HAEMATOLOGY ASSOCIATION OF IRELAND

# HAEMATOLOGY ASSOCIATION OF IRELAND ANNUAL MEETING 2024

## Europa Hotel, Belfast
## Friday 11 and Saturday 12 October 2024


**ANNUAL MEDICAL &**
**SCIENTIFIC MEETING:** **FRIDAY 11 & SATURDAY 12 OCTOBER 2024**

**ANNUAL NURSES &**
**AHPs GROUP MEETING:** **FRIDAY 11 & SATURDAY 12 OCTOBER 2024**

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HAEMATOLOGY ASSOCIATION OF IRELAND

**OCTOBER 2024**

Dear Colleagues,

It is my pleasure on behalf of our HAI committee to welcome all of you to this very special 25th anniversary meeting of the Haematology Association of Ireland. Our inaugural meeting took place in Antrim in 1999, so it is very appropriate that we return to Northern Ireland for this year's celebration of all our excellent activity and innovation in the scientific, medical, nursing and laboratory domains of haematology practice across the island of Ireland. This is reflected in over 140 excellent abstracts submitted, which will underpin the enthusiastic and interesting discussions we anticipate at our oral and poster sessions during the meeting. A special welcome to our early career and first-time participants, this is your meeting, and you represent the future of our discipline.

We would like to extend a particular thanks to our distinguished national and international guest speakers who have travelled from near and far to join us for this 25th anniversary meeting. We appreciate that each speaker has taken time out of their very busy schedule to share their knowledge, expertise and insights with us, for which we are very grateful.

I am delighted to confirm that Novartis have agreed to continue their sponsorship of the Novartis Career Development & Nursing Professional Development Awards in the amount of €10,000 and €3,000 respectively. Details of how to apply for these awards will be announced at the conference. This award will provide funding for further education, research or the acquisition of a technique or skill which would be of benefit to medical education. Our sincere thanks go to Novartis for sponsoring this Educational Grant.

In my first year as President of the HAI, I would like to extend a special thanks on our behalf to my predecessor Dr Feargal McNicholl for his excellent leadership and contribution to the further development of HAI. I also want to acknowledge the HAI Committee for all their support and hard work during the last year, with special mention of Dr Claire Andrews, Secretary/Treasurer, and Dr Kathryn Clarke, Scientific Secretary who, along with the committee, have put together a superb programme for this year's meeting. I would also like to extend my sincere thanks to everyone who has assisted in the review of abstracts as without your support, this meeting could not function.

Finally, on behalf of the HAI Committee I hope you enjoy the meeting, as we celebrate our continued progress on this 25th anniversary occasion, and renew old friendships and make some new ones.

*Paul*

***Prof. Paul Browne,***
***President***

| ***ANNUAL MEETING PROGRAMME*** ***Friday 11th October 2024, Europa Hotel, Belfast*** ***(CPD Approved)*** | |
|---|---|
| **08.00-08.45** | **Tea/Coffee/Scones/Meet the Sponsors** ***(All sponsors who support this meeting through the sponsorship of exhibition space alone have no input into the Agenda, speaker selection or content of this meeting)*** |
| **08.45-09.00** | **Opening of the Annual HAI Meeting – Prof. Paul Browne, President** |
| **SESSION 1 – Oral Presentations 6 x 10 minute Presentations Chairpersons: Prof. Paul Browne and Dr Claire Andrews** | |
| **09.00-09.10** | **GUANIDINIUM-BASED COMPOUNDS AS POTENTIAL ANTI-MYELOMA AGENTS** **Yunlong Pei[1,2]**, R Amet[1,2], P Hayden[3], P Browne[3], M Minneci[4], I Rozas[4], D Zisterer[2], T McElligott[1,] [1]John Durkan Leukaemia Laboratories, Trinity College Dublin, Dublin, [2]School of Biochemistry and Immunology, Trinity College Dublin, Dublin, [3]Department of Haematology, St James's Hospital, Dublin, [4]School of Chemistry, Trinity College Dublin, Dublin |
| **09.10-09.20** | **Elevation of PD-1 expression on circulating CD19 CAR T-cells in patients with persistent disease following CAR T-cell therapy** **Hayley Foy-Stones[1]**, N Gardiner[1], DG Doherty[3], A Kilgallon[3], AM Mc Elligott[3], T Hervig[4], C Armstrong[2], N Orfali[2], E Vandenberghe[2], R Henderson[2], E Higgins[2], CL Bacon[2,] [1]Cryobiology Laboratory Stem Cell Facility, St. James's Hospital, Dublin, Ireland, [2]National Adult Stem Cell Transplant and Adult CAR-T cell Programme, St. James's Hospital, Dublin, Ireland [3]Trinity Translational Medicine Institute, Trinity College, Dublin, Ireland, [4]Irish Blood Transfusion Service, (IBTS), Dublin |
| **09.20-09.30** | **SARS-COV-2-INDUCED SYNCYTIA HAVE ENHANCED PROCOAGULANT ACTIVITY** **James V Harte[1,2,3]**, V Mykytiv[2], MP Crowley[2,3], C Coleman-Vaughan [4], JV McCarthy[1] [1]Signal Transduction Laboratory, School of Biochemistry and Cell Biology, University College Cork, Cork, [2]Department of Haematology, Cork University Hospital, Wilton, Cork, [3]EOLAS Research Group, Cork University Hospital, Wilton, Cork, [4]Department of Biological Sciences, Munster Technological University, Bishopstown, Cork |
| **09.30-09.40** | **TREATMENT OUTCOMES AND MINIMAL RESIDUAL DISEASE MONITORING IN NPM1-MUTATED AML PATIENTS RECEIVING VENETOCLAX BASED NON-INTENSIVE TREATMENT IN NORTHERN IRELAND 2020 – 2023** **Andrew Hindley[1]**, J McGimpsey[1], C Arnold[1], N Cunningham[1], MF McMullin[1,2], F McNicholl[3], D Finnegan[1], B Merron[4], M Catherwood[1,] [1]Haematology department, Belfast City Hospital, Belfast, Northern Ireland, [2]Centre for Medical Education, Queen's University Belfast, Belfast, Northern Ireland, [3]North West Cancer Centre, Altnagelvin Area Hospital, Derry, Northern Ireland, [4]Haematology Department, Antrim Area Hospital, Antrim, Northern Ireland |
| **09.40-09.50** | **INVESTIGATING THE NOVEL ALBENDAZOLE-VENETOCLAX DRUG COMBINATION FOR PAEDIATRIC ACUTE MYELOID LEUKAEMIA** **Seodhna M Lynch[1]**, R Wilson[2], T Ní Chonghaile[3], A Thompson[4,] [5], K Mills[4], R Levine[6], KB Matchett[1] [1]Personalised Medicine Centre, School of Medicine, C-TRIC, Altnagelvin Hospital Campus, Ulster University, Derry/Londonderry, UK, [2]Wellcome-MRC Cambridge Stem Cell Institute, Jeffrey Cheah Biomedical Centre, Cambridge Biomedical Campus, Cambridge, UK, [3]Department of Physiology and Medical Physics, Royal College of Surgeons in Ireland, Dublin, [4]Patrick G Johnston Centre for Cancer Research, Queen's University Belfast, Belfast, UK [5]Centre for Cancer Sciences, The Biodiscovery Institute, Faculty of Medicine & Health Sciences, University Park, Nottingham, UK, [6]Department of Medicine, Memorial Sloan Kettering Cancer Centre, New York, USA |
| **09.50-10.00** | **UTILIZING MULTIPLEX DRUG SCREENING TO IDENTIFY NOVEL COMBINATION THERAPIES FOR THE TREATMENT OF ACUTE MYELOID LEUKEMIA** **Hayley P McMillan,** LV Cairns, KM Clarke, A Jordan, KI Mills, LJ Crawford, [1]Patrick G Johnston Centre for Cancer Research, Queen's University Belfast, Belfast, Northern Ireland |
| **10.00-10.40** | **STATE OF THE ART LECTURE: Introduced by: Dr Kathryn Clarke** ***Chronic ITP: here and now*** ***Dr Gary Benson, Consultant Haematologist and ITP Centre Director, Belfast City Hospital*** |
| **10.40-11.10** | **TEA/COFFEE/POSTERS AND MEET THE SPONSORS** ***(All sponsors have supported this meeting through the sponsorship of exhibition space alone and have had no input into the Agenda, speaker selection or content of this meeting)*** |

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| **SESSION 2 – State of the Art Lectures followed by AGM**<br>**Chairpersons: Dr Conal McConville and Dr Kathryn Clarke** | |
| **11.10-11.55** | **STATE OF THE ART LECTURE: Introduced by Dr Niamh O'Connell**<br><br>**Recent advances in management of PE**<br>**Dr Karen Breen, Consultant Haematologist**<br>**Joint Clinical Director for Haematology, Haemostasis, Cellular Pathology, Oncology & Haematology Clinical Trials, Guy's and St Thomas' NHS Foundation Trust, London, UK** |
| **11.55-12.40** | **STATE OF THE ART LECTURE: Introduced by: Dr Corrina McMahon**<br><br>**Pediatric-adult care transition in patients affected with sickle cell disease**<br>**Prof. Mariane de Montelambert, Necker Hospital for Sick Children, Paris**<br>**Sickle Cell** |
| **12.40-13.10** | **AGM – All Welcome!** |
| **13.10-14.20** | **Lunch followed by Tea/Coffee and Meet the Sponsors** |
| **SESSION 3: State of the Art Lectures**<br>**Chairpersons: Dr Lesley Sutton and Dr Aaron Niblock** | |
| **14.20-15.05** | **STATE OF THE ART LECTURE: Introduced by: Dr Maryse Power**<br><br>**Novel Strategies Targeting Aggressive B-Cell Lymphomas**<br>**Dr Kieron Dunleavy, Consultant Haematologist, MedStar Georgetown University Hospital** |
| **15.05-15.50** | **STATE OF THE ART LECTURE: Introduced by: Prof. Paul Browne**<br>**Controversies in the initial Therapy of Patients with Multiple Myeloma**<br>**Prof. Graham Jackson, Freeman Hospital, The Newcastle Upon Tyne Hospitals, Newcastle** |
| **15.50-16.15** | **TEA/COFFEE/POSTERS AND MEET THE SPONSORS**<br>***(All sponsors who support this meeting through the sponsorship of exhibition space alone have no input into the Agenda, speaker selection or content of this meeting)*** |
| **SESSION 4: Presidents' Symposium – followed by the Liam O'Connell Lecture**<br>**Chairpersons: Prof. Paul Browne and Dr Claire Andrews** | |
| **16.15-16.30** | **PATHWAYS TO MYELOPROLIFERATIVE NEOPLASM PRESENTATION & DIAGNOSIS: RESULTS FROM A CROSS-SECTIONAL STUDY**<br>**Emma-Louise Tarburn[1]**, L Iversen[2], C.M McShane[3], C Robertson[4], M F McMullin[3], A Duncombe[5], C Harrison[6], L.A. Anderson[1,1]Centre for Health Data Science, University of Aberdeen, Aberdeen, UK [2]Academic Primary Care, University of Aberdeen, Aberdeen, UK, [3]Centre for Public Health, Queens University Belfast, Belfast, UK, [4]Haematology Department, Aberdeen Royal Infirmary, Aberdeen, UK, [5]Haematology Department, University Hospital Southampton, Southampton, UK, [6]Haematology Department, Guy's and St Thomas' NHS Foundation Trust, London, UK |
| **16.30-16.45** | **The (T) thrombosis (I) in patients with (L) lower (L) limb (I) injuries (R) requiring (I) immobilisation (TILLIRI) Study**<br>T OHalloran[1], **Bibi A Bassa[2]**, B Nemeth [3], S Cannegieter [3], T Breslin[2], A Wakai[4], J O Driscoll [5], S ORourke[6], N OConnell[7], F Ni Ainle [2], M Watts[1], D OKeeffe[1], The TILLIRI Study investigators, [1]Haematology , University Hospital Limerick, Limerick , [2]Emergency medicine , Mater Misericordiae University Hospital , Dublin, [3]Clinical epidemiology, Leiden University Medical Centre, Leiden, Netherlands, [4]Emergency medicine , Beaumont Hospital , Dublin, [5]Emergency medicine , Smithfield Minor Injury Unit , Dublin, [6]Emergency medicine , Midland Regional Hospital Tullamore, Tullamore, [7]Haematology, St James's Hospital, Dublin, Dublin |
| **16.45-17.00** | **INVESTIGATING THE ROLE OF OSTEOBLASTS IN CONTROLLING NATURAL KILLER CELL CYTOTOXICITY AGAINST ACUTE MYELOID LEUKAEMIA**<br>**Leonie Durkan[1]**, C Coleman[2], E Szegezdi[1]<br>[1]School of Biological and Chemical Sciences, University of Galway, Galway, [2]Regenerative Medicine Institute (REMEDI), University of Galway, Galway |

| SESSION 4: Presidents' Symposium – followed by the Liam O'Connell Lecture<br>Chairpersons: Prof. Paul Browne and Dr Claire Andrews | |
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| **17.00-17.15** | **SKY92 MOLECULAR PROFLING IN COMBINATION WITH MRD RISK PROFILING TO IDENTIFY HIGH-RISK MULTIPLE MYELOMA PATIENTS IN IRELAND (SKIP-MM)**<br>**Roisin McAvera[1],** I Cymer[1], H Black[1], J Quinn[2], P Murphy[2], P Thornton[1,2], R Cummins[3], T Cichocka[4], E Szegezdi[4], M Perera[5], G Crotty[5], R Clifford[6], N Keane[7], J Krawcyzk[7], V Mykytiv[8], E Elhassadi[9], M Coyne[10], M O'Dwyer[11], S Glavey[1,3]<br>[1]Multiple Myeloma Research Group, Royal College of Surgeons in Ireland, Beaumont, Dublin, [2]Department of Haematology, Beaumont RCSI Cancer Centre, Dublin, [3]Molecular Pathology Laboratory, Royal College of Surgeons in Ireland, Dublin, [4]Blood Cancer Network Ireland, University of Galway, Galway, [5]Department of Haematology, Midland Regional Hospital Tullamore, Tullamore, [6]Haematology, University Hospital Limerick, Limerick, [7]Haematology Department, Galway University Hospital, Galway, [8]Department of Haematology, Cork University Hospital, Cork, [9]Haematology Department, University Hospital Waterford, Waterford, [10]Department of Clinical Haematology , St Vincent's University Hospital, Dublin, [11]School of Medicine, University of Galway, Galway |
| **17.20-18.20** | **LIAM O'CONNELL LECTURE - Introduced by: Prof. Paul Browne and Dr Claire Andrews**<br><br>**Are we ready to disease modify in MPN?**<br>**Professor Claire Harrison, Deputy Medical Director - Research**<br>**Guy's and St Thomas' NHS Foundation Trust** |
| **18.30-19.45** | **OFFICIAL POSTER VIEWING AND ADJUDICATION** |

# Time: 18.30-19.45

# Moderated Poster Board Session

## (Poster Board Presentation Walkabout and Adjudication)

## Followed by:

# Conference Dinner

# *ANNUAL MEETING PROGRAMME*
# *Europa Hotel, Belfast*
# *SATURDAY 12TH OCTOBER 2024*

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| **09.20-09.30** | **Opening of Day 2 – Prof. Paul Browne, President** |
| **SESSION 5: Chairpersons: Dr Aaron Niblock and Dr Conal McConville** | |
| **O9.30-10.30** | **Oral Presentations – 6 x 10 Minute Oral Presentations followed by State of the Art Lecture** |
| **09:30-09:40** | **ALL-IRELAND RELAPSED/REFRACTORY (R/R) LARGE B-CELL LYMPHOMA (LBCL) CHIMERIC ANTIGEN RECEPTOR T-CELL (CAR-T) OUTCOMES – REFERRALS TO KING'S COLLEGE HOSPITAL (KCH)**<br>**Adrian Maraj[1],** A Kuhnl[1], E Kumar[1], AS Moya Davila[1], O Stewart[1], P Patten[1], P Hardefeldt[1], D Yallop[1], R Benjamin[1], V Potter[1], R McCormick[5], P Elder[6], S McCloskey[4], O Sheehy[3], CL Bacon[2], E Higgins[2], E Vandenberghe[2], S Lawless[3], R Sanderson[1]<br>[1]Haematology, King's College Hospital, London, United Kingdom, [2]Haematology, St. James's Hospital, Dublin, Ireland [3]Haematology, Belfast City Hospital, Belfast Trust, Belfast, Northern Ireland, [4]Haematology, Antrim Hospital, Northern Trust, Antrim, Northern Ireland, [5]Haematology, Ulster Hospital, South-Eastern Trust, Belfast, Northern Ireland, [6]Haematology, Altnagelvin Hospital, Western Trust, Londonderry, Northern Ireland |
| **09:40-09:50** | **ALLOGENEIC TRANSPLANTATION OUTCOMES IN MYELOFIBROSIS: A 25 YEAR REVIEW**<br>**Mohammad K Khan[SJH]**, MNC Chonghaile[SJH], GL lee[SJH], CA armstrong [SJH], CMF Flynn[SJH], NO Orfali[SJH], EC Conneally [SJH,]<br>[1]Haematology , St James's Hospital, Dublin |
| **09:50-10:00** | **Application of a Novel Artificial Intelligence Algorithm to Understand Spatial Immune Cell Relationships in Newly Diagnosed Multiple Myeloma**<br>**Paraic Behan[1]**, S Sarihan[1], M Chiasson[1], P Zainulabdeen Jan Sarhandi[1], J Fay[2], J Quinn[3], P Murphy[3], K Sheehan[2], S Glavey[1]<br>[1]Departments of Haematology and Pathology, Beaumont RCSI Cancer Centre, Dublin, [2]Department of Pathology, Beaumont RCSI Cancer Centre, Dublin, [3]Department of Haematology, Beaumont RCSI Cancer Centre, Dublin |
| **10:00-10:10** | **Interferon alpha upregulates the ATF4/CHOP arm of the unfolded protein response and is synergistic in combination with proteasome inhibitors in *JAK2* V617F positive cells**<br>**Graeme Greenfield[1],** Y Sheng[1], L Crawford[1], Y Atlasi[1], D Longley[1], K Mills[1], MF McMullin[1,] [1]PGJCCR, Queen's University Belfast, Belfast, UK |
| **10:10-10:20** | **SINGLE-CENTRE EXPERIENCE USING A RAPID VENETOCLAX DOSE-ESCALATION STRATEGY FOR B-CELL CHRONIC LYMPHOCYTIC LEUKAEMIA**<br>**David Parfrey,** C Waldron, L Bacon, R Henderson, G Faulkner, M Martin, E Vandenberghe, [1]Department of Haematology, St James's Hospital, Dublin, Ireland |
| **10:20-10:30** | **GROUP O-WHOLE BLOOD - A NEW POTENTIAL ROLE IN ST. VINCENT'S UNIVERSITY HOSPITAL**<br>**Rebecca Reid[1],** D Menzies[1, 3], MA Connaughton[2], D Neary[2], K Morris[2], J Fitzgerald[1, 2]<br>[1]School of Medicine , University College Dublin, Belfield, Dublin 4, [2]Department of Haematology and Blood Transfusion, St. Vincent's University Hospital, Elm Park, Dublin 4, [3]Department of Emergency Medicine, St. Vincent's University Hospital, Elm Park, Dublin 4 |
| **10.30-11.15** | **STATE OF THE ART LECTURE: Introduced by: Dr Joan Fitzgerald**<br><br>**Using Blood Wisely: a national program to decrease inappropriate red blood cell transfusion in Canada**<br>**Dr Yulia Lin, Division Head, Transfusion Medicine & Tissue Bank, Sunnybrook Health Sciences Centre and Professor, Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Canada** |
| **11.15-11.40** | **TEA/COFFEE AND MEET THE SPONSORS**<br>***(All sponsors who support this meeting through the sponsorship of exhibition space alone have no input into the Agenda, speaker selection or content of this meeting)*** |

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| **11.40-13.15** | **SESSION 6: Chairpersons: Prof. Paul Browne and Dr Claire Andrews**<br>**Clinical Vignettes Presentations – 6 x 5 Minute Presentations followed by State of the Art Lecture** |
| **11.40-11.45** | **ACUTE MYELOID LEUKAEMIA IN A PATIENT WITH A HISTORY OF A GERMLINE BRCA1 MUTATION AND METASTATIC TRIPLE NEGTIVE BREAST CANCER**<br>**Lauren Mc Connell[1]**, K Clarke[2], M Catherwood[1], D Finnegan[2,] [1]Regional Molecular Diagnostics Service, Belfast Health and Social Care Trust, Belfast, UK, [2]Department of Haematology, Belfast Health and Social Care Trust, Belfast, UK. |
| **11.45-11.50** | **ACQUIRED HAEMOPHILIA A AS A COMPLICATION OF GRAFT-VERSUS-HOST-DISEASE FOLLOWING ALLOGENEIC STEM CELL TRANSPLANTATION: A CASE REPORT**<br>**Janet YC Tan[1]**, CCW Tan[1], N Orfali[2], M Crowley[1], V Mykytiv[1,]<br>[1]Department of Haematology & Comprehensive Coagulation Centre, Cork University Hospital, Cork, [2]Department of Haematology, St James's Hospital, Dublin |
| **11.50-11.55** | **Long-Term survival of patient with mast cell leukemia progressing from Systemic Mastocytosis treated with Avapritinib**<br>**Camillo QH Coccia[1]**, M Coyne[1], K Fadalla[1], J Fitzgerald[1], K Murphy [1], M Power[1], L Smyth [1], C Andrews[1]<br>[1]Department of Haematology, St Vincent's University Hospital, Elm Park, Dublin 4 |
| **11.55-12.00** | **Hyperhaemolysis and Pernicious Parvovirus in a Sickle Cell Patient**<br>**P Behan[1]**, C Sheehan[1], N Ngwenya[1], E Crampton[1], B Crowley[2], E Algar[1], E Tuohy[1], C McMahon[3]<br>[1]Department of Haematology, St. James's Hospital, Dublin 8, [2]Department of Virology, St. James's Hospital, Dublin 8<br>[3]Department of Haematology, CHI Crumlin, Dublin 12 |
| **12.00-12.05** | **A COMPLEX CASE OF MULTIFACTORIAL ANAEMIA**<br>**Aisling Busher[1]**, R O'Brien[1], S Holt[2], E McCarthy[3], A Al Baghdadi[1], S Ni Loingsigh[2], R Clifford[1], H O'Leary[1], C McEllistrim[1], D O'Keeffe[1]<br>[1]Haematology Department, University Hospital Limerick, Limerick, [2]Irish Blood Transfusion Service, Cork, [3]Blood Transfusion Laboratory, University Hospital Limerick, Limerick, |
| **12.05-12.10** | **TREATMENT OF A STAT5B::RARα POSITIVE CASE OF APL IN A PATIENT NOT ELIGIBLE FOR INTENSIVE CHEMOTHERAPY**<br>**Jason P Patterson[1]**, KC Clarke [1], KM Mokretar[4], MM Maurya[2], AL Logan[2], NC Cunningham [1], MC Catherwood [2], MF McMullin [3]<br>[1]Department of Haematology, Belfast Health and Social Care Trust, Belfast, Northern Ireland, [2]Regional Molecular Diagnostics Service,, Belfast Health and Social Care Trust, Belfast , Northern Ireland, [3]Centre for Medical Education,, Queens University Belfast, Belfast, Northern Ireland, [4]Department of Academic Haematology, University College London, London, United Kingdom |
| **12.10-12.45** | **STATE OF THE ART LECTURE: Introduced by: Prof. Paul Browne**<br>**Integrated diagnostics in Hematological Cancers**<br>**Pr. Elizabeth Macintyre, Professor of Diagnostic Hematology, Necker Hospital and Université Paris Cité and past –president of EHA.** |
| **12.45** | **Close of Conference and Awarding of Educational Awards** |
| **13.00** | **Lunch** |
| **14.15-16.30** | **Educational Session for SpRs, Registrars & Trainees in Haematology**<br>**Guest speakers:**<br>***Career Development, opportunities and Bio Diagnostics***<br>**Prof. Elizabeth Macintyre, Professor of Diagnostic Hematology, Necker Hospital and Université Paris Cité and past –president of EHA**<br>***Introduction to Blood Bank Serology***<br>**Dr Yulia Lin, Division Head, Transfusion Medicine & Tissue Bank, Sunnybrook Health Sciences Centre and Professor, Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Canada** |

| ***HAI NURSES & AHPs ANNUAL MEETING PROGRAMME<br>FRIDAY 11 OCTOBER, 2024*** | | |
|---|---|---|
| 08.00 – 09.30 | **REGISTRATION AND MEET THE SPONSORS/DISPLAY POSTERS** | |
| ***CHAIRS: Louise Gribben and Fidelma Hackett*** | | |
| **TIME** | **TOPIC** | **SPEAKER** |
| 09.30-09.40 | **Welcome and Introduction** | ***Louise Gribben,*** *Chairperson, HAI Nursing/AHP Group* |
| 09.40-10.40 | ***Fertility Preservation: Hope for the Future*** | ***Dr Joanne McManus, Consultant Gynaecologist & Sub-specialist in Reproductive Medicine in the Belfast Trust, Belfast*** |
| 10.40-11.10 | ***Tea/Coffee/Meet the Sponsors/Posters*** | |
| 11.10-12.10 | ***Transplant- "It takes a village"*** | ***Prof. Catherine Flynn, St James's Hospital and Dr Nicholas Cunningham, Belfast City Hospital***<br><br>***Tracey McGuigan, Transplant Co- Ordinator Belfast City Hospital***<br><br>***Carmel Ann Galligan, Transplant Advanced Nurse Practitioner, St James Hospital*** |
| 12.10-12.40 | ***Death and Bereavement: Safe and Sensitive Care*** | ***Laura Creaney, Bereavement Co-ordinator SHSCT Leona Laverty, Bereavement Co-ordinator for NHSCT*** |
| *12.40-14.00* | ***Lunch followed by Tea/Coffee and Display posters*** | |
| **CHAIRS: Caroline McCaughey and Carmel Ann Galligan**<br><br>**Oral Presentations – 6 x 10 Minute presentations** | | |
| 14.00-14.10 | **Implementing Exercise Equipment on the Hematopoietic Stem Cell Transplant Unit – Exploring Patients Opinions and Experiences** | ***Sophie Grehan, Senior Physiotherapist in Haematology, St James's Hospital, Dublin*** |
| 14.10-14.20 | **Benefits of an ANP Red flag Clinic** | ***Louise Gribben, Advanced nurse Practitioner, SHSCT*** |
| 14.20-14.30 | **Community Haematology Oral Anticancer Medication Clinic - Creating More Value with Fewer Resources** | ***Mary Kelly, Advanced nurse Practioner, Midland Regional Hospital, Tullamore*** |
| 14.30-14.40 | **ANP led Pre-assessment of Patients on Daraumumab-A quality Improvement Project** | ***Lisa Lyons, Advanced Nurse Practitioner, Northern HSCT*** |
| 14.40-14.50 | **The Development of a National Creative Arts Therapy Service for Children, Adolescents & Young Adults(CAYA) with or in Survivorship of Cancer and their Siblings** | ***Roisin Hayes, CAYA, Irish Cancer Society, Dublin*** |
| 14.50-15.00 | **Lessons learned from the development of a nursing education pathway for haematopoietic stem cell transplant (HSCT) in the national bone marrow transplant unit in St James Hospital, Dublin** | ***Deirdre Byrne, Clinical Support Nurse \| HOPE \| St James's Hospital, James Street, Dublin*** |
| 15.00-15.45 | ***Getting critical care right for Haematology Patients*** | **Gavin Cooper, Clinical Practice Facilitator in Critical Care Haematology at University College London Hospitals** |
| 15.45-16.15 | **Tea/Coffee/Meet the Sponsors and Poster Viewing** | |

| *HAI NURSES & AHPs ANNUAL MEETING PROGRAMME*<br>*FRIDAY 11 OCTOBER, 2024* | | |
|---|---|---|
| ***CHAIRS: Kerrie Sweeney and Deirdre Cleary*** | | |
| 16.15-17.15 | **Meet the Expert:**<br><br>***Multiple Myeloma – Background and the Changing Landscape***<br><br>***Managing long term Myeloma Treatment in the Real World***<br><br>***Nursing considerations for the management of multiple myeloma patients on Talquetamab - A patient case study*** | <br><br>***Prof. Graham Jackson,***<br>**Freeman Hospital, The Newcastle Upon Tyne Hospitals,**<br><br>***Lisa Lyons, ANP, Northern Health and Social Care Trust***<br><br>***Melissa Martin, CNS,***<br>***St James's Hospital, Dublin*** |
| 17.20-18.20<br>**(Main Plenary Session)** | ***LIAM O'CONNELL LECTURE - Introduced by: Prof. Paul Browne***<br><br>***Professor Claire Harrison, Deputy Medical Director – Research, Guy's and St Thomas' NHS Foundation Trust*** | ***Professor Claire Harrison*** |
| 18.30-20.00 | **Poster viewing followed by Conference Dinner** | |

| *HAI NURSES & AHPs ANNUAL MEETING PROGRAMME*<br>*SATURDAY 12th October 2024* | | |
|---|---|---|
| **CHAIRS:** ***Lorna Storey and Aoife McCormack*** | | |
| **TIME** | **TOPIC** | **SPEAKER** |
| 09.45-10.15 | **Nursing/AHP AGM** | ***All Welcome!*** |
| 10.15-11.00 | ***ANP Cancer Career Pathway "My ANP Journey"*** | ***Louise Gribben, Haematology ANP, SHSCT*** |
| 11.00-11.15 | **Highlights from the main conference** | ***Prof. Paul Browne*** |
| **11.15-11.40** | **Tea/Coffee/Meet the Sponsors and Poster Viewing** | |
| 11.40-12.45 | **CHAIRS: Susan Smyth and Niamh O'Sullivan** | |
| 11.40-12.45 | **Workshop**<br><br>**"Supporting the neurodivergent person in clinical practice"** | **Christine Kearney, Director of Development, Autism NI** |
| 12.45-13.00 | **Awarding of Prizes and Close of Annual Meeting** | **Louise Gribben, Chairperson** |
| 13.00 | **Lunch** | |

HAEMATOLOGY ASSOCIATION OF IRELAND

## *Diagnostic Laboratory Haematology and Transfusion Session Programme*
## *Friday 11 October 2024, Europa Hotel, Belfast*

| TIME | TOPIC | SPEAKER |
|---|---|---|
| 13.30-14.00 | Tea/Coffee/Pastries | |
| CHAIRS: Dr Claire Wynne and Mr Paul Fitzsimons | | |
| 14.00-14.30 | *Virtual Presentation*<br><br>*Why we make mistakes in morphology reporting from the UKNEQAS CPD Digital morphology scheme* | Michelle Brereton,<br>Lead Biomedical Scientist at Manchester University NHS Foundation Trust |
| 14.30-15.00 | *Laboratory diagnosis of VWD; understanding the importance of the phenotype-genotype relationship* | *Catriona Keenan Ph.D.*<br>*Senior Clinical Scientist at the Haemostasis Molecular Diagnostic (HMD) Laboratory, part of the National Coagulation Centre, St. James's Hospital, Dublin*<br><br>*Mairead Doyle*<br>*Senior Medical Scientist at the National Coagulation Laboratory (NCL), part of the National Coagulation Centre, St. James's Hospital, Dublin* |
| 15.00-15.30 | *Major Haemorrhage Guideline and Major Haemorrhage Simulations* | *Conor McMahon,*<br>*Medical Scientist,*<br>*Beaumont/TU Dublin Practice Educator* |
| 15.30-16.00 | *Tea/Coffee/Poster Viewing* | |
| CHAIRS: Dr Irene Regan and Mr Paul Fitzsimons | | |
| 16.00-17.00 | *Short presentations selected from abstract submissions* | |
| 16.00-16.15 | *DEVELOPMENT OF A HIGH-SENSITIVITY FLOW CYTOMETRY ASSAY FOR THE DETECTION OF GPI-DEFICIENT CLONES IN PAROXYSMAL NOCTURNAL HAEMOGLOBINURIA AND RELATED BONE MARROW FAILURE SYNDROMES* | *Ciara Liptrot, Haematology , Mater Misericordiae University Hospital, Dublin* |
| 16.15-16.30 | *A REVIEW OF MALARIA DIAGNOSIS, SEVERITY AND MANAGEMENT 2019-2023 UNIVERSITY HOSPITAL GALWAY* | *Ellen Sugrue, Galway University Hospital* |
| 16.30-16.45 | *A CASE SERIES OF UNUSUAL HAEMOGLOBIN VARIANTS DETECTED AT THE SPECIALIST RED CELL LABORATORY, BELFAST CITY HOSPITAL* | *Colleen Williamson, Haematology Department, Belfast Health and Social Care Trust, Belfast* |
| 16.45-17.00 | *THREE-SITE COMPARISON OF CELL POPULATION DATA ON SYSMEX XN-SERIES ANALYSERS* | *James Harte Presenting on behalf of Grace McMahon, Cork University Hospital* |
| 17.00 | *Close of Session*<br>*Awards will be announced at Conference Dinner* | *Dr Claire Wynne* |

**This is a CPD Event**

**Please contact Sinead on sinead@sineadcassidy.com for further details.**

**Dr Gary Benson**
Director, Northern Ireland Haemophilia Comprehensive Care Centre
Belfast City Hospital, Belfast Health and Social Care Trust
Belfast, Ireland

Dr. Gary Benson graduated from Queens University Belfast in 1999. His postgraduate training took him to Altnagelvin, Causeway and Belvoir Park Hospital before taking up specialty training in hematology in 2003 at the Belfast City Hospital. He spent at year at the East of Scotland Haemophilia Comprehensive Care Centre, Edinburgh, before taking up post as the Director of the Northern Ireland Haemophilia Centre whereby subspecialist clinics were established for to include haemophilia carriers as well as high risk obstetrics for all women with bleeding disorders.
During the last sixteen years, he has developed and progressed educational activities throughout all specialties within primary and secondary care in relation to raising awareness of the bleeding disorders.

He is the Chair of Division for Laboratory and Pharmacy, having been the past Clinical Director for Clinical Haematology/ Blood sciences for 6 years.

**Dr Karen Breen**
Dr Karen Breen is a consultant haematologist with a specialist interest in thrombosis and is Clinical Director of Haematology and supporting services at Guys and St.Thomas' NHS foundation Trust.

She trained in haematology in Ireland and moved to the UK to conduct research in antiphospholipid syndrome leading to an MD.

Her main area of clinical interest is in thrombosis, she is helping to set up and run a PERT service and works closely with the Venous vascular service in managing venous interventions at GSTT. She is currently involved in several clinical trials and in translational research in antiphospholipid syndrome.

**Gavin Cooper**

Gavin has been a Haematology nurse educator for 10 years, but for the last 2 years. He has led nursing education at University College London Hospital's Grafton Way Building (GWB) critical care unit. The GWB critical care unit is a 10 bedded, dedicated Haematology critical care, serving the needs of the largest Haematology inpatient unit in Europe. Gavin has run a haematology podcast called 'Bolus: education delivered stat' that has been listened to 100,000 times, and for which he has received a Chief Nursing Officer of England Silver Award. Two current projects that he is working on are running 6 monthly free online study days on the subject of 'Caring for the Critically Ill Haematology Patient', and writing about haematology care for the new edition of the Oxford University Press 'Critical Care Nursing' textbook.

**Laura Creaney**, Bereavement co-ordinator for the Southern Health and Social care Trust (SHSCT) and member of the Northern Ireland bereavement network.
Laura has almost 20 years' experience working in cancer services with varying roles as acute oncology and haematology clinical nurse specialist, independent nurse prescriber and Teenager and Young adult nurse.
Currently Laura Leads on the implementation of bereavement care standards from the NI Bereavement Care Strategy (DHSSPS, 2009) in the SHSCT. Promoting a supportive ethos for dying patients, bereaved families and staff, through service improvement initiatives, the development of resources, and training and education. Laura has been involved in the design and implementation of the new bereavement website for Northern Ireland ""Bereaved NI" in collaboration with the regional bereavement coordinators and stakeholders.

**Prof. Mariane de Montalembert**

Professor Mariane de Montalembert received her MD and her PhD in Ethics from the Paris Descartes Medical School. She specialized in pediatrics, statistics (option clinical research), red cell diseases, especially hemoglobinopathies, in children, and transfusion. She is co-responsible for the Hemoglobin Diseases Unit at the Necker University Hospital, which follows 600 children and the «ROFSED» healthcare network for SCD children in the Parisian area (Therapeutic Education Unit for 700 children and families). Prof de Montalembert is a member of the French Society of Pediatrics, in which she has chaired for more than 10 years the Ethic Committee, of the French Society of Hematology, the European Reference Network in rare Haematological Diseases (EuroBloodNet), the European Association (EHA), and the American Society of Hematology (ASH). She has been a member of the EHA board for the period 2020-2024 and coordinates the EHA Topic in Focus group on hemoglobinopathies. She coordinates clinical research programs, notably on hydroxyurea in children with SCD, transfusion, and iron overload.

**Dr. Kieron Dunleavy**

Dr. Kieron Dunleavy is the Director of Haematological Malignancies at Lombardi Comprehensive Cancer Center and Professor of Medicine at Georgetown University, Washington DC. He is a graduate of University College Dublin and completed medical oncology training in Dublin before starting a fellowship in oncology at the National Cancer Institute (NCI) in Bethesda, Maryland. Following his fellowship at the NCI, he was an Investigator and Clinical Director of the Lymphoid Malignancies Branch of the NCI and subsequently, Director of Lymphoma at George Washington University. Dr. Dunleavy is an expert in lymphoid malignancies with a focus on the treatment and biology of aggressive B-cell lymphomas. His research involves identifying new targets for drug development in lymphoma and designing and conducting novel trials for these diseases. He serves on the Scientific Advisory Board of the Lymphoma Research Foundation and has served as a panel advisor on the Oncology Drug Advisory Committee (ODAC) for the FDA. He has authored numerous manuscripts and book chapters on lymphoma and lectures widely.

**Dr Catherine Flynn, MD, FRCPath, MRCP(Edin) MB BCH BAO**

Dr Flynn is a consultant haematologist at St James's Hospital. She is also a consultant haematologist at the Coombe Women and Infants University Hospital since 2007. She was a previous national speciality director for Higher Specialist Training in haematology from 2011 to 2015.

Dr Flynn holds a Bachelor of Medicine, a Bachelor of Surgery and a Bachelor of Obstetrics from the Queens University of Belfast (1995). She completed specialist haematology training in Dublin. Her training took her from Ireland to the University of Minnesota, Minneapolis, USA where she started a haematology fellowship with a subspecialty interest in stem cell transplantation (2003 - 2006).
She completed her Doctor of Medicine (MD) on haematopoietic stem cells and haematopoiesis in the Katholieke Universiteit of Leuven, Belgium. She returned to Dublin in 2007 and works as a consultant haematologist in the National Adult Bone Marrow Programme.

Dr Flynn specialises in Myeloid malignancies and bone marrow failure including stem cell transplantation. Her sub-specialties include Haematological disorders in pregnancy

Dr Flynn's clinical interests include malignant myeloid diseases (myeloid leukaemia and myelodysplasia), transplantation, bone marrow failure syndromes and haematological diseases during pregnancy.

Dr Flynn's research interests include myeloid diseases, aplastic anaemia and haematological disease in pregnancy. She has published in these areas.

**Carmel Ann Galligan** - Carmel Ann, graduated from Trinity College Dublin in 2011 with a BSc in General Nursing. She continued her studies with a Higher Diploma in Cancer Care and Haematologyin 2014. Having originally started in St. James Hospital for her clinical placement during her degree, she started as Staff Nurse in Denis Burkitt Ward. Promoted to Clinical Nurse Specialist in 2017, Carmel Ann completed a MSc in Clinical Practice in UCD in 2022 and a MSc in Advanced Practice in 2023 before becoming the first Advanced Nurse Practitioner (ANP) in Acute Post-Transplant and Extracorporeal Photopheresis in St. James Hospital, Dublin.

**Louise Gribben, Haematology Advanced Nurse Practioner, Southern Health and Social Care Trust**

Qualified with Diploma in nursing in 1993 and proceeded to complete RCN degree in health studies 1994/95. Career long studies included SPQ Cancer care, QUB, Haematology and BMT course QUB, independent NMP QUB. In 2020 I completed my MSc in Advanced Nursing Practice in Ulster University, which included 2 journal publication relating to work life balance and burn out among our cancer nursing workforce.

The majority of my nursing career was within the speciality of Haematology, covering both malignant and non-malignant haematology conditions. Held a wide variety of positions within Haem/Onc, including chemotherapy staff nurse, cancer unit manager, Haematology CNS and NMP x 11 years and since 2020 have been working as a Haematology ANP delivering autonomous chemotherapy/red flag/and new urgent review clinics. Within these roles I have been in many leadership roles and positions of influence, including chair of the Nican Haematology CRG nursing group and current chair of the HAI nursing group. I also provide teaching sessions for QUB on the Haematology and BM transplant and SPQ courses. When I am not working, I love to holiday in the sun with my husband and have two beautiful children Leah and Jack.

**Prof. Claire Harrison**

Professor Claire Harrison graduated from Oxford Univeristy Medical School and became a consultant at the Guy's and St Thomas Hospital in 2001, where she is now a deputy chief medical officer.

The focus of her clinical work is myeloproliferative neoplasms (MPN), for which she has a national and international reputation. Key areas of interest are clinical trials and associated translational research. Her work has led to the approval of new therapies such a ruxolitinib, fedratinib, momelotinib and pacritinib. In the past 10 years she has published widely (>350 academic articles).

In addition she has a strong interest in patient advocacy and founded the UK MPN group www.mpnvoice.org.uk.

**Prof. Graham Jackson**

Professor Graham jackson graduated from Cambridge and the Westminster School of Medicine. He gained his MRCP in 1986 and then moved to Newcastle University to undertake his MD, which he completed in 1992. He obtained his MRCPath in 1993, followed by his FRCP in 1999 and his FRCPath in 2000. Throughout his career, Prof Jackson has received several awards, including special fellowship to the European School of Haematology and European Community Fellowship to the European School of Oncology. In 1995 he won the Mortimer M Bortin Award for Outstanding Research in Blood and Marrow Transplantation presented at the 9th Symposium of Molecular Haemopoiesis (Genoa). He has won the Van Bekkum medal at the EBMT in 2004 and in 2015 was awarded the BSH GOLD MEDAL for outstanding contribution to haematology research and patient care He is a former president of the BSH and the BSBMT and has served on the council of the RCPath. He has served on CRUK CTAAC and on the Blood wise clinical trials committee. He has been a director of Myeloma UK and scientific secretary for the UKMF. He has been CI on the MRC Myeloma 9, 11 and 11+ (the largest clinical trials ever performed in multiple myeloma) and is currently the co-CI for myeloma 14. He is part of the safety monitoring committee for all the MUK trials as well as several International studies. His research interests focus on clinical trials and safety in the treatment of myeloma, development of long-term bone marrow transplant follow-up clinics, and the cytokine profile of acute and chronic graft-versus-host disease. He has always been passionate about good doctor-patient communication and has been involved in many 'breaking bad news' training seminars. He has published over 250 peer reviewed papers as well as many book chapters and reviews. He is currently the chief medical and scientific officer for the patient facing charity Myeloma UK.

**Christine Kearney, Director, Autism NI**,

Autism NI is Northern Ireland's Autism Charity. They support autistic people and their families and campaign for autism acceptance within society.

As Director of Development, Christine Kearney is passionate about autism acceptance, inclusion and accessibility across Northern Ireland. Her work to build inclusion includes within the health and education sector, public services and private sector. Christine manages the development and facilitation of accredited training courses and the Autism Impact Award Programme, which supports organisations to demonstrate their neuroinclusive approach for autistic employees, customers and clients.

**Leona Laverty** has been a registered staff nurse for twenty four years starting her career in Intensive care. She then worked as a Staff Midwife before going on to work as an Intensive Care research nurse. After that, Leona worked for NHS Blood and Transplant for nine years as a Specialist Nurse in Organ Donation. In this capacity, she developed the SNOD role within NHSCT and was involved with regional on call services in Northern Ireland, providing support to colleagues and families throughout the organ donation process.

Leona then worked as a Nurse Education Consultant in the Clinical Education Centre where she developed and delivered programmes within the palliative and acute specialist interest groups before starting her present position as the NHSCT Bereavement Coordinator in September 2022. In this role, Leona leads on the implementation of bereavement care standards from the NI Bereavement Care Strategy (DHSSPS, 2009) in the NHSCT. Promoting a supportive ethos for dying patients, bereaved families and staff, through service improvement initiatives, the development of resources, and training and education. Leona has been involved in the design and implementation of the new bereavement website for Northern Ireland ““Bereaved NI” in collaboration with the regional bereavement coordinators and stakeholders.

**Dr Yulia Lin**

Dr. Yulia Lin is a clinician-teacher and Professor in the Department of Laboratory Medicine and Pathobiology at the University of Toronto. She is the Division Head of Transfusion Medicine & Tissue Bank at Sunnybrook Health Sciences Centre, an education scholar and affiliate scientist with the Sunnybrook Research Institute and a co-investigator in the University of Toronto Quality in Utilization, Education and Safety in Transfusion (QUEST) research program.

Her academic interests include physician education in transfusion medicine, patient blood management, and transfusion safety. She has led the expansion of the successful transfusion medicine educational program, Transfusion Camp, for postgraduate trainees nationally across Canada and to the UK and Rwanda. She is a member of provincial and national working groups in transfusion medicine including the Chair of the Ontario Transfusion Coordinators Network (ONTraC) steering committee. She is the Physician Lead for Transfusion for Choosing Wisely Canada, leading the Using Blood Wisely initiative which has designated over 150 hospitals across Canada as Using Blood Wisely hospitals.

**Prof. Elizabeth Macintyre**

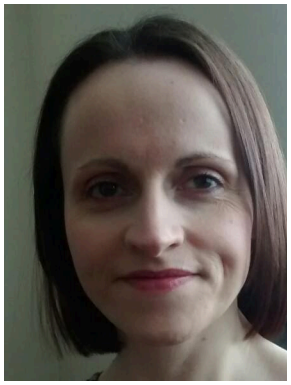
Franco-Scottish, Elizabeth Macintyre trained in Internal Medicine and Hematology in England, did her PhD in Paris, and her Post-Doctoral studies at Harvard, USA. As Assistant/Full Hematology Professor at Université Paris Cité since 1992/1997, she headed Diagnostic Hematology at Necker–Enfants Malades Hospital from 1999-2018, where she also co-directs the INSERM « Normal and Pathological Lymphoid Differentiation » Team at the INEM Research Institute https://www.institut-necker-enfants-malades.fr . Her research interests are immature T cell leukemia/lymphoma and molecular/precision diagnostics in lymphoid cancers, including from the Implementation Science and Health Technology Assessment angles. She was President of the European Hematology Association from 2021-23 and is currently president of the Biomedical Alliance in Europe https://www.biomedeurope.org, where she set up the task force on in-vitro diagnostics. She is academic coordinator of the R&I SwafS (Science with and for Society) program within the Circle U. European University Alliance https://www.circle-u.eu .

**Melissa Martin**

Currently working as a Haematology Clinical Nurse Specialist in St James's Hospital, Dublin for the last 2 years. I specialise in CLL and Multiple Myeloma and operate a nurse led treatment clinic once a week. I previously worked in Denis Burkitt Ward – National Bone Marrow Transplant Unit for 7 years. I have just completed my MSc. In Nursing with RCSI this year.

**Tracey McGuigan**

Tracey McGuigan is a Specialist Nurse who has worked within Haematology in Belfast Trust since 1999. After working for many years in the Haematology Outpatient Department, she has been a Research Nurse and a Nurse Practitioner. She holds qualifications in Specialist Practice, Health Assessment and Non-Medical Prescribing. She has managed a nurse-led clinic and worked in outpatient clinics. Her current role in the last year is Transplant Co-ordinator, involved with both autologous and allogeneic transplant patients. At the moment, she is a Practice Supervisor for a Non-Medical Prescribing student colleague. She enjoys long walks, spending time with family and would like to do more travelling.



**Dr Joanne McManus MD FRCOG**

Dr McManus is a Consultant Gynaecologist & Sub-specialist in Reproductive Medicine in the Belfast Trust. Her areas of specialist practice are Fertility and Assisted Conception, Menopause, Gynae Endocrinology and Adolescent Gynaecology. She cares for young women with haematological malignancies in the setting of fertility preservation and also hormone replacement for those whose treatment has resulted in premature ovarian insufficiency.

## GUANIDINIUM-BASED COMPOUNDS AS POTENTIAL ANTI-MYELOMA AGENTS.

**Y Pei**[1,2], R Amet[1,2], P Hayden[3], P Browne[3], M Minneci[4], I Rozas[4], D Zisterer[2], T McElligott[1]

[1]John Durkan Leukaemia Laboratories, Trinity College Dublin, Dublin,
[2]School of Biochemistry and Immunology, Trinity College Dublin, Dublin,
[3]Department of Haematology, St James's Hospital, Dublin,
[4]School of Chemistry, Trinity College Dublin, Dublin,

**Background:** Multiple myeloma (MM) is a plasma cell malignancy that accounts for around 10% of all haematological cancers. Despite advances in the understanding of the molecular pathogenesis of MM and promising new therapies only 25-35% of patients respond to therapies in the relapsed and refractory settings. Thus, there is a compelling demand for novel treatment strategies. We have recently shown anti-myeloma activity of a novel guanidine-based compound, VP79s, via a mechanism targeting the signal transducer and activator of transcription 3 (STAT3) signaling pathway [1]. Here, we further investigate the activity of VP79s and related compounds in a panel of MM cell lines and assess the potential synergistic activity of VP79s in combination with the BH3 mimetic venetoclax.

**Materials and methods:** We evaluated the anti-cancer activity of VP79s and related guanidine-based compounds in the MM cell lines, NCI-H929 and U266B1, by AlamarBlue assay. Apoptosis was assessed by staining with annexin V and propidium iodine followed by flow cytometry analysis. STAT3 activation and downstream expression of STAT3 target genes were assessed by western blotting and real-time PCR.

**Results:** Screening of VP79s and a panel of related guanidine-based compounds showed activity in the low µM range; however, VP79s remained the most potent agent. VP79s induced apoptosis in a dose and time-dependent manner in both cell lines. VP79s inhibited both constitutively active and IL-6-induced STAT3 activation within 30 minutes of treatment with concurrent decreased expression of anti-apoptotic MCL1, a STAT3 target gene. The combination of VP79s and venetoclax resulted in a synergistic induction of apoptosis.

**Conclusions:** This study advances the translational development of guanidinium-based compounds as potential anti-myeloma agents. VP79s remains the most active of these agents studied and, to further investigate its effects and mechanisms of action, global gene expression profiling of myeloma cells treated with VP79s is proposed.

1. Rebecca Amet, Viola Previtali, Helene B. Mihigo, Emily Sheridan, Sarah Brophy, Nadhim Kamil Hante, Maria Jose Santos-Martinez, Patrick J. Hayden, Paul V. Browne, Isabel Rozas, Anthony M. McElligott, Daniela M. Zisterer. A novel aryl-guanidinium derivative, VP79s, targets the signal transducer and activator of transcription 3 signaling pathway, downregulates myeloid cell leukaemia-1 and exhibits preclinical activity against multiple myeloma. Life Sciences, 290, 2022

## Elevation of PD-1 expression on circulating CD19 CAR T-cells in patients with persistent disease following CAR T-cell therapy

**H Foy-Stones**[1], N Gardiner[1], DG Doherty[3], A Kilgallon[3], AM Mc Elligott[3], T Hervig[4], C Armstrong[2], N Orfali[2], E Vandenberghe[2], R Henderson[2], E Higgins[2], CL Bacon[2]
[1]Cryobiology Laboratory Stem Cell Facility, St. James's Hospital, Dublin, Ireland
[2]National Adult Stem Cell Transplant and Adult CAR-T cell Programme, St. James's Hospital, Dublin, Ireland
[3]Trinity Translational Medicine Institute, Trinity College, Dublin, Ireland
[4]Irish Blood Transfusion Service, (IBTS), Dublin, Ireland

**Introduction:** Chimeric antigen receptor (CAR) T-cell therapy has shown notable success in treating relapsed/refractory high-grade B-cell malignancies. Despite response rates reaching up to 50%, it remains unclear what factors differentiate responders from non-responders. One potential factor is T-cell exhaustion, a state of functional impairment that results from prolonged exposure to antigenic stimulation. The mechanism of T-cell exhaustion involves the expression of multiple inhibitory receptors on T-cells and their ligands on other cells. This study presents preliminary findings on CAR T-cell exhaustion dynamics following CD19 CAR T-cell therapy.

**Materials and Methods:** We conducted a study involving 19 patients who underwent CD19 CAR T-cell therapy to treat relapsed/refractory B-cell malignancies. Peripheral blood mononuclear cells (PBMCs) were serially biobanked and flow cytometry analysis was performed at 1, 3, and 6 months following infusion. The presence of circulating CD19 CAR-T cells was quantified, and the expression of T-cell-immunoglobulin-and-mucin-domain-containing-3 (TIM-3), Programmed-cell-death-1 (PD-1), B-and-T-lymphocyte-attenuator (BTLA), Cytotoxic-T-Lymphocyte-Associated-Protein-4 (CTLA-4) and Lymphocyte-Activation-Gene-3 (LAG-3) were characterised. Data analysis was performed using FlowJo(V10.8.1) and GraphPad(V10.2.0).
We longitudinally investigated CAR T-cell recipients treated with Kymriah®(n=14) and Yescarta®(n=5). The cohort included individuals varying in age (median 60±11 years) and sex (XY: n=15, XX: n=4). At 6 months post CAR-T cell infusion, 12 patients (63%) achieved complete response (CR) and 7 patients (37%) had persistent disease (PD).

**Results:** At 1, 3 and 6 months after CAR T-cell therapy the mean CD19 CAR T-cell percentages of total $CD3^+$ cells were 2.92±3.55%, 1.88±2.62% and 1.82±2.06% respectively, with mean absolute numbers of $CD3^+CD19CAR^+$cells/µL of 3.30±5.39, 1.09±1.18 and 0.92±0.86 respectively, demonstrating a decrease in the CD19 CAR percentage and absolute numbers over time post CAR T-cell therapy. Furthermore, we assessed the mean numbers and percentages in the clinical outcome groups and found no statistically significant differences in the CR group compared to those with PD.
Analysis of exhaustion marker expression on the CD19 CAR T-cells revealed that TIM-3 exhibited the highest levels, followed by PD-1, BTLA, CTLA-4 and LAG-3. Across all time points, mean percentages of TIM-3, CTLA-4 and LAG-3 expressing CD19 CAR T-cells were higher in the CR group, but no significant differences were observed. There was a higher mean percentage expression of BTLA in the PD group at 3 months, and in the CR group at 6 months, but no significant differences were observed. PD-1 expression on CD19 CAR T-cells was notably higher in the PD group, which was statistically significant at 3 months post CD19 CAR-T cell therapy ($p=0.02$).

**Conclusions**: In this preliminary study of recipients treated with Kymriah® and Yescarta®, we observed a decrease in CD19 CAR T-cell percentages and absolute numbers over time. Exhaustion profile analysis of TIM-3, PD-1, BTLA, CTLA-4 and LAG-3 showed dynamic changes over time. Clinical outcomes showed significant elevation of PD-1 expression in the persistent disease group at 3 months post-CAR T-cell therapy, with no significant differences observed in the other markers between complete response and persistent disease groups. Our preliminary finding of significant elevation of PD-1 expression in the persistent disease group highlights a potential biomarker for the prognosis of CAR T-cell therapy.

## SARS-COV-2-INDUCED SYNCYTIA HAVE ENHANCED PROCOAGULANT ACTIVITY

**JV Harte**[1,2,3], V Mykytiv[2], MP Crowley[2,3], C Coleman-Vaughan [4], JV McCarthy[1]
[1]Signal Transduction Laboratory, School of Biochemistry and Cell Biology, University College Cork, Cork, Ireland
[2]Department of Haematology, Cork University Hospital, Wilton, Cork, Ireland
[3]EOLAS Research Group, Cork University Hospital, Wilton, Cork, Ireland
[4]Department of Biological Sciences, Munster Technological University, Bishopstown, Cork, Ireland

**Introduction:**
Haemostatic markers are frequently and substantially altered from normal physiological ranges in patients with SARS-CoV-2-associated COVID-19. The coagulopathy involves the dysregulation and dysfunction of several endogenous pathways; however, the precise pathophysiology remains poorly defined. Recently, the formation of multinucleated giant cells, known as syncytia, have been recognised as a hallmark of severe and critical disease in patients with SARS-CoV-2-associated COVID-19. Cell-cell fusion and syncytiation is a physiological and pathological phenomenon, which interestingly has been linked to the activation of the coagulation cascade *in vivo*.
Therefore, we investigated whether SARS-CoV-2-induced syncytiation could promote cellular procoagulant activity *in vitro*.

**Materials and Methods:**
Human-derived lung cells were transduced with SARS-CoV-2 virus-like particles (VLPs) to induce cell-cell fusion and syncytiation, and evaluated for changes in procoagulant activity by a modified procoagulant activity assay.

**Results:**
The procoagulant activity of human lung cells was enhanced by transduction with SARS-CoV-2 VLPs, which reduced the lagphase to protofibril formation, increased the rate of fibrin polymerisation, and increased fibrin deposition. SARS-CoV-2-induced syncytiation markedly increased the externalisation of phosphatidylserine, leading to tissue factor-dependent enhancement of procoagulant activity. Mechanistically, inhibition of calcium-dependent phosphatidylserine externalisation largely abolished the enhanced procoagulant activity, and inhibited the expansion, of SARS-CoV-2-induced syncytia. Pre-treatment with contemporary direct oral anticoagulants and heparins reversed the enhancement of procoagulant activity; however, in contrast to recent observations, treatment with anticoagulants had no effect on SARS-CoV-2-associated viral entry nor cell-cell fusion.

**Conclusions:**
Collectively, transduction of human lung cells with SARS-CoV-2 enhanced cellular procoagulant activity by increasing tissue factor-dependent coagulation at the cellular surface in response to the externalisation of phosphatidylserine. SARS-CoV-2-associated procoagulant activity can be inhibited by contemporary anticoagulants; however, anticoagulants do not appear to have innate activity against SARS-CoV-2.

## TREATMENT OUTCOMES AND MINIMAL RESIDUAL DISEASE MONITORING IN *NPM1*-MUTATED AML PATIENTS RECEIVING VENETOCLAX BASED NON-INTENSIVE TREATMENT IN NORTHERN IRELAND 2020 - 2023

**A Hindley**[1], J McGimpsey[1], C Arnold[1], N Cunningham[1], MF McMullin[1,2], F McNicholl[3], D Finnegan[1], B Merron[4], M Catherwood[1]

[1]Haematology department, Belfast City Hospital, Belfast, Northern Ireland
[2]Centre for Medical Education, Queen's University Belfast, Belfast, Northern Ireland
[3]North West Cancer Centre, Altnagelvin Area Hospital, Derry, Northern Ireland
[4]Haematology Department, Antrim Area Hospital, Antrim, Northern Ireland

Acute myeloid leukaemia (AML) remains a challenging disease to treat with outcomes remaining poor, especially in older patients ineligible for intensive chemotherapy. The approval of the *BCL2* inhibitor venetoclax in combination with hypomethylating agents (HMA) or low-dose cytarabine (LDAC) in 2022 has provided an additional non-intensive treatment option for this group of patients with historically dismal outcomes.
Evidence has shown that older AML patients harbouring an *NPM1* mutation ($NPM1^{mut}$) in particular have higher rates of complete remission (CR) and overall survival when undergoing venetoclax combination therapy.
Recent evidence has additionally demonstrated the potential of *NPM1* specific minimal residual disease (MRD) monitoring by RT-qPCR in non-intensively treated patients in providing prognostic information, having previously been documented in patients on intensive regimens. In a non-intensive cohort, overall survival of 82% vs 46% for those MRD negative within 4 cycles of treatment in comparison to those MRD positive was reported.
Furthermore, a high percentage of patients electing to stop treatment remained in treatment free remission for 2 years or longer, suggesting long term survival may be possible for a number of such patients.
This small retrospective study looked at a real world cohort of patients diagnosed with $NPM1^{mut}$ AML in Northern Ireland receiving frontline venetoclax combination therapy between 2020 and 2023 to assess overall survival, co-mutations, the relation of MRD to outcome and the frequency of MRD assessment, particularly around cycles 3-5.
A total of 53 AML patients were identified as having an *NPM1* variant present at diagnosis with 21% (11/53) of these patients receiving non-intensive venetoclax combination therapy. Of these 11 patients, one patient was enrolled on a clinical trial and 2 passed away shortly after diagnosis having failed to attain CR. Of the remaining 8 patients, median age at diagnosis was 70.5 (64 – 80), and they received between 6 and 26 cycles of treatment.
Common co-mutations observed include *TET2* (45%), *FLT3*-ITD, *FLT3*-TKD and *DNMT3A* (27%) and *IDH1* and *SRSF2* (18%). Overall survival in this group is 87.5% (7/8) with all surviving patients currently in morphological and molecular remission having been followed up for a median 17 months (11-46). Within this group, one patient stopped treatment after 6 cycles and has been in treatment-free remission for 27 months.
All patients achieving MRD negativity at any point in treatment have remained in CR and the single patient that passed away from disease progression never achieved MRD negativity, with the lowest recorded level being 12.11%. In relation to timing of MRD testing for which no guidance exists, 42.8% (3/7) of patients were assessed during cycles 3-5.
Our data is in keeping with published data showing high levels of sustained complete remission and long term survival in this subset of patients. The relation of MRD to prognosis is likely to be extremely important in the future, particularly in early stages of treatment, and may also guide possible de-intensification or cessation of treatment decisions. The variability in timing of MRD assessments highlights the requirement for guidance and standardisation as exists for intensive treatment to assist in clinical decision making and the definition of actionable MRD levels.

## INVESTIGATING THE NOVEL ALBENDAZOLE-VENETOCLAX DRUG COMBINATION FOR PAEDIATRIC ACUTE MYELOID LEUKAEMIA

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**Introduction:** Venetoclax (VEN), a potent, selective inhibitor of B-cell lymphoma (BCL)-2, has been approved for the treatment of acute myeloid leukaemia (AML) in patients >75 years. The effects of venetoclax, even when used in combination with other drugs such as azacitidine or cytarabine, are still restrictive (1-3). Furthermore, little is known about venetoclax's efficacy in paediatric AML patients. AML is a leading cause of paediatric leukaemia death with only 60% of children diagnosed with AML surviving >5 years. These poor outcomes are further complicated by toxic side effects that children experience during treatment (4-9). Therefore, there is an urgent clinical need for novel single/combination therapies, that will provide efficacy against paediatric AML and relapsed paediatric AML, whilst also reducing therapy-associated side effects.

**Material and Methods:** A single agent in-house screen was performed to identify potential novel hits using the Screen-Well® FDA drug library in primary murine cells, representative of MLL-AF9-driven paediatric AML and normal karyotype HOXA9-Meis1 driven AML. A novel hit from this screen was then evaluated for anti-leukaemia efficacy in murine and human models of childhood AML *in vitro* and *in vivo* as a single agent. In addition, the synergy of this novel drug candidate in combination with the FDA approved drug VEN was also investigated.

**Results and Discussion:** The anthelmintic agent albendazole (ABZ) was identified as a novel drug candidate. Low dose ABZ (IC50 <300 nM at 72 hours) reduced viability in human AML cell lines, while having minimal effect on normal mouse and normal human peripheral blood cells. ABZ caused G2/M arrest and PARP cleavage (at 4 hours following 100 nM ABZ treatment), leading to apoptosis as confirmed by PI and Annexin V-based flow cytometry and Western blot. RNA-seq analysis of ABZ-treated AML cells identified 98 genes with increased expression, and 14 downregulated genes. *IL1B*, *P38 MAPK* and *NF-kB* were identified as key perturbed networks following ABZ treatment. Moreover, *SELPLG* was found to be top ranked upstream regulator of the ABZ gene signature. Finally, luciferase expressing THP-1 childhood AML cells were generated and pre-treated with either vehicle or ABZ and an untreated group included. Live tracking of pSLIEW-transduced AML cells in NSG mice showed ABZ decreased leukaemia burden and extended lifespan (median survival; Control (30 days) vs ABZ (53 days)). Results have also demonstrated that the novel ABZ-VEN drug combination is synergistic in both THP-1 (which are resistant to VEN alone) and MV4-11 cells (at 24, 48 & 72 hours following treatment of cells with varying concentrations of ABZ and VEN).

**Conclusion:** The novel drug candidate ABZ has remarkable anti-leukaemia efficacy in paediatric AML both *in vitro* and *in vivo*. In addition, the ABZ-VEN drug combination is synergistic in AML cells. Based on our data, the effective anti-leukaemic concentrations of both ABZ and VEN are clinically achievable and as both drugs are FDA approved, they already have excellent toxicity profiles (10-13). Current work is focused on evaluating if ABZ alone or in combination with VEN, has potential to progress to clinical trial as an age-tailored therapy for paediatric AML.

## UTILIZING MULTIPLEX DRUG SCREENING TO IDENTIFY NOVEL COMBINATION THERAPIES FOR THE TREATMENT OF ACUTE MYELOID LEUKEMIA

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**Background:** Acute Myeloid Leukaemia (AML) is a highly heterogeneous disease with multiple sub-entities, of which are characterised by distinct genetic and epigenetic alterations. This complexity suggests that a combination of therapies is essential for effective treatment. Combination therapies offer a superior approach to leukaemia treatment: they can work synergistically, enabling lower therapeutic doses and reducing potential long-term side effects. Additionally, these therapies can overcome adaptive resistance by targeting multiple disease drivers simultaneously.

**Aim**: By combining mutational profiling and drug sensitivity testing, we aim to identify novel and effective drug combinations for the treatment of specific AML subgroups. Drug sensitivity testing was carried out *in-vitro* against a panel of 1176 pairwise combinations.

**Methods:** Our lab developed a custom panel of 49 compounds representing standard of care chemotherapy and other experimental agents. Using our all-pairs testing algorithm, these compounds were grouped into pools of 5 compounds per well generating 1176 (49 x (49-1)/2) pairwise combinations to be accommodated in 175 individual wells. Additionally, with the combination screen, a single agent screen of the 49 compounds was also performed. The biological readout for this screen was CellToxä Green Cytotoxicity multiplexed with CellTitre-Gloâ Luminescent Cell Viability Assays, fluorescence and luminescence was evaluated following 72-hour incubation. Combinations were regarded a “hit” when, collectively all 5 drugs significantly decreased cell viability (<30%), but individually did not. Five AML cell lines (OCI-AML3, THP-1, HL-60, SKM-1 and MV4-11) representing a spectrum of cytogenetic abnormalities were used for this screening approach.

**Results:** Following initial optimisation to obtain single agent IC30 dose for each of 49 compounds, we identified a hit in a specific combination comprising ATRA, cytarabine, daunorubicin, fludarabine and revumenib in MV4-11 and THP-1 cell lines. A further two, 5-compound combinations were also identified as hits in the THP-1 line. These combinations are being taken forward for deconvolution into 10 pairwise and 10 triple combinations to identify a clinically feasible combination. To enable the screen to be taken forward in *ex-vivo* AML patient samples, we have optimised culture conditions which demonstrate consistent CD34 expression over a 7-day period.

**Conclusion:** We demonstrate the use of multiplex drug screening to identify combination therapies for AML subgroups. Further investigations ex-vivo will validate these combinations for specific genetic subgroups.

## PATHWAYS TO MYELOPROLIFERATIVE NEOPLASM PRESENTATION & DIAGNOSIS: RESULTS FROM A CROSS-SECTIONAL STUDY

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**Introduction/Background**
Complexities in the diagnostic pathway of the chronic myeloproliferative neoplasms (MPNs) can lead to missed opportunities for early intervention, putting patients at risk of potentially preventable vascular complications prior to diagnosis. Prior history of vascular events is incorporated into prognostic scoring systems for MPNs, influencing disease assessment, treatment and management strategies. Evidence suggests that those with blood cancer are more likely to require multiple general practitioner (GP) appointments prior to referral than any other malignancy. As methods for early cancer detection rely on symptom recognition and appraisal, a cross-sectional study assessing risk factors for delays to presentation and diagnosis amongst MPN patients was conducted.

**Methods**
An online cross-sectional survey of MPN patients was conducted using a bespoke survey instrument. Symptoms and factors influencing patient (≥ 12 weeks from symptom onset to presentation) and GP delay (≥ 6months from initial symptomatic presentation to referral) were examined using unconditional logistic regression with adjustments for MPN subtype, age at survey completion, biological sex, educational attainment and employment status (as a proxy for socioeconomic status), marital status, smoking and alcohol consumption. Only complete responses were analysed. Symptoms were assessed both individually and as a group (blood cancer warning signs; fatigue, night sweats, unexpected weight loss, pruritus, early satiety and bruising/bleeding).

**Results**
Most respondents were female (459/620;74%). The majority reported ET (n=324;52.3%) followed by PV (n=235;37.9%), PMF (n=43;6.9%) and “Other” (n=18;2.9%). Most (80.2%) of the 620 survey respondents reported symptomatic presentation. The most common symptoms associated with patient delay were pruritus (aOR 1.89, 95%CI 1.19-3.01), headaches (aOR 1.86, 95% CI 1.13,2.82) and concentration difficulties (aOR 1.75, 95%CI 1.12,2.76). Attributing symptoms to ageing (aOR 1.92, 95% CI 1.19,3.11) and not wanting to burden the GP (aOR 2.17, 95% CI 1.35,3.50) were associated with patient delay. Concern from a family member/friend was the only facilitator to early presentation identified (aOR 0.52, 95% CI 0.32-0.83).
Numerous symptoms were associated with GP delay including dizzy spells (aOR 1.52, 95% CI 1.75,3.65), headaches (aOR 1.47, 95% CI 1.69,3.63), concentration difficulties (aOR 1.44, 95% CI 1.66,3.62), paraesthesia (aOR 1.30, 95% CI 1.58-3.35), fatigue (aOR 1.96, 95% CI 1.26-3.07) and bone pain (aOR 1.02, 95% CI 1.37,3.01). Those reporting ≥3 blood cancer warning signs were more likely to experience GP delay than those experiencing fewer (aOR 3.26, 95%CI 1.75,6.29), and lack of relational continuity of GP care was significantly associated with GP delay (aOR 3.41, 95%CI 1.65,7.28). Initial clinical outcome was significantly associated with GP delay (diagnosed with another condition aOR 2.69, 95% CI 1.25,5.94; no action taken/told to represent if symptoms worsen aOR 3.34, 95% CI 1.54,7.52; tests ordered aOR 1.52, 95% CI 0.93,2.50) compared to referral to a specialist.

**Conclusions**
Delays in MPN diagnosis are common, driven by symptom misattribution, patient reluctance to seek help, and gaps in primary care. Improving symptom awareness, GP education, and continuity of care may support timely MPN diagnosis, prevent serious vascular complications, and improve outcomes for MPN patients.

## The (T) thrombosis (I) in patients with (L) lower (L) limb (I) injuries (R) requiring (I) immobilisation (TILLIRI) Study

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**Background:** Patients requiring temporary lower limb immobilisation after injury have an increased venous thromboembolism (VTE) risk. The extent of this risk in published studies varies. The TRiP(cast) model (Thrombosis Risk Prediction following cast immobilization) quantifies VTE risk using clinical risk factors. Delineating low from high VTE risk patients is challenging in the clinical setting.

**Aims:** To determine the 90-day incidence of symptomatic VTE following temporary lower limb immobilisation after injury in an unselected patient population. To prospectively collect data on VTE risk factors, including those incorporated in the TRiP(cast) model, to calculate TRiP(cast) scores.

**Methods:** TILLIRI is a prospective multicentre cohort study including 10 sites within the Irish Network for VTE Research (INViTE). Patients ≥ 18 years with an immobilised injured lower limb following injury were included. Twenty-one clinical variables were collected at presentation. Thromboprophylaxis was prescribed according to clinical gestalt. Patients were followed up at 90-days to determine if a VTE occurred.

**Results:** Between November 2018 and February 2023, 1243 patients were recruited. Follow up was complete for 1200 patients. 43 patients (3.5%) were lost to follow up. 44 (3.6%) patients and 126 (10%) patients were prescribed an anticoagulant and aspirin respectively. VTE incidence at 90-day follow-up was 7/1222 (0.57%; CI 0.15%-1.00%). TRiP(cast) scores were calculated for 1177/1222 patients. 846 patients (71.9%) had a TRiP(cast) Score < 7, received no prophylaxis and had no VTE.

**Conclusion:** TILLIRI indicates a low incidence of VTE in an unselected patient population following lower limb immobilization with low rates of anticoagulation and aspirin use. The proportion of patients with low TRiP(cast) scores and no symptomatic VTE rate suggests that thromboprophylaxis may potentially be avoided in patients with a TRiP(cast) score < 7, with a low risk of VTE at 90 days. Future studies examining targeted strategies to identify high risk groups and the optimal pharmacological strategies in preventing VTE are needed.

## INVESTIGATING THE ROLE OF OSTEOBLASTS IN CONTROLLING NATURAL KILLER CELL CYTOTOXICITY AGAINST ACUTE MYELOID LEUKAEMIA

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**Introduction:**
Natural killer (NK) cell-based therapies have entered clinical testing as a novel cancer immunotherapy thanks to their inherent anti-tumour cytotoxicity. Acute myeloid leukaemia (AML) is one cancer for which NK cell therapies are being developed. When adoptive NK cells are administered to patients, their therapeutic efficacy may be reduced as the NK cells encounter and navigate the complex bone marrow environment. Osteoblasts, the cells lining the surface of bone trabeculae in the bone marrow are known to regulate haematopoiesis and drive drug resistance in leukaemia. We hypothesised that osteoblasts may supress the anti-leukaemic activity of NK cells and so the aim of this work was to investigate the potential effect of osteoblasts on NK cell functionality.

**Materials and Methods:**
Bone marrow mesenchymal stromal cells (BMSCs) isolated from AML patients were obtained from the Blood Cancer Network Ireland biobank. Non-AML, 'healthy' donor BMSCs were obtained from consenting donors undergoing hip replacement surgery. Osteoblast cultures were obtained by the *ex vivo* differentiation of BMSCs by culturing the cells in the presence of dexamethasone, ascorbic acid-2-phosphate and β-glycerophosphate. Osteogenic differentiation was confirmed with alizarin red staining. NK cells were derived from peripheral blood of healthy donors and expanded using lymphoblastoid feeder cells in the presence of interleukin-2. NK cell functionality after exposure to BMSCs and osteoblasts was assessed in cytotoxicity assays by combining NK cells with fluorescently tagged AML cells (MOLM-13 cell line) and measuring the viability of the AML target cells with flow cytometry.

**Results:**
Both AML patient-derived and healthy donor-derived BMSCs could differentiate into osteoblasts after culture in osteogenic differentiation medium for 14-16 days. Direct co-culture of NK cells with osteoblasts from both donor sources impaired NK cell cytotoxicity, reducing their ability to kill target AML cells. Inhibition of NK cell function was also seen after co-culture with undifferentiated BMSCs. NK cell viability from both osteoblast and BMSC co-cultures was also reduced. Preliminary results indicate that this impairment may be contact dependent.

**Conclusions:**
This study revealed that osteoblasts may act as a barrier to NK cell activity in the bone marrow which could have an impact on the success of adoptive NK cell therapy for AML treatment. Similar to others, we found that BMSCs also inhibit anti-leukaemic NK cell function. Our next objective is to determine the mechanism(s) behind this NK cell inhibition and identify potential gene editing strategies for the generation of a suppression-resistant NK cell therapy.

## SKY92 MOLECULAR PROFLING IN COMBINATION WITH MRD RISK PROFILING TO IDENTIFY HIGH-RISK MULTIPLE MYELOMA PATIENTS IN IRELAND (SKIP-MM)

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**Background:**
Multiple Myeloma (MM) is extremely heterogeneous and cytogenetic abnormalities detected by FISH can be used for risk-stratification. However, this approach lacks standardisation. Additionally, minimal residual disease (MRD) negativity is a strong predictor of survival, but the impact of high-risk (HR) MM on reaching this goal is not fully understood. In Ireland, risk-status of this population has not been described. In this study, we evaluate new methods for genetic risk-stratification of MM.
Aims:
We aimed to assess for the first time the gene expression profile (GEP) of transplant-eligible (TE)-MM patients across Ireland, to define risk status using the SKY92 gene signature (MMProfiler™), and evaluate the achievement of MRD negativity in these patients by NGS.

**Methods:**
TE-MM patients from seven major cancer centres were recruited at diagnosis. Bone marrow samples from TE-MM (n=120) at diagnosis and 100 days post-ASCT were collected. Briefly, these were enriched for mononuclear cells (MNCs) and CD138+ cells, and DNA/RNA extracted. The MMProfiler™ microarray was performed in-house to detect SKY92 (HR, predicted survival <2 years at diagnosis) and several cytogenetic abnormalities. Data was validated using FISH and digital multiplex ligation-dependent probe amplification (MLPA). Diagnostic samples were assessed for clonal IGH rearrangements using LymphoTrack™ NGS assays (IGH-FR1 and IGK) on an Illumina MiSeq platform. MRD was monitored using a single LymphoTrack™ assay according to the clonotype identified at diagnosis.

**Results:**
MMProfiler™ test success rate is >80%, which outperforms FISH. The SKY92 HR signature was detected in 29.7% of patients, this is higher than international published averages of 19-24%. These patients were more likely to present with HR cytogenetics t(4;14) and gain(1q) ($p<0.05$), and the majority were classed as ISS stage II/III, whilst standard-risk (SR) were mostly ISS stage I. Abnormalities detected by FISH and MMProfiler™ were concordant for most cases (75%), with the MMProfiler™ demonstrating superior sensitivity for abnormalities missed by FISH. Identification of gain(1q) was consistent between the MMProfiler™ and MLPA. Additionally, MLPA identified del(13) in 29% of cases, and del(1p) in 35%.
IGH-FR1 and IGK assays detected clonal rearrangements in 86.7% of diagnostic samples. We have determined MRD status in 21 follow-up samples reaching the recommended sensitivity of $10^{-5}$ (7/21 MRD-). Data indicates MRD status is independent of risk-status at diagnosis with similar rates of MRD negativity in both groups (33.3% SR vs 40% HR).
**Conclusion:**
This is the largest study conducted to date in Ireland, profiling risk status in this population. Almost one third of TE-MM patients present with HR disease as defined by MMProfiler™ and validated by independent FISH and MLPA. The reasons for the high prevalence of HR-MM at diagnosis is not clear and further in-depth genomic profiling is needed. This data underpins the need for national risk-stratified clinical trials. We show high clonal characterisation of diagnostic TE-MM MNCs using NGS, which can be used for sensitive MRD detection in real-world practice. These methods have improved risk stratification of TE-MM patients, and in future aid with risk-adapted therapy approaches. Work is underway to transition these tests into clinic.

## ALL-IRELAND RELAPSED/REFRACTORY (R/R) LARGE B-CELL LYMPHOMA (LBCL) CHIMERIC ANTIGEN RECEPTOR T-CELL (CAR-T) OUTCOMES – REFERRALS TO KING'S COLLEGE HOSPITAL (KCH)

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**Background**
The UK has successfully established autologous anti-CD19 CAR-T for LBCL with axicabtagene ciloleucel (axi-cel) and tisagenlecleucel (tisa-cel) with improved NHS outcomes of LBCL treated with CD19 CAR-T demonstrated over time. CAR-T is now approved in both 2nd and 3rd line treatment for r/r LBCL in the UK. This study describes the experience of the initial cohort of Irish patients who travelled to KCH (London) for this therapy.

**Methods**
From October 2019 to August 2024, 43 patients with r/r LBCL were referred from centres across Ireland to KCH with all patients assessed according to the same NHS CAR-T eligibility criteria ratified by the KCH CAR-T MDT. Northern Irish patients additionally were presented at the UK National CAR-T Clinical Panel (NCCP) for 2nd or 3rd line axi-cel / 3rd line tisa-cel. All patients required 10+ day admission post infusion to KCH and remained in London until follow-up PET scan at 1-month post infusion.

**Results**
Of 43 patients, 95% were 3L+ approval with the remaining 2L. Disease histology was DLBCL-NOS 68%, transformed follicular lymphoma 22%, relapsed-concomitant secondary CNS lymphoma 5% and 2% each: post-transplant lymphoproliferative disorder-DLBCL, transformed marginal zone lymphoma, high-grade B-cell lymphoma-NOS, Richter transformation.
At CAR-T MDT approval, 84% had stage IV disease, 19% 2+ extranodal sites, 26% bulky disease, 40% elevated LDH. Median number of prior treatment lines was 2, 33% had 3+ lines. 63% were male with median age 58 (range 20-78); 91% recorded ethnicity as White Irish or British.
Of 43 patients referred, 95% underwent leukapheresis (2 patients deferred for progressive disease) and 93% proceeded to infusion, where 88% had PS0-1, 12% PS2. Median time from CAR-T MDT approval to infusion was 49 days (range 38–210 days). 83% infused patients received bridging, 39% systemic chemotherapy, 22% radiotherapy ±steroids, 22% combined modality treatment, 17% no bridging.
Of the 40 patients proceeding to infusion, 12% had GFR<60ml/min and 12% had EF<50%. 93% received axi-cel , 7% received tisa-cel. 98% developed cytokine release syndrome (CRS) with 5% grade 3+. 50% developed immune effector cell-associated neurotoxicity syndrome (ICANS) with 12% grade 3+. 88% received tocilizumab, 68% dexamethasone, 12% anakinra. 27% required ICU admission - of these, 8% required organ support (2 inotropes, 1 intubation). There were no non-relapse mortality (NRM) deaths during admission or within the 1st month following infusion in London.
Best ORR by PET at 1 month was 85% (58% CMR). At data cut-off in August 2024, 29 patients (67% ITT; 73% infused patients) were alive. All deaths were related to infection and PD. Of relapsed patients 5 proceeded to bispecific antibodies. Progression free and overall survival data will be presented at the meeting.

**Conclusion**
Outcomes for this all-Ireland r/r LBCL cohort post-CAR-T are very encouraging, with best ORR and CMR rates comparable to published ZUMA-1 and UK real-world series in this unique population required to travel for treatment. The feasibility of this shared care pathway is further strengthened by the minimal high-grade toxicity we observed, alongside no NRM within the first month, reflective of good patient selection.

**ALLOGENEIC TRANSPLANTATION OUTCOMES IN MYELOFIBROSIS: A 25 YEAR REVIEW**

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**Introduction:**

Myelofibrosis (MF) is a clonal neoplasm characterised by abnormal myeloproliferation, pathological bone marrow fibrosis and extra-medullary haematopoiesis. Median survival in primary MF currently approaches 7 years, however survival is variable with a poorer outcome in those with intermediate-2 and high risk disease. Jak2 inhibitors are the mainstay of current treatment, but the only curative treatment option is allogenic hematopoietic stem cell transplantation (AlloHSCT).

International experience of AlloHSCT in Myelofibrosis has shown a higher Treatment Related Mortality (TRM) than other myeloid malignancies and is also associated with a considerable relapse rate. We here examine outcomes in Irish practice and compare to published international data.

**Methods:**

A retrospective review of patients transplanted for MF in St James' Hospital between November 1999 and December 2023 was completed. The data was extracted from our transplant registry to identify the MF patients who underwent an allogeneic transplant in SJH. Patients were risk stratified by their prognostic score, identification of driver mutations and presence of additional mutation burden (where available) and prior treatment with Ruxolitinib. We assessed treatment related mortality (TRM) and overall survival (OS) at 1 and 5 years.

**Results:**

59 patients with MF proceeded to alloHSCT. Driver mutation status was known for 51 patients, 60% carried a JAK2 mutation, 29% CALR, 6% MPL and 5% were triple negative. 64% (n=38) were male and 36% (n=21) were female. The median age at transplant was 54 years (18-68). The median time from diagnosis to transplant was months 17 months (2-132). The majority of patients were conditioned with reduced-intensity regimens (90%, n=53), with FluBuATG being the most frequently used regimen. 63% (n=37) received SIB and 37% (n=22) received MUD HSCT

The 1 year OS is estimated at 74% with a 5 year estimated OS was 56% with a median survival of 6 years. The median time to death post-transplant was 6 months (1-72). The treatment related mortality was 25% with GVHD accounting for approximately 50% of this. The relapse rate was 33% (20/59) with half of the patients still alive. Since the introduction of Ruxolitinib in 2014 survival has increased to an estimated 1 and 5 year OS of 81% and 68% respectively.

**Conclusion:**

Our data demonstrates internationally comparable 1 and 5 year OS and encourages the use of AlloHSCT in select MF patients as a curative modality. The use of small molecular inhibitors pre-transplant and now throughout the early transplant phase, coupled with incremental refinements in transplant supportive care has likely contributed to the improved survival seen in recent years. However, this dataset also highlights the challenges of significant TRM and post-transplant relapse, which occur collectively in over half of patients. Research and international collaboration is needed to further improve the prognosis of transplant-eligible MF, particularly focusing on timing of transplantation, optimising pre-transplant disease control, limiting conditioning toxicity, enhancing immune reconstitution and effectively managing the re-emergence of disease post-transplant.

**Application of a Novel Artificial Intelligence Algorithm to Understand Spatial Immune Cell Relationships in Newly Diagnosed Multiple Myeloma**

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**Background:**
The unique features of the implicated plasma cell clone and its interaction with the tumour microenvironment are integral to the understanding of the pathophysiology of multiple myeloma (MM). It has been postulated that the colocalization of bone marrow plasma cells (BMPCs) and other immune cells, such as eosinophils, in the bone marrow may provide a permissive niche for BMPC survival via APRIL and IL-6 production. To understand if spatial relationships of cellular components within the bone marrow microenvironment in newly diagnosed multiple myeloma (ND-MM) are functionally relevant in patients, we combined whole slide imaging (WSI) with a novel artificial intelligence (AI) and machine learning algorithm to assess cellular proximity, spatial relationships and plasma cell density.
**Methods:**
Bone marrow (BM) trephine WSIs were retrospectively analysed from 29 treatment naïve, ND-MM patients. WSIs were created by scanning the H&E trephine slides at X40 magnification using a high-power digital scanner (Objective Imaging). The HALO AI (Indica Labs, NM, USA) DenseNet v2 tissue classifier was trained to segregate bone, cellular and adipose tissue compartments, followed by quantification of BMPCs and eosinophils (nuclear phenotyping). The HALO Spatial analysis module was then used to assess the distribution of BMPCs within the marrow cellular compartment (spatial analysis) and the proximity of eosinophils to BMPCs (proximity analysis). Clinical biomarkers (e.g. Beta-2-microglobulin [B2M], LDH, peripheral white cell counts) were compared with AI generated data examining the spatial relationships between BMPCs and key immunological elements of the bone marrow microenvironment.
**Results:**
The median age of the 29 ND-MM patients was 66 years with a balanced male to female ratio (52% and 48% respectively). Based on cytogenetic and clinical data, 90% of patients were stratified as having IMWG R-ISS standard-risk disease and the remaining 10% were stratified as having high-risk MM. The tissue classification analysis by AI correctly classified ND-MM in all 29 cases by establishing mean BMPC number, density BMPCs in mm and the total BMPC percentage. This was possible on H&E stained slides and did not require immunohistochemistry for CD138. There was positive diagnostic concordance ($R=0.56, p<0.01$) between nuclear phenotyping by AI on H&E slides and the BMPC percentage on CD138 stained slides as estimated by an independent histopathologist. Spatial analysis demonstrated that increasing BMPC density at incremental distances from the bony trabecula positively correlated with B2M. Incremental B2M was positively correlated with both BMPC density in mm ($R=0.46, p<0.05$) and BMPC distance from the bony interface to the deeper bone marrow compartment of 120 to 300µm ($R=0.5\text{-}0.61, p<0.05$) indicating that B2M may predict invasive behaviour and homotypic interactions of BMPCs. Proximity analysis demonstrated an increased intercellular distance between eosinophils and BMPCs in kappa restricted MM ($R=0.74\text{-}0.8, p<0.001$) which may indicate altered immune cell cross-talk in this subtype of MM. The absolute neutrophil count in the peripheral blood was found to be correlated with an intermediate distance between eosinophils and plasma cells of 100-140µm ($R=0.61\text{-}0.65, p<0.001$) indicating that PC trafficking may be altered in patients with neutrophilia at diagnosis.
**Conclusion:**
Our AI algorithm can robustly and correctly identify MM from BM trephine H&E WSI, negating the need for CD138 staining, which may facilitate earlier diagnostic certainty. Additionally, our AI analysis indicates that immune cell-PC spatial relationships within the bone marrow microenvironment are altered in high disease burden states (higher B2M) and are impacted by the clonal subtype of MM and neutrophil-eosinophil localisation, perhaps indicating a pro-inflammatory milieu in the bone marrow.

**Interferon alpha upregulates the ATF4/CHOP arm of the unfolded protein response and is synergistic in combination with proteasome inhibitors in *JAK2* V617F positive cells**

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**Introduction**

Disease modifying therapies which are both tolerable and effectively eradicate the mutant *JAK2* V617F positive clone are a critical unmet need for patients with advanced forms of myeloproliferative neoplasms (MPN). Interferon alpha (IFN-α) is a first line treatment for chronic phases of MPN and can bring about sustained molecular responses. Unfortunately, the dynamics of these responses are gradual, taking many years to achieve modest allele burden reductions and therefore it is not suitable for most patients with advanced forms of MPN. Combination treatments which potentiate the effects of IFN-α in *JAK2* V617F positive cells could offer a potential novel approach for this patient group.

**Methods**

*JAK2* V617F positive UKE1, HEL and SET2 cell line models were investigated. Gene expression analysis was undertaken using RNA-sequencing and validated using real time PCR (qPCR). Chromatin accessibility was assessed using ATAC sequencing. Western blotting was used to evaluate protein level expression. Knockout and knockdown models were established using CRISPR-Cas9 by nucleofection of the ribonucleoprotein complex. Synergy was determined using SynergyFinder Plus.

**Results**

IFN-α was observed to induce apoptosis in UKE1, SET2 and HEL cells. An IFN-α resistant UKE1 MPN cell line (UKE1-NR) was established and directly compared using RNA-sequencing to the parental model (UKE-P) which remained sensitive. Both UKE1-P and UKE-NR upregulate canonical IFN pathways and increase phosphorylation of STAT1 to a similar extent after exposure to IFN-α. Differential gene expression analysis demonstrated a transcriptional upregulation of the PERK/ATF4/CHOP arm of the unfolded protein response (UPR) and the pro-apoptotic gene *PMAIP1* (NOXA) in the sensitive UKE1-P cells. Using qPCR we validated this in all three cell line models observing upregulation of the UPR genes *ATF3* and *DDIT3* (CHOP) and *PMAIP1* (NOXA) following IFN-α exposure. ATAC sequencing demonstrated differential loss of chromatin accessibility at genomic loci identified as binding sites for ATF3, ATF4 and CHOP in the non-responsive UKE1-NR cells. ISRIB is a small molecular inhibitor of ATF4 activation. Co-treatment with IFN-α in UKE1 cells antagonised the effect of IFN-α consistent with an important role of this pathway.

Proteasome inhibitors induce the UPR. Co-treatment with bortezomib was observed to increase apoptosis in all three cell line models in a synergistic manner. Combination treatment significantly increased expression of *ATF3, DDIT3* (CHOP) and *PMAIP1* (NOXA) in comparison to either single agent. This combination also demonstrated efficacy in the UKE-NR cells. UKE1 cells are *TP53* wild-type whilst HEL and SET2 cells are *TP53* mutant demonstrating independence of this combination on p53 status. This was confirmed using a *TP53* knockdown model. NOXA knockout was observed to partially antagonise the effect of the combination. Initial results suggest further synergy in combination with the BCL-2 inhibitor venetoclax.

**Conclusion**

IFN-α induces apoptosis which is characterized by an upregulation of the UPR and NOXA in *JAK2* V617F positive cells. This induces a therapeutic vulnerability which can be exploited in combination with proteasome inhibition and offers a novel approach for further investigation in *JAK2* V617F positive MPN.

## SINGLE-CENTRE EXPERIENCE USING A RAPID VENETOCLAX DOSE-ESCALATION STRATEGY FOR B-CELL CHRONIC LYMPHOCYTIC LEUKAEMIA.

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### Introduction

Chronic lymphocytic leukaemia (CLL) affects predominantly older patients and is the commonest leukaemia identified in the western world. In the past decade effective oral therapies have become available and venetoclax (a BCL-2 antagonist) combined with anti-CD20 therapy (Rituximab or Obinutuzumab)(Ven-O/R) has become the standard of care for time-limited CLL treatment. Venetoclax potency results in a significant risk of tumour lysis syndrome (TLS) in high tumour load CLL, leading to complex blood test and hydration scheduling for TLS monitoring and management, mandating weekly hospital admissions for dose escalation for up to 5 weeks. Anti-CD20 therapy can also result in acute CRS-type toxicity in patients with significant lymphocytosis and is challenging for frail patients in a day unit setting.
We adopted a rapid dose-escalation strategy based on a French study, which suited both the older, co-morbid local population and our national referral practice, avoided dose escalation delays and resulted in efficient use of hospital resources. Anti-CD20 treatment was initiated during the inpatient stay. The strategy was audited and the results are presented.

### Materials and Methods

Consecutive patients treated with rapid escalation Ven-O/R treated between 2022-2024 were included. Patient data, including clinical, laboratory, and medication records, were obtained using the hospital's electronic medical record. Patients were admitted, venetoclax was initiated with appropriate TLS management and escalated every 48 hours if tolerated. Anti-CD20 therapy was initiated when the lymphocyte count was <20 x $10^9$/L.

### Results

Sixteen patients were included of whom 14 (88%) patients were male, with a median age of 66 (*range 55-77)* years. Binet staging was progressive Binet A; 3 (19%), Binet B; 8 (50%), Binet C; 5 (31%) and 2 patients (13%) had auto-immune haemolytic anaemia. Ten patients were treatment naïve, 3 (19%) received ibrutinib, 2 (13%) received *Fludarabine-Cyclophosphamide-Rituximab* and 1 received a steroid pre-phase. Nine patients had significant co-morbidities, 7 (44%) with cardiovascular disease, and 2 (13%) with renal disease.
Pre-therapy the median white cell count (WCC) was 47.9 x$10^9$/L *(range: 2.4 to 556.7),* 11 (69%) had WCC >20 x$10^9$/L. Median creatinine clearance at initiation was 84 *(range 43-131)* ml/min. All patients completed escalation to full dose venetoclax with no episodes of clinical/biochemical TLS (*Howard* criteria). On discharge, median WCC was 4.05 x$10^9$/L *(range 1.7-13.3).*
Eleven patients (69%) initiated anti-CD20 therapy during initiation, 3 following admission, one pre-admission (Obinutuzumab in 13, Rituximab in 2) and the final patient had Venetoclax monotherapy. The median inpatient stay was 10.5 days *(range 8-22).*

### Conclusions

The rapid dose-escalation of Ven-O/R was used safely in 16 patients, was well tolerated with no TLS or CRS episodes and was administratively efficient in this frequently older, co-morbid cohort. The strategy provides a safe alternative to conventional initiation of Ven-O/R in CLL.

## GROUP O-WHOLE BLOOD - A NEW POTENTIAL ROLE IN ST. VINCENT'S UNIVERSITY HOSPITAL

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**Background**: In recent years the potential role for use of group-O whole blood has become prominent, notably in traumatic haemorrhage and pre-hospital settings. This has been highlighted by the release of group O-whole blood for clinical evaluation by the Irish Blood Transfusion Service. Though the nation's levels of donors are critically low as of late, group O-positive is Ireland's most common blood bank resource. We thus conducted a comprehensive audit of St. Vincent University Hospital's (SVUH) emergency release O-negative blood, with aim to achieve insight into our applicability to this new initiative.

**Materials and methods**: A retrospective audit of all emergency O RhD negative blood released for an eleven month period was conducted. This was carried out with reference to the NCEC29 Guidelines for Life-Threatening Intraoperative Haemorrhage, and Local hospital Guidelines. The sample size was identified using Blood Track in combination with blood bank logs. All units that were transfused as part of a Code Red Emergency blood request were noted, and this was cross-referenced with Major Haemorrhage Audit Criteria to consider the percentage of which complied. The LIMS allowed for an analysis of the temporal data involving each individual. Patient data and reason for transfusion was acquired via LIMS and Maxims.

**Results**: 42 patients needed emergency release of O-Negative blood during the audit period, with a total of 88 units being transfused. A Code Red status was activated in the case of 28 out of 42 patients, of which only 39.29% fulfilled the SVUH Blood Bank's Major Haemorrhage Audit Criteria. The mean was equal to the median (21 days) when considering the age of each unit at time of transfusion, while the modal age was 25 days. The maximum age was 35 days and the minimum was 2 days old. Acute gastrointestinal bleeding was the modal clinical reason requiring transfusion, and the Emergency Department was the most common location of all transfused O-negative emergency release units (55 units). In terms of patient demographics, the data displayed an approximate female:male ratio of 1:2. Of all 15 females, 11 were ≥ 55 years of age at the time of transfusion. All 27 males were ≥ 18 years of age at the time of transfusion. According to the suggested IBTS criteria, 90.47% of all those audited were potentially suitable for O-Positive whole blood transfusion in the place of O-Negative Emergency Release blood.

**Conclusions**: This audit highlights a strong potential for the successful implementation in SVUH of the new IBTS drive to decrease unnecessary O-negative emergency blood product usage. There was an obvious predominance of gastrointestinal bleeds requiring emergency O-Negative blood, with the majority of all units being transfused in the SVUH Emergency Department, which may be an important area of focus for future implementation.

## ACUTE MYELOID LEUKAEMIA IN A PATIENT WITH A HISTORY OF A GERMLINE BRCA1 MUTATION AND METASTATIC TRIPLE NEGTIVE BREAST CANCER

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**Introduction:**
Patients with defective DNA repair mechanisms are at greater risk for developing cancer. The *BRCA1/2* genes encode tumour suppressor proteins involved in homologous recombination DNA repair. Patients with an inherited pathogenic/likely pathogenic BRCA1/2 mutation resulting in loss of function have increased risk of several cancers, particularly breast and ovarian cancer.
AML is the most common acute leukaemia diagnosed in adults, occurring more frequently in males than females and diagnosed at a median age of 73 years. It is unclear to what extent germline *BRCA1/2* mutations impact the risk of developing de novo AML however increasing incidence of myelodysplastic syndrome (MDS) and AML in these patients suggests a possible link. Conversely, the development of therapy-related myeloid neoplasms such as AML (t-AML), accounting for 5-10% of all AML cases, is a well-recognized complication of cytotoxic, radiation or immunosuppressive solid tumour treatment.
Here we present a case of a 30-year-old female, identified at the age of 22 as being *BRCA1* positive after her father and paternal cousin were identified as *BRCA1* carriers. Following the birth of her two children at the age of 27, the patient identified a lump in her right breast and was subsequently diagnosed with bilateral triple negative breast cancer (TNBC) following biopsies. The patient completed only three rounds of neo-adjuvant chemotherapy, proceeded with a bilateral mastectomy and concomitant reconstruction with delayed healing. Five months later, metastatic disease was confirmed in the liver, lung and lymph nodes and the patient commenced Atezolizumab and Olaparib treatment. At follow-up oncology clinic, full blood count demonstrated pancytopenia and blood film confirmed circulating blasts.

**Materials and methods:**
Flow cytometry confirmed the presence of myeloid blasts in both peripheral blood and bone marrow. Molecular and cytogenetic analyses for AML-associated variants including karyotyping, FISH and myeloid NGS were performed on the patient's bone marrow.
Results
Patient had an abnormal karyotype 45,X,-X,t(8;21)(q22;q22)[10] with a *RUNX1::RUNX1T1* rearrangement detected by both FISH and PCR. The patient was negative for *FLT3* and *NPM1* mutations and no other relevant variants were detected with NGS. These results are consistent with an AML with a *RUNX1::RUNX1T1* fusion.

**Conclusions:**
This patient has a confirmed germline BRCA1 mutation, metastatic TNBC and AML with a *RUNX1::RUNX1T1* fusion. The patient has received prior chemotherapy containing topoisomerase II inhibitors, immunotherapy and Olaparib to treat TNBC and is currently receiving anti-metabolite chemotherapy.
It is well-documented that topoisomerase II inhibitors can cause t-AML in some patients, as breakage at topoisomerase II sites can cause abnormal recombination and translocations involving *KMT2A, RUNX1* or *RARA*. In these cases, AML typically presents 1-3 years post-treatment and precursor MDS is rare, which fits with this patient's AML presentation. The possibility of a de novo AML with a *RUNX1::RUNX1T1* fusion however, whilst rare, cannot be ruled out.
This is a challenging case and a multidisciplinary approach is warranted for accurate diagnosis and prognosis as de novo *RUNX1::RUNX1T1* AML has a more favorable prognosis than t-AML. Presentation of this case may generate a consensus diagnosis and audience participation is welcomed.

## ACQUIRED HAEMOPHILIA A AS A COMPLICATION OF GRAFT-VERSUS-HOST-DISEASE FOLLOWING ALLOGENEIC STEM CELL TRANSPLANTATION: A CASE REPORT

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Graft-versus-host disease (GVHD) is a significant and potentially life-threatening complication of allogeneic stem cell transplantation (allo-SCT). Acquired Hemophilia A (AHA), characterized by the development of autoantibodies against factor VIII, can lead to severe bleeding[1]. Although AHA is well-documented following autologous SCT, its occurrence in the context of GVHD post-allo-SCT is notably uncommon[2]. This case report details the presentation, diagnosis and management of AHA in a patient with GVHD following allo-SCT.

A 67-year-old female with acute myeloid leukemia (TET2, SRSF2 mutated, normal karyotype) underwent a reduced-intensity (FLU/BU ATG) conditioned allo-SCT from a sibling-matched donor in July 2021. Due to partial chimerism detected in May 2022 (day +278), a pre-emptive donor lymphocyte infusion was administered on day +338 in July 2022. By day+398, she developed mucocutaneous and ocular GVHD, necessitating initiation of high-dose prednisolone.

During a routine clinical visit on day +488 (13/12/22), she presented with extensive bruising and an isolated prolonged activated partial thromboplastin time (APTT) of 60 seconds (normal: 21-29s). Laboratory investigations revealed a nearly undetectable factor VIII level of 0.01 IU/ml and a positive inhibitor screen with elevated titres (31 BU/ml), confirming the diagnosis of acquired factor VIII deficiency secondary to GVHD.

In response to the diagnosis of AHA, her corticosteroid dose was increased, and weekly rituximab therapy was initiated, with the first cycle administered on 15/12/22. Two days after her first rituximab, she self-presented to the Emergency Department with severe right thigh bruising and pain, raising clinical suspicion of an intramuscular bleed. She received recombinant Novoseven and subsequently five doses of plasma-derived FEIBA over five days, leading to significant clinical improvement.

The patient completed four cycles of rituximab on the 5/1/23 and her corticosteroids were tapered off in February 2023. Four weeks post-AHA diagnosis, her inhibitor screen returned negative. For continued management of chronic GVHD, she was transitioned to ruxolitinib, which was discontinued in October 2023 due to cytopenias. She remains in clinical remission from both GVHD and AHA.

This case highlights the complex interaction between immune dysregulation in GVHD and the development of AHA, emphasizing the rarity and clinical significance of this complication post-allo-SCT. Managing AHA in the context of GVHD poses unique challenges, requiring a delicate balance between inhibitor eradication and graft preservation[3]. A multidisciplinary approach, including hematologists, transplant specialists, and coagulation experts, is crucial for optimal management and outcomes.

The development of AHA in a patient with GVHD post-allo-SCT underscores the need for vigilance in monitoring for bleeding complications in this population. This case reinforces the importance of a tailored, multidisciplinary approach to manage the dual challenges of autoimmunity and graft maintenance, ensuring favorable patient outcomes through close monitoring and timely intervention.

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**Long-Term survival of patient with mast cell leukemia progressing from Systemic Mastocytosis treated with Avapritinib**

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Systemic mastocytosis (SM) is a rare, heterogeneous group of disorders characterised by abnormal accumulation of mast cells in various tissues, often involving the skin, bone marrow, liver, spleen, and gastrointestinal tract. SM most commonly presents in its indolent form, but in rare cases, it progresses to more advanced forms of the disease, such as aggressive SM (ASM), SM with an associated hematologic neoplasm (SM-AHN), and mast cell leukemia (MCL). Advanced forms of SM are associated with a poor prognosis, with median survival ranging from two to four years, particularly in MCL[1].The prognosis is largely influenced by the presence of the KIT D816V mutation, which is present in approximately 90% of cases and is a key driver of the disease[2]. Recent advances in targeted therapies, such as Avapritinib, a potent inhibitor of KIT D816V, have significantly improved outcomes, including symptom control, reduction in disease burden, and overall quality of life in patients with SM.
We present the case of a 55-year-old male who presented to St. Vincent's University Hospital in 2020 with gastrointestinal and cutaneous manifestations of indolent SM, with associated significant organomegaly, including splenomegaly. Initial laboratory investigations revealed a serum tryptase level of 748 µg/L (RR 2.0 to 14.0 µg/L), Bone marrow biopsy demonstrated a 25% infiltration of mast cells, and molecular testing confirmed the presence of the KIT D816V mutation. The patient was enrolled in the PIONEER trial at Guy's and St Thomas' Hospital in London, UK, and was commenced on a low-dose regimen of Avapritinib at 25 mg daily. He remained clinically stable on this dose for 18 months, with significant symptomatic relief and no major adverse events reported. However, in April 2022, his disease progressed to MCL, as evidenced by a 35% infiltration of mast cells in a restaging bone marrow biopsy. This progression was hypothesised to be due to a reduction in marrow fibrosis, allowing mobilisation of mast cells into the peripheral blood. Consequently, his Avapritinib dose was escalated to 200 mg on alternate days, later adjusted to 100 mg daily after stabilisation of the disease.
Follow-up bone marrow evaluation in February 2024 revealed a reduction in mast cell infiltration to 20%. This quantitative improvement was paralleled by a decrease in aberrant mast cell markers. Clinically, the patient reported significant improvement in his symptoms, with no anaphylactic episodes since 2022 and notable improvement in his levels of fatigue and overall well-being. Additionally, his serum tryptase level had reduced to 50 ug/L and had remained stable for 18 months
This case highlights the potential of Avapritinib to not only stabilise but also reduce disease burden in advanced SM, even in cases progressing to MCL which usually has a dismal prognosis. Ongoing research isnecessary to better understand the durability of these responses and the optimal dosing strategies in SM which remains an unmet clinical need.

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## Hyperhaemolysis and Pernicious Parvovirus in a Sickle Cell Patient

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**Introduction:**
Hyperhaemolysis is a rare but potentially life threatening complication in sickle cell disease characterised by a rapid decline in haemoglobin, intravascular haemolysis and associated haemoglobinuria. It is typically a complication of red cell transfusion and can lead to multiorgan failure in severe cases. The literature recommends restricting transfusion and instituting immunosuppression.
Human Parvovirus B19, on the other hand, is a viral infection which has been implicated in a variety of diseases. One of the most frequently reported complications is transient aplastic crisis in patients with chronic haemolytic anaemia, such as in sickle cells disease.

**Case:**
We present the case of a 24 year old male patient with a background of homozygous HbSS disease who presented with lower back pain and bilateral shoulder pain. He was not compliant with his prescribed disease modification (hydroxycarbamide) pre admission. He was not enrolled in a red cell exchange or top up programme.
At presentation, his Hb was 5.6g/dl (usual baseline 8-9g/dl) and this did not increment following initial red cell transfusion. Parallel investigations demonstrated a suppressed reticulocyte count of 67 x $10^9$/l, elevated LDH of 1156IU/l and an elevated bilirubin of 27umol/l. While there was a concern raised for hyperhaemolysis, the parameters as described did not conform completely to the diagnosis and so the decision was taken to proceed with another two units of red cells.
Following transfusion, the haemoglobin did not increment and therefore the decision was taken to introduce immunosuppression for hyperhaemolysis with high dose methylprednisolone and intravenous immunoglobulin. He also received iron, vitamin B12 and folic acid supplementation. Over the subsequent 6 days, the Hb declined further to a nadir of 4.5g/dl. On day 8 of admission, with no improvement in the haemoglobin, eculizumab (complement inhibitor – 1 dose) and erythropoietin (daily for 5 days) were deemed necessary.
In the midst of the immunosuppression, the reticulocyte count continued to decline, demonstrating a nadir of 25 x $10^9$/l on day 8. There was a concern raised regarding parvovirus B19 infection but this was felt to be unlikely due to admission serology (ELISA) which resulted negative for both IgM and IgG. We sought the advice of our virology colleagues who recommended PCR testing. This was resulted on day 6 of admission and demonstrated DNA levels of >100,000,000IU/ml. Subsequent testing, taken on day 10 of admission demonstrated IgM positivity for PB19 and convalescent sampling on day 16 of the admission demonstrated IgM and IgG seroconversion. The patient was discharged on day 24 following admission with a Hb of 7.5g/dl (baseline).

**Conclusions:**
Hyperhaemolysis is a well documented complication of red cell transfusion and typically occurs in the context of an acute or recent sickle cell crisis and consequent pro-inflammatory state. This case demonstrates that hyperhaemolysis can be a challenging entity to recognise and manage, especially when presentations occur in the context of another diagnostic entity causing bone marrow suppression, namely parvovirus B19.
PB19 is increasingly recognised worldwide as a threat to patients with chronic haemolytic disorders such as sickle cell disease due to increasing community transmission and the lack of exposure to the virus in childhood in some countries with low incidence of the virus. As is evident from our case report, serology for PB19 can prove unhelpful in the early phase of the condition as seroconversion of IgM has not yet occurred (this usually occurs 7-10 days following acquisition of the infection).

## A COMPLEX CASE OF MULTIFACTORIAL ANAEMIA

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A 54 year old woman presented to University Hospital Limerick with severe fatigue and pallor. Her haemoglobin (Hb) on presentation was 2.3g/dL, reticulocyte count $4x10^9$/l, LDH 2142U/L with a concurrent acute liver injury with ALT 2522 U/L, bilirubin 54µmol/L. A blood film demonstrated profound anaemia with rare polychromatic cells. This was on a background of recent mild SARS-CoV-2 infection three weeks prior and mild iron deficiency anaemia treated six months prior to presentation.

The initial crossmatch sample demonstrated a cold-reactive autoantibody. This required five adsorptions as strongly Direct Antiglobulin Test (DAT) + (4+ IgG, 4+ Complement, 3+ control). The patient had never previously received a blood transfusion but had two pregnancies. She was admitted to the intensive care unit for transfusion of cross matched warmed red cells. The aetiology of the liver insult was deemed to be viral or ischaemic. This settled quickly and her haemoglobin incremented to 7.9 g/dL post transfusion. During this admission, the patient received eight units of red blood cells, two of which were $Jk^a$+.

A bone marrow examination demonstrated a hypercellular sample with decreased erythropoiesis with evidence of dysplasia and an infiltrate of 27% mature lymphocytes, immunophenotypically in keeping with marginal zone lymphoma. CT mesenteric angiogram showed borderline hepatomegaly, mild splenomegaly and abdominopelvic/inguinal lymphadenopathy with max diameter 20 mm.

The virology screen revealed parvovirus B19 IgM and IgG were strongly positive with DNA 271 IU/ml. Her follow up FBC one week post discharge demonstrated Hb of 7.7g/dL. The patient continued oral folic acid and iron supplementation. The working hypothesis was of red cell aplasia secondary to acute parvovirus infection on the background of bone marrow involvement with marginal zone lymphoma.

The patient presented six days later with jaundice, pallor and worsening fatigue. Her haemoglobin was 2.5g/dL, raised reticulocyte count of 60 $x10^9$/l, bilirubin 83 µmol/L, LDH 1528U/L and fever of 38.5degrees with markedly improved liver transaminases. A blood film demonstrated nucleated red blood cells, spherocytes and polychromasia. The working diagnosis was of an autoimmune haemolytic anaemia secondary to bone marrow involvement for which the patient commenced oral prednisolone.

A repeat crossmatch sample detected an anti- $Jk^a$+ alloantibody in addition to the autoantibody seen on presentation. In light of this recent $Jk^a$+ positive transfusion, a delayed haemolytic transfusion reaction (DHTR) could account for this patient's second presentation. On tapering prednisolone, Hb level decreased by 1g/dl with increasing reticulocyte count. Therefore, oral prednisolone 1mg/kg has been continued with Hb maintained at 8.3g/dL.

This case highlights a challenging diagnosis and need to undertake comprehensive investigations at presentation. Parvovirus B19 is a notorious cause of red cell aplasia in hereditary anaemias (1). This correlation has not been well established in low grade lymphoma. This case also demonstrates the importance of the Kidd blood group system in transfusion medicine due to its association with delayed transfusion reactions and fluctuant antibody titres (2). Our patient's case highlights the importance of communication between transfusion specialists and clinical haematologists in the management of complex anaemia.

## TREATMENT OF A STAT5B::RARα POSITIVE CASE OF APL IN A PATIENT NOT ELIGIBLE FOR INTENSIVE CHEMOTHERAPY

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Acute promyelocytic leukaemia (APL) with a STAT5b::RARα gene fusion is an extremely rare subtype of APL characterised by resistance to conventional therapies and poor prognosis. A sixty-year-old male presented to the local accident and emergency department feeling unwell with shortness of breath, icteric sclera and jaundice. Initial FBC showed pancytopenia with the blood film revealing a leucoerythroblastic picture. A bone marrow aspirate and trephine was performed which was hypercellular, almost entirely replaced with medium/large blasts/promyelocytes with variable amounts of cytoplasm containing fine azurophilic granules, some with budded cytoplasm and many with a folded nucleus. These morphologic features raised suspicion of APL. Immunophenotyping was performed and was in keeping with APL. The patient was commenced on ATRA 45 mg/m2, awaiting urgent FISH and real time quantitative PCR (RQ-PCR). The patient tested negative for a PML::RARα rearrangement by both FISH & RQ-PCR. Subsequent FISH analysis, this time using a Vysis LSI RARα dual colour break-apart probe, displayed one intact copy of RARα along with two copies of the centromeric portion of the RARα probe. These copies were confirmed by metaphase FISH to be located on the der(17). Based on karyotyping and FISH analysis the results therefore represented a variant RARα rearrangement with an unknown cryptic partner gene. NGS uncovered a cryptic inv(17) or del(17) STAT5b::RARα variant. This was confirmed by sanger sequencing. Therefore, based on these genomic findings, the favoured classification according to the 2022 WHO classification is – “APL with a variant RARα translocation”.

The patient was insensitive to ATO and ATRA and due to extensive co-morbidities was not a candidate for intensive chemotherapy. Therefore, he was commenced on five cycles of LDAC, 20mg/m2 given subcutaneously once daily on days 1-10 of each 28 day beginning on cycle 1 day 1 and Ven 100mg from day 4 to day 28 orally with an azole after dose escalation from days 1-4. Morphological remission was achieved at this point, demonstrating a clear sensitivity to a LDAC/Ven regimen. However, STAT5b::RARα mutant transcripts were still detectable by molecular and flow MRD. Cycle 2 was well tolerated. However, venetoclax dosage was reduced to 14 days following prolonged cytopenias. Cytogenetic remission was achieved following this cycle. The patient proceeded with cycles three and four respectively with a delay in cycle five due to cytopenias and probable cellulitis. A subsequent bone marrow aspirate unfortunately revealed progressive disease morphologically. The patient was transferred to ICU with neutropenic sepsis. Unfortunately, the patient continued to deteriorate and died in ICU. This case highlights that whilst APL with variant RARα translocations are rare, they do pose significant challenges diagnostically and in their clinical management. This case demonstrates the importance of using a combination of molecular techniques, including NGS, alongside morphology and immunophenotyping in cases of APL that appear negative by confirmatory testing. Secondly, our patient represents the first documented example of this rare disease that has been managed with and shown sensitivity to LDAC/Ven. This case demonstrates that although treatment options are limited for patients ineligible for intensive chemotherapy non-intensive options show increasing promise.

**Implementing Exercise Equipment on the Hematopoietic Stem Cell Transplant Unit – Exploring Patients Opinions and Experiences.**

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**Background**

The benefits of exercise in patients undergoing hematopoietic stem cell transplants (HSCT) is an ongoing area of research, with exercise proving to have a positive impact on patient length of stay and quality of life as well as common side effects of treatment. Common barriers to exercise during transplant include nausea and decreased willpower while facilitators include easy and simple exercises, with support from exercise specialists.
The aim of this project was to determine the effects of exercise equipment to encourage physical activity during an inpatient admission for HSCT. To determine the level of frequency that patients used the equipment to exercise and to determine patient experience and recommendations to our service.

**Methods**

To encourage and promote physical activity during an inpatient admission for HSCT, individual activity boxes and exercise bikes were introduced to our transplant unit. Included in the boxes were weights, resistance bands and platelet guided exercise booklets.
Between the months of March and May 2024, all patients admitted to the transplant unit were seen by a physiotherapist, given an introduction and demonstration of the activity box and exercise bikes on the unit. Each patient was subsequently given a questionnaire to complete which explored their opinions and experience of exercise and use of the activity boxes. This questionnaire was designed by both senior and rotational physiotherapy staff working in haematology, and reviewed by a Consultant Haematologist. Questionnaires were then completed anonymously by patients and given to nursing staff for collection with subsequent collection of results by physiotherapy staff.

**Results**

Eighteen questionnaires were completed, 83.3% (n=15) of these found the activity boxes useful. Of those who did not find them useful (n=3), two reported low platelets being the main barrier to exercise. Fifty percent (n=9) reported they used the activity boxes daily.
Fifteen participants responded to the section relating to the effect of the boxes on their confidence to exercise. Of the 60% (n=9) who felt they had a positive impact, one participant reported the boxes gave clear instructions as to what they should be doing, while two others reported the boxes led to a higher level of motivation to exercise. Of those who reported the boxes did not increase their confidence, one person reported that they were affected by general feelings of sickness which impacted their ability to exercise.
Six participants suggested other pieces of equipment that they would have found useful, including a treadmill (n=4), a mat (n=1) and a step (n=1). Sixteen patients surveyed were seen by physiotherapy on the same admission. One patient who was not seen by physiotherapy reported feeling unable to exercise during that admission due to low platelets.

**Conclusion**

During an inpatient admission for HSCT, more than 80% of patients reported positive experiences with activity boxes. Barriers identified were low platelet counts and low confidence levels towards exercising. The results of this survey will guide further changes and improvements to the activity boxes and guide plans for funding for further equipment.

**Benefits of an ANP Red flag Clinic**

Louise Gribben Haematology Advanced nurse Practioner SHSCT

**Background**

The NI Cancer Control Programme was published in November 2006. Within the Strategy there is a commitment to ensuring the timeliness of referral, diagnosis and treatment for suspected cancer patients.
The commissioning plan Direction set by the Department of Health dictates that 95% of patients urgently referred by a GP, as a suspected cancer, should begin their first definitive treatment within a maximum of 62 days. (Cancer Access Standards 2008)

**Recognising and identifying current challenges within the haematology service in SHSCT**

As a result of the persistent shortage within the consultant workforce I SHSCT ( 2.8 WTE where 5.0 WTE is required) Traditional consultant red flag review of haematology referrals, resulted in long unacceptable waiting times for patients referred into the service. With suspected or confirmed cancers. Some patients up to 137 days waiting!

**METHODOLOGY**

Scoping exercise carried out in 2020 as to what category of patients were creating this unacceptable waiting list in SHSCT and if and how the ANP could use their expertise and knowledge, in the evolving ANP role, to challenge existing practices and procedures and discuss potential alternatives to delivery of services that would improve the health care for our Haematology population. The initial patient group included patients with CLL and MGUS and drenching night sweats requiring investigation. The success of the red flag clinic within 2 years then led to expanding this service to include patients with MPN's, lymphomas and myeloma. Additional to initial review, the ANP autonomously schedules and requests full work up , ordering of investigations, delivery of results and diagnosis, presents cases at regional MDM and discusses the plan of care with patient.

**OVERALL AIM**

Diagnose, inform and support cancer/Haematology patients in a safe and timely manner.
Improve mental and emotional well-being of patients, by delivery of specialist intervention and support.
Achieve DOH cancer waiting time direction targets.
Reduce burden and demand on specialist consultant clinics.
Use/maximize existing resources by upskilling the Haematology ANP
Implement a new service design where new patients with a Haematological diagnosis can be seen by another health professional on their first appointment.

**2023 results:** Jan -Dec 2023 the **ANP** red flag clinic reviewed 203 patients for their first haematology appointment when referred with suspect cancer.

**Conclusion**

The development of this ANP led clinic has improved the care pathway, while providing safe, appropriate and timely review of red flag referrals by the most appropriate health care professional reflecting the recommendations of many strategic drivers such as;
Transforming Your Care (2014),
Quality 2020 leadership strategy: Delivering Improvement (2014
The health and well-being; Delivering Together 2026
Cancer Access Standards (2008)

**Community Haematology Oral Anticancer Medication clinic- creating more value with fewer resources**
Kelly, M. Midland Regional Tullamore, Co. Offaly.

**Background**
Analysis of Haematology Oral Anticancer Medications (OAM) patient cohort and existing management approach revealed opportunities for efficiencies and improvement in the service. Factors including changing demographics, with a growing population of over 65s, and associated longevity due to increasing medical treatments necessitated the initiative. Challenges included meeting increasing demands and safely managing patients with finite resources in the appropriate setting.

**Need**
To move from a hospital based care model to an integrated nurse led community clinic.

**Aims /benefits**
- Patient centric service
- Aligned with key stakeholders' objectives
- Specialization of existing resources
- Better use of resources and budget
- More efficient processes, reduced waiting times

**Methodology**
Change management methodologies, provided a series of goalposts which guided and underpinned the change process. Clinic accommodation was obtained and supporting governance documents and requirements incorporated.

**Outcomes/Results**
The clinic has been implemented on a weekly basis with a view to expansion following review. Key performance indicators (KPI) have been developed to measure outcomes.
Efficiencies have increased with appropriate use of staff, specialization of resources and accommodation, elimination of unnecessary steps in reviewing patients, reduction in waiting times and waiting lists, and increased patient safety and satisfaction. Staff cost saving of 54% are achieved, with consultants released to focus on more complex patients.

**Implications for Practice & Conclusion**
The use of existing resources, including staff and accommodation,
resulted in efficiency and cost savings. Challenges including resistance and conflict occurred highlighting the need for greater focus on the impact of change on individuals and management of crisis points in the change journey.
**Recommendations**

• Budget costings and business case proposal and submission for pharmacy support.

• Greater involvement of nursing staff in the directorate strategic plan.

• Need greater spread of change locally and nationally through communication e.g. newsletter,
presentations, written publication and media clips in collaborations with communications and
research teams.

• Monthly team meetings and quarterly directorate report

• Patient and staff satisfaction survey with service.

• Dissemination of learnings from this change to assist the planning of future projects

**ANP led Pre-assessment of Patients on Daraumumab-A quality Improvement Project**

Lisa Lyons, Michaela Cunning & Claire Stewart

**Background:** Daratumumab, a CD38-directed monoclonal antibody used to treat multiple myeloma (MM), is licenced in both the front line and relapsed setting. In Northern Ireland approximately 179 people are diagnosed with myeloma annually (Cancer Research UK, 2024). Many of these patients will receive a Daratumumab containing regimen which requires frequent subcutaneous injections during the initial treatment phase, moving to monthly injections until relapse or toxicity. Patient questionnaires revealed that patients on Daratumumab spent an average of 3.5 hours in the department on the day of their assessment and treatment. This means that a patient starting on Daratumumab could spend 77 hours waiting in the department during their first year of treatment, reducing to 42 hours each year thereafter. Given that 50% of patients remain on Daratumumab after five years therefore, steps to improve the patient experience became a priority for the haematology team. To address this the haematology ANP proposed changing the model of review from consultant led (same day assessment and treatment) to an ANP led model, with assessment and treatment on separate days, with treatment scheduled to a pre agreed time slot. In a bid to further reduce time spent in the department the ANP, in collaboration with pharmacy colleagues, implemented changes to the premedication schedule for Daratumumab.

**Objectives:**

- Improve patient experience by reducing waiting times.
- Decrease chair time in the chemotherapy day unit.
- Free up slots at consultant led clinic

**Methods:**

A Plan-Do-Study-Act (PDSA) methodology was employed for this quality improvement project. Under the new ANP-led pathway, patients were provided with dexamethasone for self-administration 1-3 hours prior to their scheduled appointment. The premedication regimen was streamlined by discontinuing chlorphenamine and paracetamol, which were previously administered 1 hour before treatment (Kumar et al (2022). The ANP conducted pre-assessments, ordered treatment, and scheduled specific appointment times, allowing for a more efficient administration of Daratumumab upon patient arrival.

Results:

Transitioning to ANP-led reviews has markedly improved patient experience by reducing patient waiting times. The initiative has been highly evaluated, and patients now report an average visit duration of 30 minutes. The elimination of chlorphenamine and paracetamol has not only streamlined the premedication process but also reduced pharmacy costs and nursing workload. Furthermore, removing sedating antihistamines has lessened the risk of side effects such as drowsiness and confusion in older adults. The ANP-led model has been positively received, giving patients greater autonomy over their medication schedule as well as freeing capacity at the consultant clinics.

**Conclusions and Next Steps:**

The ANP-led pre-assessment and revised premedication regimen have significantly enhanced the efficiency of Daratumumab administration, benefiting both patients and staff. As many patients will continue Daratumumab therapy long-term, exploring patient or caregiver administration of the drug at home could further reduce travel burdens and improve patient autonomy. Expanding self-administration practices, as established in other therapeutic areas like rheumatoid arthritis and multiple sclerosis, may offer additional benefits in terms of convenience and resource optimisation.

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**The Development of a National Creative Arts Therapy Service for Children, Adolescents & Young Adults(CAYA) with or in Survivorship of Cancer and their Siblings.**

R Hayes[1], A Nolan[1, 2], **C McCall[1]**
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**Introduction:** 180 Adolescents and Young Adults (AYA) receive a cancer diagnosis each year in Ireland. Significant psychosocial risks including anxiety, depression, adjustment challenges, post- traumatic stress symptoms, family difficulties and social isolation exist (Steele et al., 2015). Creative Arts Therapies (CATs) is a collective term used for art therapy (AT), dramatherapy (DT) and music therapy (MT). They are evidenced-based professions that provide client-led, psychosocial support by utilising creativity as an alternative and additional means of communication. CATs effectively support symptom distress associated with cancer (pain perception, nausea, fear and anxiety). CAT's provide a supportive outlet that fosters healthy relationships, sense of identity, self-esteem and support social, emotional and overall development negatively impacted by regular hospitalisations, cancer diagnosis or treatment. For AYA effected by cancer the CATs have been shown to be an effective form of psycho-social support (Raybin et, al. 2023; Purrezaian et. al. 2020; Daveson 2001).

**Objectives:** To establish and deliver a National Creative Arts Therapy Service that provides accessible and inclusive therapies for Children, Adolescents & Young Adults (CAYA) affected by Cancer and evaluate its impact.

**Methods:** The Authors engaged in;
i. A literature review of available research regarding CAYA cancer, survivorship and creative arts therapies.
ii. A national mapping of current creative arts therapy support provided in cancer support-centres nationwide.
iii. PPI via engagement of the Young People's Advisory Group (YPAG) to help shape the service offering.
iv. Engagement with the Irish Association of the Creative Arts Therapists to ensure standardisation of qualification for all therapists.
v. Establishing referral pathways internally and externally via hospital multi-disciplinary teams and client's self-referrals.
vi: Developed and distributed feedback surveys for families and therapists. These results were collated and examined to inform the service offering.

**Results:** Our preliminary findings indicate a lack of affordable, community-based psychosocial support for CAYA with or in survivorship of cancer and their siblings. A national network of 70 professional CATs were recruited; AT (50%) MT (31%), DT (19%). Since November 2023 we have received referrals for 112 families. Child with cancer (97), siblings (71), adolescence and young adults (16) located across the country. 114 sessions have been completed since commencing November 2023. Referrals are pre-assessed via phone by a senior creative arts therapist to identify the most appropriate form of CAT. Following completion of the therapy cycle the client and therapist are provided with an evaluation survey. Results are collated establishing the impact on future developments of the service.

**Conclusion:** This service aligns with the Irish Psycho-oncology Model of Care (NCCP, 2023). It provides accessible community psycho-social support to young people affected by cancer.

## Lessons learned from the development of a nursing education pathway for haematopoietic stem cell transplant (HSCT) in the national bone marrow transplant unit in St James Hospital, Dublin.

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**Introduction/Background:** Nursing knowledge is often transferred by expert to novice via preceptorship model. Busy clinical environments, increasing numbers of new nurses and the availability of expert nurses can present challenges. Patients undergoing HSCT have complex nursing care needs and require specific education and training.
As no national HSCT education pathways were available, this action research project developed a bespoke educational pathway for nurses that was designed to comply with JACIE 8th edition standards. The curriculum incorporated clinical knowledge from national and international experts in delivering HSCT, was evidence-based and adhered to national and international policy.
This paper presents an overview of the final three step pathway (self-directed, clinical simulation and clinical practice) and the lessons learned from this research. It is hoped that these lessons would be useful for people hoping to develop bespoke education pathways for nurses.

**Materials and methods:** An action research methodology was adopted, development was iterative and incorporated previously used processes (Byrne 2022, Gillespie et al. 2022). The co-creation team consisted of domain specialists (nursing and medical), nursing education, quality and technology specialists from St James Hospital and School of Nursing and Midwifery, Trinity College Dublin. The team maintained a research document that was reviewed at the end of the project and lessons learned extracted and reviewed by the co-creation team.

**Results:** The final pathway has three steps - self-directed, clinical simulation and clinical practice. To date 5 learners have completed the pathway with a further 48 learners enrolled, and feedback has been resoundingly positive. The main lessons learned are presented as 5 T's:
**Topic:** HSCT is a complex topic, and the project proved to be much bigger than initially anticipated. We found that breaking the topic down into smaller components, for example, separating out the allogeneic from autologous HSCT helps learners but also helped the development process.
**Team:** The co-creation team should include clinical expertise, education, quality and technology. Where this is not possible, the team should be able to access this expertise as required.
**Testing:** Evaluation of pathway is important and rather than a 'big bang' approach, we suggest it is a continuous process.
**Types:** A range of educational materials and delivery methods was incorporated to facilitate different learning styles, for example, self-directed and simulated-based learning.
**Time:** There is a considerable time commitment by all stakeholders and the research team found it useful to share the workload where possible.

**Conclusion:** The project was based on a need to provide evidenced based education in an evolving nursing landscape. The underpinning standards were JACIE 8th edition. The project met these needs. The lessons learned are presented as 5 T's – topic, team, testing, types and time. It is hoped that these lessons would be useful for people hoping to develop bespoke education pathways for nurses. Further research is being conducted to evaluate this list of lessons learned.

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**PVD-PACE regimen as salvage therapy for extramedullary disease in multiple myeloma: a case report**

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**Introduction**

Myeloma treatments are evolving fast but patients presenting with extramedullary disease seem to have a worse prognosis. The relapse/refractory setting is a particularly challenging situation for clinicians as the outcomes with immunotherapy based treatments such as bispecific antibodies or CAR-Ts have been disappointing. The factors predisposing to develop an aggressive extramedullary disease are being investigated, but one hypothesis is that new clones are emerging while patients are on maintenance therapy.

**Clinical Case**

A 57 year-old woman presented in June 2021 with abdominal symptoms and nausea. Initial PET scan showed an avid metabolic large tissue mass (7cm) adjacent to the gastric pylorus, and a second FDG-avid focus in porta-caval region. The tumour biopsy confirmed a malignant plasmocytoid proliferation with Ki67 40-50%, positivity of cells for CD138, CD38, kappa light chains (KLC). The bone marrow examination did not show plasma cell infiltration. FISH analysis showed no evidence of deletion of TP53, CDKN2C, or rearrangement of the IGH locus, and the normal diploid complement of CKSB1 (1q21) was detected. KLC at diagnosis were 31.5 mg/L with ratio kappa/lambda 2.8 and there was a faint Ig A kappa monoclonal band.

With the diagnosis of extramedullary peri-gastric plasmacytoma, the patient was treated with 4 cycles of lenalidomide-velcade-dexamethasone (RVD) followed by ASCT performed in November with melphalan conditioning. The PET scan in February 2022 confirmed a complete metabolic response, the KLC were 23 mg/L after the transplant. She went on maintenance therapy with lenalidomide initially at 15 mg then 10 mg since June 2023 because of haematologic toxicity.

In december 2023 the KLC started rising and the patient begun to develop gastric symptoms and nausea. A repeat PET scan in January 2024 showed a large extraosseous plasmacytoma in right upper quadrant of abdomen adjacent to gastric antrum, also an FDG avid plasmacytoma in left frontal skull and right distal femur. A new biopsy of the mass confirmed the relapse of the disease. The bone marrow did not show infiltration of plasma cells and FISH analysis failed.

The case was discussed in MDM and an intensive approach with pomalidomide-velcade-dexamethasone (PVD) – PACE regimen with pomalidomide 2 mg 7 days per cycle was decided. Radiotherapy was not considered due to high volume and risk of bowel toxicity. Unfortunately, the PET scan after 2$^{nd}$ cycle showed increase in size of the plasmacytoma, increase of metabolically active lytic lesions in the right medial femoral condyle and left frontal skull.

After the treatment, KLC were 389 mg/L with a ratio kappa/lambda> 100. The patient is currently receiving daratumumab-carfilzomib-dexamethasone and depending on the response could be eventually candidate for Car-T cell therapy, if available.

**Conclusion**

This is the case of an Ig A kappa multiple myeloma in a young patient with a large abdominal extramedullary plasmacytoma relapsing one year after transplant and refractory to PVD- PACE regimen. Unfortunately we do not have data about cytogenetics but the aggressive nature of the disease is consistent with high risk myeloma. Prospective studies are required to define best therapeutic approach for patients with extramedullary disease at presentation and in the relapse setting.

**Extramedullary hematopoesis presenting as a subpleural mass in a patient with homozygous sicke-cell disease.**

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**Introduction:**

A 47 year-old African male with homozygous sicke cell disease diagnosed at age 4 presented with severe bilateral hip pain and chest oppression. Oxygen saturation was 88% on room air, he was afebrile. The Hb was 6,5 g/dL (previous was 7,5), CRP was normal and D dimer was 4114 ng/mL

A CT pulmonary angiogram showed a subpleural soft tissue mass of the right lower lobe, in the paravertebral area. There was no evidence of pulmonary embolism.

Images were discussed in a multidisciplinary team and radiologist confirmed high suspicion of focal extramedullary hematopoesis.

The patient was managed with hyperhydration and opioid analgesia initially for pain control. Evolution was rapidly favourable. Haematinics showed a mild iron deficiency so the patient received IV iron supplements and a single EPO injection.

One month later the patient was clinically stable and Hb rate was 9,1 g/dL.

**Discussion:**

Sicke cell disease is a inherited blood disorder that affects haemoglobin and causes red cells to have a “crescent moon” shape. Patients have chronic anemia and can develop vaso- occlusive crisis, bone pain, strokes and have an impaired quality of life.

Extramedullary haematopoesis has been described in sicke cell patients as a mechanism to try and synthetize more Haemoglobin. It can also be seen in other haematological conditions, mainly as a compensatory alternative for ineffective haematopoiesis of the bone marrow. It can affect visceral organs like the liver, spleen, lymph nodes but in patients with haemoglobinopathies the thorax is the most reported location.

The CT typically shows a lobulated mass with soft tissue attenuation. Biopsy of those lesions is usually not recommended as masses are usually hypervascular

This case is to illustrate that any mass with soft tissue attenuation in the paravertebral area should raise possibility of extramedullary haematopoesis in the context of sicke cell disease.

## A CASE OF HODGKIN'S LYMPHOMA IN PREGNANCY: A UNIQUE CLINICAL COMPLEXITY.

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### Introduction

Hodgkin's lymphoma (HL) is the most common haematological malignancy in pregnancy, reported in approximately 1:1000-6000 pregnancies. This accounts for up to 3% of all HL cases[1]. HL in pregnancy represents a unique clinical complexity requiring the careful consideration of multi-disciplinary specialities. The challenge is balancing the delivery of optimal curative therapy to the mother while minimising the risks to her pregnancy.

### Case Report

A 28 year-old female was referred with a five month history of a neck lump. Assessment revealed a 2cm left supraclavicular node without B symptoms. At presentation she had a positive pregnancy test. Her past medical history was significant only for pubic symphysis in a prior pregnancy.
Histology demonstrated Reed-Sternberg cells with surrounding small lymphocytes, histiocytes and eosinophils. They positively expressed CD15, CD30, MUM1 with weak expression of PAX5, consistent with classical Hodgkin's Lymphoma (HL). Bone marrow examination showed no lymphomatous involvement. Whole-body-MRI revealed lymphadenopathy above and below the diaphragm, consistent with Stage IIIA HL. The Hasenclever International Prognostic Score was 1.
She was counselled on the diagnosis and the use of chemotherapy in pregnancy. Her pregnancy was much sought after. She elected to continue with the pregnancy and was closely followed by obstetrics. ABVD (Doxorubicin, Bleomycin, Vinblastine, Dacarbazine) chemotherapy was deferred until the second trimester. She received prophylactic enoxaparin. Whole-body-MRI after two cycles demonstrated interval response to treatment. The 20 week gestational scan showed normal growth and organogenesis. She completed four further cycles of AVD with interval scans showing growth appropriate for gestational age. She successfully delivered her healthy female baby after 39 weeks. End of treatment PET-CT postpartum demonstrated complete metabolic remission and she remains well after five months of follow-up.

### Discussion

HL in pregnancy represents a unique complexity that raises clinical and ethical dilemmas. The goal is to deliver curative therapy to the mother, while trying to maintain a healthy pregnancy. When HL is diagnosed in pregnancy it is almost always possible to control the lymphoma and allow the pregnancy to continue to full term. PET-CT is avoided for staging in pregnancy to avoid the risks of fetal irradiation[2,3]. Whole-body-MRI is the preferred modality. Generally, chemotherapy is avoided in the first trimester due to risks of fetal malformation during this period of organogenesis[2,3,4,5]. ABVD is considered the standard of care in pregnancy with survival outcomes comparable to non-pregnant cases[6,7]. The evidence is limited to retrospective series. Some have reported increased rates of preterm labour and premature rupture of membranes with antenatal chemotherapy[6].
Regimens such as escalated-BEACOPP or those containing brentuximab-vedotin are not recommended in pregnancy[2].It is optimal to delay delivery until at least 36 weeks, where possible, avoiding the complications of prematurity[3,4]. Long term follow-up studies of children haven't demonstrated an increased risk of haematological malignancy, cardiac or developmental toxicity[8,9].

## The Detection of Potential Germline Variants through Somatic Sequencing

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### Introduciton

The DEAD-box RNA helicase 41 (DDX41) is a member of the DEAD box protein family, which are involved in cellular processes such as RNA splicing and translation initiation. DDX41 mutations are responsible for approx. 80% of germline myeloid neoplasms. DDX41 mutations are not fully penetrant and a secondary mutation is often needed for transformation into a high grade myeloid neoplasm. Secondary somatic DDX41 mutations are seen in almost 80% of MN cases with a germline DDX41 mutation (gmDDX41). Patients with gmDDX41 often respond poorly to haematopoietic stem cell transplants (HSCT).

Patients with germline DDX41 mutations display a distinct pattern of physiological and cytological markers. There is a higher penetrance in males with a male: female ratio of 3:1. Bone marrow analysis tends to show hypocellularity and evidence of erythroid dysplasia. A normal karyotype is present in 70-80% of cases and a family history of malignancies (not always haematological) are often seen. Late onset of disease is a feature of gmDDX41 and so the association with potential germline origin is not always made in these cases.

A 68y/o man presented at ED with a short history of increasing fatigue and shortness of breath. Full blood count at presentation showed haemoglobin 59 g/l, MCV 119 fl, white cell count 2 x 109/l, platelets 36 x 109/l and neutrophils 0.37 x 109/l. Bone marrow trephine features were in keeping with that of an acute myeloid leukaemia (AML).

### Materials and Methods

FLT3/NPM1 fragment analysis, myeloid NGS panel, flow cytometry and karyotyping were all performed on the initial diagnostic sample. Secondary Sanger sequencing was performed on a bone marrow sample following 1$^{st}$ remission using primers designed for the specific DDX41 mutation detected by NGS.

### Results

Initial results from this patient showed a normal karyotype and no mutations in NPM1 and FLT3. Flow cytometry was in keeping with a CD33+ AML. The bone marrow trephine showed hypocellularity and rouleaux. Family history questioning revealed his brother is currently being treated for lung adenocarcinoma.

The NGS results showed 4 pathogenic/likely pathogenic variants in the DDX41 c.415_418dup p.(Asp140GlyfsTer2) VAF 38%, DDX41 c.1574G>A p.(Arg525His) VAF 6%, PHF6 c.86_87insC p.(Gln30ThrfsTer6) 5% and JAK2 c.1849G>T p.(Val617Phe) 4%.

Sanger sequencing results of the bone marrow sample taken post remission showed the presence of the DDX41 c.415_418dup p.(Asp140GlyfsTer2) mutation.

### Conclusions

Based on the Sanger sequencing results is was determined this patient had a gmDDX41 mutation. This patient showed all the classical indications of a germline DDX41 variant. His marrow was hypocellular and showed evidence of erythroid dysplasia. He had 2 hits of DDX41 – one germline and one somatic. At 68 he is within range of median presentation of AML although this age is significantly older than age of onset of other predisposed malignancies. The detection of the gmDDX41 changed this patient's treatment plan from potential HSCT to an intensive chemotherapy. This man has and his family have also been sent to the regional genetics service for counselling. This case highlights the importance of detecting potential germline variants during somatic testing.

# THE ROLE OF CONVENTIONAL SALVAGE CHEMOTHERAPY IN TRIPLE CLASS RELAPSED/REFRACTORY (R/R) MULTIPLE MYELOMA

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## Introduction

Triple class R/R myeloma is defined as refractoriness to an IMiD, a proteasome inhibitor and an anti-CD38 antibody. Extramedullary disease is associated with an adverse prognosis and tends to be triple class refractory. Thus, conventional salvage chemotherapy agents are used in rapid tumour debulking or as a bridge to transplant. One such regimen is VTP-PACE.

## Clinical Case

We describe the case of a 58 year old gentleman diagnosed with IgG Kappa Multiple Myeloma in late 2020. He presented with renal failure, hypercalcaemia and an extramedullary plasmacytoma at the skull base causing a partial cranial nerve palsy. He was R-ISS stage III with a b2m of 25.48. FISH studies were incomplete but did show a 1p deletion. He received induction therapy with RVD, with local radiotherapy to his skull base, followed by autologous stem cell transplant. The patient achieved complete remission and commenced maintenance Lenalidomide. In July 2023, he represented with multiple intramuscular plasmacytomas within the thorax and pelvis, requiring further radiotherapy. His monoclonal band was 5g/L with FKLC >100, and he received CyBorD-Dara for 3 cycles. After the third cycle, he again presented with new extramedullary disease in the right paraspinal region T8-L1. Unfortunately, access to Bispecifics and CAR-T was unavailable at the time of his progression. Given the aggressive behaviour of his disease, he was treated with salvage chemotherapy in the form of VTP-PACE, followed by second autologous SCT in January 2024. The patient is currently in stringent CR with normalisation of his serum immunoglobulin and light chains, and continues on dual maintenance with pomalidomide and bortezomib.

## Conclusion

Despite the continuing development of novel anti-myeloma agents, there remains a subset of patients with aggressive R/R disease who may benefit from conventional salvage chemotherapy for induction remission pre transplant.

## A CASE OF MARGINAL ZONE LYMPHOMA PRESENTING WITH HYPERLEUKOCYTOSIS AND ASSOCIATED PAPILLOEDEMA AND VISUAL SYMPTOMS

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**Case:**

We report the case of a 56-year-old woman who presented with a 4-month history of non-remitting visual blurring. Ophthalmological assessment demonstrated bilateral papilloedema which prompted medical workup. A full blood count demonstrated a profound leukocytosis (WCC 175), predominantly lymphocytosis. Her blood film displayed large mature lymphoid cells with prominent nucleoli. A staging CT demonstrated mild splenomegaly without lymphadenopathy. An MRI of the brain and cerebrospinal fluid analysis* were unremarkable.
Bone marrow aspirate was notable for small to medium-sized lymphocytes with cytoplasmic blebbing accounting for >80% of the total nucleated cell count. Trephine showed dense lymphocytic infiltrates which stained positive for CD20 and weakly for CD5. Cyclin D1 and SOX-11 were negative. Molecular studies for t(11:14), MYD88, TP53 and del17p were negative. Cytogenetics demonstrated C-Myc positivity. Flow cytometry demonstrated a clonal population of B-Cells which were CD5 positive, CD10 and CD23 negative, lambda restricted, with dim expression of CD200 and FMC7. Her case was discussed at haematology/pathology multidisciplinary meeting and was felt to represent marginal zone lymphoma.
She was treated with 6x cycles of R-CHOP as well as 2 doses of high-dose methotrexate. Resolution of visual symptoms was achieved with cytoreduction. An interim PET was Deaville 1 showing resolution of splenomegaly, and an end-of-treatment bone marrow biopsy showed no residual disease. Following completion of initial therapy, the patient was commenced on maintenance rituximab.
*CSF analysis not performed until WCC normalised

**Discussion:**

Marginal zone lymphoma (MZL) is typically an indolent lymphoma categorised into splenic marginal zone lymphoma (SMZL), nodal marginal zone lymphoma (NMZL), and extranodal marginal zone lymphoma (EMZL). It is a rare subtype of non-Hodgkin's lymphoma, ~3% of all diagnosed lymphoid malignancies.[1] SMZL is typically most associated with higher levels of circulating lymphocytes. MZL is frequently CD5 negative though this can be positive in approximately 20% of cases of SMZL. CD5 positivity has been associated with more profound lymphocytosis and marrow involvement.[2]
The major differential diagnosis in our case is atypical CLL. CLL has a pathognomonic immunophenotype and is characteristically strongly positive for CD5 and co-expresses CD19, CD20, and CD23.[3]
Our case represents an unusual presentation of a rare condition highlighting the need to consider a broad differential diagnosis in the evaluation of lymphocytosis and the importance of a collaborative effort between different diagnostic modalities.

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## PHLEGMONOUS GASTRITIS IN NEUTROPENIC SEPSIS: A CASE REPORT

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### Introduction

Phlegmonous gastritis (PG) is a rare suppurative bacterial infection of the gastric wall with a high mortality rate. We present a case of PG affecting a patient with MDS and neutropenic sepsis.

### Case Report

An 82 year old male presented acutely unwell with vomiting, fever and malaise. Past history included NK Cell LGL with subsequent MDS with increased blasts. He received nine cycles of azacitidine therapy. Neutrophil count was 0.8x109/L and CRP 170.7mg/L at presentation. He was treated for febrile neutropenia with piperacillin-tazobactam and gentamicin.

Extended septic screen was non-contributory. On day 8 of antibiotics he spiked a fever, following discussion with microbiology, treatment was switched to cefotaxime. Septic screen remained negative. With continued fevers, epigastric tenderness, emesis and rising CRP of 265mg/L, a CT Chest/Abdomen was performed. This demonstrated a markedly oedematous gastric wall, with mucosal hyper-enhancement in keeping with a severe gastritis. PPI was escalated to IV, with sucralfate, IV vancomycin and metronidazole commenced.

Despite three days of escalated therapy, he complained of worsening epigastric pain, emesis and obstipation. Examination revealed diffuse tenderness, with guarding. Bowel sounds were quiet and muffled. Repeat CT abdomen was performed. The stomach wall had become more grossly oedematous and inflamed, having worsened in the short interval. Due to progression, radiological features and following discussion with gastroenterology and microbiology, a diagnosis of PG with acute infection in the setting of neutropenic sepsis was made. Treatment escalation consisted of PPI infusion, IV ciprofloxacin with continued vancomycin and metronidazole. Despite this, persistent fevers continued with CRP at 242mg/L, vancomycin was switched to IV linezolid. After 5 days, a follow-up CT showed near complete resolution of the oedema.Our patient was subsequently discharged.

### Discussion

PG is a rare entity with 1 case per year over the last century. Global mortality rates are reported as wide ranges from 26% to 64%. The commonest organism in PG is Streptococcus, followed by Enterococcus and Staphylococcus with the former accounting for 70% of cases. We were unable to detect the causative pathogen in this case. Endoscopic findings are nonspecific but include an erythematous and oedematous mucosa/gastric folds, ulcer with slough, and mucous-pus adhesion. Gastroscopy with biopsy was not performed in this case as the clinical course, symptoms and CT conveyed significant data to conclude PG. CT findings can include gastric wall thickening, low signal intensity areas suggesting abscess, and accumulation of gas. A review of the literature between 2013 and 2023 identifies only seven cases of PG in haematology/oncology patients in the context of neutropenia. Conservative management with prompt initiation of antibiotics is the treatment of choice.

### Conclusion

We reported a case of PG in a patient with neutropenic sepsis. Conservative management with prompt initiation of antibiotics is the treatment of choice. Given the mortality rate of the condition, it should remain on the list of differential diagnosis in pyrexia of unknown origin in patients complaining of epigastric pain where routine septic screens have been non-contributory.

**A rare case of Tretinoin induced acute myocarditis complicating induction therapy for acute promyelocytic #leukaemia.**

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**Background-**

Tretinoin (all-trans retinoic acid/ATRA) is a critical component of induction therapy regimens for acute promyelocytic leukaemia (APL) but is associated with significant potential complications. We present a case of an unusual complication of ATRA therapy which has been rarely reported in the literature to date (1).

Clinical presentation-

A 20 year old man presented to our hospital in November 2022 with fever, easy bruising and fatigue. A blood film showed circulating promyelocytes and blasts with a white cell count of 21. Bone marrow aspirate and trephine biopsy with molecular studies subsequently confirmed PML-RARA+ acute promyelocytic leukaemia (APL). He was commenced on Tretinoin (ATRA) 45mg/$m^2$ daily and Idarubicin 12mg/$m^2$ day 1,3,5,7 – high risk APL therapy- and initially tolerated this well.

On day 27 of ATRA therapy, the patient reported sharp central chest pain, worse on exertion and relieved by sitting forward. Electrocardiogram (ECG) showed subtle dynamic changes with ST flattening and depression. A troponin leak of 5922ng/L, with NTproBNP of 1100ng/L, was detected. No arrhythmia was demonstrated on telemetry and no evidence of clinically decompensated heart failure was present. CT pulmonary angiogram was negative for pulmonary embolism. Echo showed subtle regional wall motion abnormalities and an ejection fraction of 45-50%. Cardiac MRI showed basal inferolateral wall segments with increased T1 mapping at 1,200 (baseline 1,760), increased T1 STIR and evidence of late GAD enhancement consistent with oedema. These findings were consistent with myocarditis. No other features of differentiation syndrome were present- no unexplained fever, weight gain, respiratory distress, interstitial pulmonary infiltrates and pleural or pericardial effusion. The patient was reviewed by Cardiology and diagnosed with isolated ATRA induced myocarditis.

ATRA was held and dexamethasone 10mg BD IV was commenced. Ramipril 3.75mg once daily, eplerenone 25mg once daily and bisoprolol 1.25mg once daily were added and he was monitored with telemetry and daily cardiac biomarkers. Dexamethasone was tapered over 7 days after 8 days of full dose therapy. Consolidation therapy with ATRA and arsenic trioxide was commenced as an inpatient on normalisation of ECG, ejection fraction, troponin and NT-proBNP 4 weeks after initial diagnosis of myocarditis. Cardiac medications were continued throughout therapy with ATRA and he was monitored closely with weekly ECG and cardiac biomarkers and monthly echo. Myocarditis did not recur and the patient achieved a molecularly confirmed remission at end of consolidation.

**Conclusion-**

This is a rare case of isolated ATRA induced myocarditis requiring interruption of ATRA therapy. This occurred at a later timepoint in therapy than previous reported cases (1). ATRA was reintroduced. With careful cardiac monitoring and close multidisciplinary management, treatment was tolerated without recurrence of myocarditis to completion of consolidation and achievement of remission. Despite severe cardiac toxicity in this case, reintroduction of ATRA was achievable and resulted in molecular remission.

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## A CASE OF AN ACQUIRED INHIBITOR TO CLOTTING FACTOR XII IN ASSOCIATION WITH COLD HAEMAGGLUTININ DISEASE (CHAD)

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Factor XII deficiency is a rare coagulation disorder which causes prolongation of the activated partial thromboplastin time (aPTT). This is an in-vitro phenomenon which, unlike other clotting factor deficiencies, does not correlate with an increased bleeding risk. Factor XII deficiency can be inherited in an autosomal recessive pattern due to mutations of the F12 gene located on the long arm of chromosome 5 (5q33-qter). It can also be acquired, with reported causes including nephrotic syndrome, cirrhosis, ARDS, DIC and shock. Deficiencies of various clotting factors due to the presence of inhibitor antibodies have been well reported in literature, however not previously in association with cold haemagglutinin disease (CHAD).

CHAD is a complement-dependent, classical pathway-mediated autoimmune disorder which is characterised by haemolytic anaemia with antibodies typically active between 3 to 4 degrees Celsius.
We report the case of a 49 year old woman diagnosed with CHAD who was managed with a combination of IV immunoglobulin, high dose steroids and Rituximab. Extensive work-up did not reveal an underlying cause.
The following year she was referred to the coagulation haematology service for investigation of a prolonged aPTT noted prior to elective abdominal surgery. The aPTT had been persistently prolonged (range 38.1-50.7 seconds) since her diagnosis of CHAD the previous year. Prior to this time, any previous aPTTs had been within the normal range. It was advised to postpone the elective procedure pending haemostatic workup. Of note, the patient had no significant bleed history, either before or after developing a prolonged aPTT, despite multiple major haemostatic challenges.

The aPTT did not correct with initial 50:50 mixing studies with normal plasma, suggesting an inhibitor effect. A lupus anticoagulant (LA) was expected to be the most likely explanation but this was negative when tested on two separate occasions (both using silica clotting time and delayed Russell viper venom time)
Clotting factor assays and a von Willebrand screen were then performed. Clotting factors VIII, IX and XI were all found to be within the normal ranges; as were von Willebrand Factor antigen and activity (vWF:RCo). Factor XII however was low at 0.34 iu/mL (0.52-1.64). This was deemed to be the likely cause of her prolonged aPTT and the decision was made to proceed with her surgery without haemostatic cover.
This patient had successful surgery with no bleeding intra- or post-operatively. She did however have a drop in her haemoglobin which deemed to have been due to haemolysis as opposed to bleeding. This stabilised after a repeat course of IVIg. She had an uneventful post-op recover with no major issues.

**CONCLUSION**
This case report demonstrates a previously unreported association: the simultaneous development of CHAD with an acquired inhibitor to clotting factor XII. There was no bleeding with major surgery in this case, suggesting that acquired Factor XII deficiency behaves like inherited Factor XII deficiency, and does not convey an increased bleeding risk.

## THERAPEUTIC PLASMA EXCHANGE IN LIVER DISEASE PATIENTS: INDICATIONS AND OUTCOME - A SINGLE-CENTRE EXPERIENCE (2022-2024)

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**Introduction:**
Acute liver failure (ALF) is characterised by an acute decline in liver function with associated coagulopathy, jaundice and encephalopathy. It can exhibit high mortality rates in the absence of liver transplantation with estimated mortality rate reaching up to 60%. The introduction of Liver transplant in the mid-1980s significantly improved survival. However, other adjunctive therapies for critically ill liver failure patients who cannot receive or access liver transplantation are limited.
The multi-organ failure syndrome associated with ALF is believed to be driven by overwhelming systemic inflammation triggered by both microbial and non-microbial factors. Therapeutic plasma exchange (TPE) has been shown to reduce inflammatory cytokine levels, modulate adaptive immunity, potentially lessen susceptibility to infections, and decrease levels of albumin-bound and water-bound toxins in liver failure. High-volume TPE has been shown to improve transplant-free survival and decrease multiorgan dysfunction.
Pruritus can be a common debilitating complication of cholestatic liver diseases (CLD) which can significantly impair the quality of life. Symptoms can persist despite maximum drug therapy and patients might require salvage therapy with invasive interventions such as ultraviolet B phototherapy, endoscopic nasobiliary drainage or plasmapheresis.
The aim of this audit is to evaluate the indications and outcomes of TPE in liver disease patients at a single centre from 2022 to 2024. The findings are expected to provide valuable insights for improving clinical practice and patient care.

**Materials and Methods:**
This retrospective audit examines patient records from a single centre, targeting Patients with liver diseases who underwent TPE between 2022 and 2024. Data collected included patient demographics, indications for TPE, number and frequency of TPE sessions, clinical outcomes, and complications. Descriptive statistics were used to analyse demographics and clinical characteristics, while outcomes were measured in terms of improvement rates, complication rates, and survival rates.

**Results:**
Fifteen patients underwent TPE for liver disease, with 60% treated for ALF and 40% for intractable itching associated with CLD. The median age of the patients was 43 years (range: 27-68), and 66.6% were female. A median of 3 TPE sessions were performed, with a median total exchange volume of 4 liters. Among patients with cholestatic liver disease, 83% reported an improvement in itching, which lasted for an average of 12 weeks. In the ALF group, there was a significant improvement in biochemical variables post-TPE, including ALT, AST, bilirubin, APTT, and alkaline phosphatase ($P < 0.05$). Overall survival was 73.3%, and there were no treatment-related deaths.

**Conclusions:**
Therapeutic plasma exchange can improve biochemical markers in patients with acute liver disease and may provide temporary support for those awaiting liver transplantation, though further research is needed to assess the long-term impact of these biochemical improvements. Additionally, TPE can be an effective treatment for pruritus in liver disease, offering significant relief for some patients that may last up to six months.

**Compliance with VTE Prophylaxis Guidelines and assessment of patient weighing : A Closed-Loop Audit in Mayo University Hospital**

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**Background**: Venous thromboembolism (VTE) is a significant and well-documented complication in hospitalized patients, with various established risk factors. Recognized standards of care include pre-admission VTE risk assessments, alongside the implementation of mechanical and chemoprophylaxis, as endorsed by both the Health Service Executive (HSE) and national guidelines. Proper prophylaxis for VTE is vital to prevent these potentially life-threatening complications during hospital stays.

**Methods**: A snapshot audit was conducted on a single day across two medical wards in Mayo University Hospital (MUH), encompassing 33 inpatients. The primary goal of this audit was to assess the appropriateness of VTE prophylaxis prescriptions and the completion of the VTE prophylaxis checklist. Additionally, the audit aimed to determine whether the provision of accurate patient weights had an impact on prescribing errors. Following the initial audit, a series of interventions were introduced. This included an educational session for doctors focusing on the importance of VTE prophylaxis, as well as instructions to nursing staff to prioritize weighing patients upon admission. Furthermore, nursing homes were directed to ensure that patients transferred to the hospital had documented weights.

**Results**: In the initial audit, 33 patients were evaluated. It was found that 72% of the patients received appropriately prescribed VTE prophylaxis. However, 19% of the patients either received VTE prophylaxis inappropriately or did not receive it at all. Additionally, 9% of the patients were prescribed incorrect dosages based on either weight or creatinine clearance. VTE prophylaxis checklist completion was notably low, with only 10% of checklists being completed. Alarmingly, patient weights were inaccurately documented in 71% of the cases.
After the interventions were implemented, a follow-up audit involving 37 patients showed an improvement in the appropriate prescription of VTE prophylaxis, increasing to 82%. The percentage of patients with inappropriate or unprescribed prophylaxis decreased to 9%, although dosing errors persisted at 9%. Patient weight documentation saw an improvement, with accurate documentation increasing to 47%. However, checklist completion showed only a marginal increase to 11%. In both audits, none of the stroke patients who did not require chemoprophylaxis were prescribed mechanical prophylaxis, although due to nursing protocols were receiving mechanical prophylaxis in spite of this.

**Conclusion**: The audit demonstrated that enhanced patient weighing significantly improved the accuracy of VTE prophylaxis prescriptions at MUH. However, the persistent 9% error rate in VTE prophylaxis dosing remains a concern. Despite the educational interventions aimed at improving VTE prophylaxis practices, the overall documentation of VTE decision-making continued to be suboptimal. While inaccurate weight documentation accounts for some of the dosing errors, it does not explain all the inaccuracies observed. Continuous efforts are needed to address these persistent gaps in practice to ensure patient safety and adherence to best practices in VTE prophylaxis

## VERIFICATION OF LUPUS ANTICOAGULANT TESTING AND REVIEW OF THE CURRENT EPIDEMIOLOGICAL PROFILE OF PATIENTS SENT FOR SCREENING IN A STANDALONE MATERNITY HOSPITAL

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**Abstract**
Lupus Anticoagulant (LA) becomes more prevalent during pregnancy and can result in thrombosis or pregnancy complications. The objective of this study was to verify the LA assay on the ACL TOP 550 Analyser and review the current epidemiological profile of patients sent for LA screening over the last year in the National Maternity Hospital (NMH). After the epidemiological profile was reviewed, it revealed that NMH patients were sent for LA screening because of recurrent miscarriages, thrombocytopenia, postnatal screening, family history of DVT's and stillbirth. Performance qualifications parameters were evaluated as part of the LA test validation, which included the measurement of precision, the measurement of accuracy, the method of comparison and extra testing performance. This study found that the method comparison provides great correlation and agreement between the Silica Clotting Time Confirm (SCT-C) and the Dilute Russel Viper Venom Screen (DRVVT-S) LA screening tests from analysis in NMH and in St. Vincent's University Hospital (SVUH). The measurement of precision displayed that internal quality control (IQC) results were precise and reliable. A great measurement of accuracy was concluded after an external quality assurance (EQA) sample was sent for external laboratory assessment. The extra testing parameter was not completed due to sample unavailability, this will be ongoing after completion of this project.

## RE-AUDIT ON THE HAEMATOLOGICAL MANAGEMENT OF MASSIVE POSTPARTUM HAEMORRHAGE IN CORK UNIVERSITY MATERNITY HOSPITAL

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### Background

Postpartum haemorrhage (PPH) is a leading cause of maternal mortality across the world. PPH has traditionally been defined as >500ml of blood loss from the genital tract following birth, or >1000ml of blood loss following Caesarean section (1). The British Society for Haematology (BSH) released guidelines on the haematological management of major haemorrhage in 2022 (2). Using this guideline as standards, an audit was performed in August 2022 in Cork University Maternity Hospital (CUMH) to assess the haematological management of massive PPH followed by formal training in CUMH.
New Health Service Executive (HSE) guidelines on the prevention and management of primary postpartum haemorrhage was released in December 2022 (1). When compared to the BSH guidelines there is significant overlap with identical targets in the haematological management of blood products. This makes perfect opportunity to re-audit the haematological management of primary PPH in CUMH using both guidelines with identical targets as standard.

### Methods

This is a retrospective audit performed in CUMH. All patients who suffered from PPH with blood loss >1500ml or requiring >5 units of red blood cells (RBC) during from January 2023 to August 2024 were included in the study. Data was collected using the blood transfusion laboratory massive haemorrhage protocol logbook, the CUMH hospital electronic record system, MNS-CERNER, and the APEX laboratory system. The transfusion laboratory logbook allowed us to identify patients, and record blood products distributed with APEX showing the products administered, their timing and blood investigations performed. The MNS-CERNER system was used to identify maternal and neonatal risk factors, blood loss and outcomes. All results were compared against best practice recommendations in the BSH and HSE guidelines in the management in PPH. This data was analysed using Excel and SPSS.

### Results

This audit is currently ongoing and these results are not yet finalised. Extrapolating from the initial results we estimate 20 patients to fulfil our criteria. A plasma: RBC ratio of more that 1:2 is seen in 90% of cases. Point of care testing is utilised in all cases as well as testing for coagulopathy including fibrinogen levels. On mean units of blood product used was 5.3 RBC, 3.6 plasma, 1.3 platelet, and 3.16 fibrinogen per patient. Point of carte testing was utilised in all cases and coagulation testing in 90%. Massive haemorrhage protocol standdown was documented in 20% and product return documented in 40%.

### Conclusion

Management of the haematological aspect of PPH should closely follow the BSH and HSE guidelines and this re-audit will identify efficacy of formal training as well as adherence so further training can be put in place.

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# INTERVENTIONAL RADIOLOGIST- PERFORMED BIOPSIES DURING THE COVID19 PANDEMIC - IMPACT ON DIAGNOSTIC YIELD AND TREATMENT DECISIONS FOR PATIENTS WITH LYMPHOMA.

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## Introduction

Lymphoma guideline (NICE, 2016) recommended performing an excision biopsy as the first diagnostic procedure at first presentation. The Covid19 pandemic resulted in theatre closures, leading to surgical specialties curtailing excision biopsy services since 2020. Patients presenting with lymphadenopathy were instead referred to the Interventional Radiologist (IR) for core biopsies. The IR approach represents a deviation from best practice.

## Aims

1. To examine the quality of IR-performed core biopsies and its impact on histological, IHC & molecular studies (diagnostic yield).
2. To examine its consequent impact on MDM decisions regarding patient management.

## Method

Consecutive patients managed in the haematology department SET were studied during a four-month FY1 doctor's attachment. Patient records on ECR and EPIC were accessed to extract patient demographics, IR / histology reports and MDM outcomes. The data was collated on an excel worksheet and results analysed. Inclusion criteria: All patients have a final diagnosis of lymphoma. Exclusion criteria: Bone and bone marrow biopsies.

## Results

*Patient demographics:*
Lymphoma patients 25 were studied, 2 were excluded. IR performed core needle biopsy in 19/23 (82.6%) patients, while only 4/23 (17.4%) patients had surgical excision biopsy as first-line diagnostic procedure. Among the 23 lymphoma patients, Subtype: DLBCL = 11, FL = 4, HL = 4, high grade B cell (nos) = 1, Mantle cell = 1, Richter's transformation of CLL to DLBCL = 1 and to HL = 1).
Median age 70y (age range 23-83y).
Gender: M=13, F=10.
*Core biopsy sample quality:* Mean number of needle passes by IR = 3.25 (range 1-7 passes). The number of passes were not stated in 3 patients. Mean number of cores received by Histopathologist = 3.2 (range 1-7 cores). The histology report did not state number of cores in 3 cases. Core biopsy yielded a definitive diagnosis in 14/19 (73.7%) patients, and a 'probable' or 'suspicious' diagnosis in 5/19 (26.3%) patients. MDM decisions were hampered by two 'suspicious of HL' and a 'probable lymphoma' core biopsy histological reports, leading to surgical biopsy in 3/19 (15.8%) patients. Surgical biopsy confirmed HL in a 22 and a 25 yo patient, and FL in a 72 yo patient.

## Conclusion

The majority of biopsies as first-line procedure were performed by IR. The majority of IR performed core biopsies led to a definitive diagnosis and treatment decision. Following a successful core biopsy, very few excision biopsies were required. However, a significant proportion of MDM outcomes were hampered by the quality of the core biopsy. In particular, suspected HL in younger patients were more likely to hinder MDM decisions and required large volume surgical biopsy.

## Recommendation

To improve diagnostic yield, IR-performed core biopsies should obtain multiple, large calibre cores. Surgical large volume biopsy should be performed on younger patients with suspected HL at presentation. A speedy surgical biopsy pathway should be made accessible to primary and secondary care doctors to improve diagnostic yield.

## AUDITING THE USE OF WARFARIN FOR ANTICOAGULATION IN PATIENTS WITH ATRIAL FIBRILLATION

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**Background:**
Anticoagulation has a central role in stroke risk in patients with atrial fibrillation (AF) and increased $CHA_2DS_2VASc$ score. Treatment of choice has evolved from warfarin to direct oral anticoagulants (DOAC), however some patients remain on warfarin. DOACs exhibit more favourable safety and efficacy profiles in this population (Carnicelli et al Circulation 2022) and current guideline recommend first line use of DOAC in AF.
This project aimed to identify patients attending the St James's Hospital warfarin clinic with AF who could be potentially suitable for switch to a DOAC. Suitable individuals would be offered information on DOACs to enable shared patient centred decision making regarding their ongoing anticoagulation management.

**Methods:**
Patients were identified via DAWN dosing system. All individuals attending with a target INR 2-3 attending were ascertained whose sole indication was AF. For each individual the most recent Creatinine Clearance (CrCl) was calculated and liver function testing (LFTs) recorded.
Patients were divided into three groups
**Group A** - Those unsuitable to switch to DOAC due to CrCl <30ml/min or abnormal LFTs
**Group B** - Those potentially suitable to switch (CrCl >30ml/min in last 2 years, normal LFTs)
**Group C -** Those with no recent data available
**Results:**
818 patients attended the SJH warfarin clinic in 2023, 628 with a target INR of 2-3. From this group, AF was the sole indication in 207 patients (median age of 82 years).
Of the 207 patients, only 158 were evaluable. 16 patients were deceased, with 33 patients possibly deceased (no data in >10 years). Of the 158 evaluable patients, only 84 had CrCl/LFTs available from the last 2 years.
Patients were sorted into cohorts in line with study aims:
**Group A** – Less suitable for DOAC – Creatinine Clearance (CrCl) <30ml/mins or abnormal LFTs - n=15 (9.5%)
**Group B**- Those potentially suitable to switch (CrCl >30ml/min in last 2 years, normal LFTs), n=69 (43.7%)
**Group C** – No recent blood results – n=74 (46.8%)
All patients in Group A will have their DAWN file annotated accordingly and will continue on warfarin. Those in Group B are scheduled for an education session on DOAC and medication check with the anticoagulation nurse at their next INR check. Group C will have routine bloods at their next INR check and be reassessed.

**Conclusions:**
This audit of patients attending SJH Warfarin clinic service has identified that AF (target INR 2-3) continues to represent 25.3% of all users. At least 44% of those with AF could potentially benefit for consideration of change to a DOAC. Many patients (47%) lacked recent bloods to assess suitability while only 9.5% had a reduced CrCl complicating the use of DOAC medications.

## Unmasking the offender: a case report of Cold Haemagglutinin Syndrome as the presenting feature in Systemic Lupus Erythematosus

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**Background**

Systemic Lupus Erythematosus (SLE) has a variety of haematological manifestations[1] with autoimmune haemolytic anaemia (AIHA) occurring in less than 10% of patients, predominantly warm autoimmune haemolysis[2]. AIHA can occur years prior to or following the diagnosis of SLE[2] and is considered a rare initial presenting feature[3].

**Case Report**

A 75 year old lady with no major comorbidities presented with a 9 month history of pathological weight loss (15%), anorexia, lethargy and features suggesting anaemia. Questioning at a subsequent presentation 3 weeks later confirmed a subacute history of aches in her hands and wrists with associated finger discolouration in cold weather. Examination at original presentation revealed low volume palpable, soft, mobile lymphadenopathy (cervical, supraclavicular, axillary) and a tip of spleen. At the time of re-presentation, synovitis was noted at the left wrist and a PIP joint in the left hand.

Cold haemagglutinin syndrome (CAS) was diagnosed, but driving causes remained unclear at the time of her original presentation with no discriminative clinical features and autoimmune panel results still awaited. At a re-presentation 3 weeks later, the diagnosis of SLE was made based on the history of Raynaud's phenomenon, clinical evidence of arthritis, the presence of AIHA and supportive serology.

**Investigations**

Initial FBC: WCC 5.4, Neutrophils 3.86, Lymphocytes 1.09, Hb 5.9, MCV 104.7, RDW 18.3, Platelets 310.
Blood film: left shifted myeloid series, cold agglutinins present, polychromasia, nucleated red blood cells.
Haemolytic screen: Total Bilirubin 31, Direct Bilirubin 11, LDH 626, Haptoglobin <0.1, Reticulocyte count 92 (7.3%), direct coombs test failed due to strength of cold reactive auto-antibody.
Haematinics: Transferrin saturation 20%, Total Iron Binding Capacity 37.7, Ferritin 6015, Vitamin B12 287, Folate 6.2.
Virology panel (HIV, HBsAg, anti-HCV, EBV IgM, CMV IgM): negative.
SPEP: No monoclonal paraprotein, normal kappa-lambda ratio.
Myeloproliferative panel (JAK2, JAK2 exon 12, CALR, MPL): negative.
Auto-immune panel: ANA >32, Anti-dsDNA 318, RF <10, ENA panel negative, p-ANCA positive (yet anti-MPO 0.3, anti-PR3 <1.0), C3 0.4, C4 <0.02.
CT TAP: No lymphadenopathy or hepatosplenomegaly.
Bone marrow: A hypocellular aspirate with no evidence of a lymphoproliferative disorder on either aspirate or trephine.
Flow cytometry: T cells predominate, no monoclonal B cell population.

**Management**

Initial management included blood transfusions with a blood warmer and avoidance of cool temperatures. On diagnosis of SLE, Prednisolone 1mg/kg daily was initiated with a view to transitioning to a more definite immunosuppressive regimen.

Nephrology workup was commenced given an acute kidney injury with nephrotic range proteinuria, establishing the clinical diagnosis of lupus nephritis.

Despite high dose steroids, she remained transfusion dependent. Mycophenolate was initiated as per MDM discussion between Haematology, Rheumatology and Nephrology. The qualification for immunosuppressive therapy based on haematological parameters regardless of renal involvement negated the requirement for a renal biopsy at that stage.

**Outcome**

The patient's haemoglobin stabilized at a level greater than 10 without transfusion support. She currently remains symptomatic with nephrotic syndrome.

**Conclusion**

This case adds to the small evidence base[4-7] in current literature for cold AIHA as the presenting feature in SLE, highlights a poor haematological response to steroid initiation and finally emphasizes the importance of diagnostic perseverance.

## The cost of a poor diet: a case report of severe Vitamin B12 and Folic Acid deficiency complicated by thrombotic microangiopathy

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**Background**
Megaloblastic anaemia results from abnormal DNA synthesis in maturating haemopoietic cells with associated apoptosis and intramedullary haemolysis. However, extramedullary (intravascular) haemolysis in the form of microangiopathic haemolytic anaemia (MAHA) is a rare association with severe Vitamin B12 (and potentially Folic Acid) deficiency and described in isolated case reports in international literature [1-5]. Aetiological theories implicate homocysteine buildup (as a precursor in nucleic acid synthesis) in microthrombi and endothelial dysfunction via oxidative pathways[6] or alternatively consider mechanical damage to erythrocytes with decreased erythrocyte deformability and impaired passage through microvasculature[7]. Although Vitamin B12 and Folic Acid deficiencies are benign and easily treatable, their haematological manifestations may mimic more sinister conditions.

**Case Report**
A teenage girl with no comorbidities and only on an oral contraceptive presented with a presyncopal event. She reported a 2 month history of progressive malaise, exertional palpitations and presyncope. She also noted recent bruising on minimal trauma, but denied B-symptoms or weight loss. She had sober habits, denied illicit substance use and was a leaving cert pupil, but some challenging family dynamics were apparent during her inpatient stay. Her diet included regular protein intake (mostly white meat) and poor vegetable intake. She had no mental health problems or significant recent stressors.
She had a normal BMI. There was conjunctival pallor, but no scleral icterus or palpable lymphadenopathy. Cardiovascular exam revealed a presumed flow murmur. The rest of her systemic examination, including neurological exam, was unremarkable.

**Investigations**
Initial FBC: WCC 2.92/ Hb 4.5/ MCV124.0/ RDW21.4/ Plt 38
Renal function: Urea 2.7, Creatinine 45, eGFR >90
Haemolytic markers: Reticulocyte count 28, LDH 1270, Haptoglobin <0.1, Total Bilirubin 39, Direct Bilirubin 22
Haematinics: Folate <2.0, Vit B12 <150, Ferretin 353, Iron 40.6, Transferrin 1.8, Transferrin sats 90%, TIBC 45.2
Blood film: Polychromasia, schistocytes. Hypogranular, hypersegmented neutrophils. Leucopaenia. Thrombocytopaenia.
Coeliac screen: Anti-tTG <0.2, Total IgA 0.75
Pernicious anaemia screen: Anti-Parietal cell Ab and Anti-Intrinsic Factor Ab negative
Helicobactor Pylori Faecal antigen: negative
Pregnancy test: negative

**Management**
A broad differential diagnosis was established and systematically excluded: acute leukaemia, haemolytic uraemic syndrome (HUS), thrombotic thrombocytopaenic purpura (TTP), pregnancy related HELLP syndrome, hypertensive emergency, malignancy, disseminated intravascular coagulation (DIC) and severe systemic infection. The diagnosis was established as severe Vitamin B12 and Folic Acid deficiency complicated by megaloblastic anaemia, pancytopaenia and MAHA. Gastrointestinal causes for the haematinic deficiencies were excluded.
She was initiated on subcutaneous Vitamin B12 and oral Folic Acid replacement without transfusion support, given her clinical stability. She was reviewed by the Dietetic and Psychiatric services, with the consensus that there was no evidence of an eating disorder; rather disordered eating.

**Outcome**
She had a fully normalised FBC on follow up.

**Conclusion**
This case adds to the limited evidence base to support MAHA in the context of severe Vitamin B12 deficiency. It demonstrates that a poor diet alone may results in severe haematinic deficiencies and its haematological consequences. A restrictive transfusion approach may be followed despite severe anaemia, permitting the patient is clinically uncompromised, not bleeding and does not have ischaemic heart disease.

**MORE THAN JUST A NUMBER: IMPACT OF IMMUNE THROMBOCYTOPENIA ON PSYCHOSOCIAL QUALITY OF LIFE IN PEDIATRIC PATIENTS—INSIGHTS FROM A TERTIARY CARE CENTRE IN HYDERABAD, PAKISTAN**

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**Introduction**

Immune Thrombocytopenia, characterized by low platelet counts due to immune system dysfunction, poses unique challenges for children and their families due to risk of serious bleed. It is one of the long-term conditions affecting multiple aspects of an individual's life which ultimately leads to a lower QoL. Though not an uncommon scenario in haematology clinics, the data showing impact of ITP on a patient's life from a physician's perspective is scarce. Since the exact etiology is unknown, the management options are very limited while working in a resource restricted setting. Lack of awareness or inaccessibility, unaffordability being the major reasons influencing the management of ITP. This study will contribute to the global discourse on the psychosocial aspects of chronic illnesses in pediatric populations, with specific relevance to the unique socio-cultural context of Pakistan.

**Objectives:**

• Assess the impact of ITP on psychosocial quality of life
• Evaluate the clinical and demographic spectrum of childhood ITP

Methods: Descriptive, Cross-sectional study, conducted at the Haematology Clinic LUMHS, Jamshoro.
A detailed predesigned, pre-structured questionnaire was filled by the physician in OPD, history taken from the patient or next of kin who came for follow-up. Specific investigations were added where available.
The questionnaire comprised five sections and collected information on demographics and diagnosis, symptoms of ITP, QoL (psychosocial) associated with ITP in patient, impact of ITP on parents' life, treatment received.

**Results:**

Total 46 ITP patients, Median age: 5.8 years (1.5 yr-16yrs), Mean Platelet count: 17 x 109/L. (range 3-61)×109/L. Platelet transfusion history was positive in 77%. Overall QoL was low with limited access to school, outdoor activities, travel and sports. Children with visible bruises experienced negative social attention. 68% parents reported discontinuing therapy at some point due to economic reasons.

**Discussion:**

Though a benign disorder with a wait and watch approach in most patients, ITP does pose an undue pressure on the child as well as parents, limiting their overall exposure to the common challenges of life. Limited treatment modalities, non-responding to steroids often leads to main reliance on transfusion of platelet concentrates leaving the patient exposed to various transfusion related infections.

**Conclusion:**

More researches are required to guide the school and other community centre about childcare in case of a chronic bleeding disorder like ITP. Sense of security and care will add more colours to the patient as well as parents' life living with immune thrombocytopenia. Adopting right practices should be done in daily routine activities in order to make them less challenging.

**Keywords:**
Immune Thrombocytopenia, Quality of life, Psychosocial, Bleeding, Paediatric, Transfusion

**NAVIGATING THE PEAKS AND VALLEYS: CHALLENGES AND TRIUMPHS IN MANAGING MYELOPROLIFERATIVE NEOPLASM**

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Current pharmacotherapeutic options for MPNs are not curative and have not shown a significant improvement in survival rates. Additionally, adherence to prescribed medications and their side effect profile poses a challenge for these patients. These factors can severely undermine treatment effectiveness. However, adherence interventions and switch to next best availabe agent tailored to the individual needs of each patient can significantly enhance the patient and family's experience, leading to better quality-of-life outcomes and reducing the impact of the disease.

A 61 year old lady presented in September 2012 with persistently elevated Hb, haematocrit and platelets.
She had no significant medical history apart from a previously resected carcinoid tumor of the caecum. She was non-smoker, did not consume alcohol, and was not on any regular medication. Clinical examination revealed small palpable splenomegaly, which was confirmed by ultrasound. Following initial investigations, she was diagnosed with JAK2V617F-positive polycythemia vera (PV). After receiving both written and verbal information, she was started on aspirin and hydroxycarbamide (HC) and scheduled for regular hematology reviews, including venesections as needed.

In December 2012, HC was discontinued due to significant mucocutaneous side effects that adversely affected her oral intake and quality of life. She was then started on weekly subcutaneous injections of pegylated interferon at 135 mcg. Initially, she tolerated the treatment well, experiencing only mild flu-like symptoms and myalgia. However, over the next few weeks, she developed periorbital dermatitis, lethargy, and a reduced appetite. Additionally, liver function tests showed abnormalities, prompting the discontinuation of interferons and further investigations. During this period, she continued only on antiplatelet therapy and was closely monitored. Her symptoms gradually resolved, liver function normalized, and her blood counts remained stable for about 18 months without cytoreductive or immunomodulatory therapy. She required only infrequent venesections to maintain her hematocrit levels below 0.45. However, surveillance revealed rising platelet and white cell counts, leading to the introduction of anagrelide and discontinuation of aspirin due to the increased bleeding risk associated with their combination.

Unfortunately, the patient struggled with anagrelide due to the recurrence of mouth ulcers and dry, painful eyes, necessitating its discontinuation and the resumption of aspirin. Regular follow-ups were arranged to monitor disease progression while she remained off definitive therapy. During these follow-ups, she developed iron deficiency anemia, leading to an urgent iron deficiency workup. An oesophagogastroscopy (OGD) revealed duodenal mucosal erosion, prompting the discontinuation of aspirin and initiation of proton pump inhibitor therapy with esomeprazole. Her blood counts remained stable, requiring few venesections, and she reported no concerning symptoms. Although initially, she had no cardiovascular risk factors or thrombosis and aws low risk, but the increased age and newly diagnosed hypertension in 2017 put her into high risk category.
Over the next five years, she remained stable under regular hematology review. However, in 2023, gradual increase in blood parameters, spleen size, and the emergence of symptoms such as reduced appetite, abdominal pain, and mild frequent headaches were observed. Blood film analysis showed leukoerythroblastic features, and a bone marrow aspirate and trephine biopsy confirmed disease transformation to secondary myelofibrosis with grade 3 fibrosis. After discussing the disease transformation with her, ruxolitinib was initiated as the best available therapy. Initially, she experienced minor side effects, but they quickly resolved, and she demonstrated significant clinical improvement, including a reduction in symptom burden and evidence of spleen regression on clinical and radiological evaluations.

**SECOND SPLENECTOMY? A ROCKY JOURNEY OF REFRACTORY IMMUNE THROMBOCYTOPENIA**

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**Introduction/Background:**

Immune thrombocytopenia (ITP) is an acquired autoimmune disorder characterized by increased platelet destruction and deficient megakaryocyte maturation. Patients with ITP are largely heterogenous and about 10% of them become refractory to treatment. An international working group defined refractory ITP as disease that does not respond to or relapse after splenectomy and that requires treatment to reduce the risk of clinically significant bleeding[1]. Patients with refractory ITP are at severe risk of bleeding and infection with higher mortality compared to the general population[2].

We thereby present an interesting case study of a refractory chronic ITP patient who had undergone multiple lines of combination therapy and is on his rare journey to his second elective splenectomy. To date, he is the only one in Ireland on a spleen tyrosine kinase inhibitor.

**Case study:**

A 46-year-old gentleman from Slovakia was diagnosed with ITP in April 2013. He first presented with epistaxis and was found to have an isolated thrombocytopenia of less than 5. He had a very transient response to intravenous immunoglobulins (IVIG) and corticosteroids, lasting for only 2 weeks. Since then, he had multiple hospital admissions with platelet < 5 despite being on 1mg/kg of prednisolone. He failed Rituximab and was intolerant to eltrombopag. He initially responded to Romiplostim and had a full splenectomy, including splenunculus in 2013. Unfortunately, he relapsed 6 months post-splenectomy. He became steroid responsive post-splenectomy however response was quickly lost once steroid was tapered. For the next decade, he remained in and out of hospital with bleeding, always needing pulses of high dose steroid as rescue. He had been trialed on on eltrombopag, romiplostim, mycophenolate, azathioprine, ciclosporin, avatrombopag and daratumumab in different combinations without a sustained response.

In November 2023, he became the first patient in Ireland to be started on Fostamatinib, in addition to daratumumab and romiplostim. Unfortunately, over the Christmas period, he presented with a life-threatening severe gastrointestinal bleed that required multiple red cell transfusions. Very unexpectedly, a full-size spleen was found on CT scan with no accessory spleen seen. With high dose methylprednisolone, IVIG and platelet transfusions, his platelet eventually improved. Since then, the goal has been trying to achieve a safe platelet count to have a second splenectomy. His platelet count continued to rise while on weekly romiplostim and twice daily fostamatinib and weekly daratumumab. Unfortunately, he developed an arterial thrombus affecting his right toe, requiring antiplatelet and therapeutic anticoagulation which delayed his splenectomy. While on aspirin and apixaban for 4 weeks, he developed worsening intermittent limb claudication and on investigation, was found to have a new large suprarenal aortic clot where his apixaban dose had to be increased, again postponing his splenectomy. To date, he is still awaiting the optimal circumstances for his second splenectomy, with his fluctuating platelet count while on aspirin and apixaban.

**Conclusion:**

In treating refractory ITP, combination therapy targeting multiple biological mechanisms concurrently works better than single-agent therapy. Regrowth of full-sized spleen following initial splenectomy remains undescribed in the literature.

**Stroke versus Lymphoma: An unusual differential**

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Intravascular large B-cell lymphoma is a rare, aggressive form of lymphoma. Difficulties in diagnosis and management stem from a relatively non-specific presentation, wide differential diagnosis on radiological imaging and high risk and technically difficult biopsy procedures.

We herein report a case of a 63 year old female with intravascular large B-cell lymphoma. The patient presented in September 2023 with TIA-like symptoms – transient visual disturbances, weakness and confusion. CT imaging of the brain at that time showed no abnormality and she was managed as a TIA. Symptoms progressed despite treatment. MRI was performed which showed multiple foci of restricted diffusion in keeping with tiny infarcts throughout the cerebrum. A broad range of differential diagnoses were considered, including vasculitis, embolic disease and intravascular lymphoma.

Cerebrospinal fluid was submitted for cytological examination and flow cytometry, which showed no evidence of lymphoma. Brain biopsy was performed and histological examination showed ischaemic change related to an intravascular proliferation of malignant cells in the cortex and white matter. The intravascular malignant cells showed a positive CD20, CD5, BCL6, CD10, and MUM1 immunophenotype with a high MIB1 proliferation index, in keeping with large B-cell lymphoma.

She was treated with 6 cycles of Pola R-CHP with CNS prophylaxis. Prior to treatment she was bed bound with confusion, visual disturbance, and neglect. Following treatment she made a complete neurological recovery.

**Reviewing the diagnosis of von Willebrand disease using new laboratory tests and recent consensus guidelines in paediatric patients attending the Paediatric Coagulation Centre at Children's Health Ireland at Crumlin**

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**Introduction**: Von Willebrand disease (VWD) is a common inherited bleeding disorder characterised by quantitative or qualitative deficiencies in von Willebrand factor (VWF). Diagnosis and classification is important for prognosis and treatment, but is challenging. The von Willebrand factor antigen (VWF: Ag) assay measures the amount of von Willebrand factor. Function of von Willebrand factor is measured in CHI at Crumlin using two separate tests: 1. VWF: CB measures the binding of VWF to collagen and VWF: 2. VWF: RCo measures the platelet binding activity of VWF. VWF: RCo/VWF: Ag ratio <0.7 is indicative of type 2 VWD, a qualitative deficiency of VWF. Type 2 VWD is associated with known mutations in the *VWF* gene. Patients with VWF: RCo/VWF: Ag ratio <0.7 without a corresponding type 2 *VWF* mutation, and those with isolated low VWF: RCo and otherwise normal assays were classified as having low VWF.
Recent guidelines for the diagnosis of VWD recommend the use of newer assays to measure the platelet binding activity of VWF (VWF: GP1b assay). The VWF: RCo assay has lower reproducibility and increased false positive rates in comparison to the VWF: GP1b assay. The relatively recently described D1472H polymorphism in the *VWF* gene can be associated with artificially low VWF: RCo results. This polymorphism has no effect on VWF: GP1b assays.
The objective of this audit is to re- assess the diagnosis and classification of paediatric patients with low VWF in line with recent guidelines using the VWF: GP1b assay and genetic tests for D1472H polymorphism, and to identify those patients who would benefit from use of these tests.

**Methodology**: All patients registered with low VWF were identified and analysed using the national haematology register/electronic patient record (nhl.indici.ie) and the laboratory results portal. Data collected included age, gender, reason for initial referral, FVIII, VWF: Ag, VWF: RCo and VWF: CB. Data on VWF: GP1bM levels, *VWF* gene D1472H polymorphism and multimer abnormalities were collected where available. Patients with VWF: RCo/VWF: Ag ratio <0.7 and/or those with an isolated low VWF: RCo were identified for further assessment.

**Results:** 403 patients were identified as having low VWF (218 males and 185 females). 139 patients had a VWF: RCo/VWF: Ag ratio of <0.7, including 57 patients with a VWF: RCo/ VWF: Ag ratio of <0.6. Amongst the remaining patients, 82 patients had an isolated low VWF: RCo result. When available, the VWF: GP1b and genetic polymorphism results were reviewed in these patients. These results will be presented. This audit identified 221 patients who would benefit from further analysis to confirm or change their diagnosis. Of 15 patients who have currently received further testing, 9 have been discharged, with 2 patients retaining the diagnosis of low VWF. 2 patients had their diagnosis changed to possible bleeding disorder, with 2 others changed to bleeding disorder of unknown aetiology. Further analysis will be presented.

**Discussion/ Conclusion:** This audit has identified a large group of patients needing reassessment of their diagnosis using new tests (VWF: GP1bM and *VWF* gene D1472H polymorphism status). This will result in patients no longer having a diagnosis of VWD or a change in classification of their subtype of VWD with significant impact on patient quality of life and treatment choice (if changed subtype) and on the work of the haematology service.

## SPLANCHNIC VEIN THROMBOSIS AS A FIRST PRESENTATION OF JAK2 POSITIVE MYELOPROLIFERATIVE NEOPLASM

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### Introduction

Polycythaemia Vera (PV), Essential Thrombocythemia (ET) and Primary Myelofibrosis (PMF) are Philadelphia-chromosome negative group of chronic Myeloproliferative Neoplasms (MPN), characterized by clonal proliferation of abnormal haemoatopoietic progenitor cell. The commonest trigger for screening is erythrocytosis or thrombocytosis. Splanchnic vein thrombosis (SVT) is frequent complication of MPN. The aim of this study is to characterize patients diagnosed with SVT with MPN and examine therapeutic interventions and relevant outcomes.

### Methods

A retrospective study was performed, including patients over 18 with non-malignant / non cirrhotic PVT and BCS diagnosed with MPN by WHO criteria at St Vincent's University Hospital (SVUH) between 2011 – 2023. Patients were identified from the SVUH haematology database.

### Results

A total of 14 patients were included. The average age at diagnosis of SVT was 37.9 years (21-72 range). Female patients accounted for 85.7% (12). In 12 patients (85.7%), the thrombotic episode preceded diagnosis of MPN. All patients had *JAK2V617F* mutation, none of them had *CALR* or *MPL*. Next Generation Sequencing was available for 9 patients. Two of them had additional mutations, (*SRSF2*, *TET2 and U2AF1*). Cytogenetic abnormalities were t(3;17) and trisomy 8. At the time of diagnosis, 78.57% (11) patients had normal blood counts, 1 had erythrocytosis and 2 thrombocytosis. Bone marrow biopsy confirmed MPN in 12 patients, and it was not done for 2. Thirteen patients (92.85%) received anticoagulants, one stopped due to bleeding. One patient was on antiplatelet therapy. Cytotoxic therapy was used in 9 (64.2%) patients. Seven (50%) used Hydroxyurea and two (14.28%) Pegylated Interferon. Four patients suffered from recurrent thrombosis: two underwent TIPPS procedure; another 2 patients suffered from thrombosis in other sites (subclavian vein and sagittal sinus). All patients had portal hypertension and varices, 50% (7) suffering from variceal bleeding, with 28% (4) requiring banding and 14% (2) requiring splenectomy. One patient underwent multi-visceral transplant and one liver transplant. All patients are alive at the time of this study.

### Discussion

SVT is a rare type of venous thromboembolism. Despite a small number of patients, our study confirmed that SVT is frequently the first manifestation of MPN driven by *JAK2 p.V617F.* It also demonstrates that the demographic of this population tends to be younger females. The diagnosis of MPN in these patients may be delayed due to absence of erythrocytosis or thrombocytosis especially in patients with hypersplenism or iron deficiency. This highlights the need for early screening for MPN in patients with SVT. The management is complex and include venesection, anticoagulation, antiplatelet and cytotoxic therapy, endoscopy and surgical procedures including splenectomy and transplant.
Our study highlights the need for further investigations that will aid optimisation of treatment in this cohort of patients.

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**Assessing the outcome of Positive D Dimers in primary care**

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**Introduction**

- The D-Dimer test is a laboratory assay used to quantitate Fibrin Degradation products and is clinically useful for delineating between those who require further investigation for potential Venous Thromboembolic events (VTE) by means of CT Pulmonary Angiogram (CTPA) or Proximal Leg vein ultrasound. Current NICE Guidelines recommend testing D-Dimer levels if Wells Score ≤1 and if positive, pursuing further appropriate imaging i.e. proximal leg vein ultrasound or CTPA. The utility of D-Dimer testing in this case is due to its high sensitivity for VTE, however the relatively low specificity of the test leads to potentially unnecessary further imaging due to false positives.
- This project aimed to assess the utily of D-Dimer use by primary care.

**Methods**

- The current ULN for D-Dimer testing is 250ng/ml. All positive (>250ng/ml) D-Dimer tests sent in via primary care were investigated.
- Patient GP data was collected by Antrim Area Hospital Haematology Laboratory and covered results from December 2021 – March 2022.
- In total 366 patients had positive D-Dimer test results but 27 were excluded due to having multiple D-Dimers sent. Therefore, analysis was performed on 339 total patients.
- Of patients who proceeded to imaging, timing of imaging was also examined.

**53 patients with positive D-Dimers had CTPA imaging**

- **39 cases would have had image-proven VTE**

- **31 Deep Vein Thrombosis and 8 Pulmonary Embolism**

- **All confirmed cases were within Range; 359-5398ng/ml**

- **1 Case had less than 400ng/ml – this patient had a previous VTE 2 months previously.**

- **339 cases had a positive D-Dimer. Of those**

- **88 cases (26%) had no appropriate imaging**
- **193 cases had a D-Dimer <500ng/ml. Of those, 68 cases (35%) did not have appropriate imaging.**
- **58 cases had a D-Dimer >1000ng/ml. Of those, 6 cases (10%) did not have appropriate imaging.**

**Discussion**

- Could increasing the upper limit of normal of the D-Dimer test reduce rates of unnecessary imaging without increasing risk of false negative for VTE.
- If the upper limit of normal were to be adjusted to 300ng/ml rather than 250ng/ml, **No** cases of VTE would have been missed in this time period (December 2021 – March 2022). If the ULN of 300ng/ml were to be used, 25 unnecessary proximal Leg Vein Ultrasound tests and 8 CTPAs would have been avoided.

- Reduction in costs of imaging (approx. £50/scan for CTPA), therefore saving the trust ~£400 pounds in imaging costs alone. This does not take into consideration the associated labour costs of performing and interpreting such scans.
- Minimising exposure to radiation.
- Changing the threshold would lead to incongruities between health and social care trusts within Northern Ireland. Additionally, to alter assay standards, extensive cooperation and collaboration between laboratory and clinical staff would be required to maintain clarity on guidelines.
- limitations to this data, firstly the data only applies to patients referred from primary care. There be may value in examining data from a secondary care perspective to provide further insight into its significance.
- This area needs further investigation and research, potentially covering more trusts, secondary care and over a longer timeframe.

## Could adjustment of the D-Dimer range improve its specificity?

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**Introduction:**
NICE Guidelines suggest that if imaging cannot be offered within 4 hours of a positive D-Dimer then interim anticoagulation should be offered with imaging performed within 24 hours. This can often be a challenging management problem in primary care.
We assessed the possibility of

**Methods:**
We assessed all positive D-Dimers received in the lab over a 3 month period exclusively from primary care.
We divided this into the following questions
1) Was appropriate imaging performed?
2) Was the likelihood of imaging being performed related to the quantitative value?
3) Was the imaging performed in a timely fashion for both CTPAs and US Dopplers?
We also reviewed all cases that led to the diagnosis of VTE:
1) To what extent does the quantitative value relate to likelihood of VTE

**Results:**
26% of all cases did not have any appropriate imaging performed
This was much more likely to occur at lower quantitative values with 68/193 cases not having imaging performed with values of 250-499ng/mL compared to only 6/58 cases with values of >1000ng/mL
We found that of the 192 patients that attended for US Doppler, 13 took place the same day with 109 the following day.
Of the 53 patients that attended for CTPAs 10 attended the same day with 33 the next day.
The use of interim anticoagulation was not able to be accurately audited due to limited access to GP systems.
A total of 39 cases would subsequently get a positive VTE diagnosis with 31 DVT and 8 PE.
The range of values for positive cases were within the range of 359-5398 ng/mL. Only 1 patient had a value of <400 ng/mL and this patient had previous DVT within 8 weeks.

**Discussion:**
1) By raising the lower limit of a positive value even slightly to 300 ng/mL then 0 cases of VTE would be missed with 25 US Dopplers and 8 CTPAs avoided.
2) The main limitation of the study is that it was exclusive to primary care. Is this reproducible to secondary care.
3) A high proportion of D-Dimers are sent inappropriately as reflected by the 26% of cases without follow-up imaging. Is there a way to minimize this?

## JAK2+VE MYELOPROLIFERATIVE NEOPLASMS PRESENTING WITH CEREBRAL VENOUS SINUS THROMBOSIS (CVST) - A CASE SERIES

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### INTRO AND BACKGROUND

Essential thrombocytosis (ET) is a myeloproliferative neoplasm (MPN) characterised by persistent thrombocytosis in the absence of any provoking cause, with megakaryocyte proliferation. 50% of cases are asymptomatic while another 50% are associated with an increased thrombotic and haemorrhagic risk. The JAK2-V617F mutation is seen in approximately 50% of cases of ET and is associated with an increased risk of venous and arterial thrombosis. MPL and CALR gene mutations are also associated with ET, albeit with lower thrombotic risk. Cerebral Venous Sinus Thrombosis (CVST) is a potential complication of ET that rarely manifests at initial diagnosis.

### MATERIALS AND METHODS

Three separate cases of patients involving an 39-year-old male, 38-year-old female and 21-year-old male in a 30 month period are described in this case series, all presenting with extensive CVST and thrombocytosis and subsequently diagnosed with JAK2+ MPN most consistent with ET. Chart reviews were performed and radiology data was obtained from the National Integrated Medical Imaging System (NIMIS).

### RESULTS

All three patients presented with symptoms of persistent headaches lasting months, as well as other associated symptoms of CVST such as nausea and vomiting. Patient 1 and Patient 3 had previously been referred to the haematology service with elevated platelets routinely prior to their acute admissions. Patient 2 was found to have thrombocytosis on laboratory testing after referral to the emergency department by their optician with papilloedema. Platelet counts ranged from 550 to 850 $x10^9$/L at presentation. All were initially commenced on therapeutic low molecular weight heparin (LMWH). Patient 1 and 2 were switched on discharge to Warfarin (target INR 2.0- 3.0) while patient 3 was changed to Apixaban 5mg twice daily, a direct oral anticoagulant (DOAC). Cytoreductive therapy in the form of hydroxyurea was commenced for Patients 1 and 2 pending MPN panel result given the likelihood of ET and their perceived high risk. Both were then transitioned to pegylated interferon (Peg-IFN) as an outpatient. Patient 3 had pegylated interferon commenced once JAK2+ status was confirmed. Available follow-up imaging for patients 2 and 3 demonstrated significant reductions in thrombus burden at 6-12 months.

### CONCLUSIONS

CVST can be a rare and life-threatening first presentation of JAK2+ ET. Therapeutic anticoagulation should be commenced without delay in these cases and LMWH is preferred as the first line agent, prior to an oral switch after 1 week. Although there is little RCT data for anticoagulation in CVST, let alone in the context of an MPN, the oral anticoagulant we have most experience with to date is Warfarin. However there is a growing trend internationally to prescribe DOACs for CVST, as we chose to do with patient 3, after appropriate counselling. Due to a high recurrence rate, lifelong anticoagulation is usually recommended after venous thrombosis in patients with a JAK2+ MPN. It's important to be aware of potential haemorrhagic risk in patients with higher platelet counts >1000x$10^9$/L.
Unexplained thrombocytosis in patients with acute thrombosis should lead clinicians to suspect an underlying MPN and consider sending an MPN panel. Cytoreduction should be considered to further reduce recurrent thrombotic risk.

# REVERSAL OF ANTICOAGULANT THERAPY-RELATED MAJOR BLEEDING: PROJECTED COST IMPLICATIONS IN THE SETTING OF INCREASED ACCESS TO EXPANDED PROTHROMBIN COMPLEX CONCENTRATE OPTIONS AND ANDEXANET ALFA

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## Introduction

Prothrombin complex concentrate (PCC) is licensed for reversal of warfarin-induced anticoagulation. However, the direct oral anticoagulants (DOACs) have largely replaced warfarin for most indications and so reversal strategies for DOAC therapy (specifically for the factor Xa inhibitors apixaban, rivaroxaban and edoxaban) are also required. PCC is frequently used as a non-specific antidote for FXa-inhibitor associated bleeding but efficacy data are lacking. Andexanet alfa (AA), a recombinant modified FXa decoy protein, was developed as a specific antidote to rivaroxaban/apixaban and while it has been licensed for life-threatening bleeding, efficacy data are limited with respect to clinical outcomes, particularly with regards to intra-cranial haemorrhage (ICH). Recent safety data has highlighted a risk of thrombosis, including ischaemic stroke, following AA use in ICH patients which has prompted the HSE to alter its current guidance relating to AA use.
AA use is associated with significant cost implications. Wholesale costs of a single dose are estimated at €20,000-€40,000. Equivalent costs for PCC preparations (such as Octaplex) are substantially lower and increased availability of other 4-factor PCC products in the Irish market over coming months may lead to further cost savings (e.g. Prothromplex) in the region of 30%.
In this study we aimed to estimate potential AA cost implications based on patterns of PCC use in our institution during the 6-month period prior to the introduction of AA to the Irish market in 2023.

## Methods

Records of PCC administration maintained by the blood transfusion laboratory identified PCC-treated patients during the study period. Clinical details relating to indication for administration were obtained from patient health records.

## Results

38 patients received PCC (warfarin reversal n=18; DOAC reversal n=20). In the DOAC group, the indication for PCC was major bleeding in just 13 cases, of which ICH accounted for 7. In the warfarin group, the median dose of PCC administered was 2000 units (IQR 1875-2625). In the DOAC group, the median PCC dose was 2750 units (IQR 2000-3000).
The total cost of PCC usage (n=20) for DOAC reversal during this period is estimated (based on wholesale Octaplex costings) at €35,760. Using an alternative 4-factor PCC option (Prothromplex) for a similar level of PCC usage would be associated with potential cost savings (estimated costs €24,760). Had AA been available during this period it likely would have been considered for the 13 DOAC-treated patients who received PCC for major bleeding. If AA was available for use in these cases it would have resulted in wholesale costs in the region of €300,950 – 541,710 (depending on dosing band), in contrast to the estimated Octaplex PCC costs in this subgroup of €23,244. If cases of ICH were excluded from AA use, AA costs would still have been estimated to amount to between €162,050 to €291,690.

## Conclusion

Limited options exist for effective and safe anticoagulation reversal. AA is associated with significant cost implications and should be used judiciously, taking into account the available safety and efficacy data. Senior-decision making is crucial in order to ensure this agent is used appropriately.

## ANTICOAGULATION REVERSAL - BUT AT WHAT COST? A CASE FOR ANTICOAGULATION STEWARDSHIP

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**Introduction:**
Anticoagulation Stewardship is a systematic, pharmacist-led approach to anticoagulant management which includes a focus on the appropriate use of anticoagulants and their reversal agents. The primary goal of such a programme is to improve patient safety with the use of this high-risk medication group. It should also aim to achieve cost-savings to hospitals by ensuring judicious use of anticoagulants and their expensive reversal agents. Factor Xa inhibitors apixaban and rivaroxaban are two of the direct oral anticoagulant (DOAC) medications licenced for use in stroke prevention in non-valvular atrial fibrillation, and for venous thromboembolism treatment and prevention. Bleeding is the most significant adverse event associated with their use and can be life-threatening. Andexanet alfa, a recombinant human factor Xa protein, acts as a direct reversal agent for apixaban and rivaroxaban, and can be used in place of previous standard of care in some but not all circumstances. It was approved for reimbursement in Ireland in April 2023 and became available for use at Beaumont Hospital in June 2023. This study analyses the overall use and cost of Andexanet alfa, prothrombin complex concentrate (PCC), and tranexamic acid (TXA) in the 12 months before and after Andexanet alfa availability in Beaumont Hospital.

**Materials and Methods:**
Dispensing records and cost information for Andexanet alfa, PCC, and TXA for the periods 1st June 2022 - 31st May 2023, and 1st June 2023 - 31st May 2024, were obtained from Beaumont Hospital Pharmacy and Blood Bank. Total expenditure for the two time periods was calculated, and a direct cost comparison was made.

**Results:**
Prior to June 2023, PCC, with or without TXA, was used to manage DOAC-related life-threatening or uncontrolled bleeding. PCC and TXA costs amounted to €125,030 and €14,007, respectively, from June 2022 to May 2023, totalling €139,037. From June 2023 to May 2024, PCC utilisation and cost decreased by 33.9%, down to €82,588, while TXA costs increased marginally to €14,946.
From June 2023 to May 2024, 151 units of Andexanet alfa were used for apixaban or rivaroxaban reversal, costing a total of €558,310 at approximately €15,000 to €30,000 per single dose. The total expenditure on reversal agents in the first 12 months after Andexanet alfa availability was €655,844, reflecting a marked 372% overall cost increase of €516,807.
Initially, Andexanet alfa was stocked in pharmacy and released only on a named patient basis, but this led to delays in timely access in emergent cases. It has been stored in the Emergency Department since July 2023, which has made auditing of its use more challenging.

**Conclusions:**
DOAC use confers increased bleeding risk which may be life-threatening and warrant urgent reversal. However, direct reversal agents, such as Andexanet alfa, are expensive, and need to be used appropriately. The introduction of a pharmacist-led, physician-supported Anticoagulation Stewardship Programme in our hospital would greatly facilitate appropriate prescribing and administration of anticoagulation reversal agents, and accurate tracking and auditing of their use. This will enable us to maximise patient outcomes and reduce the high systems costs associated with these medications.

# The Pivotal Role Of Formal Post-Pulmonary Embolism Follow-Up In The Early Detection Of Chronic Pulmonary Vascular Disease: Outcomes From A Pilot Initiative from the National Pulmonary Hypertension Unit and Haematology Service of the Mater Hospital.

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## Introduction

Pulmonary embolism (PE) represents a leading cause of cardiovascular morbidity globally. Fortunately, with effective anticoagulant therapy the vast majority of patients will be expected to survive and experience complete resolution of pulmonary vascular occlusion. However, a small proportion of patients remain symptomatic with persistent vascular obstruction (chronic thromboembolic pulmonary disease; CTEPD), which in some cases (3-4% overall) progresses to chronic thromboembolic pulmonary hypertension (CTEPH; potentially life-threatening condition). CTEPD/CTEPH is likely under-recognised and frequently presents at an advanced stage with registry data suggesting a mean duration of symptoms of two years or more prior to diagnosis. Current guidelines recommend that all PE patients are assessed for signs of CTEPD/CTEPH following completion of initial anticoagulation and recent data suggests that the establishment of haematology/respiratory post-PE clinics leads to more timely diagnosis and, critically, improved clinical outcomes.

## Methods

A 'post-PE' dual haematology/respiratory clinic (DHRC) has been established at the Mater Misericordiae University Hospital (MMUH) in a collaborative initiative between the coagulation service and the Respiratory/National Pulmonary Hypertension Unit. The purpose of the clinic is to undertake specialist assessment of PE patients with persistent cardio-respiratory symptoms. As standard, all PE patients in the MMUH undergo a screening visit at a either a haematology, respiratory or ANP clinic at 3 months following diagnosis at which point patients requiring DHRC review are identified. At the DHRC patients are assessed by a Consultant Haematologist and Consultant Respiratory physician with specialist interest in pulmonary vascular disease. Selected patients are referred for investigations including VQ scanning, echocardiography, invasive pulmonary angiography (IR-PAgram), right heart catheterisation (RHC) and other respiratory investigations as indicated. The DHRC aims to review all referred patients within 6 months of PE diagnosis and to complete screening investigations within 6 months of first DHRC assessment. In this study, we present the initial data from the first 20 patients referred for DHRC review.

## Results

Twelve patients were referred following provoked PE with 8 referred following an unprovoked event. The mean age was 56.7 years (range 25-89). The majority of patients (n=11) had been referred following a presentation with intermediate-risk PE (ESC Criteria: Intermediate-high, n=7; Intermediate-low, n=4). Following DHRC assessment, 15 were referred for VQ scan/IR-PAgram which has revealed a diagnosis of CTEPD in 6 of 10 scans completed to date, with IR-PAgram confirming chronic vascular occlusion in all 6 cases and revealing probable CTEPH in 3 cases. Referral of these 3 patients for RHC has confirmed CTEPH in one case with 2 results awaited. While unprovoked PE was associated with a 1.6-fold increased likelihood of CTED/CTEPH, this did not reach statistical significance in this small cohort.

## Conclusion

In this pilot phase of a specialist DHRC, a diagnosis of symptomatic CTEPD has already been made in 40% of the first 20 referred patients, despite completion of investigations still being awaited in 5 cases. Three patients have been diagnosed with possible CTEPH (21%; 1 confirmed on RHC; 2 awaiting confirmation). This DHRC model permits rapid and more streamlined detection of chronic pulmonary vascular diseases including CTEPH.

## LABORATORY EVALUATION OF INTERFERENCES ASSOCIATED WITH FACTOR XIA INHIBITORS ASUNDEXIAN AND MILVEXIAN IN ROUTINE COAGULATION ASSAYS

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Direct oral anticoagulants (DOACs) are increasingly used for the treatment of thrombosis. While inhibitors of factor IIa and factor Xa have shown effectiveness, the risk of bleeding remains a significant concern. Recently, direct factor XIa (FXIa) inhibitors - including asundexian and milvexian have emerged as potential anticoagulation therapies with minimised bleeding risk, based on clinical observations that patients with FXIa deficiencies seldom present with spontaneous bleeding tendencies. The interferences associated with DOACs in routine and specialised coagulation assays are well-described; however, the interferences associated with emerging FXIa inhibitors are largely uncharacterised.

Here, we briefly report the impact of asundexian and milvexian in routine coagulation assays using in vitro plasma-based systems. In addition, we report the efficacy of activated charcoal (AC) as a potential adsorbent material to minimise FXIa inhibitor-associated interferences.

Asundexian and milvexian induced concentration-dependent prolongations in APTT-based assays with curvlinear regressions with no interferences observed for PT-based assays. The responsivity of APTT-based assays may be suitable for the measurement of pharmacodynamic effects at peak levels ex vivo. Subsequent treatment of asundexian- and milvexian- containing plasma material with AC effectively adsorbed all concentrations evaluated and efficiently removed any FXIa inhibitor-associated interferences.

This study highlights that FXIa inhibitors may contribute to pre-analytical interferences in coagulation asssays, as well as highlighting the importance of having methodologies to remove such interferences prior to laboratory testing.

## An Evaluation of the Sysmex XR Haematology Cell Counter Analyser and Comparison with the Capabilities of the Sysmex XN Series

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The full blood count (FBC) is one of the most common tests in the clinical laboratory and provides valuable information which influences the decisions of clinicians in the treatment and care of patients. It is essential that the results reported by haematology laboratories are precise, accurate, and delivered within an appropriate timeframe, therefore, FBC analysers must be evaluated to assess whether they are fit for purpose. The XR-series is the latest haematology analyser launched by Sysmex. The XR-series holds the same measurement channels and principles as the previous model by Sysmex, the XN-series, but with novel features such as a new reagent system for the white cell differential (WDF) channel (Lysercell WDF II) as well as the graphical presentation of results on a three-dimensional scattergram, and a quicker throughput than the XN-series. The aim of this study was to evaluate the performance of the Sysmex XR-1000 and compare it to the Sysmex XN-20, the FBC analyser currently in use in the haematology laboratory in St. James's Hospital.
As recommended by the International Council for Standardization in Haematology (ICSH) guidelines for the evaluation of blood cell analysers, accuracy, intra-assay and inter-assay precision, linearity, and carryover of the Sysmex XR was evaluated in this study. A comparability study of the Sysmex XR and the Sysmex XN was performed which included a comparison of leukocyte differentials to evaluate the new Lysercell WDF II reagent and assess whether it improved white blood cell differential counts, and the flagging performance of both analysers was also examined. The evaluation of the Sysmex XR was carried out on anonymised surplus Ethylenediaminetetraacetic Acid (EDTA) anticoagulated peripheral whole blood samples from out-patients and inpatients at St. James's Hospital which required no further testing and would otherwise have been discarded. Samples were analysed within 4-8 hours from the time of venesection as recommended by the ICSH guidelines. For accuracy and inter-assay precision, XN CHECK (Sysmex Corporation) control material was used which had greater stability than fresh whole blood samples.
The findings of this study revealed that the XR had good accuracy, intra-assay and inter-assay precision, linearity, and carryover. For the comparability study, Bland-Altman and linear regression analysis showed that the XR provided similar results as the XN. The leukocyte differentials of both analysers were similar apart from three cases in which the XR achieved better separation of neutrophils and eosinophils than the XN. The XR displayed a faster throughput of 112.43 samples/hour compared to 97.25 samples/hour by the XN. The sensitivity and specificity of the flagging performance of both analysers appeared to be insufficiently sensitive to identify all true cases, however, exhibited sufficient specificity that positive results were likely to be genuine. To summarise, this study found that the Sysmex XR functions well as a FBC analyser and it performs similarly to the Sysmex XN, but with a greater throughput, and suggested improved leukocyte separation, which could be confirmed by further and more extensive studies.

## Understanding the mechanism of natural killer cell exhaustion in multiple myeloma

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**Introduction:**
Multiple myeloma (MM), an arduous haematological malignancy of plasma cells. Immune suppression plays a significant role in myeloma progression. In our previous investigation, a comprehensive analysis of single-cell transcriptomic data from multiple myeloma patient samples revealed a positive correlation between the proportion of exhausted NK cells and disease progression. With further gene-regulatory network analysis, transcription factors associated with NK cell exhaustion were identified.

**Aims:**
Through mechanistic studies targeting these transcription factors, we aim to determine their significance in driving NK cell exhaustion. This study endeavours to validate the in silico results and develop genetically engineered NK cells resistant to exhaustion driven by bone marrow microenvironmental factors of MM patients.

**Methods:**
For functional and mechanistic analysis of drivers of NK cell exhaustion, *in vitro* NK cell exhaustion assays were used. Transcription factors associated with NK cell exhaustion were identified using single-cell RNA sequencing and gene network analysis. Candidate transcription factors were inhibited with pharmacological inhibitors and NK phenotypic changes were monitored in long-term *in vitro* cytotoxicity assays.

**Results:**
Using long-term co-culture of primary, *ex vivo* expanded NK cells and multiple myeloma cancer cell lines, we have established an *in vitro* model of NK cell exhaustion. We assembled a comprehensive single-cell RNAseq dataset of patient-derived samples covering all key stages of multiple myeloma development, from monoclonal gammopathy of undetermined significance (MGUS), smouldering myeloma (SMM), primary myeloma to refractory/relapsed multiple myeloma (RRMM). In this dataset we have found that NK cell exhaustion is present from the earliest stages of disease development (at MGUS) and the frequency of exhausted NK cells increases with disease progression. With gene-network analysis, we have identified over 40 genes, including 10 transcription factors closely associated with NK cell exhaustion.

**Conclusions:**
We have developed an *in vitro* model of NK cell exhaustion that facilitates the detection of exhausted NK cells. Using this model, we aim to identify novel key transcription factors in exhausted NK cells, whose expression can be modulated to reverse their exhausted phenotype.

# DEVELOPMENT OF A HIGH-SENSITIVITY FLOW CYTOMETRY ASSAY FOR THE DETECTION OF GPI-DEFICIENT CLONES IN PAROXYSMAL NOCTURNAL HAEMOGLOBINURIA AND RELATED BONE MARROW FAILURE SYNDROMES

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**Introduction:** Paroxysmal nocturnal haemoglobinuria (PNH) is a haematopoietic stem cell disorder caused by a somatic mutation of the PIG-A gene. Progeny of mutated cells have either a reduced expression or absence of glycosylphosphatidylinositol (GPI), resulting in the reduction or absence of GPI-anchored proteins. The absence of GPI is readily detected by flow cytometry, the gold standards laboratory diagnosis of PNH. Aplastic anaemia (AA) is a bone marrow failure syndrome characterised by pancytopenia and a hypocellular marrow. Approximately 60% of AA patients have a minor GPI-deficient clone at diagnosis. In cases of AA, the identification of a minor GPI-AP deficient clone, >1%, is of clinical significance. Expansion of clones may indicate disease progression and/or the need for intervention. Recent British Society for Haematology guidelines recommend that all patients diagnosed with AA should be tested for the presence of GPI-deficient clones at diagnosis using high-sensitivity flow cytometry. Expert groups, the ICCS and ESSCA published consensus guidelines on the detection of GPI-deficient clones using high-sensitivity flow cytometry. The purpose of this study was to validate a high-sensitivity flow cytometry assay for the detection of GPI-deficient cells, in accordance with these guidelines, enabling the MMUH laboratory to identify and monitor minor GPI-deficient clones.

**Methods:** The development of this high-sensitivity assay was achieved by optimising cytometer settings, determining optimal antibody concentrations required, and the development of sequential gating strategies. Analysis of results was performed using BD FACSDiva software. Sequential gating strategies were developed to isolate populations of interest; single red blood cells, neutrophils and monocytes, and to assess them for the presence or absence of corresponding GPI associated proteins. Cytometer was set up and compensated as per the method outlined by Sutherland *et al.,* (2018). For the validation of optimised PNH assays, spiking studies were performed as per the methods described by Illingworth *et al.,* (2018a). In brief, for both red and white cell assays, the LOB and LOD was determined by assessing 10 normal samples using optimised cytometer setting and antibody concentrations. To verify assay sensitivity (LLOQ) serial dilutions of a known PNH sample and a normal sample were performed, creating a range of GPI-deficient clones of assumed linearity. Serial dilutions were performed in triplicate to assess assay precision.

**Results:** Assay sensitivity (LLOQ) was assessed by performing spiking studies with a known PNH sample. Desired assay sensitivities were observed for the detection of GPI-deficient red cells, 0.01%, neutrophils, 0.03% and monocytes, 0.3%.

**Conclusion:** The aim of the MMUH flow cytometry laboratory is to validate this assay for routine use in place of current methods. Not only is the developed assay capable of assessing minor GPI-deficient clones, as seen in AA and occasionally MDS, but it is also capable of accurately and reliably detecting larger GPI-deficient clones for the diagnosis of haemolytic PNH. Implementation of this assay would allow for the identification and quantitation of minor GPI-deficient clones in patients with AA and MDS, as well as monitoring clonal expansion and potential need for therapeutic intervention.

## QUALITY IMPROVEMENT PROJECT: IMPROVING MORPHOLOGY TEACHING FOR HAEMATOLOGY TRAINEES IN NORTHERN IRELAND

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**Introduction:**
Haematology is a unique specialty that has both clinical and laboratory aspects. Part of training is lab based reporting blood films and bone marrow aspirate/trephines. To complete specialty registrar training it is a requirement to pass the FRCPath examinations. A large part of this exam is morphology based. Given such a large portion of the job and exams consist of morphology and other specialised diagnostic tests I felt it would be useful to introduce regular dedicated sessions to the departments weekly teaching program.

**Plan:**
To improve trainee knowledge and confidence with morphology and lab based tests it was planned to introduce monthly sessions dedicated to morphology and integrated diagnostics to the department teaching programme.

**Do/Study:**
An initial questionnaire was sent to those who regularly attend the weekly teaching (mainly Haematology SpRs, Specialty doctors and Clinical Scientists. A total of 10 people responded to the questionnaire. Results confirmed that there was infrequent formal teaching sessions covering this area (less than once per year) and 100% of respondents felt they would be useful.

**Act:**
As diagnostic Haematology consists of morphology as well as many specialised tests feedback from the initial questionnaire suggested it might be useful to add some teaching on these techniques to the programme. Therefore, a programme was developed to try to include the different areas of the haematology specialised integrated diagnostics.
A regular morphology teaching session at the start of each month.

- January – Case based morphology
- February – combined case based morphology with flow cytometry
- March – Red cell disorders and benign Haematology
- April – combined case based morphology with molecular Haematology
- May – Cased based morphology from the new patient clinic

**Re-evaluate:**
Following the first 5 sessions a repeat questionnaire was sent to those who attended with eight responses. Results showed that 100% of the sessions took place as planned. 100% of attendees found the sessions either useful or extremely useful. 100% wanted these sessions to continue on a regular basis and liked the combined sessions
Other feedback: Some attendees found the overhead project poor quality and some who attended online found the sound was low volume if the speaker moved

**Future:**
Given the positive feedback, the plan for the future is to try to keep these sessions going on a regular occurrence. For improvement of the facilities, a new camera and microphone has been acquired and discussions about acquiring a new projector/screen have been started with managers.

**Conclusion:**
Due to increasing complexity of diagnostic tests within haematology it was felt that improved education was needed to help improve knowledge and confidence in interpreting morphology and other specialised tests. The feedback after these sessions has shown that trainees are becoming more confident in laboratory Haematology. These sessions were also extended to the clinical scientists within the department and feedback has also found the sessions extremely useful in both improving their knowledge of these tests but also seeing the clinical context behind the tests. Given the positive feedback, I plan to continue these sessions regularly within the department's teaching programme.

## A Case Series of Unusual Haemoglobin Variants Detected at from the Specialist Red Cell Laboratory, Belfast City Hospital

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### Introduction

Haemoglobinopathies are disorders of globin chain synthesis. They are spilt into two groups- haemoglobin variants and thalassaemia. Most are caused by mutations in the alpha or beta genes and can result in both qualitative and quantitative defects in globin chain production e.g.structurally abnormal globin chains in sickle cell disease, or reduced globin chains in thalassaemia.
5% of the world's population have haemoglobin mutations. Certain haemoglobinopathies are linked with certain ethnic groups i.e. a high incidence of HbS in Africa and alpha 0 thalassaemia in Asia.
The Red Cell Laboratory Belfast, processes ~1500 haemoglobinopathy samples a year. In 2023, the most significant abnormalities detected were 304 haemoglobin variants and 37 alpha 0 thalassaemia.
There are 35 adults and 19 children currently living in Belfast with a major haemoglobinopathy.

### Laboratory Methods

The Sickle Cell and Thalassaemia Screening Program suggests haemoglobinopathy detection must be confirmed by two methods. The Belfast Trust employs capillary electrophoresis (CE) and Isoelectric Focusing (IEF). The results of both are compared, interpretated and reported together. Samples can be forwarded to Oxford red cell reference laboratory for confirmation. The patient's ethnicity and FBC results are also used to identify haemoglobinopathies.
Here we present a series of unusual haemoglobinopathies detected at the Red Cell Laboratory, Belfast City Hospital

### Case Presentations

Case 1.
A 31 year old Irish female was offered testing after her newborn's heel prick was inconclusive. Her red cell indices were normal. CE detected a 16% peak in the HbD region (a clinically significant Hb variant), however IEF detected 2 variant bands not consistent with HbD. Hb Etobicoke was confirmed by molecular testing. Although Hb Etobicoke is an alpha gene mutation it has no known clinical significance or reproductive implications.
Case 2.
A 31 year old female was investigated as part of her antenatal booking bloods. Family origin questionnaire indicated patient was from Saudi Arabia (high risk area). The patient had a normal Hb and red cell indices. CE identified a peak in the HbS region of 18% but and IEF excluded HbS. The variant detected was not consistent with any common variants. Subsequent molecular testing confirmed the presence of Hb Setif a rare, mildly unstable haemoglobin. In these cases testing of the patient's partner is also offered to gauge prenatal risk. In this case, no variants were detected in the father.
Case 3
Routine FBC testing of a 22 year old Asian female detected microcytosis (Hb 127, MCH 20 pg). No abnormal peaks were detected on CE or IEF but the sample was forwarded for molecular testing due to high risk for alpha 0 thalassaemia. Although alpha 0 thalassaemia was suggested, εγδβ+ thalassaemia was detected. A deletion of a whole region of the beta globin gene, which affects the expression of beta, gamma and delta globin. This is the first time that this mutation has been described therefore effects can only be predicated to result in beta thalassemia. Further Actions – screening should be offered to any partner to assess the risks to a child. Family members should also be considered for testing.

# VALIDATION AND PRELIMINARY IMPLEMENTATION OF SHORT TANDEM REPEAT (STR) CHIMERISM STATUS TESTING IN PATIENTS TREATED WITH ALLOGENIC HAEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT)

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## Introduction

Allo-HSCT has become a well-established, effective method for the treatment of several malignant and non-malignant haematological malignancies. Relapse is the main cause of patient death following allo-HSCT. An increase in recipient alleles is usually indicative of a relapse of the patient's malignant cells, and therefore, the likelihood of relapse can be predicted following two successive increases in recipient chimerism within post-transplant whole blood or bone marrow samples. Currently, the method of choice for monitoring chimerism is STR PCR, a technique capable of determining the percentage of both donor and recipient cells. Their increased polymorphism means there is a high probability that a panel of STR markers will enable the differentiation of individual genomes. BHSCT currently has no in-house chimerism testing in place for HSCT patients.

## Materials & Methods

Using the PowerPlex® 16 STR system, we sort to establish chimerism analysis on NEQAS and retrospective PB samples, as well as PB, CD3+ and CD15+ cell subsets on prospective samples; as part of a validation of the chimerism testing method employed by the referral laboratories, with the aim of replicating, and subsequently introducing this method into routine diagnostic testing.

## Results

In this study, we have confirmed that the wide range of sensitivity, in addition to the flexibility of the protocol ensures that chimerism analysis in patient samples with minimal DNA material can be performed. Using the PowerPlex® 16 HS protocol, full STR profiles were generated for all samples analysed. Additionally, during analysis, we were able to detect both fully informative and informative markers in the sample cohort. We urther demosntrate that, the use of more than 3 informative markers increases the quality of chimerism analysis, and highlighted that, reducing the reaction volume is a viable option for chimerism analysis in patients with minimal DNA concentration or template volume, albeit with extreme care. Most significantly, we successfully generated full STR profiles from CD3+ and CD15+ DNA extracted from PB.

## Conclusions

With continuous training on analysis, chimerism monitoring assessments will be implemented and performed on a weekly basis in our department using the quantitative fluorescence-based STR-PCR with capillary electrophoresis for PCR product resolution presented herein. Chimerism analysis will be performed during engraftment in PB, CD3+ T-cell subsets and CD15+ myeloid subsets, in line with published guidelines, to aid clinicians to implement clinical interventions to ensure optimal patient management across the province as a whole.

## DON'T HOLD YOUR BREATH TO DIAGNOSE MULTIPLE MYELOMA

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Multiple myeloma is a prevalent plasma cell malignancy primarily affecting bones, but with the potential to infiltrate soft tissues, including the airway, leading to significant respiratory compromise. The systemic nature of the disease underscores the need for prompt diagnosis and comprehensive treatment.

We present the case of a 78-year-old male with a background of atrial fibrillation, bronchiectasis, ischemic heart disease (IHD) with prior percutaneous coronary intervention (PCI), and previously treated prostate cancer. The patient presented in February 2023 with dysphagia, food regurgitation, hoarseness, and unintentional weight loss over a six-month period. A CT neck-thorax-abdomen-pelvis (NTAP) scan identified a 4.7 cm soft tissue mass in the right larynx with invasion into adjacent soft tissues and significant airway narrowing. This was accompanied by extensive lytic skeletal metastases. Interestingly, a biopsy of the left supraglottic region revealed only mild cytological atypia without high-grade dysplasia or malignancy. In contrast, core biopsy samples from the neck and left lateral chest wall showed diffuse sheets of CD138-positive plasmacytoid cells, negative for cytokeratin and S100, confirming plasma cell infiltration.

Bone marrow biopsy demonstrated 60% plasma cell infiltration, consistent with multiple myeloma, with kappa light chain restriction. Plasma cells comprised of 8% of the aspirate. Laboratory results showed β2-microglobulin at 4.6 mg/L and albumin at 23 g/L, indicating Revised International Staging System (R-ISS) stage II myeloma. Serum immunofixation confirmed IgG kappa paraproteinemia at 32 g/L.

During hospitalization, the patient developed acute respiratory distress necessitating intubation and transfer to the intensive care unit (ICU). Following a prolonged ICU stay, a tracheostomy was performed for prolonged intubation. The patient was then transferred to St. James Hospital, where he completed a course of radiotherapy (25 Gray in 5 fractions) in March 2023. Subsequently, he was initiated on D-VTD (Daratumumab, Bortezomib, Thalidomide, and Dexamethasone), completing four cycles by July 2023. Response to treatment was mild, with interval CT scans showing only slight reduction in tumor size. However, new soft tissue growth was noted in the right mandibular body (3.3 x 3.6 x 3 cm) in June 2023, for which the patient received additional radiotherapy (8 Gy in a single fraction) to the right mandible in July.

In August 2023, the patient commenced a new regimen of Ixazomib, Lenalidomide, and Dexamethasone, completing three cycles. Repeat bone marrow biopsy in September 2023 showed plasma cell infiltration of less than 5%. However, chemotherapy was paused due to frailty and episodes of diarrhea. Follow-up CT scans demonstrated stability of both the supraglottic tumor and mandibular soft tissue swelling.

This case underscores the complexity of managing refractory multiple myeloma with airway involvement in a frail patient. Despite discontinuation of chemotherapy, the patient remained clinically stable with a multidisciplinary approach to care, highlighting the importance of personalized management strategies in advanced multiple myeloma.

## Analysis of T cell subsets in the first-line treatment of chronic lymphocytic leukaemia (CLL) using the Venetoclax-Obinutuzumab (VO) fixed duration regimen

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**Introduction:**
Following the outcome of the CLL14 trial, the fixed-duration Venetoclax-Obinutuzumab (VO) regimen was made available through the NCCP on March 1st 2022 for the first line treatment of standard risk CLL. Since then, this regimen has gained popularity due to the high rates of undetectable MRD, manageable safety profile and finite duration. However, given that CLL is an inherently immunosuppressive condition in an elderly cohort, T cell suppression is of concern.
We assessed the effect of VO on total lymphocyte counts, T cell subsets and the incidence of Pneumocystis Jirovecii (PJ), varicella zoster (VZ) and respiratory viral infections. We also recorded the use of infection prophylaxis.

**Methods:**
All patients who are undergoing or have completed the VO regimen from January 1st 2023 to August 1st 2024 were included. A retrospective chart review captured the following: demographics, high risk molecular data (17p deletion and TP53 mutations), nadir lymphocyte counts, median quarterly nadir CD4+ and CD8+ counts, the use of co-trimoxazole and valaciclovir prophylaxis and the incidence of VZV, PJP, SARS-CoV-2, influenza A+B, respiratory syncytial virus, parainfluenza, human metapneumovirus and adenovirus infections. The mode of VO delivery was also recorded i.e. as a rapid ramp-up (RR) or by the standard dose escalation (SDE) route. Every lymphocyte count below $1x10^9$/L was correlated with active infection and the administration of Obinutuzumab within 72 hours.

**Results:**
15 patients were included: 5 female, 10 male. Median age: 69 years on commencement of VO. 10/15 (67%) were delivered by the RR route and 5/15 (33%) by SDE. None of the cohort had 17p deletion or TP53 mutations.
The lymphocyte nadirs ranged from 0.1-1.4 x $10^9$/L (RR: 0.1-0.5, SDE: 0.4-1.4), 10/15 (66%) occurred within 72 hours of Obinutuzumab, 2/15 (13%) had infections, 2/15 (13%) had a rash and 1/15 (6%) was unaccounted for. The lymphocyte count returned to >0.5 in all cases within 7 days regardless of aetiology.
The median nadir CD4 counts (cells/$mm^3$) for each quarter were: 444 (range 75-1361), 627 (range 196-1349), 1084 (range 466-1918) and 420 (range 402-1281) for quarters 1-4 respectively. The median nadir CD8 counts (cells/$mm^3$) for each quarter were: 235 (range 55-629), 224 (range 55-1187), 448 (range 227-1678) and 286 (range 138-349) for quarters 1-4 respectively. There was no difference in the RR and SDE groups in terms of quarterly CD4 and CD8 counts.
10/15 (67%) and 14/15 (93%) were on co-trimoxazole and valaciclovir prophylaxis respectively. 3/15 (20%) of patients contracted SARS-CoV-2, none required ICU admission. There were no cases of PJP or VZV infections.

**Conclusions:**
The findings of this study suggest that VO does not lead to T cell depletion – the quarterly CD4 and CD8 results demonstrate T cell reconstitution as treatment progresses. Lymphocyte nadirs were transiently lower in the RR group likely due to the rapid debulking caused by full-dose Venetolax prior to starting Obinutuzumab. None of the patients contracted PJP or VZV infections irrespective of being on prophylaxis. Interestingly, all the covid infections occurred in quarters 1 and 2 of treatment.
This study suggests that valaciclovir and co-trimoxazole prophylaxis may not be required in combination the VO regimen. Larger studies are required to confirm our findings.

## AN AUDIT OF DIAGNOSTIC RADIOLOGICAL INVESTIGATION FOR NEWLY DIAGNOSED PLASMA CELL DISORDERS AT AN IRISH TERTIARY HOSPITAL

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### Introduction

The International Myeloma Working Group (IMWG) recommends using cross-sectional imaging in the initial diagnostic evaluation of patients with multiple myeloma (MM) and smoldering multiple myeloma (sMM). Current recommendations for suitable imaging modalities are whole-body low-dose CT, whole-body MRI, or PET-CT, depending on availability and resources. We carried out an audit of imaging techniques selected for initial diagnostic investigation of MM and sMM in a tertiary Irish hospital.

### Methods

A retrospective audit of diagnostic imaging modalities for patients with newly diagnosed MM and sMM attending a tertiary Irish hospital over a 2-year period (2021-2023). Data extracted from patient records included date of confirmed diagnosis, primary imaging modality at diagnosis, interval between diagnosis and completion of imaging, and the presence or absence of MM-related findings on diagnostic imaging.

### Results

68 patients were identified with a new diagnosis of MM (n=55), sMM (n=10), and solitary plasmacytoma (n=3) over the study period. The most frequently utilised diagnostic imaging modality in this cohort was PET-CT with 32% (n=22) of patients receiving this test. 18% of patients had a whole-body MRI and 12% underwent a CT-TAP. 18% of the cohort had x-ray based skeletal survey (SS) as a baseline diagnostic scan. 20.6% (n=14) of patients did not have initial whole-body imaging, 3 of whom had a diagnosis of sMM (21%) and 1 with a diagnosis of solitary plasmacytoma (7%). In patients who received diagnostic whole-body imaging (n=54), 68.5% (n=37) had radiological features consistent with a diagnosis of multiple myeloma. One of the patients with a sMM diagnosis who received baseline imaging had radiological findings of MM, thus resulting in a revised diagnosis to active disease. In patients with solitary plasmacytoma (n=3), skeletal survey was the primary imaging modality (n=2). The average time between initial diagnosis and whole-body imaging was 51 days. Patients received CT-TAP at an average interval of 14.6 days, whereas average duration between diagnosis and PET-CT was 46 days and 69 days for whole-body MRI

### Conclusion

This audit outlines the diagnostic radiological investigation of patients with newly diagnosed MM, sMM, and plasmacytoma over a 2-year period at an Irish tertiary hospital. This time period follows the publication of the IMWG consensus recommendations on the optimal use of imaging for plasma cell disorders.[1] Our findings highlight the variability in diagnostic imaging modalities utilised for this cohort and associated time intervals. Whole-body MRI had the longest delay between diagnosis and imaging. The absence of baseline radiological investigation in 20% of patients is a significant finding, given the importance of accurate detection of bone and bone marrow lesions. Furthermore, 30% of patients with sMM did not receive whole-body imaging, which is of particular significance, given the diagnostic, prognostic and therapeutic implications of MM radiological features in this cohort. Whole-body CT +/- PET and MRI modalities provide significantly superior sensitivity compared with x-ray. In our cohort, 18% of patients underwent SS as their diagnostic imaging modality, possibly reflecting barriers to timely access of recommended radiological investigations.

## *JAK2*$^{V617F}$ ALLELE BURDEN ASSESSMENT IN MYELOPROLIFERATIVE NEOPLASMS

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Introduction: Myeloproliferative Neoplasms (MPNs) encompass blood disorders marked by excessive myeloid lineage cell proliferation, namely essential thrombocythaemia, polycythaemia vera, and primary myelofibrosis. MPN patients hence face heightened risks of haemorrhages and thromboses, which may be preventable with early detection and appropriate treatment. Current treatment pathways include ruxolitinib, interferon, hydroxyurea and anti-coagulants. Additionally, MPNs may progress to acute myeloid leukaemia (AML), shortening patients' lifespans and posing challenges for treatment due to their non-curative nature. The *JAK2*$^{V617F}$ mutation, prevalent in a majority of MPN cases, drives the cell proliferation seen in these disorders through the associated gain-of-function and dysregulation of the *JAK2/STAT5* pathway. It currently serves as a diagnostic biomarker, aiding in MPN diagnosis alongside other clinical features as detailed in WHO guidance. Recent research suggests its potential as a prognostic indicator, as reductions in its mutational burden have been correlated with symptom control, this study aimed to explore and quantify the impact of treatment on *JAK2*$^{V617F}$ variant allele frequency (VAF).
Materials and Methods: This research was conducted in collaboration with the Belfast Health and Social Care Trust's Regional Molecular Diagnostic Service. DNA was extracted from peripheral blood from patients diagnosed with MPNs. This project was part of a routine service evaluation according to the NHS research policy framework. The *JAK2*$^{V617F}$ VAF was measured in a cohort of 37 MPN patients between 4-50 months post-diagnosis. These patients received either ruxolitnib (n=4), interferon (n=4), hydroxyurea (n=20) or anti-coagulants (n=9). The *JAK2*$^{V617F}$ VAF was quantified using real time Q-PCR. Statistical analyses were performed using Wilcoxon test and $P<0.05$ was accepted to indicate statistical significance.
Results: Patients across the four treatment types had statistically significant differences in blood count analysis when comparing baseline and follow-up; white blood cells, haemoglobin, haematocrit, and platelets all showed a statistically significant decrease in-line with improved blood count control. There was no statistically significant difference in *JAK2*$^{V617F}$ VAF observed between baseline and follow-up in patients receiving anti-coagulants monotherapy, interferon or ruxolitinib. However, the hydroxyurea group had a statistically significant decrease in *JAK2*$^{V617F}$ VAF between baseline and follow-up, with a p value of 0.0240.
Conclusions: *JAK2*$^{V617F}$ VAF has been shown to have variable responses in different treatments, and this is an on-going area of research which currently has shown no prognostic benefit for the treatment pathways of patients. As *JAK2*$^{V617F}$ VAF is linked to risk stratification it should remain a diagnostic biomarker and may be used prognostically if it has significant impact on treatment algorithms, which this study has not deduced. The significant reduction in *JAK2*$^{V617F}$ VAF within the hydroxyurea cohort remains elusive, and as such may present an opportunity for further research, particularly with a sample size larger than this study. However, the *JAK2*$^{V617F}$ VAF has allowed for early detection in patients which is imperative for the prevention of thrombotic events and transformation.

# A novel clinic-pathological subtype of Mantle Cell Lymphoma; the importance of diagnostic Immunoglobulin assessment

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## Introduction

Mantle cell lymphoma (MCL) is a rare, clinically aggressive B-non-Hodgkin lymphoma (B-NHL) characterized by a t(11;14)(q13;q32), which upregulates CCND1. New diagnostic and treatment pathways have led to improved outcomes, which coupled with real world data (RWD) collection help identify clinically relevant biomarkers. We analysed a rare subgroup of patients with inflammatory presentations and polyclonal hypergammaglobulinemia. The assessment of paraprotein incidence/type was performed simultaneously, as little published data is available on this simple disease tracking bio-marker.

## Methods

Consecutive, consented patient attending haematology between 2004-2024 were analysed for demographics, stage, pathology subtype, SPEP, clinical features at presentation, treatment, Overall survival(OS) and Progression Free Survival(PFS). Patients who did not have an SPEP at diagnosis were excluded. Patients' clinical features with hyper-gammaglobulinaemia (IgG >14.96, IgA>2.9, IgM>1.82) gms/L were reviewed in detail and patients with a paraprotein identified.

## Results

54 patients identified and 4 patients without diagnostic SPEP were excluded. The clinical profiles was as follows: Males; n=36 (66%), mean age; 65 (*range 37-90)* years, ECOG3/4; n=17 (31%), Stage IV; n=36 (72%), B symptoms n=19 (38%). The pathology subtypes available on 46 (92%) patients included classical, n=33(72%), blastic, n=8(17%), pleomorphic, n=3(6.5)% and indolent n=2 (4.3%). Nine (18%) were hypergammaglobulinaemic, and detailed clinical features were available on 7. Three had an isolated raised IgA (mean 4.95; *range 4.78-5.05*) with no unusual clinical features or response to treatment. Four patients with generalised hypergammaglobulinaemia; IgG (mean 25.27; *range 18.96-39.03*), IgA (mean 9.67; *range 7.04-12.69*) and IgM (mean 2.99; *range 2.58-3.39*) described a 6-12 month prodrome of myalgia/arthralgia/muscle weakness including PUO (n=2) and 3 had been investigated for connective tissue disorders. Two received chemo-immunotherapy(CIT) resulting in a life threatening clinical flare of symptoms (including AKI with normal urate in 1 patient). Two patients on a clinical trial of first line BTKi had no symptom flare and rapid resolution of systemic symptoms. An IgG paraprotein <4 gms/L was detected in 3(7%) patients, who did not have associated hypergammaglobulinaemia. An IgG paraprotein <4gms was noted in 3 (6%) patients. The median follow up of the cohort was 7.2 years, the OS and PFS at 10 years was 65% and 40%, with no difference noted in the hyper gammaglobulinaemic cohort.

## Discussion

Diagnostics SPEP are carried out in most patients at diagnosis in B-NHL, providing an accessible biomarker. The pathogenesis of polyclonal hypergammaglobulinaemia is unclear, is not a feature of other B-NHLs and may be caused by an interaction between the MCL and host immune system. Isolated hyper-IgA appears to have no clinical consequences, however the patients with pan-hypergammaglobulinaemia had a delayed diagnosis because of the atypical presentation. The two patients treated with CIT experienced severe treatment related toxicity whereas the patients treated with BTKi benefitted from outpatient treatment and immediate symptom resolution, so recognition of pan-hypergammaglobulinaemia is clinically important. Paraproteins can be used to track a minority (6%) of MCL patients non-invasively. Extending the RWD dataset could be a clinically relevant national project.

## Mutational profiling of myelodysplastic syndrome by next generation sequencing and impact of molecular data on risk stratification

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### Introduction

Myelodysplastic syndrome (MDS) is a malignant disorder characterised by ineffective haematopoiesis and is associated with progression to acute myeloid leukaemia. MDS typically presents with cytopenias on routine blood testing. However, diagnosis relies on the identification of dysplastic changes within the bone marrow. Additional laboratory testing by karyotyping and next generation sequencing (NGS) provide information to aid in classification and prognostication of patients. Our aim was to investigate the molecular patterns present in MDS sub-types and determine the impact of molecular data on risk classification.

### Method

A cohort of 149 patients with a diagnosis of MDS according to the WHO diagnostic criteria were included in this study. Classification of MDS patients was performed according to the WHO-2022 criteria. Total genomic DNA from bone marrow or peripheral blood was sequenced using a Myeloid NGS assay covering common sequence, structural and copy number variations in genes involved in myeloid neoplasms. Alignment, de-duplication and variant calling was performed using the MyeloidTS_WF bioinformatics pipeline v1.1.

### Results

Of the 149 MDS patients included in the study the majority were classified as MDS with low blasts (MDS-LB) (43%). The remaining patients were MDS with low blasts and *SF3B1* (MDS-*SF3B1*) (15%), MDS with increased blasts 2 (MDS-IB2) (15%), MDS with increased blasts 1 (MDS-IB1) (11%), MDS with fibrosis (MDS-f) (5%), MDS with biallelic *TP53* inactivation (MDS-bi*TP53*) (5%), MDS hypoplastic (MDS-h) (3%) and MDS with isolated 5q deletion (MDS-5q) (3%). Mutational burden differed by MDS subtype with a higher number of mutated genes per patient associated with increased blast count and fibrosis, MDS-IB2 (2.77) and MDS-f (2.88) compared to MDS-LB (1.73). The genes in which variants most often occurred in our MDS cohort were TET2 (26%), ASXL1 (19%) and SRSF2 (19%). However, the prevalence of specific mutated genes differed by MDS sub-types with high risk MDS-IB2 primarily associated with variants in the RUNX1 (46%) and ASXL1 (32%) genes, whilst the predominant variants in low risk MDS-LB were in the TET2 (28%) and U2AF1 (22%) genes. Finally, risk classification was performed for a subset of 88 patients by both IPSS-R and IPSS-M. Of these, 60% had the same classification with both risk calculators. Of the remaining 40% whose risk score changed, 30% moved to a higher risk score and 10% moved to a lower risk score by IPSS-M vs IPSS-R.

### Discussion

This study compared the mutational landscape of MDS sub-types assessed by NGS and evaluated the impact of including molecular data when calculating risk. We have identified changes in the prevalence of specific mutations in each MDS sub-type with higher levels of RUNX1 and ASXL1 in high risk sub-types. However, while the prevalence differed the overall mutational profile was similar between MDS sub-types. Low numbers in some of the MDS sub-types limits the efficacy of this data to draw conclusions on the molecular profile of these specific sub-types. Inclusion of molecular data when calculating a patients risk group resulted in a change of classification for 40% of patients. These data highlight the importance of including molecular data for risk stratification in MDS.

# PRIMARY INTRAOCULAR LYMPHOMA – A RARE CLINICAL CHALLENGE IN HIGH-GRADE LYMPHOMA

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## Introduction

Primary intra-ocular lymphoma (PIOL) is a rare form of primary CNS lymphoma with an estimated 50 annual cases occurring in the United States[1,2]. PIOLs arise in the intraocular compartment without brain involvement. The majority are high-grade diffuse large B cell lymphoma of the activated-B-cell type. Mutations in MYD88 are frequent[3]. PIOL can result in permanent visual impairment and has a 60-90% risk of CNS relapse which represents the major cause of death[4]. Multi-centre prospective evidence is lacking, with expert consensus based on retrospective series. Optimal treatment involves systemic intensive CNS-directed chemotherapy with consideration of consolidative autologous stem cell transplantation (autoSCT) in fit individuals, with or without local intra-vitreal treatments or ocular radiotherapy, to minimise the risk of CNS relapse and improve prognosis[1,2].

## Methods

Patients treated for PIOL in St Vincent's University Hospital, in conjunction with the Royal Victoria Eye and Ear Hospital, between 2017 and 2024 were retrospectively reviewed. Data was collected from the electronic and paper records.

## Results

Five patients were included in the cohort, 3 female and 2 male. The median age at diagnosis was 74 years (range 66-82). Histopathological diagnosis was confirmed by vitrectomy in all cases. Staging included MRI-Brain/Orbits and PET-CT to exclude systemic disease. MYD88 mutation status was available for n=3 at diagnosis, with MYD88 p.L265p mutation detected by PCR in all three cases. The median LDH at diagnosis was 221IU/ml (184-260). Vitreous IL-10 and IL-6 levels at diagnosis were available in n=4. The median IL-10 level was 582pg/ml (399-2976) and all 4 cases had a positive IL-10/IL-6 ratio >1, median ratio 19.8 (4.5-58.8), consistent with PIOL.
Four patients (80%) received intra-ocular therapy which consisted of intra-vitreal rituximab +/- intra-vitreal methotrexate.
Two patients (40%) received systemic chemotherapy with the MATRIX (Methotrexate, cytarabine, thiotepa, rituximab) regimen. Chemotherapy was stopped after 3 cycles in one patient due to treatment-related toxicity with an ICU admission for neutropenic sepsis. The other patient completed a planned 4 cycles of MATRIX however treatment was complicated by two re-admissions for neutropenic fevers. Due to treatment-related morbidity neither patient progressed to a previously planned consolidative autoSCT.
Two patients (40%) completed consolidative ocular radiotherapy with a further patient referred for same. Response was monitored with ophthalmology follow up, clinical assessment and imaging which included MRI-B/Orbits +/- PET-CT. The median duration of follow up was 18 months (6-80).
Three patients (60%) relapsed at a median time to relapse of 18 months (5-78). Two (40%) had localised intra-ocular relapse without brain involvement. One patient was treated with intra-vitreal rituximab/methotrexate with a plan for addition of temzolomide. The other is planned for intra-vitreal rituximab/methotrexate and MDT discussion regarding further therapy. One patient (20%) experienced CNS relapse with multi-focal frontal lobe involvement and was treated with palliative radiotherapy.

## Conclusion

PIOL represents a unique clinical challenge in high-grade lymphoma with a requirement for multi-disciplinary specialty coordination including ophthalmology, haematology, radiology and pathology. Local ocular treatment improves visual symptoms but doesn't mitigate the risk of CNS relapse. Systemic CNS-directed chemotherapy is intensive and is optimal in fit patients.

## TESTING TUMOUR GROWTH, DRUG RESPONSIVENESS AND SYSTEMIC DISSEMINATION IN A PATIENT-CENTRIC CHICK EMBRYO MODEL OF MULTIPLE MYELOMA

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**Introduction:** Multiple myeloma (MM) is an incurable malignancy, featuring uncontrolled proliferation of plasma B cells in the bone marrow (BM). ~400 individuals are diagnosed with MM annually in Ireland, and it accounts for 10-15% of all haematological malignancies. In the era of immunotherapies, novel immunocompetent models are urgently required to reproduce disease. This project aims to develop and refine a non-rodent MM xenograft model in the immunocompetent chick embryo chorioallantoic membrane (CAM) system, validating it with a clinically-relevant selection of MM therapeutics, assessing the impact of stromal cell support on plasma cell drug responsiveness, and quantifying systemic dissemination in end organs. Alongside planned immune characterization, this will act as a valuable preclinical tool to complement traditional mouse xenograft studies of MM.

**Materials and Methods:** Fertilised hen eggs were incubated at 37$^{o}$C on Embryonic Development Day (EDD) 0. On EDD3, albumin was withdrawn, and a dorsal window was exposed and re-covered with semi-permeable tape. On EDD9, human MM cell lines +/- HS5 stromal cells or CD138+/- plasma cells derived from patient bone marrow biopsies were implanted onto the CAM. Following xenograft growth, Bortezomib and Lenalidomide (or vehicle), were topically applied daily. On EDD16, tumour xenografts and their surrounding CAM were imaged, excised and immunohistochemically stained for the plasma cell marker CD138. The slides were scanned using a high-power digital scanner at 40X (Glissando Objective Imaging). Tumour burden was quantified using the HALO-AI (Indica Labs) multiplex IHC platform. Genomic DNA was isolated from the chick liver, brain and heart, and qPCR performed to detect human-specific Alu sequences of systemically-disseminated plasma cells.

**Results:** Xenograft tumours were successfully generated in the CAM model with two conditions. Matrigel was the most effective matrix, yielding highly-vascularized, macroscopically-visible tumours from high-risk cell lines JJN3 and KMS18 (n=44/50). Inoculation of 1x10^6 cells consistently produced tumours measuring ~5x5x3mm (mean) in successful JJN3 replicates, and larger (10x10x4mm) KMS18 tumours. Gelatin-rich haemostatic film supported xenografts of standard-risk cell lines RPMI8226 and U266 (n=20/25), but resulted in inferior vasculature and fewer live cells across all four cell lines. MM tumour growth was confirmed by Haematoxylin and Eosin staining and CD138+ immunohistochemistry. Notably, Bortezomib and Lenalidomide treatment significantly reduced JJN3 and KMS18 tumour size and CD138+ plasma cell infiltration. Digital quantification of CD138+ cell staining in JJN3 and KMS18 xenografts revealed a 71% reduction between vehicle controls and those treated twice with 0.3mg Bortezomib (n=4). Similarly, control KMS18 xenografts versus those treated with a combination of Bortezomib (2.4mg) and Lenalidomide (0.06mg) showed a 91% decrease in CD138+ cells. Finally, MM patient-derived xenografts were successfully grown using cell numbers as low as $2.24x10^5$-$5x10^5$ cells per implant.

**Conclusions:** The MM CAM xenograft model successfully replicates MM growth and recapitulates sensitivity to currently-used MM patient therapies, suggesting future use as a cheap, effective and speedy non-rodent alternative for preclinical studies. At time of abstract writing, the systemic homing of MM cells from primary tumour site to organs is currently being interrogated under drug-naïve and drug-treated conditions through qPCR.

## NOVEL DRUG COMBINATION STRATEGIES FOR CHRONIC LYMPHOCYTIC LEUKAEMIA

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### Introduction

Chronic lymphocytic leukaemia (CLL) is an incurable B-cell malignancy that accounts for over one third of all leukaemia in the developed world, with Ireland having one of the highest incidence rates. Despite the success of targeted therapies in recent years, the occurrence of resistance and off-target effects, as well as the low complete response rate achieved by these drugs, calls for the development of new combination treatments. This study investigates the therapeutic potential of the B-cell receptor signalling (BCR) pathway inhibitor, ibrutinib, in combination with standard and novel microtubule targeting agents (MTAs) in both cell lines and ex vivo CLL cells. CLL cells are characterized by cytoskeletal abnormalities and tubulin is tightly associated with BCR-mediated signalling molecules, suggesting an enhancement of the effects of these agents in combination with the potential of broadening therapeutic alternatives in CLL.

### Methods

IC50 values and the cytotoxic effect of single agent ibrutinib and MTAs, vincristine, colchicine, and the novel agent PBOX-15, were determined using MTT proliferation assays on EHEB and I83-E95 CLL cell lines. Drug-induced modulation of the cell cycle was assessed by flow cytometry following propidium iodide staining. The levels of apoptosis induced by these agents individually and in combination was determined by annexin-V/propidium iodide staining and flow cytometry in cell lines and patient derived CLL cells.

### Results

CLL cell lines and patient samples displayed sensitivity to ibrutinib, vincristine, colchicine and PBOX-15. The ibrutinib/vincristine and ibrutinib/PBOX-15 combination treatments resulted in greater apoptosis in comparison to the respective single agents at all concentrations and treatment durations in CLL cell lines. Enhanced induction of apoptosis in ex vivo CLL cells was observed following treatment with ibrutinib/vincristine combination treatment compared to treatment with single agents alone.

### Conclusion

This work demonstrates that the use of ibrutinib in combination with microtubule targeting agents may show promise as a novel treatment strategy in CLL.

## Investigating metabolic dynamics and BCL-2 dependency in Multiple Myeloma: Unveiling New Therapeutic Targets

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### BACKGROUND

Multiple myeloma (MM) is a blood cancer marked by abnormal plasma cell growth in the bone marrow (BM). Despite therapeutic advancements, managing MM remains challenging due to its heterogeneity, recurrence, and treatment resistance. The survival and proliferation of MM cells critically depend on BCL-2 family proteins, which enable these cells to evade programmed cell death, thereby driving disease progression and therapeutic resistance. Alongside this resistance to apoptosis, the metabolic phenotype in multiple myeloma is highly heterogeneous, characterised by diverse alterations in energy production pathways, metabolic dependencies, and nutrient utilization, reflecting the tumour's adaptability and resistance mechanisms. Therefore, cell death mechanisms and metabolic processes are pivotal in MM progression, sustaining MM cell survival in the BM milieu. Our aim is to test if interaction between MM and bone marrow (BM) fibroblasts alters the metabolic phenotype or the apoptotic dependence. With a goal to understand unique vulnerabilities for innovative therapeutic interventions for MM patients.

### METHODS

To investigate the metabolic dependencies and vulnerabilities of MM patient samples, we utilised SCENITH profiling to assess single-cell metabolism. This innovative flow cytometry-based technology uses protein translation as a functional readout of metabolism, with 2-deoxy-D-glucose (2DG) applied to inhibit glycolysis and oligomycin to inhibit oxidative phosphorylation (OXPHOS). To further examine how the bone marrow microenvironment influences the metabolic profile of MM, we co-cultured MM cell lines (SK-MM2, KMS27, MM1S, and H929) with bone marrow stromal cells (BMSCs) and performed Seahorse assays to measure cellular bioenergetics. Using the Seahorse XFe96 analyser, we evaluated two critical aspects of cellular metabolism: the glycolytic rate, indicated by extracellular acidification rate (ECAR), and mitochondrial respiration, indicated by oxygen consumption rate (OCR).

### RESULTS AND CONCLUSION

Our observations revealed that MM cell lines with different anti-apoptotic dependencies also exhibited distinct metabolic profiles. Specifically, BCL-2-dependent cell lines (SK-MM-2 and KMS27) displayed reduced glycolysis, mitochondrial mass, and mitochondrial potential compared to MCL-1-dependent cell lines (H929 and MM1S). Interestingly, after co-culturing these cells with BM fibroblasts, we observed that the bone marrow environment promoted increased glycolytic activity and preserved mitochondrial function in BCL-2-dependent cell lines compared to MCL-1-dependent ones. Furthermore, we observed that MCL-1-dependent cell lines acquire BCL-2 sensitivity after co-culture with bone marrow fibroblasts. We are currently trying to understand the cell line selective nature of the microenvironment. Furthermore, using the SCENITH assay on plasma cells from MM patients, we were able to optimise a rapid metabolic profiling *ex vivo*. The results showed that primary samples reliant on BCL-2 for survival were more susceptible to oligomycin inhibition leading us to hypothesise a possible link between oxidative phosphorylation (OXPHOS) reliance and BCL-2 dependency within MM cells. Moving forward, we plan to investigate the impact of BM microenvironment on MM cells and to understand the metabolic pathways linked to BCL-2 dependency. Our goal is to harness the metabolic pathways in conjunction with BH3 mimetics for more effective treatments for relapsed MM patients.

## THERAPY-RELATED B-LYMPHOBLASTIC LEUKAEMIA SECONDARY TO TREATMENT OF MULTIPLE MYELOMA - A CASE SERIES

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### Introduction

New therapeutic options for the treatment of multiple myeloma (MM) continue to confer improved outcomes and prolonged remission rates, but are associated with the development of secondary primary malignancies (SPMs). The majority of SPMs in MM are secondary myeloid neoplasms. Therapy-related acute lymphoblastic leukaemia (t-ALL) is emerging as a distinct clinical entity in recent years, and is reported to represent 3-9% of all adult ALL cases. We report three patients with therapy related-B-cell ALL in the setting of treatment for MM.

### Case 1

A 58 year old gentleman attended ENT outpatients with a 6 week history of nasal congestion and muffled speech. Clinical examination revealed a large mass arising from the nasopharynx. Histological examination demonstrated a solitary extramedullary plasmacytoma which was treated with radiotherapy. 6 months later, repeat PET scan showed new extensively metabolically active disease in the long bones and liver. These were confirmed as plasmacytoid lesions and he received 4 cycles of CyBorD, followed by VRD and autologous stem cell transplant, with bortezomib/lenalidomide maintenance. 6 years after initial diagnosis, he presented with a new pancytopenia and 26% B-lymphoblasts on immunophenotyping. Plasma cells were <5%. The patient was commenced on treatment with UKALL 60 protocol, followed by allogeneic SCT. The patient continued to progress with splenic and liver plasmacytomas. He was commenced on Daratumumab monotherapy, but in light of his frailty, was made palliative and discharged to hospice care.

### Case 2

A 57 year old female was diagnosed with IgG Kappa MM following a compression fracture of L1 vertebra and widespread lytic disease. Her treatment included local radiotherapy and 4 cycles of CyBorD, followed by consolidation with autologous SCT and lenalidomide maintenance. 5 years later, bloods revealed pancytopenia with 30% blasts in peripheral blood. Bone marrow aspirate immunophenotyping was consistent with pre-B acute lymphoblastic leukaemia. Cytogenetic analysis revealed a complex karyotype; FISH was negative for t(9;22). She was commenced on induction therapy with UKALL protocol. Her treatment course was complicated by episodes of sepsis and development of a perianal abscess. After repeat admissions with sepsis, her care was redirected to palliative measures.

### Case 3

A 69 year old male patient was known to the Haematology department for 6 years with a diagnosis of IgG Kappa MM. Previous treatment consisted of CyBorD followed by autologous SCT, 4 cycles of consolidation with RVD, and maintenance Lenalidomide. Routine bloods revealed an acutely raised white cell count >100 with thrombocytopenia. An urgent bone marrow biopsy revealed >95% blasts; immunophenotyping was consistent with B-cell acute lymphoblastic leukaemia. Cytogenetic studies reported a mutated TP53, and deletions of 9q34 and 22q11. BCR-ABL rearrangement was not detected. The patient was admitted to the ward and received induction with Hyper-CVAD protocol. This was tolerated well, and a bone marrow at the end of treatment demonstrated morphological remission. The patient is post five cycles of HyperCVAD and remains MRD negative.

### Conclusion

B-lymphoblastic leukaemias are increasingly recognised as a consequence of cytotoxic chemotherapy. Larger studies are required to further characterise the biology of t-ALL, its development and treatment strategies.

**Current Trends In Veno-Occlusive disease In Adult Allogeneic Stem Cell Transplant Recipients**

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**Introduction**:

Veno-occlusive disease or Sinusoidal obstruction syndrome (VOD/SOS) is a rare but potentially fatal complication of allogeneic stem cell transplantation (alloSCT) with an estimated incidence of 3-5% in adults. Sinusoidal endothelial injury with subsequent obstruction and post-sinusoidal portal hypertension leads to a clinical syndrome of hyper-bilirubinaemia, hepatomegaly, ascites and weight gain. Risk factors include heavy pre-treatment, prior exposure to Gemtuzumab or Inotuzumab ozogamycin (GO/IO) and myeloablative (MAC) conditioning regimens. The mortality of severe VOD/SOS is high (up to 80%). Defibrotide is an oligonucleotide mixture purified from porcine intestinal mucosa that improves survival in severe VOD/SOS when initiated early. This agent however is costly with a 14-day course for a 70kg patient priced at €66,500. We sought to examine our VOD/SOS epidemiology and outcomes in recent years, noting that GO received Irish reimbursement in November 2020.

**Methods:**

We conducted a retrospective review of patients treated with Defibrotide for VOD/SOS at the National Adult Stem Cell Transplant Unit between January 2021 and June 2024. Patients were identified by interrogating the electronic patient record (EPR) for defibrotide exposure. We used the EBMT criteria for diagnosis and severity scoring. Total alloSCT numbers were extracted from our EBMT dataset.

**Results:**

Sixteen patients were initially identified as defibrotide recipients: 14 met EBMT diagnostic criteria for VOD/SOS, while 2 were diagnosed on convincing clinical grounds.

The majority (94%) of VOD/SOS occurred in patients with myeloid disease: AML (n=12), MDS/PNH (n=1), CML (n=1), proliferative CMML (n=1). The remaining patient had T-LBL. 14 patients received a MAC alloSCT, 1 a sequential conditioning regimen and 1 a reduced-intensity regimen.

For patients with acute leukaemia, the median number of prior intensive chemotherapy cycles was 3 (range 1-7). This included 2 patients who had previously received alloSCT. 5 patients had received GO. 6 patients had received Midostaurin - 5 of these 6 patients had received combination Midostaurin and GO. The single patient with CML had received 3 tyrosine kinase inhibitors.

The median day of VOD/SOS onset was D+23 (range 5-44D). 11 patients developed “very severe” VOD/SOS, 7 of whom were transferred to ICU. 4 patients died resulting in a mortality rate of 25%. The median duration of defibrotide treatment was 20 days (range 8-94d).

The incidence of VOD/SOS in our adult alloSCT population for this period was 5%. While an increased risk of VOD/SOS following midostaurin has not to date been reported, we specifically examined the incidence of VOD/SOS in FLT3-mutated alloSCT recipients and found this to be 16%.

**Conclusion:**

Our 5% incidence of VOD/SOS is comparable to international figures. With early clinical suspicion and prompt initiation of defibrotide, we report a mortality rate of 25%. We observe a higher incidence of VOD/SOS in FLT3-mutated patients and a possible safety signal that co-administration of both GO and midostaurin may increase risk. At this time there is no published data to support these agents in combination, particularly in patients proceeding to alloSCT but studies are ongoing. We favour avoiding the combination where possible and adopt increased vigilance during alloSCT for these patients.

# GENOMIC INSIGHTS FOLLOWING NEXT GENERATION SEQUENCING OF EXTRAMEDULLARY MYELOMA: DIAGNOSTIC AND THERAPEUTIC IMPLICATIONS

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## Introduction

Multiple myeloma(MM) is characterised by clonal proliferation of plasma cells in the bone marrow(BM). Extramedullary disease(EMD) is an aggressive manifestation of MM, characterised by the ability of a malignant clone and/or subclone to develop and thrive independent of the BM microenvironment.The incidence of EMD has markedly increased in recent years, likely reflecting the longer survival of MM patients due to therapeutic advances and the emergence of treatment-resistant EMD at disease relapse.
EMD presence at diagnosis or relapse is associated with poor treatment response and significantly reduced overall survival(OS). This suboptimal therapeutic response extends to advanced cellular therapies, where this cohort have shorter progression free survival and OS following CAR-T therapy, with EMD being the primary site of relapse. Notably, a significant proportion of patients without EMD develop relapse at extramedullary sites post-CAR-T. Thus, EMD is becoming an increasingly relevant clinical issue.The genomic mechanisms driving EMD development and therapeutic resistance are poorly understood, but pivotal for targeted treatment development. This study aimed to identify genomic drivers of EMD, performing Whole Genome Sequencing(WGS) on paired sequential samples (BM & EMD) at diagnosis and relapse.

## Methods

Biopsy samples from BM and EMD sites of 8 patients were obtained and underwent DNA extraction. EMD sites included intracranial soft tissue lesions, colon, mesentery, pleural effusion, and skin. CD138 staining was used to mark involved tissue for tumour selection and subsequent macrodissection from formalin-fixed-paraffin-embedded tissue. DNA was sequenced on an IlluminaNovaSeq6000 platform with paired-end 150 bp reads. Data analysis involved performing quality assessments using FastQC and Trimmomatic, followed by aligning the quality-filtered reads to the human genome, version GRCh38, using BWA-MEM. Post-processing steps, including sorting and indexing, were completed according to GATK best practice using SAMTools, Picard and GATK4. Variant calling was completed using Mutect2.Clinical data for patient characterisation was collected by retrospective chart review.

## Results

One of the most frequently identified mutations in our cohort (n=6) was DUOX2, which was mutated in 67% of patients and has recently been identified as a novel candidate driver gene in relapsed/refractory MM(R/RMM). Mutations in EHMT1, involved in epigenetic gene repression, were the most frequent in our cohort (83%). EHMT1 mutations were identified in 100% of patients with primary EMD and 1 patient with relapse EMD. EHMT1 is closely related to EZH2, which was recently linked to EMD and mutated in 50% of cohort. TP53 and KRAS mutations were each identified in 67% of our cohort, predominantly at EMD sites and not BM. KRAS mutations were more prevalent in primary EMD. Mutation overlap was greater for relapse EMD(28%) than primary(8%). There was significant variability in the mutational profile between BM and EMD sites, demonstrating spatial heterogeneity, with a higher mutational burden at EMD sites.

## Conclusion

Genomic analysis of EMD demonstrates heterogeneity between the BM and EMD sites in patients, in addition to variability in the mutational profile of primary versus relapse EMD. This has implications for therapeutic strategy and underscores the need for a personalised approach. Mutations in DUOX2 were prevalent in our cohort, suggesting the need for its further evaluation in EMD. Other genomic mutations of significance in our study include KRAS, TP53 and EHMT1.

# Real World Analysis of Bi-specific Antibodies in the Management of Patients with Multiple Myeloma in Northern Ireland.

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Bispecific antibodies are currently altering the therapeutic landscape of relapsed and refractory multiple myeloma (RRMM). In clinical trials these drugs have displayed high response rates, resulting in durable remissions lasting over a year. While two new bi-specific agents (teclistimab and elranatamab) have just received NICE approval patients with RRMM were able to gain access to three agents Teclistimab, Talquetamab and Elranatamab via compassionate use programmes spanning a 26 month period. Here we present real world data on efficacy and toxicity.

**Methods**

A retrospective analysis identified 21 patients between 1st May 2022 to 30th June 2024. Two patients received two bi-specific agents and one patient received all three. The age range was 48-78 with a median of 66. 12 male patients and 9 female patients. Patients had 3-8 prior lines of therapy with a median of 5. All patients were triple class refractory.

15 patients received elranatamab (March 2024-July 2024), 7 patients received talquetamab (June 2023-November 2023) and 3 patients received teclistimab (May 2022-Feb 2023).

**Efficacy**

The overall response rate was 67%.

The CR was 38 %(n=9), VGPR 8% (n=2), PR 21% (n=5), SD 4% (n=1), PD 29% (n=7). Unable to assess response in 1 patient as treatment commenced due to plasmacytoma and imaging not updated.

Median time to best response was 2 months.

**Toxicity**

56% (n=14) of patients experienced Cytokine Release Syndrome (CRS) on starting a new bi-specific. 52% experienced grade 1-2 CRS and 1 patient had grade 3 CRS.

64% (9 of 14) of patients received tocilizimab. The patient that had grade 3 CRS required 2 doses of tocilizimib and symptoms settled within 48hours. There were no ICU admissions due to CRS.

Sadly 1 patient developed grade 4 ICANS following D4 elranatamab with an acute deterioration in GCS. He required ICU for vasopressor and ventilator support. He passed away 11 days after starting elranatamab.

**IVIg**

43% (n=9) received IVIg. 5 of these 9 patients were not on IVIG prior to starting bi-specific – these were all started pre-emptively. IgG levels were low prior to commencing IVIG and ranged between <0.05 and 4.0.

**Infections**

76% (16 of 21) patients had an infection while on a bi-specific with 48% (10 of 21) requiring at least one admission.

78% (7 of 9) patient on IVIG had a documented infection and 33% (3 of 9) patients on IVIG required admission for treatment of infection. 75% (9 of 12) patients not on IVIG had a documented infection however 58% (7 of 12) required hospital admission for treatment.

**Conclusion**

When we compare our real world experience to the outcomes in the in MajesTEC-1 and MagnestisMM-3 trials the ORR and CR rates within our cohort are reassuringly similar.

CRS is common but often low grade but our experience also highlights risk of ICANs in these patients. Importantly we show the significant reduction in the need for hospital admission due to infections on those receiving IVIG.

This data will help inform colleagues with wider role out of these agents

# MPL mutation positive Essential thrombocythemia, an audit to assess compliance with the BSH guidelines on investigation and management

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**Introduction:**
In 2006, sequence analysis of the *MPL* gene coding the TPO receptor led to discovery of a new molecular abnormality in JAK-2 mutation-negative MPN patients (Pickman, 2006). These mutations can be found in up to 10% of primary myelofibrosis patients and in around 8.5% ET cases in the large PT1 study (Beer et al, 2008). BSH guidelines outline criteria for diagnosis of E.T. one of which is the finding of a driver mutation in either *JAK2*, *CALR* or *MPL.* We undertook an audit to assess adherence to BSH guidelines in a cohort of patients with *MPL* mutations.

**Methods:**
Data was collected from electronic health care records on MPL mutation positive patients, detected between 2015 and 2022 in the molecular lab, Belfast trust. Samples originated from all 5 HSC trusts in Northern Ireland. Data was collected on diagnosis, thrombosis and bleeding history, blood counts, spleen size, treatment with anti-platelet drugs, anticoagulants and use of cytoreductive agents. Data was also collected on response to treatment. Overall outcomes including progression to post E.T. myelofibrosis, acute myeloid leukemia or death was recorded.

**Results summary:**
29 patients diagnosed with MPL mutation positive myeloproliferative neoplasms (MPN), 100% of patient's diagnosis as E.T. fulfilled the BSH guidelines diagnostic criteria.
The majority of patients with MPL mutations were female. This is in line with published data in this group of patients. The patients were overwhelmingly of an older age group and this was also reflected in the literature (Vannucchi et al. 2008).
A third of the E.T. patients underwent a bone marrow biopsy and half the patients had spleen assessment by ultrasound. A third of the these were shown to have splenomegaly.
All patients were risk assessed and all high-risk patients (86% of total patients) were appropriately managed with cytoreductive therapy. This was in the form of hydroxycarbamide in all but one patient. Watchful waiting was appropriately followed in all low risk patients. A total of 80% of patients were on platelet antagonists while in 20% anticoagulation was indicated.
A complete response was seen in two thirds of the patients and a partial response in another third.
Thrombotic complications were documented in 62.5% of patients. None of the E.T. patients were reported to have progressed to either post E.T. myelofibrosis or acute myeloid leukemia.

**Discussion:**
This audit highlights close adherence to the BSH guidelines in diagnosis of E.T., in these MPL mutation across the Northern Ireland haematology services.
The age or frailty of the patients influenced the decision to proceed to a bone marrow biopsy. This did not, however, effect the subsequent management decisions.
There was a relatively higher percentage of thrombosis diagnoses in this cohort when compared to that published in the literature for MPL mutated ET patients (62.5% versus 18 – 20%). This may reflect the older age of the patients in this group and the presence of pre-existing cardiovascular risk factors in 50% of patients.

**Recommendation:**
Prospective study of E.T. patients with JAK2V617F and CAL-R mutations in Northern Ireland over a similar time frame, assessing the adherence to BSH guidelines and updated WHO 2016 diagnostic criteria.

## Diagnosis and Management of Systemic AL Amyloidosis; A Single Centre's Experience

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**Introduction/Background:**
Systemic Light chain (AL) Amyloidosis is a monoclonal proliferative plasma cell dyscrasia that results in amyloidgenic protein deposition with multi organ involvement. Secondary to the insidious onset and varied presentation of AL Amyloidosis as a result of multi organ involvement, diagnosis and subsequent treatment can be delayed. Awareness and knowledge of this condition and its early detection in patients can assist with its prompt diagnosis and appropriate commencement of therapy. Documentation and review of AL Amyloidosis patient data can help with our understanding and insight of this complex condition.

**Materials and methods:**
A retrospective analysis of all Systemic Light chain (AL) Amyloidosis patients treated in Cork University Hospital (CUH) from the year 2020 to 2024 inclusive was completed. Patients with localised disease were excluded. Plasma Cell/Myeloma multi-disciplinary meeting patient lists and Dayward treatment schedules allowed us to identify all treated patients over said period. Patient's paper records were accessed along with their data from the ICM and Aria databases here in CUH. This information was utilised to compose a dataset for each corresponding patient including details of their initial presentation, treatment schedules and diagnostic investigations.

**Results:**
20 patients were identified through our retrospective analysis (median age 67.19 years [y], range 45.58-81.1 y; 55% Male). Amyloidosis was detected by Congo Red staining on a variety of tissues including; Bone Marrow 15%, Cardiac 10%, Gastrointestinal 20%, Renal and Genitourinary 40%, Lung 10% and Fat Pad biopsy 5%. Subtyping to confirm AL amyloidosis was performed in the Royal Free Hospital in the United Kingdom. At diagnosis B-type natriuretic peptide (BNP) (median 466pg/ml), High Sensitivity Troponin (TnT) (median 27ng/L) and Urinary Creatinine (UCr) (median 4007umol/L range 1341-18531umol/L) were all assessed. 70% of patients had proven renal involvement at diagnosis, 50% had evidence of amyloid deposition on Echocardiogram and all 20 patients had evidence of a plasma cell disorder in their bone marrow. 80% of patients had a scan for lytic lesions on diagnosis with 6.25% of them having a PET-CT and 93.75% completing a CT skeletal survey. A FISH analysis was completed on bone marrow aspirate which demonstrated 20% of patients being positive for a 1q gain. 65% of patients had Daratumumab prescribed at one point in their therapy and 2 patients underwent an upfront Autologous Bone Marrow Transplant. The median survival was 42 months with a range of 1-182 months.

**Conclusion:**
Patients with Systemic Light chain (AL) Amyloidosis present late with progressive disease as is illustrated by the median BNP and UCr demonstrated in this retrospective analysis. Diagnosis can prove challenging as evident by the array of organ biopsies and referrals from other specialities that are required for this group of patients. Improved understanding and knowledge of this complex disorder is required to expedite diagnosis and enhance our ability to appropriately treat these patients.

**Investigating the effects of Targeted Cellular and Immunotherapies on T-cell reconstitution post Haematopoietic Stem Cell Transplant.**

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The repertoire of new cancer immunotherapies is rapidly expanding along with the indications for haematopoietic stem cell transplantation (HSCT). Immune-modulating therapies include monoclonal antibody (mAb) therapies and adoptive transfer of genetically modified T-cells expressing chimeric antigen receptor (CAR) targeting cancer-specific antigens. Immune-modulating approaches are increasingly used in an attempt to cure disease with less toxicity compared to HSCT. Timely T cell recovery is the strongest predictor factor of survival after HSCT. It also protects from viral reactivation. T-cell reconstitution can be delayed or incomplete. The mechanisms behind inadequate T-cell recovery are largely unknown or how targeted cellular and immunotherapies impact immune reconstitution when given prior to HSCT. To test the hypothesis that immune-modulating therapies prior to HSCT may impair T cell reconstitution we compared two paediatric patients with acute leukaemia, who either did (HSCT+T) or did not (HSCT) receive prior cellular/immunotherapy. Using an optimised assay we performed flow cytometry on serial fresh peripheral blood samples (2, 4 and 6 weeks post-transplant), using specific markers to examine T cell reconstitution (CD3/CD4/CD8) and exhaustion (CD57). Two patient groups were used; HSCT+T (*n=1*) and HSCT (*n=1*). Both patients were in disease remission at the time of HSCT and received a HLA-matched unrelated bone marrow transplant following similar conditioning. An expected reversed CD4/CD8 ratio was noted in both the HSCT+T (0.63) and HSCT (0.17) following myeloablative conditioning. We found that the mean CD8+ expansion was higher following HSCT (80.66% of total T-cells) compared with HSCT+T (50.96% of total T-cells). Furthermore, CD8+ T cells in the HSCT+T setting had a higher expression of CD57, a marker of T cell exhaustion and replicative senescence. Expansion of donor derived CD8+ T-cells is critical in order to protect the host from viral reactivation and infection (1). These findings support the hypothesis that treatment with immune-modulating therapies prior to HSCT impairs T cell reconstitution through reduced expansion of functional CD8+ T cells leading to a potential increase risk for viral reactivation. Notably, the patient who received prior immune-modulating therapies developed HHV6 encephalitis 7 weeks post HSCT. Further research is needed to confirm these results and explore the mechanisms involved.

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## AZACYTIDINE / VENETOCLAX AND RUXOLITINIB MAY PROVIDE A BRIDGE TO TRANSPLANT FOR PATIENTS WITH ACCELERATED AND BLAST PHASE MYELOPROLIFERATIVE NEOPLASMS

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### Introduction

Accelerated phase(AP) and blast phase (BP) Myeloproliferative Neoplasm (MPN) remains a devastating diagnosis. Overall survival (OS) of blast phase MPN remains around 3–6 months with or without intensive chemotherapy. The only potential for cure is bone marrow transplant. Phase 2 study previously showed that combination of hypomethylating agent and Ruxolitinib achieved prolonged OS for MPN in AP and BP. In this report we describe the characteristics and outcomes of patients treated with combination of Azacitidine / Venetoclax and Ruxolitinib.

### Methods

Retrospective study was performed on all patients over 18 who transformed to Accelerated Phase (blasts between 10-19%) or Blast Phase (blasts >20%) MPN as per WHO in St Vincents University Hospital. Azacytidine was given at 75mg/$m^2$ over 7 days over a 28 day cycle and Venetoclax was titrated up to a dose of 400mg. Two patients received Ruxolitinib daily at >10mg BD/day.

### Results

Four patients were included in our study. All were *JAK2V617F* positive. The average time between diagnosis of MPN and progression to AP / BP was 9 years (108 months), with range between 10 months and 15.25 years (183 months). The average age at diagnosis of MPN AP/ BP was 70.2 years. At the time of leukemic transformation, one patient had post ET myelofibrosis, one had PV, one had PMF and one had MDS/MPN with neutrophilia. NGS revealed mutations in *TP53, ASXL1, EZH2, SRSF2* and *DNMT3a.* Unfavourable cytogenetics present in two patients included del(20q), trisomy 8, trisomy 9, monosomy 5 and monosomy 7. One patient who received only Azacitidine/Venetoclax opted for palliative route after the first cycle and since passed away. Remaining 3 patients achieved CR1 and proceeded to bone marrow transplant. Of them, the patient with the most unfavourable NGS and Cytogenetics (including *TP53* mutation and monosomy 5 and 7), relapsed post-transplant, however she is alive currently 19 months post leukemic transformation. Two other patients remain in remission, currently 11 and 5 months post progression to MPN-AP/BP.

### Discussion

In this study we report the outcomes of a small group of patients diagnosed with accelerated phase or blast phase MPN, treated with triple – based combination of Azacitidine / Venetoclax and Ruxolitinib. Despite the small number of patients in our study, the results appear promising. Combination of the three agents was tolerated well, with both patients achieving CR and able to undergo marrow transplant. Three patients that underwent marrow transplant are alive at the time of this report. One relapsed post-transplant, however her survival time has significantly exceeded the usual OS seen in blast phase MPN. Long term follow up will allow for accurate measurement of OS. Further studies are required to investigate this combination as a potential bridging strategy to bone marrow transplant.

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Mascarenhas JO, Rampal RK, Kosiorek HE, Bhave R, Hexner E, Wang ES, et al. Phase 2 study of ruxolitinib and decitabine in patients with myeloproliferative neoplasm in accelerated and blast phase. Blood Adv. 2020;4:5246–56.

# A MULTI-CENTRE REAL-WORLD OBSERVATIONAL STUDY OF PATIENTS WITH MULTIPLE MYELOMA TREATED WITH BELANTAMAB MAFODOTIN IN NORTHERN IRELAND

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## Introduction

Multiple myeloma remains incurable and patients who are multiply relapsed and refractory to standard therapies remain difficult to manage. Belantamab mafadotin (Belamaf) is a novel antibody-drug conjugate targeting B-cell maturation antigen (BCMA) with a cytotoxic payload of monomethyl auristatin F. The DREAMM-2 study (NCT03525678) showed good efficacy from Belamaf monotherapy in patients with relapsed/refractory multiple myeloma (RRMM). On this basis it was available for compassionate use to patients in Northern Ireland since 2021 provided their disease was refractory to at least one proteasome inhibitor, one immunomodulatory agent, and an anti-CD38 monoclonal antibody, and their outcomes are reviewed here.

## Methods

Retrospective analysis was carried out on all patients in Northern Ireland to receive Belamaf up to 01/08/2024. The initial dose was 2.5mg/kg every 21 days, reduced to 1.9 mg/kg every 21 days when required due to toxicities. Cytogenetic risk and treatment response assessments were as per International Myeloma Working Group criteria. Survival analysis was compared using the log-rank test. Response comparisons between cytogenetic risk groups used Fisher's exact test.

## Results

Belamaf was given to 29 patients after a median of 4 prior lines of therapy (range 3-6). The median age was 60 (range 41-77), 74% were male, and 65% (15/23 available) had high risk cytogenetics at the most recent testing prior to commencement. 46% were stage I, 23% stage II and 31% stage III (of 26 available) using the International Staging System (ISS), and 11% stage I, 59% stage II and 30% stage III (of 27 available) using the Revised International Staging System (R-ISS).

Patients received a median of 4 cycles of Belamaf (range 1-16), with 8 remaining on treatment at the time of analysis. 10 stopped due to ocular toxicities with any grade keratopathy seen in 45% (13/29) and at least grade 3 in 10% (3/29). The overall response rate (ORR) was 48% (14/29), of which 10% (3/29) gained a very good partial response (VGPR) and 38% (11/29) a partial response (PR).

The median overall progression free survival (PFS) was 3 months and overall survival (OS) 14 months. Those gaining at least PR achieved significantly better outcomes than those who didn't with PFS 9.5 months vs. 1 month ($p$<0.01) and OS 22 months vs. 6 months ($p$<0.01). There was no significant difference in the likelihood of reaching at least PR between those with high or standard risk cytogenetics ($p$=0.22).

## Conclusion

The Northern Ireland experience of Belamaf is comparable with those of the DREAMM-2 trial and other real-world observational studies. Ocular toxicities are common, but with limited options available for patients with RRMM who are already heavily treated, Belamaf offers significant improvements in PFS and OS for those responding.

# SCREENING FOR OSTEOPOROSIS AND USE OF BONE PROTECTIVE MEDICATIONS IN THE MANAGEMENT OF PATIENTS WITH LYMPHOMA TREATED WITH HIGH DOSE STEROIDS

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## Introduction

Osteoporosis is a major morbidity in patients treated with high dose steroids. The risk of osteoporotic bone fracture is significant with an 18-month cumulative incidence of 11% in UK based large B-cell lymphoma patients. Recent clinical practice guidelines published by the British Society of Haematology recommended clinically assessment of osteoporosis risk in all patients with newly diagnosed large B-cell lymphoma prior to treatment.[1] An audit on clinical practices in our centre was conducted due to clinical concern regarding several patients returning after treatment of lymphoma with osteoporotic insufficiency fractures.

## Aims

Our practices prior to the new BSH guidelines did not typically incorporate the formal assessment of osteoporotic risk factors and often a heterogeneous approach was adopted. This audit aims to assess our current practice against the new standard based on current guidelines in order to introduce changes to improve clinical outcomes.

## Methods

A retrospective review was completed of all lymphoma patients' medical notes who attended haematology day ward within a 30-day period. Their clinical data including relevant background, risk factors, interventions were collected. This was organized into an audit tool with relevant characteristics as per the new BSH guidelines.

## Results

15 lymphoma patients attended within a 30-day period for treatment. M:F ratio 0.875. The median age was 70 (Range 50-87). 4 of 15 patients had low grade lymphoma, the remainder were high grade (11/15). 14/15 patients were receiving or had received high dose steroids as part of their chemotherapy regimen over the previous 6 months. 1/15 had not previously received high dose steroids. 2/15 patient had a known diagnosis of osteoporosis at baseline and only 1 patient was currently on treatment with a bisphosphonate or RANK-L inhibitor. None of the patients had a documented fracture risk assessment (FRAX score). 12 of 15 patients were identified to have at least one osteoporotic risk factor. Only 1 patient had a formal DEXA scan completed. All patients had serum calcium checked while none had vitamin D levels checked. Of note 1 patient developed a significant osteoporotic fracture during treatment.

## Discussion

This audit highlighted a gap in our current clinical practice. Osteoporotic risk assessment is not part of our current supportive care protocol in lymphoma patients treated with high dose steroids. Our patient group reflects a cohort with high risk of developing osteoporosis and we have identified a need to address this. Limitations to adoption of these guidelines include access to resources including timely access to DEXA scanning, establishment of management pathways in consultation with endocrinology.
As per the BSH guidelines we recommend baseline testing of calcium and vitamin D, fracture risk assessment, and treatment where appropriate.
We will aim to implement these measures and repeat the audit in 3 months' time.

## References

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**Chimeric antigen receptor T cell (CAR-T) for refractory high grade lymphoma in St James Hospital. A review of the first 30 months of the clinical service.**

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**Introduction**

Chimeric antigen receptors (CAR) are engineered receptor proteins designed to redirect T cells to eliminate cancer cells expressing a specific target antigen. Tisagenlecleucel (tisa-cel, Kymriah) and Axicabtagene ciloleucel (axi-cel, Yescarta) are now licensed in Ireland to treat adult patients with relapsed or refractory diffuse large B cell lymphoma (DLBCL) and primary mediastinal large B cell lymphoma (PMBCL), after two or more lines of systemic therapy. The first CAR T infusion took place in St James's Hospital in Ireland in December 2021. This study describes the outcomes of the first 66 patients undergoing this therapy.

**Materials and Methods**

All patients who underwent CAR T therapy from December 2021 to May 2024 in St James's Hospital were included. May 2024 was chosen as a cut-off to ensure there was 3 full months of follow up data available. All patients had a PET CT scan pre infusion, and at 1, 3, and 6 months post. CRS, ICANS and ICU admission rates are reported.

**Results**

Of the 66 patients, 73% were male. 47% had primary refractory DLBCL, 24% had relapsed DLBCL and 8% had relapsed PMBCL. Of the remainder, 3% had Richter's transformation and 18% had transformed follicular lymphoma.

In terms of therapy, 36% of patients had 2 previous lines of therapies, 18% had 3 previous lines, 9% had 4 previous lines and 3% had 5 previous lines of therapy. 6% of patients had a previous autologous stem cell transplant.

92% of patients received bridging therapy – 64% chemotherapy, 24% radiotherapy and 5% combined modality. 49% received tisa-cel (Kymriah) and 51% received axi-cel (Yescarta). PET CT prior to CAR T showed Deauville 1-3 in 27% of patients, and 73% were Deauville 4-5.

85% of patients developed cytokine release syndrome (CRS) of any grade. 52% of patients developed grade 1 CRS, 29% grade 2, 2% grade 3 and 2% grade 4. 73% of patients received tocilizumab (2-4 doses) and 6% received dexamethasone. 23% of patients developed immune effector cell-associated neurotoxicity syndrome (ICANS) of any grade and 9% had grade 3-4. ICU admission was required for 24% of patients in total. There were no therapy-related deaths.

Currently, 79% of infused CAR T patients are alive. Overall response rate (ORR) assessed at PET CT at 3 months was 65%, with 50% of patients demonstrating complete metabolic response (CMR). 3 patients who relapsed subsequently underwent allogeneic stem cell transplants, one of whom is still alive in a complete remission. 2 patients developed MDS, and 1 patient developed AML following CAR T.

**Conclusion**

Considering the high risk nature of this patient cohort, the outcomes are encouraging. The ORR and CMR rates reflect international data. Grade 3 and 4 side effects were rare. CAR T therapy being delivered nationally is a significant advancement in our ability to care for this high risk cohort of patients.

## RITUXIMAB-POLATUZUMAB-BENDAMUSTINE AT MIDLANDS REGIONAL HOSPITAL TULLAMORE

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### Introduction

Relapsed/refractory diffuse large B cell lymphoma (DLBCL) remains difficult to treat, particularly in the transplant-ineligible population. There is no clear standard of care, with current regimens demonstrating poor response rates and high levels of toxicity. Polatuzumab-vedotin is an anti-CD79a monoclonal antibody-drug conjugate and is combined with rituxumab and bendamustine (Pola-BR) as second line therapy for relapsed/refractory diffuse large B cell lymphoma, for transplant-ineligible patients. A phase Ib/phase II trial (Sehn et al. 2020)[1] demonstrated improved CR rates with Pola-BR compared to BR alone, with consistent data subsequently published in a 2-year follow-up study (Sehn et al. 2022)[2].
Polatuzumab-vedotin is of particular interest, given that the combination with Rituxumab, Cyclophosphamide, Doxorubicin and Prednisolone (R-Pola-CHP) demonstrated superior progression-free survival compared to R-CHOP (Tilly et al. 2022)[3]. This regimen has been recommended for use as first line therapy in recent BSH guidelines (Fox et al. 2024)[4] and has recently been approved as a first line therapy for patients with DLBCL in Ireland.
Our aim is to document our response rates of Pola-BR and compare them to the published trial data.

### Methods

A retrospective analysis was carried out on patients who received Pola-BR in Midlands Regional Hospital Tullamore from 2022 to present. Data was collected from patient charts, Net-acquire laboratory systems, and the National Integrated Medical Imaging System. Data collected included patient demographics, lymphoma subtypes, IPI scores at diagnosis, response rates, survival data, and toxicity data.

### Results

In total, 7 patients have received Pola-BR in MRHT to date. The median age of this cohort was 78. Diagnoses included DLBCL NOS (n=4), testicular DLBCL (n=1), FL transformed to DLBCL (n=1), and one case of an EBV+ lymphoproliferative disorder. IPI scores at diagnosis were as follows: 2 patients had low-risk R-IPI, one patient had intermediate-risk R-IPI, and 4 patients had high-risk R-IPI. 2 patients had primary-refractory disease, one patient had an early relapse (<6 months), 3 patients had late relapses (median 42 months). 6 patients had one previous line of therapy, and 1 patient received 2 prior lines of therapy.
Regarding response rates, 4 patients achieved a complete response (CR) determined by end-of-treatment PET-CT. 2 patients had progressive disease on interim PET-CT scans. 2 patients in our cohort died, with one case of Covid pneumonitis, and one case of progressive disease. Overall survival was 71% and Progression-free survival was 54%, with a median follow up of 13 months (range 6-26 months).
The regimen was well tolerated. There were 2 cases of febrile neutropenia during treatment. Only one patient reported peripheral neuropathy, which was grade 1, and did not require dose reduction. Fatigue (grade 1) was reported in 2 cases.

### Conclusion

Pola-BR has shown efficacy for relapsed DLBCL for transplant-ineligible patients. Our data shows relatively comparable response rates to published data, albeit with a limited sample size. The treatment is well tolerated with low rates of infection and peripheral neuropathy. Use of polatzumab in Ireland has recently been approved as a first line agent in patients with DLBCL.

## BiTEs in the treatment of Non-Hodgkins Lymphoma in a Tertiary Referral Hospital over a Three Year Period

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### Introduction / Background

In the Republic of Ireland, approximately 830 cases of Non-Hodgkins Lymphoma (B-NHL) are diagnosed annually (Irish Cancer Society). B-NHL are a heterogeneous group of neoplasms incorporating over 40 subtypes, including Diffuse Large B-Cell Lymphoma (DLBCL) and Follicular Lymphoma (FL). In the relapsed/refractory setting, treatment strategies utilising highly active immunotherapies that work in concert with the host immune system, have revolutionised the treatment landscape in B-NHL.
Bispecific T-cell engagers (BiTEs) are antibody constructs with two binding domains: the first recognising expressed lymphoma antigens (CD20 in B-NHL) and the second recognising CD3 (immune effector T-Cells). Through this mechanism, BiTEs lead to T-Cell activation and tumour killing. Currently available BiTEs approved in the treatment of B-NHL include Epcoritamab, Glofitamab and Mosunetuzumab. Real world prescribing patterns for these drugs currently remains under explored.

### Aims

This study sought to evaluate prescribing patterns of BiTEs in the treatment of adult patients with B-NHL in a tertiary referral hospital over a three year period between 2022 – 2024. This analysis also sought to evaluate efficacy and side effect profile, including cytokine release syndrome (CRS) and Immune effector cell-associated neurotoxicity syndrome (ICANS).

### Methods

A retrospective review of electronic patient records was performed on all patients with B-NHL treated with BiTE therapy at a St James Hospital, Dublin, from January 2022 to August 2024. Data collected included baseline demographics, disease subtype, previous treatment, BiTE used, side effect profile and associated side effects, Progression free survival and Overall Survival. Data was collated on Microsoft excel.

### Results

Between 2022 and 2024 eleven patients received BiTes, five males and six females; three patients (27%) with DLBCL, two patients (18%) with transformed follicular lymphoma and six patients (54%) with follicular lymphoma. One patient (9%) was treated with Epicoritamab, three patients (27%) were treated with Glofitamab, and seven patients (63%) received Mosunetuzumab. Of the patients treated, six (54%) had a BiTE as their third line treatment while five (46%) received a BiTE as their fourth line or greater treatment. CRS occurred in three patients (27%), with grade 1 CRS occurring in two patients (18%) and grade 3 CRS occurring in one patient requiring admission to intensive care. No patients in this cohort developed ICANS. Two patients (18%) required steroids and two patients (18%) required tocilizumab for the management of their BiTE associated CRS.

### Conclusions

In this audit we provide real world data on the use of BiTEs in a tertiary referral hospital in Ireland, including observed side effects and efficacy. BiTEs offer an “off-the-shelf” option for redirecting T-cells against B-NHL. Due to the ability to initiate treatment quickly in rapidly evolving disease settings, they are being increasingly integrated into a broader range of treatment paradigms for lymphoma in Ireland.

## CURRENT PRACTICE AND UNMET NEEDS IN THE TREATMENT AND MANAGEMENT OF CHRONIC MYELOID LEUKAEMIA (CML) IN IRELAND

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**Introduction/background:** This survey aimed to understand the current practice and unmet needs of patients (pts) with CML-CP in Ireland.

**Materials and Methods:** 15 haematology healthcare professionals (HCPs) completed structured interviews between February & June 2024 (Consultants (n=7), Clinical Nurse Specialists (n=4) & Advanced Nurse Practitioners (n=4) with Medical Science Liaisons from Novartis. Responses were analysed descriptively.

**Results:** Most respondents (47%) saw 6-7 newly diagnosed CML-CP patients per year. In addition to routine tests, BRC::ABL1 transcript levels and bone marrow are assessed in CML work-up. Cardiovascular (CV) history, comorbidities, smoking, blood pressure, co-medications & alcohol are routinely captured in pts notes regarding CV risk. 73% do not use a CV assessment tool before initiating tyrosine kinase inhibitors (TKIs), mostly referring to GPs for CV risk management. However, CML prognosis is assessed (93%), usually by Sokal (67%).
The main treatment goal (>80%) for 1L & following 1L intolerance is deep molecular response. At later lines, major molecular response (MMR) becomes the target (60-73%). Efficacy, tolerability, comorbidities, safety profile, quality-of-life (QoL) & guidelines drive TKI selection (≥73%). After 2L resistance, QoL, guidelines & treatment-free remission (TFR) reduce in importance. Mutation status becomes more important following resistance (>80%).
93% of HCPs monitor pts every 3 months during the first year of TKI therapy. This frequency drops to 53% once a pt achieves MMR at 12 months; while 33% reduce monitoring to every 6 months. Early kinetics of response is used by 67% HCPs in their evaluation of TKI response. Failure pts are seen in-person monthly by 87% of respondents; while 60% & 40% of HCPs see intolerant patients & warning pts every 1-2 months, respectively.
TKI resistance is defined as not achieving complete haematological response by 3 months by 73% HCPs. Therapy switch & mutation analysis are likely at >1 warning response (73%, 93%) or failure (both 100%); evaluating compliance is most likely after only 1 warning response (93%). TKI intolerance is associated with impacting QoL (100%), grade 3 adverse events (93%) & tolerability affecting compliance (87%). Most (80%) switches to 2$^{nd}$ line TKI are due to resistance. Allogeneic stem cell transplant work-up should be considered at 4L failure (86%), or disease progression if aged <65 years (75%).
Key unmet needs in CML (1L, 2L, 3L) are TKI toxicity (27%, 60%, 67%) and improving QoL (20%, 47%, 47%). Achieving TFR (33%) and avoiding resistance (53%) become increasingly important at 2L and 3L, respectively. At 3L, lack of treatment options (40%) and T315I mutation (40%) concern many. Most (60%) think ELN2020 guidelines fall short, many citing 3L treatment advice and pregnancy. Education (molecular testing techniques, TFR management) is desired; registrars & CNSs are most likely to benefit.
**Conclusions:** These findings suggest management of CML in Ireland is broadly in line with ELN2020 recommendations. However, they also emphasise the need for improvement of optimal pt management including CV risk and mutational analysis in all warning/failure pts. In addition, HCPs need improvements in pt QoL and reduced TKI toxicity; as well as better advice on pt management in later lines.

## A SINGLE CENTRE RETROSPECTIVE REVIEW OF TRANSPLANT INELIGIBLE MANTLE CELL LYMPHOMA PATIENTS

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### Introduction

Mantle cell lymphoma (MCL) is a rare mature B cell non-Hodgkin lymphoma that largely affects older adult males. Over 95% of cases have the t(11;14) associated IGH::CCND1 fusion which leads to the overexpression of cyclin D1. Whilst the clinical course in MCL is variable, ranging from in situ mantle cell neoplasm (ISMCN) to classical MCL or leukaemic non-nodal MCL, the disease generally is associated with a poor prognosis. The majority of patients diagnosed with MCL will require treatment with immunochemotherapy, with those fit enough referred for consolidation with autologous stem cell transplant (ASCT). The aim of this study was to retrospectively review patients attending the Mater Misericordiae University Hospital (MMUH) with MCL who were ineligible for stem cell transplant, to assess their demographics and analyse their outcomes.

### Materials and methods (MMUH)

This is a single centre retrospective review of patients diagnosed with mantle cell lymphoma who attended the haematology department in the MMUH. Data was collected from electronic patient records and BD Cato Software. Data collected included patient demographics, MIPI at diagnosis, response at interim and end-of-treatment imaging, patients consolidated with radiotherapy, survival data and treatment tolerability.

### Results

From 2009 to 2023, 35 patients were diagnosed with MCL in the MMUH. Of these 51.4% (n=18) were deemed transplant ineligible; these patients made up our study cohort. Two-thirds of this cohort (n=12) were male, with 6 females. The median age at diagnosis was 69 years old (range 43 to 85 years). Thirteen of these patients had a bone marrow biopsy performed at diagnosis; 11 patients had bone marrow involvement with MCL, whilst two patients did not. Three patients (16.7%) were diagnosed with indolent MCL and, at the time of writing, remain treatment naïve under active surveillance. Thirteen patients received combination immunochemotherapy, with the majority (n=11, 78.6%) receiving rituximab-bendamustine followed by rituximab maintenance. One patient was unfit for any treatment. Five patients subsequently relapsed after first line treatment; the majority of these relapses (80%) were treated with rituximab-ibrutinib. Six of the 18 patients (33%) had died by time of writing.

### Conclusion

The majority of our transplant ineligible patients received immunochemotherapy; most of our cohort received rituximab-bendamustine upfront with ibrutinib reserved for relapsed/refractory disease. However, outcomes remain poor. Patients with indolent disease requiring no treatment at all represented a minority. Further research is needed into optimum treatment algorithms for these patients potentially incorporating novel targeted therapies into earlier lines of treatment.

## Targeted Inhibition of JAM-A: A Novel Therapeutic Strategy to Suppress Proliferation in High-Risk Multiple Myeloma

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Junctional Adhesion Molecule-A (JAM-A), encoded by the *F11R* gene and located on chromosome 1, is a tight junction protein whose upregulation in various solid tumours has been linked with adverse patient outcomes. Recent reports have newly indicated that elevated JAM-A levels in multiple myeloma (MM) patients also associate with reduced overall survival (OS). MM is a blood cancer featuring uncontrolled proliferation of plasma B cells, which, despite treatment advances, remains incurable. Since amplifications of chromosome 1 associate with inferior survival in MM patients, it is crucial to explore the druggability of novel potential targets such as JAM-A. Homo-dimerization of JAM-A, occurring within the same cell (in *cis*) is thought to associate with oncogenic traits such as angiogenesis and metastasis. Therefore, the purpose of this study was to interrogate JAM-A expression trends alongside progression parameters in MM patients, and to design and test JAM-A *cis*-dimerization inhibitors in MM models.

Patient databases (CoMMpass and GEO Accession) were analyzed to correlate *F11R* expression with MM patient survival along the established pathway of MM (premalignant to newly-diagnosed to refractory disease). In parallel, a peptide library was designed using Molecular Operating Environment software to antagonize JAM-A *cis*-dimerization. Top-ranking peptides, engineered to exhibit maximum binding stability to critical *cis*-dimer residues in the crystal structure of human JAM-A, were tested via CellTiterGlo viability assays using MM cell lines expressing variable levels of JAM-A (OPM2, MM1S, KMS12BM and KMS18). Common cell death pathways (apoptosis and necrosis), cellular senescence and proliferation were interrogated in parallel. Additionally, the testing of lead peptides in an *in-vivo* xenograft model on the chick chorioallantoic membrane (CAM) has begun. Database analysis demonstrated increased *F11R* expression alongside MM disease progression (from healthy to relapsed disease). MM patients with high JAM-A gene expression exhibited significantly reduced OS, supporting the hypothesis that JAM-A antagonism merits exploration. A newly-designed panel of anti-JAM-A peptides exhibited energetically-favourable binding to amino acid residues responsible for JAM-A *cis*-dimer formation. *In vitro* testing revealed significant reductions in cellular ATP levels following treatment with these novel peptides ($LogIC_{50}$ values ranging from 0.5-2μM over a 3-day period with daily treatments; n=3-4 experiments). Subsequent testing ruled out apoptosis and necrosis as methods of cellular death, and revealed a curious dissociation between ATP results and traditional proliferation assays. Nonetheless, the first *in vivo* xenograft results were promising in evoking macroscopic reductions in tumour size using peptides NM1 and NM3 compared to untreated controls.

In conclusion, our *in silico* findings confirm that increased JAM-A gene expression in MM associates with diminished OS of MM patients, and newly demonstrate that its expression increases sequentially along a disease progression spectrum. Multiple novel anti-JAM-A peptides have been designed, and show promising *in vitro* bioactivity against MM cells. Efforts are now turning to interrogating the impact of novel peptides on the cell cycle, and further testing peptide bioactivity in the *in vivo* CAM model. By completion, this project promises to open a timely discourse on the potential use of JAM-A antagonists in future MM targeted therapy approaches.

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## BORTEZOMIB AND HUWE1 INHIBITOR QDD-7 ACT SYNERGISTICALLY TO INDUCE DNA DAMAGE AND APOPTOSIS IN MULTIPLE MYELOMA CELLS

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**Introduction:**
Despite significant advances in Multiple Myeloma (MM) treatment, it remains a largely incurable malignancy with most patients experiencing several periods of relapse and remission, highlighting the need for novel treatments. Previous work from our lab identified the E3 ligase HUWE1 as a potential therapeutic target in MM, demonstrated a key role in regulating genomic instability and developed a novel HUWE1 inhibitor QDD-7. HUWE1 has more recently been identified in promoting the formation of c-MYC multimers surrounding replication forks which prevent collapse and thus protect against DNA damage. Treatment with Bortezomib, a standard of care therapy in MM, leads to an increase in c-MYC multimer formation. The aim of this study is to investigate whether disruption of MYC multimer formation through HUWE1 inhibition can enhance the efficacy of Bortezomib.

**Materials and methods:**
*Dose Response:* JJN3, OPM2, KMS12 and MOLP8 cell lines were seeded in a 96-well plate at $3x10^5$ /mL and treated with Bortezomib and QDD-7 either simultaneously, or through sequential pre-treatment of one drug 4 hours before the addition of the second drug. Cell viability was assessed using Cell-Titre Glo® luminescent assay 24 and 48 hours after treatment. Synergy was calculated in SynergyFinder+ using the Bliss Synergy Model.
*Western Blot:* Cells were seeded in T80 flasks at $3x10^5$ /mL treated with the IC 50 values of Bortezomib and QDD-7 either as single agents, simultaneously, or through pre-treatment. Protein lysates were obtained at 6h, 24h and 48h.

**Results:**
Combinations of Bortezomib and QDD-7 were analysed in SynergyFinder+ whereby a bliss synergy score >10 indicates synergy, a score between -10 and 10 shows an additive effect and <-10 is antagonistic. Through this Bortezomib pre-treatment was identified as the most effective way to combine the two compounds with bliss synergy scores of ≥ 16.82, while simultaneous combinations were additive (≥1.58); there was no clear trend with QDD-7 pre-treatment. Western Blot analysis showed that at 24 hours, all combination treatments caused increased γH2AX expression in JJN3 cells and induced cleaved caspase 3 expression in JJN3 and OPM2 cell lines, indicating an increase in DNA damage and activation of apoptotic pathways respectively. C-MYC expression was reduced in combination treatments suggesting that the combination impacts MYC multimer formation.

**Conclusions:**
Sequential treatment of Bortezomib and QDD-7 results in strong synergy across MM cell lines, associated with an increase in DNA damage, apoptotic activation and a decrease in c-MYC expression. Future work will further investigate the effect of drug combinations on c-MYC multimer formation surrounding stalled replication forks through immunofluorescence imaging.

# TARGETING THE INHIBITOR OF APOPTOSIS PROTEIN BIRC3 SENSITISES MULTIPLE MYELOMA CELLS TO PROTEASOME INHIBITORS

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**Introduction:**
Whilst there have been significant advances in the treatment of multiple myeloma (MM), including proteasome inhibitors (PIs) as a standard of care, this disease is still considered incurable due to inevitable therapy resistance. Thus, it is essential that resistance mechanisms are elucidated, and novel targets are identified to advance treatment and overcome resistance. Network analysis of 20 MM cell lines was carried out using data from SynLeGG (Synthetic Lethality with Gene Expression and Genomics; www.overton-lab.uk/synlegg) to predict PI-sensitiser genes for targeting in conjunction with PI treatment to increase sensitivity. The network analysis identified BIRC3 as a potential target gene. BIRC3 codes for an inhibitor of apoptosis protein (cIAP2) which is largely involved in regulating both the canonical and non-canonical NF-κB pathways. The aim of this study was to validate BIRC3 as a PI-sensitiser gene and to investigate its potential as a therapeutic target.

**Materials and methods:**
Four MM cell lines (JJN3, U266, AMO1, OPM2) representing three main cytogenetic subgroups [t(14;16), t(11;14), t(4;14)] were analysed. BIRC3 was silenced using siRNA-mediated knockdown (KD) or chemically inhibited using the bivalent SMAC mimetic BV-6. CellTiter-Glo® Luminescent Cell Viability Assay (Promega) was performed to determine viability. Percentage viability values, following combination treatment, were analysed using SynergyFinder to calculate Bliss Synergy scores. Scores <-10 indicate an antagonistic relationship, -10 to 10 indicates an additive relationship, and >10 indicates synergy. Western blot analysis was also performed to elucidate the mechanism of action of this drug combination.

**Results:**
siRNA-mediated KD of BIRC3 significantly reduced viability of MM cell lines compared to control siRNA ($p<0.05$), and increased sensitivity to carfilzomib (CFZ). Subsequent analysis using the bivalent SMAC mimetic BV-6 in combination with PIs (carfilzomib/bortezomib) across two cell lines, revealed at least an additive relationship between these drugs (Bliss Synergy score ≥ -10). Western blot analysis of BV-6 in combination with PIs revealed an accumulation of NF-κB-inducing kinase (NIK) compared to untreated controls and single agents, occurring within 6 hrs of treatment. NIK normally undergoes continuous degradation by BIRC3 and TRAF3 to prevent constitutive activation of the non-canonical NF-κB pathway. Therefore, accumulation of this protein suggests BV-6/CFZ combination treatment prevents NIK degradation. Furthermore, at 24 hrs this drug combination induced cleavage of caspase-3/-8/-9, suggesting both intrinsic and extrinsic apoptotic cell death.

**Conclusions:**
The results of this study reveal that BIRC3 is a PI-sensitiser gene which, when targeted therapeutically, increases PI sensitivity. Future work for this study will include further delineating the mechanism of action of this drug combination, with a particular focus on the NF-κB pathway. Analysis will also be carried out to assess the impactof BIRC3/TRAF3 mutational status. Ultimately, the discovery of this synergistic drug combination could have important implications in developing new strategies to overcome treatment resistance in MM.

## HUWE1 mutations are associated with a delayed Replicative Stress Response and Genomic Instability in Multiple Myeloma

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### Introduction

Despite continuous advances in therapies over the last few decades, Multiple Myeloma (MM) remains an incurable malignancy, highlighting the need for new more personalized treatment options. Recent genomic studies have uncovered novel mutational driver genes in MM, including the E3 ligase HUWE1 which is mutated in 5% of patients. HUWE1 has been implicated in the regulation of cellular processes including stress response, apoptosis, and DNA replication and repair, through its interaction with a diverse set of substrates. Our lab and others have previously reported dysregulated HUWE1 in MM and identified its potential as a therapeutic target. In this study we investigated the role of wild type (WT) and mutant HUWE1 in DNA replication and DNA damage response pathways in MM.

### Methods

Cells were transfected with SMARTvector Inducible Human HUWE1 shRNA (Dharmacon, USA). Replicative stress was induced by treatment with 2 mM Hydroxyurea (HU) and assessed using immunofluorescence staining and iPOND (isolation of proteins on nascent DNA) analysis. Genomic instability was assessed using the PIG-A mutation assay and micronucleus analysis (Litron Labs) in a panel of HUWE1 mutant and WT MM cell lines.

### Results

Proteomic profiling and co-immunoprecipitation studies identified and validated Replication Protein A (RPA), as a novel substrate of HUWE1. RPA is a heterotrimeric subunit complex which plays a critical role in the recruitment of DNA repair proteins. We observed significantly less ubiquitination ($p=0.00213$) and phosphorylation ($p=0.0064$) of RPA in the absence of HUWE1, with an associated decrease in RPA localisation to DNA following treatment with HU to induce replicative stress. Subsequent iPOND analysis determined that this was accompanied by reduced recruitment of repair proteins, including RAD51, to DNA. Moreover, induced replicative stress in HUWE1 depleted/inhibited cells resulted in significantly higher levels of DNA damage at 6hrs ($p=0.00421$) and 24hrs ($p=0.0219$) post HU treatment. The presence of a HUWE1 mutation also led to a reduced ability to rectify DNA damage, with HUWE1 mutant MM cell lines exhibiting a delayed response to replicative stress. A strong interaction between HUWE1 and the repair proteins RPA and H2AX was observed in HUWE1 WT cell lines after 3hrs of HU treatment, mutant cell lines did not achieve a similar interaction until 24hrs. WT cells experienced a rapid induction of H2AX phosphorylation by 3hrs in response to HU treatment which had dissipated by 24hrs while mutants did not display a DNA repair response until the 24hrs timepoint. This corresponded to a greater ability to sense and subsequently resolve DNA damage among WT cell lines compared to their mutant counterparts. Mutant cell lines also exhibited a significantly higher mutation rate ($p=0.0023$) and increased levels of micronuclei formation ($p<0.0001$) than HUWE1 WT cells. Furthermore, MM patients with a HUWE1 mutation identified in the CoMMpass data set (A13 release) were found to exhibit similar phenotypes of genomic instability with higher levels of both nonsynonymous ($p<0.0001$) and somatic ($p<0.0001$) mutations.

### Conclusion

We have identified RPA as a novel substrate for HUWE1 and demonstrate that aberration of HUWE1 results in increased replication stress and a dampened DNA repair capacity in MM cells, underpinned by reduced recruitment of repair proteins. This work outlines a clear role for HUWE1 in genome stability and highlights that exploitation of the replication stress response may represent a therapeutic vulnerability for MM patients with a HUWE1 mutation.

## Targeting the SF3B1$^{K700E}$ mutation in myeloid malignancy

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Introduction/Background: Splicing is a crucial post-transcriptional process that removes intronic sequences from pre-mRNA to produce mature transcripts for cytoplasmic export. The spliceosome is a large multi-ribonuclear complex which orchestrates this process, comprised of multiple snRNPs and associated splicing factors; SF3B1, SRSF2, U2AF1 and ZRSR2. These splicing factors are commonly mutated in haematological malignancies, and are known as "founder mutations", commonly identified in CHIP (clonal haematopoiesis of indeterminate potential). Moreover, individuals harbouring spliceosome mutations are at increased risk of developing myelodysplastic syndromes (MDS)/ acute myeloid leukaemia (AML). MDS is characterised by peripheral blood cytopenia, leading to symptoms of bone marrow failure. One third of patients with MDS experience disease progression and advance to secondary acute myeloid leukaemia (sAML), which is notoriously more difficult to treat than *de novo* AML. Notably, spliceosome mutations are prevalent in about 50% of cases within both MDS and AML contexts. Aim: Identify unique genetic dependencies in K700E *SF3B1* mutated cancers (*SF3B1*$^{K700E}$) using a genome-wide CRISPR knockout screen, alongside an FDA approved drug screen, in order to establish compounds capable of mimicking the effects of genetic knockout and induce synthetic lethality in the presence of this *SF3B1* mutation.
Materials and Methods: The Toronto Knockout Library v3, a pooled genome-wide CRISPR knockout screen, was performed over a 14 day period using our isogenic *SF3B1* mutant and wild-type K562 cell line models. The MAGeCK pipeline was implemented to analyse guide dropout/enrichment and identify targets that induce synthetic lethality.
Results: Using the genome-wide CRISPR KO screen, we identified 34 unique genetic dependencies in *SF3B1*$^{K700E}$ cells, further encompassing a group of functionally enriched pathways related to mitosis and proteasomal degradation processes. Subsequent pharmacological and genetic validation studies confirmed that proteasomal degradation preferentially targets *SF3B1*$^{K700E}$ mutant cells.
Conclusion: This data highlights the potential to use a pool of novel, targetable dependencies that are specific to the *SF3B1*$^{K700E}$ mutation, offering an opportunity to intervene and target "founder mutations" to prevent myeloid disease progression.

# PATIENT SUPPORT GROUP IS A USEFUL ASPECT FOR ACHIEVING THE LONG TERM NEEDS OF A PATIENT LIVING WITH MYELOMA.

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**Background**
Myeloma remains a chronic incurable cancer, resulting in a wide range of physical effects, long-term sequela and psychosocial concerns. Patients are at risk of anxiety and depression, which impacts mortality and quality of life. The long-term needs of a patient living with myeloma is evolving; as novel treatments bring unique challenges, as well as prognosis improving rapidly resulting late effects. Support groups are recognised for their potential to reduce isolation and build support networks. The Cancer Focus Myeloma Support Group runs every 6 weeks with approximately 30 attendees. A scoping exercise was conducted to establish a co-produced program, with invited guest speakers addressing concerns such as mental health, finances, fatigue/mobility and side effects.

**Methods**
A baseline patient-led group activity was carried out exploring the top concerns experienced by attendees. An extensive questionnaire was completed to further explore concerns, symptoms and levels of anxiety or depression. Questionnaires were adapted from elements of the MyPOS scale (a palliative care outcome scale, validated for use in myeloma patients), as well as the validated PHQ-9 depression screening tool and GAD-7 anxiety screening tool.
At the same time the patient's carer also completed a separate questionnaire capturing the impact on their own mental health.
14 patients and 10 carers completed the initial questionnaires.
To evaluate the impact of the groups, a follow-up questionnaire was completed by 33 patients and 11 carers, after 6 months.

**Results**
Baseline:

- Top priorities included information on disease/ treatments, side-effects, fatigue, worry regarding loved ones and coping with uncertainly.
- Most common symptoms included fatigue (85%), tingling in hands or feet (77%), pain (69%), difficulty remembering things (69%) and poor mobility (69%).
- 79% experienced worry regarding disease progression, 64% regarding infections and 57% death or dying.
- Depression and anxiety was identified in 69% and 38% of patients retrospectively
- Anxiety demonstrated in 40% of carers
- 75% of patients reported an impact on work, home or getting along with people.
- Only 57% of patients reported having enough information on what may happen in the future and 36% having enough information on planning for the future.

Evaluation:

- 100% felt the groups had helped with understanding their disease, treatments and side-effects, 80% in relation to finances and 61% in relation to planning for the future.
- 97% of patients and 90% of loved ones reported an improvement in overall emotional well-being.
- 92% of patients who had previously experienced isolation/ loneliness reported this had improved.
- Carers anxiety fell to 27%
- Anxiety in patients remained unchanged, slight improvement of 17% in depression noted.
- Benefits of meeting and sharing experiences with others frequently identified in additional comments

**Conclusion**
Findings reflect the significant impact of a myeloma diagnosis on patients' well-being. Tailored support groups such as these have potential to promote self-management while providing interpersonal support. Evidence of anxiety and depression remains, however improvements in overall all well-being, reduction in isolation/ loneliness and a greater understanding of their illness/ treatments were identified. One patient stated the groups have "given me the confidence to plan ahead and start living my life again". A holistic approach to myeloma care is essential to help improve the patient's quality of life and experience of care

## CLINICAL CHARACTERISTICS AND OUTCOMES OF MYELOPROLIFERATIVE NEOPLASMS IN ADOLESCENTS AND YOUNG ADULTS: A SINGLE-CENTER IRISH EXPERIENCE

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**Introduction:**
Myeloproliferative neoplasms (MPNs) are clonal haematopoietic disorders commonly diagnosed in the seventh decade of life. With increasing access to blood surveillance, the number of adolescent and young adults (AYAs) diagnosed with MPNs is increasing. AYAs with MPN demonstrate unique patterns of driver mutations and thrombotic events and remain at risk for progression to more aggressive disease states. In this review, we present a comprehensive retrospective review of the clinical features, disease course and management of AYA patients with MPN seen at our institution.

**Methods:**
We retrospectively reviewed charts of patients whose ages were 16-39, (defined as AYA patients per NCCN guideline recommendations on AYA cancers), diagnosed with MPN (adhering to the World Health Organization criteria) at our institution from 2006-2024. Conventional statistical methods were used for analyses.

**Results:**
The AYA MPN population consisted of 28 patients, with median follow-up 6.4 years (0-15). Most patients (93%; 26/28) had a diagnosis of essential thrombocytosis (ET), the remaining two patients had polycythaemia vera (PV). There was a female preponderance (57%) and median age at diagnosis was 31.1 years (18-38). JAK2 V617F was the most common driver mutation detected (46%), followed by CALR (32%); the remaining cases were triple negative (21%).
The majority of AYA MPNs were diagnosed following incidental detection of thrombocytosis (71%). 29% were symptomatic at presentation, five with thrombosis, one with bleeding, one with headaches and one with erythromelalgia. Median platelet count at ET diagnosis was 1049 $\times 10^9$/L (570-2605 $\times 10^9$/L). Median haemoglobin and haematocrit at PV diagnosis was 17.2g/dl and 50% respectively.
Of the thrombotic presentations all were JAK2 V617F positive. Both PV patients presented with thrombosis, along with three ET patients. Four were arterial events with one venous event. There were no additional thrombotic events post diagnosis.
One triple negative case presented with bleeding and was found to have acquired von Willebrand syndrome (AVWS) in the context of extreme thrombocytosis (platelets >1000 $\times 10^9$/L). There were three additional cases of AVWS identified post diagnosis, all were CALR positive with extreme thrombocytosis.
Treatment information was available in twenty-seven cases, two patients had no treatment to date (7%). 74% (20/27) are receiving anti-platelet therapy. 85% have received cytoreductive therapy (23/27) including Hydroxyurea (48%; 13/27), Interferon (37%; 10/27), Anagrelide (30%; 8/27) and Ruxolitinib (7%; 2/27). The majority have received one line of therapy (56%; 15/27), six patients are on second line therapy (22%) and two on third line therapy (7%). Symptom burden was the primary indication for cytoreduction (43%; 10/23), followed by thrombosis (22%; 5/23), extreme thrombocytosis (17%; 4/23) and bleeding/AVWS (17%; 4/23).
Two patients have transformed to myelofibrosis (both JAK2 V617F positive), all patients are still alive.

**Conclusion:**
AYA MPN patients have unique characteristics. Our data highlights the female preponderance, high incidence of CALR mutation and increased burden of symptoms. Symptom burden is hugely important for these patients with the potential for significant impact on quality of life. Given the likely long length of time they will live with their disease, specific AYA MPN directed risk stratification and therapeutic guidelines are necessary to inform age-appropriate and holistic patient care.

## ADOLESCENT AND YOUNG ADULT (AYA) CANCER EPIDEMIOLOGY IN IRELAND - A RETROSPECTIVE REVIEW OF NATIONAL CANCER REGISTRY DATA FROM 2002 TO 2018.

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**Background:** Adolescents and Young Adults (AYA) with cancer are now recognised as a distinct group in Ireland. The AYA cancer population in Ireland is defined as patients aged 16 - 24 + 364 days at the time of diagnosis of cancer. Cancer is the leading cause of disease related death in this group. This cohort of patients have unique disease biology and additional challenges to their care as compared to their paediatric and older adult counterparts.

**Aim:** To characterise the epidemiology of Adolescent and Young Adult Cancer in Ireland.

**Methods:** Retrospective data of all patients diagnosed with cancer in Ireland aged 16 - 24 + 364 days between 2002 and 2018 was obtained from the National Cancer Registry of Ireland. Ethical approval was granted for the project from Trinity College Dublin and approval from the HRCDC was sought to undertake the project.
Results: The total number of diagnoses in this age group over this time was 2828. 51% M : 49% F. The average number of AYA cancer cases diagnosed in Ireland each year was 166. There was a steady increase in cancer incidence with increasing age. 11.6% of patients died as a result of cancer. The cancer of highest incidence in this age group was Hodgkin Lymphoma, accounting for 15% of all AYA cancers. Non Hodgkin Lymphoma and Leukaemia each accounted for 6% of AYA cancer cases.
There were 431 cases of Hodgkin Lymphoma in this age group over the time period studied. The number of cases per year fluctuated between 16 and 32. 55% of cases were female and 45% were male. The peak age of incidence was 19 and 20. The breakdown by subtype was 85% Classical Nodular Sclerosis, 10% Mixed Cellularity and 5% Nodular Lymphocyte Predominant. The stage at presentation was stage 1 in 15%, stage 2 in 61%, stage 3 in 12% and stage 4 in 12% of cases. There was approximately 1 death per year due to Hodgkin Hymphoma in this group.

**Conclusion:** Cancer remains the leading cause of disease related death in Adolescents and Young Adults in Ireland, however survival is increasing. Haematological malignancies account for 30% of cancer cases in this age group, with Hodgkin Lymphoma being the most predominant cancer seen in this group. Data collected by the NCRI is lacking detailed information on treatment and treatment toxicities and specific challenges of AYA cancer care such as fertility preservation, access to clinical trials, time to diagnosis from presentation and access to additional supports and members of the MDT.

## BLOOD CANCER BIOBANK IRELAND: A NATIONAL RESOURCE FOR ADVANCING BLOOD CANCER RESEARCH

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**INTRODUCTION/BACKGROUND:**

Established in 2016, Blood Cancer Biobank Ireland (BCBI) is a national biobank dedicated to blood cancer research. It represents a collaborative effort involving nine hospitals and universities across Ireland, focusing on the collection and storage of biospecimens from consented patients diagnosed with various blood cancers. BCBI's primary aim is to provide precious biospecimens for translational and preclinical research, facilitating advances in understanding and treating blood cancers such as chronic lymphocytic leukemia (CLL), acute myeloid leukemia (AML), and multiple myeloma (MM).

**MATERIALS AND METHODS:**

The core activities of BCBI involve the systematic collection, processing, and storage of blood and bone marrow samples from patients diagnosed with various blood cancers. These samples are collected with informed consent and are meticulously processed to ensure high-quality biospecimens suitable for a range of research applications. The type of specimens stored are live leukemic cells, stromal cells, serum/plasma and some of the samples are processed to isolate DNA and RNA; these sample types are critical for understanding the molecular and cellular mechanisms of blood cancers. The biobank also maintains a comprehensive database that collects detailed information associated with each biospecimen, thus providing a valuable resource for data-driven research. BCBI utilizes standardized protocols to ensure consistency and reliability across the entire process.

**RESULTS:**

To date, BCBI has a collection of over 15,000 samples from approximately 900 patients, positioning it as a central repository for blood cancer research in Ireland. The biobank has already supported numerous high-impact studies, contributing to significant scientific discoveries and the publication of 19 influential papers since 2017. These studies have explored various areas, including cellular biology, in-silico analyses of cellular mechanisms, the development of novel immunotherapy strategies, and the identification of potential drug candidates through innovative screening techniques. Notably, BCBI has played a pivotal role in the DISCOVER EU project determining the role of tumor necrosis factor signalling in the tumour microenvironment, the CLL Interactome project, a collaborative research initiative aiming to investigate the role of long-non-coding RNA in CLL and to conduct comprehensive genomic screenings to uncover CLL-specific genetic aberrations and to research projects investigating novel cellular immunotherapies.

**CONCLUSIONS:**

BCBI significantly contributes to the advancement of blood cancer research. BCBI's collaborative efforts, both nationally and internationally, highlights its commitment to enhancing cancer research and improving patient outcomes. Through initiatives including  like the CLL Interactome project and the recent partnerships with the European Myeloma Network, BCBI continues to drive innovative research, shape the future of blood cancer treatment, and offer hope for better therapeutic outcomes for patients.

**FIRST YEARS' EXPERIENCE OF FRONT LINE VENETOCLAX-OBINUTUZUMAB IN PREVIOUSLY UNTREATED PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKAEMIA IN CORK UNIVERSITY HOSPITAL, A SINGLE CENTRE AUDIT.**

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**Introduction:** The combination Venetoclax plus Obinutuzumab is approved as a fixed duration first line treatment for patients with TP53 intact Chronic Lymphocytic Leukaemia (CLL). However, there is a considerable risk of tumour lysis syndrome (TLS) and cytopaenias at initiation of treatment, necessitating careful monitoring and communication with patients by clinical nurse specialists.
Since April 2022 we have treated 32 patients in Cork University Hospital (CUH) using the NCCP approved Ven-O protocol, which includes a 5 weekly venetoclax ramp-up from day 22. Patients are admitted overnight for 2 nights at the initiation of obinutuzumab; but are otherwise treated as day patients; some requiring supportive G-CSF. The aim of this audit was to assess the real world data and experience of adopting a new protocol to CUH.

**Materials and Methods:** This audit gathered retrospective data from patients commencing treatment over 24 months (April 2022 to March 2024). We used multiple sources for data collection including the APEX laboratory management system, Aria Oncology Information System, and iSofts Clinical manager (iCM). We obtained patient data including demographics, laboratory results, TP53/IgHV status and radiology results. We compared our patient characteristics, experiences and outcomes to recently published studies**.**

**Results:** 32 patients received VenO in CUH: 24 males and 8 females. Ages from 43 to 79 with a median age of 66.5. The time range from diagnosis to treatment was 0 - 227 months; with a median of 46 months. 20 had a documented ECOG of 0, with 8 undocumented. All patients were discussed at MDT and met iWCLL indications for treatment; thrombocytopaenia (10 patients), anaemia (13), immune phenomena (11), splenomegaly (10) and B symptoms (7). 16 patients had more than one indication for treatment. 29/30 patients were TP53 intact. 16/30 patients were IgHV unmutated, 11/30 mutated and 3/30 were borderline.
The overall survival (OS) rate was 90% at the time of data collection: 1 patient developed AML, and 2 underwent Richter's transformation (1 while actively on treatment), all 3 patients died. 2 patients discontinued after 1 month due to treatment intolerance but the remaining cohort continued treatment. No patients required 2nd line treatment to date. 12 patient completed 12 months of treatment, and 100% were in complete remission.
At the onset of treatment, 40% of patients had haemoglobin less than 10g/dL, but after 4 months, they had achieved CR (per iWCLL criteria). 23% of patients had a platelet count below 50 at initiation; resolving to 0 patients after 4 months. None developed clinical/biochemical TLS.
14 patients developed mild neutropenia (neutrophils 1-1.5x$10^9$/L); 2 patients developed severe neutropenia. These data are confounded by the administration of G-CSF. Rates of neutropaenia peaked at 21% during months 1-4, and declined thereafter. 11 patients required hospital admission- median length of stay of 5 days.

**Discussion:** The data indicate that VenO is an effective first line therapy against CLL and can be successfully administered as an outpatient in CUH and is comparible to published data. The majority of patients responded to treatment and managed to avoid hospital admissions. This regime however required significant time input from haematology CNSs.

**Bi-specific antibody therapy for the treatment of relapsed/ refractory multiple myeloma and diffuse large B cell Lymphoma: a single centre experience**

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**Introduction:**
Bispecific antibody therapies offer a therapeutic option for patients who are refractory to standard lines of therapy for both multiple myeloma and diffuse large B-cell lymphoma (DLBCL). The aim of this retrospective cohort study was to report on the practice patterns and clinical outcomes of patients treated with talquetamab and teclistamab,for patients with relapsed/refractory multiple myeloma, and epcoritimab and glofitamab for patients with relapsed/refractory DLBCL.

**Method:**
We conducted a retrospective review of all patients who had received bispecific antibody therapy for the treatment of multiple myeloma and DLBCL in our patient cohort up until July 2024. Data were collected on baseline characteristics of the patients, the number of prior lines of therapy they had received, response rates to the bispecific antibodies, and the incidence CRS, ICANS , and other adverse events where available.

**Results:**
A total of 16 patients were identified as having received bispecific antibody therapy. Of these, 6 patients (37.5%) received Teclistamab, 4 patients (25%) received Talquetamab, 3 patients (18.7%) received Glofitamab, and 3 patients (18.7%) received Epcoritamab.

In the cohort of patients receiving Teclistamab and Talquetamab for relapsed/refractory multiple myeloma (n=10), the median age at the time of commencement of BITE therapy was 74 years for Teclistamab and 70.5 years for Talquetamab. These patients were heavily pre-treated, with 83% of patients in the Teclistamab group and 100% of the patients in the Talquetamab group being penta-refractory (having failed 2 IMiDs, 2 proteasome inhibitors, and an anti-CD38 antibody). The median number of lines of therapy prior to commencing BITE therapy was 6.5, with 80% of patients having received a prior autologous stem cell transplant. The median Progression-Free Survival (PFS) was 3.2 months in the Teclistamab group and 2.7 months in the Talquetamab group. One episode of Grade 1 ICANS and one episode of CRS were noted in the Teclistamab group. Grade 3 adverse events were identified in 3 patients (30%).

In the cohort of patients receiving Glofitamab and Epcoritamab for relapsed DLBCL (n=6), the median age at the time of commencement of BITE therapy was 65 years in the Glofitamab group and 51 years in the Epcoritamab group. The median NCCN-IPI score was 2 in the Glofitamab group and 4 in the Epcoritamab group. The median number of prior lines of therapy was 2 in both groups. One patient in the Glofitamab group had received a prior allogeneic stem cell transplant, and one patient in the same group had received prior CAR T-cell therapy. In our cohort, one patient in the Epcoritamab group achieved a partial response with a PFS of 3 months, and one patient in the Glofitamab group achieved complete metabolic remission (CMR) with PFS of 6 months, with the rest of the cohort experiencing disease progression on interval imaging. One episode of Grade 1 ICANS was reported in the Glofitamab group, and one episode of Grade 3 CRS was reported in the Epcoritamab group.
**Conclusion:**
Bispecific antibodies represent a valuable addition to the current therapeutic landscape for patients with relapsed/refractory multiple myeloma and DLBCL who have exhausted conventional therapies. Our real-world experience provides insight into the utility of these in the current era.

## EXPLORING THE EPIDEMIOLOGICAL PROFILE OF MULTIPLE MYELOMA IN THE UNITED KINGDOM

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**Introduction/background:**
Multiple myeloma (MM) is an incurable haematological cancer affecting plasma cells in the bone marrow and is associated with male sex and older age. According to estimates from the global cancer observatory, MM is most common in high-income settings. MM incidence has previously been reported to vary by UK nation. To explore this further, an in-depth report of MM epidemiology was produced for the UK.

**Materials and methods:**
Publicly available data for MM (C90.0) incidence and mortality were retrieved from the English National Cancer Registration and Analysis Service, the Scottish Cancer Registry and Intelligence Service, the Welsh Cancer Intelligence & Surveillance Unit and the Northern Ireland Cancer Registry. The year 2020 was selected as the most recent year reported on by all cancer registries. Incidence and mortality rates over time (1993 onwards) were also considered. Where available (England, Scotland and Wales), outcomes were evaluated across the individual healthcare Boards/Trusts of each nation.
European age-standardised rates (EASRs) for incidence and mortality are presented for each nation, enabling comparisons which are not influenced by differing population and age structures. These rates are based on the 2013 European standard population in all datasets.

**Results:**
A total of n=5,775 MM cases were reported in 2020. The highest MM incidence rate was reported in Northern Ireland (NI; EASR 10.2/100,000, 95%CI 8.7-11.8), followed by England (9/100,000, 95%CI 8.8-9.3), Scotland (8.5/100,000, 95%CI 7.7-9.3) and Wales (7.1/100,000, 95%CI 6.3-8.2). MM incidence steadily increased over time for all nations except for Wales, which reported a slight decrease in incidence (2002-2006 vs 2016-2020: 9.9 vs 8.2 per 100,000).
No clear geographical pattern emerged for MM cases diagnosed in 2020 across each nation. For nations reporting incidence by Trust/Health Board, the highest incidence rates within each nation were observed in: England's South East London Integrated Care Board (13.2/100,000), Scotland's Ayrshire & Arran NHS Board (10.8/100,000) and Wales's Powys Teaching Health Board (13.3/100,000).
For mortality, in 2020 Wales reported the highest mortality rate (EASR 5.2/100,000), followed by England (4.9/100,000), NI (4.6/100,000), and Scotland (4.4/100,000). Each nation's mortality rates remained relatively consistent over time from the earliest years in their respective cancer registries.

**Conclusions:**
This report presents the latest epidemiological findings for MM across the UK, offering a detailed geographical analysis of MM in each UK nation. This report aligns with previous reports documenting higher incidence in England and NI and highlights the need for further research in this area.

## MULTIPLE MYELOMA: PRELIMINARY INCIDENCE AND MORTALITY PROJECTIONS FOR THE UNITED KINGDOM UP TO 2050

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**Introduction/background:**
This study aims to anticipate the future multiple myeloma (MM) landscape in the UK, supporting MM service planning and provision. Projections for MM incidence and mortality for the UK and its constituent regions are presented up to 2050.

**Materials and methods:**
Publicly available cancer registry data on MM diagnoses (ICD-10: C90.0) across the UK from 2002-2020 were extracted from each UK nations' individual cancer registries; the English National Cancer Registration and Analysis Service, the Scottish Cancer Registry and Intelligence Service, the Welsh Cancer Intelligence & Surveillance Unit and the Northern Ireland Cancer Registry. For population projections, Office for National Statistics gender specific estimates up to 2050 were used.
Joinpoint regression was used to identify trends in incidence and mortality for MM from 2002-2020, using Power 5 models to calculate projections up to 2050. European age-standardised rates (EASRs) for incidence and mortality were generated by UK region, standardising to the 2013 European standard population. Projected incidence and mortality rates for 2050 were compared to an average from 2015-19.

**Results:**
During 2015-19, n=30,080 MM cases were diagnosed in the UK, of which 57.5% (n=17,297) were male and 42.5% (n=12,783) female. By 2050, newly diagnosed MM cases across the UK are projected to be 72.3% higher than 2015-19, increasing from an annual average of n=6,016 (2015-19) to n=10,364 (2050). MM cases in England are projected to increase by 76.0%, Scotland by 31.7%, Wales by 50.1% and NI by 104.7%. In terms of incidence rates, increases are projected for England (from EASR 10 to 11.6 per 100,000), and NI (9.3 to 12.2/100,000). No changes are projected for Wales (6.8/100,000) while a slight reduction in incidence is projected for Scotland (9 to 8.9/100,000). In terms of mortality, by 2050, mortality rates for MM are projected to increase for England (EASR 5.0/100,000 to 5.8/100,000), Wales (3.5/100,000 to 5.5/100,000) and NI (5.3/100,000 to 5.4/100,000) but decrease for Scotland (4.8/100,000 to 3.6/100,000).

**Conclusions:**
Over the next 30 years, MM case numbers are projected to increase by over 70% with variations projected for each UK nation. For smaller nations such as NI, projection estimates may be impacted by smaller sample sizes. Nonetheless, appropriate clinical and support services will be required to support the increased number of MM patients.

## INVESTIGATING THE RISK OF MGUS PROGRESSION TO HAEMATOLOGICAL MALIGNANCIES: A SYSTEMATIC REVIEW WITH META-ANALYSIS AND NARRATIVE SYNTHESIS

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**Introduction/background:**
Monoclonal gammopathy of undetermined significance (MGUS) is an asymptomatic pre-cancer which precedes multiple haematological malignancies (HMs), mainly multiple myeloma (MM). Current International Myeloma Working Group (IMWG) guidelines state that MGUS progresses to HM at a rate of "around 1% per year", however estimates vary across the literature. To address this, a systematic review was conducted to investigate MGUS's rate of malignant progression to any HM and to MM specifically.

**Materials and methods:**
Four electronic databases were searched: MEDLINE ALL (1946), EMBASE (1974), PubMed (1964) and Web of Science (1988), with no language restrictions, restricted to humans where possible. Databases were searched from inception to 28/3/24.
Returns were de-duplicated in Endnote and Covidence, where screening also took place. The pre-specified screening criteria selected for epidemiological studies in humans which reported on malignant MGUS progression and excluded case reports/series and non-primary data. All studies were screened by the lead reviewer (SQ) and another team member; conflicts were resolved by team discussion.
Hospital-based populations were included, however studies which exclusively evaluated specialised populations –such as cohorts with diabetes or a specified exposure-- were excluded.
Meta-analysis and narrative synthesis were performed; to enable this, studies were required to report the rate of malignant MGUS progression at 1-/5-/10-years, or the number of malignant progressions with the number of person-years (PY) follow-up.

**Results:**
A total of n=47 studies were included; publication dates ranged from 1991-2024 and reports were included from n=17 countries across Europe, the USA and Asia. Cohorts were typically assembled from hospital databases and median follow-up ranged from 2.1-34.2 years.
For meta-analysis, n=12 studies reported on progression to HM and n=12 reported on progression to MM (different reports were included between these two pools). The overall estimate of MGUS progression to HM was 12 events per 1000 PY (95%CI: 10-15), which was approximately equivalent to a 1.2% rate of progression per year. For the meta-analysis of MGUS progression to MM only, the overall estimate was 8 events per 1000 PY (95%CI: 7-11), which was approximately equivalent to a 0.8% rate of progression per year. There was a notably high heterogeneity in both meta-analyses, however (HM- $I^2$:96.7; $X^2$:331.6, p<0.0001; MM- $I^2$:95.8; $X^2$:263.4, p<0.0001).
In narrative synthesis, a wide range of findings were reported for progression to HM and MM. For progression to HM, n=23 studies reported on samples ranging from n=87-17,963 patients. Progression occurred at a rate of 1-1.6% at 1 year, 3-13% at 5 years and 6.6-33.6% at 10 years. For progression to MM, n=15 studies reported on sample sizes ranging from n=114-10,847. Progression rates ranged from 0-2% at 1 year, 3-12% at 5 years and 7-28.5% at 10 years.

**Conclusions:**
This systematic review broadly supports the IMWG's current consensus regarding MGUS progression, but highlights the varying rates reported across the literature. This displays the need for further research to identify potentially underappreciated sources of variance in MGUS progression.

## MULTIPLE MYELOMA SERVICE PROVISION ACROSS THE UNITED KINGDOM: A FREEDOM OF INFORMATION STUDY

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### Introduction

Multiple myeloma (MM) is an incurable haematological malignancy arising from plasma cells in the bone marrow. Given the ageing population and the projected increase in MM diagnoses, it is crucial to assess current service provision to support future service planning. This study aims to provide the first detailed summary of MM care provision across the UK.

### Materials and methods

Freedom of information requests were sent to the individual Boards/Trusts of Scotland, Wales and Northern Ireland (NI) (date: 22/1/2024) and individual health trusts in England (13/5/24). Using 1 January 2024 as date cutoff, each Board/Trust was asked to provide information on the number of hospitals providing oncology services, haematology staff including those specialising in MM (consultant haematologists, specialist haematology registrars and clinical nurse specialists), and multidisciplinary team (MDT) meetings (frequency and membership). Responses from individual English Trusts were collated to summarise practice for Integrated Care Boards. The number of haematology staff was compared to each Board/Trust's population coverage to calculate the number of haematology professionals per 100,000 population. Mid-year population estimates from 2022 census data were used to provide population estimates.

### Results

Of the n=237 health Boards/Trusts across the UK, 89% responded including all from Northern Ireland and Wales. The response rates were 93.3% for Scotland and 88.1% for England.
While nearly all Boards/Trusts reported providing oncology services, the number of hospitals providing these services within each Board/Trust varied by population served (e.g. English Boards ranged from 15-38 hospitals, while in NI 4 out of 5 Health and Social Care Trusts reported having one hospital providing oncology services). Some of the smaller Boards/Trusts reported referring MM patients to other Boards/Trusts for care (for example, Powys Teaching Health Board and Velindre University NHS Trust in Wales, and the Shetland, Orkney and Western Isles NHS Boards in Scotland).
Aligning with this, variations in the number of haematology healthcare professionals was observed by nation. As of 1 January 2024, across the responding Health Boards/Trusts there were an estimated n=1,694 haematology professionals (consultant haematologists, specialist haematology registrars and clinical nurse specialists), with n=241 specialising in MM (as a consultant haematologist or clinical nurse specialist) in the UK. Caution is however warranted as some professionals may provide services to multiple Boards/Trusts and therefore be counted more than once here. Most Trusts/Boards ranged between n=2-5 professionals per 100,000 population, (min 0.7– max 9.9).
When asked about how MM patients were managed, most Boards/Trusts reported that MM patients were discussed at general haematology MDTs, which typically occurred weekly. Few Boards held MM-specific MDTs, however this did occur in n=14 English Boards and n=1 Welsh Board. In some cases, a weekly general haematology MDT was supplemented by a monthly MM-specific MDT.

### Conclusion

This report offers the first summary of MM care provision across UK health Boards/Trusts, enabling service evaluation against outcomes and planning for the future.

**Predictive value of free light chain burden in patients newly diagnosed with AL amyloidosis treated with CyBorD or DaraCyBorD**

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**Background:** A difference between involved and non-involved free light chain (dFLC) exceeding 180 mg/L is part of the 2012 Mayo staging system. We hypothesized that depth of response in AL amyloidosis patients treated with bortezomib-containing regimens is independent of free light chain burden.

**Methods:** This is a retrospective, multicentre study including 223 newly diagnosed AL amyloidosis patients seen at our institutions between 2012 to 2024. We investigated the relationship between baseline iFLC and dFLC at day 28 and 3, 6, 9 and 12 months from commencement of CyBorD or DaraCyBorD therapy. The study was IRB approved.

**Results:** We identified 132 patients treated with CyBorD and 91 treated with DaraCyBorD. Forty patients in the CyBorD cohort and 3 in the DaraCyBorD cohort did not respond to therapy. Lack of response was independent of baseline iFLC. At day 28, we identified no correlation (r2=0.02) between baseline iFLC and dFLC response in patients receiving DaraCyBorD (Fig 1A), while patients receiving CyBorD had lower cytoreduction (r2=0.53) when iFLC measured >1000mg/L (Fig 1B). Similar trends were noted at 3, 6, 9 and 12 months from therapy start.

**Conclusion:** Depth and rapidity of response is independent from iFLC at diagnosis in patients treated with DaraCyBorD. CyBorD response also appears independent of baseline iFLC up to approximately 1000 mg/L. Data from our cohort are not mature to assess overall survival, but it questions the importance of free light chain burden measured by conventional methods (sFLC) in the era of DaraCyBorD.

## INVESTIGATING THE IMPACT OF THE ADAM17 SHEDDASE COMPLEX ON PAEDIATRIC ACUTE MYELOID LEUKAEMIA

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Leukaemia is the most common cancer and cause of cancer mortality in children around the world. Paediatric Acute myeloid leukaemia (AML) contributes around 15% to 25% of all childhood leukaemia cases. Unfortunately, around 15% of paediatric AML patients suffer from primary chemotherapy resistance and only around 33% of these patients survive. A subgroup of AML found predominantly in children defined by the NUP98::NSD1 fusion has a particularly poor prognosis. Recent evidence from McNeer et al. (PMID:30760869) identified an increased copy number of the Frmd8/iTAP gene within the NUP98::NSD1 subgroup in patients exhibiting resistance to induction chemotherapy. Additionally, they observed an increased copy number following clonal evolution in response to chemotherapy. Frmd8/iTAP is a major regulator of the ADAM17 sheddase complex, which has recently been shown to control inflammation and tumour growth. The sheddase complex is responsible for releasing various soluble forms of cell surface proteins such as cytokines, growth factors, cell adhesion molecules and receptors such as EGFR, FLT3 ligand. I am currently developing models to investigate the role of Frmd8/iTAP in NUP98::NSD1-positive AML and in chemoresistance. This will clarify the relationship between the ADAM17 sheddase complex and childhood AML and elucidate the role of the sheddase complex in humans myeloid cell biology.

**EXTRACELLULAR VESICLE-MEDIATED MOLECULAR MECHANISMS IN THE PROGRESSION OF MULTIPLE MYELOMA.**

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**Introduction/Background:** Despite treatment advances, MM remains incurable due to inevitable relapse and drug resistance (DR), highlighting the need for new therapeutic targets. Complex interactions within the BM microenvironment (BMM) contribute to DR, with extracellular vesicles (EVs) recently identified as key players in establishing a resistant phenotype. EVs are nanosized vesicles formed by most cell types and are crucial for local and systemic cell communication. A genome-wide CRISPR screen of a range of haematological cell lines identified EV biogenesis as essential for MM survival. Analysis of publicly available patient data found that MM patients at relapse with higher expression of some EV biogenesis genes had poorer prognosis. Therefore, this research aims to investigate the role of EV's in drug resistance in order to aid identification of potential targets.

**Materials and Methods:** Two MM cell line models (AMO-1 and RPMI-8266) reflecting proteasome inhibitor (PI) sensitive and resistant disease were used. Both parental cell lines have isogenic bortezomib-resistant (BR) and carfilzomib-resistant (CR) counterparts. AMO-1 and RPMI parental and resistant cell lines were cultured in RPMI supplemented with 10% EV-free FCS and 5% Pen-Strep for 48H. EVs were isolated by removing cells, centrifuging media at 1,000g for 30 minutes to remove debris, and concentrating conditioned media to ~1mL. EVs were pelleted using the Total Exosome Isolation Kit (Thermo Fisher). Pharmacological inhibition of EV biogenesis was conducted using 10μM GW4869 (Sigma). PIs were used at a concentration of 5nM (IC50). Cell viability was measured using Cell Titer Glo (Promega).

**Results:** EVs were isolated from cell lines and confirmed via nanoparticle tracking analysis (NTA) (NanoSight N300), transmission electron microscopy (TEM) and Western blot using EV markers TSG101, HSP70, Alix, and CD9 in accordance with MISEV guidelines. AMO-1 CR cells exhibited increased EV number (1,126,666,666 particles/mL) compared to PI-sensitive AMO-1 cells (798,666,667 particles/mL), along with higher expression of EV marker HSP70. In contrast, there was no difference in EV number between RPMI-8226 PI-sensitive (1,128,333,333 particles/mL) and RPMI-8226 BR cells (1,167,666,666 particles/mL). Fewer EVs were obtained from RPMI-8226 CR cells (740,666,666 particles/mL), and expression of EV markers HSP70 and CD9 was reduced in PI-resistant cells compared to RPMI-8226 PI-sensitive cells. The differences in EV production are reflective and demonstrates the heterogeneity of the resistance mechanisms within MM.
AMO-1 PI-resistant cells were more sensitive to the EV biogenesis inhibitor GW4869 than AMO-1 PI-sensitive cells, suggesting they may be more reliant on this pathway. Combining GW4869 with CFZ significantly reduced viability in CFZ-resistant cells compared to either agent alone by 72H, suggesting that inhibiting EV biogenesis may resensitize cells to CFZ. CFZ-resistant AMO-1 cells released EVs capable of altering the sensitivity of AMO-1 sensitive cells to CFZ. AMO-1 sensitive cells co-cultured with CFZ-resistant EVs and treated with CFZ became more resistant to CFZ at both 24H and 48H post-treatment (≥5-fold increase in cell viability), than those cultured without EVs.

**Conclusions:** The differential response of PI-resistant cells to GW4869 suggests a role for EVs in the transfer of DR from PI-resistant cells to PI-sensitive cells. Future studies will quantify and profile the RNA and protein content of EVs from sensitive vs. resistant cell lines to elucidate targetable pathways and biomarkers for patient translation.

## MANAGEMENT OF MONOMORPHIC BURKITT-LIKE PTLD WITH LOW-INTENSITY CHEMO-IMMUNOTHERAPY IN A PAEDIATRIC LIVER TRANSPLANT RECIPIENT

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Post-transplant lymphoproliferative disorders (PTLD) (recently termed lymphomas arising in immune dysregulation by WHO update) are serious complications following organ transplantation and can be clinically aggressive lymphomas.
This case report presents a 9-year-old girl with a history of liver transplantation for biliary atresia, who developed monomorphic Burkitt-like PTLD. She presented with severe back pain, and imaging identified a large retroperitoneal mass (9 x 9 x 24cm) with splenic and mediastinal involvement. A biopsy confirmed high-grade B-cell lymphoma with Burkitt-like morphology and an extremely high Ki67 index. While FISH was negative for MYC translocations – the optimal treatment strategy for PTLD with Burkitt like morphology is unclear and options have often included intensive chemo-immunotherapy. While the outcomes for paediatric patients treated with intensive regimens R-COPADM / R-CYM (CCLG guidelines) is excellent, the treatment is inpatient based and includes high doses of methotrexate (5-8g/m2). Nearly all patients experience grade 3/4 toxicities including febrile neutropenia and mucositis with real potential for treatment related mortality.
A recent paediatric case series has demonstrated low-dose chemo-immunotherapy could be effective in Burkitt-like PTLD (and indeed in cases with MYC translocations), which could spare patients toxicities associated with intensive regimens. Based on these observations the patient was started on a regimen of Rituximab, Cyclophosphamide, and Prednisolone (R-CP) per a COG protocol. After an initial induction and monitoring for tumour lysis syndrome – the patient discharged to complete treatment on an outpatient basis and has no grade 3 toxicities. PET-CT scanning post the first 2 cycles of chemotherapy has demonstrated an excellent response.
This case underscores the potential of low-intensity chemo-immunotherapy in managing paediatric PTLD. The outcomes align with recent studies suggesting that low-dose treatment can be effective, offering a less toxic alternative to traditional high-dose chemotherapy in selected patients with promising survival rates and reduced treatment-related morbidity.

## EXPLORING HOW TIME-TO-TREATMENT IS REPORTED AMONG CHILDREN AND YOUNG ADULTS WITH CANCER GLOBALLY: A SCOPING REVIEW

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### Introduction

The global incidence of cancer in children and young adults (CAYA) is increasing. While cancer survivorship among CAYAs is high in high-income countries (HICs), only 20% of children in low-income countries (LICs) receiving treatment are cured, and only 10% cured. Delays in the cancer care pathway may influence survival among CAYAs. A scoping review exploring time-to-treatment including reporting practices for CAYA was undertaken.

### Methods

The Arksey and O'Malley Scoping Review Framework was followed. Three databases, namely Ovid Medline, Embase and Web of Science Core Collection were searched using relevant key words and subject headings. Studies were eligible for inclusion if they reported on 0-24-year-old patients receiving their first treatment for their first cancer. Rayyan was used to manage the scoping review. Two reviewers independently screened titles and abstracts, and assessed the full-text against the eligibility criteria. Findings were charted to explore reporting differences in definitions used for TTT, and factors reported to influence TTT among CAYA. We focus here on the findings from studies focusing on haematological malignancies.

### Results

A total of 21 articles reporting on 60,003 CAYAs were included. All studies reported on TTT, and 66.7% reported on factors influencing TTT. More studies were published in 2013-2023 compared to the previous decade. The majority (52.4%) of studies were from HICs. Fourteen studies included haematological malignancies in their investigation. Of the 14 studies focusing on haematological malignancies identified, n=9 reported on leukaemia, including n=4 by subgroups (e.g., acute lymphoblastic leukaemia). One study described TTT for haematological malignancies overall. Five studies reported TTT for cancer overall, not specifying site. Of the n=14 studies investigating haematological cancers, n=4 explicitly referenced the Aarhus statement which defines TTT as the interval between diagnosis and treatment. Two studies implemented other definitions such as the time between index hospital admission to date of first systemic chemotherapy. Some studies reported TTT as a median and others as a mean. For haematological malignancies, TTT ranged from a median of 1 day to 21 days, but this varied by population including country and age group studied. Of the factors influencing TTT investigated in the literature, age was the most commonly investigated factor. Financial factors were also commonly investigated in low-middle-income countries.

### Discussion

To the best of our knowledge, this is the first scoping review investigating the reporting of TTT in the CAYA population and its influencing factors. This review comprehensively maps current literature reporting TTT in CAYAs which will inform future research in this area. Future application of the Aarhus statement and the International Classification of Childhood Cancers would benefit the comparability of studies.

**Paediatric use of rivaroxaban for cerebral venous sinus thrombosis: A multi-centre clinical audit**

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**Background:** Paediatric cerebral venous sinus thrombosis (CVST) is a rare, life-threatening event. Treatment with anticoagulation is not currently standardised and was previously controversial due to associated intracranial haemorrhage. The EINSTEIN-Jr trial demonstrated treatment with rivaroxaban had low risk of major bleeding, high rates of recanalisation and good clinical outcomes.

**Aims:** To provide “real-world” data of rivaroxaban use in CVST in the paediatric setting compared to previous standard of care.

**Methods:** A multi-centre retrospective audit was performed reviewing the use of anticoagulation for paediatric patients diagnosed with CVST, comparing treatment with previous standard of care anticoagulation and rivaroxaban. Patients aged 0 – 18 years treated for CVST at Alder Hey Children’s, Birmingham Children’s, and Glasgow Children’s Hospital between January 2017 – November 2023 were reviewed.

**Results:** 67 patients diagnosed with CVST started on anticoagulation between January 2017 and November 2023 were included. Ages ranged from 15 days – 16 years at diagnosis. Patients were grouped into ‘standard treatment’ (anticoagulation with warfarin or heparin, n=31) or rivaroxaban (n=36) treatment groups. Anticoagulation was continued for <3 months in three patients (4%), 3-6 months in 44 patients (66%), >6 months in four patients (6%) and treatment is ongoing in nine (13%) patients. Of the nine patients still receiving anticoagulation at the time of this audit, seven are on rivaroxaban. Duration of anticoagulation was not available for seven (24%) patients. Bleeding complications, all of which were in the standard treatment group, occurred in three (4%) patients, one of which was defined as a major bleed as per the International Society on Thrombosis and Haemostasis. Recurrent thrombus occurred in four (6%) patients, three receiving standard treatment and one receiving rivaroxaban group. Thrombus recurrence included deep vein thromboses and bilateral pulmonary embolism. Recanalisation data was available for 62 patients. Complete recanalisation occurred in 30 (48%) patients, of which 14 (47%) were from rivaroxaban and 16 (53%) from standard treatment group. 28-day survival was 100% in both treatment groups.

**Conclusion:** This data shows that outside of a clinical trial, treatment of CVST with rivaroxaban in paediatrics is safe and effective when compared to previously available anticoagulation. Ongoing anticoagulation therapy in the Rivaroxaban group will likely yield higher rates of complete recanalisation once treatment is completed. Since the EINSTEIN-Jr trial and subsequent rivaroxaban licensing, it has been used widely. This non-monitored oral medication provides clear practical advantages for children and families.

## HYDROXYUREA – TREATMENT EFFICACY AND LIMITATIONS IN A PAEDIATRIC SICKLE CELL POPULATION

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### Background

Hydroxyurea (HU) reduces sickling in patients with sickle cell disease (SCD) by increasing HbF production, which inhibits HbS polymerisation. Children with SCD on HU with a HbF% >20 are less likely to be hospitalised with SCD complications, such as vaso-occlusive events (VOE), than those with a HbF% <20. Despite HU therapy, admissions with VOE still occur; reasons for this include non-adherence, non-response and sub-optimal dosing.

### Aim

The aim of this study was to identify and characterise hospitalisations by SCD patients on HU, with a focus on those admitted with VOE.

### Methods

This was a single centre retrospective review of admissions by SCD patients on HU from 1/9/22 to 31/8/23 inclusive. Data was collected locally from electronic patient records and a departmental database.

### Results

150 patients received HU during the study period, 75 male/75 female, aged 3-22, mean age 14.5 years. HbSS patients accounted for 210 admissions, with 78 admission (37.1%) by 53 patients on HU for > 6 months. 48 admissions (61.5%) were on HU alone and 30 admissions (38.5%) on a combination of HU and blood transfusion (BT) program.

Admissions in the HU & BT group were for infection (n=16, 53.3%), VOE (7, 23.3%), splenic sequestration (4, 13.3%) and other (3, 10%). The 7 VOE admissions were by 5 patients (4 males, 1 female); 1 male (poorly compliant with BT program) was admitted 3 times. Mean age of admissions in this VOE group was 16.4 years old (range 10–20 years). Mean HbS on admission was 44.8% (range 6.1- 77.9%), with mean Hb on 9.5g/dL (range 8.5-10.0 g/dL).

Of the HU alone cohort (48 events), VOE was the commonest reason for admission (n=21, 43.7%), then infection (n=20, 41.7%), splenic sequestration (n=3, 6.25%), other (n=3, 6.25%) and 1 unknown.

Males made up 66.7% of VOE admissions (n=14). 17 patients accounted for the 21 admissions. The mean age of admissions was 12 years (range 2-21 years). The mean total time on HU was 74.8 months (range 21-145 months). Four of the admissions with VOC on HU had HbF% of >20; the remaining 17 admissions, made up of 14 patients, had a HbF% of <20 (range 1.5% to 19.4%). 12 of these 17 admissions were by males (70.6%), with 5 by females (29.4%). The mean age was 13.3 years (median 17 years, range 3 years-21 years). Admissions by those less than 14 years old had a higher mean HbF than those who were 14 years or older (mean 12.8%, range 6.4 to 19.4%, and mean 10.3%, range 1.5 to 16.1% respectively). The 17 admissions had a mean MCV of 85.9 (range 63.6-119.3) and reticulocyte count of 220.2 (range 64.7 - 384.2) respectively.

### Summary/Conclusion

In our patient cohort on HU, VOE remains a significant cause for admission, especially in adolescent males. Whilst further research is needed into why this is the case, HbF levels <20% in this group, with lower MCVs, suggest medication compliance may be a contributory factor.

## ANALYSIS OF CENTRAL LINE-ASSOCIATED BLOODSTREAM INFECTIONS IN PAEDIATRIC HAEMATOLOGY PATIENTS AT A PRIMARY TREATMENT CENTRE

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**Background:**
Central Line-Associated Bloodstream Infections (CLABSIs) pose a significant risk to paediatric haematology patients, who rely on central venous catheters (CVCs) for the administration of chemotherapy, transfusions, and other supportive care. Understanding infection rates and associated factors is crucial for informing prevention strategies and optimizing patient outcomes.

**Methods:**
A retrospective analysis was conducted using data from patients diagnosed with acute leukaemia or lymphoma over a two-year period. The dataset included information on central line insertions, infections, and outcomes. Key variables analysed included the date of line insertion, the date of infection, line type, number of lumens, and associated microbiological findings. The primary outcome measures were the number of infections per line day (i.e., the time a line was in situ), and the time to infection, calculated as the number of days between CVC insertion and the first documented infection. Descriptive statistics were used to summarize the data, and Kaplan-Meier curves were constructed to analyse the time to first infection and time to line removal due to infection.

**Results:**
The dataset included data on over 90 patients with central line insertions. The majority of these patients had their lines inserted for the treatment of acute lymphoblastic leukaemia (ALL) and experienced prolonged exposure to indwelling central venous catheters. Most patients had at least one documented CLABSI; however, only a fraction of these cases necessitated line removal. In many cases, treatment with antibiotic locks or systemic antibiotics successfully salvaged the line.

**Conclusion and Discussion:**
The results underscore the importance of continuous monitoring and strict adherence to infection control protocols, particularly during the first few months following CVC insertion. Future research should focus on identifying patient-specific risk factors to further refine prevention strategies and reduce the incidence of CLABSI in this vulnerable population. The practice of using therapeutic locks within the centre appears beneficial. However the use prophylactic antimicrobial locks could be considered. Taurolidine, a novel taurine-derived broad-spectrum antimicrobial compound with a unique mechanism of action, has been shown to reduce the incidence of CLABSI in various patient groups. Its use has yielded impressive results in similarly sized paediatric haematology centres and could be a valuable addition to infection prevention strategies.

## A WOLF IN SHEEP'S CLOTHING: IS IMMUNOPHENOTYPE PROGNOSTIC IN KMT2A-R INFANT ACUTE LYMPHOBLASTIC LEUKAEMIA – THE IMPACT OF CD10 AND NG2 STATUS.

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Childhood acute lymphoblastic leukaemias (ALL) typically have a promising prognosis, with a current EFS of over 90%. Unfortunately, not all subtypes of ALL share this prognosis. Infantile ALL has significantly poorer outcomes and we still tend to see survival rates of less than 50%.
Infants with ALL often present with extremely high white cell counts, CNS involvement and immature Pro B phenotype defined by the absence of surface CD10 – the vast majority being associated with underlying translocations involving KMT2A (MLL) gene. The presence of KMT2A translocations is deemed highly negatively prognostic and dictates treatment protocols.
In this report, we discuss the case of a 9 month old infant that presented with trivial leukocytosis and no CNS involvement. Flow cytometry of the blasts revealed a CD10+/ CD19+/cCD79a+/NG2-/cIgM-/CD34-/TdT- immunophenotype. This presentation is consistent with a precursor-B ALL (pre-B ALL).
The presence of CD10 and lack of NG2 expression would have had a high negative predictive value for the presence of KMT2A rearrangements.
Despite the mature immune phenotype and clinical picture more in keeping with ALL of older childhood, FISH testing confirmed the KMT2a:MLLT1 rearrangement t(11:19)(q23:p13.3) – the patient was therefore treated as per infant protocol Interfant 2021; and experienced a rapid response with an excellent end of induction MRD response.
CD10 status historically has been used as a prognostic factor with expression associated with favourable outcomes in infant ALL. Despite this, its strong association with KMT2A status means that its impact is confounded. Here we examine the impact of immunophenotype within the KMT2A infant ALL cohort.

## ASSESSMENT OF BLEEDING AMONG PAEDIATRIC PATIENTS AT A TERTIARY CARE CENTRE UNVEILED LOW VITAMIN K LEVELS

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**Background:** Vitamin K works as a vital cofactor of coagulation factors II, VII, IX, and X, anticoagulation proteins C and S. Vitamin K is not transported across the placenta efficiently, and infants are born with low to undetectable concentrations of Vitamin K and elevation of Protein Induced by Vitamin K Absence or Antagonism (PIVKA). VKDB is a potentially devastating consequence of vitamin K deficiency in the neonatal period. Limited data are available on the relative frequencies of early, classic, and late vitamin k deficiency bleeding and exact level of vitamin K has not been assessed before in the population of Sindh.

**Objectives:**
**1-** To assess Vitamin K level in pediatric patients presenting with bleeding.
**2-** To determine demographic profile of Vitamin K deficiency bleeding patients.
**Methods:** This descriptive cross-sectional study was conducted at the department of Pathology and department

of Pediatrics LUMHS. Patients who met the criteria were selected from Paediatrics department.
Detailed bleeding history and clinical examination of each patient was done. All patients underwent primary screening for bleeding including PT and APTT that was performed on Coagulation Analyzer CA- 600. All the samples were analyzed for levels of Vitamin K1.

**RESULTS:**
Sample size was 114, with age ranging from day 01 up to day 180 (up to 6 months) out of which 56 were males and 58 were females. The mean age was 44.01 days. PT, aPTT, were prolonged in most of the cases.

**Conclusion:** Vitamin K deficiency still remains a cause of concern in newborn and infant visiting Emergencies & Outpatient setting due to bleeding. It presents with variable bleeding pattern. It is more frequent in male and in preterm neonates. Further studies should be conducted in order to lower the burden caused by such preventable causes of early age morbidity and mortality.

**Keywords:** Vitamin K Deficiency Bleeding, Hemorrhagic Disease of Newborn, Coagulation factors

## Compliance with single unit transfusion protocol in Wexford General Hospital between June 1st 2024 and June 30th 2024

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This audit aimed to assess the adherence to guidelines for single-unit red cell transfusions at Wexford General Hospital (WGH) during June 2024. A single-unit transfusion is defined as administering one red cell unit followed by a post-transfusion haemoglobin measurement before considering the administration of a second unit. The objective was to determine the percentage of transfusion episodes that adhered to this protocol, reflecting a more conservative approach to red cell transfusions that aligns with best practices and enhances patient safety.
The methodology involved reviewing inpatient transfusion records for the period between June 1st and June 30th, 2024, using the Apex Web Enquiry System. The inclusion criteria comprised all inpatients at WGH who received red cell transfusions during the specified period. Patients who were actively bleeding, haemodynamically unstable, or had planned red cell transfusions (RCC) were excluded from the analysis. This exclusion was necessary to accurately measure adherence to the single-unit transfusion guideline, as the excluded cases typically require multiple units due to their critical nature.
During the audit period, a total of 109 red cell units were transfused to 76 patients. Of these, 52 transfusions (47.71%) were single-unit transfusions, while 57 transfusions (52.29%) involved multiple units. The multiple transfusions were further analysed to identify their causes: 20 (35.09%) were due to active bleeding, 10 (17.54%) involved planned RCC transfusions through outpatient services, 2 (3.51%) were due to haemodynamic instability with a haemoglobin level below 8 g/dL, and the remaining 25 (43.86%) were attributed to other causes, including stable upper gastrointestinal bleeding (36%), congestive heart failure with haemoglobin less than 8 g/dL (32%), haematological or oncological malignancies with haemoglobin less than 8 g/dL (24%), and breathlessness with haemoglobin less than 8 g/dL (8%).
Out of the 109 transfusion episodes, 77 were included in the final analysis after excluding those involving bleeding, haemodynamic instability, or planned transfusions. Among these 77 transfusion episodes, a post-transfusion haemoglobin check was performed in 52 cases (67.53%), 25 (32.47%) did not have a haemoglobin check after a single unit and went on to have multiple units with no obvious indications.
These finding highlights that while the single-unit transfusion practice was applied in a significant number of cases, there is still considerable room for improvement in adherence to guidelines, particularly concerning the mandatory haemoglobin measurement before a second unit is considered. The audit underscores the need for enhanced compliance with the NICE guidelines for single-unit transfusions at WGH. The data suggest that there is a reliance on multiple-unit transfusions, which could be reduced by stricter adherence to guidelines. The hemovigilance department will continue to advocate for single-unit transfusions where feasible and provide education and support to clinical teams to foster better practices. By promoting a more cautious approach to transfusions, WGH aims to improve patient outcomes, reduce the risks associated with transfusion therapy, and align with national and international best practices for transfusion safety. Following teaching sessions to all Non-Consultant hospital doctors, a re-audit will be carried out.

## A RETROSPECTIVE MULTICENTRE ANALYSIS OF THERAPEUTIC APHERESIS IN IRELAND: INDICATIONS AND RESOURCE DISTRIBUTION 2019-2023

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**Background:**
Therapeutic apheresis(TA), is a well established means of removal of pathogenic substances (e.g autoantibodies or toxic agents), cells (e.g. leucopheresis) and/or reconstitution of patients plasma with that of a healthy donor (e.g thrombotic thrombocytopenic purpura(TTP)). It is indicated as an absolute, relative and rescue intervention requiring multidisciplinary management, often involving critically ill patients [1]. In Ireland, provision has been ad hoc without central planning or funding. Therapeutic advances may affect the distribution of indications but emerging indications seem likely to replace these. Collecting information on indications and the activity involved is a necessary step to improvement in service provision. The aim of this study is to provide a retrospective analysis of the indications, distribution across specialty groups and volume of procedures for TA across three large tertiary referral centres from 2019-2023.

**Methods:**
Patients were included in this study if referred for TA to the Munster Regional Transfusion Centre (2019-2023), University Hospital Galway (2019-2023) or St. Vincent's University Hospital (2019-2022), excluding red cell exchange. The study database was collated from anonymised local Microsoft Excel databases maintained at each centre. Statistical analysis was performed using GraphPad Prism software. Quantitative data related to procedure volume is expressed as median with interquartile range (IQR).

**Results:**
A total of 187 patient referrals resulting in 1268 procedures were recorded. This represents an average of 30.2 referrals per year across the three centres. The most frequent sources of referral were Neurology (47.3%), Nephrology (23.1%) and Haematology (22.6%) resulting in a median of 5,7 and 2 procedures respectively. The most commonly referred conditions were ANCA-vasculitis (12.9%), Goodpasture's disease (anti-GBM) disease (12.9%), Autoimmune neurological disease (NOS) (9.1%), Guillain-Barré Syndrome (9.1%), Hyperviscosity (8.6%) and TTP (7%). Thirteen cases were exchanged for presumed TTP, 3/13 were discontinued after 48 hours. Other sources comprised of 7% of referrals. Of those referred, three cases severe hypertriglyceridaemia, three cases amanita-phalloides poisoning and three cases of refractory immune checkpoint inhibitor toxicity were observed.

**Conclusions:**
In this study, we describe the indications and volume of TA procedures in three centres in Ireland (variable referral patterns across specialties hinder ability to quantify the population served but is estimated over 1.5 million people). Neurology indications were the commonest specialty source, however ANCA-vasculitis and anti-GBM disease mediated renal impairment were the commonest individual indications requiring the highest number of procedures in this data set. Haematological indications, although predominantly urgent, were of lower resource burden as regards volume of procedures but varied depending on indication. Establishment of a national plasma exchange database would allow accurate data capture for resource planning and better monitoring of efficacy, adverse events and emerging indications.

**References:**
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## AUDIT OF TRANSFUSION INCREMENTS IN ANAEMIC HAEMATOLOGY ADULT IN-PATIENTS

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**Introduction:**
The British Committee for Standards in Haematology (BCSH 2012) guidelines suggest that haemoglobin(Hb) levels should increase by 1 g/dL following the transfusion of 1 unit Red Cell Concentrate (RCC) to an adult of approximately 70kg . However, this expected increment varies in patients admitted with different haematological conditions.

**Aims:**
This audit aimed to compare the actual Hb increment post transfusion with the expected rise as per the BCSH guidelines and to assess the patient population relative to these published standards. The goal was to identify any correctable factors contributing to a lower than expected Hb increase after transfusion.
Patients and Methods :
This retrospective audit examined 45 transfusion episodes involving 20 patients with haemoglobin levels below 8 g/dL or symptomatic anaemia, admitted under haematology care at Cork University Hospital, over 3 months, from 1st Nov 2023 to 31st January 2024. The adult patients, aged 30 - 81 years, with a mean weight of 72kg (ranging from 50 to 107kg) , were identified through daily inpatient lists. Transfusion data was gathered from the laboratory information system (Apex), validated by the Blood Track system, and confirmed through patient's paper charts. Post transfusion Hb levels were measured opportunistically and fell within 3 to 23 hours after receiving transfusion. Variables collected included the number of RCC units transfused, timing of post transfusion Hb checks, underlying haematological conditions, ongoing treatments, and clinical stability.

**Results :**
In 45 transfusion episodes, mean haemoglobin increase was 1.00 g/dL per unit of RCC transfused, with values ranging from 0.50 to 1.70 g/dL. 20 episodes showed an increment of less than 1 g/dL. Of these, 14 patients had increases less than 0.50-0.80 g/dL. Clinical background of these 14 revealed conditions such as newly diagnosed leukaemias with severe cytopenias, undergoing intensive chemotherapy, ICU admission with sepsis and intubation, or end-stage refractory hematologic malignancy. Remaining 6 ( out of 20 ) patients, who were recovering from stem cell transplants or rehabbing after intensive care, showed slightly higher increments (0.80-1.00 g/dL) despite ongoing infections. Meanwhile, 25 episodes achieved haemoglobin rises of ≥1 g/dl, predominantly in patients with recovering bone marrow function, well-controlled infections without any vital instability and those who were transfusion dependent but without underlying systemic illness. Surprisingly, the timing of post-transfusion Hb check did not correlate with the Hb increment observed (R value: 0.12), showing no dependency of extent of Hb rise to time post transfusion Hb checked. For instance, Hb measured 11 hours after transfusion, in 4 patients, showed increments ranging from 0.70 to 1.70 g/dL.

**Conclusion :**
Stable clinical status and bone marrow function leads to better haemoglobin increments post transfusion. We confirmed the importance of factors such as severe neutropenia, common red cell antibodies, immune suppression, and vital instability affecting post transfusion Hb response. Our audit is limited by small sample size and unidentified variables like hydration status, ongoing GCSF or erythropoeitin injections, post chemo bone marrow suppression phase and rare red cell antibodies. However we confirmed that in our sick inpatients (average weight 72kg), 1 unit RCC, raised Hb by 1g/dL, consistent with BCSH guidelines.

## AUDIT ON IRON CHELATION THERAPY IN MERCY UNIVERSITY HOSPITAL HAEMATOLOGY DEPARTMENT

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### Background

Patients receiving regular red cell transfusions in haematology are at high risk of iron overload, a condition that can lead to multisystem organ damage due to excess iron deposition. Early initiation of iron chelation therapy is crucial to mitigate these risks. Our audit aimed to evaluate compliance with the British Society of Haematology (BSH) guidelines for monitoring and managing iron overload in patients with haemoglobinopathies and rare anaemias, published in October 2021.

### Methodology

We conducted a retrospective analysis of nine adult haematology patients at Mercy University Hospital in Co Cork, who are on regular red cell transfusion programmes. Using the BSH guidelines as a reference, we developed a comprehensive questionnaire to collect data on patient demographics, primary haematological diagnosis, transfusion history, and iron chelation therapy status. For those on iron chelation, we recorded ferritin levels before therapy, the rationale for therapy initiation, the type of chelation used, and compliance with pre-initiation and ongoing monitoring protocols. For patients not on iron chelation, we explored the reasons behind this decision.

### Results

Our cohort consisted of nine patients, with a median age of 75 years, comprising four males and five females. Diagnoses included transfusion-dependent beta-thalassemia (1 patient), refractory anaemia secondary to myelodysplasia (6 patients), severe aplastic anaemia (1 patient), and myelofibrosis (1 patient). Four out of the nine patients were on iron chelation therapy, with two on deferasirox (Exjade) and two on desferrioxamine. While we were adherent to most of the BSH guidelines, we identified important gaps in several areas, including interval urinalysis, endocrinology assessments, audiometry, and ophthalmology reviews.

### Discussion

This audit revealed several challenges in optimizing care for patients on iron chelation therapy in our centre. The small patient cohort limited the statistical significance of our findings. Additionally, data collection was complicated by the fact that some essential investigations, such as audiometry and ophthalmology reviews, were conducted at different hospitals with documentation off site.
In response to these findings, we developed departmental guidelines to improve the identification of patients at risk of iron overload and to standardize the initiation and monitoring of iron chelation therapy. A checklist was also introduced to ensure that all necessary investigations are conducted regularly for patients on iron chelation therapy.
We plan to re-audit our iron chelation practices at Mercy University Hospital after implementing these guidelines to assess improvements in patient care and guideline compliance.

### Conclusion

Optimizing iron chelation therapy in haematology patients is critical to preventing iron overload and its associated complications. Our audit highlights areas for improvement and has led to the development of targeted guidelines to enhance patient management. Ongoing audits and adherence to updated protocols are essential for ensuring high standards of care.

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# SAFE PRESCRIBING OF BONE PROTECTION IN NEWLY DIAGNOSED MULTIPLE MYELOMA PATIENTS WITHIN THE SOUTHERN HEALTH AND SOCIAL CARE TRUST: A SERVICE EVALUTION

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**Background:** Bisphosphonates are the only therapy recommended by National Institute of Clinical Excellence (NICE) for the prevention of myeloma bone disease, zoledronate is the agent of choice (NICE 2016).In the Southern Health and Social Care Trust, zoledronate is currently prescribed on a handwritten paper prescription chart which is not reviewed by a pharmacist. This is not in accordance with other prescribed therapies in haematology. As a result, there is potential for an increased risk of prescribing errors with zoledronate. Kantilal and Fatani (2021) concluded the introduction of simple interventions led to improvements in both blood monitoring and dental reviews for patients receiving bisphosphate infusions.

**Objective:** To determine the following at baseline and post-intervention.

- Are newly diagnosed multiple myeloma (NDMM) patients prescribed a bisphosphonate?
- What is the bisphosphonate of choice?
- Is there a record of pre-treatment dental assessment?
- Has pre-treatment serum vitamin D been requested?
- Have blood tests (Urea and electrolyte, Serum Adjusted Calcium, phosphate and Magnesium) been requested and recorded on the bisphosphonate prescription?
- Has a calculated creatinine clearance (CrCl) been recorded on the bisphosphonate prescription?
- Was bisphosphonate dose reviewed for renal function (by calculated CrCl)?
- Has weight (within three months) been recorded for CrCl calculation?
- Has the prescription been clinically checked by a pharmacist?
- Have planned frequency and duration of bisphosphonate treatment been recorded?

**Materials and Methods:** Data collection sheets were designed and used to systematically assess, 47 NDMM patients who commenced first-line treatment after 1st July 2022, case notes andcare plans at baseline, and post-intervention. These results were compared and analysed.

**Results:** 46 patients were reviewed, 29 of whom were commenced on zoledronate. 107 doses of zoledronate are included in this study. From baseline to post-intervention a small increase from 84.7% to 89.3% of doses being prescribed in accordance with calculated CrCl was observed, significant association was not demonstrated. Since presentation of baseline findings and introduction of a standardised prescription chart, there was a 30% increase in documented education, a 27% increase in documented frequency, a 15.2% increase in recent recorded weights, and a 13.9% increase in recorded calculated CrCl, all of which demonstrated significant association between patient groups. Excellent practice for completion of pre-treatment dental reviews, co-prescribing calcium and vitamin D supplement, as well as the requesting and recording of serum creatinine, eGFR, and adjusted calcium was observed in both groups.

**Conclusion:** The presentation of findings and introduction of a standardised prescription chart has resulted insafer prescribing of zoledronate in myeloma patients. Safe prescribing was optimised with a significant increase in recorded education, frequency, calculated CrCl, and recent weight. However, further optimisation is required to derive significant improvement in doses being prescribed in accordance with calculated CrCl.

**References**

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**The Power of Connection - Youth Support Workers**

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The Youth Support Worker (YSW) is a unique role, and one which is solely focused on the practical, social, and emotional needs of young people. Those who provide the support are sought from a range of professions, but who are committed to meeting the needs of Adolescents and Young Adult's (AYA). They can build rapport, connection and trust, who can be creative, adaptive and work as part of a multi-disciplinary team. This support is a 'unique offer' of psychosocial care, not seen in adolescent healthcare generally (Cable, 2023)

Cancer Fund for Children have developed the role of YSW's throughout the Island of Ireland in part, as a response to a needs-based analysis of parents of children with Cancer (The Katie Nugent Foundation, Trinity Collage Dublin & Children's Health Ireland, 2019), and direct needs analysis with adolescents and young adults (Cancer Fund for Children, 2022), that revealed gaps in emotional support. Many parents reported inadequate assistance during their child's hospital stay (The Framework of AYA Cancer Care, 2021-2026)

Building upon this needs-based analysis, Cancer Fund for Children has taken action by the deployment of three YSW's across the Island of Ireland, working with young people aged 11-24 years. In Northern Ireland, this includes the main children and adults' hospital. In the Republic of Ireland, the YSW is based in the Childrens hospital alone, with plans for this to be enhanced further across Ireland.

YSW's establish genuine relationships with AYA's throughout their cancer journey, providing emotional support and becoming a critical support and advocate throughout an AYA's cancer experience. Parents, too, find comfort and support in these connections. Shared experiences create a deeper understanding, and through shared stories, laughter, and tears, YSWs become trusted companions on the path to recovery.
Empowering AYA's to express themselves, YSWs offer encouragement and gentle reminders of their inner strength. Amid the routines of hospital life, YSW's infuse joy—whether through games, creative exercise, projects, makeup sessions, or creating small moments of light.

The role embodies the power of connections by providing opportunities for young people to connect with others in similar situations to themselves through groupwork and peer support. YSW's emphasise youth resilience and independence throughout the treatment experience and beyond, described as 'integral to the specialist TYA psychosocial team' (Cable, 2023).

"My daughter used to hate coming into the hospital, wanting to be there as little as possible. Now, with the YSW, she will even ask the nurses to delay her treatment so she can spend more time with her." (St Johns Ward, Crumlin)
''The YSW would call in and bring a bit of brightness and cheer, distraction from the horrible hell he's been in.'' (Royal Victoria Hospital for Sick Children)

**Lessons learned from the development of a nursing education pathway for haematopoietic stem cell transplant (HSCT) in the national bone marrow transplant unit in St James Hospital, Dublin.**

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**Introduction/Background:** Nursing knowledge is often transferred by expert to novice via preceptorship model. Busy clinical environments, increasing numbers of new nurses and the availability of expert nurses can present challenges. Patients undergoing HSCT have complex nursing care needs and require specific education and training.
As no national HSCT education pathways were available, this action research project developed a bespoke educational pathway for nurses that was designed to comply with JACIE 8th edition standards. The curriculum incorporated clinical knowledge from national and international experts in delivering HSCT, was evidence-based and adhered to national and international policy.
This paper presents an overview of the final three step pathway (self-directed, clinical simulation and clinical practice) and the lessons learned from this research. It is hoped that these lessons would be useful for people hoping to develop bespoke education pathways for nurses.

**Materials and methods:** An action research methodology was adopted, development was iterative and incorporated previously used processes (Byrne 2022, Gillespie et al. 2022). The co-creation team consisted of domain specialists (nursing and medical), nursing education, quality and technology specialists from St James Hospital and School of Nursing and Midwifery, Trinity College Dublin. The team maintained a research document that was reviewed at the end of the project and lessons learned extracted and reviewed by the co-creation team.

**Results:** The final pathway has three steps - self-directed, clinical simulation and clinical practice. To date 5 learners have completed the pathway with a further 48 learners enrolled, and feedback has been resoundingly positive. The main lessons learned are presented as 5 T's:
**Topic:** HSCT is a complex topic, and the project proved to be much bigger than initially anticipated. We found that breaking the topic down into smaller components, for example, separating out the allogeneic from autologous HSCT helps learners but also helped the development process.
**Team:** The co-creation team should include clinical expertise, education, quality and technology. Where this is not possible, the team should be able to access this expertise as required.
**Testing:** Evaluation of pathway is important and rather than a 'big bang' approach, we suggest it is a continuous process.
**Types:** A range of educational materials and delivery methods was incorporated to facilitate different learning styles, for example, self-directed and simulated-based learning.
**Time:** There is a considerable time commitment by all stakeholders and the research team found it useful to share the workload where possible.

**Conclusion:** The project was based on a need to provide evidenced based education in an evolving nursing landscape. The underpinning standards were JACIE 8th edition. The project met these needs. The lessons learned are presented as 5 T's – topic, team, testing, types and time. It is hoped that these lessons would be useful for people hoping to develop bespoke education pathways for nurses. Further research is being conducted to evaluate this list of lessons learned.

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## An exploration of the patients experience of survivorship when diagnosed with relapsed/ refractory multiple myeloma

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**BACKGROUND:** Multiple myeloma is a complex haematological malignancy characterised by the disorderly over production of plasma cells in the bone marrow that causes painful lytic bone lesions and abnormal levels of paraprotein in the blood and urine. It is a progressive and incurable disease but in recent years there has been an explosion in the development of treatment strategies such as novel therapies, autologous stem cell transplant and CAR-T cell therapy that has led to patients living longer with the disease. Due to the chronicity of the disease survivorship consists of intermittent episodes of symptoms that require treatment followed by episodes of remission. Patients are at greater risk of developing late effects from treatment and complications associated with disease. There is scant literature exploring the survivorship experience of myeloma patients particularly in relapsed and refractory disease.

**AIM:** The aim of this review was to synthesise all qualitative evidence on the experience of survivorship for patients diagnosed with relapsed/refractory multiple myeloma and gain a better understanding of their survivorship care needs.

**SEARCH:** Qualitative research articles from 2008 to June 2024 were located in the electronic databases – CINAHL, Medline and PubMed. The search strategy was formed according to the PEOS acronym to allow for a more precise search to locate the relevant studies and literature to answer the research question. Since no existing review answering the research question was found during the preliminary examination of the databases a systematic search was conducted. The search resulted in seven studies that met the inclusion criteria.

**DATA EVALUATION:** The studies that met the inclusion criteria were sent forward for quality assessment using Bruton's 10 item checklist and the Critical Appraisal Skills Programme tool. The seven studies were of medium to high quality. The Data was extracted using an adapted data extraction tool and all extracted data was coded. SYNTHESIS: Thomas and Hardens (2008) guide to thematic analysis was used to synthesis the findings. Findings were four main analytical themes. 1) the burden of treatment and disease 2) psychological impact of living with uncertainty 3) the relapsing experience and 4) supportive care needs.

**CONCLUSION:** The findings mostly align with trends already familiarised in existing literature regarding myeloma in that it identifies the very individual journey patients experience and the many negative effects on quality of life that disease and treatment cause. This review was the first to provide an overview of the patients' survivorship experience and created a broadened understanding of the chronicity of myeloma and identified the patients challenges throughout their cancer journey. Relapsed/refractory myeloma patients have very specific supportive care needs dependent on where in their myeloma journey they were. Healthcare professionals have a valuable role in providing patients and their families with information and support specific to their needs. There is an increasing need for evidence synthesis in myeloma now that patients are living longer with the disease and likely to experience multiple relapses and eventually treatment refractoriness along their cancer trajectory. More qualitative synthesis would provide crucial information regarding patients' expectations of their care and existential needs.

**NATIONAL STANDARDISED PATIENT INFORMATION FOR THE ACUTE HAEMATOLOGY ONCOLOGY NURSING SERVICE IN IRELAND - A PATIENT AND NURSING PARTNERSHIP**

Gillespie, M., Whelan, D., O' Mahony, L., Diggins, J., Campbell, A.

**Background: Introduction and Objectives:**
The requirement for this project was to provide evidence-based patient information for the acute haematology oncology nursing service, this need was highlighted by Cancer Patient Advisors, The National Cancer Strategy[1] and The NCCP SACT model of care[2].

**Methods:** An agile project management approach was utilised throughout the project. This meant that adjustments could be made quickly on key documents when reviewed by domain experts and advisors. Action research methodology ensured ongoing reflection, planning and acting throughout the project cycle.[3]

The collaboration of skills between the patient advisors and professionals was key to the success of this project. A review of all current patient facing service information was essential to agreement of what was required.
A co-inquiry group was established for an initial workshop to determine the project requirements and the following were determined to be in scope:

- Agree a standard national name for the acute haematology oncology nursing telephone triage line
- Produce two standardised artefacts for national usage: standard patient information leaflet (PIL) and standard alert card

The co-inquiry group agreed that all patient information would be in line with UKONS[4] assessment imagery. Incorporating the red, amber, green imagery had the benefit of clear patient information, standardised imagery for patients and staff and a distinct identity for immediate recognition by staff of the patient cohort when a patient presents the alert card.
This was noted to be especially important as we work to build links with colleagues across hospital in-patient units, emergency departments and in community care.

Clarity of information was also a key focus and use of plain English was prioritised in line with National Adult Literacy Agency Information[5]. Accepting the findings of the Acute
Haematology Oncology temperature working group was key to ensuring consistency of advice on temperature parameters.
Several iterations of PIL and alert card went through rigorous review and approval processes until the final drafts were agreed in March 2024.
The final drafts were further reviewed by patients in three pilot sites (a type one, two and three hospital) using a questionnaire. Results were submitted anonymously.

**Results:** The feedback has been resoundingly positive and the PIL and alert card have now been implemented nationally.

**Conclusion**: National roll out of new name of telephone triage line **SOS (Sort Out my Symptoms) Hotline** and new PIL and alert card complete. Patient and professional partnership ensured the success of this project. Standardising information nationally meets key recommendations.

**Next Steps:**

- Patient information has been translated into the most commonly used languages (Irish, Polish, Ukrainian, Russian, Hungarian) Evaluation of service user needs are ongoing and further translations will be developed if required.
- Development of digital braille option of patient information for visually impaired service users.
- Evaluate requirement for easy read version of patient information for people with learning difficulties or who cannot read - develop if required
- Evaluate requirement for audio/ audio visual information - develop if required
- Ongoing discussion with social inclusion colleagues/ key stakeholders to identify further project requirements, develop bespoke patient information and promote consistent messaging as required to meet service user needs
- Evaluate requirement for standardisation for paediatric patient information/develop if required.

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# Implementing Exercise Equipment on the Hematopoietic Stem Cell Transplant Unit – Exploring Patients Opinions and Experiences.

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## Background

The benefits of exercise in patients undergoing hematopoietic stem cell transplants (HSCT) is an ongoing area of research, with exercise proving to have a positive impact on patient length of stay and quality of life as well as common side effects of treatment. Common barriers to exercise during transplant include nausea and decreased willpower while facilitators include easy and simple exercises, with support from exercise specialists.
The aim of this project was to determine the effects of exercise equipment to encourage physical activity during an inpatient admission for HSCT. To determine the level of frequency that patients used the equipment to exercise and to determine patient experience and recommendations to our service.

## Methods

To encourage and promote physical activity during an inpatient admission for HSCT, individual activity boxes and exercise bikes were introduced to our transplant unit. Included in the boxes were weights, resistance bands and platelet guided exercise booklets.
Between the months of March and May 2024, all patients admitted to the transplant unit were seen by a physiotherapist, given an introduction and demonstration of the activity box and exercise bikes on the unit. Each patient was subsequently given a questionnaire to complete which explored their opinions and experience of exercise and use of the activity boxes. This questionnaire was designed by both senior and rotational physiotherapy staff working in haematology, and reviewed by a Consultant Haematologist. Questionnaires were then completed anonymously by patients and given to nursing staff for collection with subsequent collection of results by physiotherapy staff.

## Results

Eighteen questionnaires were completed, 83.3% (n=15) of these found the activity boxes useful. Of those who did not find them useful (n=3), two reported low platelets being the main barrier to exercise. Fifty percent (n=9) reported they used the activity boxes daily.
Fifteen participants responded to the section relating to the effect of the boxes on their confidence to exercise. Of the 60% (n=9) who felt they had a positive impact, one participant reported the boxes gave clear instructions as to what they should be doing, while two others reported the boxes led to a higher level of motivation to exercise. Of those who reported the boxes did not increase their confidence, one person reported that they were affected by general feelings of sickness which impacted their ability to exercise.
Six participants suggested other pieces of equipment that they would have found useful, including a treadmill (n=4), a mat (n=1) and a step (n=1). Sixteen patients surveyed were seen by physiotherapy on the same admission. One patient who was not seen by physiotherapy reported feeling unable to exercise during that admission due to low platelets.

## Conclusion

During an inpatient admission for HSCT, more than 80% of patients reported positive experiences with activity boxes. Barriers identified were low platelet counts and low confidence levels towards exercising. The results of this survey will guide further changes and improvements to the activity boxes and guide plans for funding for further equipment.

**Benefits of an ANP Red flag Clinic**

Louise Gribben Haematology Advanced nurse Practioner SHSCT

**Background**

The NI Cancer Control Programme was published in November 2006. Within the Strategy there is a commitment to ensuring the timeliness of referral, diagnosis and treatment for suspected cancer patients.
The commissioning plan Direction set by the Department of Health dictates that 95% of patients urgently referred by a GP, as a suspected cancer, should begin their first definitive treatment within a maximum of 62 days. (Cancer Access Standards 2008)

**Recognising and identifying current challenges within the haematology service in SHSCT**

As a result of the persistent shortage within the consultant workforce I SHSCT ( 2.8 WTE where 5.0 WTE is required) Traditional consultant red flag review of haematology referrals, resulted in long unacceptable waiting times for patients referred into the service. With suspected or confirmed cancers. Some patients up to 137 days waiting!

**METHODOLOGY**

Scoping exercise carried out in 2020 as to what category of patients were creating this unacceptable waiting list in SHSCT and if and how the ANP could use their expertise and knowledge, in the evolving ANP role, to challenge existing practices and procedures and discuss potential alternatives to delivery of services that would improve the health care for our Haematology population. The initial patient group included patients with CLL and MGUS and drenching night sweats requiring investigation. The success of the red flag clinic within 2 years then led to expanding this service to include patients with MPN's, lymphomas and myeloma. Additional to initial review, the ANP autonomously schedules and requests full work up , ordering of investigations, delivery of results and diagnosis, presents cases at regional MDM and discusses the plan of care with patient.

**OVERALL AIM**

Diagnose, inform and support cancer/Haematology patients in a safe and timely manner.
Improve mental and emotional well-being of patients, by delivery of specialist intervention and support.
Achieve DOH cancer waiting time direction targets.
Reduce burden and demand on specialist consultant clinics.
Use/maximize existing resources by upskilling the Haematology ANP
Implement a new service design where new patients with a Haematological diagnosis can be seen by another health professional on their first appointment.

**2023 results:** Jan -Dec 2023 the **ANP** red flag clinic reviewed 203 patients for their first haematology appointment when referred with suspect cancer.

**Conclusion**

The development of this ANP led clinic has improved the care pathway, while providing safe, appropriate and timely review of red flag referrals by the most appropriate health care professional reflecting the recommendations of many strategic drivers such as;
Transforming Your Care (2014),
Quality 2020 leadership strategy: Delivering Improvement (2014
The health and well-being; Delivering Together 2026
Cancer Access Standards (2008)

**The Development of a National Creative Arts Therapy Service for Children, Adolescents & Young Adults(CAYA) with or in Survivorship of Cancer and their Siblings.**

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**Introduction:** 180 Adolescents and Young Adults (AYA) receive a cancer diagnosis each year in Ireland. Significant psychosocial risks including anxiety, depression, adjustment challenges, post- traumatic stress symptoms, family difficulties and social isolation exist (Steele et al., 2015). Creative Arts Therapies (CATs) is a collective term used for art therapy (AT), dramatherapy (DT) and music therapy (MT). They are evidenced-based professions that provide client-led, psychosocial support by utilising creativity as an alternative and additional means of communication. CATs effectively support symptom distress associated with cancer (pain perception, nausea, fear and anxiety). CAT's provide a supportive outlet that fosters healthy relationships, sense of identity, self-esteem and support social, emotional and overall development negatively impacted by regular hospitalisations, cancer diagnosis or treatment. For AYA effected by cancer the CATs have been shown to be an effective form of psycho-social support (Raybin et, al. 2023; Purrezaian et. al. 2020; Daveson 2001).

**Objectives:** To establish and deliver a National Creative Arts Therapy Service that provides accessible and inclusive therapies for Children, Adolescents & Young Adults (CAYA) affected by Cancer and evaluate its impact.

**Methods:** The Authors engaged in;
i. A literature review of available research regarding CAYA cancer, survivorship and creative arts therapies.
ii. A national mapping of current creative arts therapy support provided in cancer support-centres nationwide.
iii. PPI via engagement of the Young People's Advisory Group (YPAG) to help shape the service offering.
iv. Engagement with the Irish Association of the Creative Arts Therapists to ensure standardisation of qualification for all therapists.
v. Establishing referral pathways internally and externally via hospital multi-disciplinary teams and client's self-referrals.
vi: Developed and distributed feedback surveys for families and therapists. These results were collated and examined to inform the service offering.

**Results:** Our preliminary findings indicate a lack of affordable, community-based psychosocial support for CAYA with or in survivorship of cancer and their siblings. A national network of 70 professional CATs were recruited; AT (50%) MT (31%), DT (19%). Since November 2023 we have received referrals for 112 families. Child with cancer (97), siblings (71), adolescence and young adults (16) located across the country. 114 sessions have been completed since commencing November 2023. Referrals are pre-assessed via phone by a senior creative arts therapist to identify the most appropriate form of CAT. Following completion of the therapy cycle the client and therapist are provided with an evaluation survey. Results are collated establishing the impact on future developments of the service.

**Conclusion:** This service aligns with the Irish Psycho-oncology Model of Care (NCCP, 2023). It provides accessible community psycho-social support to young people affected by cancer.

**Community Haematology Oral Anticancer Medication clinic- creating more value with fewer resources**

Kelly, M. Midland Regional Tullamore, Co. Offaly.

**Background**

Analysis of Haematology Oral Anticancer Medications (OAM) patient cohort and existing management approach revealed opportunities for efficiencies and improvement in the service. Factors including changing demographics, with a growing population of over 65s, and associated longevity due to increasing medical treatments necessitated the initiative. Challenges included meeting increasing demands and safely managing patients with finite resources in the appropriate setting.

**Need**

To move from a hospital based care model to an integrated nurse led community clinic.

**Aims /benefits**

- Patient centric service
- Aligned with key stakeholders' objectives
- Specialization of existing resources
- Better use of resources and budget
- More efficient processes, reduced waiting times

**Methodology**

Change management methodologies, provided a series of goalposts which guided and underpinned the change process. Clinic accommodation was obtained and supporting governance documents and requirements incorporated.

**Outcomes/Results**

The clinic has been implemented on a weekly basis with a view to expansion following review. Key performance indicators (KPI) have been developed to measure outcomes.
Efficiencies have increased with appropriate use of staff, specialization of resources and accommodation, elimination of unnecessary steps in reviewing patients, reduction in waiting times and waiting lists, and increased patient safety and satisfaction. Staff cost saving of 54% are achieved, with consultants released to focus on more complex patients.

**Implications for Practice & Conclusion**

The use of existing resources, including staff and accommodation,
resulted in efficiency and cost savings. Challenges including resistance and conflict occurred highlighting the need for greater focus on the impact of change on individuals and management of crisis points in the change journey.

**Recommendations**

• Budget costings and business case proposal and submission for pharmacy support.

• Greater involvement of nursing staff in the directorate strategic plan.

• Need greater spread of change locally and nationally through communication e.g. newsletter,
presentations, written publication and media clips in collaborations with communications and research teams.

• Monthly team meetings and quarterly directorate report

• Patient and staff satisfaction survey with service.

• Dissemination of learnings from this change to assist the planning of future projects

**LIVING WITH MULTIPLE MYELOMA & AL AMYLOIDOSIS PODCAST SERIES- USING A DIGITAL MEDIUM TO RAISE AWARENESS OF, AND EDUCATE ON LIVING WITH BOTH CONDITIONS**

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**Background**

Multiple Myeloma (MM) is a bone marrow cancer and though it is the second most common blood cancer, it only represents 1% of cancers. On average 384 patients are diagnosed with MM annually.
AL Amyloidosis (immunoglobulin light chain amyloidosis) is a rare disease that occurs when a protein called Amyloid builds up in a patient's organs preventing them from working correctly.
Most people are unaware of myeloma and AL Amyloidosis, therefore a diagnosis can be life changing. Multiple Myeloma Ireland (MMI) is the only charitable organisation focused on supporting (MM) and AL Amyloidosis patients, families and carers. In partnership with stakeholders, we recorded a podcast series to provide information, support and raise awareness on all aspects of Living with MM & AL Amyloidosis.
Topics included personal patient and carer experiences, managing the emotional impact of the diagnosis, research and treatment updates, managing side effects, stem cell transplantation, partnerships with the Royal free Amyloidosis centre and living with relapsed disease.
Interviewees are chosen from a wide range of backgrounds. A TV personality with medical background was selected as interviewer for conversational style interviews and a professional media production agency company was engaged.
Resources utilised include Funding by MM, a budget of €10,000 annually and a nurse with specialist interest and experience present for recordings to provide support. A patient reviewer is also on board who gives feedback before publication.

**Methods**

A retrospective statistical analysis was performed from data collected from the hosting site reports with the aim of assessing patients experience of the podcast and with the goal of improving the production and content going forward.
Further qualitative data was collected at information days and support group meetings, which assessed patient feedback and suggestions for improving the podcast.

**Results**

Twenty-two podcasts have been recorded to date. Three on AL Amyloidosis, 13 on MM and 6 on wellbeing.
A retrospective statistical analysis of the **first 16 shows** revealed, episodes were downloaded 20,024 times and a survey of listeners revealed:

- 69% found it very useful
- 70% were people living with MM
- 25% were a Family Member / Carer of someone living with MM
    - 98% would recommend the series to someone living with MM and their family members / Carers.
- 93% would recommend to a Healthcare Professional.

The respondents (patient support group members) stated that the patient experience episodes (downloaded over 6,800 times) were the most informative (42%).
19% of respondents found episodes providing an overview and giving general information about the diseases most helpful and informative.
18% of respondents from the MMI network were unaware of series. Going forward, we will examine further how to publicise the series within our network of support groups to reach a greater cohort of patients and their families.

The most popular episode, (downloaded 3,302 times) was with Irish Times Journalist, Mr Michael O'Regan who shared his experience of diagnosis and living with myeloma.

Suggested themes or future podcasts include, Updates on Future Treatments, how to support family members, particularly children. Many of the respondents focussed on well-being, requesting information on mental health, self-care and psychosexual health.

**Conclusions and Implications for Practice**

- The Podcast Series was nominated for an Irish Podcast Award and was awarded bronze winner in the Bullseye award category.
- The successful partnership between patients' carers and HCPs led to an effective podcasts series, easily accessible by patients and families.
- An interview with a public figure living with MM is an important element of the podcasts. Public figures have wider audience appeal and attract greater listenership numbers.
- A postproduction survey advertised on various social media platforms provided feedback to inform future topics.
- The podcasts are available as a resource to listen to on the MMI website at https://www.multiplemyelomaireland.org/resources/ as well as on most podcast media platforms
- Podcasting is an effective medium to reach a larger diverse audience and should be incorporated more healthcare.

**'The Hangout - The Story So Far'**

Joy Lewis,
Adolescent & Young Adult (AYA) Cancer CNS, St James's Hospital, Dublin

'The Hangout' is a partnership between business enterprise and healthcare. The Adolescent and Young Adult (AYA) Cancer Team along with multi-disciplinary team members from St James's Hospital, meet monthly with AYA cancer patients in a non-medical space at the Guinness Enterprise Centre, Dublin.

**Aim**

'The Hangout' is a monthly event where AYA cancer patients can 'hangout' with multidisciplinary team members including nurses, doctors, occupational therapist, physiotherapist, psychologist, dietitian, social worker in a non-medical environment where any concerns they have can be highlighted. The AYA cancer patients who attend 'The Hangout' also benefit from interactive sessions with the businesses represented in the GEC.

**Method**

Following on from a single-centre pilot of 'The Hangout' this joint initiative between St James's Hospital and the GEC has evolved further. In April 2024, the AYA Cancer patients received an email inviting them to complete a short anonymous online survey to give their feedback about 'The Hangout'

**Results**

Response rate to the online survey was over 70%. All of the 13 respondents agreed that other AYA cancer patients would benefit from 'The Hangout' being available at their hospital. When asked what they liked best about The Hangout, almost half of the respondents selected 'Meeting other young people'.

**Discussion**

In qualitative studies, Adolescents and Young Adults (AYA's) who experience a cancer diagnosis highlight a need for peer support. The Guinness Enterprise Centre (GEC) in Dublin is the venue for 'The Hangout'. It is more than a venue, the businesses based at the GEC regularly collaborate with one another and now this collaboration extends to the AYA cancer patients and healthcare staff attending.

**An Activity Analysis undertaken to understand the complexity of the AYA Cancer CNS role**

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**Introduction:** Clinical Nurse Specialist roles and their contribution to patient care and outcomes needs to be documented. We must show the complexity and specialist nature of our role. The evidence of contribution and credibility of the CNS role needs to be measurable to highlight activities and performance. It is imperative we justify our worth. The Evaluation of Nurse Specialist roles can be challenging. It is acknowledged that Specialist Nursing work is complex and this then leads to difficulty in developing and applying appropriate techniques for analysis of the clinical nurse specialist role. We hope demonstrate how we spend our time and its value to care of Adolescents and Young Adults (AYA) cancer patients. AYA's facing a cancer diagnosis require specialised care that considers their unique developmental, emotional, and psychosocial needs. Effective nursing care is pivotal in providing comprehensive support to this population. However, understanding the intricacies of AYA nurse specialist care delivery and optimising time management remains a challenge. This abstract presents the development and implementation of a novel tool aimed at capturing a day in the life of the AYA nursing team.

**Methods:**The development of the tool involved a literature review to guide us towards the most common interactions of AYA cancer Nursing care and considerations. This project requires a Multidisciplinary team collaboration to identify key domains that are essential for AYA nursing care delivery. These domains include physical, psychological and social and within these domains we created more specific interventions that the AYA cancer CNS provides. Based on these domains, Microsoft Excel was adapted to capture various aspects of the nursing team's daily activities, the tool was piloted and refined through interactive feedback sessions. To gain a reasonable picture of our activities we will aim to collect 70-100 hours of work over 2-3 weeks.

**Results:** The developed tool will provide a comprehensive framework for AYA nursing team members to document their daily activities and time allocation. The tool allows for real-time data collection and analysis, enabling AYA Cancer CNS's to identify trends, assess workload distribution, and optimise resource allocation. The implementation of the tool will demonstrate nursing team efficiency and will promote holistic care.

**Conclusion:** The development of this tool will offer valuable insights into the complexities of AYA Cancer care provision and will facilitate continuous quality improvement efforts. By leveraging guidance from the Cassandra app, the AYA Cancer nursing team can effectively audit time spent on various activities, identify areas for optimisation, and enhance the delivery of tailored and developmentally appropriate care to AYA patients. This poster presentation aims to share our experiences, and future directions in utilising innovative tools to support AYA Cancer nursing practice.

## ANP led Pre-assessment of Patients on Daraumumab-A quality Improvement Project

Lisa Lyons, Michaela Cunning & Claire Stewart

**Background:** Daratumumab, a CD38-directed monoclonal antibody used to treat multiple myeloma (MM), is licenced in both the front line and relapsed setting. In Northern Ireland approximately 179 people are diagnosed with myeloma annually (Cancer Research UK, 2024). Many of these patients will receive a Daratumumab containing regimen which requires frequent subcutaneous injections during the initial treatment phase, moving to monthly injections until relapse or toxicity. Patient questionnaires revealed that patients on Daratumumab spent an average of 3.5 hours in the department on the day of their assessment and treatment. This means that a patient starting on Daratumumab could spend 77 hours waiting in the department during their first year of treatment, reducing to 42 hours each year thereafter. Given that 50% of patients remain on Daratumumab after five years therefore, steps to improve the patient experience became a priority for the haematology team. To address this the haematology ANP proposed changing the model of review from consultant led (same day assessment and treatment) to an ANP led model, with assessment and treatment on separate days, with treatment scheduled to a pre agreed time slot. In a bid to further reduce time spent in the department the ANP, in collaboration with pharmacy colleagues, implemented changes to the premedication schedule for Daratumumab.

**Objectives:**

- Improve patient experience by reducing waiting times.
- Decrease chair time in the chemotherapy day unit.
- Free up slots at consultant led clinic

**Methods:**

A Plan-Do-Study-Act (PDSA) methodology was employed for this quality improvement project. Under the new ANP-led pathway, patients were provided with dexamethasone for self-administration 1-3 hours prior to their scheduled appointment. The premedication regimen was streamlined by discontinuing chlorphenamine and paracetamol, which were previously administered 1 hour before treatment (Kumar et al (2022). The ANP conducted pre-assessments, ordered treatment, and scheduled specific appointment times, allowing for a more efficient administration of Daratumumab upon patient arrival.

Results:

Transitioning to ANP-led reviews has markedly improved patient experience by reducing patient waiting times. The initiative has been highly evaluated, and patients now report an average visit duration of 30 minutes. The elimination of chlorphenamine and paracetamol has not only streamlined the premedication process but also reduced pharmacy costs and nursing workload. Furthermore, removing sedating antihistamines has lessened the risk of side effects such as drowsiness and confusion in older adults. The ANP-led model has been positively received, giving patients greater autonomy over their medication schedule as well as freeing capacity at the consultant clinics.

**Conclusions and Next Steps:**

The ANP-led pre-assessment and revised premedication regimen have significantly enhanced the efficiency of Daratumumab administration, benefiting both patients and staff. As many patients will continue Daratumumab therapy long-term, exploring patient or caregiver administration of the drug at home could further reduce travel burdens and improve patient autonomy. Expanding self-administration practices, as established in other therapeutic areas like rheumatoid arthritis and multiple sclerosis, may offer additional benefits in terms of convenience and resource optimisation.

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## A FORMATIVE SERVICE EVALUATION EXPLORING THE EXPERIENCE AND LEVELS OF SATISFACTION OF PATIENTS ATTENDING THE NURSE LED BONE MARROW CLINIC

**L Lyons**
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### Background
The incidence of haematological malignancy is increasing, and the bone marrow biopsy plays a key role in the diagnostic process. Due to the increasing demand, haematology clinics are frequently operating beyond their capacity. In response to this challenge, a nurse-led bone marrow clinic was established by the Trust in 2014. However no formal evaluation of this service had been conducted.

### Aim
To explore the experience and satisfaction among patients who have attended the bone marrow biopsy clinic and identify areas for service improvement.

### Method
A qualitative evaluation of the service was conducted using semi-structured interviews, which were analysed using a content analysis approach. A non-probability, purposive sampling method was used. Six females and three males who attended in the last 3 months were interviewed, their ages ranged from 56 to 83 years, they were diagnosed with various haematological conditions.

### Findings
Four themes, “influence of personality type on stress and coping before the procedure,” “interplay between experience and expectations”,” impact of person-centered nursing care” and “Potential areas for Improvement” emerged from the analysis. All participants positively evaluated the nurse-led clinic, expressing a high level of satisfaction with the care they received. Of particular note was that the procedure was much less painful than what participants had expected as well as the positive impact of person-centred care on the patient experience. Suggested improvements included better information about car parking and clinic location, and a change in the bone marrow biopsy clinic environment which participants felt lacked the privacy required for this invasive procedure.

### Conclusions
This evaluation's findings serve as an important reminder of the significance of connecting with patients on a human level and meeting patients “where they are at” to enable them to feel safe and supported during their procedure.

## EMPOWERING CANCER CARE: OPTIMISING STOP SMOKING BRIEF INTERVENTIONS THROUGHOUT CANCER TREATMENT.

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**Aims:** To provide cancer patients who smoke equal access to stop smoking supports. Empower staff to optimise brief interventions with their patients throughout all stages of cancer treatment (diagnosis, treatment and survivorship).To provide easy access /direct referral from the acute pilot site to the community stop smoking services. Establish and integrate a collaborative professional relationship between the acute cancer services and community stop smoking services in the South East.

**Background**: Research shows that cancer patients are less likely to be offered brief interventions for smoking cessation or referred to stop smoking services while attending cancer treatment services as they would if attending other hospital services. There is a disproportionate rate of smoking cessation rates among cancer survivors when compared to the general population.Within this research cancer patients also identify that they want health care professionals to discuss smoking cessation with particular emphasis on the short term benefits.

**Benefits of stopping smoking for cancer patients include:**
Reduced risk of recurrence of cancer
Fewer second primary cancers
Better treatment outcomes
Fewer treatment related complications & toxicities
Better survival rates
Lung cancer mortality is lower with decreased smoking
These complications decrease by 19% per week after cessation.

**Barriers for Healthcare professionals:**
Barriers identified in research include:
Perceptions such discussions were not appropriate.
Likely to be ineffective.Stigmatising.
Inadequate training in smoking cessation.

**Methods:** Using a Knowledge Transition Framework and national clinical guidelines to underpin the importance of these stop smoking brief interventions, this project will assist staff that want best outcomes for to integrate a care pathway to the already established community services that can provide specialist stop smoking services, with the right care in the right place at the right time. This project is based on a collaborative, integrated tailored approach between community and acute services transforming research into practice.
A steering group has been formed to develop an interdisciplinary educational resource for staff. Initially a staff survey will take place to provide the foundation of the requirements for this resource. This group will also integrate a new electronic referral pathway for cancer services to directly and efficiently refer to stop smoking services in the South East.

**Discussion:** It is envisaged that staff, following educational interventions, will show an increased awareness of the evidence for stop smoking brief Interventions for cancer patients. This will create a cultural awareness within the work environment and a willingness by staff to provide these brief interventions.
It is anticipated that referrals from the new electronic direct referral from the pilot site to South East community healthcare community stop smoking services will provide a baseline and give an insight into numbers of referrals. It is planned to utilise a closed loop referral system to enable feedback to the referring health care professional.
This project is the first cancer specific smoking cessation intervention within Ireland. Therefore this has potential to be replicated locally within other specialist cancer services (diagnostic, radiation oncology and surgical) but also at national level, through the NCCP as an educational resources for all cancer services within cancer centres in Ireland. The project team believes that there are further opportunities to develop dedicated stop smoking services within the acute setting with collaborative links to community services as an integrated service during cancer treatment.

# INCREASING PRESCRIBING CAPACITY IN HAEMATOLOGY OUTPATIENT SERVICES: INTEGRATION OF NURSE AND PHARMACIST PRESCRIBERS

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## Introduction

Treatment of haematology malignancies within Southern Health and Social Care Trust (SHSCT) relies on collaborative working and innovative approaches to the delivery of care. The combination of an aging population, expanding treatment options and improved survival has resulted in an exponential rise in patients within this speciality.[1] Increased demand on services is compounded by the shortage of consultant and trainee haematologists.

It was recognised by the Department of Health[2] that the reliance on medical staff to prescribe every systemic anticancer treatment (SACT) cycle was not sustainable and suitably trained non-medical prescribers (NMP) could be utilised.

SHSCT haematology outpatient services currently has the support of one Advanced Nurse Practitioner, one Clinical Nurse Specialist (CNS) prescriber, and three Specialist Haematology Pharmacist prescribers for the prescribing of SACT.

This audit aims to review nurse and pharmacist SACT prescribing in haematology outpatients, SHSCT. Data will be used to evaluate the service, and help guide future development.

## Objectives

- Outline timeline for evolution of non-medical prescribing service in haematology, SHSCT
- Determine number of haematology clinic appointments in 2023 delivered by NMPs
- Determine remit of non-medical SACT prescribing in haematology
- Explore patient and staff opinions of NMP clinics

## Method

1. Collate timeline for introduction of non-medical prescriber (NMP) clinics within haematology
2. Review data on haematology outpatient clinic activity between January and December 2023
3. Develop NMP staff survey to determine clinical remit of each prescriber
4. Develop questionnaire to determine patient and staff experience of haematology NMPs

## Results

Timeline for non-medical prescribing in haematology services:
2010: First nurse led haematology prescribing clinic commenced.
2014: Second nurse led clinic commenced.
2019: First pharmacist led clinic commenced.
2020: Second pharmacist clinic commenced.
2022: Temporary funding secured, third pharmacist clinic commenced.
2024: 6 NMP SACT prescribing clinics per week ongoing - delivered by one Advanced Nurse Practitioner, one CNS and three pharmacists.

Number of haematology clinic appointments (review and SACT prescribing) by non-medical prescribers (January 2022 – December 2022) = 3695
This equates to 1232 hours of clinic time (20 minute appointments).

Nurses and pharmacists prescribed SACT for patients across a range of haematological malignancies, including multiple myeloma, lymphoma, MPN, CLL and CML. Examples of SACT agents prescribed include lenalidomide, daratumumab, hydroxycarbamide, ibrutinib and rituximab. All NMPs surveyed had completed SACT competency training and are authorised to prescribe SACT from cycle 2 onwards.

An audit of patient opinion of the service was completed in 2020, all feedback was positive, a repeat patient satisfaction survey is planned for 2025. An audit haematology staff opinion was completed in 2023[4]. Feedback was also positive.

**Conclusion**

Nurse and Pharmacist Led Haematology clinics are well established in SHSCT, and demonstrate increased capacity within a service with ongoing medical staff shortages.

NMPs prescribe across a range of disease states within the remit of haematological malignancies.

There is scope to diversify in the future, based on the evolving needs of the service. The provision of over 3500 clinic slots per year by collaborative working between the nurse and pharmacist team increases capacity within consultant led clinics.

**References**


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**The impact and limitations of an Acute Haematology Oncology Nursing Service in a large Dublin Hospital**

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An Acute Oncology Service was developed in Beaumont Hospital in 2019 with an aim to improve patient safety and experiences as outpatients following systemic anti-cancer therapy (SACT). This service was extended to include Haematology patients in 2020 which coincided with the national rollout of the acute haematology oncology nursing service by the National Cancer Control Programme (NCCP). This national service now extends to 26 Hospitals across the Republic of Ireland and has grown massively since its inception.

Within Beaumont there is currently 2.5 WTE Clinical Nurse Specialists working in the Acute Haematology Oncology Service. This service acts as a source of risk assessment and advice for patients undergoing SACT. As the service has become more established its impact on unscheduled hospital attendances can be measured in the amount of patients using the service who require hospital review/admission for their symptom/side effect. When compared with overall telephone triage contacts, the number of patients referred on to attend ED or Day Ward is approximately 10%. The remaining patients issues are resolved via phone consultation or in liaison with community services such as GP, PHN, community Palliative care.

Unfortunately, the impact of vacant posts is clear when the number of triage calls is compared to a period with a full staffing cohort. With 1 WTE CNS absent the service noted a decrease of approximately 50% in calls received.

## Introducing a Systemic Anti-Cancer Therapy (SACT) Safety Pause to improve clinical practice

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**Introduction:** SACT is administered to patients daily within haematology. Multiple patients receive treatment, with some patients receiving more than one agent. Regimens are intricate and carefully followed. Patient safety is therefore of paramount importance and at the forefront of nursing care.

**Background:** A SACT omission occurred where a patient did not receive one of their chemotherapy drugs. The patient's safety was placed at risk, it negatively impacted upon patient trust. In addition, the remorse felt by the nursing staff involved in the incident was immense and affected their confidence.

**Methods:** During a hot debrief of the incident the areas that had not been adhered to where discussed. SACT should be checked with the patient to ensure that they are getting the correct drug but as the chemo was never in the nurses hands this step was missed. It was noted that there was no documented process with SACT in relation to the use of a daily safety pause. It was evident that not enough time was taken to confirm what SACT was to be administered, thus the idea of introducing a SACT Safety Pause into clinical practice was borne.

The 'Safety Pause' is not a new concept. The World Health Organistion (WHO) (2008) launched the Surgical Safety Checklist, which advocated a mandatory pause before, during and after surgery. Since implementation, it has improved outcomes for patient worldwide.

Others have looked at whether safety briefings improve patient safety in the acute setting. Findings showed that safety briefings achieved beneficial outcomes and improved safety culture (Ryan et al, 2019)
Initially the implementation of a paper based SACT Safety Pause was introduced. This would increase staff awareness, improve communciation, enhance education, prevent omissions, maintaining patient safety and trust. The Nurse in Charge would complete the document with the team.

**Results:** Completion of this document was encouraged and championed by the management staff. The tool was trialled and evaluated by those using it. Nursing staff liked the idea of a specific SACT Safety Pause but felt that the paper-based nature of the tool made it feel like a 'pen pushing exercise' and 'yet another thing to complete' within an already busy work environment. Furthermore, whilst completion of the tool moderately improved communication within the nursing team it was not fully embraced by all.

To encourage use by the entire team the concept needed to be altered. Drawing upon suggestions from the nursing team the 'paper-based' SACT Safety Pause was abandoned in favour of a more visible tool. Bright yellow posters sectioned off into rows, one row for each bed, were placed at each nursing station. At handover nursing teams were encouraged to gather the SACT charts, initiate safe space discussion of the SACT administrations for that day and write these on the visible posters.

**Conclusions:** Since the introduction of the SACT Safety Pause no SACT errors or omissions have occured. A feedback process is in progress from all staff, which will be collated by mid-October.

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World Health Organisation (2008) 'WHO Surgical Safety Checklist' Accessed from: https://www.who.int/teams/intregrated-health-services/patient-safety/research/safe-surgery/tools-and-resources
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# DEVELOPMENT OF A BESPOKE 'END OF TREATMENT' SUMMARY FOR ADOLESCENTS AND YOUNG ADULTS WITH HODGKIN'S LYMPHOMA

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**Background**
Hodgkin's lymphoma (HL) is a common cancer in adolescents and young adults (AYAs). While most are cured with upfront chemotherapy +/- radiotherapy, patients are at risk of specific late-effects as a result of their disease and treatment. Additionally AYAs face significant psychosocial/ mental health concerns and risk of education/ employment failure. Guidance by NHS England recommends AYAs are provided with an end of treatment (EOT) summary and careplan outlining any specific late-effects and required monitoring.
The British Society for Haematology (BSH) sets out recommendations in relation to late-effects and survivorship in HL. Patients should be educated on their risk of cardiovascular/ pulmonary toxicity, secondary malignancy, risk to fertility or early menopause. Additionally patients require life-long irradiated blood products. Females aged 35 or younger who revieve radiotherapy to breast tissue, should be offered entry to early breast screening programs, and those who have had irradiation to the neck/ upper mediastinum, should have regular thyroid screening.

**Methods**
An audit was carried out in the Northern Health and Social Care Trust (NHSCT) which included 17 AYAs with HL who presented to the trust between 2016 and 2023. Audited standards included key BSH recommendations related to late effects and survivorship in HL. Relevant electronic and paper medical records were screened to assess adherence to these standards.

**Results**

- 100% of AYAs (n=3) who received radiotherapy to breast tissue- appropriately referred to early breast cancer screening program
- 100% AYAs (n=17) were counselled regarding their lifetime risk of secondary malignancy, risk of cardiovascular/ pulmonary disease, potential impact to fertility impact and/ or menopausal status.
- 100% of AYAs (n=17) were educated regarding life-long irradiated blood.
- 80% of AYAs (n=4) who received radiotherapy to neck/ upper mediastinum were having regular thyroid function screening.

The AYA team recognised the benefits that an EOT summary could provide in ensuring AYAs and their primary care teams have an accessible record of their diagnosis and treatment history, outlining potential late effects or long-term monitoring requirements. An AYA EOT summary was therefore co-produced with 6 young people who had experienced cancer as an AYA. Completed summaries are shared electronically with AYAs and their General Practitioner. Additionally, information postcards were developed to give to AYAs alongside the EOT summary, providing information on specific topics such as fertility, work, finances, mental health and education. At the time of the audit 59% of AYAs (n=10) had evidence of an EOT summary completed. AYAs reported positively on the EOT summary and in particular felt it was 'very important' that it had been developed in collaboration with other AYAs.

**Conclusion**
Excellent adherence to recommendations related to late-effects and survivorship in HL was demonstrated in this audit. However an AYA EOT summary further ensures both patients and their primary care team have an accessible record of their diagnosis, treatment history, long-term monitoring required or potential late-effects that they may be at risk of. Completion of the EOT summary also offers opportunity for patient education and health promotion. This co-produced AYA EOT summary has been successfully piloted in 2 trusts in NI, with current plans to adopt across all health trust in NI.

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