ASH 2025 Clinical and AI / ML Preview

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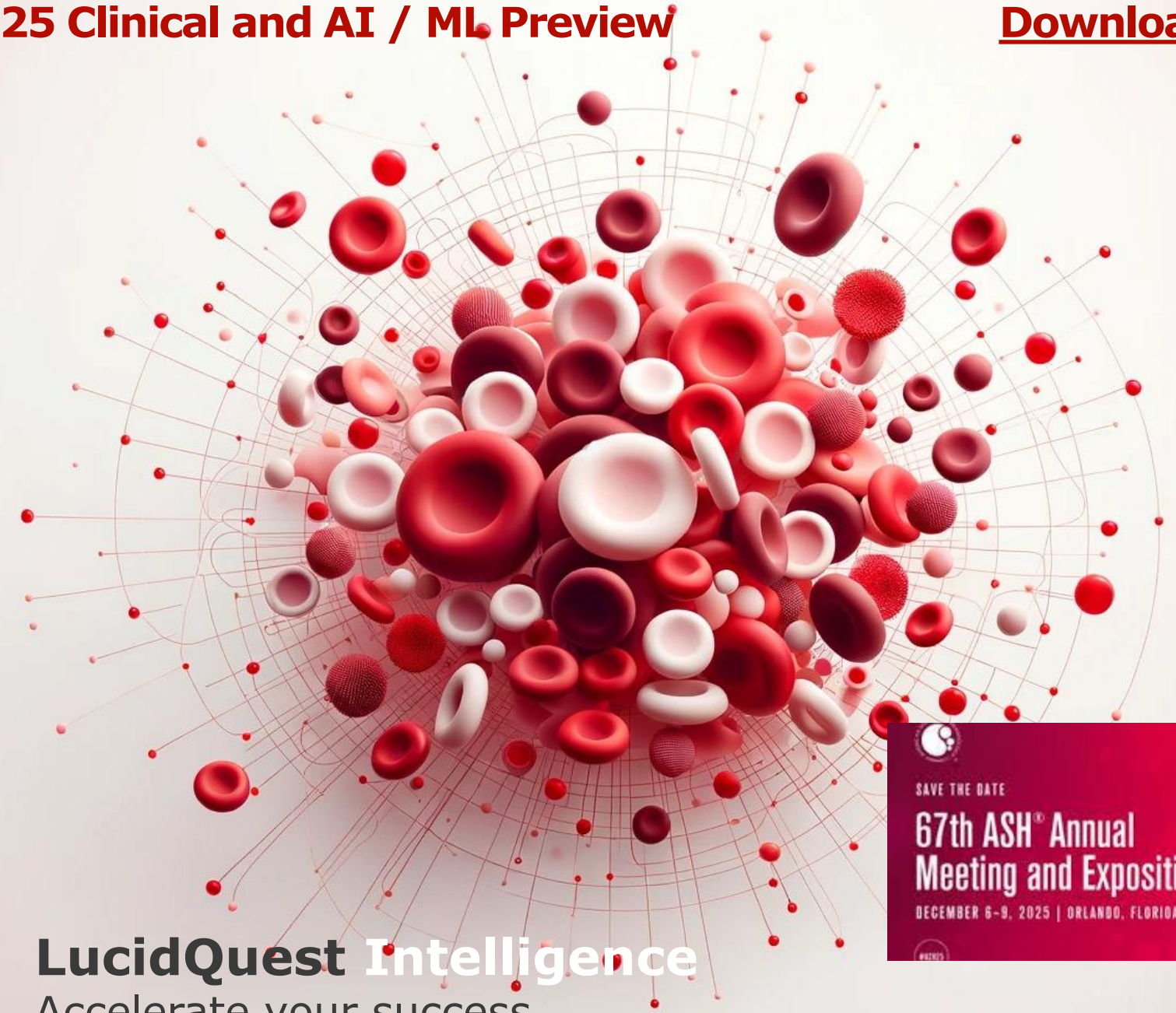

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ASH 2025 – General Overview

- **Record Late-Phase Activity:** ASH 2025 will feature dense Phase 2/3 readouts across leukemias, lymphomas, myeloma, and benign hematology, reshaping several first-line and relapsed standards of care
- **Cellular Therapies Maturing:** Long-term CAR-T and engineered cell therapy data are expected to clarify durability, retreatment options, and comparative roles versus transplant and bispecifics
- **Targeted–Immunotherapy Convergence:** Combinations of small molecules, antibodies, and T-cell engagers will deepen remissions while carefully limiting myelosuppression, infections, and resistance
- **Fixed-Duration Treatment Focus:** Trials are expected to refine finite, MRD-guided strategies in CLL, AML, and myeloma, balancing depth, toxicity, cost, and patient preference
- **Patient-Centred Outcomes Priority:** QOL, symptom burden, and functional endpoints will feature prominently, influencing regulatory and reimbursement perspectives in chronic MPNs, ITP, and myeloma
- **High-Resolution Translational Insights:** Genomic and immune profiling will refine disease subtypes and resistance markers, enabling tightly biomarker-guided trial designs across hematologic malignancies and benign disorders

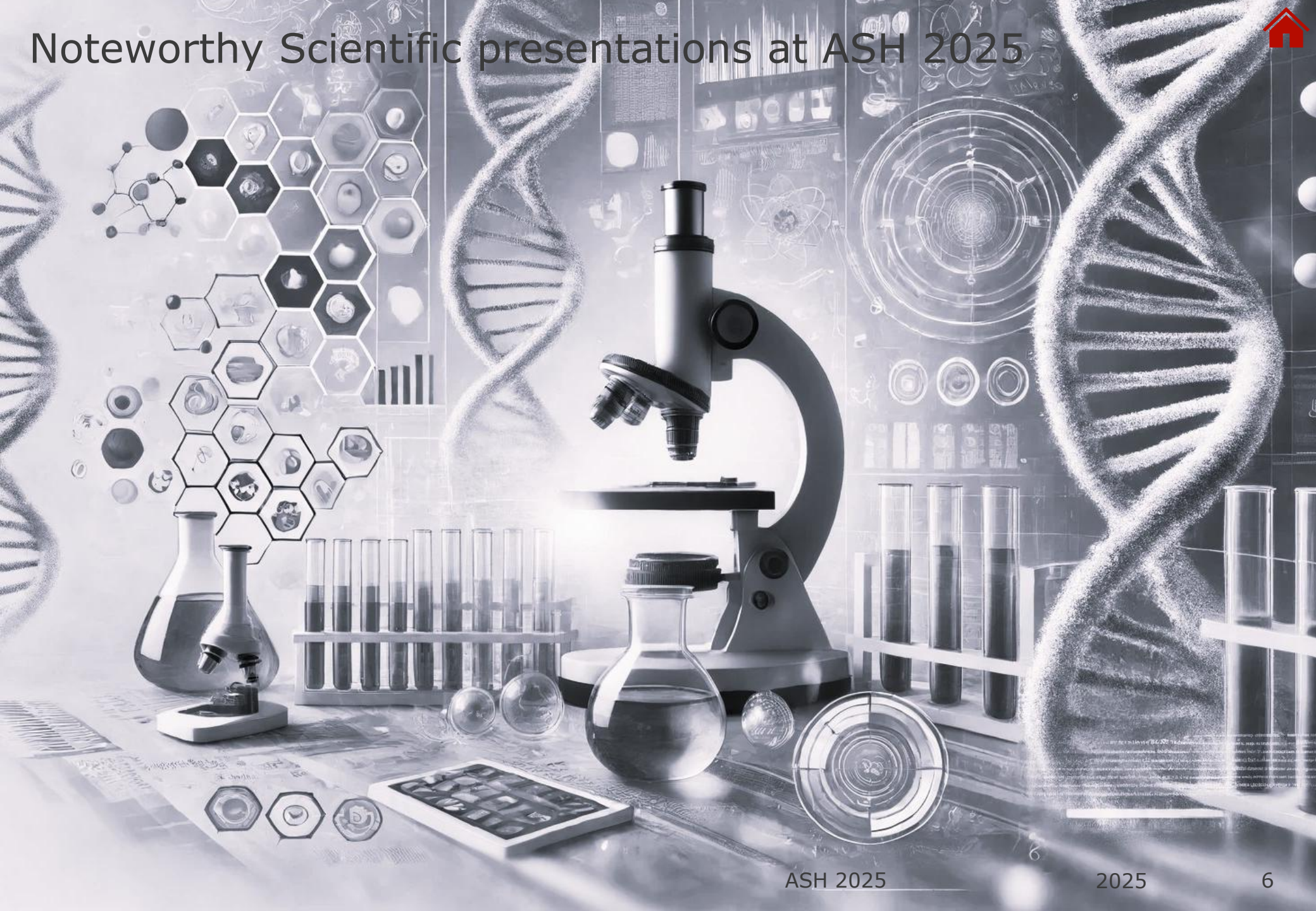
ASH 2025– Conference Themes (1/2)

- **BTK/BCL2 optimization:** Studies are going to refine sequencing and combinations of covalent and non-covalent BTK inhibitors with venetoclax and anti-CD20 antibodies in CLL, MCL, and immune cytopenias
- **MRD-guided care:** MRD-directed algorithms are going to adjust treatment intensity and duration in ALL, AML, follicular lymphoma, and myeloma, reshaping transplant, consolidation, and maintenance decisions
- **Bispecifics moving upstream:** CD20, CD19, BCMA, and GPRC5D bispecifics are expected to enter earlier lines, including consolidation and maintenance, challenging current CAR-T and autologous transplant positioning
- **Rewriting AML induction:** Triplet venetoclax regimens and targeted combinations are going to redefine induction, MRD clearance, and bridge-to-transplant strategies in genomically defined AML subsets
- **Refined MDS/MPN modifiers:** JAK-based doublets, telomerase blockers, and hepcidin-axis agents are going to target true disease modification in MDS, CMML, MF, ET, and PV

ASH 2025– Conference Themes (2/2)

- **Transforming hemoglobinopathies:** Novel HbF inducers and sickling-pathway modulators are going to focus on VOC reduction, transfusion independence, and organ preservation in SCD and thalassemia
- **Complement and thrombotic disorders:** Next-generation complement inhibitors and ADAMTS13 replacement are going to expand precision options for PNH, TTP, and complex thrombotic microangiopathies
- **Next-generation GVHD control:** GVHD prevention will merge graft engineering, targeted antibodies, microbiome modulation, and cellular therapies to enhance allogeneic HCT tolerance and long-term outcomes
- **Evolving CAR-T paradigms:** Allogeneic, multispecific, and consolidation CAR-T approaches are going to emphasize durability, toxicity mitigation, and rational sequencing with bispecifics and targeted agents
- **Smarter trial methodology:** Adaptive and AI-enabled trial models will streamline hematology development and improve real-world applicability

Noteworthy Scientific presentations at ASH 2025



Key Topics From Notable Presentations (1/8)

- **Acute Myeloid Leukemia (AML):** Targeted therapies like bleximenib and venetoclax are set to show promising results in treating high-risk and difficult-to-treat AML subtypes, with a focus on improving survival rates and bridging patients to stem cell transplantation
  - High-Risk AML and Novel Conditioning Regimen: A Phase 2 trial combining myeloablative busulfan, cladribine, thiotepa, venetoclax, and post-transplant cyclophosphamide showed promising outcomes in high-risk AML, with 3-year progression-free survival (PFS) of 58%. TP53 wild-type patients had notably better outcomes
  - Bleximenib in KMT2A and NPM1m AML: The Phase 3 HOVON 181 trial evaluates bleximenib, a menin inhibitor, in combination with standard chemotherapy for KMT2A rearranged (KMT2Ar) and NPM1 mutated (NPM1m) AML. This study seeks to improve event-free survival (EFS) and overall survival (OS) in these challenging subtypes
  - Venetoclax in Pediatric and Elderly AML: The ITCC-101/APAL2020D study explores venetoclax combined with standard treatments for relapsed pediatric AML. Additionally, studies like DEC3-VEN in elderly or unfit AML patients have shown promising complete remission (CR) and minimal residual disease (MRD) negativity rates, demonstrating its effectiveness

Key Topics From Notable Presentations (2/8)

- **Acute Lymphoblastic Leukemia (ALL):** Experts will discuss Innovative therapies like blinatumomab, CAR-T, and targeted TKIs that can improve outcomes in ALL, with increased MRD negativity and reduced reliance on traditional chemotherapy or stem cell transplantation

  - Blinatumomab and MRD: Blinatumomab showed improved MRD negativity and remission rates in adult B-ALL, highlighting its effectiveness in specific molecular subgroups and the potential for targeted therapies

  - FMA vs Cy/8TBI: A study comparing FMA and Cy/8TBI regimens found no significant survival differences, suggesting reduced-intensity conditioning (RIC) regimens can be viable for older, high-risk ALL patients

  - CAR-T in First-Line B-ALL: First-line CD19-directed CAR-T therapy demonstrated high MRD-negative rates and long-term leukemia-free survival, positioning it as a potential alternative to traditional chemotherapy in newly diagnosed B-ALL

Key Topics From Notable Presentations (3/8)

- **Lymphoma (Hodgkin & Non-Hodgkin):** The session will explore how novel combinations like acalabrutinib, odronextamab, and pembrolizumab-based therapies are showing high efficacy and manageable safety profiles in various lymphoma subtypes, including LBCL and Hodgkin lymphoma, and may represent promising alternatives to traditional chemotherapy regimens
  - Acala in Untreated Large B-Cell Lymphoma (LBCL): A Phase 2 trial combining acalabrutinib (acala) with frontline chemotherapy showed broad efficacy across LBCL genetic subtypes, particularly in MCD/N1. Acalabrutinib responded in 50% of patients, with a 2-year progression-free survival (PFS) rate of 84.8%
  - Odronextamab in Untreated DLBCL: The Phase 1A of the OLYMPIA-3 trial evaluated combining odronextamab (Odro) with chemotherapy for untreated DLBCL, showing a 100% ORR in one group. Safety was manageable, with cytokine release syndrome (CRS) being the most common side effect
  - Brentuximab Vedotin and Pembrolizumab in Hodgkin Lymphoma: A combination of pembrolizumab, gemcitabine, vinorelbine, and liposomal doxorubicin (GVD) in R/R cHL patients achieved a 95% CR rate with 100% PFS at 13.5 months, providing a durable long-term outcome

Key Topics From Notable Presentations (4/8)

- **Multiple Myeloma & Plasma Cell Disorders:** Session will discuss about novel therapies like KRd, Iberdomide maintenance, and CAR-T therapies are significantly improving outcomes in multiple myeloma, offering deeper and more durable responses, particularly in transplant-ineligible and relapsed/refractory patients. Further studies will solidify their roles in transforming the treatment landscape

  - KRd vs. VRd: KRd showed superior MRD-negative CR rates (31% vs 18%) and PFS compared to VRd in newly diagnosed multiple myeloma (NDMM), supporting its use as an induction regimen

  - Iberdomide Maintenance: Iberdomide improved MRD-negative CR rates (31%) post-transplant, with the 0.75 mg dose offering efficacy and tolerability, showing 92% PFS at 2 years

  - CAR-T Therapy for Relapsed/Refractory Multiple Myeloma (RRMM): The iMMagine-1 trial demonstrated that anito-cel, an anti-BCMA CAR-T therapy, achieved 97% overall response rate (ORR) and 93% MRD negativity in RRMM patients. The treatment showed strong efficacy and manageable safety, with most adverse events related to cytopenias and cytokine release syndrome (CRS)

Key Topics From Notable Presentations (5/8)

- **Myelodysplastic Syndromes & Myeloproliferative Neoplasms:** Sessions will highlight that emerging therapies such as rusfertide, pacritinib, and durable CR in MDS are set to provide new treatment avenues, enhancing symptom control and survival, especially in underserved populations with myeloproliferative disorders

  - Rusfertide in PV: The VERIFY study confirmed rusfertide's sustained efficacy in reducing hematocrit and phlebotomy needs in polycythemia vera (PV) patients, improving fatigue and disease symptoms with manageable safety

  - Durable CR in HR-MDS: In higher-risk myelodysplastic syndromes (HR-MDS), durable complete response (CR) >6 months was shown to correlate with significant survival benefit, offering a reliable surrogate for assessing treatment efficacy

  - Pacritinib for High-Risk MF: Pacritinib significantly improved spleen size and symptom burden in high-risk myelofibrosis (MF) patients, offering superior outcomes over standard treatments, positioning it as a key option for these patients

Key Topics From Notable Presentations (6/8)

- **Bone Marrow Failure & Aplastic Anemia:** Experts will discuss how combining eltrombopag with standard therapies (IST, CSA) improves treatment responses and offers promising new approaches for both severe and moderate aplastic anemia, with lasting benefits and manageable safety profiles

  - Eltrombopag in AA: The Phase 3 trial showed that adding eltrombopag (EPAG) to hATG + CsA improves immune responses in severe aplastic anemia (AA), with naïve Tregs identified as key predictors of treatment success

  - Romiplostim for AA: A multicenter study demonstrated that romiplostim (ROMI) combined with immunosuppressive therapy (IST) led to sustained long-term responses in AA, with a 77.1% overall response rate (ORR) and high survival rates

  - EPAG in Moderate AA: The EMAA trial revealed that eltrombopag combined with cyclosporine A (CSA) significantly improved hematologic responses in moderate aplastic anemia (MAA) compared to placebo, offering a potential new standard of care

Key Topics From Notable Presentations (7/8)

- **Benign Haematology:** The ongoing studies on novel treatments for hematologic disorders like HES, hemophilia, PNH, and thalassemia will show promising results in reducing bleeding events, improving quality of life, and offering potential disease-modifying therapies. Benralizumab, marstacimab, KP104, and other therapies will pave the way for better management of these conditions, with an emphasis on safety and long-term efficacy

  - Benralizumab in Hypereosinophilic Syndrome (HES): The Phase 3 NATRON trial demonstrated that benralizumab significantly reduced flare risk and delayed hematologic relapse in HES patients, improving fatigue with a favourable safety profile

  - Marstacimab in Hemophilia: The BASIS study found that marstacimab significantly reduced annualized bleeding rates (ABR) and improved quality of life in hemophilia A/B patients with inhibitors, showcasing its potential as a key treatment option

  - KP104 in PNH: The Phase 2 BASIS trial showed that KP104 led to sustained hemoglobin increases and normalization, with no serious adverse events, presenting it as a promising monotherapy for PNH

Key Topics From Notable Presentations (8/8)

- **Transplantation & Cell Therapy (CAR-T, GVHD, conditioning regimens):** Ongoing research into novel therapies like itolizumab, TSC-101, and G-CSF receptor blockade in transplantation and cell therapy will demonstrate significant improvements in patient outcomes, such as reduced relapse rates, improved survival, and reduced complications, marking promising advancements in these areas
  - Itolizumab for Acute Graft-Versus-Host Disease (aGVHD): The Phase 3 EQUATOR trial showed that while itolizumab did not meet the primary endpoint for Day 29 complete response, it improved secondary outcomes such as duration of complete response and one-year survival, highlighting its potential in aGVHD management
  - TSC-101 in Hematologic Malignancies: The ALLOHA study showed promising efficacy of TCR-engineered T-cell therapy (TSC-101) in preventing relapse post-HCT, with early results showing improved relapse-free survival and overall survival in patients with AML, MDS, or ALL
  - G-CSF Receptor Blockade in Sickle Cell Disease (SCD): A preclinical study found that G-CSF receptor blockade significantly reduced vaso-occlusive crisis (VOC) severity in SCD mice, suggesting a new therapeutic approach for managing VOC in SCD patients

Focus of Key Industry-Sponsored Sessions at ASH 2025 (1/5)

- **AbbVie:**
  - Focus Areas: Multiple Myeloma & CLL
  - Discussions will explore the clinical impact of BCL-2 inhibitors as the backbone of fixed-duration therapy in CLL and advancements in BCMA-directed bispecific antibody therapies for relapsed/refractory multiple myeloma (RRMM)
- **Lundbeck:**
  - Focus Areas: Lymphoma & MCL
  - Presentations will highlight updates on CAR-T therapies in follicular lymphoma (FL) and the expansion of BTK inhibitors in the upfront treatment of mantle cell lymphoma (MCL)

Focus of Key Industry-Sponsored Sessions at ASH 2025 (2/5)

- **Genentech (Roche):**
  - Focus Areas: DLBCL & Thalassemia
  - Sessions will focus on advancements in diffuse large B-cell lymphoma (DLBCL) therapies and new treatments for thalassemia, showcasing therapeutic advancements and patient outcomes
- **Bristol Myers Squibb:**
  - Focus Areas: Haematological Malignancies
  - Discussions will explore the growing role of CAR-T in multiple myeloma, with new data on earlier lines of therapy, and investigating CELMoDs in myeloma and their clinical implications
- **Johnson & Johnson:**
  - Focus Areas: Myeloma & CLL
  - Presentations will cover new treatment options for relapsed/refractory CLL, including advances in BTK inhibitors, and CAR-T strategies in multiple myeloma for earlier intervention

Focus of Key Industry-Sponsored Sessions at ASH 2025 (3/5)

- **Pfizer:**
  - Focus Areas: Hemophilia & DLBCL
  - Sessions will examine subcutaneous treatments in hemophilia care, including HYMAVZI (marstacimab), and advancements in DLBCL care with bispecific antibodies in 3L+ settings.
- **Novartis:**
  - Focus Areas: PNH & Myelofibrosis
  - Discussions will highlight new therapies for Paroxysmal Nocturnal Hemoglobinuria (PNH) and advancements in myelofibrosis treatment, with a focus on novel approaches to enhance patient outcomes
- **Regeneron Pharmaceuticals:**
  - Focus Areas: Myeloma & Lymphoma
  - Presentations will focus on clinical evidence for bispecific antibody treatments in RRMM and advances in personalized care for CLL patients using next-generation therapies

Focus of Key Industry-Sponsored Sessions at ASH 2025 (4/5)

- **Takeda Pharmaceuticals:**
  - Focus Areas: Myeloproliferative Neoplasms (MPNs)
  - Sessions will cover emerging therapies for polycythemia vera and other MPNs, with a focus on addressing clinical unmet needs and improving disease modification.
- **Kura Oncology:**
  - Focus Areas: AML & NPM1 Mutations
  - Discussions will explore new treatments for NPM1-mutated acute myeloid leukemia (AML), focusing on managing resistant subtypes and improving clinical outcomes.
- **Incyte Corporation:**
  - Focus Areas: Non-Hodgkin Lymphoma & MCL
  - Presentations will focus on leveraging bispecific antibodies in DLBCL and follicular lymphoma (FL), examining integration into clinical care for advanced lymphoma patients

Focus of Key Industry-Sponsored Sessions at ASH 2025 (5/5)

- **Sanofi:**
  - Focus Areas: Hemophilia & Immune Thrombocytopenia
  - Sessions will explore marstacimab (HYMAVZI) in hemophilia care, and new approaches in managing immune thrombocytopenia (ITP) with rilzabrutinib and other targeted therapies
- **GSK:**
  - Focus Areas: Myeloma & Lymphoma
  - Discussions will focus on BCMA-directed therapies for multiple myeloma and long-term efficacy data supporting combination strategies in relapsed/refractory multiple myeloma (RRMM)
- **Amgen:**
  - Focus Areas: Myeloma & Immune Thrombocytopenia
  - Presentations will highlight T-cell redirecting therapies for myeloma and the impact of therapies in chronic immune thrombocytopenia (ITP), aiming for improved patient outcomes

Notable Presentations And Late-breaking Sessions At ASH 2025

Notable Presentations At ASH 2025
Acute Myeloid Leukemia (AML) (1/12)

Date	Title	Author	Summary
06 Dec 2025	Myeloablative fractionated busulfan, fludarabine, cladribine, thiotepa, and venetoclax (Cladillac) conditioning for high-risk AML: A phase 2 trial	Uday Popat	• **Introduction:** Pts with high-risk acute myeloid leukemia (AML) face poor outcomes post-stem cell transplantation (SCT), primarily due to non-relapse mortality (NRM) and relapse. These are exacerbated by infections, toxicity, and graft-versus-host disease (GVHD). This study explores a novel conditioning regimen to address these challenges • **Methodology:** A Phase 2 trial evaluated high-risk AML pts using myeloablative busulfan, cladribine, thiotepa, venetoclax, and post-transplant cyclophosphamide (PTCy). The primary endpoint was progression-free survival (PFS), with 50 pts enrolled across multiple donor types. • **Results:** One-year PFS was 60%, with 3-year PFS of 58%. TP53 wild-type pts had significantly better outcomes. The 3-year overall survival (OS) rate was 64%, with a relapse rate of 26%. Acute GVHD was observed in 20%, and chronic GVHD at 3 years was 13%. • **Conclusions:** This regimen demonstrated promising outcomes for high-risk AML pts, especially in TP53 wild-type cases, supporting further investigation of this novel approach.
06 Dec 2025	Bleximenib or placebo in combination with standard induction and consolidation therapy followed by maintenance for the treatment of pts with newly diagnosed KMT2A-rearranged or NPM1-mutant Acute Myeloid Leukemia eligible for intensive chemotherapy: A double-blind Phase 3 study (HOVON 181 AML / AMLSG 37-25)	Marc Raaijmakers	• **Introduction:** KMT2A rearranged (KMT2Ar) and NPM1 mutated (NPM1m) acute myeloid leukemia (AML) are associated with poor outcomes, especially in older pts. While the standard of care involves intensive chemotherapy (IC) with '7+3,' there are no approved therapies targeting these specific mutations. Bleximenib, a menin inhibitor, has shown promise in preclinical studies and Ph 1 trials in combination with '7+3' for treating these AML subtypes • **Methodology:** The Phase 3 HOVON 181 AML study is a double-blind, placebo-controlled, multicenter trial evaluating the efficacy of bleximenib versus placebo in combination with '7+3' chemotherapy, followed by maintenance therapy. Eligible participants are ≥18 years with ND KMT2Ar or NPM1m AML and fit for IC. • **Results:** Participants in the bleximenib arm will receive induction therapy with bleximenib plus cytarabine and daunorubicin/idarubicin, followed by consolidation with bleximenib or stem cell transplantation, and maintenance therapy with bleximenib. The study will assess event-free survival (EFS), overall survival (OS), complete remission (CR) rates, and adverse events. • **Conclusions:** The HOVON 181 AML study aims to evaluate whether bleximenib, in combination with SoC chemotherapy, can improve outcomes in high-risk AML pts, with the primary endpoint being event-free survival. Enrollment is expected to begin in late 2025.

Notable Presentations At ASH 2025
Acute Myeloid Leukemia (AML) (2/12)

Date	Title	Author	Summary
06 Dec 2025	ITCC-101/APAL2020D: A randomized Phase 3 trial of fludarabine/cytarabine/gemtuzumab ozogamycin with or without venetoclax in children with relapsed Acute Myeloid Leukemia	Sae Ishimaru	• **Introduction:** Survival after relapse in pediatric AML is poor, especially in children unable to receive anthracycline-based therapies due to prior cardiac toxicity. Venetoclax, a BCL-2 inhibitor, has shown promise in adults but is not approved for pediatric use. Previous studies suggest its safety and efficacy in combination with standard treatments for relapsed pediatric AML. • **Methodology:** The ITCC-101/APAL2020D trial is a Phase 3 study investigating venetoclax with fludarabine/cytarabine (FLA) and gemtuzumab ozogamicin (GO) in pediatric relapsed AML. pts are randomized to venetoclax or placebo. The primary endpoint is overall survival (OS), with secondary endpoints including safety and measurable residual disease (MRD). • **Results:** As of August 2025, 71 pts were enrolled, with 46% in the late first relapse cohort, higher than expected. The trial is ongoing at 80 sites across 20 countries, with no early safety concerns. Study enrollment adjustments are being considered. • **Conclusions:** The APAL2020D study aims to assess venetoclax in pediatric relapsed AML, particularly for those ineligible for anthracyclines. Early data suggests favorable outcomes in the late relapse cohort, supporting further study adjustments and potential new treatment options.
06 Dec 2025	A randomized phase 2 trial of CPX-351 vs. CLAG-m (Cladribine, High-Dose Cytarabine, G-CSF, and Mitoxantrone) in medically less-fit adults with previously untreated acute myeloid leukemia (AML) or other high-grade myeloid neoplasms	Anna Halpern	• **Introduction:** This study aims to evaluate CPX-351 versus CLAG-M in frail adults with untreated AML or high-grade myeloid neoplasms. • **Methodology:** This randomized trial enrolled adults ≥18 years with AML and a Treatment-Related Mortality (TRM) score ≥13.1. pts were randomized to receive CPX-351 or CLAG-M for induction and consolidation therapy, with primary endpoints assessing 3-month overall survival (OS) and secondary endpoints including remission rates and relapse-free survival (RFS). • **Results:** 60 pts were enrolled (median age 72). Response rates were numerically higher with CLAG-M (MRD-negative complete remission: 37% vs. 13%). Early mortality at day 28 was similar between groups. CLAG-M showed non-significantly higher OS (10.5 vs. 5.8 months) and RFS (8.9 vs. 4.3 months), with a 3-month OS of 70% vs. 60%. • **Conclusions:** CLAG-M showed numerically higher remission rates and survival compared to CPX-351 in frail AML pts, though differences were not statistically significant. Further studies comparing intensive and lower-intensity therapies in similar populations are planned.

Notable Presentations At ASH 2025
Acute Myeloid Leukemia (AML) (3/12)

Date	Title	Author	Summary
06 Dec 2025	10-day decitabine versus conventional chemotherapy ("3+7") followed by allografting in AML pts ≥ 60 years: Long-term follow-up results of the randomized phase III trial AML21 of the EORTC leukemia group, GIMEMA and german MDS Study group	Michael Lübbert	• **Introduction:** This study compares 10-day DEC therapy with the standard "3+7" induction regimen in fit elderly AML pts, aiming to assess survival outcomes and post-HSCT results • **Methodology:** A Phase III, open-label, randomized trial was conducted across 54 hospitals in 9 countries. pts aged ≥60 with newly diagnosed AML were randomized to receive DEC or 3+7 chemotherapy. Primary endpoints included overall survival (OS) and secondary endpoints included progression-free survival (PFS), disease-free survival (DFS), and HSCT outcomes. • **Results:** 606 pts were enrolled (median age 68). Six-year OS was similar between groups (DEC: 23.7%, 3+7: 25.5%), with a hazard ratio of 1.02. PFS and DFS were comparable. HSCT rates were similar, and OS post-HSCT was nearly identical in both groups (DEC: 41.6%, 3+7: 41.2%). Notably, DEC pts not in CR/CRi at HSCT had similar long-term survival to those in CR/CRi. • **Conclusions:** DEC therapy provided similar survival outcomes to 3+7 with a better safety profile and quality of life. The trial confirmed that non-CR/CRi pts can still achieve favorable long-term survival post-HSCT, supporting DEC as a viable alternative in older, fit AML pts.
06 Dec 2025	Elevation of fetal hemoglobin is a biomarker for response to decitabine in AML: Results of the AML21 randomized phase III trial of the EORTC leukemia group, gimema and german MDS study group	Julia Stomper	• **Introduction:** This study aims to validate HbF as a biomarker for HMA response in the EORTC AML21 trial. • **Methodology:** In the AML21 trial, pts aged ≥60 with newly diagnosed AML were randomized to receive either DEC or 3+7 chemotherapy. HbF levels were measured at baseline and day 10 of DEC treatment in the DEC arm, using high-performance liquid chromatography. • **Results:** In the DEC arm, an increase in HbF from baseline to day 10 was associated with a higher likelihood of achieving complete remission (CR) or CR with incomplete count recovery (CRi) (OR 2.40, p=0.020). However, baseline HbF levels did not correlate with CR/CRi or overall survival. No significant associations were observed in the 3+7 arm. The increase in HbF was a predictive biomarker for CR/CRi in the DEC arm. • **Conclusions:** This study is the first large prospective trial to assess HbF as a biomarker for HMA response. The findings suggest that HbF increase, measured early during treatment, could be a useful predictor of response in DEC-treated AML pts, warranting further investigation in future studies.

Notable Presentations At ASH 2025
Acute Myeloid Leukemia (AML) (4/12)

Date	Title	Author	Summary
06 Dec 2025	Therapy related core binding factor Acute Myeloid Leukemia (CBF-AML) responds favorably to fludarabine, cytarabine, GCSF (FLAG) based therapy: Exploratory Analysis from a Phase 2 trial	Jayastu Senapati	• **Introduction:** Study explores the outcomes of FLAG therapy with or without GO in T-CBF pts. • **Methodology:** This phase 2 trial enrolled adults with newly diagnosed CBF-AML, randomized to receive FLAG therapy with or without GO. The primary endpoints were RFS and OS, with secondary endpoints including measurable residual disease (MRD) and complete remission (CR). Quantitative PCR was used to monitor CBF-specific transcripts. • **Results:** Among 219 CBF-AML pts, 32 (15%) had T-CBF. In the DEC arm, 41% achieved optimal PCR response (OPR) after induction, with a higher rate in FLAG-GO pts (53% vs. 29%). At median follow-up of 113 months, 5-year RFS and OS rates were similar between T-CBF and DN-CBF (74.7% vs. 70.6% for RFS, 74.2% vs. 70.5% for OS). FLAG-GO treatment showed trends toward higher OPR in T-CBF but RFS and OS were comparable with FLAG-IDA. • **Conclusions:** FLAG therapy, including FLAG-GO, yields comparable survival outcomes in T-CBF and DN-CBF pts. Although FLAG-GO shows a trend toward better OPR rates in T-CBF, RFS and OS were similar between FLAG-GO and FLAG-IDA, suggesting no significant difference in survival outcomes for T-CBF pts.
07 Dec 2025	A phase 2 dose confirmation trial of oral ASTX030, a combination of oral azacitidine with cedazuridine among pts with myelodysplastic syndromes, chronic myelomonocytic leukemia, and acute myeloid leukemia	Guillermo Garcia-Manero	• **Introduction:** The ASTX030-01 trial explores its efficacy and safety in high-grade myeloid malignancies. • **Methodology:** In this Phase 2 trial, pts with MDS, CMML, MDS/MPN, or AML were randomized to receive ASTX030 or SC AZA. The primary endpoint was the ratio of AZA exposure in ASTX030 versus SC AZA. Secondary endpoints included clinical response, PK, and safety. Pharmacokinetic measurements were taken at baseline and during cycles. • **Results:** Thirty pts were treated, with a median age of 74.5 years. The geometric mean ratio (GMR) for AZA exposure was 0.913, with BSA influencing exposure. In MDS pts, 50% achieved an overall response, and 22.7% achieved complete remission (CR). Transfusion independence was achieved in 30.8% of RBC transfusion-dependent pts. Adverse events (AEs) included nausea (70%), constipation (66.7%), and thrombocytopenia (43.3%), with 83.3% of AEs being grade ≥3. • **Conclusions:** Oral ASTX030 demonstrated PK, pharmacodynamic, and clinical profiles comparable to SC AZA. The study highlighted the importance of BSA-based dosing to optimize exposure. The ongoing Phase 3 trial (AZTOUND) incorporates BSA-based dosing and is recruiting participants, further supporting ASTX030 as a viable oral alternative.

Notable Presentations At ASH 2025
Acute Myeloid Leukemia (AML) (5/12)

Date	Title	Author	Summary
07 Dec 2025	Results from paradigm - a phase 2 randomized multi-center study comparing azacitidine and venetoclax to conventional induction chemotherapy for newly diagnosed fit adults with acute myeloid leukemia	Amir Fathi	• **Introduction:** This study compares aza-ven to IC in fit AML pts to assess if it can challenge the current standard. • **Methodology:** This Phase II trial randomized IC-eligible AML pts (≥18 years) to aza-ven or IC. The primary endpoint was event-free survival (EFS), with secondary endpoints including overall response rate (ORR), overall survival (OS), toxicity, and quality of life (QOL). • **Results:** 172 pts were randomized. Aza-ven showed a higher ORR (88% vs. 62%) and composite complete response (CCR) rate (81% vs. 55%). The 1-year EFS was 53% for aza-ven vs. 39% for IC (HR 0.61). Aza-ven also improved QOL, with fewer ICU admissions and lower symptom burden. • **Conclusions:** Aza-ven demonstrated superior EFS and response rates compared to IC. It also improved quality of life, with fewer infections and hospitalizations, supporting its potential to replace IC in fit AML pts.
07 Dec 2025	Tagraxofusp, azacitidine, and venetoclax (TAG-AZA-VEN) triplet therapy shows efficacy, tolerability, and transplant potential in pts with blastic plasmacytoid dendritic cell neoplasm (BPDCN): Results of a phase 2 trial	Andrew Lane	• **Introduction:** This study explores the triplet therapy of TAG, azacitidine (AZA), and venetoclax (VEN) in BPDCN, building on previous findings showing AZA-VEN's efficacy in AML. • **Methodology:** This Phase 2 trial (NCT03113643) enrolled untreated or relapsed/refractory (R/R) BPDCN pts, randomized to receive TAG-AZA-VEN or standard therapy. The primary endpoint was event-free survival (EFS), with secondary endpoints including response rates, overall survival (OS), and measurable residual disease (MRD). • **Results:** 27 pts (16 in 1L, 11 in R/R) were treated. In the 1L cohort, 88% achieved composite CR (CR + CRi). In the R/R cohort, 64% achieved composite CR. The median OS in 1L was not reached, with 1- and 2-year OS of 60%. In R/R, median OS was 8.4 months. 1L pts had 1- and 2-year progression-free survival (PFS) of 58%. Treatment was well-tolerated, with common adverse events including neutropenia, thrombocytopenia, and capillary leak syndrome (CLS). • **Conclusions:** TAG-AZA-VEN showed high efficacy in both 1L and R/R BPDCN pts, with many proceeding to transplant in remission. The safety profile was consistent with previous studies, and the therapy may improve outcomes compared to single-agent TAG. This combination is a promising treatment option for BPDCN.

Notable Presentations At ASH 2025
Acute Myeloid Leukemia (AML) (6/12)

Date	Title	Author	Summary
07 Dec 2025	Revumenib for pts with relapsed or refractory (R/R) Nucleophosmin 1–Mutated (NPM1m) Acute Myeloid Leukemia (AML): Outcomes by prior treatment in the phase 2 AUGMENT-101 study	Martha Arellano	• **Introduction:** NPM1m AML has poor prognosis, especially in R/R cases, with limited treatment options. Despite therapies like venetoclax (VEN), the survival rate is low. Revumenib, a menin-KMT2A inhibitor, has shown promise in treating R/R NPM1m AML. • **Methodology:** This Phase 2 AUGMENT-101 study evaluated revumenib in R/R NPM1m AML pts, with CR+CRh as the primary endpoint and safety as a secondary endpoint. A post hoc analysis assessed DOR based on prior treatments. • **Results:** Of 77 efficacy-evaluable pts, 26% achieved CR+CRh. Response rates varied by prior treatment: 19.3% with VEN, 12.9% with FLT3i, 40% with IDH1i, 60% with IDH2i, and 27.8% with HSCT. Median DOR was 4.7 months. TRAEs were manageable, with 78.6% of pts experiencing them. • **Conclusions:** Revumenib showed activity in R/R NPM1m AML, with similar response rates and DOR across prior treatments. Further data is needed to optimize treatment sequencing.
07 Dec 2025	Phase 2 study of SLS009 in combination with azacitidine and venetoclax for relapsed/refractory AML with MDS-related changes (AML-MR) after prior venetoclax treatment	Joshua Zeidner	• **Introduction:** This study explores the combination of SLS009, AZA, and VEN in R/R AML pts. • **Methodology:** This Phase 2a trial enrolled R/R AML pts who had previously been treated with VEN-based regimens. pts received SLS009 (30 mg IV BIW), AZA (75 mg/m²), and VEN (400 mg) in 28-day cycles. The primary objective was to assess efficacy, safety, and tolerability. • **Results:** 44 pts were enrolled, with a median of 2 prior treatments. The overall response rate (CR+CRi+MLFS) in evaluable pts was 44%, including 29% with CR/CRi. Higher response rates were seen in pts with fewer prior treatments: 60% in Cohort 3 (1 prior treatment), 40% in Cohort 4 (2 prior treatments), and 36% in Cohort 5 (3+ prior treatments). Median overall survival (mOS) was 4.7 months, with longer survival in those with fewer prior lines of therapy. • **Conclusions:** The addition of SLS009 to AZA/VEN was safe and showed clinical activity in R/R AML, especially in pts with ASXL1 mutations. The treatment was most effective in pts with one prior line of VEN-based therapy, suggesting its potential in overcoming resistance to HMA and VEN combinations. Further studies in newly diagnosed high-risk AML are planned.

Notable Presentations At ASH 2025
Acute Myeloid Leukemia (AML) (7/12)

Date	Title	Author	Summary
07 Dec 2025	Preliminary results from RIVER-81, a phase 2 study of romaciclib (RVU120) + venetoclax in pts with acute myeloid leukemia failing first-line venetoclax + hypomethylating agent (HMA)	Pau Montesinos	• **Introduction:** This Phase 2a study evaluates the combination of romaciclib and VEN in R/R AML pts after prior VEN-based therapies. • **Methodology:** RIVER-81 is a dose-escalation, open-label trial assessing the efficacy, safety, and optimal dosing of romaciclib + VEN in R/R AML pts. The primary endpoint is composite complete remission (CR/CRh/CRi), with secondary endpoints including duration of response (DoR), overall survival (OS), and pharmacokinetics (PK). The study includes three parts: dose escalation, and efficacy assessment at the recommended dose. • **Results:** 48 pts were treated, with a median age of 76. No dose-limiting toxicities (DLTs) were observed. PK analysis confirmed dose-proportional increases in romaciclib exposure. The most common adverse events (AEs) were nausea (54%) and vomiting (42%). Of 28 evaluable pts, 43% achieved CR/CRi, with 23% in Stage 1 of Part 2 and 50% in Cohort 4. Responses lasted 0.6–7 months. Serious AEs occurred in 69 pts, with 5 possibly drug-related. • **Conclusions:** Romaciclib combined with VEN shows promising activity in R/R AML, with observed CR/CRi suggesting potential to overcome VEN resistance. These results support continued study of romaciclib + VEN, with enrollment and long-term follow-up ongoing.
07 Dec 2025	Camelot-2: A phase 3 randomized, double-blind, placebo-controlled, study of bleximenib, venetoclax and azacitidine for the treatment of participants with newly diagnosed Acute Myeloid Leukemia harboring KMT2A rearrangements or NPM1 mutations, who are ineligible for intensive chemotherapy	Elias Jabbour	• **Introduction:** KMT2A rearranged (KMT2Ar) and NPM1 mutated (NPM1m) AML are challenging, particularly in older or unfit pts who cannot tolerate intensive chemotherapy (IC). These pts are often treated with azacitidine (AZA) and venetoclax (VEN). Bleximenib, a menin inhibitor, targets KMT2Ar and NPM1m AML and may enhance the efficacy of VEN + AZA. • **Methodology:** The Phase 3 cAMeLot-2 study (NCT06852222) is a randomized, double-blind trial evaluating bleximenib with VEN + AZA in pts with newly diagnosed KMT2Ar or NPM1m AML ineligible for IC. Primary endpoints include complete remission (CR) rate and overall survival (OS), with secondary endpoints like event-free survival (EFS) and transfusion independence. • **Results:** 600 participants will be randomized to receive bleximenib 100 mg BID or placebo with VEN + AZA. Bleximenib has shown preclinical activity, with low differentiation syndrome rates and no significant drug-drug interactions. Safety and efficacy will be evaluated in this trial. • **Conclusions:** The cAMeLot-2 study aims to assess the efficacy of bleximenib with VEN + AZA for treating KMT2Ar and NPM1m AML in IC-ineligible pts, potentially offering a new treatment option for this group.

Notable Presentations At ASH 2025
Acute Myeloid Leukemia (AML) (8/12)

Date	Title	Author	Summary
07 Dec 2025	Phase 1b safety run-in study followed by Phase 2 study of ficlatuzumab, azacitidine and venetoclax in untreated Acute Myeloid Leukemia pts aged ≥ 60 years old	Emily Curran	• **Introduction:** Hepatocyte growth factor (HGF) promotes AML survival through MET signaling, correlating with poor survival. Ficlatuzumab, an anti-HGF antibody, shows promise in AML, particularly in combination with venetoclax (VEN) and azacitidine (AZA), as these treatments offer benefits but remain non-curative. • **Methodology:** This Phase 1b/2 study, part of the Beat AML Master Trial, evaluates ficlatuzumab with VEN/AZA in older AML pts unfit for intensive therapy. Phase 1b identifies a safe dose, while Phase 2 assesses complete remission (CR) and composite CR rates, comparing to a control group. • **Results:** The study uses a Bayesian optimal design in Phase 1b to determine the safe dose of ficlatuzumab (20 mg/kg or 15 mg/kg). Secondary endpoints include safety, tolerability, survival, and remission duration. Phase 2 will test CR rates in two arms with different doses, aiming for 55% CR. • **Conclusions:** This study investigates ficlatuzumab combined with VEN/AZA for non-intensive treatment of AML. Early safety and efficacy data will guide Phase 2 dosing, with promising potential for improving outcomes in this challenging patient population.
07 Dec 2025	CYP3A4 inhibitors (CYP3A4i) and myelosuppression in pts (Pts) with newly diagnosed mutant isocitrate dehydrogenase 1 (mIDH1) Acute Myeloid Leukemia (AML) in the phase 3 AGILE study	Andre Schuh	• **Introduction:** Ivosidenib (IVO), a targeted inhibitor for mIDH1 AML, is combined with azacitidine (AZA) to treat newly diagnosed pts. However, potential drug interactions, especially with CYP3A4 inhibitors (CYP3A4i), may affect treatment outcomes. This study evaluates IVO's safety and efficacy in combination with VEN and AZA, focusing on the impact of concomitant CYP3A4i. • **Methodology:** This analysis included pts from the AGILE study (NCT03173248), evaluating IVO + AZA with concomitant CYP3A4i use. Pharmacokinetics (PK) of IVO were assessed, and myelosuppression rates were analyzed across strong, moderate, and mild/no CYP3A4i categories. • **Results:** In total, 72 pts received IVO+AZA, with 38% using strong CYP3A4i. Myelosuppression occurred in 75% of IVO+AZA pts, with neutropenia more common in the IVO group, especially with mild/no CYP3A4i. PK modeling showed modest increases in IVO exposure when co-administered with CYP3A4i. • **Conclusions:** IVO + AZA with CYP3A4i showed similar myelosuppression rates as PBO + AZA, despite increased IVO exposure. This suggests that CYP3A4i use does not significantly increase myelosuppression risk, supporting IVO's use with CYP3A4i in AML treatment.

Notable Presentations At ASH 2025
Acute Myeloid Leukemia (AML) (9/12)

Date	Title	Author	Summary
07 Dec 2025	ALIDHE: An ongoing open-label phase 3b study investigating ivosidenib with azacitidine in clinical practice in adult pts with newly diagnosed mutant isocitrate dehydrogenase 1 (mIDH1) Acute Myeloid Leukemia (AML) ineligible for intensive induction chemotherapy (IC)	Paresh Vyas	• **Introduction:** The AGILE study demonstrated the long-term benefits of IVO+AZA. However, real-world data on its efficacy and safety in clinical practice, particularly for older or unfit pts, remains limited. The ALIDHE study investigates IVO+AZA in this population. • **Methodology:** ALIDHE is a Phase 3b, single-arm, open-label study evaluating IVO+AZA in newly diagnosed mIDH1 AML pts ineligible for intensive chemotherapy. Primary endpoints include treatment-emergent adverse events (TEAEs) and serious AEs. Secondary endpoints focus on event-free survival (EFS), disease response, and time to response. • **Results:** 92 pts were enrolled with a median age of 75 years. The most common mutations included DNMT3A and ASXL1. Safety data showed high rates of neutropenia (32.6%) and nausea (29.2%). The composite complete response (CR+CRh) rate was 45%, with 58% achieving overall response (ORR). MRD negativity was achieved in 31.3% of pts in CR/CRh. • **Conclusions:** Preliminary results from ALIDHE align with the AGILE study, showing that IVO+AZA is effective and well-tolerated in clinical practice. The study is ongoing, with future analyses focusing on effectiveness and quality of life. These findings provide valuable real-world insights for IVO+AZA in treating mIDH1 AML.
07 Dec 2025	Venetoclax combined with three-day multi-frequency decitabine (DEC3-VEN) VS venetoclax combined with azacitidine in elderly pts with Acute Myeloid Leukemia : a phase III, prospective, multicenter, randomized controlled trial	ZePing Zhou	• **Introduction:** This study evaluates the efficacy and safety of DEC3-VEN, combining venetoclax with three-day decitabine, as induction therapy for these pts. • **Methodology:** This Phase III, multicenter, randomized controlled study compares DEC3-VEN to VEN+AZA in elderly or unfit AML pts. The primary endpoint is event-free survival (EFS). Secondary endpoints include response rates and minimal residual disease (MRD) negativity. • **Results:** 120 pts were enrolled; the DEC3-VEN group showed a cCR rate of 76.9%, with a CR rate of 73.1% and MRD negativity in 77.5% of cases. In the VEN+AZA group, the cCR rate was 60.8%, CR rate was 52.9%, and MRD negativity was 51.6%. DEC3-VEN significantly improved CR and MRD negativity compared to VEN+AZA. • **Conclusions:** DEC3-VEN demonstrated superior efficacy and tolerability compared to VEN+AZA in elderly or unfit AML pts, showing significantly higher CR and MRD negativity rates. Longer follow-up is needed to assess overall survival (OS) and event-free survival (EFS).

Notable Presentations At ASH 2025
Acute Myeloid Leukemia (AML) (10/12)

Date	Title	Author	Summary
07 Dec 2025	A pre-emptive bridge-to-transplant therapy for measurable residual disease with venetoclax and azacitidine in NPM1-mutated Acute Myeloid Leukemia: Updates from the ongoing GIMEMA AML2521 phase 2 trial	Chiara Sartor	• **Introduction:** This study investigates the efficacy of VEN-AZA in bridging pts to allogeneic stem cell transplantation (alloSCT) after molecular relapse or progression. • **Methodology:** The GIMEMA AML2521 trial is a Phase 2, non-randomized study enrolling fit NPM1m AML pts with molecular relapse after at least two cycles of IC. pts receive VEN and AZA, with the primary endpoint being MRD negativity (MRDneg). Secondary endpoints include overall response rate (ORR), event-free survival (EFS), and bridging to alloSCT. • **Results:** 25 pts were enrolled with a median age of 57 years. The ORR was 86%, and 80% achieved MRDneg, with a median time to MRDneg of 2.33 months. 84% of pts were successfully bridged to alloSCT, with a median time to transplant of 3.71 months. The most common Grade 3 adverse events were neutropenia and thrombocytopenia. • **Conclusions:** VEN-AZA effectively prevents relapse and reduces MRD in NPM1m AML pts in MF, with a high rate of successful bridging to alloSCT. The regimen showed promising safety and efficacy, supporting its use in this high-risk patient group. Further updates will be provided as the study progresses.
08 Dec 2025	A Phase 2 study of sequential administration of gilteritinib after MEC chemotherapy in Relapsed/Refractory FLT3-mutated Acute Myeloid Leukemia in adults: Japan adult leukemia study group (JALSG) RR-FLT3-AML220 study	Yuichi Ishikawa	• **Introduction:** This study evaluates the combination of gilteritinib with MEC chemotherapy in improving response rates and survival outcomes. • **Methodology:** The Phase 2, single-arm study enrolled 42 adult pts with R/R FLT3-mutated AML. pts received MEC chemotherapy followed by gilteritinib maintenance for up to 13 cycles. The primary endpoint was complete remission (CR) rate, with secondary endpoints including composite CR (CRc), overall response rate (ORR), and survival metrics • **Results:** The CR rate was 48.8%, with a CRc rate of 87.8%. For pts undergoing allo-HSCT, the CR rate was 44%, while non-transplanted pts had a CR rate of 18.8%. Median overall survival (OS) was 32.2 months, and relapse-free survival (RFS) for CRc pts was 29.3 months. The most common grade 3-4 adverse events were anemia, neutropenia, and thrombocytopenia. • **Conclusions:** Sequential MEC chemotherapy with gilteritinib demonstrates high response rates and manageable toxicity in R/R FLT3-mutated AML. The combination improves CR and CRc rates, with promising outcomes, especially in pts proceeding to allo-HSCT.

Notable Presentations At ASH 2025
Acute Myeloid Leukemia (AML) (11/12)

Date	Title	Author	Summary
08 Dec 2025	Initial results from a phase 2 study of cladribine, cytarabine, and granulocyte-colony stimulating factor with gemtuzumab ozogamicin (CLAG-GO) for the treatment of pts with relapsed/refractory acute myeloid leukemia	David Chen	• **Introduction:** This study evaluates the efficacy and safety of the CLAG-GO regimen in R/R AML. • **Methodology:** The study is a Phase II, single-arm trial involving adult pts with R/R AML. pts receive a combination of cladribine, cytarabine, G-CSF, and GO. The primary endpoint is the efficacy of CLAG-GO as a salvage therapy, while secondary endpoints include measurable residual disease (MRD) status, duration of response, and overall survival (OS). • **Results:** Of 19 enrolled pts, 42% achieved a composite CR (36% CR, 5% CRi), with 37% receiving consolidation and 32% proceeding to alloSCT. Median overall survival was 9.53 months. Hematologic AEs, including febrile neutropenia, thrombocytopenia, and anemia, were the most common, with no cases of veno-occlusive disease. • **Conclusions:** CLAG-GO demonstrates a comparable response rate to other salvage regimens in R/R AML, with manageable toxicity. Deep responses allowed many pts to proceed to alloSCT. CD33-PGx6 analysis suggested a correlation between low CD33 levels and poor response. Enrollment continues with further patient analysis.
08 Dec 2025	Revumenib for pts with relapsed or refractory (R/R) KMT2Ar acute leukemia: Outcomes by leukemia type in the phase 2 AUGMENT-101 study	Ibrahim Aldoss	• **Introduction:** KMT2A-rearranged (KMT2Ar) acute leukemia (AL) has poor prognosis, and treatment options for relapsed/refractory (R/R) cases are limited. Revumenib, a selective inhibitor of the menin-KMT2A interaction, has shown efficacy in treating R/R KMT2Ar AL across various leukemia types, including AML, ALL, and MPAL. • **Methodology:** The Phase 2 AUGMENT-101 study evaluated revumenib in R/R KMT2Ar AL pts, assessing its safety, efficacy, and MRD reduction. pts received revumenib 163 mg every 12 hours in 28-day cycles. The primary endpoint was CR+CRh rate, with secondary endpoints including overall response rate (ORR) and duration of response (DOR). • **Results:** Among 97 pts, ORR was 67% in AML, 46% in ALL, and 67% in MPAL. CR+CRh rates were 23% in AML, 23% in ALL, and 17% in MPAL. MRD negativity was achieved in 64% of AML responders, 33% of ALL, and 100% of MPAL. Safety analysis showed common grade ≥3 adverse events, including differentiation syndrome and febrile neutropenia. • **Conclusions:** Revumenib monotherapy demonstrated clinically meaningful responses and high MRD negativity rates in R/R KMT2Ar AL, across AML, ALL, and MPAL. The safety profile was consistent with previous studies, supporting its potential as a therapeutic option for R/R KMT2Ar AL pts.

Notable Presentations At ASH 2025
Acute Myeloid Leukemia (AML) (12/12)

Date	Title	Author	Summary
08 Dec 2025	Phase 3 Study of ivosidenib (IVO) and azacitidine (AZA) with or without venetoclax in adult pts with newly diagnosed IDH1-mutated AML or MDS/AML ineligible for intensive chemotherapy (EVOLVE-1)	Hartmut Döhner	• **Introduction:** The EVOLVE-1 study aims to assess whether IVO/AZA with VEN improves outcomes compared to IVO/AZA with placebo. • **Methodology:** The EVOLVE-1 study (NCT06465953) is a phase 3, multicenter, randomized, double-blind, placebo-controlled trial. pts with newly diagnosed mIDH1 AML or MDS/AML ineligible for intensive chemotherapy will be randomized to receive IVO/AZA with VEN or placebo. The primary endpoint is event-free survival (EFS), with secondary endpoints including overall survival (OS), CR/CRh rates, and duration of response. • **Results:** Expected enrollment is approximately 227 pts. The trial will evaluate the efficacy of IVO/AZA with VEN compared to IVO/AZA with placebo. Treatment involves 28-day cycles with IVO 500 mg/day, AZA 75 mg/m²/day for 7 days, and VEN 400 mg/day for 7 days (ramped up in cycle 1). • **Conclusions:** The EVOLVE-1 study will address the unmet need for better treatment options in newly diagnosed mIDH1 AML or MDS/AML pts ineligible for intensive chemotherapy. The primary endpoint of EFS and secondary endpoints will provide crucial data on the efficacy and safety of the IVO/AZA/VEN regimen.
08 Dec 2025	A phase 2 clinical study on intensifying idarubicin dosage for inducing remission in acute myeloid leukemia pts aged 65 and younger	Mark Lee	• **Introduction:** This study investigates the safety and efficacy of an intensified idarubicin dose to improve outcomes in adult AML pts. • **Methodology:** A phase 2 study enrolled 37 pts aged 20-65 years with newly diagnosed or secondary AML. pts were treated with 18 mg/m² idarubicin for 3 days and 100 mg/m² cytarabine for 7 days. Survival was analyzed using Kaplan-Meier. • **Results:** The complete remission (CR) rate was 70.3%, with 5-year event-free survival (EFS) of 38.1% and overall survival (OS) of 52.3%. Significant differences in EFS and OS were noted between CR vs non-CR groups. EFS and OS varied by risk category, with favorable risk pts showing the best outcomes. • **Conclusions:** Intensifying idarubicin doses effectively induced remission in AML pts. Further phase 3 trials are needed to confirm this regimen, particularly for pts without mutated FLT3.

Notable Presentations At ASH 2025
Acute Lymphoblastic Leukemia (ALL) (1/7)

Date	Title	Author	Summary
06 Dec 2025	Genomic determinants of treatment outcome and identification of a new genomic subset of adult acute lymphoblastic leukemia from the ECOG-ACRIN E1910 randomized phase III trial	Xiaoming Zhong	• **Introduction:** This study aims to identify key genomic markers in newly diagnosed adult B-ALL and assess their association with minimal residual disease (MRD) negativity, enabling blinatumomab randomization. • **Methodology:** The study analyzed 569 pts with B-ALL, utilizing RNA-seq, whole exome, and genome sequencing. pts were classified into 22 molecular groups, and outcomes were assessed in a subgroup of 319 treated with blinatumomab. • **Results:** 268 driver genes were identified, with pathways including B-cell development and Ras signaling. A novel "CEBPalt" subgroup emerged, marked by CEBPA/CEPB alterations. Blinatumomab improved outcomes in certain subgroups, with MRD negativity achieved in 80% of responders. • **Conclusions:** This study identifies a new molecular subgroup of adult B-ALL, providing insights into blinatumomab efficacy across distinct genetic subgroups, especially in MRD-negative cases.
06 Dec 2025	Incorporation of 8Gy total body irradiation into reduced intensity conditioning does not improve allogeneic transplant outcomes for high-risk adult acute lymphoblastic leukemia: Results from the randomised prospective phase 2 UK multicentre ALL-RIC impact study	Anna Castleton	• **Introduction:** Previous trials, such as UKALL14, reported the FMA regimen's 55% overall survival (OS) at 4 years but with high relapse rates. The use of total body irradiation (TBI) is thought to improve outcomes, prompting a study comparing FMA with cyclophosphamide plus 8Gy TBI (Cy/8TBI). • **Methodology:** This multicenter, randomized trial compared FMA and Cy/8TBI regimens in adult ALL pts. Eligible pts had high-risk ALL and received either FMA (fludarabine, melphalan, alemtuzumab) or Cy/8TBI. The primary endpoint was disease-free survival (DFS), with secondary endpoints including OS, relapse, and graft-versus-host disease (GvHD) rates. • **Results:** 102 pts were randomized, with 89 proceeding to allo-SCT. The 3-year DFS was similar for FMA (50%) and Cy/8TBI (48%) (HR 1.12, p=0.7). No significant differences were seen in cumulative incidence of relapse (CIR) or non-relapse mortality (NRM). OS was 61% for FMA and 58% for Cy/8TBI at 3 years (HR 1.1, p=0.8). GvHD rates were comparable across arms, with no significant differences in serious adverse events (SAEs) or infection rates.. • **Conclusions:** Cy/8TBI did not demonstrate superiority over FMA for RIC in adult ALL pts, showing similar DFS and OS. TBI incorporation into RIC was well-tolerated, with no additional toxicity. This trial emphasizes the need for randomized trials to refine conditioning regimens for older adults undergoing allo-SCT. The feasibility of such trials is supported by the successful enrollment and patient participation.

Notable Presentations At ASH 2025
Acute Lymphoblastic Leukemia (ALL) (2/7)

Date	Title	Author	Summary
06 Dec 2025	Front-line consolidation with CAR-t therapy in newly diagnosed adult ph-negative b-acute lymphoblastic leukemia: Results from a prospective, phase 2 study	Shaowei Qiu	• **Introduction:** Achieving deep remission is essential for durable responses in B-cell acute lymphoblastic leukemia (B-ALL). CD19-directed CAR-T therapy has shown promise in relapsed/refractory cases, but its role as a front-line consolidation therapy to improve long-term outcomes, reduce chemotherapy toxicity, and improve survival has not been fully explored. • **Methodology:** This Phase 2 trial enrolled adult pts with newly diagnosed Ph-negative B-ALL. pts received pediatric-inspired induction therapy followed by 1-2 cycles of consolidation. Afterward, they received second-generation 4-1BB-CD19 CAR-T therapy during remission, followed by maintenance therapy and CNS prophylaxis. • **Results:** 44 pts received CAR-T therapy. All achieved MRD negativity, with 96.9% of pts free from NGS-detectable MRD. The 1-year overall survival rate was 100%, with a 97.7% leukemia-free survival rate. Cytokine release syndrome (CRS) occurred in 59.1%, but all were grade 1, with no cases of immune effector cell-associated neurotoxicity syndrome (ICANS). • **Conclusions:** First-line CAR-T therapy as consolidation in B-ALL is effective in eradicating leukemia cells and shows a favorable safety profile. It reduces treatment duration while maintaining long-term remission, supporting its potential in upfront treatment.
06 Dec 2025	The addition of inotuzumab ozogamicin to frontline hyper-CVAD and sequential blinatumomab leads to durable survival outcomes in adults with newly diagnosed B-cell acute lymphoblastic leukemia: Four-year follow-up of a phase 2 study	Hannah Goulart	• **Introduction:** This study investigates whether InO added to frontline Hyper-CVAD and blina improves outcomes in newly diagnosed (ND) pts. • **Methodology:** This Phase II trial enrolled adults with ND Ph-negative B-ALL, receiving induction therapy, followed by Hyper-CVAD and blina, with InO added from patient #39. Maintenance included venetoclax and POMP chemotherapy. • **Results:** Of 75 pts, 100% achieved CR, with 95% MRD-negative by flow cytometry. InO improved MRD negativity by NGS (79% vs 50%). After median follow-up, 4-year OS was 91%, EFS was 83%. InO addition improved OS (HR 12.5, p=0.02). • **Conclusions:** InO with Hyper-CVAD and blina resulted in high survival rates, with many pts in remission without allo-SCT. Further randomization studies are ongoing.

Notable Presentations At ASH 2025
Acute Lymphoblastic Leukemia (ALL) (3/7)

Date	Title	Author	Summary
06 Dec 2025	Blinatumomab and ponatinib demonstrates ongoing efficacy as frontline therapy in Philadelphia positive B-cell acute lymphoblastic leukemia: Long-term follow-up from a phase 2 Study	Hannah Goulart	• **Introduction:** This study updates results from a Phase 2 trial evaluating the efficacy of this chemotherapy-free regimen over 3 years. • **Methodology:** Adults with Ph+ B-ALL received up to 5 cycles of blina and ponatinib, followed by continued ponatinib. Protocol amendments included increased intrathecal chemotherapy and high-dose methotrexate for high white blood cell counts. • **Results:** Among 85 pts, 95% achieved complete remission (CR), with 97% achieving MRD negativity. The 3-year event-free survival (EFS) was 78%, and overall survival (OS) was 89%. Relapses occurred in 12% of pts, with a 3-year cumulative incidence of relapse of 17%. WBC >70x10^9/L at baseline correlated with higher relapse risk. • **Conclusions:** Blina and ponatinib offer durable remission for Ph+ B-ALL pts without requiring allogeneic stem cell transplant. The addition of CNS-directed therapy improved outcomes, with no new safety concerns identified.
06 Dec 2025	Brexucabtagene autoleucel (Brexucel) as a consolidation therapy in B-cell acute lymphoblastic leukemia (B-ALL) post HCVAD/minihcvd-inotuzumab-blinatumomab regimens: Initial Results of a prospective Phase 2 trial.	Jayastu Senapati	• **Introduction:** This study evaluates brexucel as frontline consolidation therapy in high-risk (HR) or relapsed/refractory (R/R) Ph-negative B-ALL to improve long-term outcomes and reduce the need for allogeneic stem cell transplant (ASCT). • **Methodology:** Adult pts with HR B-ALL or R/R B-ALL received initial chemotherapy followed by leukapheresis and brexucel infusion. The primary endpoint was event-free survival (EFS), with secondary endpoints including overall survival (OS) and molecular remission. • **Results:** Among 14 pts with follow-up >1 month, the 4-month EFS was 88%, with 88% OS and sustained NGS-MRD negativity. Most pts had a strong CAR-T expansion, and adverse events (CRS) were manageable (all grade 1). 11 pts remained NGS-MRD-negative. • **Conclusions:** Brexucel consolidation in HR and R/R B-ALL showed promising efficacy, sustained molecular remission, and a favorable safety profile, suggesting its potential to replace ASCT. The study continues to recruit pts.

Notable Presentations At ASH 2025
Acute Lymphoblastic Leukemia (ALL) (4/7)

Date	Title	Author	Summary
06 Dec 2025	Results of POLARIS-1, a global Phase 3 study (Part A): Olverembatinib combined with low-intensity chemotherapy in pts with newly diagnosed (ND) Philadelphia chromosome-positive (Ph+) acute lymphoblastic leukemia (ALL)	Suning Chen	• **Introduction:** This phase 3 study evaluates the efficacy and safety of olverembatinib in newly diagnosed (ND) Ph+ B-ALL. • **Methodology:** pts with ND Ph+ B-ALL received olverembatinib plus chemotherapy, with treatment cycles consisting of induction, consolidation, and maintenance phases. Primary endpoints were MRD negativity after 3 induction cycles, with secondary endpoints including overall survival (OS) and safety. • **Results:** The MRD-negative CR rate was 64.2% after induction. The most common treatment-emergent adverse events (TEAEs) included neutropenia, leukopenia, and anemia. Most pts tolerated the treatment well, with minimal toxicity and favorable outcomes, even in pts with poor prognostic genotypes like IKZF1+. • **Conclusions:** Olverembatinib combined with chemotherapy achieved deep molecular responses and showed a favorable safety profile in newly diagnosed Ph+ B-ALL. The regimen may improve outcomes and extend treatment options, especially for pts with poor prognostic features.
06 Dec 2025	Blinatumomab versus high-dose chemotherapy in the first-line therapy of high-risk childhood B-cell acute lymphoblastic leukemia: The results of a Phase 3 trial of the cALL-pol consortium in Poland	Wojciech Michal Mlynarski	• **Introduction:** This phase 3 trial aimed to evaluate the safety, efficacy, and MRD reduction when blinatumomab was used instead of chemotherapy in children with newly diagnosed high-risk BCP-ALL. • **Methodology:** The trial involved 87 children with high-risk BCP-ALL who were randomly assigned to either chemotherapy blocks or blinatumomab treatment in the post-induction phase. Primary endpoints included toxicity (adverse events) and MRD negativity, with exploratory analysis on event-free survival. • **Results:** Blina treatment significantly reduced the risk of clinically relevant adverse events (32.4% vs 81.1%) and achieved superior MRD negativity (97.3% vs 56.8% after the first block). MRD status after treatment cycles correlated with improved event-free survival. Blinatumomab showed better outcomes in toxicity reduction and MRD control compared to chemotherapy. • **Conclusions:** Blinatumomab replaced chemotherapy in high-risk BCP-ALL, significantly reducing toxicity and improving MRD reduction, with a favorable impact on event-free survival. Further follow-up is necessary to confirm these findings.

Notable Presentations At ASH 2025
Acute Lymphoblastic Leukemia (ALL) (5/7)

Date	Title	Author	Summary
07 Dec 2025	First results of the Phase III GIMEMA ALL2820 trial comparing ponatinib plus blinatumomab to imatinib and chemotherapy for newly diagnosed adult ph+ acute lymphoblastic leukemia pts	Sabina Chiaretti	• **Introduction:** This phase III study aimed to compare the efficacy and safety of a chemo-free approach using blinatumomab and olverembatinib versus the standard TKI plus chemotherapy regimen in newly diagnosed adult Ph+ ALL. • **Methodology:** Adults with newly diagnosed Ph+ ALL were randomized to receive either a chemo-free regimen with blinatumomab or a standard TKI plus chemotherapy. The primary endpoint was complete hematologic remission (CHR), with secondary endpoints including measurable residual disease (MRD) negativity and event-free survival (EFS). • **Results:** The chemo-free approach showed superior results with a higher CHR rate (94.4% vs. 79.4%) and greater MRD-negativity (70.2% vs. 52.7%) at day 133. The 18-month EFS was also better in the chemo-free arm (89.9% vs. 76.8%). A crossover from the chemotherapy arm to the chemo-free arm improved MRD-negativity in 62.1% of pts. Fewer relapses and deaths were observed in the experimental arm. • **Conclusions:** This study demonstrates that a chemo-free approach using blinatumomab significantly improves outcomes in Ph+ ALL compared to the traditional TKI/chemotherapy approach, with higher CHR rates, better MRD responses, and improved event-free survival.
07 Dec 2025	Single CAR-t infusion during front-line consolidation induces deep and sustained remission in newly diagnosed adult ph+b-ALL: A prospective phase 2 study	Runxia Gu	• **Introduction:** Frontline treatments combining tyrosine kinase inhibitors (TKIs) and immunotherapy, such as blinatumomab, have shown strong efficacy in treating Philadelphia-positive B-cell acute lymphoblastic leukemia (Ph+ B-ALL). The potential of adding a single infusion of CD19-directed CAR-T therapy as front-line consolidation, combined with TKI therapy, remains underexplored. • **Methodology:** This Phase 2 study enrolled 35 adults with newly diagnosed Ph+ B-ALL. After TKI-based induction therapy, pts received a single CAR-T infusion during first remission. Maintenance therapy included chemotherapy and TKI, with CNS prophylaxis. • **Results:** All pts achieved complete remission (CR) and MRD negativity by flow cytometry after CAR-T therapy. After 1 year, overall survival (OS) and leukemia-free survival (LFS) rates were both 100%. No pts experienced relapse, and 74.3% experienced mild cytokine release syndrome (CRS). No cases of immune effector cell-associated neurotoxicity syndrome (ICANS) occurred. • **Conclusions:** Front-line CAR-T therapy for newly diagnosed Ph+ B-ALL pts is safe, effective, and leads to deep remission, offering a promising alternative to intensive chemotherapy.

Notable Presentations At ASH 2025
Acute Lymphoblastic Leukemia (ALL) (6/7)

Date	Title	Author	Summary
07 Dec 2025	Ibrutinib plus blinatumomab in Relapsed/Refractory B-cell acute lymphoblastic leukemia: Results of A phase 2 study	Brian Jonas	• **Introduction:** Blinatumomab (BLIN), a CD19xCD3 bispecific T-cell engager, improves outcomes in relapsed/refractory (R/R) B-ALL. The combination of BLIN with ibrutinib (IBR), a BTK inhibitor, is hypothesized to enhance T-cell–mediated cytotoxicity and improve complete remission (CR) rates in R/R B-ALL. • **Methodology:** This multicenter Phase 2 trial (NCT02997761) evaluated IBR + BLIN in adults with R/R B-ALL. pts received two cycles of IBR and BLIN followed by consolidation cycles for responders. The primary endpoint was the CR rate. • **Results:** Out of 19 enrolled pts, the CR rate was 50%, with 55.6% achieving CR/CR with incomplete count recovery. Median overall survival (OS) was 12.3 months. Adverse events included anemia (32%) and febrile neutropenia (32%), with CRS in 47% and neurotoxicity in 16%. • **Conclusions:** The IBR + BLIN combination showed encouraging efficacy with high MRD-negative CR rates and was generally well-tolerated. Further randomized trials are warranted to explore this immunomodulatory synergy in B-ALL.
07 Dec 2025	Phase 2 study of brexu-cel in minimal residual disease positive B-cell acute lymphoblastic leukemia	Bijal Shah	• **Introduction:** Minimal residual disease (MRD) after induction is a key predictor of relapse in B-cell acute lymphoblastic leukemia (B-ALL), with ~30% of pts experiencing poor outcomes due to persistent MRD. Blinatumomab can induce MRD clearance, but durable remissions typically require allogeneic HSCT, which carries substantial mortality. CAR T-cell therapy, including brexucel, has improved outcomes in relapsed/refractory B-ALL and may offer an early, less toxic option for MRD-positive adults. • **Methodology:** This multicenter Phase 2 trial (NCT06144606) evaluates brexucel in adults with MRD-positive B-ALL after induction chemotherapy. MRD detected by NGS triggers treatment with brexucel following fludarabine–cyclophosphamide lymphodepletion. Primary endpoint: relapse-free survival (RFS). Secondary endpoints: clinical response, molecular RFS, overall survival. Exploratory analyses: T-/B-cell recovery and cytokine signatures. • **Status:** Opened November 2023; 16 of 60 planned pts have been infused. Enrollment continues, with expansion underway at major cancer centers.

Notable Presentations At ASH 2025
Acute Lymphoblastic Leukemia (ALL) (7/7)

Date	Title	Author	Summary
08 Dec 2025	Toxicities on the E1910 phase III randomized trial of blinatumomab plus chemotherapy in adults with BCR:ABL-1 negative acute lymphoblastic leukemia	Anjali Advani	• **Introduction:** This study aims to explore the efficacy of brexucel for adult B-ALL pts who are MRD positive by NGS after induction chemotherapy (NCT06144606). • **Methodology:** This Phase 2 multicenter study enrolls adults with MRD-positive B-ALL after induction chemotherapy. pts receive brexucel after lymphodepletion with fludarabine and cyclophosphamide, followed by optional consolidation with allogeneic transplant or tyrosine kinase inhibitor maintenance. The primary endpoint is relapse-free survival (RFS), with secondary endpoints including safety, molecular and clinical response, and overall survival. Exploratory endpoints include CAR T-cell expansion and cytokine profiling. • **Status:** The trial began enrolling in November 2023, with 16 of 60 pts infused to date. Accrual is ongoing, with plans for extension at major cancer centers.

Notable Presentations At ASH 2025
Lymphoma (Hodgkin & Non-Hodgkin) (1/13)

Date	Title	Author	Summary
06 Dec 2025	Response-adapted Phase 2 study of acalabrutinib window prior to frontline chemotherapy in untreated large B-cell lymphoma: Molecular correlates of response to acalabrutinib	Mark Roschewski	• **Introduction:** A Phase 2 study of acala prior to frontline chemotherapy to explore the molecular profiles of BTKi-responsive tumors in LBCL was conducted. • **Methodology:** This multicenter, single-arm trial enrolled pts with untreated LBCL. Participants received 14 days of acala followed by DA-EPOCH-R or R-CHOP chemotherapy. pts with a ≥25% reduction in tumor burden continued acala. Molecular profiling of tumors was conducted, and response was evaluated after 2 cycles of therapy. • **Results:** Among 110 screened, 99 pts enrolled, with 50% responding to acala. The response rate varied by tumor subtype: 43% in GCB DLBCL, 53% in ABC DLBCL, and 83% in unclassified LBCL. Acala was active across all LymphGen subtypes, particularly in MCD/N1. Toxicity was mainly hematologic, with G3/G4 neutropenia in 63% of DA-EPOCH-R + acala cycles. The 2-year progression-free survival (PFS) was 84.8% overall. No survival difference was observed between responders and non-responders. • **Conclusions:** Acala showed broad efficacy across genetic subtypes of LBCL, especially in MCD/N1. The combination of acala with chemotherapy was well tolerated. Molecular profiling and MRD assessment may be useful for predicting responses to acala in frontline LBCL therapy.
06 Dec 2025	Odronextamab plus chemotherapy in pts with previously untreated diffuse large B-cell lymphoma (DLBCL): First Results from part 1 of the Phase 3 Olympia-3 study	Jean-Marie Michot	• **Introduction:** Results from Part 1A of the study, investigating the safety and efficacy of Odro-CHOP were presented. • **Methodology:** Part 1A enrolled pts with untreated CD20+ DLBCL. Participants received 14 days of Odro at escalating doses, followed by 6 cycles of CHOP. The primary endpoint was dose-limiting toxicities (DLTs), with secondary endpoints evaluating response rates, duration of response (DOR), and cytokine changes. • **Results:** Of the 22 pts treated, 77.8% (DL1) and 92.3% (DL2) completed 6 cycles. No DLTs were observed. The most common treatment-emergent adverse events (TEAEs) were neutropenia (77.8% DL1, 84.6% DL2), CRS (33.3% DL1, 76.9% DL2), and anemia (33.3% DL1, 53.8% DL2). The objective response rate (ORR) was 77.8% for DL1, with a 66.7% complete response (CR). DL2 had a 100% ORR and CR rate. • **Conclusions:** Odro-CHOP induction therapy was well tolerated, with no new safety signals. The efficacy of the combination was encouraging, with a 100% CR rate in the DL2 group. This suggests that rituximab may not be necessary to achieve a deep response with Odro in untreated DLBCL. Further data will be presented.

Notable Presentations At ASH 2025
Lymphoma (Hodgkin & Non-Hodgkin) (2/13)

Date	Title	Author	Summary
06 Dec 2025	Final analysis of the Phase III GHSG HD21 trial: PET-guided brecadd vs. ebeacopp in advanced-stage classical Hodgkin lymphoma	Justin Ferdinandus	• **Introduction:** The final efficacy and safety results were reported, including long-term progression-free survival (PFS), overall survival (OS), and late toxicity. • **Methodology:** This phase III trial randomized adults with AS-cHL to receive 4–6 cycles of eBEACOPP or BrECADD, guided by PET after two cycles. Primary endpoints were TRMB reduction and superior PFS with BrECADD. • **Results:** 1,500 pts were enrolled. The 5-year PFS for BrECADD was 93.6%, vs. 90.6% for eBEACOPP. In PET2-negative pts, the PFS benefit was more pronounced (96.2% for BrECADD vs. 92.4% for eBEACOPP). HR for PFS was 0.64 in favor of BrECADD. Male sex and hemoglobin < 10.5 g/dL were associated with higher risk. OS remained 98% for both arms. Secondary malignancies (SPMs) were more frequent in the BrECADD arm (2.8% vs. 2.1%). • **Conclusions:** With 5 years of follow-up, BrECADD shows high cure rates and long-term safety, establishing it as a standard treatment for newly diagnosed AS-cHL with benefits from response-adapted strategies.
06 Dec 2025	Interim PET-adapted de-escalation chemotherapy regimen for advanced stage classical Hodgkin lymphoma using brentuximab vedotin, pembrolizumab, doxorubicin, and dacarbazine: Phase 2 study	Hun Lee	• **Introduction:** This study investigates the combination of pembrolizumab with Bv+AD and PET-adapted de-escalation to reduce chemotherapy exposure in untreated pts. • **Methodology:** Adult pts with newly diagnosed stage I/II bulky mediastinal disease or stage III/IV AS-cHL received 3 cycles of BvP+AD. PET scans after cycle 3 guided de-escalation for those with negative interim scans, with those achieving <90% reduction continuing full treatment. The primary endpoint was the complete remission (CR) rate at the end of therapy (EOT). • **Results:** 25 pts (median age 31) were enrolled. 88% (22/25) achieved CR at EOT, with no progressions. The most common treatment-related AEs were nausea (80%), fatigue (60%), and ALT increase (60%). No treatment-emergent immune-mediated adverse events (IMAEs) were observed. PET scans showed significant tumor reduction, with 80% achieving a DS2 at EOT. Three pts had DS4, with no evidence of lymphoma in biopsies. No consolidative radiation therapy was used. • **Conclusions:** PET-adapted de-escalation with BvP+AD showed promising efficacy with a favorable safety profile, reducing chemotherapy exposure without compromising effectiveness. Further follow-up with a larger cohort is needed for robust evidence.

Notable Presentations At ASH 2025
Lymphoma (Hodgkin & Non-Hodgkin) (3/13)

Date	Title	Author	Summary
06 Dec 2025	Valemetostat monotherapy in pts with relapsed or refractory B-cell lymphoma: Final results of the Phase 2 valym study from the lysa	Emmanuel Bachy	• **Introduction:** This Phase 2 study evaluates its efficacy in various lymphoma subtypes, including large B-cell lymphoma (LBCL), follicular lymphoma (FL), mantle cell lymphoma (MCL), marginal zone lymphoma (MZL), and Hodgkin lymphoma (HL). • **Methodology:** The study enrolled 120 pts with R/R B-cell lymphoma. Pts received oral valemetostat 200 mg daily in 28-day cycles until disease progression or unacceptable toxicity. The primary endpoint was overall response rate (ORR), assessed per Lugano 2014 criteria. • **Results:** At a median follow-up of 28.6 months, ORR was 17.1% for LBCL, 62.2% for FL, 11.1% for MCL, 20.0% for MZL, and 20% for HL. Complete response rates were 12.2% for LBCL and 20.0% for FL. The median progression-free survival (PFS) was 2.6 months for LBCL, 9.7 months for FL, and 2.0 months for MCL. Safety profiles were manageable, with the most common adverse events being diarrhea (25%) and thrombocytopenia (21%). • **Conclusions:** Valemetostat showed modest activity in MCL, MZL, and HL, with encouraging efficacy in FL. The safety profile supports its further investigation, particularly in combination therapies.
06 Dec 2025	Promising response rates and manageable safety with mosunetuzumab plus lenalidomide (Mosun-Len) in pts with relapsed/refractory (R/R) follicular lymphoma (FL): US extension cohort from the Phase III CELESTIMO study	Dahlia Sano	• **Introduction:** . This study reports the focused enrollment strategies for the US extension (Arm C), highlighting its effectiveness in achieving rapid enrollment and demographic representation. • **Methodology:** pts with untreated advanced FL received Mosun-Len in a non-randomized, single-arm study. Recruitment strategies included site expansion, targeted materials, and 1:1 investigator interactions. Primary endpoints included objective response rate (ORR) and complete response rate (CRR), with safety and cytokine release syndrome (CRS) monitored. • **Results:** 54 pts enrolled in Arm C, with 87% White, 5.6% Asian, and 3.7% African American. Median age was 62 years. ORR was 96.3%, and CRR was 87.0%. Most common AEs included neutropenia (40.7%) and infections (57.4%). CRS was reported in 27.8%, resolving in all cases. Serious AEs occurred in 27.8% of pts. One fatal AE was linked to Mosunetuzumab (pneumonia). • **Conclusions:** 54 pts enrolled in Arm C, with 87% White, 5.6% Asian, and 3.7% African American. Median age was 62 years. ORR was 96.3%, and CRR was 87.0%. Most common AEs included neutropenia (40.7%) and infections (57.4%). CRS was reported in 27.8%, resolving in all cases. Serious AEs occurred in 27.8% of pts. One fatal AE was linked to Mosunetuzumab (pneumonia).

Notable Presentations At ASH 2025
Lymphoma (Hodgkin & Non-Hodgkin) (4/13)

Date	Title	Author	Summary
06 Dec 2025	Phase 2 bellwave-003 cohort f: Updated clinical outcomes of nemtabrutinib in participants with relapsed or refractory marginal zone lymphoma	Muhit Ozcan	• **Introduction:** This study evaluated the efficacy and safety of nemtabrutinib in pts with R/R MZL who had progressed after ≥2 prior therapies, including covalent BTK inhibitors. • **Methodology:** This Phase 2, multicenter, open-label study (BELLWAVE-003) enrolled pts with R/R MZL who had failed prior BTKi or chemoimmunotherapy. pts received nemtabrutinib 65 mg daily until disease progression or unacceptable toxicity. The primary endpoint was objective response rate (ORR), with secondary endpoints including duration of response (DOR), progression-free survival (PFS), and overall survival (OS). • **Results:** 23 participants with R/R MZL were treated. The ORR was 52% by blinded independent central review (BICR) and 48% by investigator review. The median duration of response was 7.4 months. The most common adverse events were pneumonia, pyrexia, anemia, and diarrhea. Grade 3 or 4 adverse events occurred in 52% of participants, with pneumonia and anemia being the most frequent. • **Conclusions:** Nemtabrutinib demonstrated sustained antitumor activity and a manageable safety profile in heavily pretreated pts with R/R MZL. These results support further clinical exploration of nemtabrutinib in this patient population.
06 Dec 2025	Phase 3 study (inMIND) of tafasitamab plus lenalidomide and rituximab for relapsed or refractory follicular lymphoma: Clinical characteristics and outcomes of pts receiving second-line treatment	Ajay Gopal	• **Introduction:** This post hoc analysis evaluates tafa's efficacy and safety in 2L treatment. • **Methodology:** pts aged ≥18 with R/R FL who received ≥1 prior therapy were randomized to tafa or placebo with lenalidomide and rituximab for up to 12 cycles. Primary endpoint: PFS; secondary endpoints: ORR, CRR, and IRC-assessed PFS. • **Results:** In 300 pts, tafa showed significant improvements in PFS, ORR, CRR, and TTNT compared to placebo. Median investigator-assessed PFS was 24.0 months with tafa versus 15.4 months with placebo (HR 0.40). In pts with prior anti-CD20 therapy, median PFS was 24.0 months with tafa versus 14.4 months with placebo (HR 0.45). Common AEs were neutropenia, diarrhea, and fatigue, with similar safety profiles across arms. • **Conclusions:** Tafa combined with lenalidomide and rituximab significantly improved PFS and other responses in R/R FL, with manageable safety. Tafa is a valuable option for 2L treatment.

Notable Presentations At ASH 2025
Lymphoma (Hodgkin & Non-Hodgkin) (5/13)

Date	Title	Author	Summary
06 Dec 2025	Optimal dose regimen of epcoritamab in combination with lenalidomide and rituximab in relapsed or refractory follicular lymphoma - analyses of pharmacokinetics and exposure-response relationships of epcore FL-1 Phase 3 study	Behnam Noorani	• **Introduction:** This study evaluates epcoritamab's pharmacokinetics (PK) and exposure-response (E-R) relationship when combined with rituximab and lenalidomide (R2) in the EPCORE FL-1 trial. • **Methodology:** pts received 48 mg (Arm A) or 24 mg (Arm B) of epcoritamab with R2. A step-up dosing (SUD) regimen was used to mitigate cytokine release syndrome (CRS). PK, safety, and efficacy were assessed, and the optimal dose was determined. • **Results:** PK analyses showed a clear E-R trend for time-to-event endpoints like duration of response (DOR), progression-free survival (PFS), and overall survival (OS), with 48 mg showing superior outcomes over 24 mg. Safety profiles were similar, with no increase in adverse events at higher doses. A 3-step SUD regimen (0.16/0.8/3 mg) reduced CRS risk compared to the 2-step regimen. • **Conclusions:** The 48 mg dose with a 3-step SUD regimen demonstrated optimal efficacy and safety for R/R FL pts. Dosing strategy provides improved efficacy with manageable safety.
06 Dec 2025	Pembrolizumab plus gemcitabine, vinorelbine, and liposomal doxorubicin as second-line therapy in relapsed or refractory Hodgkin lymphoma: 5-year update of a multicenter, Phase 2 trial	Kishan Patel	• **Introduction:** Here, a 5-year update of the trial (NCT03618550) was presented. • **Methodology:** This investigator-initiated, single-arm, phase II trial enrolled R/R cHL pts after one prior chemotherapy line. pts received pembrolizumab (200 mg) with gemcitabine, vinorelbine, and liposomal doxorubicin every 21 days. pts achieving CR proceeded to high-dose therapy with BEAM and autologous stem cell transplantation (HDT/AHCT). Primary endpoint: CR with pembrolizumab-GVD. Secondary endpoints: PFS and overall survival (OS). • **Results:** 39 pts enrolled (median age 38, range 21–71). At enrollment, 41% had stage I/II disease and 59% had stage III/IV. 41% had primary refractory disease. After 4 cycles of pembrolizumab-GVD, CR was achieved in 95% of pts, with a 100% overall response rate (ORR). 36 pts proceeded to HDT/AHCT. After a median follow-up of 57 months, 5-year PFS and OS were 91% and 94%, respectively. Only 1 patient relapsed and 2 died from non-relapse causes. No new safety signals were identified. • **Conclusions:** Pembrolizumab-GVD followed by consolidative HDT/AHCT achieves durable long-term responses in R/R cHL with a manageable safety profile. A randomized study comparing HDT/AHCT versus pembrolizumab maintenance for pts who achieve CR is underway.

Notable Presentations At ASH 2025
Lymphoma (Hodgkin & Non-Hodgkin) (6/13)

Date	Title	Author	Summary
06 Dec 2025	Interim and end-of-treatment FDG-PET demonstrate limited ability to predict 3-year progression-free survival with nivolumab-AVD in first-line treatment of advanced stage Hodgkin lymphoma: Imaging sub-analysis of Phase 3 S1826 study	Nancy Bartlett	• **Introduction:** The Phase 3 S1826 trial showed superior progression-free survival (PFS) with nivolumab-AVD (Nivo-AVD) versus BV-AVD in untreated advanced Hodgkin lymphoma (HL). However, the prognostic value of interim (iPET) and end-of-treatment (EoT) PET using the 5-point scale (5PS) for Nivo-AVD had not been defined. • **Methodology:** pts with stage 3–4 HL were randomized to Nivo-AVD or BV-AVD. iPET after Cycle 2 and EoT PET after Cycle 6 were centrally reviewed. 5PS 1–3 indicated complete remission; 4–5 indicated residual disease or progression. • **Results:** Among 994 enrolled pts, 742 had iPET and 863 had EoT PET. Three-year PFS was 86% overall and 87% for centrally assessed iPET cases. PFS was 89% for iPET-negative and 77% for iPET-positive pts. For EoT PET, PFS reached 93% for negative scans and 52% for positive scans. pts positive on both iPET and EoT PET had markedly lower PFS (60%). Discordance between investigator and central reads occurred in 20% (iPET) and 12% (EoT). • **Conclusions:** EoT PET was more prognostic than iPET. Notably, many iPET- or EoT-positive pts treated with Nivo-AVD remained progression-free at 3 years, indicating therapy should not be modified based solely on iPET. The results underscore the need for improved response tools such as ctDNA.
06 Dec 2025	A Phase 2, multicenter, open-label, single-arm study assessing a 4-weekly dosing schedule for mogamulizumab in pts with mycosis fungoides/Sézary syndrome (MOGA-2MG-Q4W)	Julia Scarisbrick	• **Introduction:** Mogamulizumab (moga), a CCR4-targeting monoclonal antibody, is approved for R/R mycosis fungoides/Sézary syndrome (MF/SS) after ≥1 systemic therapy. A Phase 2 study evaluated a reduced-frequency schedule (2.0 mg/kg every 4 weeks) in stage IB–IV MF/SS. • **Methodology:** pts received 1.0 mg/kg weekly during Cycle 1, then 2.0 mg/kg every 4 weeks. Primary endpoint: safety. Secondary endpoints: PK, efficacy, duration of response (DOR). Exploratory work assessed gene expression and mutations associated with response. • **Results:** Thirty-four pts were treated (median age 64). Common TEAEs were drug eruption (38.2%) and infusion reactions (23.5%). Among 32 evaluable pts, ORR was 37.5% with 2 CRs. ORR was 30.8% in MF and 66.7% in SS. Median PFS was 6.3 months. Moga exposure rose with successive cycles, reaching steady state by Cycle 3. Immune and mutational signatures correlated with response and drug-eruption risk. • **Conclusions:** The 4-week 2.0 mg/kg schedule was well tolerated with safety comparable to 1.0 mg/kg Q2W. Exploratory immune and genomic findings may aid response prediction and refine patient management.

Notable Presentations At ASH 2025
Lymphoma (Hodgkin & Non-Hodgkin) (7/13)

Date	Title	Author	Summary
06 Dec 2025	Tislelizumab combined with zanubrutinib and high-dose methotrexate in newly diagnosed primary central nervous system DLBCL: A phase 2 study	Xia Zhao	• **Introduction:** PCNS-DLBCL is a rare subtype with poor prognosis. The TZM regimen, combining tislelizumab, zanubrutinib, and methotrexate, shows promise in improving outcomes. This Phase 2 trial (ChiCTR2300071346) assesses its efficacy and safety. • **Methodology:** 38 newly diagnosed pts aged 18-90 were enrolled across five centers in China from May 2022 to May 2025. Data on response rates, survival, and adverse events were collected. • **Results:** The median age was 65.5 years. After 2 cycles, ORR was 97.1%, and CRR was 8.6%. After 6 cycles, ORR reached 100%, with CRR of 85.7%. At 18 months, OS and PFS were 86.8% and 73.4%. Adverse events included renal injury, infections, and mild hematological toxicity. • **Conclusions:** The TZM regimen significantly improved survival in PCNS-DLBCL with manageable safety.
06 Dec 2025	Phase 2 Study of polatuzumab vedotin, zanubrutinib and rituximab (Pola-ZR) in untreated elderly and frail DLBCL pts: Molecular features and follow-up updates	Yuhong Ren	• **Introduction:** This Phase 2 trial (NCT05940064) further investigates Pola-ZR's efficacy and safety with revised prophylaxis for infections. • **Methodology:** Untreated DLBCL pts aged ≥70 or aged 60-69 with performance status 2-4 were enrolled. Exclusion criteria included central nervous system involvement. The primary endpoint was CR rate after 6 cycles of Pola-ZR, with secondary endpoints of safety, overall response rate, and 24-month PFS. Molecular analysis was conducted via ctDNA and whole-exome sequencing (WES). • **Results:** 30 pts were enrolled, median age 72 (range 67-83). 80% were ≥70, 73.3% had an IPI score of 3-5, and 63.3% had non-GCB subtype. After 6 cycles, the CR rate was 71.4%. Median PFS was 18.5 months, with median OS not reached. The safety profile showed manageable lung infections (10%) and leukopenia (26.7%). No dose de-escalation of polatuzumab vedotin was required. WES revealed 21 genotyped cases: 6 A53, 5 MCD, 3 N1, 4 ST2, 2 BN2, 1 EZB. RNA sequencing showed 8 GCB and 10 ABC subtypes. • **Conclusions:** Pola-ZR demonstrated sustained efficacy with manageable safety in elderly and frail DLBCL pts. Prophylaxis for pneumocystis jirovecii pneumonia controlled infections. WES and RNA sequencing results were consistent with clinical findings. Ongoing analysis will provide further insights into treatment efficacy and molecular mechanisms.

Notable Presentations At ASH 2025
Lymphoma (Hodgkin & Non-Hodgkin) (8/13)

Date	Title	Author	Summary
06 Dec 2025	Phase 2 trial of polatuzumab vedotin, rituximab and dose attenuated CHP in pts 75 years and older with large B-cell lymphoma	Patrick Reagan	• **Introduction:** This study investigates CMOP with or without rituximab (CMOP±R) for treatment-naïve NHL pts. • **Methodology:** A phase 3, single-arm, open-label study treated adults with NHL using CMOP±R for up to 6 cycles. The primary endpoint was complete response rate (CRR). Secondary endpoints included ORR, PFS, OS, and safety. MAIC used historical data from POLARIX and Ro-CHOP studies. • **Results:** 27 pts were included, median age 56 years. The CRR was 70.4%, and ORR was 100%. After 6 cycles, CRR increased to 76.5%. The median follow-up was 5.3 months, with only two progressions. MAIC showed CMOP±R achieved better responses than conventional regimens, especially in DLBCL and PTCL. Common grade 3-4 adverse events included neutropenia, leukopenia, and anemia. • **Conclusions:** CMOP±R demonstrates promising efficacy as a first-line treatment for NHL with a manageable safety profile. Further updates will be reported with more pts.
06 Dec 2025	Mitoxantrone hydrochloride liposome-based CMOP±R regimen achieves superior response in treatment-Naïve non-Hodgkin lymphoma: A phase III clinical trial with matching-adjusted indirect comparison	Tao You	• **Introduction:** This study aimed to evaluate CMOP with or without rituximab (CMOP±R) as first-line therapy for treatment-naïve NHL. • **Methodology:** This phase 3 study included adults with newly diagnosed NHL. pts received CMOP±R every 4 weeks for up to 6 cycles, or until disease progression or unacceptable toxicity. Primary endpoint: complete response rate (CRR); secondary endpoints: objective response rate (ORR), duration of response (DoR), progression-free survival (PFS), overall survival (OS), and safety. • **Results:** 27 pts were enrolled. Median age: 56 years; 59.3% had diffuse large B-cell lymphoma (DLBCL), 29.6% PTCL. CRR was 70.4%, and ORR was 100%. After 6 cycles, CRR was 76.5% in pts completing treatment. With a median follow-up of 5.3 months, only 2 progressions occurred and no deaths. MAIC analysis showed superior responses with CMOP±R over conventional treatments. Most common grade 3-4 adverse events: neutropenia (33.3%), leukopenia (25.9%), anemia (11.1%), thrombocytopenia (11.1%). • **Conclusions:** The CMOP±R regimen showed promising efficacy as a first-line treatment for NHL with a manageable safety profile. Further updates will be provided with additional pts.

Notable Presentations At ASH 2025
Lymphoma (Hodgkin & Non-Hodgkin) (9/13)

Date	Title	Author	Summary
06 Dec 2025	Subgroup analysis based on prior treatment from the Phase 3 allele study of tabelecleucel for epstein-barr virus-driven post-transplant lymphoproliferative disease	Sarah Nikiforow	• **Introduction:** This phase 3 ALLELE trial investigates its efficacy and safety in pts after hematopoietic cell transplant (HCT) or solid organ transplant (SOT). • **Methodology:** pts who had failed prior rituximab or rituximab/chemotherapy were treated with tabelecleucel (2 x 10^6 cells/kg) in 35-day cycles. The primary endpoint was objective response rate (ORR), and secondary endpoints included time to response (TTR), overall survival (OS), and safety. • **Results:** As of September 2024, 29 HCT and 57 SOT pts were treated. The ORR was 48.3% in HCT and 47.4% in SOT. Median OS was 18.6 months for HCT and not reached for SOT. The estimated 1-year OS rate was 54.3% (HCT) and 62.6% (SOT). Serious adverse events (SAEs) were reported in 58.6% of HCT and 66.7% of SOT pts, with no treatment-related fatalities. • **Conclusions:** Tabelecleucel demonstrates promising efficacy and manageable safety in treating R/R EBV+ PTLD. These findings support its use as a novel treatment option.
06 Dec 2025	Epcoritamab with lenalidomide and tafasitamab in pts with relapsed/refractory diffuse large B cell lymphoma (ECLAT), a phase 2 investigator-initiated trial	Pallawi Torka	• **Introduction:** A phase 3 multicenter, open-label trial (NCT03394365) is exploring tabelecleucel's efficacy and safety in pts after hematopoietic cell transplant (HCT) or solid organ transplant (SOT). • **Methodology:** Eligible pts received tabelecleucel at 2 x 10^6 cells/kg on days 1, 8, and 15 in 35-day cycles. Objective response rates (ORR), time to response (TTR), and overall survival (OS) were the primary and secondary endpoints, respectively. • **Results:** 29 HCT and 57 SOT pts were treated, with ORR of 48.3% for HCT and 47.4% for SOT. For SOT-R and SOT-RC, the ORR was 52.4% and 44.4%, respectively. Median OS for HCT was 18.6 months, while OS for SOT was not reached. • **Conclusions:** Tabelecleucel shows promising efficacy in R/R EBV+ PTLD with manageable safety. No new safety concerns were identified, supporting its potential as a treatment option for pts with poor survival prospects.

Notable Presentations At ASH 2025
Lymphoma (Hodgkin & Non-Hodgkin) (10/13)

Date	Title	Author	Summary
07 Dec 2025	Combined mosunetuzumab and zanubrutinib for the treatment of pts with newly diagnosed high-burden follicular lymphoma: First results of the multicenter phase 2 mithic-FL2 trial	Lorenzo Falchi	• **Introduction:** The first results of the MITHIC-FL2 trial evaluating this combination in untreated FL pts were presented. • **Methodology:** Eligible pts (≥18 years, ECOG PS 0-2) with grade 1-3A FL received mosunetuzumab and zanubrutinib for 12 cycles. The primary endpoint was the complete response (CR) rate at the end of study therapy. • **Results:** 47 pts were enrolled, with a median age of 59 years. The CR rate was 74%, and the best overall response rate (ORR) was 85%. The most common treatment-emergent adverse events (AEs) were injection site reactions (62%), cytokine release syndrome (56%), and dry skin (53%). Grade 3 AEs occurred in a small number of pts, including neutropenia (4%). • **Conclusions:** The combination of zanubrutinib and mosunetuzumab demonstrates high efficacy and manageable safety in pts with untreated high-burden FL. Updated data will be presented as the study continues.
07 Dec 2025	Tucidinostat plus R-CHOP in untreated MYC/BCL2 double-expressor diffuse large B-cell lymphoma : topline efficacy and safety results from the randomized phase 3 DEB study	Wei Li Zhao	• **Introduction:** Epigenetic dysregulation is linked to the progression of diffuse large B-cell lymphoma (DLBCL). Tucidinostat (chidamide), a selective histone deacetylase (HDAC) inhibitor, has shown promise in combination with R-CHOP for treating double-expressor lymphoma (DEL), a subtype associated with poor outcomes. • **Methodology:** The phase 3 DEB trial compared tucidinostat plus R-CHOP to R-CHOP alone in untreated DEL pts. pts were randomized to receive either 20 mg tucidinostat or placebo alongside six cycles of R-CHOP. The primary endpoint was event-free survival (EFS), with secondary endpoints including CR rate, progression-free survival (PFS), and overall survival (OS). • **Results:** Of 423 pts, 211 received tucidinostat and 212 received placebo. At a median follow-up of 44.9 months, tucidinostat plus R-CHOP significantly improved EFS (HR 0.72, P=0.02), with EFS rates of 60.3% at 2 years and 56.8% at 3 years, compared to placebo (50.5% and 47.7%, respectively). The CR rate was 73.0% for tucidinostat vs 61.8% for placebo (P=0.01). Safety was manageable, with more hematologic AEs in the tucidinostat group, but no unexpected toxicity. • **Conclusions:** Tucidinostat combined with R-CHOP significantly improves EFS and CR rate in untreated DEL pts, with a tolerable safety profile.

Notable Presentations At ASH 2025
Lymphoma (Hodgkin & Non-Hodgkin) (11/13)

Date	Title	Author	Summary
07 Dec 2025	Smart start with tislelizumab as frontline treatment in advanced-stage classical Hodgkin lymphoma : a PET-adapted, chemotherapy-sparing phase 2 study	Zhiming Li	• **Introduction:** Around 10-30% of classical Hodgkin's lymphoma (cHL) pts relapse or become refractory after chemotherapy. To balance efficacy and toxicity, the phase II study (NCT04843267) explored tislelizumab sequentially combined with AVD as first-line treatment for advanced-stage cHL. • **Methodology:** Untreated cHL pts with advanced-stage disease were treated with 2 cycles of tislelizumab monotherapy, followed by a PET-CT evaluation. PET-2 responders received 4 more cycles of tislelizumab, while partial responders received tislelizumab plus AVD. The primary endpoint was the PET-2 complete response rate (CRR). • **Results:** Thirty-two pts were enrolled, with 31 evaluable for response. PET-2 CRR was 32.3%, and the overall response rate (ORR) was 96.8%. After 36 months of follow-up, 28 pts (90.3%) achieved CR, and 3 (9.7%) had PD. The 3-year progression-free survival (PFS) was 70.5%, with OS remaining at 96.7%. Females and pts aged <45 had significantly better PFS. The treatment was well tolerated, with no treatment-related severe adverse events (SAEs). • **Conclusions:** Tislelizumab plus AVD showed high CR rates and reduced chemotherapy exposure, especially in younger and female pts, suggesting potential for reducing or omitting chemotherapy in some cHL pts.
07 Dec 2025	Pembrolizumab + GVD with ctdna-guided consolidation for relapsed/refractory classic Hodgkin lymphoma: A multicenter phase 2 Study of the University of California hematologic malignancies consortium	Michael Randall	• **Introduction:** This phase 2 trial aims to guide consolidation treatment using PET and circulating tumor DNA (ctDNA) to omit ASCT for patients achieving metabolic CR and undetectable ctDNA. • **Methodology:** This single-arm study will enroll 38 adult patients with R/R cHL across six California sites. Patients will receive 2 cycles of pembro-GVD, followed by PET and ctDNA assessment. Those achieving metabolic CR and undetectable MRD will receive non-transplant consolidation with pembrolizumab and/or radiotherapy. • **Results:** The primary endpoint is the MRD-negative CR rate after pembro-GVD, with secondary endpoints including 2-year progression-free survival (PFS), overall survival, and quality of life. The study hypothesizes that over 60% of patients will achieve MRD-negative CR and be eligible for non-transplant consolidation. • **Conclusions:** This study investigates whether high-dose chemotherapy and ASCT can be omitted for select R/R cHL patients, using ctDNA as a response assessment tool.

Notable Presentations At ASH 2025
Lymphoma (Hodgkin & Non-Hodgkin) (12/13)

Date	Title	Author	Summary
07 Dec 2025	Chidamide-BEAM conditioning plus autologous stem cell transplantation forperipheral t-cell lymphoma: A single-arm, single-center, phase 2 trial	Meng-Meng Ji	• **Introduction:** Chidamide, a histone deacetylase inhibitor, has shown therapeutic promise in T-cell lymphoma (TCL). This study evaluates the efficacy and safety of Chidamide combined with BEAM conditioning, followed by autologous stem cell transplantation (ASCT) and Chidamide maintenance in patients with peripheral T-cell lymphoma (PTCL). • **Methodology:** From June 2022 to June 2023, 26 eligible PTCL patients were enrolled. Patients received Chidamide-BEAM conditioning, followed by ASCT and Chidamide maintenance. The primary endpoint was 2-year progression-free survival (PFS), with secondary endpoints including overall survival (OS), complete remission rate, and adverse events. • **Results:** Of 23 evaluable patients, 2-year PFS was 95.7% and 2-year OS was 100%. The most common grade 3-4 adverse events were infections (13%), hepatic toxicity (8.7%), and vomiting/mucositis (4.3%). • **Conclusions:** The Chidamide-BEAM regimen, followed by ASCT and maintenance, demonstrated high efficacy and a manageable safety profile in PTCL patients.
07 Dec 2025	Duvelisib in patients with relapsed/refractory peripheral T-cell lymphoma: Final results from the phase 2 PRIMO trial - impact of prior therapy and expanded safety analysis	Pier Luigi Zinzani	• **Introduction:** Peripheral T-cell lymphomas (PTCL) represent a heterogeneous and aggressive group of lymphomas with poor prognosis, and current treatments offer modest responses. Duvelisib, an oral dual inhibitor targeting PI3K-δ and PI3K-γ, has shown promise in other hematologic cancers and is being investigated in relapsed/refractory (R/R) PTCL. The PRIMO trial (NCT03372057) explored duvelisib monotherapy in R/R PTCL. • **Methodology:** The phase 2 PRIMO-EP trial enrolled patients with R/R PTCL, receiving 75 mg BID of duvelisib for 2 cycles, followed by 25 mg BID for 12 cycles, until progression or unacceptable toxicity. The primary endpoint was overall response rate (ORR), and secondary endpoints included progression-free survival (PFS), overall survival (OS), and safety. • **Results:** The study enrolled 123 patients (median age 65), with a median treatment duration of 8.3 weeks. The overall response rate (ORR) was 48%, with a complete response rate (CRR) of 33%. The median PFS was 3.4 months, and the median OS was 12.4 months. Subgroup analysis of AITL patients showed better outcomes with an ORR of 62%, CRR of 51%, and a median PFS of 8.3 months. Safety analysis revealed common grade 3-4 adverse events, including neutropenia (13%) and infections (13%). • **Conclusions:** Duvelisib showed promising efficacy in heavily pretreated R/R PTCL patients, particularly in AITL, with manageable safety. These findings support further investigation in more homogenous PTCL populations.

Notable Presentations At ASH 2025
Lymphoma (Hodgkin & Non-Hodgkin) (13/13)

Date	Title	Author	Summary
07 Dec 2025	Golidocitinib combined with CHOP in treatment-Naïve monomorphic epitheliotropic intestinal T-cell lymphoma: Preliminary results from A phase 2 multicenter, single-arm goal study	Yu-Ran Qiu	• **Introduction:** Monomorphic epitheliotropic intestinal T-cell lymphoma (MEITL) is a rare and aggressive PTCL with poor prognosis and limited treatments. CHOP chemotherapy provides suboptimal results. Golidocitinib, a selective JAK1 inhibitor, shows promise in PTCL and was tested in combination with CHOP for MEITL. • **Methodology:** This phase 2 trial enrolled patients with treatment-naïve MEITL, receiving golidocitinib (150 mg daily) and CHOP for 6 cycles. Primary endpoint: complete response rate (CRR) at EOT. Secondary endpoints: ORR, DOR, PFS, OS, and safety. • **Results:** Seven patients enrolled (median age 60). After 6.2 months' follow-up, ORR was 85.7%, CRR 71.4%. JAK/STAT mutations were seen in responders. Common Grade ≥3 AEs were hematologic, with severe GI events and CMV reactivation in two patients. • **Conclusions:** Golidocitinib plus CHOP showed strong efficacy in MEITL, with JAK/STAT activation and immune microenvironment as potential biomarkers.
07 Dec 2025	Pola-R-edch shows high response rates in high-risk aggressive B-cell lymphomas or PMBCL: A phase 2 study	Wei LIU	• **Introduction:** This study evaluates the safety and efficacy of combining Pola with R-EDCH in high-risk aggressive non-Hodgkin's lymphoma or PMBCL. • **Methodology:** Patients aged 18-65 with newly diagnosed aggressive B-cell lymphoma, including DLBCL, HGBL-NOS, and HGBL-DH, received six 21-day cycles of Pola-R-EDCH. • **Results:** 16 patients were enrolled, with 81.3% having non-GCB subtype. The best overall response rate was 100%, with 81.3% achieving CR. The 1-year PFS rate was 62.5%, and the OS rate was 87.5%. The most common grade ≥3 AEs were neutropenia (93.8%) and thrombocytopenia (31.3%). Febrile neutropenia occurred in 43.8%, and peripheral neuropathy in 50%. • **Conclusions:** The Pola-R-EDCH regimen showed high response rates with manageable toxicity. TP53 abnormalities correlated with increased risk of progression.

Notable Presentations At ASH 2025
Multiple Myeloma & Plasma Cell Disorders (1/8)

Date	Title	Author	Summary
06 Dec 2025	Carfilzomib, lenalidomide, and dexamethasone (KRd) versus bortezomib, lenalidomide and dexamethasone (VRd) in patients with newly diagnosed multiple myeloma (NDMM) – interim results from the randomized Phase III COBRA trial.	Dominik Dytfeld	• **Introduction:** KRd and VRd are standard regimens for newly diagnosed multiple myeloma (NDMM). The phase III COBRA trial (NCT03729804) compared KRd vs VRd, evaluating the efficacy and safety of both in patients with NDMM. • **Methodology:** Patients were randomized to receive KRd or VRd. KRd included carfilzomib, lenalidomide, and dexamethasone, while VRd included bortezomib. The study's primary endpoints were MRD-negative complete response (CR) and progression-free survival (PFS). • **Results:** Of 250 patients, 126 received KRd and 124 received VRd. KRd demonstrated significantly better MRD-negative CR rates (31% vs 18%; p = 0.016) and PFS (median not reached vs 49 months; HR = 0.57; p = 0.0095). The CR rate was higher in KRd (71% vs 53%; p = 0.005). Adverse events were common in both groups, with KRd showing more neutropenia and peripheral neuropathy. • **Conclusions:** KRd showed superior efficacy to VRd in NDMM, with a similar safety profile. These results support further evaluation of KRd as an induction regimen in NDMM.
06 Dec 2025	Iberdomide maintenance after autologous stem-cell transplantation in newly diagnosed multiple myeloma: An update from the phase 2 EMN26 trial	Niels W.C.J. van de Donk	• **Introduction:** An updated analysis with a median follow-up of 30.2 months was presented • **Methodology:** The EMN26 study (NCT04564703) enrolled MM patients (≥18 years) with at least partial response after induction therapy and autologous stem cell transplants (ASCT). Three cohorts received 0.75, 1.0, or 1.3 mg Iberdomide daily. The primary endpoint was response improvement, and secondary endpoints included MRD conversion, progression-free survival (PFS), and safety. • **Results:** A total of 120 patients were enrolled, with a median follow-up of 23.4–33.4 months. At 12 months, MRD-negative complete response (CR) rates were 31%, 19%, and 7%, respectively. Best response achieved ≥CR in 78%, 60%, and 70%. PFS at 2 years was 92%, 82%, and 84%. The most common grade ≥3 adverse events were neutropenia (48%–60%) and infections (8%–18%). • **Conclusions:** Iberdomide shows superior efficacy in response improvement compared to historical data with lenalidomide maintenance. The 0.75 mg dose demonstrated comparable efficacy with improved tolerability and is recommended for future evaluations.

Notable Presentations At ASH 2025
Multiple Myeloma & Plasma Cell Disorders (2/8)

Date	Title	Author	Summary
06 Dec 2025	A phase 2 trial of abbreviated fixed-duration (Default 4 Cycles) linvoseltamab immuno-consolidation to deepen responses post newly diagnosed multiple myeloma combination therapy for minimal residual disease positivity (the IMMUNOPLANT Study)	Dickran Kazandjian	• **Introduction:** This updated analysis includes a median follow-up of 30.2 months. • **Methodology:** The EMN26 study (NCT04564703) enrolled patients with MM who achieved at least a partial response after induction and ASCT. Three cohorts (0.75, 1.0, and 1.3 mg) of Iberdomide were evaluated. Primary endpoints were response improvement, and secondary endpoints included MRD conversion, progression-free survival (PFS), and safety. • **Results:** A total of 120 patients were enrolled. At 12 months, MRD-negative CR rates were 31%, 19%, and 7%. Best response achieved ≥CR in 78%, 60%, and 70%. PFS at 2 years was 92%, 82%, and 84%. The most common grade ≥3 adverse events were neutropenia (48%–60%) and infections (8%–18%). • **Conclusions:** Iberdomide provides superior response improvement compared to historical data with lenalidomide maintenance. The 0.75 mg dose demonstrated comparable efficacy with improved tolerability, recommended for future evaluations.
06 Dec 2025	A phase 2 trial of iberdomide, carfilzomib, daratumumab and dexamethasone quadruplet therapy for relapsed/refractory multiple myeloma: The rekindle study	Benjamin Diamond	• **Introduction:** This study evaluates the combination of Iberdomide with Carfilzomib (K), Daratumumab (Dara), and dexamethasone (IberKDd) in early relapse/refractory MM. • **Methodology:** The Phase II ReKInDLE trial (NCT05896228) enrolled patients with 1-3 prior lines of therapy, including lenalidomide. Patients received Iberdomide (1mg) with Dara and K for up to 8 cycles, followed by Iberdomide monotherapy for up to 3 years if response was ≥SD. • **Results:** Of 30 patients, 40% achieved MRD-negative (10^{-5}) complete response (CR), with an overall response rate (ORR) of 92%. Most patients remained on treatment, and 27% de-escalated to Iberdomide monotherapy. Common grade ≥3 adverse events included neutropenia (50%) and lymphocytopenia (40%). • **Conclusions:** IberKDd provides high MRD-negative response rates in early relapse/refractory MM with manageable toxicity and the option for de-escalation to monotherapy.

Notable Presentations At ASH 2025
Multiple Myeloma & Plasma Cell Disorders (3/8)

Date	Title	Author	Summary
06 Dec 2025	Phase 2 registrational study of anitocabtagene autoleucel for the treatment of patients with relapsed and/or refractory multiple myeloma: Updated results from iMMagine--1	Krina Patel	• **Introduction:** Anitocabtagene autoleucel (anito-cel), an autologous anti-BCMA CAR T-cell therapy, shows promise for relapsed/refractory multiple myeloma (RRMM) patients. The iMMagine-1 Phase 2 trial evaluates its efficacy and safety in this population. • **Methodology:** Patients with RRMM received anito-cel after 3+ prior therapies. The primary endpoint was overall response rate (ORR), with secondary outcomes including MRD negativity, progression-free survival (PFS), and safety. MRD was assessed by NGS. • **Results:** 117 patients were treated, with 97% achieving ORR, and 68% achieving complete response (CR). 93% of patients achieved MRD negativity at 10^{-5}. PFS at 12 and 18 months was 79% and 66%, respectively. The safety profile was manageable, with most adverse events being cytopenias and CRS. • **Conclusions:** The iMMagine-1 trial shows anito-cel's strong efficacy and manageable safety in heavily pre-treated RRMM patients. No delayed neurotoxicities or IEC-associated enterocolitis were observed. Updated data will be presented.
06 Dec 2025	A phase 2 Study of teclistamab in combination with daratumumab in elderly patients with newly diagnosed multiple myeloma: The IFM2021-01 teclille trial, cohort a	Salomon Manier	• **Introduction:** This phase 2 study (IFM2021-01) evaluates the combination of teclistamab and daratumumab (Tec-Dara) as frontline therapy in transplant-ineligible patients with newly diagnosed multiple myeloma (NDMM). • **Methodology:** 37 patients ≥65 years with NDMM, ineligible for autologous stem cell transplant, were enrolled. The primary endpoint was the very good partial response (VGPR) rate after 4 cycles. Secondary endpoints included overall response rate (ORR), complete response (CR) rate, minimal residual disease (MRD) negativity, progression-free survival (PFS), and overall survival (OS). • **Results:** 78% of patients achieved VGPR or better. The ORR was 100%, and 51% of patients achieved MRD negativity at 10^{-6}. At a median follow-up of 7.6 months, there was no disease progression or death, with 100% PFS and OS. Safety included grade ≥3 adverse events in 76% of patients, with neutropenia being most common. • **Conclusions:** Tec-Dara shows promising efficacy and a favorable safety profile in elderly NDMM patients. Further investigation is warranted for this all-antibody-based regimen.

Notable Presentations At ASH 2025
Multiple Myeloma & Plasma Cell Disorders (4/8)

Date	Title	Author	Summary
06 Dec 2025	Sustained minimal residual disease (sMRD) negativity in transplant ineligible newly diagnosed multiple myeloma treated with isatuximab plus lenalidomide and dexamethasone with bortezomib (Isa-VRd) versus isa-rd: 12-24-month data from the phase 3 benefit trial (IFM 2020-05)	Arthur Bobin	• **Introduction:** MRD negativity between 12 and 24 months in newly diagnosed multiple myeloma (NDMM) transplant-ineligible (TI) patients from the BENEFIT study was assessed. • **Methodology:** BENEFIT is a phase 3 randomized trial comparing isatuximab-lenalidomide-dexamethasone with or without bortezomib (Isa-Rd ± V) in NDMM TI patients. Data are presented in the intention-to-treat (ITT) population. • **Results:** With a median follow-up of 33.4 months, the Isa-VRd arm showed significantly higher MRD negativity at 10^{-5} (OR 2.26, p=0.002) and sustained MRD negativity (OR 2.73, p=0.0007). Similar results were observed for sMRD at 10^{-6}. In the t(11;14) subgroup, MRD negativity rates were lower. No new safety signals were observed • **Conclusions:** Isa-VRd improves sustained MRD negativity in NDMM TI patients, supporting its use as a new standard of care for patients aged 65–79 years, including those with high-risk multiple myeloma (HRMM).
06 Dec 2025	Role of bortezomib maintenance therapy in the anti-CD38 antibody era: Interim analysis results of a randomized Phase III study for transplant-ineligible newly diagnosed multiple myeloma (JCOG1911/B-DASH Study)	Tomotaka Suzuki	• **Introduction:** This study evaluates whether adding bortezomib to Dara maintenance therapy (Dara + Bortezomib, or Dara-Bor) improves outcomes in TI-NDMM patients. • **Methodology:** Patients aged ≥65 or aged 20–64 and ineligible for autologous stem cell transplant were randomized to receive either Dara alone (Arm A) or Dara + Bortezomib (Arm B). The primary endpoint was PFS after the second registration. • **Results:** At the pre-specified interim analysis (March 2025), 224 patients were enrolled. The 2-year PFS rates were 80.2% in Arm A and 72.5% in Arm B, showing no significant improvement with added Bortezomib (HR 1.53, p=0.33). The study was terminated early due to a low predictive probability of Arm B demonstrating superiority. • **Conclusions:** Adding bortezomib to Dara maintenance did not improve PFS. Tolerability issues and the high incidence of adverse events in Arm B likely influenced these results. Further studies are needed to optimize maintenance therapy strategies.

Notable Presentations At ASH 2025
Multiple Myeloma & Plasma Cell Disorders (5/8)

Date	Title	Author	Summary
06 Dec 2025	Impact-AL: A phase 2 clinical trial of teclistamab and daratumumab in previously untreated AL amyloidosis	Rajshekhar Chakraborty	• **Introduction:** The study investigates teclistamab-daratumumab (Tec-Dara) as a frontline treatment for transplant-ineligible newly diagnosed multiple myeloma (NDMM), aiming to improve MRD negativity and overall response. • **Methodology:** Phase 2, single-arm, open-label trial with patients ≥65 years. Patients received step-up dosing of teclistamab plus daratumumab for 4 cycles. • **Results:** 97% ORR, 68% CR rate. At 6 months, 51% achieved MRD negativity at 10^{-6}. No progression or death reported. • **Conclusions:** Tec-Dara shows high efficacy and safety, offering deep responses and a favorable safety profile for elderly NDMM patients, supporting its potential as a standard frontline therapy.
06 Dec 2025	Long-term responders from the Phase 3 dreamm-7 study of belantamab mafodotin plus bortezomib and dexamethasone vs daratumumab plus bortezomib and dexamethasone in Relapsed/Refractory multiple myeloma	Vania Hungria	• **Introduction:** The DREAMM-7 trial compared BVd vs. DVd in relapsed/refractory multiple myeloma (RRMM), showing BVd improved PFS and OS. This post hoc analysis explores long-term responders (LTRs) for deeper insights. • **Methodology:** Patients were randomized to BVd or DVd, treated until progression or other events. LTRs had PFS ≥36 months. Primary endpoint: PFS; secondary: DOR, MRD negativity, and OS. • **Results:** 125 LTRs were identified, with 78 (32%) in BVd and 47 (19%) in DVd. BVd-treated LTRs had higher rates of ≥CR and MRD negativity. Median PFS, DOR, and OS were not reached for BVd LTRs.. • **Conclusions:** BVd resulted in higher response rates and longer remissions than DVd. The safety profile was consistent, supporting BVd's efficacy for long-term remission in RRMM.

Notable Presentations At ASH 2025
Multiple Myeloma & Plasma Cell Disorders (6/8)

Date	Title	Author	Summary
06 Dec 2025	Deep responses and durable outcomes in patients treated with belantamab mafodotin plus pomalidomide and dexamethasone from long-term follow-up of the Phase 3 dreamm-8 study	Suzanne Trudel	• **Introduction:** Daratumumab plus bortezomib, pomalidomide, and dexamethasone (BPd) demonstrated significant efficacy in the DREAMM-8 trial for relapsed/refractory multiple myeloma (RRMM), showing improvements in progression-free survival (PFS) compared to the standard pomalidomide, bortezomib, and dexamethasone (PVd) regimen. • **Methodology:** 302 patients were randomized to receive BPd or PVd. The primary endpoint was PFS, with secondary endpoints including overall survival, MRD negativity, and duration of response (DOR). Safety was also assessed. • **Results:** BPd showed a median PFS of 32.6 months vs. 12.5 months for PVd (HR 0.49). BPd patients had higher rates of complete response (43% vs. 17%) and MRD negativity (28% vs. 6%). BPd also provided more durable responses, with a median DOR not reached vs. 16.4 months in PVd. • **Conclusions:** BPd significantly improved response depth and durability compared to PVd in RRMM. Its safety profile was manageable, making BPd a potential new standard of care for RRMM, particularly in patients with lenalidomide-refractory disease.
06 Dec 2025	Efficacy and safety of aponermin-carfilzomib-dexamethasone-based regimens for relapsed/refractory multiple myeloma: A Phase 2 prospective multi-center study	Huixing Zhou	• **Introduction:** Aponermin, a recombinant TRAIL, targets tumor cell death and is combined with carfilzomib and dexamethasone (Apo-KD) for relapsed/refractory multiple myeloma (RRMM). This combination has shown promise, particularly in patients who are heavily pretreated. • **Methodology:** A prospective, multi-center phase 2 trial was conducted in RRMM patients with ≥2 prior treatments. Apo-KD was administered in 28-day cycles, with primary endpoints including overall response rate (ORR) and secondary endpoints assessing progression-free survival (PFS), overall survival (OS), and safety. • **Results:** 40 patients were enrolled, with a 70% ORR and 32.5% VGPR. In extramedullary disease patients, ORR was 71.3%. The median PFS was 11.4 months, with manageable adverse events, including bone marrow suppression and infections. • **Conclusions:** Apo-KD demonstrated promising efficacy in heavily pretreated RRMM, including those with extramedullary disease and TCE. Safety was manageable, supporting its potential as a viable treatment option.

Notable Presentations At ASH 2025
Multiple Myeloma & Plasma Cell Disorders (7/8)

Date	Title	Author	Summary
06 Dec 2025	The SCOPE trial: A phase 2 Study of selinexor in combination with pomalidomide and dexamethasone for patients with relapsed and/or refractory multiple myeloma	Prashant Kapoor	• **Introduction:** The SCOPE trial explored an all-oral regimen combining selinexor, pomalidomide, and dexamethasone (SPd) in RRMM patients with prior exposure to proteasome inhibitors and lenalidomide. • **Methodology:** This phase 2 study administered SPd for 18 cycles to RRMM patients. The primary endpoint was overall response rate (ORR), and secondary endpoints included progression-free survival (PFS), duration of response (DOR), overall survival (OS), and safety. • **Results:** Of 29 patients, 61% achieved ORR, with 21% achieving MRD-negative complete response. Median PFS was 24 months, and the 2-year OS rate was 93%. Hematologic toxicities occurred in 43% of patients, and non-hematologic toxicities in 46%. • **Conclusions:** SPd showed promising efficacy and manageable safety, making it a viable all-oral option for RRMM. Further investigation in a phase 3 trial is ongoing.
06 Dec 2025	A Phase 2/3, multicenter, randomized, open-label study evaluating the efficacy and safety of etentamig and daratumumab compared to daratumumab, lenalidomide, and dexamethasone in frailer transplant-ineligible patients with newly diagnosed multiple myeloma	Anders Svensson	• **Introduction:** Elderly or frail patients with newly diagnosed multiple myeloma (NDMM) often face suboptimal outcomes with current standard-of-care (SoC) regimens. Etentamig, a bispecific antibody targeting BCMA and CD3, may provide a promising, tolerable option for this population. • **Methodology:** This Phase 2/3 global, randomized, open-label study (NCT07095452) will evaluate etentamig+daratumumab (etentamig+D) versus DRd in transplant-ineligible (TI) NDMM patients, with the Phase 2 part determining the optimal dose. • **Results:** Primary endpoints include overall response rate and clinical activity in Phase 2, while Phase 3 evaluates measurable residual disease (MRD) negativity and progression-free survival (PFS). • **Conclusions:** Etentamig+D could be a promising option for frail or elderly patients with NDMM, addressing the unmet need for effective, tolerable treatment regimens.

Notable Presentations At ASH 2025
Multiple Myeloma & Plasma Cell Disorders (8/8)

Date	Title	Author	Summary
06 Dec 2025	BCMA CAR T-cell therapy in newly diagnosed transplant-ineligible multiple myeloma: An open label, single-arm, phase 2 study (CAREMM-001)	Wenqiang Yan	• **Introduction:** BCMA-directed CAR-T therapies show promising efficacy in relapsed/refractory multiple myeloma, but data on their use in transplant-ineligible (TIE) newly diagnosed multiple myeloma (NDMM) patients is limited. This study reports on the CAREMM-001 trial, evaluating CAR-T therapy as a frontline treatment for TIE NDMM. • **Methodology:** This Phase 2, single-arm trial enrolled TIE NDMM patients after VRd-based induction therapy, followed by CAR-T infusion, consolidation, and lenalidomide maintenance. Primary endpoints included safety and MRD negativity, with secondary endpoints of overall response rate, progression-free survival (PFS), overall survival (OS), and duration of remission (DOR). • **Results:** Of 36 treated patients, all achieved MRD negativity by day 28 and sustained it for ≥12 months. The overall response rate (ORR) was 100%, with 88.9% achieving stringent complete response (sCR). Median PFS, OS, and DOR were not reached. Common AEs included grade ≥3 neutropenia and lymphopenia, with manageable CRS and ICAHT. • **Conclusions:** BCMA CAR-T therapy induced deep, durable responses in TIE NDMM patients, including those with high-risk features. These findings support its potential as a transformative first-line treatment.
06 Dec 2025	Trial in progress: QUINTESSENTIAL-2—a phase 3 study of arlocabtagene autoleucel versus standard of care in adult patients with relapsed and refractory multiple myeloma (RRMM) exposed to lenalidomide	Eyal Lebel	• **Introduction:** Arlocabtagene autoleucel (arlo-cel), a GPRC5D-directed CAR T-cell therapy, has shown impressive results in a Phase 1 trial, with high response rates in patients with RRMM. • **Methodology:** The QUINTESSENTIAL-2 study (NCT06615479) is a Phase 3, randomized, open-label trial comparing arlo-cel to standard of care (SOC) in adults with RRMM. Patients with 1-3 prior lines of therapy and measurable disease were randomized to receive either arlo-cel or SOC. Primary endpoints include progression-free survival (PFS) and MRD negativity. • **Results:** The study is ongoing, with 440 patients expected to enroll across 126 sites globally. The primary endpoints include PFS and MRD negativity in complete response. Secondary endpoints include overall survival, overall response rate (ORR), and pharmacokinetics. Patients will be followed for up to 5 years. • **Conclusions:** The QUINTESSENTIAL-2 trial will further investigate arlo-cel as a potential new treatment for RRMM, offering promising results with a targeted approach.

Notable Presentations At ASH 2025
Myelodysplastic Syndromes & Myeloproliferative Neoplasms (1/12)

Date	Title	Author	Summary
06 Dec 2025	Rusfertide or placebo plus current standard-of-care therapy for polycythemia vera: Durability of response and safety results through week 52 from the randomized controlled phase 3 VERIFY study	Andrew Kuykendall	• **Introduction:** This study investigates rusfertide's long-term efficacy and durability in PV patients, focusing on the sustained control of Hct and PHL reduction. • **Methodology:** The VERIFY study (Phase 3) randomized patients to receive rusfertide or placebo (PBO) along with standard-of-care therapy. Part 1b assessed the durability of rusfertide's effects, including the absence of PHL eligibility and Hct control. • **Results:** Of 294 patients, 61.9% of rusfertide-treated patients maintained PHL eligibility absence through Week 52. For patients who crossed over from PBO, 78.0% achieved the same outcome by Week 52. Median time to first Hct ≥45% was not reached in the rusfertide group. Treatment showed durable improvements in fatigue and disease symptoms, with manageable adverse events (AEs) such as injection site reactions and fatigue. • **Conclusions:** Rusfertide provided sustained efficacy in controlling Hct and PHL, even in patients previously receiving PBO. Its safety profile remains consistent with prior data, supporting its potential as a durable treatment option for PV.
06 Dec 2025	Efficacy and safety of the LSD1 inhibitor bomedemstat in participants with polycythemia vera (PV) resistant or intolerant to cytoreductive therapy: The Phase 2 shorespan-004 study	Lindsay Rein	• **Introduction:** Polycythemia vera (PV) is a JAK2-driven myeloproliferative disorder, with current treatments failing to address the disease's progression effectively. Bomedemstat, an LSD1 inhibitor, has shown promise in other myeloproliferative neoplasms, and its potential for treating PV in patients who are resistant to prior therapies is being explored. • **Methodology:** In the SCOPE trial, patients with PV, resistant to ≥1 therapy, received bomedemstat combined with pomalidomide and dexamethasone. Primary endpoints included hematocrit reduction to <45%, while secondary endpoints included progression-free survival and platelet/white blood cell reduction. • **Results:** Of 20 patients treated, 45% achieved sustained hematocrit reduction by Week 36, with 85% reaching this outcome at any point. Significant platelet and WBC reductions were also observed. There was a meaningful reduction in disease symptoms, with a 31% improvement in the patient-reported health status. • **Conclusions:** Bomedemstat showed manageable safety and significant clinical efficacy, reducing hematocrit, platelet, and WBC counts in PV patients. These findings support its potential as a viable treatment option for PV.

Notable Presentations At ASH 2025
Myelodysplastic Syndromes & Myeloproliferative Neoplasms (2/12)

Date	Title	Author	Summary
06 Dec 2025	Subgroup analyses from the randomized, Phase 3 VERONA study of venetoclax with azacitidine (Ven+Aza) versus placebo with azacitidine (Pbo+Aza) in patients with treatment-naïve, intermediate and higher-risk Myelodysplastic Syndromes (HR MDS)	Guillermo Garcia-Manero	• **Introduction:** Polycythemia vera (PV) is a JAK2-driven myeloproliferative neoplasm with current treatments offering limited disease progression control. Rusfertide, a hepcidin mimetic, has shown promising efficacy in reducing phlebotomies and improving hematocrit control in previous studies. • **Methodology:** In the VERIFY study, patients were randomized to receive rusfertide or placebo alongside standard-of-care therapy. In Part 1b, patients who continued rusfertide or crossed over from placebo were assessed for long-term benefits, including hematocrit control and patient-reported outcomes. • **Results:** Rusfertide demonstrated durable control of hematocrit levels, with 61.9% of patients maintaining absence of phlebotomy eligibility by week 52. Significant reductions in platelet and WBC counts were also observed. The safety profile was consistent with prior studies. • **Conclusions:** Rusfertide provided durable benefits for PV patients, improving hematocrit control and reducing phlebotomies. Its safety profile remains manageable, making it a promising treatment for PV.
06 Dec 2025	Durability of complete response outperforms complete response rates as a surrogate endpoint for advancing to phase III trials in high-risk myelodysplastic syndromes	Julie Braish	• **Introduction:** This study explores whether durable complete response (CR) can be a more reliable surrogate endpoint for survival benefits than CR alone. • **Methodology:** A retrospective analysis was conducted on patients with HR-MDS treated with HMA-based therapy. Durable CR was defined as CR lasting more than 6 months, and overall survival (OS) was analyzed using Cox regression and landmark analysis. • **Results:** mong 980 patients, durable CR was associated with a significant reduction in mortality risk. Only durable CR (≥6 months) showed survival benefit, with a 44% reduction in the hazard of death. Short-duration CR did not impact survival. Subgroup analyses confirmed durable CR's relevance in patients with TP53 mutations. • **Conclusions:** Durable CR (>6 months) is a clinically meaningful surrogate endpoint for HR-MDS, providing a better assessment of treatment efficacy and supporting its role in accelerating drug development.

Notable Presentations At ASH 2025
Myelodysplastic Syndromes & Myeloproliferative Neoplasms (3/12)

Date	Title	Author	Summary
06 Dec 2025	Pacritinib in patients with high-risk myelofibrosis: Outcomes from post-hoc analyses of two Phase 3 studies	Pankit Vachhani	• **Introduction:** This analysis evaluates the efficacy of PAC versus best available therapy (BAT) in high-risk MF patients. • **Methodology:** A pooled analysis of the PERSIST-1 and PERSIST-2 trials assessed week 24 outcomes for PAC versus BAT in high-risk MF. Key endpoints included spleen volume response (SVR35), symptom score response, transfusion independence (TI-R), and patient-reported outcomes. • **Results:** PAC significantly outperformed BAT in SVR35 (17% vs. 3%) and PGIC response (29% vs. 8%). For patients with baseline platelets ≥50x10^9/L, PAC showed superior responses in SVR35, TSS50, and PGIC. Median OS was 126 weeks for PAC vs. 62 weeks for BAT. Safety profiles were similar between groups. • **Conclusions:** PAC demonstrated significant improvements in spleen size, symptom burden, and survival in high-risk MF patients compared to BAT. These findings position PAC as an important treatment option for this underserved patient population.
06 Dec 2025	Shorespan-017: Phase 3 extension study for safety of bomedemstat in participants with essential thrombocythemia who received bomedemstat from a prior clinical study	Monia Marchetti	• **Introduction:** This extension study evaluates its long-term safety, tolerability, and efficacy in participants with ET who were previously treated with bomedemstat. • **Methodology:** The Shorespan-017 extension study (NCT06351631) enrolled participants who had previously received bomedemstat in feeder studies. Participants continued treatment at the same dose used in earlier studies. The primary endpoint was the safety and tolerability of bomedemstat. • **Results:** 56 participants, including 40 with ET, were treated. Median follow-up was 8.1 months. Most participants (98%) remained on treatment. Common adverse events included diarrhea (23%), contusions (13%), and abdominal pain (10%). Serious treatment-related adverse events included grade 2 constipation. Grade 3 or 4 adverse events were observed in 20% of participants, but no deaths occurred. • **Conclusions:** Bomedemstat demonstrated a manageable safety profile and clinical benefit in ET patients, with most participants remaining on treatment. These results support bomedemstat's potential as a long-term therapeutic option for ET.

Notable Presentations At ASH 2025
Myelodysplastic Syndromes & Myeloproliferative Neoplasms (4/12)

Date	Title	Author	Summary
06 Dec 2025	RALLY MF: A phase 2 Study of DISC-0974, an anti-hemojuvelin antibody, in patients with myelofibrosis and anemia	Naseema Gangat	• **Introduction:** Hepcidin is elevated in myelofibrosis (MF) patients, contributing to anemia by limiting iron availability. DISC-0974, an investigational antibody, blocks hemojuvelin to reduce hepcidin and improve anemia. Early studies showed promise in reducing transfusion dependence. • **Methodology:** This Phase 2 study (NCT05320198) evaluated DISC-0974 in nTD, TD low, and TD high cohorts, with an exploratory cohort including momelotinib or pacritinib. DISC-0974 was administered monthly at 50 mg, escalating to 75 mg if necessary. • **Results:** Preliminary data show sustained hepcidin reduction and hematologic responses similar to the Phase 1b study, suggesting efficacy in both nTD and transfusion-dependent patients. • **Conclusions:** DISC-0974 showed a favorable safety profile and promising early responses in MF patients, supporting further development, especially with momelotinib or pacritinib
06 Dec 2025	A phase 2, open-label study of the safety, tolerability, pharmacokinetics, pharmacodynamics, and efficacy of DISC-3405 in participants with polycythemia vera (PV)	Marcus Carden	• **Introduction:** Polycythemia vera (PV) is a myeloproliferative disorder characterized by excessive erythrocyte production, often driven by JAK2 mutations. Current treatments, including phlebotomy and cytoreductive therapies, are burdensome and can lead to iron deficiency. DISC-3405 is a novel monoclonal antibody targeting TMPRSS6, stimulating hepcidin production to reduce hematocrit (HCT) levels. • **Methodology:** This Phase 2, open-label study evaluates DISC-3405's efficacy in reducing HCT and phlebotomy (PHL) requirements in PV patients. Participants receive up to 300 mg of DISC-3405 biweekly for 52 weeks, with an optional 2-year continuation phase. • **Results:** The study assesses therapeutic response, HCT reduction, and PHL eligibility. Efficacy endpoints include the proportion of participants maintaining HCT <45% and reduced PHL needs. • **Conclusions:** DISC-3405 offers a potential treatment for PV, targeting iron regulation to reduce HCT and PHL requirements, with long-term safety and efficacy to be further evaluated.

Notable Presentations At ASH 2025
Myelodysplastic Syndromes & Myeloproliferative Neoplasms (5/12)

Date	Title	Author	Summary
06 Dec 2025	Long-term outcomes from the randomized, double-blind, placebo (PBO)-controlled, phase 3 imerge trial of imetelstat (IME) for lower-risk myelodysplastic syndromes (LR-MDS)	Valeria Santini	• **Introduction:** This analysis aims to evaluate long-term outcomes, including overall survival (OS), progression-free survival (PFS), and safety. • **Methodology:** In the IMerge trial, patients with LR-MDS and RBC-TD anemia were randomized to receive IME or placebo (PBO). Primary endpoints included OS, PFS, and the association with RBC-TI. • **Results:** At a median follow-up of 45 months, IME-treated patients showed a favorable trend in OS and PFS. The median OS was 47.8 months for IME versus 44.8 months for PBO (HR=0.82), with most subgroups showing improved outcomes with IME, particularly those with SF3B1 mutations. Secondary endpoints like PFS and AML progression also favored IME. • **Conclusions:** IME demonstrated a favorable trend in OS and PFS, supporting its potential as a therapeutic option for RBC-TD LR-MDS. Durable responses correlated with RBC-TI and hemoglobin rise, emphasizing IME's clinical benefit despite statistical limitations in subgroup analysis.
07 Dec 2025	A phase 2 study of canakinumab in patient with myelofibrosis: Results from part 1	Andrew Kuykendall	• **Introduction:** This Phase 2 study evaluates its effect on symptom burden and cytopenias in patients with R/R MF. • **Methodology:** The study enrolled patients with MF, including those ineligible for or refractory to JAK inhibitors. Canakinumab (200 mg) was administered subcutaneously in 21-day cycles for 24 weeks. Primary endpoints included overall response rate (ORR) and symptom improvement. • **Results:** Of 13 treated patients, 23% achieved symptom response, with 46% showing disease progression. Significant symptom improvement was observed in 85% of patients, with median MF-SAF TSS declining. Hemoglobin and platelet counts improved, while spleen volume remained stable. CRP reduction was seen in 62.5% of patients with elevated baseline CRP. Most adverse events were hematologic, with non-hematologic AEs being mild. • **Conclusions:** Canakinumab improved symptoms and blood counts in R/R MF patients, showing a manageable safety profile. Despite limited impact on splenomegaly, the study demonstrated promising results in treating MF symptoms, leading to the amendment of the study for patients on stable JAK inhibitors.

Notable Presentations At ASH 2025
Myelodysplastic Syndromes & Myeloproliferative Neoplasms (6/12)

Date	Title	Author	Summary
07 Dec 2025	Ropeginterferon alfa-2b in essential thrombocythemia of all risk levels ineligible for standard cytoreduction: 12-month primary endpoint analysis from the ROP-ET phase 3 study	Jean-Jacques Kiladjian	• **Introduction:** Essential thrombocythemia (ET) is a myeloproliferative neoplasm with high platelet counts, leading to vascular events and disease progression. Despite existing therapies, many patients are intolerant, resistant, or ineligible. Ropeginterferon alfa-2b is being studied as a potential disease-modifying therapy for these patients. • **Methodology:** 132 adults with ET, who were intolerant or resistant to cytoreductive therapies, were treated with ropeginterferon alfa-2b every two weeks, with dose adjustments. The primary endpoint was a durable response after 12 months, including symptom improvement, blood count remission, and absence of thrombotic/hemorrhagic events. • **Results:** At baseline, median platelet count was 579 $\times 10^9$/L, with 83.3% having prior cytoreductive therapy. Ropeginterferon alfa-2b was well-tolerated, with 3% discontinuing due to adverse events. The primary endpoint analysis is ongoing, with the final visit in Q3 2025. Secondary endpoints include molecular response and long-term outcomes. • **Conclusions:** Ropeginterferon alfa-2b demonstrated manageable safety in this hard-to-treat population. The study aims to assess its efficacy for patients needing cytoreduction but unable to tolerate current therapies. Final results will follow the primary endpoint analysis.
07 Dec 2025	ASTX727 delivers superior response rates and associated survival benefit versus hydroxycarbamide/best supportive care in CMML and other MDS/MPN overlap syndromes: First results from the Phase 2 UK multicenter randomized ammo trial	Daniel Wiseman	• **Introduction:** Chronic myelomonocytic leukemia (CMML) and related MDS/MPN overlap syndromes have poor prognosis with limited treatment options. Hypomethylating agents (HMA) are standard for CMML but less effective in proliferative disease. ASTX727, an oral combination of decitabine and cedazuridine, offers a potential alternative treatment with a favorable safety profile. • **Methodology:** The AMMO phase 2 RCT compared ASTX727 vs hydroxycarbamide (HC)/best supportive care (BSC) in advanced MDS/MPN. Primary endpoint was the overall response rate (ORR) at cycle 6. Secondary endpoints included progression-free survival (PFS), transformation-free survival (TFS), and overall survival (OS). • **Results:** Of 77 patients, ASTX727 achieved a significantly higher ORR (53%) compared to HC/BSC (30%). Median PFS for ASTX727 was 23.5 months vs. 13.9 months for HC/BSC (HR 0.44, p=0.017). Median OS was 23.5 months for ASTX727 vs. 16.9 months for HC/BSC (HR 0.42, p=0.017). Treatment-related toxicities were higher in ASTX727, but manageable. • **Conclusions:** ASTX727 demonstrated significant survival benefit over HC/BSC, with longer PFS, TFS, and OS, marking the first randomized survival benefit in MDS/MPN in ~30 years. Its efficacy and safety profile support it as a new standard of care for advanced MDS/MPN.

Notable Presentations At ASH 2025
Myelodysplastic Syndromes & Myeloproliferative Neoplasms (7/12)

Date	Title	Author	Summary
07 Dec 2025	Long-term rusfertide treatment in polycythemia vera: Initial results from the phase 2 THRIVE extension study	Naveen Pemmaraju	• **Introduction:** This analysis presents the long-term outcomes and safety of rusfertide in the ongoing THRIVE extension study. • **Methodology:** Patients from the REVIVE study, who completed ≥12 months of rusfertide therapy, transitioned to THRIVE for up to 2 more years of treatment. Efficacy was measured by Hct levels and PHL requirements, while safety data, including adverse events (AEs) and thromboembolic events (TEs), were also collected. • **Results:** Out of 46 patients who transitioned to THRIVE, 96% remained on study at the data cutoff. Median treatment duration was 48 weeks in THRIVE, and median combined treatment duration (REVIVE + THRIVE) was 3.8 years. Hct remained stable with a significant reduction in the annual PHL rate, from 9.2 to 0.7 PHL/year. The most common AEs were injection site reactions, fatigue, and COVID-19. New-onset cancers occurred in 13% of patients, and 20% had prior TEs. • **Conclusions:** Rusfertide, with or without cytoreductive therapy, provided sustained long-term Hct control and reduced PHL needs, with a manageable safety profile over 3.8 years of treatment. These results highlight its potential as a treatment option for PV.
07 Dec 2025	Evaluation of levofloxacine as antibiotic prophylaxis in MDS and AML patients treated with azacitidine: Results from the randomized open-label phase III azabac study	Juliette Pénichoux	• **Introduction:** This phase 3 trial assessed the efficacy of levofloxacin prophylaxis in reducing febrile events in these patients. • **Methodology:** Patients with AML or high-risk MDS were randomized to receive either levofloxacin prophylaxis or no prophylaxis during AZA treatment. The primary endpoint was the incidence of febrile neutropenia leading to hospitalization and systemic antibiotics. Secondary endpoints included overall survival (OS). • **Results:** 59 patients were enrolled, with 29 in the levofloxacin arm and 30 in the control arm. No significant difference in febrile event incidence was observed between groups (17.2% vs 26.7%, p=0.58). However, grade 4-5 events were more frequent in the control group. OS was similar between arms (p=0.16). • **Conclusions:** Levofloxacin did not significantly reduce febrile events or improve survival, though its potential benefit in preventing severe febrile events warrants further investigation in larger trials.

Notable Presentations At ASH 2025
Myelodysplastic Syndromes & Myeloproliferative Neoplasms (8/12)

Date	Title	Author	Summary
07 Dec 2025	Prospera (ABNL-MARRO 002): A randomized phase 2 study of pacritinib vs. hydroxyurea in patients with advanced proliferative chronic myelomonocytic leukemia (CMML)	Zhuoer Xie	• **Introduction:** Chronic myelomonocytic leukemia (CMML) is a hematologic malignancy with overlapping features of dysplastic and proliferative diseases. Standard therapy with hydroxyurea (HU) only offers temporary control, highlighting the need for more effective treatments. Pacritinib, a selective multikinase inhibitor, targets key drivers of CMML and is be • **Methodology:** PROSPERA (NCT07033598) is a phase 2 study enrolling 66 patients with proliferative CMML. Participants are randomized to receive pacritinib (200 mg twice daily) or HU for 48 weeks. The primary endpoint is the clinical benefit rate (CBR) at Week 24, with secondary endpoints including event-free and overall survival. • **Results:** The trial evaluates pacritinib's efficacy vs. HU, with correlative studies on clonal dynamics and cytokine signaling. Patients on the HU arm may crossover to pacritinib after Week 24 if no clinical benefit is seen.. • **Conclusions:** PROSPERA aims to assess pacritinib's disease-modifying potential in advanced CMML, addressing the unmet need for effective treatments in this high-risk group.
08 Dec 2025	Elritercept shows durable responses in lower-risk myelodysplastic neoplasms (LR-MDS) with transfusion dependence: Updated Results from an ongoing Phase 2 trial	Lynette Chee	• **Introduction:** This study updates results on hematologic improvement, response durability, and prior ESA exposure. • **Methodology:** Phase 2 trial assessed transfusion independence (TI) and hematologic improvement-erythroid (HI-E) in LR-MDS patients. Genomic analysis examined benefits of elritercept in patients with mutations, especially SF3B1. • **Results:** Of 78 patients, 38.5% achieved TI for ≥8 weeks, and 26.9% for ≥24 weeks. HI-E response was 61.5%, with a median response time of 3.1 weeks. SF3B1 mutations were present in 64%, with better responses in SF3B1-positive patients. • **Conclusions:** Elritercept showed durable efficacy in LR-MDS patients, including those with SF3B1 mutations and prior ESA exposure. These findings support further development, with a Phase 3 trial underway.

Notable Presentations At ASH 2025
Myelodysplastic Syndromes & Myeloproliferative Neoplasms (9/12)

Date	Title	Author	Summary
08 Dec 2025	Preliminary analysis of a phase 2b, randomized, active-control study of flonoltinib maleate (FM) vs. ruxolitinib in intermediate-2 or high-risk myelofibrosis patients	Ting Niu	• **Introduction:** This phase IIb trial compares FM with ruxolitinib (Rux) in JAKi-naïve MF patients. • **Methodology:** Seventy-five MF patients were randomized to FM 50 mg (FM L), 100 mg (FM H), or Rux for 24 weeks. Primary endpoint: SVR35 at week 24. Secondary endpoints included TSS50 response and hematologic parameters. • **Results:** At 12 weeks, FM L and FM H achieved superior SVR35 (80%, 100%) vs. Rux (50%). TSS50 response rates were also higher in FM groups (FM L: 66.7%, FM H: 83.3%) vs. Rux (61.1%). At 24 weeks, FM groups maintained significant benefits in SVR35 and TSS50. Patients with CALR mutations had a marked response in FM arms. FM-treated patients showed higher platelet counts and improved bone marrow fibrosis compared to Rux. • **Conclusions:** FM demonstrated better spleen response and symptom improvement in MF patients compared to Rux with manageable toxicity. FM is a promising novel therapy for MF, targeting JAK2 inhibition. A phase III trial is under discussion.
08 Dec 2025	Hematological and clinical improvements with elritercept (KER-050, TAK-226) at the recommended Phase 2 dose (RP2D) in patients with myelofibrosis (MF) receiving ruxolitinib: Updated results from the Phase 2 restore trial	Ciro Rinaldi	• **Introduction:** This Phase 2 RESTORE trial (NCT05037760) evaluates elritercept with ruxolitinib for MF patients. • **Methodology:** RESTORE enrolled MF patients with anemia treated with elritercept (3.75 mg/kg) plus ruxolitinib. Effects on hematology, spleen size, symptoms, and mutations were assessed. Participants were transfusion-dependent (TD) or non-transfusion-dependent (NTD). • **Results:** At 24 weeks, 30.4% of TD patients achieved transfusion independence (TI), and 56.5% had a ≥50% reduction in RBC transfusions. In NTD patients, 38.5% had a ≥1.5 g/dL hemoglobin increase. 14.3% had spleen volume reduction ≥25%, and 36% improved fatigue. Some showed reduced JAK2 V617F mutation. • **Conclusions:** Elritercept with ruxolitinib improved anemia, thrombocytopenia, spleen size, and symptoms in MF. Early signs of hematopoietic restoration and mutation reduction suggest its potential in MF treatment.

Notable Presentations At ASH 2025
Myelodysplastic Syndromes & Myeloproliferative Neoplasms (10/12)

Date	Title	Author	Summary
08 Dec 2025	Durable efficacy and long-term safety with pelabresib plus ruxolitinib in JAK Inhibitor–Naive myelofibrosis: 96-week Results from the Phase III MANIFEST-2 study	Raajit Rampal	• **Introduction:** The MANIFEST-2 study investigates PELA+Rux in JAKi-naive MF patients, showing significant benefits. • **Methodology:** MANIFEST-2 is a double-blind, randomized Phase III trial of JAKi-naive MF patients, randomized to PELA+Rux or placebo+Rux. Primary endpoint: ≥35% spleen volume reduction (SVR35) at 96 weeks. Secondary endpoints include total symptom score (TSS) reduction and overall survival (OS). • **Results:** At 96 weeks, 91.5% of PELA+Rux patients achieved SVR35 vs 57.5% on PBO+Rux (difference, 34%). TSS50 response was 36.9% vs 28.2%, respectively. Hgb response was 17.8% vs 11.6%. PELA+Rux showed fewer red blood cell transfusions, with better symptom and spleen volume control. Leukemic transformations were similar between arms (5.1% vs 3.7%). Median OS was 47.8 months for PELA+Rux, showing clinical benefit. • **Conclusions:** PELA+Rux provided deep, durable benefits, improving spleen response, TSS, and anemia with manageable safety. Long-term data suggests potential for disease modification and improved survival in MF patients.
08 Dec 2025	Should dermatologic examinations become routine standard of care in patients with polycythemia vera? Observations from the phase 3 VERIFY study prior to rusfertide exposure	Joseph Shatzel	• **Introduction:** Polycythemia vera (PV) patients are at increased risk for skin cancers. As part of the phase 3 VERIFY study (NCT05210790), dermatologic screening was conducted to identify pre-existing skin malignancies in patients prior to treatment with rusfertide. • **Methodology:** Patients with PV requiring frequent phlebotomies were randomized 1:1 to rusfertide or placebo. Dermatologic examinations were performed during screening, at Week 32, and at other study periods to identify skin cancers before treatment exposure. • **Results:** Out of 399 screened, 293 were randomized. 40 patients had a history of skin cancer, and 11 developed new skin malignancies during screening. 6 patients in the placebo group developed skin cancers during treatment, with BCC, SCC, and malignant melanoma cases. Prior cytoreductive therapy was common in these patients • **Conclusions:** This is the first phase 3 study to prospectively screen PV patients for skin cancers before investigational treatment. Screening identified both malignant and non-malignant lesions, supporting routine dermatologic screening as part of PV management.

Notable Presentations At ASH 2025
Myelodysplastic Syndromes & Myeloproliferative Neoplasms (11/12)

Date	Title	Author	Summary
08 Dec 2025	Comprehensive analyses of patient-reported outcomes from the phase 3 VERIFY study of rusfertide or placebo plus current standard of care for polycythemia vera	Aniket Bankar	• **Introduction:** Polycythemia vera (PV) causes symptoms like fatigue and pruritus, leading to a poor quality of life. Rusfertide, a hepcidin mimetic, controls erythrocytosis and has shown efficacy in the VERIFY study (NCT05210790). This report focuses on patient-reported outcomes (PROs) assessing fatigue and symptoms. • **Methodology:** In the VERIFY Part 1a study, patients requiring frequent phlebotomy received either rusfertide or placebo, in addition to standard care. Key secondary endpoints included the change in PROMIS Fatigue SF-8a T-score and MFSAF TSS7 scores. • **Results:** 293 patients were randomized to rusfertide (n=147) or placebo (n=146). Rusfertide showed significant improvements in fatigue (p=0.025) and symptom burden (p=0.024) compared to placebo. In symptomatic patients at baseline, rusfertide led to greater reductions in fatigue and PV symptoms. Improvements were observed in the MPN-SAF concentration item (p=0.027). • **Conclusions:** Rusfertide significantly reduced fatigue and overall symptom burden, improving quality of life in PV patients, particularly those with moderate-to-severe symptoms. The results highlight its potential clinical benefit in managing PV.
08 Dec 2025	Validation of the international working group (IWG) 2023 criteria for clinical benefit in higher risk Myelodysplastic Syndromes (HR-MDS) using a large, international, randomized Phase 3 clinical trial dataset	Maximilian Stahl	• **Introduction:** Polycythemia vera (PV) increases the risk of non-PV malignancies, including skin cancers. The VERIFY study (NCT05210790) included dermatologic screening at baseline and Week 32 to monitor skin lesions in PV patients receiving rusfertide. This report focuses on the outcomes of those screenings. • **Methodology:** The VERIFY phase 3 study enrolled PV patients requiring frequent phlebotomy. Patients underwent dermatologic screening at baseline and Week 32, with lesions identified and treated as appropriate. Skin cancer diagnoses were tracked, and patients were followed up as they transitioned to Part 1b. • **Results:** Of 399 screened, 293 patients were randomized (147 rusfertide, 146 placebo). 13.7% had a history of skin cancer. Screening identified 11 patients with skin malignancies, including BCC, melanoma, and SCC. By Week 32, 6 patients in the placebo group developed new skin cancers. 66.7% of these patients had prior CRT. • **Conclusions:** This study highlights the importance of dermatologic screening in PV patients, with high rates of skin malignancies observed. Routine screening should be considered standard practice for optimal PV management.

Notable Presentations At ASH 2025
Myelodysplastic Syndromes & Myeloproliferative Neoplasms (12/12)

Date	Title	Author	Summary
08 Dec 2025	Validation of the international working group (IWG) 2023 criteria for clinical benefit in higher risk Myelodysplastic Syndromes (HR-MDS) using a large, international, randomized Phase 3 clinical trial dataset	Maximilian Stahl	• **Introduction:** Polycythemia vera (PV) increases the risk of non-PV malignancies, including skin cancers. The VERIFY study (NCT05210790) included dermatologic screening at baseline and Week 32 to monitor skin lesions in PV patients receiving rusfertide. This report focuses on the outcomes of those screenings. • **Methodology:** The VERIFY phase 3 study enrolled PV patients requiring frequent phlebotomy. Patients underwent dermatologic screening at baseline and Week 32, with lesions identified and treated as appropriate. Skin cancer diagnoses were tracked, and patients were followed up as they transitioned to Part 1b. • **Results:** Of 399 screened, 293 patients were randomized (147 rusfertide, 146 placebo). 13.7% had a history of skin cancer. Screening identified 11 patients with skin malignancies, including BCC, melanoma, and SCC. By Week 32, 6 patients in the placebo group developed new skin cancers. 66.7% of these patients had prior CRT. • **Conclusions:** This study highlights the importance of dermatologic screening in PV patients, with high rates of skin malignancies observed. Routine screening should be considered standard practice for optimal PV management.
08 Dec 2025	Pacritinib in transplant-eligible myelofibrosis: Final analysis of the phase 2 HOVON-134 trial	Ruben Van Dijck	• **Introduction:** The HOVON-134 study evaluates the use of PAC in transplant-eligible MF patients, aiming to assess its feasibility and impact on spleen and symptom responses, safety, and the ability to proceed to allogeneic stem cell transplantation (alloHSCT). • **Methodology:** HOVON-134 was a phase 2, single-arm study involving transplant-eligible MF patients. PAC was administered at 200 mg twice daily for 3-4 cycles before conditioning with alloHSCT. The primary endpoint was the proportion of patients able to proceed to alloHSCT, while secondary endpoints focused on symptom and spleen responses. • **Results:** Among 61 patients, 64% had JAK2V617F mutations, and 38% had prior ruxolitinib (RUX) exposure. After treatment, 36% of patients showed symptom response, and 43% showed spleen response. 95% proceeded to alloHSCT. 1- and 5-year overall survival rates were 80% and 57%, respectively. At 1 year post-transplant, progression-free survival was 79%, with GVHD-free relapse-free survival of 42%. • **Conclusions:** PAC is a feasible pre-transplant treatment for MF patients, enabling a high rate of successful alloHSCT and achieving durable symptom and spleen responses. These findings support its potential in improving clinical outcomes in transplant-eligible MF patients.

Notable Presentations At ASH 2025
Bone Marrow Failure & Aplastic Anemia (1/2)

Date	Title	Author	Summary
06 Dec 2025	Deep immune signature of immune-mediated aplastic anemia pts shows distinct subsets of regulatory T cells associated with response to treatment: Results from the phase 3, randomized EBMT race clinical trial	Sila Gerlevik	• **Introduction:** Immune-mediated aplastic anaemia (AA) involves T-cell-driven destruction of hematopoietic stem cells, causing pancytopenia. About two-thirds respond to standard IST with ATG and cyclosporine (CsA). Eltrombopag (EPAG) improves outcomes, but immunologic predictors of response remain poorly defined. • **Methodology:** This phase 3 study enrolled 130 untreated severe/very-severe AA pts, randomized to hATG + CsA ± EPAG. Baseline and 6-month immune profiling of T-, B-, myeloid, and NK-cell subsets was performed via CyTOF to identify predictors of treatment response. • **Results:** Baseline profiles showed marked immune dysregulation, with reduced myeloid/NK cells and expanded effector T cells. Very severe AA showed further myeloid depletion and enriched effector Th1 CCR4^{+} and CD8^{+} subsets. Complete responders had higher naïve Tregs and fewer memory Tregs. By 6 months, both arms demonstrated innate immune recovery and greater differentiated T cells, with responders showing a consistent shift toward naïve Tregs. • **Conclusions:** AA features pronounced immune activation and impaired innate immunity. Naïve and memory Treg distributions emerge as independent predictors of treatment outcome.
6 Dec 2025	Long-term follow-up of pts with aplastic anemia enrolled in two phase 2/3 trials of immunosuppressive therapy plus romiplostim as a first-line treatment: Final report for up to 5 years	Jong Wook Lee	• **Introduction:** Immune-mediated aplastic anemia (AA) arises from T-cell-driven destruction of hematopoietic stem cells, causing pancytopenia. Many pts respond to immunosuppressive therapy (IST), and adding romiplostim (ROMI) appears to enhance outcomes. Long-term evidence on IST + ROMI has been limited, leading to this multicenter observational follow-up. • **Methodology:** Pts from two phase 2/3 trials (531-003 and 531-004) treated with IST + ROMI were followed for up to 5 years to assess overall response rate (ORR), complete (CR) and partial (PR) responses, transfusion needs, and safety outcomes. • **Results:** Thirty-six pts were included (median follow-up 4.1 years). The 5-year ORR was 77.1%, with CR 40% and PR 37.1%. ORRs were 86.7% (531-003) and 70% (531-004). Transfusion dependence declined markedly—platelets to 9.4% and RBCs to 13.9%. No new cytogenetic abnormalities or AML/MDS transformation occurred. 5-year survival reached 88.6%. • **Conclusions:** IST + ROMI produced durable responses with a strong safety profile, and some pts achieved treatment-free remission. This combination supports use as a first-line option for IST-naïve adults with AA who are not transplant candidates.

Notable Presentations At ASH 2025
Bone Marrow Failure & Aplastic Anemia (2/2)

Date	Title	Author	Summary
08 Dec 2025	Adding eltrombopag to immunosuppressive treatment with cyclosporine as front-line therapy for moderate aplastic anemia improves trilineage hematologic response: One-year analysis of the randomised, placebo-controlled, double-blind Phase III trial eltrombopag for moderate aplastic anemia (EMAA Trial)	Britta Hoechsmann	• **Introduction:** Immune-mediated aplastic anemia (AA) is a life-threatening condition where T-cell-mediated destruction of hematopoietic stem cells leads to pancytopenia. Eltrombopag (EPAG) combined with antithymocyte globulin (ATG) and cyclosporine A (CSA) has been shown to improve hematologic responses in severe AA. However, no studies have yet explored EPAG's effectiveness in moderate aplastic anemia (MAA), a condition where treatment regimens remain unclear. • **Methodology:** The EMAA trial (NCT02773225) is a phase 3, randomized, double-blind, placebo-controlled study that enrolled 85 treatment-naïve MAA pts. Participants were randomly assigned to receive either EPAG (150 mg/day) with CSA or placebo with CSA for 24 weeks. The primary endpoint was the proportion of pts achieving trilinear hematologic response at week 24. • **Results:** Of the 75 pts assessed at week 24, the EPAG arm had a significantly higher overall response rate (ORR) of 71.4% compared to 42.5% in the placebo arm (p = 0.011). Complete remission (CR) rates were 11.4% in the EPAG group versus 5.0% in the placebo group. MRD negativity rates were higher in the EPAG group at both 24 and 48 weeks, with continued responses in the majority of pts. The 5-year survival rate was 88.6%, and no new chromosomal abnormalities were observed. • **Conclusions:** Adding EPAG to CSA in first-line treatment for MAA significantly improves hematologic response compared to placebo, with a favorable safety profile. The regimen offers a promising new treatment approach for MAA pts. EPAG combined with CSA should be considered as a new standard of care for MAA.

Notable Presentations At ASH 2025
Benign Haematology (1/21)

Date	Title	Author	Summary
6 Dec 2025	Efficacy and safety of benralizumab in patients with hypereosinophilic syndrome: Results from the Phase 3 natron study	Amy Klion	• **Introduction:** Hypereosinophilic syndrome (HES) is a rare disorder marked by persistent eosinophilia and organ damage. Benralizumab, an IL-5 receptor α antibody, shows promise in treating eosinophilic conditions like severe asthma and eosinophilic granulomatosis with polyangiitis. This study evaluates benralizumab's efficacy in HES patients. • **Methodology:** NATRON (NCT04191304) is a phase 3, randomized, double-blind, placebo-controlled trial assessing benralizumab in HES. Participants (≥12 years) were randomized to benralizumab (30 mg) or placebo for 24 weeks, alongside standard therapy. Primary endpoint: time to first HES flare. • **Results:** 133 patients were enrolled. Benralizumab significantly reduced the risk and delayed time to first flare (HR: 0.35, P=0.0024). The annualized flare rate was lower with benralizumab (0.41 vs 1.23). Hematologic relapse was delayed, and fatigue improved significantly. AEs were similar between groups. • **Conclusions:** Benralizumab added to standard therapy significantly reduced flare risk, hematologic relapse, and improved fatigue in HES patients. Safety was consistent with its profile, showing potential as a therapeutic option for HES.
6 Dec 2025	Marstacimab prophylaxis in participants with Hemophilia A or B with inhibitors: Results from the Phase 3 BASIS trial	Davide Matino	• **Introduction:** Marstacimab is a monoclonal antibody designed to enhance thrombin generation and restore hemostasis in hemophilia patients. The BASIS study evaluated its safety and efficacy in individuals with hemophilia A (HA) or B (HB) with inhibitors, who are typically challenging to treat with traditional bypassing agents. • **Methodology:** This open-label, single-arm study enrolled males aged ≥12 with high-titer inhibitors, transitioning from bypassing agents to marstacimab. The primary endpoint was the annualized bleeding rate (ABR) for treated bleeds, comparing marstacimab prophylaxis to previous on-demand therapy. • **Results:** Sixty participants (median age 23) demonstrated significant reductions in ABR with marstacimab, from 19.78 in the observational phase to 1.39 in the active phase (P<0.0001). Marstacimab also improved health-related quality of life across multiple domains, with minimal adverse events reported. • **Conclusions:** Marstacimab significantly reduced bleeding rates and improved quality of life in hemophilia patients with inhibitors. Its safety profile was favorable, supporting its potential as a key treatment option.

Notable Presentations At ASH 2025
Benign Haematology (2/21)

Date	Title	Author	Summary
6 Dec 2025	KP104, a bifunctional C5 mAb–Factor h fusion protein, demonstrates sustained long-term efficacy and safety in complement inhibitor–naïve PNH patients: 2-year results from A phase 2 study with 8-week post-treatment safety follow-up.	Li Zhang	• **Introduction:** Paroxysmal nocturnal hemoglobinuria (PNH) is a life-threatening hematologic disorder driven by complement dysregulation. KP104 is a novel bifunctional recombinant protein targeting both terminal and proximal complement pathways, showing promise as a treatment for complement inhibitor–naïve PNH patients. • **Methodology:** The Phase 2 BASIS trial enrolled 18 patients to assess KP104's efficacy and safety. After an initial dose-escalation phase, patients transitioned to an optimal biologic dose (OBD) and received treatment for up to two years. Post-treatment follow-up was conducted over 8 weeks. • **Results:** KP104 demonstrated sustained clinical improvements, with 100% of patients maintaining a ≥2 g/dL hemoglobin increase. 82.4% achieved hemoglobin normalization. No serious adverse events (SAEs) or discontinuations occurred. During the post-treatment phase, 83.3% maintained hemoglobin normalization at week 4. • **Conclusions:** KP104 showed durable efficacy, with sustained hemoglobin and LDH improvements, even after discontinuation, and a favorable safety profile, making it a promising monotherapy for PNH.
6 Dec 2025	Safety data from the non-transfusion-dependent dose-confirmation cohort: A phase 2a study of luspatercept in pediatric patients with β-thalassemia	Vip Viprakasit	• **Introduction:** β-thalassemia is characterized by ineffective erythropoiesis, leading to chronic anemia. While pediatric non-transfusion-dependent (NTD) patients require fewer RBC transfusions, they still face complications like iron overload and anemia. Luspatercept has shown efficacy in adult patients with β-thalassemia, and this study evaluates its safety in pediatric NTD patients. • **Methodology:** This ongoing Phase 2a study enrolled adolescents (12–18 years) with NTD β-thalassemia to confirm the safety of 1.0 mg/kg luspatercept administered subcutaneously every 3 weeks for 4 cycles. • **Results:** Three patients were enrolled, showing a median baseline hemoglobin of 7.8 g/dL. The most common treatment-emergent adverse events (TEAEs) were upper respiratory tract infections and gastroenteritis. No serious TEAEs or dose-limiting toxicities occurred. • **Conclusions:** Luspatercept was well-tolerated in pediatric NTD patients, with no new safety concerns. TEAEs were non-hematologic and unrelated to the drug. Ongoing recruitment aims to expand the cohort.

Notable Presentations At ASH 2025
Benign Haematology (3/21)

Date	Title	Author	Summary
6 Dec 2025	Revisiting erythroid response in the phase 3 BELIEVE trial of luspatercept in patients with transfusion-dependent β-thalassemia using real-world criteria	Khaled Musallam	• **Introduction:** β-thalassemia patients often require RBC transfusions, and luspatercept has shown efficacy in transfusion-dependent (TD) patients. The BELIEVE trial demonstrated a significant erythroid response with luspatercept, but the 33% reduction in RBC transfusion burden (TB) used as the primary endpoint may not fully capture the clinical benefit. A modified framework was proposed to assess the broader spectrum of benefits observed in real-world settings. • **Methodology:** This post hoc study reanalyzed erythroid response data from the BELIEVE trial, using a modified response framework that categorized responses as excellent, good, satisfactory, or no response, based on TB reduction and hemoglobin (Hb) changes. • **Results:** Luspatercept showed higher response rates compared to placebo. At 24 weeks, 51.3% of luspatercept-treated patients achieved an excellent or good response vs 16.1% with placebo (P<0.0001). The odds of achieving excellent response were 9.9 times higher with luspatercept. • **Conclusions:** Modified response categories revealed a broader benefit of luspatercept treatment, with higher response rates and a need for extended evaluation beyond 24 weeks to capture delayed responses. This approach enhances understanding of patient benefit in routine clinical practice.
6 Dec 2025	A phase III, multicenter, randomized, placebo controlled, double-blind study to assess efficacy and safety of crizanlizumab (5 mg/kg) versus placebo, with or without hydroxyurea/hydroxycarbamide therapy, in adolescent and adult sickle cell disease patients with frequent vaso-occlusive crises: The sparkle study	Andrew Campbell	• **Introduction:** Crizanlizumab, a P-selectin blocker, is FDA-approved for reducing vaso-occlusive crises (VOCs) in sickle cell disease (SCD). While the Phase II SUSTAIN trial showed efficacy, the Phase III STAND trial did not demonstrate superiority, possibly due to COVID-19-related disruptions. The SPARKLE trial is designed to confirm crizanlizumab's efficacy in reducing VOCs. • **Methodology:** The Phase III SPARKLE trial is a 52-week, multicenter, randomized, double-blind study comparing crizanlizumab to placebo in patients with frequent VOCs. Participants will receive crizanlizumab (5.0 mg/kg) or placebo with or without Hydroxyurea/Hydroxycarbamide. • **Results:** The primary endpoint is the annualized rate of healthcare professional (HCP)-managed VOCs. Secondary endpoints include all VOCs (HCP- and self-managed), time to first VOC, and duration of HCP-managed VOCs. Safety will include adverse events and tolerability assessments. • **Conclusions:** The SPARKLE trial aims to validate crizanlizumab's effectiveness in reducing both HCP-managed and total VOCs, potentially offering an alternative to existing therapies, with study results expected by 2030.

Notable Presentations At ASH 2025
Benign Haematology (4/21)

Date	Title	Author	Summary
6 Dec 2025	Improved health-related quality of life (HRQoL) and bleeding scores with oral bruton tyrosine kinase (BTK) inhibitor rilzabrutinib in the open-label (OL) period of the multicenter Phase 3 LUNA3 study in adults with immune thrombocytopenia (ITP)	Nicola Cooper	• **Introduction:** Rilzabrutinib, a BTK inhibitor, showed positive results in the Phase 3 LUNA3 study for immune thrombocytopenia (ITP), improving platelet response, reducing bleeding, and enhancing physical fatigue. The open-label (OL) period further demonstrated rilzabrutinib's durable benefits. This study evaluates its impact on health-related quality of life (HRQoL) and bleeding scores. • **Methodology:** Adult ITP patients with prior treatments were randomized to rilzabrutinib or placebo during the double-blind (DB) phase, followed by rilzabrutinib in the OL phase. HRQoL and bleeding were assessed using ITP-PAQ, IBLS, EQ-5D-5L, and EQ-VAS scores at week 53. • **Results:** At week 53, rilzabrutinib significantly improved HRQoL, fatigue, and bleeding scores. Key domains (e.g., physical health, activity, psychological health) exceeded clinically meaningful thresholds. IBLS scores showed reduction, and EQ-VAS scores improved. Patients transitioning from placebo to rilzabrutinib also benefited. • **Conclusions:** Sustained improvements in fatigue, HRQoL, and bleeding support rilzabrutinib's potential in ITP treatment. Continued exposure enhanced outcomes, including in patients who switched from placebo, reinforcing rilzabrutinib's clinical benefits.
6 Dec 2025	Reduction in corticosteroid use with rilzabrutinib and sustained response in adults with persistent/chronic immune thrombocytopenia in the long-term extension period of the Phase 3 LUNA3 study	David Kuter	• **Introduction:** Immune thrombocytopenia (ITP) leads to thrombocytopenia and increased bleeding risk. Long-term corticosteroid (CS) use in ITP is associated with toxicity. Rilzabrutinib, a selective BTK inhibitor, demonstrated rapid and durable platelet responses and improved fatigue and bleeding scores in the LUNA3 study. This analysis focuses on the long-term extension (LTE) period, emphasizing CS use changes. • **Methodology:** Patients with ITP who met predefined response criteria entered the LTE, receiving rilzabrutinib 400 mg bid. Concomitant CS or thrombopoietin-receptor agonists (TPO-RA) were allowed, and dose adjustments or discontinuations were permitted. • **Results:** 69 patients entered the LTE, with 62% completing ≥12 months. Platelet counts were maintained or increased, and 49% reduced or discontinued CS use. Fatigue and bleeding symptoms remained improved. Safety was favorable, with no serious adverse events related to treatment. • **Conclusions:** Rilzabrutinib showed sustained efficacy in ITP patients, enabling CS tapering or discontinuation. These findings support rilzabrutinib's role as a durable, steroid-sparing treatment with disease-modifying potential.

Notable Presentations At ASH 2025
Benign Haematology (5/21)

Date	Title	Author	Summary
6 Dec 2025	Concizumab efficacy in patients with Hemophilia A/B without inhibitors from the Phase 3 explorer8 study: A post-hoc sensitivity analysis for the intra-patient comparison of concizumab with previous prophylaxis	Anthony Chan	• **Introduction:** Concizumab, a monoclonal antibody targeting the tissue factor pathway inhibitor (TFPI), is approved for hemophilia A/B with or without inhibitors. In the Phase 3 Explorer8 study, concizumab demonstrated superior efficacy over on-demand treatment for hemophilia A/B without inhibitors, although non-inferiority compared to previous prophylaxis was not confirmed. A post-hoc analysis aimed to investigate the impact of extreme annualized bleeding rates (ABRs) on this comparison. • **Methodology:** Explorer8 enrolled male patients with hemophilia A/B who received concizumab, and a subset was included in an intra-patient analysis. Sensitivity analyses with imputed values for extreme ABRs were conducted using parametric and non-parametric methods. • **Results:** Sensitivity analyses showed that imputation reduced the ABR ratio for concizumab versus previous prophylaxis, indicating non-inferiority for most patients. For hemophilia A, the ABR ratio improved from 1.39 to 0.75, and for hemophilia B, from 1.75 to 1.00. • **Conclusions:** Post-hoc sensitivity analyses demonstrated that, for most patients, concizumab was non-inferior to previous prophylaxis. The study supports concizumab as an efficacious and well-tolerated therapy for hemophilia A/B, though individual responses may vary.
6 Dec 2025	Recombinant von willebrand factor for perioperative management of bleeding in pediatric patients with severe von willebrand disease: Interim results from a phase 3 multicenter study and a phase 3b continuation study	Eric Mullins	• **Introduction:** Von Willebrand disease (VWD) is a common bleeding disorder in children, and recombinant von Willebrand factor (rVWF) has shown efficacy in adults with severe VWD. This study evaluates the hemostatic efficacy and safety of rVWF, with or without recombinant factor VIII (rFVIII), in pediatric patients undergoing minor surgeries. • **Methodology:** In an open-label, multicenter Phase 3 study, pediatric patients aged <18 years with severe VWD underwent minor surgeries. rVWF dosing was tailored based on surgery type and pharmacokinetic (PK) assessments, with rFVIII added if necessary to achieve target factor VIII levels. • **Results:** Eight patients (mean age 10.4 years) underwent 9 surgeries. Perioperative hemostatic efficacy was rated "Excellent" for all surgeries. rVWF was administered in 62 infusions, with most patients not requiring rFVIII. Four treatment-emergent adverse events (TEAEs) were reported, none related to the study drug. • **Conclusions:** rVWF, with or without rFVIII, was effective in managing perioperative bleeding in pediatric VWD patients undergoing minor surgeries. No new safety concerns were identified, supporting rVWF's use in this population.

Notable Presentations At ASH 2025
Benign Haematology (6/21)

Date	Title	Author	Summary
7 Dec 2025	Benefits of hydroxyurea in hemoglobin SC: Results of the open-label phase of the prospective identification of variables as outcomes for treatment (PIVOT) trial	Luke Smart	• **Introduction:** The PIVOT Phase 2 trial evaluates hydroxyurea's efficacy and safety in HbSC patients, with a focus on dose-limiting toxicities (DLT) and clinical outcomes, especially after 12 months of open-label treatment. • **Methodology:** The PIVOT trial included patients with HbSC disease, randomized to hydroxyurea or placebo for 12 months, followed by 12 months of open-label hydroxyurea. Hematologic effects, sickle-related adverse events, and hospitalizations were analyzed, with a focus on the development of DLT. • **Results:** A total of 196 patients continued into the open-label phase, with hydroxyurea dosing reduced slightly in both arms. DLT were mild and transient, with 33% in the hydroxyurea arm and 23% in the placebo arm. Hydroxyurea-treated patients showed sustained benefits, including reduced vaso-occlusive pain, malaria, and hospitalizations. The placebo group showed similar improvements after switching to hydroxyurea. • **Conclusions:** Open-label hydroxyurea treatment demonstrated significant clinical and laboratory benefits for HbSC patients, including reduced vaso-occlusive events and malaria. These findings support hydroxyurea's role as a disease-modifying treatment for HbSC disease and provide a basis for a Phase 3 trial.
7 Dec 2025	Mim8 prophylaxis in adults and adolescents with hemophilia A: 52-week efficacy and safety outcomes from the phase 3 FRONTIER2 study	Steven Lentz	• **Introduction:** The Phase 3 FRONTIER2 study demonstrated the efficacy of Mim8 in reducing bleeding rates in HA patients. This report presents the 52-week extension phase results, assessing the long-term efficacy and safety of Mim8 compared to previous treatments. • **Methodology:** The Phase 3 study randomized patients to receive either Mim8 once-weekly (QW) or once-monthly (QM) or continued on-demand treatment. After 12 months, all participants switched to open-label Mim8. Primary endpoint: number of treated bleeds; secondary endpoints included injection-site reactions (ISRs) and immunogenicity. • **Results:** In the extension phase, 88% of Mim8 QW and 70% of Mim8 QM patients had zero treated bleeds. Significant reductions in annualized bleeding rates (ABR) were observed, with minimal adverse events (AEs). ISRs were mild and infrequent. Anti-Mim8 antibodies were detected in 7% of patients but showed no clinical impact. • **Conclusions:** Mim8 demonstrated sustained bleed protection and a favorable safety profile over 52 weeks. With low rates of ISRs, no thromboembolic events, and no clinically relevant antibody development, Mim8 provides an effective and convenient prophylactic option for HA patients.

Notable Presentations At ASH 2025
Benign Haematology (7/21)

Date	Title	Author	Summary
7 Dec 2025	Clinical outcomes up to 4 years of once-weekly efanesoctocog alfa prophylaxis in previously treated adults, adolescents, and children with severe hemophilia A: Interim analysis of the Phase 3 XTEND-ed long-term extension study	Lynn Malec	• **Introduction:** Efanesoctocog alfa is a first-in-class FVIII replacement therapy for hemophilia A, designed to decouple FVIII from endogenous von Willebrand factor. The XTEND-1 and XTEND-Kids studies demonstrated its effectiveness in bleeding protection. The XTEND-ed extension study evaluates the long-term safety and efficacy of efanesoctocog alfa in preventing bleeds in both adults and children with severe hemophilia A. • **Methodology:** Participants from XTEND-1 and XTEND-Kids received once-weekly 50 IU/kg efanesoctocog alfa for continued bleeding protection in the XTEND-ed study. The primary endpoint was FVIII inhibitor development, with secondary endpoints including annualized bleed rates (ABRs), efficacy for bleed treatment, and safety. • **Results:** No FVIII inhibitors developed in any participant. Over 52 weeks, efanesoctocog alfa showed sustained efficacy, with mean ABRs of 0.45 (adults) and 0.64 (children). A majority of bleeds were resolved with one injection, and high rates of zero bleeds were reported. Treatment-emergent adverse events were mild, with no serious treatment-related events. • **Conclusions:** Efanesoctocog alfa demonstrated continued, highly effective bleed protection and was well-tolerated in both adults and children with severe hemophilia A. The study supports its use as a long-term prophylactic treatment without FVIII inhibitor development.
7 Dec 2025	Hibiscus 2 (Trial-in-Progress): A global, Phase 3, randomized, double-blind, placebo-controlled study evaluating the efficacy and safety of etavopivat in adolescents and adults with sickle cell disease	Guanglin Wu	• **Introduction:** Etavopivat, a selective PKR activator, aims to improve RBC health by increasing ATP and decreasing 2,3-DPG. The HIBISCUS 2 study is designed to further evaluate its efficacy in improving Hb levels and reducing VOCs in adults and adolescents with SCD. • **Methodology:** HIBISCUS 2 is a global, multicenter, Phase 3, randomized, double-blind, placebo-controlled trial. Participants aged ≥12 years with moderate-to-severe anemia and frequent VOCs are randomized to receive 400 mg of etavopivat or placebo for 52 weeks. The primary endpoint is the number of VOCs, with secondary endpoints including Hb change, time to first VOC, and fatigue scores. • **Results:** Etavopivat showed significant improvements in Hb and VOC frequency in earlier phases, with 400 mg providing stronger and more consistent responses than 200 mg. In HIBISCUS 2, primary and secondary endpoints will assess the impact on VOC frequency, Hb levels, and fatigue. Secondary endpoints include laboratory markers and functional outcomes. • **Conclusions:** HIBISCUS 2 will provide robust data on etavopivat's ability to reduce VOCs, increase Hb levels, and reduce fatigue in SCD patients. The study is expected to further confirm etavopivat's potential as a disease-modifying therapy for SCD.

Notable Presentations At ASH 2025
Benign Haematology (8/21)

Date	Title	Author	Summary
7 Dec 2025	Reproductive health in patients with primary immune thrombocytopenia (ITP) receiving rilzabrutinib: A subgroup analysis from the Phase 3 LUNA3 multicenter study	Michele Lambert	• **Introduction:** Rilzabrutinib, a BTK inhibitor, improves platelet counts and bleeding in ITP. Women with ITP experience additional challenges, such as heavy menstrual bleeding. This analysis evaluates rilzabrutinib's impact on women's reproductive health (WRH) in the LUNA3 study. • **Methodology:** Participants received rilzabrutinib (400 mg BID) or placebo for 24 weeks. WRH was assessed using the ITP-PAQ WRH domain, focusing on menstrual symptoms and reproductive impacts. • **Results:** Rilzabrutinib improved WRH scores, notably for menstrual bleeding and pregnancy likelihood, with changes at weeks 13 and 25. Placebo showed minimal or negative changes. • **Conclusions:** Rilzabrutinib improved WRH in women with ITP, especially for menstrual bleeding, suggesting potential HRQoL benefits. Further studies are needed to confirm these findings.
7 Dec 2025	Iguratimod plus low-dose rituximab as second-line treatment in adults with primary immune thrombocytopenia: A multicenter, open-label, randomized, controlled, Phase 2 trial	Qiu-Sha Huang	• **Introduction:** Corticosteroid-resistant or relapsed immune thrombocytopenia (ITP) remains challenging to treat. Iguratimod, an antirheumatic drug, and low-dose rituximab (LD-RTX) target T and B cells, respectively. This study evaluates the efficacy and safety of combining iguratimod with LD-RTX compared to LD-RTX monotherapy in ITP patients. • **Methodology:** Adult patients with corticosteroid-resistant or relapsed ITP were randomized to receive iguratimod (25 mg BID for 12 weeks) plus LD-RTX (100 mg weekly for 4 weeks) or LD-RTX alone. The primary endpoint was initial overall response (OR), and secondary endpoints included sustained response (SR) at 6 months. • **Results:** The combination therapy showed a higher OR (75%) and SR (55%) compared to LD-RTX alone (51.7% and 38.3%, respectively). Time to response was shorter in the combination group (18 vs. 35 days). Both groups showed improvements in HRQoL, with the combination therapy group having better results in symptoms, fatigue, and social activity. • **Conclusions:** Iguratimod plus LD-RTX significantly improved initial and sustained response rates and shortened time to response, showing promise as a treatment for corticosteroid-resistant or relapsed ITP.

Notable Presentations At ASH 2025
Benign Haematology (9/21)

Date	Title	Author	Summary
7 Dec 2025	Trial in progress: Study design of a randomized, phase 3 trial evaluating the efficacy and safety of mezagitamab (TAK-079) compared with placebo in adults with chronic primary immune thrombocytopenia	David Kuter	• **Introduction:** Mezagitamab, an anti-CD38 monoclonal antibody, depletes plasma cells that produce anti-platelet autoantibodies. A Phase II study showed promising efficacy, with early responses observed after a single dose. This Phase III study aims to assess the efficacy and safety of mezagitamab in adults with chronic primary ITP. • **Methodology:** This global, multicenter, double-blind, placebo-controlled Phase III study will randomize participants (≥18 years) to receive mezagitamab 600 mg or placebo weekly for 8 weeks, followed by a treatment-free period and additional 8 weeks of treatment. Primary endpoint: durable platelet response at Week 24. • **Results:** Primary efficacy endpoints include platelet counts ≥50,000/μL at least 4 times during Weeks 19-24. Secondary endpoints include time to platelet count ≥50,000/μL, cumulative weeks with platelet counts ≥50,000/μL, and bleeding events. Safety will be assessed by adverse events and abnormal laboratory tests. • **Conclusions:** This Phase III study will evaluate mezagitamab as a potential new treatment for ITP patients who have failed prior therapies, with promising early results from anti-CD38 treatment.
7 Dec 2025	Management of breakthrough bleeds in participants with hemophilia A or B without inhibitors receiving marstacimab prophylaxis in the phase 3 BASIS study	Travis Gould	• **Introduction:** Marstacimab is a monoclonal antibody targeting tissue factor pathway inhibitor, approved for prophylaxis in hemophilia A (HA) and B (HB) without inhibitors. The BASIS study demonstrated marstacimab's efficacy in reducing bleeds. This analysis focuses on managing breakthrough bleeds in patients receiving concurrent factor replacement therapy (FRT) during marstacimab prophylaxis. • **Methodology:** In the BASIS study, patients received 300 mg marstacimab followed by 150 mg weekly. Acute breakthrough bleeds were treated with FRT, and FRT usage and bleeding episodes were recorded. • **Results:** 75% of patients experienced breakthrough bleeds, treated with FRT. Most bleeds required a single FRT infusion, with plasma-derived or standard half-life (SHL) FVIII products being the most common treatment. No thromboembolic events were reported. • **Conclusions:** Marstacimab, when combined with FRT, effectively managed breakthrough bleeds in HA and HB patients, demonstrating safety and efficacy. Most bleeds were resolved with a single FRT infusion.

Notable Presentations At ASH 2025
Benign Haematology (10/21)

Date	Title	Author	Summary
7 Dec 2025	Concizumab plasma concentration measurements for personalized dose adjustment in patients with Hemophilia A/B with and without inhibitors: Data from the Phase 3 explorer7 and explorer8 studies	Hermann Eichler	• **Introduction:** Concizumab, a monoclonal antibody targeting tissue factor pathway inhibitor, is approved for prophylaxis in hemophilia A/B with inhibitors. This study investigates pharmacokinetics (PK) and bleeding outcomes with one-time concizumab dose adjustments based on plasma concentration in two Phase 3 studies (Explorer7 and Explorer8). • **Methodology:** Patients receiving concizumab (300 mg loading dose, followed by 150 mg weekly) had plasma concentrations measured at week 4. Dose adjustments were made based on these concentrations: increased to 0.25 mg/kg if <200 ng/mL, decreased to 0.15 mg/kg if >4,000 ng/mL, or maintained at 0.20 mg/kg for others. • **Results:** 70% of patients maintained the 0.20 mg/kg dose. Adjustments to 0.25 mg/kg improved plasma concentration and reduced the annualized bleeding rate (ABR) from 7.2 to 3.8. No significant differences in ABR were observed for those adjusted to 0.15 mg/kg or who remained on 0.20 mg/kg. • **Conclusions:** Concizumab dose adjustments based on plasma concentrations optimized prophylaxis, reducing bleeding rates effectively in hemophilia A/B patients. This approach ensures personalized therapy and supports concizumab's use for long-term management of hemophilia
7 Dec 2025	Long-term safety and efficacy of iptacopan in patients with paroxysmal nocturnal hemoglobinuria: 4- and 5-year follow-up of patients from Phase 2 studies who entered the roll-over extension program	Antonio Risitano	• **Introduction:** Paroxysmal nocturnal hemoglobinuria (PNH) is a life-threatening condition characterized by complement-mediated hemolysis. Iptacopan, an oral proximal complement inhibitor targeting factor B, has shown sustained efficacy in controlling hemolysis in PNH patients. This analysis reports 4- and 5-year follow-up data on the long-term safety and efficacy of iptacopan in patients from Phase 2 studies. • **Methodology:** The PNH-REP study (NCT04747613) enrolled patients from two Phase 2 studies, assessing the impact of iptacopan 200 mg BID. Key efficacy endpoints included hemoglobin (Hb) levels, transfusion avoidance, LDH levels, and reticulocyte count normalization. Safety was evaluated by breakthrough hemolysis (BTH) and major adverse vascular events (MAVEs). • **Results:** At 4 and 5 years, most patients maintained Hb levels ≥12 g/dL and achieved transfusion independence. LDH <1.5×ULN was observed in 81.8% and 83.3%, respectively. BTH occurred in 11.5% of patients, and MAVEs in 1 patient. No new safety concerns emerged. • **Conclusions:** Iptacopan demonstrated sustained efficacy in managing PNH, improving Hb levels, transfusion independence, and hemolysis markers. It was well tolerated, with no new safety findings, supporting its potential as a long-term treatment for PNH.

Notable Presentations At ASH 2025
Benign Haematology (11/21)

Date	Title	Author	Summary
7 Dec 2025	Patient perspectives on the burden of hypereosinophilic syndrome: Results from the Phase 3 natron interview sub-study	Amy Klion	• **Introduction:** Hypereosinophilic syndrome (HES) is characterized by high eosinophil levels, leading to organ damage and reduced quality of life. Despite treatment, patients may experience persistent symptoms. This study reports symptoms and health-related quality of life (HRQoL) impacts in HES patients from the NATRON trial. • **Methodology:** The NATRON study included a qualitative interview sub-study with 29 patients from Poland and the US. Interviews focused on the diagnosis journey, symptoms, treatment expectations, and personal definitions of treatment success. • **Results:** Patients reported 60 symptoms across 13 domains. Common symptoms included fatigue, shortness of breath, and muscle pain. HRQoL impacts were most significant in daily activities, physical activity, and work. Key reasons for study participation were health improvement and avoiding corticosteroids. • **Conclusions:** HES significantly impacts patients' daily lives, with notable HRQoL impairment. These findings highlight the need for timely diagnosis and effective treatment options. Further research into patients' experiences with HES and treatment is necessary.
8 Dec 2025	G-CSF receptor is a signaling node linking thrombo-inflammation to vaso-occlusion in sickle cell disease: Target for a new phase 2 trial	Gregory Kato	• **Introduction:** G-CSF receptor (G-CSFR) blockade has emerged as a potential therapeutic approach to prevent VOC in SCD by targeting this pathway. This preclinical study investigates the role of G-CSFR blockade in reducing VOC severity. • **Methodology:** SCD mice were exposed to G-CSF, oxy-hemoglobin, or lipopolysaccharides (LPS) to induce VOC. Mice were treated with VR81, an anti-G-CSFR monoclonal antibody (mAb), to evaluate its impact on VOC prevention. Biomarker analysis and intravital microscopy assessed the effects on blood flow, inflammation, and neutrophil-platelet aggregates. • **Results:** VR81 inhibited G-CSFR signaling, preventing skin and lung microvascular occlusions. It reduced pro-inflammatory biomarkers, prevented NET formation, and improved chronic organ injury markers, including pulmonary hypertension. Transcriptomic analysis showed that G-CSF gene signatures were enriched in SCD patients during VOC, supporting the therapeutic potential of G-CSFR blockade. • **Conclusions:** G-CSFR blockade effectively prevented VOC and reduced inflammation in SCD mice, suggesting that targeting this pathway could be a promising approach for managing VOC in SCD patients. Phase 2 trials are planned to confirm these findings in humans.

Notable Presentations At ASH 2025
Benign Haematology (12/21)

Date	Title	Author	Summary
8 Dec 2025	Sutacimig, a novel bispecific antibody for prophylactic treatment of glanzmann thrombasthenia: Analysis of a Phase 2 study	Paul Saultier	• **Introduction:** Sutacimig is a bispecific antibody designed to enhance thrombin generation at sites of vascular injury in Glanzmann thrombasthenia (GT), a bleeding disorder caused by defective platelet aggregation. No prophylactic therapy exists, and patients experience significant morbidity. Early results from a study evaluating sutacimig showed a >50% reduction in the median annualized treated bleeding rate (ATBR), with promising safety. • **Methodology:** This multicenter, open-label Phase 2 study enrolled adults (18-67 years) with confirmed GT. Participants were given subcutaneous sutacimig following a 6-week run-in period, with primary endpoints assessing safety and additional pharmacokinetics (PK), pharmacodynamics (PD), and preliminary efficacy. • **Results:** The study enrolled 34 participants across four dosing regimens. Most adverse events were mild to moderate, with common side effects including headache, nasopharyngitis, and fatigue. Sutacimig achieved >50% reduction in median ATBR compared to the run-in period. PK and PD data showed dose-proportional increases in FVIIa. • **Conclusions:** Sutacimig demonstrated clinical activity with a significant reduction in ATBR and was well tolerated in patients with GT. Ongoing analyses will support dose selection and inform the planning of Phase 3 trials for prophylactic therapy in GT.
8 Dec 2025	Phase 3 ESLIM-01 study: Final analysis of efficacy and safety of long-term treatment with sovleplenib in adults with chronic primary immune thrombocytopenia	Yu Hu	• **Introduction:** Sovleplenib, an oral SYK inhibitor, has shown promising results in treating chronic primary ITP. In the phase 3 ESLIM-01 study, sovleplenib demonstrated efficacy in reducing bleeding episodes and improving platelet counts. This analysis reports long-term efficacy and safety data from participants who received sovleplenib treatment. • **Methodology:** Adult patients with chronic ITP were randomized to receive sovleplenib 300 mg once daily or placebo for 24 weeks. Those who completed the study entered an open-label extension sub-study. Main endpoints included durable response (platelet count ≥50×10^9/L) and complete response rate (platelet count ≥100×10^9/L). • **Results:** 179 patients were included in the final analysis. 61.5% of patients who received sovleplenib showed durable responses. The complete response rate was 67.6%. Safety data showed that treatment-related adverse events were predominantly mild, with no mortality events reported. • **Conclusions:** Sovleplenib provided sustained platelet responses with a favorable safety profile, supporting its potential as a treatment option for adults with chronic ITP.

Notable Presentations At ASH 2025
Benign Haematology (13/21)

Date	Title	Author	Summary
8 Dec 2025	Secondary analysis results from VAYHIT3, a phase 2 study of ianalumab in patients with primary immune thrombocytopenia previously treated with at least two lines of therapy	Philip Choi	• **Introduction:** Ianalumab, a monoclonal antibody targeting BAFF-R, shows efficacy in treating refractory primary immune thrombocytopenia (ITP). In the Phase 2 VAYHIT3 study, 44% of patients achieved a confirmed response (ConfR), and over half maintained stable responses (SR) at 6 months. Here, we present secondary analyses from VAYHIT3. • **Methodology:** Adults with ITP, refractory to corticosteroids and thrombopoietin receptor agonists (TPO-RAs), received 4 doses of ianalumab 9 mg/kg. ConfR and SR were key endpoints, analyzed by treatment history, age, and sex. • **Results:** 41 patients were analyzed. Rapid B-cell depletion was observed. ConfR rates were consistent across subgroups, with 22% achieving complete response (CR) by Week 25. Bleeding events decreased significantly. • **Conclusions:** Ianalumab demonstrated robust efficacy and improved bleeding symptoms in heavily pretreated ITP patients.
8 Dec 2025	Recombinant ADAMTS13 prophylaxis in patients with congenital thrombotic thrombocytopenic purpura: Final analysis from A phase 3 randomized, controlled study	Marie Scully	• **Introduction:** The phase 3 study (NCT03393975) evaluated recombinant ADAMTS13 (rADAMTS13) versus plasma-based therapy (PBT) in patients with congenital thrombotic thrombocytopenic purpura (cTTP). This final analysis assessed the efficacy, safety, and patient satisfaction with rADAMTS13. • **Methodology:** Adult patients with cTTP were randomized to receive either rADAMTS13 or PBT for 24 weeks, followed by crossover. The primary endpoint was the incidence of acute TTP events. Secondary endpoints included bleeding manifestations and safety. • **Results:** No acute TTP events occurred with rADAMTS13. Lower annualized event rates were observed for TTP manifestations and subacute events with rADAMTS13. Safety profiles were comparable, and treatment satisfaction improved. • **Conclusions:** rADAMTS13 demonstrated superior efficacy and treatment satisfaction compared to PBT in patients with cTTP.

Notable Presentations At ASH 2025
Benign Haematology (14/21)

Date	Title	Author	Summary
8 Dec 2025	Danicopan add-on therapy demonstrates positive efficacy and safety outcomes in advanced age adults with paroxysmal nocturnal hemoglobinuria and clinically significant extravascular hemolysis: A sub-analysis of the phase 3 ALPHA trial	Austin Kulasekararaj	• **Introduction:** Danicopan, a factor D inhibitor, was evaluated as add-on therapy to ravulizumab or eculizumab in patients with paroxysmal nocturnal hemoglobinuria (PNH) and clinically significant extravascular hemolysis (csEVH). This sub-analysis of the ALPHA trial (NCT04469465) focuses on the efficacy and safety of danicopan in patients aged ≥65 years. • **Methodology:** Patients were randomized to receive either danicopan or placebo for 12 weeks. Key outcomes included hemoglobin (Hb) levels, absolute reticulocyte count (ARC), and Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) scores. • **Results:** Danicopan significantly improved Hb levels, ARC, and FACIT-F scores compared to placebo. Transfusion independence was achieved in 75% of older patients on danicopan. • **Conclusions:** Danicopan add-on therapy is effective and well-tolerated in elderly patients with PNH and csEVH, supporting its use in this population.
8 Dec 2025	Efficacy and safety of NTQ5082 monotherapy in complement-inhibitor-Naïve patients with paroxysmal nocturnal hemoglobinuria: A proof-of-concept, multicenter, randomized, open-label phase 2 study	Fengkui Zhang	• **Introduction:** NTQ5082, a novel oral complement factor B (CFB) inhibitor, is being evaluated for treating paroxysmal nocturnal hemoglobinuria (PNH). The Phase 2 study showed promising results with once-daily dosing. • **Methodology:** In a multicenter, open-label Phase 2 study, patients with complement inhibitor-naïve PNH received NTQ5082 at doses of 100 mg or 200 mg once daily for 12 weeks. Primary endpoint: the proportion of patients achieving an Hb increase ≥20 g/L at Week 12. • **Results:** NTQ5082 showed a significant increase in Hb levels, with 100% of patients achieving the primary endpoint. LDH and bilirubin levels were also reduced. The treatment was well-tolerated with mild to moderate adverse events. • **Conclusions:** NTQ5082 is effective and well-tolerated, offering a robust treatment for PNH with a favorable safety profile.

Notable Presentations At ASH 2025
Benign Haematology (15/21)

Date	Title	Author	Summary
8 Dec 2025	LP-005, a bifunctional C5 antibody fusion protein, efficacy and safety in PNH patients with active hemolysis: Updated results from a Phase 2 study at 12/24 weeks	Guangsheng He	• **Introduction:** PNH is a rare blood disorder marked by hemolysis, thrombosis, and bone marrow failure. LP-005, a bifunctional anti-C5 antibody, targets both the alternative and terminal complement pathways. This Phase 2 study investigates the efficacy and safety of LP-005 in PNH patients. • **Methodology:** Adult patients with active hemolysis were randomized to receive LP-005 (900 mg or 1200 mg) for 12 weeks, followed by dose optimization. Primary endpoints included changes in LDH and Hb levels. • **Results:** At Week 12, LP-005 reduced LDH by 49% (Cohort 1) and 82% (Cohort 2). Hb levels increased by 69%, with 90% of patients achieving ≥2 g/dL Hb increase. Safety was favorable, with no treatment-related SAEs. • **Conclusions:** LP-005 offers significant clinical improvements and a favorable safety profile, suggesting its potential as a superior treatment for PNH.
8 Dec 2025	Efficacy and safety of mitapivat in pediatric patients with pyruvate kinase deficiency who are not regularly transfused: Results from the Phase 3, global, randomized, double-blind, placebo-controlled ACTIVATE-Kids trial	Satheesh Chonat	• **Introduction:** PK deficiency, a rare chronic hemolytic anemia, often requires transfusions and splenectomy, with no approved therapies for children. Mitapivat, a first-in-class oral PK activator, aims to address this unmet need. • **Methodology:** ACTIVATE-Kids (NCT05175105) is a Phase 3, randomized, double-blind, placebo-controlled study of mitapivat in pediatric PK deficiency patients who are not regularly transfused. Primary endpoint: ≥1.5 g/dL increase in Hb. • **Results:** Mitapivat significantly improved Hb levels in 31.6% of patients vs 0% in the placebo group. It also reduced indirect bilirubin and LDH. TEAEs were similar between groups, with no discontinuations or deaths. • **Conclusions:** Mitapivat demonstrated efficacy and safety in children with PK deficiency, showing potential for broader clinical use in pediatric hemolytic anemias.

Notable Presentations At ASH 2025
Benign Haematology (16/21)

Date	Title	Author	Summary
8 Dec 2025	A phase 2 study of luspatercept in adults and adolescents with α-thalassemia: Findings from the dose-confirmation cohort in adolescents	Pablo Gurman	• **Introduction:** α-thalassemia HbH disease, a rare condition causing anemia, lacks approved treatments. Luspatercept, an investigational therapy, is being studied for its efficacy and safety in adolescent patients with transfusion-dependent (TD) and non-transfusion-dependent (NTD) α-thalassemia HbH disease. • **Methodology:** ACTIVATE-Kids is a Phase 3, open-label study where adolescents with α-thalassemia HbH received luspatercept 1 mg/kg for 21 days. Primary endpoints: safety, Hb response, and markers of hemolysis. • **Results:** Luspatercept was well-tolerated with no dose-limiting toxicities. Significant improvements in Hb and hemolysis markers were observed, with minimal adverse events. • **Conclusions:** Luspatercept demonstrated promising efficacy and safety, supporting its potential as a treatment option for adolescent patients with α-thalassemia HbH disease.
8 Dec 2025	Impact of long-term luspatercept treatment on iron parameters in patients with transfusion-dependent and non-transfusion-dependent β-thalassemia: Results from the phase 3b long-term follow-up study	Ali Taher	• **Introduction:** α-thalassemia hemoglobin H (HbH) disease causes chronic anemia and complications like iron overload. Luspatercept, an erythroid maturation agent, is being tested for its potential to improve anemia in α-thalassemia HbH patients. • **Methodology:** The ACTIVATE-Kids trial (NCT05175105) assessed luspatercept's efficacy in adolescents (12–17 years) with non-transfusion-dependent (NTD) or transfusion-dependent (TD) α-thalassemia HbH. Patients were randomized to receive luspatercept (1–5 mg/kg) or placebo for 21 days. The primary endpoint was a ≥1.5 g/dL increase in hemoglobin (Hb). • **Results:** Six patients (3 TD, 3 NTD) were enrolled. Luspatercept significantly increased Hb by 0.90 g/dL in TD and 1.11 g/dL in NTD patients. 90% had Hb increases ≥2 g/dL, and 60% reached Hb ≥10 g/dL. Hemolysis markers (LDH, reticulocytes) improved, and fatigue scores increased. • **Conclusions:** Luspatercept improved Hb and hemolysis markers in adolescents with α-thalassemia HbH, with no major safety concerns, indicating its potential as a treatment option for this condition. Further studies are needed.

Notable Presentations At ASH 2025
Benign Haematology (17/21)

Date	Title	Author	Summary
8 Dec 2025	Efficacy and safety of osivelotor in participants with sickle cell disease in a 12-week phase 2, multicenter, open-label, dose-finding trial and extension study	Santosh Saraf	• **Introduction:** Osivelotor, a sickle hemoglobin (HbS) polymerization inhibitor, is being investigated for treating sickle cell disease (SCD). Preliminary phase 2 results showed promising improvements in hemoglobin (Hb) levels and hemolysis markers. • **Methodology:** A seamless phase 2/3 study evaluated osivelotor's efficacy and safety in adults with SCD (HbSS/HbSβ0). In the phase 2 portion, participants received 100 or 150 mg osivelotor daily for 12 weeks, with the primary endpoint being Hb change from baseline. • **Results:** In the phase 2 study, Hb significantly increased by +2.6 g/dL (100 mg) and +3.4 g/dL (150 mg) by Week 12. In the open-label extension (OLE), Hb gains were sustained, and annualized vaso-occlusive crises (VOC) decreased from 1.9 to 1.2 events/year. Osivelotor was generally well tolerated, with most treatment-emergent adverse events (TEAEs) being mild. • **Conclusions:** Osivelotor showed sustained Hb improvement and a favorable safety profile, supporting its potential for treating SCD. The results encourage continued clinical development.
8 Dec 2025	A phase 2 open-label study of epeleuton in patients with sickle cell disease	Biree Andemariam	• **Introduction:** Sickle cell disease (SCD) is a genetic disorder characterized by sickle hemoglobin (HbS), leading to hemolysis, inflammation, and vaso-occlusion. There is an unmet need for new treatments that address multiple aspects of SCD. Epeleuton, a synthetic derivative of 15(S)-HEPE, has shown promise in preclinical studies by improving RBC membrane health and reducing sickling. • **Methodology:** This phase 2, open-label, multicenter study (NCT05861453) will enroll 35 adults with SCD. Participants will receive 2g of epeleuton twice daily for 16 weeks. Key endpoints include annualized VOC rates, RBC health, and cellular adhesion. • **Results:** Results will assess the impact of epeleuton on RBC function, VOC rates, and disease markers. • **Conclusions:** Epeleuton may offer a disease-modifying therapy for SCD. Findings will guide future trials

Notable Presentations At ASH 2025
Benign Haematology (18/21)

Date	Title	Author	Summary
8 Dec 2025	Early multi-immune modulation with rilzabrutinib in patients with primary ITP after first-line treatment failure: A phase 3b study (LUNA 4)	David Kuter	• **Introduction:** Immune thrombocytopenia (ITP) is an autoimmune disorder causing low platelet counts, bleeding, and impaired quality of life. Current treatments, including corticosteroids, offer limited response. Rilzabrutinib, a selective BTK inhibitor, targets immune pathways involved in ITP, showing promise in earlier trials for improving platelet counts, reducing bleeding, and enhancing quality of life. • **Methodology:** LUNA4 (NCT07007962) is a phase 3b, open-label study assessing early multi-immune modulation with rilzabrutinib in adults with ITP. Participants will receive 400 mg of rilzabrutinib twice daily for 28 weeks, with primary outcomes focused on durable platelet response and secondary measures including fatigue and immune markers. • **Results:** Results will assess durable platelet responses, fatigue reduction, and the impact on ITP progression, with key outcomes including response rates and safety evaluations. • **Conclusions:** LUNA4 will demonstrate rilzabrutinib's potential in modifying ITP disease progression and improving clinical outcomes, potentially offering a new treatment option for early intervention in ITP.
8 Dec 2025	Characterization of participants with elevated bleeding rates responding to prophylactic marstacimab treatment in the phase 3 BASIS trial	Pascal Klaus	• **Introduction:** Hemophilia A (HA) and B (HB) are bleeding disorders with high morbidity. Marstacimab, a monoclonal antibody targeting tissue factor pathway inhibitor, is approved for prophylaxis in patients with HA or HB without inhibitors. The BASIS study demonstrated its effectiveness in reducing the annualized bleeding rate (ABR) compared to on-demand (OD) or routine prophylaxis (RP) therapy. • **Methodology:** This study aimed to identify prognostic factors for patients with elevated ABRs in BASIS. Prognostic factors evaluated included age, region, hemophilic arthropathy, and baseline hemophilia joint health score. • **Results:** 12 patients had an ABR >12. Elevated ABRs correlated with older age, hemophilic arthropathy, and more target joints. Despite this, 41.7% saw a 55.4% decrease in ABR after dose escalation. • **Conclusions:** Older age, Asian residence, and worse joint health were linked to elevated ABRs, but most patients still responded to marstacimab, suggesting dose escalation may benefit some patients.

Notable Presentations At ASH 2025
Benign Haematology (19/21)

Date	Title	Author	Summary
8 Dec 2025	Outcomes of marstacimab treatment in adolescent participants with Hemophilia A or B without inhibitors compared with prior routine prophylaxis: Results from the phase 3 BASIS trial	Anthony Chan	• **Introduction:** The BASIS study (NCT03938792) evaluated marstacimab in adolescents with severe hemophilia A (HA) or B (HB) without inhibitors. Marstacimab, a monoclonal antibody targeting TFPI, reduced the annualized bleeding rate (ABR) of treated bleeds compared to prior therapy. • **Methodology:** Adolescents aged 12–18 received a 300 mg loading dose, followed by 150 mg weekly in the 12-month active treatment phase. Dose escalation to 300 mg QW was allowed for some patients. Outcomes included ABR, safety, pharmacokinetics (PK), and pharmacodynamics (PD). • **Results:** Marstacimab significantly reduced ABR in adolescents, with median ABR of 0.00 for joint and target joint bleeds. Plasma levels were 2–2.5 times higher than adults. Safety was generally favorable, with few adverse events. • **Conclusions:** Marstacimab reduced bleeding and was well tolerated in adolescents. PK differences were weight-dependent, with no significant PD differences from adults, supporting its use in younger patients.
8 Dec 2025	Fibrinogen concentrate versus cryoprecipitate for bleeding in cardiac surgery patients stratified by surgery risk in the phase 3 fibres Study	Jeannie Callum	• **Introduction:** The FIBRES study evaluated fibrinogen concentrate (FC) vs cryoprecipitate in cardiac surgery patients with acquired hypofibrinogenemia. FC was non-inferior to cryoprecipitate in reducing bleeding post-surgery, with a focus on surgical risk factors influencing outcomes. • **Methodology:** Adult patients with hypofibrinogenemia undergoing cardiac surgery were randomized to receive either FC or cryoprecipitate. Patients were stratified into high or non-high surgical risk groups based on preoperative conditions. Primary endpoint: allogeneic blood products (ABPs) transfused during the first 24 hours post-CPB. • **Results:** FC reduced ABPs transfused in non-high-risk patients (mean ratio 0.84, $p<0.0001$). In high-risk patients, FC was non-inferior but not superior. TEAEs occurred less frequently in FC-treated patients in both groups. • **Conclusions:** FC was superior to cryoprecipitate in non-high-risk patients and non-inferior in high-risk patients, supporting FC for managing bleeding in cardiac surgery with hypofibrinogenemia.

Notable Presentations At ASH 2025
Benign Haematology (20/21)

Date	Title	Author	Summary
8 Dec 2025	Oral iptacopan monotherapy demonstrates clinically meaningful hemoglobin increases in patients with paroxysmal nocturnal hemoglobinuria with baseline hemoglobin levels 10 to <12 g/dl on anti-C5 therapy: Subgroup analysis of the appulse-pnh Phase 3b trial	Austin Kulasekararaj	• **Introduction:** Paroxysmal nocturnal hemoglobinuria (PNH) is a rare blood disorder often treated with anti-C5 therapies, but some patients remain anemic due to extravascular hemolysis. Iptacopan, an oral factor B inhibitor, was tested in the APPULSE-PNH study, which demonstrated superior efficacy in patients with PNH and Hb ≥10 g/dL on anti-C5 therapy. • **Methodology:** In this Phase 3b study, 52 patients with PNH on stable anti-C5 therapy switched to iptacopan 200 mg twice daily for 24 weeks. The primary endpoint was the change in hemoglobin (Hb) levels, with subgroup analyses for patients with baseline Hb 10 to <12 g/dL. • **Results:** In the subgroup (n=32), Hb increased by +2.4 g/dL (95% CI: 2.0–2.7), surpassing noninferiority and superiority thresholds. No patients required transfusions. Significant improvements in fatigue (FACIT-F) and treatment satisfaction (TSQM-9) were observed. • **Conclusions:** Iptacopan significantly increased Hb and improved quality of life in patients with Hb 10 to <12 g/dL, supporting its use as a potential treatment for PNH.
8 Dec 2025	Study design of A phase 3, open-label trial for pozelimab and cemdisiran combination therapy in patients with paroxysmal nocturnal hemoglobinuria with inadequate control of intravascular hemolysis	Jun Ho Jang	• **Introduction:** Paroxysmal nocturnal hemoglobinuria (PNH) is a rare disease characterized by complement-mediated hemolysis. Current C5 inhibitors like eculizumab, ravulizumab, and crovalimab can leave residual intravascular hemolysis. The combination of pozelimab (C5 activation inhibitor) and cemdisiran (C5 production inhibitor) is being explored as a novel therapy to achieve better control of intravascular hemolysis. • **Methodology:** This phase 3, single-arm, multicenter study (EU CT:2024-519709-37-00) will enroll 35 PNH patients with persistent LDH >1.5 × ULN despite current C5 inhibitor therapy. Patients will receive pozelimab 400 mg SC and cemdisiran 200 mg SC every 4 weeks for 28 weeks, followed by a 52-week extension. • **Results:** The primary endpoint is the percentage change in LDH from baseline to week 28. Secondary endpoints include normalization of LDH, transfusion avoidance, and safety assessments. • **Conclusions:** This study aims to assess the combined efficacy of pozelimab and cemdisiran in controlling hemolysis in PNH patients inadequately controlled by C5 inhibitors.

Notable Presentations At ASH 2025
Benign Haematology (21/21)

Date	Title	Author	Summary
8 Dec 2025	Sustained improvements in patient-reported outcomes after intravenous efgartigimod in adults with primary immune thrombocytopenia in a Phase 3 clinical trial (ADVANCE IV) and the first 52 weeks in its open-label extension study (ADVANCE IV+)	Monica Carpenedo	• **Introduction:** Primary immune thrombocytopenia (ITP) is an autoimmune disorder causing thrombocytopenia, bleeding, and impaired quality of life. Many patients do not respond to treatments and require additional therapy. The ADVANCE IV trial demonstrated the efficacy and safety of intravenous efgartigimod in adults with chronic and persistent ITP. • **Methodology:** The ADVANCE IV+ extension study evaluates long-term safety and the impact of efgartigimod on health-related quality of life (HRQoL) and patient-reported outcomes (PRO) using surveys such as SF-36, FACIT-Fatigue, and FACT-Th6. • **Results:** Improvements in HRQoL were observed, with significant increases in SF-36, FACIT-Fatigue, and FACT-Th6 scores. Efgartigimod-treated patients showed continued HRQoL improvements in the open-label extension. • **Conclusions:** Efgartigimod improved HRQoL in ITP patients, including those who switched from placebo. Ongoing studies aim to further evaluate its impact on HRQoL in long-term treatment.
9 Dec 2025	Primary results from VAYHIT2, a randomized, double-blind, phase 3 trial of ianalumab plus eltrombopag versus placebo plus eltrombopag in patients with primary immune thrombocytopenia (ITP) who failed first-line corticosteroid treatment	Hanny Al-Samkari	• **Introduction:** Paroxysmal nocturnal hemoglobinuria (PNH) is characterized by complement-mediated hemolysis, and patients on C5 inhibitors often experience inadequate control due to residual intravascular hemolysis. Iptacopan, an oral selective factor B inhibitor, is being evaluated for its ability to address this gap in treatment. • **Methodology:** APPULSE-PNH (NCT05630001) is a Phase 3b trial evaluating iptacopan in patients with PNH and Hb ≥10 g/dL on anti-C5 therapy. Patients were switched to iptacopan monotherapy for 24 weeks, with primary and secondary endpoints including change in hemoglobin (Hb) levels and patient-reported outcomes. • **Results:** Patients with baseline Hb 10–12 g/dL showed a significant increase in Hb (+2.4 g/dL) after switching to iptacopan. Improvements in lactate dehydrogenase (LDH), reticulocyte count, fatigue, and treatment satisfaction were also observed. No RBC transfusions were required during the treatment period. • **Conclusions:** Iptacopan demonstrated substantial efficacy in increasing Hb and managing PNH symptoms. It was well-tolerated with no increase in infection risk, supporting its potential as a disease-modifying treatment for PNH.

Notable Presentations At ASH 2025
Transplantation & Cell Therapy (CAR-T, GVHD, conditioning regimens) (1/9)

Date	Title	Author	Summary
6 Dec 2025	Primary results from Equator, a Phase 3 double-blind, randomized placebo-controlled study evaluating itolizumab in combination with corticosteroids as initial treatment of acute graft-versus-host disease.	John Koreth	• **Introduction:** Itolizumab, a monoclonal antibody targeting CD6, was evaluated in the EQUATOR Phase 3 trial as a first-line treatment for acute graft-versus-host disease (aGVHD) in combination with corticosteroids. • **Methodology:** 158 high-risk aGVHD patients were randomized to receive itolizumab or placebo. Primary endpoint: Day 29 complete response (CR). Secondary endpoints included overall response rate (ORR), durable CR (DCR), overall survival (OS), and failure-free survival (FFS). • **Results:** Itolizumab showed no statistically significant difference in Day 29 CR but improved secondary endpoints like duration of CR and FFS. Itolizumab also demonstrated a lower 1-year mortality rate compared to placebo. • **Conclusions:** While primary endpoint was not met, itolizumab prolonged responses and improved survival outcomes, suggesting potential benefits for aGVHD management.
6 Dec 2025	Trials in progress: Design of a registrational Phase 2 trial (ALLOHA) using an external control arm for TSC-101 for prevention of relapse post allogeneic HCT in patients with ALL, AML, or MDS	Monzr M. Al Malki	• **Introduction:** The ALLOHA™ study (NCT05473910) is a Phase 1/2 trial investigating the safety and efficacy of TSC-101, a TCR-engineered T-cell therapy for preventing relapse in HLA-A*02:01-positive adults with AML, MDS, or ALL undergoing reduced intensity conditioning-based allogeneic HCT (RIC-HCT). • **Methodology:** The study includes a Phase 1 cohort receiving TSC-101 infusions post-engraftment. Control arm patients receive standard RIC-HCT. A Phase 2 cohort will further investigate the efficacy of two TSC-101 infusions with an external control arm from the CIBMTR registry. • **Results:** Initial Phase 1 results showed no dose-limiting toxicities and promising improvements in relapse rates, relapse-free survival (RFS), and overall survival (OS). RMAT designation was granted in 2024. • **Conclusions:** The ALLOHA study explores engineered TCR-T cell therapy post-HCT to reduce relapse and improve survival in hematologic malignancies.

Notable Presentations At ASH 2025
Transplantation & Cell Therapy (CAR-T, GVHD, conditioning regimens) (2/9)

Date	Title	Author	Summary
6 Dec 2025	Pharmacokinetics-guided ATG targeted dosing strategy in unmanipulated haploidentical haematopoietic stem cell transplantation: A randomized, multicenter, phase 3 clinical trial	Daihong Liu	• **Introduction:** This study aimed to evaluate the clinical outcomes of a pharmacokinetics-guided, dose-optimized ATG strategy in haploidentical HSCT recipients, as opposed to the standard fixed dosing (10 mg/kg) for GVHD prophylaxis. • **Methodology:** A multicenter, randomized Phase 3 trial compared targeted versus fixed ATG dosing in patients with hematological malignancies. The primary endpoint was CMV reactivation within 180 days post-transplant. Patients were enrolled between January 2022 and January 2024, with 204 participants in total. • **Results:** The targeted dose group showed a significantly lower CMV reactivation rate (30.7% vs. 54.9%, P = 0.0003) and higher GRFS at 365 days (63.7% vs. 48.0%, P = 0.007). Fewer infections were reported in the targeted group (56.9% vs. 97.1%, P < 0.001). • **Conclusions:** Pharmacokinetics-guided ATG dosing reduces CMV reactivation, improves immune reconstitution, and enhances GRFS, without increasing GVHD or graft failure
6 Dec 2025	Orca-T demonstrates favorable quality of life and healthcare resource use compared to standard allohsct plus tac/MTX for GVHD prevention in a randomized Phase 3 clinical trial (Precision-T)	Arpita Gandhi	• **Introduction:** The study explores the use of Orca-T, a high-precision engineered T-cell therapy, in preventing GVHD in haploidentical HSCT recipients compared to standard unmanipulated peripheral blood stem cells with Tac/MTX. Orca-T showed promising outcomes in reducing chronic GVHD, improving survival, and reducing infections. • **Methodology:** Patients with hematological malignancies were randomized to receive Orca-T plus tacrolimus or Tac/MTX. The study assessed HRQoL using the FACT-BMT instrument, hospitalization patterns, and treatment-related outcomes. • **Results:** Orca-T recipients had higher HRQoL scores, fewer hospitalizations, and lower rehospitalization rates. The Orca-T group showed improved recovery and higher rehospitalization-free survival at 18 months. • **Conclusions:** Orca-T offers significant HRQoL benefits, faster recovery, and fewer complications compared to Tac/MTX, suggesting a promising option for HSCT recipients.

Notable Presentations At ASH 2025
Transplantation & Cell Therapy (CAR-T, GVHD, conditioning regimens) (3/9)

Date	Title	Author	Summary
6 Dec 2025	Orca-T improves chronic graph-versus-host disease free in patients with a broad range of demographic and clinical variables: Results of randomized, Phase 3 trial	Everett Meyer	• **Introduction:** Orca-T, a novel engineered T-cell immunotherapy, demonstrated superior outcomes in preventing chronic GVHD (cGVHD) compared to standard Tac/MTX in a Phase 3 trial. This analysis explores the impact of Orca-T across subgroups in patients undergoing HSCT for hematological malignancies. • **Methodology:** Patients (n=182) were randomized to receive Orca-T or Tac/MTX after myeloablative conditioning. Subgroup analyses were conducted based on demographics, disease type, donor type, and conditioning regimen. • **Results:** Orca-T significantly improved cGVHD-free survival (cGFS) and graft-versus-host disease-free, relapse-free survival (GRFS) across various subgroups, with reduced non-relapse mortality and fewer infections compared to Tac/MTX. • **Conclusions:** Orca-T offers significant clinical benefits in preventing cGVHD, especially in older and high-risk patients, suggesting broader applicability for diverse patient populations.
7 Dec 2025	Haplo-identical transplantation in patients with myelofibrosis, a phase 2 prospective multicentric study	Marie Robin	• **Introduction:** This Phase 2 trial evaluates haploidentical HSCT using a specific conditioning regimen in myelofibrosis patients without an HLA-matched donor, aiming for improved relapse and rejection-free survival compared to historical data. • **Methodology:** Patients aged 18-70 with intermediate/high-risk myelofibrosis received haploidentical HSCT. Primary endpoint: one-year relapse and rejection-free survival. Secondary endpoints included GVHD, survival, and infections. • **Results:** The one-year relapse/rejection-free survival was 64.3%, significantly higher than historical controls (35%). Acute GVHD occurred in 64.3%, chronic GVHD in 39.3%, and overall survival was 67.9%. Non-relapse mortality was 32.1%, primarily due to GVHD and infections. • **Conclusions:** The trial met the primary endpoint but highlights the need to address non-relapse mortality, particularly due to acute GVHD and infections.

Notable Presentations At ASH 2025
Transplantation & Cell Therapy (CAR-T, GVHD, conditioning regimens) (4/9)

Date	Title	Author	Summary
7 Dec 2025	ZUMA-25 preliminary analysis: A Phase 2 study of brexucabtagene autoleucel (brexu-cel) in patients (Pts) with relapsed/refractory (R/R) burkitt lymphoma (BL), substudy C	Suzanne Van Dorp	• **Introduction:** Brexu-cel, an autologous anti-CD19 CAR T-cell therapy, is investigated for relapsed/refractory Burkitt lymphoma (R/R BL), a rare, aggressive B-cell malignancy. This Phase 2 study (ZUMA-25, Substudy C) aims to evaluate the safety and efficacy of brexu-cel. • **Methodology:** Patients aged ≥18 with R/R BL received brexu-cel after leukapheresis and conditioning. The primary endpoint was overall response rate (ORR), with secondary endpoints including progression-free survival (PFS) and overall survival (OS). • **Results:** Among 10 treated patients, ORR was 100% (50% CR, 50% PR). Median OS was 12.9 months, with durable responses in CR patients. AEs included pyrexia and cytokine release syndrome, but no treatment-related mortality. • **Conclusions:** Brexu-cel shows promising efficacy and safety for R/R BL, though further studies with longer follow-up are needed.
7 Dec 2025	CD19/CD22 bispecific CAR-t cell therapy for relapsed/refractory large b-cell lymphoma: A prospective, single-arm, single-center, phase 2 clinical trial	Liang Wang	• **Introduction:** CD19/CD22 bispecific CAR-T (CAR2219) therapy is being evaluated for R/R LBCL, a group with limited treatment options and poor outcomes from conventional therapies. This study aims to assess the safety and efficacy of CAR2219 in these patients. • **Methodology:** A Phase 2 trial enrolled 31 R/R LBCL patients, who received CAR2219 after lymphodepletion. The primary endpoint was the overall response rate (ORR) at 3 months, with secondary endpoints including complete response rate (CRR), progression-free survival (PFS), and adverse events. • **Results:** The ORR was 100%, with a CRR of 64.5%. The median PFS and OS were not reached, with 12-month PFS at 60.4% and OS at 87.1%. Safety was manageable, with common AEs including neutropenia, thrombocytopenia, and CRS. • **Conclusions:** CAR2219 shows promising efficacy and a favorable safety profile in R/R LBCL, warranting further study.

Notable Presentations At ASH 2025 Transplantation & Cell Therapy (CAR-T, GVHD, conditioning regimens) (5/9)

Date	Title	Author	Summary
7 Dec 2025	Firicabtagene autoleucel (firi-cel), a CD22-directed CAR T-cell therapy, for patients with relapsed/refractory large B-cell lymphoma: Results from the phase 2 study (FIRCE-1 Trial)	Matthew Frank	• **Introduction:** Firi-cel, a bispecific CAR-T targeting both CD19 and CD22, was evaluated in relapsed/refractory large B-cell lymphoma (r/r LBCL) patients previously treated with CD19 CAR-T (CAR19). The study aimed to assess its efficacy and safety. • **Methodology:** This Phase 2, open-label study enrolled patients with r/r LBCL, receiving firi-cel after leukapheresis and lymphodepletion. The primary endpoint was overall response rate (ORR) at 3 months, with secondary endpoints including progression-free survival (PFS) and safety. • **Results:** Among 84 infused patients, ORR was 73%, and complete response (CR) was 46%. Median PFS was 3.1 months, with OS at 12.4 months. Notable AEs included cytokine release syndrome (CRS) and immune effector cell-associated hemophagocytic lymphohistiocytosis (IEC-HS), leading to trial termination due to toxicity. • **Conclusions:** Firi-cel showed high ORR but low durable responses, potentially due to manufacturing changes and patient selection. Further studies are needed to explore the relationship between pharmacokinetics, toxicity, and efficacy.
7 Dec 2025	First-line consolidation with cemacabtagene ansegedleucel (cema-cel) in patients with large B-cell lymphoma (LBCL) and minimal residual disease (MRD) after response to standard therapy: The pivotal, randomized, open-label Phase 2 ALPHA3 study	John M. Burke	• **Introduction:** R-CHOP achieves a 60% cure rate for LBCL, but 10% of patients are refractory, and 30% relapse within two years. Cema-cel, an off-the-shelf, HLA-unmatched CD19 CAR-T, could provide an alternative for patients at high risk of relapse after first-line (1L) therapy. • **Methodology:** The ALPHA3 Phase 2 study evaluates cema-cel vs. standard observation in patients with detectable MRD post-1L therapy. Eligible patients with DLBCL or other types of LBCL, who respond to 1L therapy and are MRD-positive, are randomly assigned to either SOC or cema-cel after lymphodepletion (FC regimen). • **Results:** The study is ongoing, focusing on event-free survival, MRD clearance, and safety, with interim analyses planned. • **Conclusions:** Cema-cel shows promise for improving outcomes in MRD-positive LBCL patients post-1L therapy.

Notable Presentations At ASH 2025 Transplantation & Cell Therapy (CAR-T, GVHD, conditioning regimens) (6/9)

Date	Title	Author	Summary
7 Dec 2025	Etoposide-cytarabine-pegfilgrastim (EAP) and disease-specific chemotherapy regimens for hematopoietic stem cell mobilization in lymphoma: A randomized phase III trial	Peipei Ye	• **Introduction:** Hematopoietic stem cell (HSC) collection is crucial for successful autologous stem cell transplantation (auto-SCT) in lymphoma patients. The effectiveness of mobilization is influenced by the methods used, with the EAP regimen (etoposide, cytarabine, pegfilgrastim) showing promise over traditional chemotherapy. • **Methodology:** A multicenter Phase III trial (NCT06520163) randomized patients to receive either the EAP regimen or a disease-specific chemotherapy regimen for HSC mobilization. The primary endpoint was achieving ≥5×10⁶ CD34+ cells/kg in one apheresis session. • **Results:** The EAP regimen resulted in significantly more patients reaching the optimal collection target (73.3% vs. 28.6%, p=0.005) and required fewer apheresis sessions. Safety profiles were similar, with fewer plerixafor rescues needed for the EAP group. • **Conclusions:** The EAP regimen enhances HSC mobilization effectiveness with fewer apheresis sessions and similar safety, making it a cost-effective option for NHL patients.
7 Dec 2025	Mesenchymal stem cells for treating gastrointestinal-involved steroid-refractory acute graft-versus-host disease: A multicenter, single-arm, pivotal clinical Trial	Yawei Zheng	• **Introduction:** Steroid-refractory acute graft-versus-host disease (SR-aGVHD), especially SR-gastrointestinal (GI) aGVHD, is a major cause of morbidity and mortality after allogeneic hematopoietic stem cell transplantation (allo-HSCT). This study assesses the efficacy and safety of hUC-MSC PLEB001, a human umbilical cord-derived mesenchymal stem cells (MSCs) product, for SR-GI-aGVHD. • **Methodology:** In this multicenter, single-arm pivotal trial, patients received hUC-MSC PLEB001 (106 cells/kg) twice weekly for 4 weeks. The primary endpoint was the overall response rate (ORR) at day 28, with secondary endpoints including complete response (CR), overall survival (OS), and adverse events. • **Results:** Fifty-four patients were enrolled. The ORR at day 28 was 63.0%, with a CR rate of 55.6%. The 28-day durable CR rate was 51.9%. OS at day 360 was 65.8%. The treatment was well-tolerated, with no infusion-related toxicities reported. • **Conclusions:** hUC-MSC PLEB001 demonstrated efficacy and good tolerance in SR-GI-aGVHD, leading to its approval by the Chinese NMPA as the first MSC product for this indication.

Notable Presentations At ASH 2025 Transplantation & Cell Therapy (CAR-T, GVHD, conditioning regimens) (7/9)

Date	Title	Author	Summary
7 Dec 2025	In Vivo evaluation of autologous serum eye drops obtained via a closed-circuit collection device: Preliminary analysis of a Phase 2 pilot trial	Giancarlo Fatobene	• **Introduction:** Autologous serum eye drops (ASED) are used to treat ocular surface diseases, showing symptom improvement of 50-70%. However, the preparation process is costly and requires germ-free conditions. This study evaluates the feasibility and safety of ASED collected via a closed-circuit system device. • **Methodology:** A single-arm, phase 2 pilot trial enrolled patients with persistent dry eye disease or chronic corneal defects. ASED were processed and frozen in single-dose containers. Assessments included ophthalmological evaluations, symptom questionnaires, adherence, and adverse events at baseline, 6, and 12 weeks. • **Results:** Fourteen patients were enrolled. Objective ophthalmic measures showed no significant changes, but symptom scores improved significantly (OSDI: p=0.0002, Lee score: p=0.009). Adverse events were mild and transient, with three patients discontinuing treatment. • **Conclusions:** The closed-circuit ASED production system is feasible and safe, with patients experiencing symptomatic relief. A registration trial is underway.
7 Dec 2025	Trial in progress: A phase 3, randomized, double-blind, placebo-controlled study of axatilimab and corticosteroids as initial treatment for moderate to severe chronic graft-versus-host disease	Zachariah DeFilipp	• **Introduction:** Chronic graft-versus-host disease (cGVHD) is a common and severe complication after allo-HSCT, often leading to significant morbidity and mortality. Current treatments, particularly corticosteroids, are insufficient, with many patients progressing to second-line therapies. Axatilimab, an anti-CSF-1R monoclonal antibody, has shown promising results in phase 2 trials for relapsed/refractory cGVHD. • **Methodology:** The phase 3, double-blind, placebo-controlled study (NCT06585774) will assess the efficacy and safety of axatilimab combined with corticosteroids in patients with new-onset moderate to severe cGVHD. Approximately 240 patients will be randomized to receive either axatilimab or placebo, with primary endpoints focused on event-free survival. • **Results:** This ongoing trial will evaluate the clinical benefit of axatilimab as first-line therapy for cGVHD, with safety monitoring and secondary endpoints including ORR and symptom improvement. • **Conclusions:** This study aims to provide evidence for axatilimab's role in treating moderate to severe cGVHD in combination with corticosteroids.

Notable Presentations At ASH 2025
Transplantation & Cell Therapy (CAR-T, GVHD, conditioning regimens) (8/9)

Date	Title	Author	Summary
8 Dec 2025	MaaT013 for ruxolitinib-refractory acute graft-versus-host disease with gastrointestinal involvement: Results from the ARES phase III trial	Florent Malard	• **Introduction:** Steroid-refractory gastrointestinal (GI) graft-versus-host disease (SR-GI-aGVHD) is a major complication following allo-HSCT with poor prognosis. Fecal microbiotherapy has shown promise in treating refractory cases. This study evaluates MaaT013, a human umbilical cord-derived microbiome therapy, as second-line treatment for SR-GI-aGVHD. • **Methodology:** Patients with refractory GI-aGVHD received MaaT013 (3 doses over 10 days) after a 2-day vancomycin course. The primary endpoint was GI overall response rate (GI-ORR) at Day 28. Secondary endpoints included overall survival (OS) and safety. • **Results:** Among 66 subjects, the GI-ORR at Day 28 was 62%, exceeding the threshold of 22%. The response was sustained at Day 56 (49%) and Month 3 (44%). Median OS was not reached, with responders having significantly higher survival rates. • **Conclusions:** MaaT013 demonstrated significant efficacy and safety, offering a promising option for treating refractory SR-GI-aGVHD.
8 Dec 2025	An open-label, multi-center Phase 2 study to assess the safety and efficacy of burixafor (GPC-100) and propranolol with G-CSF for the mobilization of hematopoietic progenitor cells in patients with multiple myeloma	Jack Khouri	• **Introduction:** Autologous hematopoietic cell transplantation (AHCT) for multiple myeloma (MM) requires effective hematopoietic progenitor cell (HPC) mobilization. The use of anti-CD38 antibodies may impair mobilization. Burixafor (GPC-100), a CXCR4 inhibitor, is investigated in combination with propranolol and G-CSF to optimize HPC mobilization. • **Methodology:** This Phase 2 trial (NCT05561751) involved 20 patients. Participants received G-CSF, propranolol, and burixafor before leukapheresis. The primary endpoint was achieving ≥2x10⁶ CD34+ cells/kg in two sessions. • **Results:** 10 patients achieved ≥2x10⁶ CD34+ cells/kg. 70% collected ≥5x10⁶ CD34+ cells/kg. Adverse events were mostly mild, with no infusion reactions. All patients proceeded to AHCT, with median engraftment times of 11 days for neutrophils and 15 days for platelets. • **Conclusions:** Burixafor with propranolol and G-CSF effectively mobilized HPCs with a favorable safety profile, facilitating same-day leukapheresis.

Notable Presentations At ASH 2025 Transplantation & Cell Therapy (CAR-T, GVHD, conditioning regimens) (9/9)

Date	Title	Author	Summary
8 Dec 2025	Trial-in-progress: A phase 2 randomized trial of remodeling intestinal microbiota using fecal microbiome transplant (FMT) among recipients of chimeric antigen receptor T cells (CAR T)	Karamjeet Sandhu	• **Introduction:** Chimeric Antigen Receptor T-cell (CAR T) therapy has revolutionized B-cell lymphoma treatment, but its efficacy may be hindered by prior high-risk antibiotic use, which damages the microbiome. This study investigates whether fecal microbiota transplant (FMT) can restore microbiome diversity and improve CAR T therapy outcomes in patients with relapsed/refractory B-cell lymphoma. • **Methodology:** This Phase 2a, double-blind, randomized, placebo-controlled trial (NCT07042438) enrolls 56 patients to receive FMT or placebo, with microbiome diversity assessed pre- and post-treatment using the Shannon Index. Secondary objectives include treatment response and safety evaluations, including infections and toxicity. • **Results:** Primary endpoint is microbiome diversity improvement by Day 0. Safety and clinical response assessments will follow. • **Conclusions:** This trial explores FMT's potential to enhance CAR T therapy efficacy by restoring the gut microbiome in patients with high-risk prior antibiotic exposure.
8 Dec 2025	Eltrombopag plus G-CSF for peripheral blood stem cell mobilization: Final analysis of a single arm, Phase 2 trial	Ta-Chuan Yu	• **Introduction:** Autologous hematopoietic stem cell transplantation (auto-HSCT) is standard for relapsed/refractory lymphoma, but some patients struggle to collect sufficient peripheral blood stem cells (PBSC) for transplant. This study investigates whether eltrombopag, a thrombopoietin receptor agonist, can improve PBSC harvest success. • **Methodology:** In this Phase 2 trial, East-Asian lymphoma patients receiving ESHAP chemo-mobilization were treated with eltrombopag (75 mg daily) to enhance PBSC collection. The primary endpoint was the proportion of patients obtaining >2.0 × 10^6/kg CD34+ cells on the first apheresis day. • **Results:** Of 39 enrolled patients, 29 met the primary endpoint. The mean harvested CD34+ cells were higher with eltrombopag (13.30 × 10^6/kg) compared to historical controls (5.71 × 10^6/kg). No major eltrombopag-related adverse events occurred. • **Conclusions:** Eltrombopag safely improves PBSC harvest efficiency in auto-HSCT and warrants further investigation for confirmatory studies.

Key Industry Sponsored Sessions Information

ASH 2025 Key Industry Sponsored Sessions Information (1/8)

Date	Sponsor	Title
05 Dec 2025	AstraZeneca, Genentech, Incyte Corporation, Novartis and Regeneron	Beyond Chemotherapy: Patient Voices and Expert Insights on Using Precision Therapies to Enhance Personalized Care of Follicular Lymphoma
05 Dec 2025	BMS	MASTER MDS for Enhanced Patient Care: Modern Advances with STandard and Emerging, Risk-adapted Treatment
05 Dec 2025	Johnson & Johnson, and Kura Oncology	Menin Masters for AML Care: Guidance on Integrating Menin Inhibitor Regimens & Boosting Efficacy in Challenging AML Subtypes
05 Dec 2025	Incyte Corporation, Orca Bio, and Sanofi	Rising to the Graft-vs-Host Disease Challenge: Progress in Treatment and Post-HCT Outcomes Across Hematologic Cancers
05 Dec 2025	AbbVie and GSK	Steady Progress in Multiple Myeloma: Applying New Data and Updated Guidelines Throughout Treatment
05 Dec 2025	AstraZeneca and Lilly	Aligning Discovery With Clinical Practice: Applying Expert Consensus Guidelines To Improve Patient Outcomes in CLL/SLL
05 Dec 2025	GSK, Johnson & Johnson and Regenenon	Many Roads to Myeloma Remission: Making Sequential Choices With BCMA and non-BCMA Immunotherapies
05 Dec 2025	AstraZeneca, Novartis, Roche, Sobi and Apellis	Paroxysmal Nocturnal Hemoglobinuria: What we have learned from the introduction of new therapies

ASH 2025 Key Industry Sponsored Sessions Information (2/8)

Date	Sponsor	Title
05 Dec 2025	Agios Pharmaceuticals and BMS	Momentum in MDS: Making Progress and Shaping a Better Future
05 Dec 2025	Pharmacosmos Therapeutics	Advances in Targeting Angiogenesis and Managing Severe Anemia in Vascular Bleeding Disorders:Hereditary Hemorrhagic Telangiectasia, Von Willebrand Disease, and Beyond
05 Dec 2025	Indy Hematology Education	Reaching Clinical Trial Excellence: Practical Strategies for Achieving Generalizable and Transportable Data
05 Dec 2025	AstraZeneca	Redrawing Frontlines in MCL: The Upfront Expansion of BTKi Options & Modern Clinical Decision-making in Newly Diagnosed Disease
05 Dec 2025	AstraZeneca, BeOne Medicines, and Lilly	Pathways to Personalized Remission in CLL: Leveraging Targeted Standards & Next-Gen Advances for Upfront and Sequential Care
05 Dec 2025	AstraZeneca	Moving Forward in B-ALL: Insights on Modern and Emerging Standards With Off-the-Shelf Bispecific Antibodies
05 Dec 2025	AstraZeneca and Regeneron	Off the Shelf and in the Clinic for NHL: Leveraging Bispecific Antibody Strategies in DLBCL, FL, and Beyond
05 Dec 2025	AbbVie, Astellas, Daiichi Sankyo	Consensus or Controversy? Clinical Investigators Provide Perspectives on the Current and Future Management of Patients with Acute Myeloid Leukemia

ASH 2025 Key Industry Sponsored Sessions Information (3/8)

Date	Sponsor	Title
05 Dec 2025	Janssen	The Growing Role of CAR T-Cell Therapy in Multiple Myeloma: New Data on Earlier Lines of Therapy, Expanding Access to Treatment
05 Dec 2025	Novo Nordisk	Advancing Hemophilia Care—Uniting Expert Insights and Community Voices to Shape the Future of Non-Factor Replacement Therapy
05 Dec 2025	BMS and Kite Pharma	Advancing Outcomes in Lymphoma Care: A Master Class on Integrating the CAR T-Cell Therapies into Clinical Practice
05 Dec 2025	Kura Oncology and Rigel Pharmaceutical	Medical Crossfire®: Experts Debate the Hottest Topics in AML – FLT3, IDH1/2, KMT2Ar, NPM1, Secondary AML, Maintenance, Novel Combinations, and Emerging Therapies
05 Dec 2025	Takeda	Cases & Conversations™: Real-World Insights on Advances in the Management of Myeloproliferative Neoplasms: How the Experts Apply the Latest Developments to Clinical Practice
05 Dec 2025	Amgen	Medical Crossfire®: Advances in ALL Management Across the Patient Spectrum: Integrating Innovation and Precision Care
05 Dec 2025	Sanofi	'Four' Every Patient: Maximizing Outcomes in Newly Diagnosed Multiple Myeloma Care with Anti-CD38 Monoclonal Antibody-Based Quadruplet Therapies
05 Dec 2025	Novartis	A Master Class in CP-CML: New Agents, Treatment Goals, and Clinical Challenges

ASH 2025 Key Industry Sponsored Sessions Information (4/8)

Date	Sponsor	Title
05 Dec 2025	Abbvie., AstraZeneca, BMS, and Lilly	Cases from the Community: Investigators Discuss Available Research Guiding the Selection of Therapy for Patients with Chronic Lymphocytic Leukemia
05 Dec 2025	BMS	Myeloma Myth Busters: Investigating the Now, Soon, and Future Clinical Implications of CELMoDs
05 Dec 2025	Sanofi	Filling in the Gaps in Hemophilia Guideline Recommendations: Evidence-Based Strategies to Optimize Patient-Relevant Outcomes
05 Dec 2025	Novartis	Visualizing Novel Pathways to Optimizing Care for Patients with Paroxysmal Nocturnal Hemoglobinuria (PNH)
05 Dec 2025	Amgen, Pfizer	BRINGING EMERGING TREATMENTS TO ALL PATIENTS: Strategies for Implementing T-cell Redirection Therapies in Community Oncology Practices
05 Dec 2025	BMS	Bridging the Gaps in CAR T-Cell Therapy for Hematological Malignancies: Expert Guidance, Clinical Experience and Increased Access
05 Dec 2025	Sanofi	Achieving Comprehensive Care for Chronic Immune Thrombocytopenia: Exploring Emerging Therapies to Address Patient-centric Hematological and Non-Hematological Outcomes
05 Dec 2025	Novo Nordisk	Staying in the Lead: Navigating the Changing Course of Sickle Cell Disease Management —A CME COMPETE™: SCD Edition

ASH 2025 Key Industry Sponsored Sessions Information (5/8)

Date	Sponsor	Title
05 Dec 2025	Alnylam	Acute Hepatic Porphyria: Bridging Gaps for Better Diagnosis and Management
05 Dec 2025	BMS and GSk	Expert Second Opinion: Investigators Discuss the Optimal Management of Patients with Myelofibrosis and Systemic Mastocytosis
05 Dec 2025	Genentech	EXPERT SECOND OPINION: Investigators Discuss the Role of Novel Treatment Approaches in the Care of Patients with Follicular Lymphoma and Diffuse Large B-Cell Lymphoma
06 Dec 2025	Novartis	Clinical Management and Unmet Needs in Immune Thrombocytopenia (ITP)
06 Dec 2025	Pfizer	Enhancing Sickle Cell Disease Care Through Patient Partnership
06 Dec 2025	GSK	Evolving Patient Support Programs: Access, Education and Affordability in Oncology Care
06 Dec 2025	Takeda	Rethinking Control in Polycythemia Vera - Uncovering the Clinical Unmet Needs and Potential to Address Them with Emerging Therapies
06 Dec 2025	Genentech	A Treatment Option for Adults with Certain R/R DLBCL After ≥ 2 Prior Lines of Systemic Therapy

ASH 2025 Key Industry Sponsored Sessions Information (6/8)

Date	Sponsor	Title
06 Dec 2025	Johnson & Johnson	Frontline Therapy in Transplant-Ineligible Patients with Newly Diagnosed Multiple Myeloma
06 Dec 2025	Novartis	Hear Jen's Journey, Then Explore the Data
06 Dec 2025	Thermo Fisher Scientific	Rapid NGS: Transforming Molecular Profiling of Myeloid and Lymphoid Malignancies
06 Dec 2025	Sanofi	Shifting Currents in Hemophilia Care: Exploring the Impact of Antithrombin Lowering
06 Dec 2025	AbbVie	Unlocking the Benefits of Time-Off Treatment with a BCL-2 Inhibitor as the Proven Backbone of Targeted, Fixed-Duration Therapy in CLL
06 Dec 2025	BMS	Unlocking the Potential of CAR T: When and Why it Matters
07 Dec 2025	Johnson & Johnson	A Consideration for Patients with Relapsed or Refractory Multiple Myeloma
07 Dec 2025	Regeneron	A New BsAb Treatment for R/R Multiple Myeloma After 4 Prior Lines

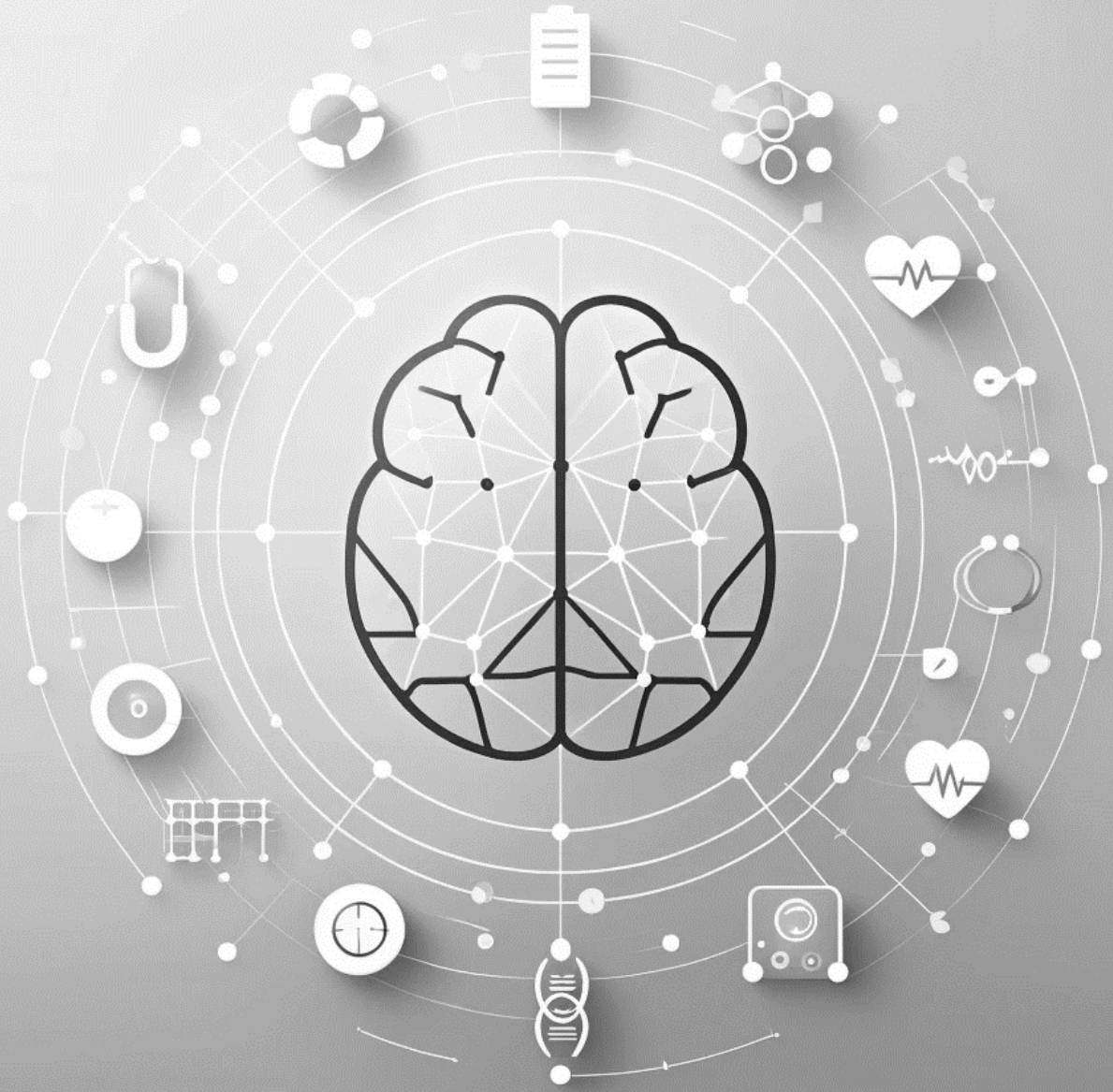
ASH 2025 Key Industry Sponsored Sessions Information (7/8)

Date	Sponsor	Title
07 Dec 2025	Pfizer	Advancing Care in RRMM: Clinical Evidence for a BCMA-Directed Bispecific Antibody Treatment Option (Program will begin with a patient's own story)
07 Dec 2025	Sanofi	Cablivi (caplacizumab-yhdp) Real-World Evidence in 1,000+ Patients: Early Initiation Matters
07 Dec 2025	GSK	A New Treatment Option in Multiple Myeloma
07 Dec 2025	Sanofi	Discover a New Way Forward with WAYRILZ
07 Dec 2025	Pfizer	Exploring a Subcutaneous Treatment Option in Hemophilia Care with HYMPAVZI (marstacimab-hncq)
07 Dec 2025	Johnson & Johnson	First-in-Class Treatment for Patients with Relapsed or Refractory Multiple Myeloma
07 Dec 2025	Genentech	Latest POLARIX Primary and 5-Year Outcomes Data
07 Dec 2025	GSK	A New Treatment Option in Multiple Myeloma

ASH 2025 Key Industry Sponsored Sessions Information (8/8)

Date	Sponsor	Title
07 Dec 2025	Eli Lilly and Company	Reignite the Spark: Clinical Conversations about Jaypirca (pirtobrutinib)
08 Dec 2025	Syndax Pharmaceuticals	Introducing a Therapeutic Option in Relapsed/Refractory Acute Leukemia
08 Dec 2025	Genmab and AbbVie	Unlocking the Potential for a Bispecific Antibody in 3L+ DLBCL and 3L+ FL
08 Dec 2025	Bristol Myers Squibb	First-Line Treatment Option for Anemia in Lower-Risk MDS COMMANDS Trial Overview
08 Dec 2025	Novartis Pharmaceuticals Corporation	From Innovation to Impact: Real Stories of Transformation in PNH Management
08 Dec 2025	Johnson & Johnson	Making the Case for Early Use of CAR-T Therapy in Multiple Myeloma
08 Dec 2025	Kura Oncology	Managing KOMZIFTI in Patients with R/R NPM1-m AML
08 Dec 2025	Incyte Corporation	MONJUVI + Rituximab & Lenalidomide: The First and Only CD19- and CD20-targeted Immunotherapy Combination Approved for 2L+ Follicular Lymphoma Patients

Noteworthy AI / ML presentations at ASH 2025



Themes from key AI / ML presentations at ASH 2025 (1/4)

- **ASH 2025 is expected to showcase how AI and machine learning will play a transformative role in hematology by enhancing diagnostic accuracy, personalizing treatment strategies, and improving risk prediction models, ultimately leading to more efficient and targeted patient care**
- Check out the key AI / ML themes at ASH 2025 below:
- **AI-Driven Personalized Treatment Approaches:**
  - AI/ML models will guide personalized treatment strategies, such as predicting treatment responses in AML, CLL, and myeloma, using a combination of transcriptomic, genomic, and clinical data
- **Gene Signature Identification in CML:**
  - The STIM2 trial (NCT01343173) identified a 48-gene signature with AUROC of 0.84, demonstrating predictive potential for treatment-free remission (TFR) in CML, offering insights into individualized care
- **Bleeding Risk Prediction in Cancer Patients:**
  - A multi-center cohort study will leverage ML models to predict bleeding risk in cancer patients using over 1,000 clinical features, achieving an 18-fold variation in bleeding rates across patient risk quintiles

Themes from key AI / ML presentations at ASH 2025 (2/4)

- **VTE Risk Prediction Using AI:**
  - A transformer-based AI/ML model developed on 80,808 cancer patients will predict venous thromboembolism (VTE) risk, showing improved identification of high-risk patients, with AUCs ranging from 0.68 to 0.77
- **Sickle Cell Disease Diagnosis via AI:**
  - SIGHT, an ML-based system, will enhance SCD diagnosis accuracy, achieving 99.3% accuracy in identifying SCD risk using CBC data, with SHAP analysis pinpointing MCHC as the primary predictor
- **AML Target Identification via ML:**
  - ML-guided drug discovery in AML will identify small molecules targeting mutant JAK2V617F HSCs, providing a selective treatment approach to reduce anemia risks, distinct from current therapies like ruxolitinib
- **Predicting AML Response Using AI:**
  - A deep learning (DL) model will analyze bone marrow images to predict IDH1 mutation status in AML patients, demonstrating AUROC values between 0.731 and 0.788, aiding in targeted therapy selection

Themes from key AI / ML presentations at ASH 2025 (3/4)

- **Predicting CAR-T Outcomes in LBCL:**
  - A machine learning model using serum metabolomics will predict CAR-T therapy response in relapsed/refractory LBCL with AUCs up to 0.99, enabling early intervention and reducing cytopenia risks
- **MDS Patient Risk Stratification via ML:**
  - ML models will predict leukemic transformation risk in MDS patients using RDW as a key biomarker, achieving AUCs from 0.75 to 0.81, and enabling early risk identification for personalized care
- **AI for AML Diagnosis and Prognosis:**
  - AI/ML models, combining multi-omics data, will classify MDS patients into 14 molecular clusters, enhancing disease understanding and providing predictive value for disease progression and treatment decisions
- **AML Survival Prediction Using AI:**
  - Bayesian network models will predict 5-year survival outcomes in AML, achieving AUC of 0.74, and integrate clinical variables for personalized treatment, improving patient-specific predictions

Themes from key AI / ML presentations at ASH 2025 (4/4)

- **Enhanced Hematology Diagnostics with AI:**
  - AI-based tools, like MobileNetV2 and YOLOv11, will improve blood cell classification and leukemia subtyping, achieving accuracy rates above 90%, streamlining hematologic diagnostics and reducing clinician workload
- **AI-Based Risk Prediction for SCD:**
  - Machine learning models will automate and improve the prediction of acute pain and CKD in SCD patients, achieving AUCs up to 0.98, and extending grading coverage to a greater patient population
- **AI-Enhanced Bone Marrow Diagnostics:**
  - The CIF AI model will assist in quantifying fibrosis severity and inter-rater agreement in bone marrow diagnostics, enhancing MPN diagnosis with strong performance metrics and reliable clinical application
- **AI for Predicting GVHD Post-Transplant:**
  - The GVHD-Intel 1.0 model will predict acute and chronic GVHD outcomes in hematopoietic stem cell transplant patients, achieving AUCs up to 0.83, offering real-time, scalable predictions

Noteworthy AI / ML presentations at ASH 2025

Notable Presentations At ASH 2025
AI / ML (1/20)

Date	Title	Author	Summary
6 Dec 2025	A machine learning approach identifies a transcriptomic signature predicting treatment-free remission in chronic myeloid leukemia	Vincent Alcazer	• **Introduction**: Treatment-free remission (TFR) is a key goal for chronic myeloid leukemia (CML) patients, yet 50% relapse post-therapy cessation. While certain factors influence TFR, no validated predictive score exists. The study aimed to predict TFR using transcriptomic data prior to imatinib (IMA) cessation. • **Methodology:** The STIM2 multicenter trial (NCT01343173) provided 96 patients with available pre-IMA cessation peripheral blood cell samples. Differential gene expression analysis using DESEQ2 and a machine learning approach identified genes associated with TFR success, splitting the cohort for training and testing. • **Results:** A gene signature with 48 stable genes demonstrated strong predictive power, with AUROC of 0.84 and 0.73 in the training and testing sets. Validation in external cohorts confirmed the signature's ability to distinguish TFR success. Multivariate analysis showed a significant association with TFR (aHR 0.32, p=0.008). • **Conclusions:** A transcriptomic signature was identified for predicting TFR in CML. Ongoing trials aim to validate and refine this approach for individual-level application.
6 Dec 2025	Dynamic machine Learning–Based prediction of major bleeding in patients receiving anticoagulant therapy: A multi-center study	Tamar Tadmor	• **Introduction**: Existing bleeding risk models fail to fully capture the complexity of modern treatments, particularly in high-risk populations like cancer patients. This study aimed to develop a machine learning (ML) model integrating over 1,000 clinical and laboratory features for more dynamic and individualized bleeding risk prediction. • **Methodology:** A retrospective, multi-center cohort study was conducted using electronic health records from six Israeli medical centers. The study included adult patients on anticoagulation, with major bleeding defined between days 91 and 455. Three ML models—logistic regression, random forest, and XGBoost—were evaluated, with performance assessed using AUC, sensitivity, specificity, and precision. • **Results:** Out of 163,596 patients, 7,705 experienced significant bleeding, with 2,503 major bleeds. Key predictors included cancer history, creatinine, hemoglobin, age, and anticoagulant class. The XGBoost model showed an AUC of 0.70, with risk stratification revealing an 18-fold difference in bleeding rates between lowest and highest risk quintiles. • **Conclusions:** The model provides an individualized risk tool, enabling targeted interventions for high-risk patients and reduced monitoring for low-risk individuals, potentially improving clinical management of anticoagulation therapy

Notable Presentations At ASH 2025
AI / ML (2/20)

Date	Title	Author	Summary
6 Dec 2025	Identification of small molecules that selectively target JAK2V617F driven cytokine-independent megakaryopoiesis by leveraging single cell RNA sequencing maps of myelofibrosis patients samples and a deep learning framework	Mauricio Cortes	• **Introduction**: Myelofibrosis (MF) driven by JAK2V617F mutations causes dysregulated hematopoiesis. Current treatments, like ruxolitinib, target both wild-type and mutant JAK2 but cause cytopenias. There's a need for therapies targeting mutant hematopoietic stem cells (HSCs). • **Methodology:** We built a transcriptomic map using patient data and iPSC models with JAK2V617F mutations. Single-cell RNA sequencing confirmed disease signatures. ML-guided drug discovery identified molecules targeting mutant HSCs. • **Results:** Lead compounds reduced PF4 and CD42+ progenitors in iHSC models, showing selectivity over normal erythropoiesis. These compounds did not bind JAK2 and displayed distinct transcriptional signatures from ruxolitinib. • **Conclusions:** ML and iPSC models identified small molecules that selectively target JAK2V617F HSCs, offering a promising therapeutic approach with reduced anemia risk.
6 Dec 2025	A deep learning model to dynamically predict cancer-associated thrombosis using electronic health records from the u.s. veterans affairs healthcare system	Tianshe He	• **Introduction**: Venous thromboembolism (VTE) is a major risk for cancer patients undergoing systemic therapy. Prophylactic anticoagulants can mitigate this risk, but real-time dynamic identification of high-risk patients is essential. AI/ML models can integrate complex patient data to improve VTE risk prediction. • **Methodology:** Using the Veterans Affairs healthcare system, we analyzed 80,808 cancer patients and developed a transformer-based AI/ML model. It used patient trajectories from diagnostic codes, laboratory results, and demographic data to predict VTE within one year of systemic treatment. The model was tested across four quarterly prediction windows. • **Results:** The model achieved AUCs of 0.68-0.77 for VTE prediction, with recall rates between 0.78-0.84. Compared to existing tools, the model significantly improved high-risk patient identification for months 6-12 post-treatment. • **Conclusions:** This transformer-based model effectively predicts VTE risk by leveraging time-dependent patient data, offering a dynamic approach to risk assessment.

Notable Presentations At ASH 2025
AI / ML (3/20)

Date	Title	Author	Summary
6 Dec 2025	Sight: Sickle cell identification from general hematological testing, a machine learning approach for rapid screening in emergency medicine	Jedrzej Konarkowski	• **Introduction**: Accurate identification of sickle cell disease (SCD) is crucial in emergency medicine, but challenges in EHR reliability and time constraints hinder diagnosis. We developed SIGHT, a machine learning (ML)-based system using complete blood count (CBC) data to identify SCD risk rapidly, addressing this diagnostic gap. • **Methodology:** Data from 8,069 CBCs were used to train an XGBoost-based ML model. The dataset, including 5.74% SCD cases, was split for training and testing. Features like RBC count and hemoglobin levels were used, and the model's performance was evaluated through various metrics, including accuracy, sensitivity, and F_1-score. • **Results:** SIGHT achieved 99.3% accuracy, 99.5% sensitivity, and 95.5% specificity. It correctly identified 84 SCD cases, with a low false positive rate (8) and false negatives (4). SHAP analysis highlighted MCHC as the most important predictor. • **Conclusions:** SIGHT offers high accuracy and reliability for SCD screening, especially in emergency settings. It provides transparent predictions and is a promising tool for identifying patients in need of further testing.
6 Dec 2025	Machine learning approach identifies targeting strategy for selective AML dependency	Enea Provenzano	• **Introduction**: Acute myeloid leukemia (AML) presents significant clinical challenges, with limited targeted therapies and poor outcomes. IRF2BP2 has been identified as a selective dependency in AML, suggesting a potential therapeutic window for targeting this protein. However, no specific inhibitors or degraders of IRF2BP2 are available due to its structure. • **Methodology:** Computational strategy combining machine learning and transcriptomic data to identify upstream regulators of IRF2BP2. Neural network models were trained on bulk RNA-seq data from AML samples to predict IRF2BP2 expression, identifying genes influencing its expression. Linear regression was used for validation, and integrative analysis prioritized robust regulators. • **Results:** IRS2 emerged as a key positive regulator of IRF2BP2 expression. Treatment with NT157, an IRS1/2 inhibitor, decreased IRF2BP2 expression and induced apoptosis in AML cells, confirming the model's predictions. • **Conclusions:** This machine learning-guided approach successfully identified regulators of IRF2BP2, offering a potential therapeutic strategy for targeting AML dependencies and advancing drug discovery for intractable targets.

Notable Presentations At ASH 2025
AI / ML (4/20)

Date	Title	Author	Summary
6 Dec 2025	Metabolomics profiling and machine learning prediction of efficacy and prolonged cytopenia in patients with large B-cell lymphoma undergoing CAR-T therapy	Hesong Zou	• **Introduction**: Achieving complete response (CR) within 3 months after CD19 CAR-T therapy is a key early indicator of prognosis in relapsed or refractory large B-cell lymphoma (R/R LBCL). However, there is no unified risk model to predict early treatment response, which could guide clinicians in selecting appropriate treatments and improving patient outcomes. • **Methodology:** Serum samples from 123 R/R LBCL patients were analyzed using untargeted metabolomic sequencing. Recursive feature elimination (RFE) and LASSO regression identified differential metabolites, and machine learning algorithms (Random Forest, Logistic Regression) were used to predict CR and the risk of prolonged cytopenia. • **Results:** Machine learning models predicted CR with high accuracy (RFE: AUC=0.99; Logistic Regression: AUC=0.82). The model was validated (RFE: AUC=1.00; Logistic Regression: AUC=0.84) and also predicted neutropenia and thrombocytopenia risks with AUCs of 0.694 and 0.754, respectively. • **Conclusions:** A serum metabolomics-based machine learning model effectively predicts early CAR-T response and prolonged cytopenia risk, enabling early interventions to improve patient outcomes.
6 Dec 2025	Identification of red cell distribution width as a key predictor of leukemic transformation in polycythemia vera and essential thrombocythemia: A machine learning approach involving 10,560 cases	Lior Rokach	• **Introduction**: Red blood cell distribution width (RDW) is an underutilized prognostic marker in diseases like AML. This study explores RDW as a predictor of leukemic transformation (LT) in patients with polycythemia vera (PV) and essential thrombocythemia (ET), focusing on its role in early risk stratification. • **Methodology:** Machine learning (ML) models were developed using clinical and laboratory data from discovery cohorts (Israel) and validated in Mayo Clinic cohorts. ROC analysis and Cox regression identified key predictors of LT, including RDW, age, and LDH levels. • **Results:** RDW >15.5 was a significant risk factor for LT in both PV and ET, with increased RDW correlating with higher HRs in both cohorts. The model achieved robust risk stratification, with AUCs ranging from 0.75 to 0.81. RDW remained a key independent prognostic factor. • **Conclusions:** Higher RDW is a strong, independent predictor of LT in PV and ET, suggesting it reflects long-term pre-leukemic clones or pro-leukemic inflammation, offering potential for early clinical intervention.

Notable Presentations At ASH 2025
AI / ML (5/20)

Date	Title	Author	Summary
6 Dec 2025	Machine learning uncovers invariant evolutionary molecular trajectories in MDS.	Matteo D'Addona	• **Introduction**: MDS (myelodysplastic syndromes) are genetically complex, making it challenging to use traditional prognostic models. This study applied machine learning (ML) to classify MDS into 14 molecular clusters (MCs), enabling better understanding of the disease's molecular underpinnings and progression dynamics. • **Methodology:** ML autoencoders were used to identify genetic similarities and classify MDS patients into MCs. The model was trained on 3588 patients and validated on an expanded cohort of 3810, including 320 patients studied serially. MCs were analyzed for transitions and progression dynamics. • **Results:** MCs exhibited distinct patterns of stability and transitions. MC13, associated with malignant progression, emerged as a key node, with 40% of progressive cases undergoing MC reassignment. In contrast, non-progressors showed limited MC shifts. MCs like MC2, associated with normal karyotype, frequently transitioned to higher-risk MCs (e.g., MC13, MC7). • **Conclusions:** This study identifies dynamic, non-random MC transitions that predict disease progression in MDS. Findings suggest that understanding MC evolution patterns could improve prognostic predictions and help identify high-risk patients earlier, guiding treatment decisions.
6 Dec 2025	Deep learning predicts IDH1 mutation status in Acute Myeloid Leukemia from bone marrow smear images	Andrew Srisuwananukorn	• **Introduction**: Acute myeloid leukemia (AML) is genetically heterogeneous, with IDH1 mutations occurring in ~8% of cases. IDH1 mutations lead to the accumulation of 2-hydroxyglutarate (2-HG), impairing differentiation and epigenetic regulation. Ivosidenib, a selective inhibitor of mutant IDH1, improves outcomes in IDH1-mutated AML. Identifying all IDH1-mutated cases is critical for prognosis and targeted therapy. • **Methodology:** A deep learning (DL) approach was used to analyze May-Gruenwald-Giemsa stained bone marrow smears from 86 IDH1-mutated and 60 wild-type AML patients. 40 tiles per slide were extracted to train eight convolutional neural networks (CNNs) for classifying IDH1 mutation status. • **Results:** The DL models achieved AUROC values between 0.731 and 0.788, with accuracy ranging from 0.728 to 0.774 and F1-scores between 0.676 and 0.741. These results demonstrate the feasibility of using image-based analysis to predict IDH1 mutations. • **Conclusions:** This study shows that deep learning can be used to predict IDH1 mutation status from bone marrow images, enabling digital screening for targetable mutations. Incorporating such tools into routine bone marrow microscopy could facilitate broader access to targeted therapies and improve patient outcomes.

Notable Presentations At ASH 2025
AI / ML (6/20)

Date	Title	Author	Summary
6 Dec 2025	Predicting CAR T-cell therapy outcomes in large B-cell lymphoma using pre-infusion clinical and inflammatory markers: A machine learning approach with explainable artificial intelligence	Cristiana Carniti	• **Introduction**: This study aims to develop machine learning (ML) models using real-world data to predict progression-free survival (PFS) based on clinical and inflammatory factors available at leukapheresis. • **Methodology:** Data from 1309 LBCL patients treated with anti-CD19 CAR T therapy were analyzed, with 779 included after exclusions. Five ML survival models were trained using 22 pre-leukapheresis clinical and inflammatory variables. Feature selection, hyperparameter tuning, and stratified cross-validation were performed, with SHAP used for explainability. • **Results:** Key predictors identified included LDH, bulky disease, hemoglobin, and prior autologous stem cell transplant. The Extra Survival Trees model achieved a C-index of 0.68 on training, cross-validation, and test sets. SHAP analysis confirmed known prognostic factors associated with poorer outcomes. External validation performance was lower (C-index = 0.55). • **Conclusions:** ML models based on routinely available pre-leukapheresis variables can predict PFS in LBCL patients undergoing CAR T therapy. The model is promising for clinical integration, offering real-time risk prediction with transparent SHAP-based explanations for personalized treatment planning.
6 Dec 2025	Field-level visual explanations for leukocyte classification using AI model: Enhancing interpretability in peripheral smear diagnostics	Manpreet Saini	• **Introduction**: AI's integration into hematopathology is limited by its lack of interpretability. This study presents a deep learning model for cell classification in peripheral smears that offers visual explanations, aligning decision-making with human diagnostic practices. • **Methodology:** A convolutional neural network (MobileNetV2 backbone) was developed to classify eosinophils, lymphocytes, monocytes, and neutrophils. The model was trained on 1,989 peripheral smear images. Three explainability techniques (Grad-CAM, LIME, Occlusion Sensitivity) were used to visualize key features influencing predictions. • **Results:** The model achieved 97% accuracy, with precision and recall above 92% for all classes. Lymphocytes and monocytes showed precision/recall >98%. Explainability methods identified clinically relevant features like nuclear architecture and granules, reinforcing model credibility. • **Conclusions:** This model provides high-performance, transparent cell classification, mimicking human visual logic. Its interpretability enables clinicians to confidently validate AI decisions, promoting safe clinical AI use. Future work will extend this framework to support early hematologic malignancy detection.

Notable Presentations At ASH 2025
AI / ML (7/20)

Date	Title	Author	Summary
6 Dec 2025	Supporting routine diagnostics: AI for interpretation of interphase FISH images	Dennis Bode	• **Introduction**: This study aims to develop an AI-based classifier for automating the interpretation of FISH images, improving efficiency and reducing the reliance on experienced personnel. • **Methodology:** A convolutional neural network (ResNet18) was trained to classify FISH images from four probes (1pq, 5pq, KMT2A, BCRABL) into normal and aberrant signal patterns. Data were collected from a large set of images, with training focused on the three dominant patterns. The model's performance was evaluated on a test set and quality measures were annotated for challenging images. • **Results:** Model achieved mean accuracy of 0.93 for 5pq, 0.92 for KMT2A, 0.88 for 1pq, and 0.83 for BCRABL. The classifier identified up to 84% of the data for 5pq and 77% for BCRABL. Imperfect signal characteristics led to higher error rates, especially for challenging images. • **Conclusions:** The AI classifier showed high accuracy, automating up to 77% of cell image classifications for 5pq. However, images with low quality or incomplete signal patterns still require manual review. Expanding the dataset with new labeled images will enhance performance and reduce manual intervention, speeding up diagnostic workflows.
6 Dec 2025	Automatic identification of blast leukemic cells types using deep learning with vision transformers.	Adriana Bornacelly	• **Introduction**: AML and ALL diagnosis in Colombia faces delays, impacting outcomes. AI models, particularly vision transformers, can aid diagnosis by differentiating myeloblasts from lymphoblasts. • **Methodology:** This study used bone marrow smears from 48 leukemia cases, trained five AI models (including ConvNeXt and Swin Transformer) for differentiation and APL classification. • **Results:** The ConvNeXt Small model achieved 99.67% sensitivity, 98.58% specificity, and an AUC-ROC of 0.998 for differentiating myeloblasts and lymphoblasts. ConvNeXt Large performed moderately for APL with 64.58% accuracy. • **Conclusions:** Vision transformers effectively differentiate myeloblasts and lymphoblasts, providing a promising diagnostic tool. Further validation is needed for clinical implementation

Notable Presentations At ASH 2025
AI / ML (8/20)

Date	Title	Author	Summary
6 Dec 2025	Deep learning-based image analysis of pretreatment FDG-PET/CT predicts CAR-T cell treatment outcome at month-12 for patients with Relapsed/Refractory large B-cell lymphomas	Stephen Schuster	• **Introduction**: This study builds on previous work using deep learning (DL) to predict CAR-T therapy outcomes in relapsed/refractory large B-cell lymphoma (r/r LBCL) patients. It compares DL-based image analysis from pre-treatment FDG-PET and low-dose CT (LD-CT) images with traditional prognostic markers, such as serum LDH and secondary International Prognostic Index (sIPI). • **Methodology:** Pre-infusion images from 102 patients treated with tisagenlecleucel were analyzed using DL models to predict treatment response at 12 months. Lesion-level predictions were aggregated using rule-based reasoning. Actual outcomes were then compared to DL predictions. • **Results:** DL-based predictions for responders (CR) showed 77% sensitivity and 51% specificity, with balanced accuracy of 64%. Compared to serum LDH and sIPI, DL-based predictions demonstrated more consistent results, though LDH had high sensitivity and low specificity. • **Conclusions:** DL-based image analysis for predicting CAR-T outcomes is feasible and performs similarly to traditional methods. With further refinement, this approach could provide valuable pre-treatment insights for optimizing CAR-T therapy.
7 Dec 2025	Machine learning-based novel surfaceome classification system for acute myeloid leukemia	Heye Yu	• **Introduction**: This study aims to enhance AML immunophenotyping through machine learning-based surfaceome profiling, using multi-omics data for a comprehensive classification system. • **Methodology:** Surface proteins from 124 AML patient samples were analyzed via LC-MS/MS, complemented by multi-omics data (transcriptomics, proteomics, metabolomics) from 79 patients. Non-negative matrix factorization (NMF) and linear discriminant analysis (LDA) were used for clustering and classification, while multi-omics factor analysis (MOFA) integrated datasets. • **Results:** 2,764 membrane proteins were identified, with surfaceome profiling aligning well with traditional flow cytometry. Seven distinct surfaceome subgroups were identified, with machine learning achieving 95.97% classification accuracy. Subgroups showed partial overlap with genetic classifications, revealing differentiation blocks and metabolic characteristics specific to each subgroup. • **Conclusions:** A machine learning-based surfaceome classification system provides a more comprehensive AML immunophenotyping method, offering insights into genetic, differentiation, and metabolic factors driving AML heterogeneity. This framework could enhance personalized treatment approaches.

Notable Presentations At ASH 2025
AI / ML (9/20)

Date	Title	Author	Summary
7 Dec 2025	Comparative performance of clinical versus genomic machine learning prognostic models in AML: A prisma-guided systematic review and meta-analysis	Xiaoyi Zhang	• **Introduction**: AI-based models are increasingly used to predict prognosis in AML, but their real-world performance and the value of genomics over clinical data remain unclear. This study provides a meta-analysis of AI prognostic models for overall and relapse-free survival in AML. • **Methodology:** We analyzed 24 studies involving 137 model cohorts and 51,055 patients, pooling AUCs from independent validation cohorts. Discrimination was assessed at 1, 2, 3, and 5 years, and model optimism was quantified by the AUC difference between development and validation datasets. • **Results:** Overall AUC for independent validation cohorts was 0.769, improving with longer prognostic horizons. Gene-centric models showed no significant improvement over non-genetic models (ΔAUC 0.035, p=0.085). Optimism averaged 0.052, with higher optimism observed for 5-year models. • **Conclusions:** Externally validated AML ML models perform well overall, with strongest results at 5 years. Clinical and laboratory models offer comparable performance to gene-centric models and should be used as initial tools, with genomics added where possible. Local validation is essential for effective implementation.
7 Dec 2025	Machine learning-powered integration of global proteomics and ex vivo sensitivity unveils a protein signature predictive of treatment success to AML therapy: Validation in patients treated with FHD-286, a SMARCA2/4 dual inhibitor	James Sorrentino	• **Introduction**: AML has a poor prognosis, with limited therapeutic progress. A major hurdle is the lack of accurate models to predict patient responses. This study uses deep learning to integrate proteomics, clinical data, and ex-vivo sensitivity to create a personalized therapeutic response model for AML. • **Methodology:** Proteomics from 200 AML patient samples and over 90 patient-derived cell lines were analyzed. The dataset, comprising >9,000 proteins and >5,000 drug assays, was integrated using deep learning and transfer learning from publicly available datasets to develop a generalizable AML therapeutic sensitivity model. • **Results:** The model successfully identified patient subpopulations based on proteomic signatures and therapeutic sensitivity. A 5-protein biomarker signature predicted clinical response to FHD-286, an investigational SMARCA2/4 dual inhibitor, with 100% accuracy in a small cohort of 7 patients. • **Conclusions:** This AI-driven model shows potential in personalizing AML treatment by predicting therapeutic responses, supporting the development of a mass spectrometry-based clinical assay for patient selection in clinical trials.

Notable Presentations At ASH 2025
AI / ML (10/20)

Date	Title	Author	Summary
7 Dec 2025	Machine learning models improve survival prediction in DLBCL: Analysis from the goya trial	Shuna Yao	• **Introduction**: The International Prognostic Index (IPI) is widely used for risk stratification in DLBCL, but its predictive accuracy is limited in the immunochemotherapy era. This study develops machine learning (ML) models integrating clinical, laboratory, imaging, and immunohistochemical data to predict overall survival (OS) in newly diagnosed DLBCL patients. • **Methodology:** Data from 1,166 patients in the GOYA trial were analyzed, incorporating clinical, laboratory, imaging, and immunohistochemical variables. ML models (Cox, random survival forest, XGBoost) were trained and evaluated using cross-validation and Harrell's C-index. Risk stratification was performed using the RSF model and cumulative hazard function. • **Results:** The RSF model outperformed other models with AUCs of 0.78, 0.71, and 0.72 for 1-, 2-, and 3-year OS prediction. SHAP and variable importance analyses identified albumin, LDH, SPD, and age as key predictors. RSF stratified patients into low, medium, and high-risk groups, with distinct OS rates. • **Conclusions:** ML models, especially RSF, improve OS prediction and risk stratification beyond IPI, with albumin, LDH, SPD, and age as key prognostic factors. These findings support integrating ML into individualized treatment planning for DLBCL.
7 Dec 2025	Machine learning-based classification of chronic lymphocytic leukemia signalotypes to allows biological and clinical insights into novel CLL subgroups	Alexander Egle	• **Introduction**: CLL's mutational landscape is shaped by genetic alterations and interactions with the microenvironment, influencing disease progression and treatment response. Signaling patterns derived from RNA expression can provide insights into these interactions, offering potential for improving prognostic accuracy and tailoring therapies. • **Methodology:** RNA-seq data from 661 chemo-naïve CLL patients, applying a custom bioinformatics pipeline to define "signalotypes" based on unique pathway activation profiles. Machine learning algorithms were used to classify CLL samples from our biobank into these clusters. We conducted in vitro drug toxicity screens to assess therapeutic responses. • **Results:** 11 distinct signalotypes, each with unique signaling and metabolic profiles, linked to clinical outcomes such as time to treatment and survival. Machine learning models classified 101 patient samples accurately, and drug screens revealed heterogeneity in response, with some agents, like Venetoclax, showing broad efficacy, while others had more selective activity. • **Conclusions:** RNA-derived signaling patterns can stratify CLL patients into biologically distinct subgroups, enabling personalized treatment strategies. Machine learning enhances patient classification and identifies core molecular features, while drug screening highlights significant variability in therapeutic responses across CLL subgroups.

Notable Presentations At ASH 2025
AI / ML (11/20)

Date	Title	Author	Summary
7 Dec 2025	Bayesian machine learning, medical history, and predictive models for early diagnosis of systemic light chain amyloidosis	Anita D'Souza	• **Introduction**: AL diagnosis is often delayed due to nonspecific symptoms. This study aims to identify clinical diagnoses preceding AL in MGUS+ patients to inform early detection strategies, using machine learning on Medicare claims data. • **Methodology:** Analyzed data from 8,681 MGUS+ patients, tracking pre- and post-diagnosis incidents for up to 5 years. BART, a machine learning method, was used to model time-to-event data, integrating red flag diagnoses and sociodemographics to predict AL progression. • **Results:** The strongest predictors of AL progression were nephrotic syndrome, cardiomyopathy, pleural effusion, and proteinuria. Age and race were significant sociodemographic factors. The model showed good performance (Harrell's C-index = 0.73). • **Conclusions:** Machine learning models can detect early patterns leading to AL in high-risk MGUS+ patients, enabling earlier intervention and potential integration into clinical practice for better outcomes.
7 Dec 2025	GVHD intel 1.0: A scalable, HLA-enhanced machine learning model for predicting acute and chronic GVHD	Naveed Syed	• **Introduction**: Graft-versus-host disease (GVHD) remains a leading cause of morbidity and mortality in allo-HSCT recipients. Existing clinical scoring systems have modest predictive power for GVHD. GVHD-Intel 1.0 is a machine learning (ML) framework developed to predict both acute (aGVHD) and chronic GVHD (cGVHD), offering real-time and scalable predictions. • **Methodology:** This retrospective study analyzed electronic health records from two centers (UAE and KHCC). The model was trained on 399 patients and validated on independent cohorts (46 and 150 patients). Key variables included donor type, disease status, HLA alleles, and conditioning agents. SHAP and LIME were used for interpretability. • **Results:** GVHD-Intel 1.0 demonstrated strong predictive performance: AUC of 0.832 for cGVHD and 0.802 for aGVHD. Metrics included high accuracy (82.7% for cGVHD, 77.6% for aGVHD), F1 scores (0.896 and 0.860), and sensitivity (0.864 and 0.799). Calibration was strong across tasks. • **Conclusions:** GVHD-Intel 1.0 outperforms conventional clinical risk scores in predicting both acute and chronic GVHD, offering a robust and interpretable tool for clinicians. Prospective validation and further refinement are planned to expand its clinical utility.

Notable Presentations At ASH 2025
AI / ML (12/20)

Date	Title	Author	Summary
7 Dec 2025	Code red (Código Rojo): Multimodal generative AI for specialized hematology education	Adrian Mosquera	• **Introduction**: Advances in artificial intelligence, particularly in Natural Language Processing (NLP) via Large Language Models (LLMs), are revolutionizing medical education. These systems, when supervised by experts, can enhance clinical understanding and support continuous professional development in hematology. • **Methodology:** CodeRed AI assistants were developed by physician teams and trained on curated, validated medical texts. These systems use retrieval-augmented generation (RAG) with OpenAI's GPT-4 and support multimodal inputs. Feedback mechanisms allow real-time updates by a medical oversight group. • **Results:** By mid-2025, CodeRed will host 230 assistants, with 22 focused on hematology, including both malignant (e.g., leukemias, lymphomas) and benign conditions (e.g., hemophilia, anemia). The platform has registered 273,831 visits, with users from multiple countries, demonstrating its global reach. • **Conclusions:** CodeRed is a pioneering multimodal AI platform for clinical education, showing promise in hematology training. Ongoing benchmarking and future improvements will enhance its reliability and clinical relevance across specialties.
7 Dec 2025	Toward precision pathology: Deep learning supported fibrosis grading augments performance of international hematopathologists in a large real-world cohort	Timothy Ebsworth	• **Introduction**: Accurate bone marrow fibrosis evaluation is crucial in diagnosing and monitoring myeloproliferative neoplasms (MPNs). The AI-based Continuous Indexing of Fibrosis (CIF) model quantifies fibrosis severity and heterogeneity, offering a robust tool for MPN diagnosis and progression detection. • **Methodology:** CIF was applied to 1,000 bone marrow trephine (BMT) samples from Oxford University Hospitals NHS Foundation Trust. A panel of 14 international hematopathologists graded the fibrosis, with and without CIF heatmap overlays, assessing intra- and inter-observer variability. • **Results:** CIF mapped fibrosis scores across all diagnoses, showing a significant improvement in inter-rater agreement with CIF support (Cohen's kappa increased from 0.51-0.84 to 0.60-0.84). Consensus on fibrosis grade improved, with pathologists' grading aligning more closely with expert consensus. • **Conclusions:** CIF successfully quantifies fibrosis in clinical settings, enhancing grading accuracy and consistency. These findings highlight the limitations of manual grading and lay the groundwork for CIF's integration into routine diagnostics, improving precision in MPN care.

Notable Presentations At ASH 2025
AI / ML (13/20)

Date	Title	Author	Summary
7 Dec 2025	Early identification of patients likely to benefit from paroxysmal nocturnal hemoglobinuria workup using machine learning on large-scale real-world data.	Sandeep Jain	• **Introduction**: Paroxysmal Nocturnal Hemoglobinuria (PNH) is a rare hematologic disorder often diagnosed late after severe events like strokes. Early identification could reduce disease burden, but diagnostic delays persist. This study explores machine learning (ML) for earlier PNH diagnosis based on clinical data, potentially improving diagnostic efficiency. • **Methodology:** Using the Atropos Health Aracadia dataset (416K patients), we developed an XGBoost model to predict PNH diagnosis within 3-12 months after an initial hemoglobin (Hb) measurement. Clinical features were derived from a 24-month lookback period. The model aimed to maximize precision, recall, and clinical relevance. • **Results:** The model identified 306 PNH cases, achieving an AUPRC of 0.09 and AUROC of 0.77. Key features included anemia history, disease burden, age, haptoglobin levels, and MDS diagnosis. Clinical review confirmed that 75-90% of false positives warranted further workup. • **Conclusions:** This ML model demonstrates potential for identifying patients requiring PNH workup, reducing diagnostic delays. Thresholds for further workup should be tested locally, considering lab variability. This approach could enhance early PNH detection and patient outcomes.
7 Dec 2025	Machine learning using bayesian networks to predict response in patients with newly diagnosed Acute Myeloid Leukemia	Onyee Chan	• **Introduction**: AML's complex genetic and clinical features lead to variable treatment responses. Current risk stratification systems lack patient-specific predictions. This study develops a Bayesian network model to predict the probability of achieving response after frontline AML therapy. • **Methodology:** A retrospective cohort of AML patients treated at Moffitt Cancer Center was used. The model incorporated 55 features (demographics, pathology, lab results) and selected key variables through Random Forest and expert input. Bayesian networks were trained on 80% of the data, with performance assessed using AUC and cross-validation. • **Results:** The model retained 10 key features (age, cytogenetic risk, mutations in NPM1, IDH1/2, RUNX1, TP53). It achieved an AUC of 0.74 and 70% accuracy in predicting response. The Bayesian network provided interpretable pathways and showed strong calibration between predicted and observed outcomes. • **Conclusions:** Bayesian networks offer an interpretable and accurate method for predicting AML treatment response, enabling personalized treatment strategies. Future work will focus on external validation and expanding the model to include MRD and longitudinal data.

Notable Presentations At ASH 2025
AI / ML (14/20)

Date	Title	Author	Summary
7 Dec 2025	Temporal external validation of an individuals machine learning clinical decision support prediction tool for hematopoietic cell transplantation for sickle cell disease	Rajagopal Chandrashekhar	• **Introduction**: Hematopoietic cell transplantation (HCT) for sickle cell disease (SCD) offers excellent outcomes, but inter-patient variability complicates decision-making. The SPRIGHT model, a machine learning tool for predicting HCT outcomes in SCD, has shown promise but requires external validation to ensure reliability and generalizability. • **Methodology:** We implemented the SPRIGHT model on a web-based platform using Gradio and deployed it on Hugging Face. This platform allows users to input data and obtain performance metrics, facilitating external validation. Temporal validation was performed using an independent cohort from 2021-2023, assessing outcomes like OS, EFS, and graft failure. • **Results:** Initial external validation showed moderate performance with AUCs ranging from 0.63 to 0.66. Data drift was identified, particularly in donor types post-2020, impacting model performance. After retraining with updated data, AUCs improved (up to 0.76 for EFS), demonstrating the model's adaptability to evolving patient populations. • **Conclusions:** Browser-based validation framework enhances model accessibility and scalability. SPRIGHT maintained solid performance post-retraining, reinforcing the need for continuous model monitoring and updates to maintain clinical utility across diverse patient populations.
8 Dec 2025	Machine learning-based body composition analysis for risk stratification in newly diagnosed diffuse large B cell lymphoma	Fabian Ullrich	• **Introduction**: Frailty, commonly observed in diffuse large B-cell lymphoma (DLBCL) patients, is a significant prognostic factor. However, its measurement is inconsistent. Body composition analysis (BCA) using routine clinical imaging offers a promising method for evaluating frailty and enhancing risk stratification in DLBCL. • **Methodology:** The study used the Body and Organ Analysis (BOA) pipeline to calculate sarcopenia index (SI) and visceral fat index (VFI) from CT data in 291 DLBCL patients from the PETAL trial. Multivariable Cox regression and machine learning models incorporating SI, VFI, and clinical features were used to predict overall survival (OS). • **Results:** Low baseline SI was associated with significantly shorter OS ($p = 0.002$). A greater decrease in SI during treatment was linked to poorer outcomes ($p = 0.0007$). Machine learning identified a low-risk group with 100% 5-year OS among iPET-negative patients. SI was confirmed as an independent prognostic factor for OS (HR 0.38, $p = 0.01$). • **Conclusions:** Sarcopenia, identified through BCA, is a key independent prognostic factor in DLBCL. Combining BCA with clinical parameters improves risk stratification, and machine learning methods can support routine clinical decision-making in DLBCL management.

Notable Presentations At ASH 2025
AI / ML (15/20)

Date	Title	Author	Summary
8 Dec 2025	Machine learning replicates and extends clinician-informed disease severity grading classification for acute pain and CKD in sickle cell disease	Minzhang Zheng	• **Introduction**: The Sickle Cell Organ Grading System (SCOGS) was developed to standardize grading, but missing data often limits its use. This study explores machine learning (ML) to replicate clinician-assigned grades and impute missing ones. • **Methodology:** Random forest classifiers were trained using longitudinal SCCRIP data, including labs, medications, and quality of life scores. Models for acute pain and CKD were evaluated using cross-validation, with performance assessed by AUC. Feature importance was analyzed using SHAP. • **Results:** ML models achieved high accuracy (AUC 0.97 for pain, 0.98 for CKD). For pain, key predictors included hemoglobin, age, and BMI. For CKD, features included creatinine, transfusion exposure, and treatment history. Model-based imputation increased CKD grading coverage from 21% to 90%. • **Conclusions:** ML accurately predicts SCOGS grades and extends grading to more patients. This approach improves structured phenotyping and can support scalable, individualized care for SCD, though further validation is needed before clinical implementation.
8 Dec 2025	Integrated machine learning analysis for automatic recognition of b-ALL MRD level in flow cytometry list mode data	Yu-Fen Wang	• **Introduction**: Minimal residual disease (MRD) detection via flow cytometry is crucial in B-acute lymphoblastic leukemia (B-ALL) but requires expert interpretation to differentiate normal cells from leukemic ones. This study presents a machine learning pipeline to automate MRD classification, improving accuracy and efficiency. • **Methodology:** Data from 772 bone marrow samples were collected and classified by experts. A hierarchical cell-level model was trained using cell annotations to filter out irrelevant populations, followed by a sample-level model using GMM-SVM frameworks for MRD classification. Expert review and model validation were conducted. • **Results:** Cell-level models showed excellent performance, with AUCs of 99.96% for lymphocyte classification and 99.94% for immature B cell differentiation. Sample-level MRD classification achieved AUCs of 94.06% and 86.40% accuracy with optimal preprocessing, significantly improving classification performance. • **Conclusions:** The integrated machine learning approach automates B-ALL MRD analysis with high accuracy. The creation of an interactive tool for reviewing discordant cases further enhances the model's utility and potential for improving clinical decision-making.

Notable Presentations At ASH 2025
AI / ML (16/20)

Date	Title	Author	Summary
8 Dec 2025	Sparse whole genome sequencing and machine learning of AML genomes reveals novel, clinically relevant genetics.	Yanming Zhang	• **Introduction**: Copy Number Alterations (CNAs) significantly impact the genetics and clinical management of acute myeloid leukemia (AML), especially in complex karyotypes. This study uses low-coverage whole genome sequencing and machine learning to explore CNAs in over 600 AML samples, revealing new genetic, biological, and clinical correlations. • **Methodology:** Sparse whole genome sequencing and machine learning, including Cox-regression and Non-negative Matrix Factorization (NMF), were applied to identify novel genetic alterations linked to clinical outcomes. These techniques were validated with data from ECOG-ARCIN trials. • **Results:** Focal deletions at 17q, 21q, and 3p were linked to inferior survival, while amplifications at 11q23 also indicated poor prognosis. The model identified cryptic variations such as 5q deletions and chromosome 8 gain. A prognostic classifier based on three genomic features demonstrated high accuracy in predicting disease outcomes. • **Conclusions:** Combining low-coverage sequencing with machine learning can enhance AML diagnosis and management. The findings support a novel approach to understanding CNAs and offer potential for clinical implementation in patient risk stratification.
8 Dec 2025	A multi-center study of a machine learning algorithm for identifying undiagnosed patients with myelodysplastic syndrome based on complete blood count data	Marek Dudziński	• **Introduction**: Myelodysplastic syndromes (MDS) are often asymptomatic in early stages, detected through subtle CBC abnormalities. This study aimed to develop a machine learning (ML) algorithm to identify high-risk MDS patients using only CBC data. • **Methodology:** Anonymized EHR data from 32,850 patients were used to develop a one-class classification model with 13 CBC features. The model was trained with 80% of the dataset and tested with 20%. Kolmogorov-Smirnov test selected differential features, with performance evaluated using recall, specificity, precision, F1 score, AUPRC, and AUROC. • **Results:** The model showed recall of 77.74%, specificity 93.08%, and AUROC of 94.66%. Deployed in four medical centers, it flagged 95 high-risk MDS patients, leading to 8 new diagnoses. The model identified patients already under evaluation or diagnosed, demonstrating strong detection potential. • **Conclusions:** This study validates the practical application of an ML algorithm for identifying high-risk MDS patients based on CBC data. Future work will enhance exclusion criteria and expand data usage for real-time integration, optimizing diagnostic alerts.

Notable Presentations At ASH 2025
AI / ML (17/20)

Date	Title	Author	Summary
8 Dec 2025	Evaluating the impact of stem cell transplantation in myelodysplastic syndrome using machine learning and comparative modeling	Ziyi Li	• **Introduction**: MDS patients typically experience poor survival outcomes, with SCT offering a potential survival benefit, but its risks complicate decision-making. Current models like IPSS-R lack personalized predictions. This study applies machine learning (ML) to improve survival prediction for MDS patients and enhance decision-making between HMA and SCT. • **Methodology:** Cox proportional hazards and ML models (RSF, GBM, XGBoost, SL) were trained on 814 SCT-naïve patients. Covariates included age, blood counts, cytogenetic risk, and gene mutations. Models were validated on separate cohorts: 555 SCT patients and 300 SCT-naïve patients. • **Results:** ML models outperformed Cox for SCT-naïve patients (C-index 0.81), while performance was lower in SCT patients (C-index 0.68–0.70). Key factors influencing SCT response included hemoglobin, age, platelet count, and cytogenetic risk. • **Conclusions:** ML models provide better survival predictions and highlight key variables for SCT response, supporting personalized treatment strategies. Further research is needed for improved SCT patient selection.
8 Dec 2025	Modeling discordant cardiac and renal recovery trajectories in AL amyloidosis using interpretable machine learning	John Hanna	• **Introduction**: In AL amyloidosis, discordance between hematologic remission and organ response is common but poorly understood. This study aims to identify predictors of discordant responses in patients achieving VGPR or better, comparing machine learning (ML) to logistic regression (LR) models for organ recovery prediction. • **Methodology:** A cohort of 376 AL amyloidosis patients was analyzed, with cardiac and renal responses assessed at 6, 12, 18, and 24 months. ML models, including XGBoost, were compared to LR models using 37 baseline variables. SHAP values helped interpret feature importance. • **Results:** Discordance was observed in 35.2% (cardiac) and 31.1% (renal) of patients at 6 months. ML outperformed LR, with XGBoost achieving higher accuracy (AUC 0.83 vs. 0.61 for cardiac response at 6 months). Key predictors of discordance included neuropathy, male sex, and hospitalization. • **Conclusions:** ML models outperform LR in predicting organ responses, highlighting key clinical factors for discordance. These models can inform personalized treatment strategies and improve early recognition of at-risk patients.

Notable Presentations At ASH 2025
AI / ML (18/20)

Date	Title	Author	Summary
8 Dec 2025	Machine learning uncovers prognostically distinct myeloma cast nephropathy phenotypes not captured by standard risk stratification systems	Michael Hughes	• **Introduction**: Myeloma cast nephropathy (MCN) remains a significant cause of renal failure in newly diagnosed multiple myeloma (NDMM). This study aims to apply machine learning (ML) to identify latent MCN phenotypes and improve risk stratification based on real-world NDMM data. • **Methodology:** Analyzed 332 patients (59 with MCN and 273 controls) using autoencoders, UMAP, and clustering techniques to generate compressed latent representations. ML models were trained to predict survival outcomes and uncover MCN-related risk phenotypes. • **Results:** Six clusters were identified, with two MCN-enriched phenotypes showing differing survival outcomes. ML-based survival stratification was superior to traditional risk models. The "high-risk MCN" group had significantly worse survival. • **Conclusions:** This study highlights ML's potential in detecting MCN-related heterogeneity and stratifying survival risk, offering insights into personalized treatment strategies for NDMM.
8 Dec 2025	Machine learning accurately predicts mortality in adult NPM1-mutant Acute Myeloid Leukemia using baseline clinical and genomic features	Rahul Thakur	• **Introduction**: Nucleophosmin 1-mutated (NPM1m) AML, while generally considered favorable risk, shows significant clinical heterogeneity. We developed baseline-only machine learning (ML) models to predict early death (ED) and treatment outcomes in NPM1m patients. • **Methodology:** Analyzed 207 patients treated at Roswell Park Cancer Center from 2006–2025. Baseline features included demographics, lab values, co-mutations, and treatment regimen. We compared Cox regression with machine learning models (Random Survival Forest, XGBoost) for survival prediction. • **Results:** ML models outperformed Cox models, with the highest performance for predicting 5-year overall survival (AUC 0.79). Key predictive factors included age, WBC, performance status, and co-mutations (e.g., FLT3-ITD, DNMT3A). • **Conclusions:** ML models accurately predict individual survival in NPM1m AML, with implications for personalized treatment strategies.

Notable Presentations At ASH 2025
AI / ML (19/20)

Date	Title	Author	Summary
8 Dec 2025	Automated AI classification in clinical flow cytometry: Transforming B-cell lymphoma diagnostics	Chrysanthi Tsamadou	• **Introduction**: Flow cytometry (FC) is essential for hematological diagnostics but is resource-intensive. The integration of AI in FC data analysis can enhance efficiency. This study develops an AI model to classify B-cell lymphoma (B-NHL) and its subtypes with high accuracy. • **Methodology:** An XGBoost-based model was trained on FC data from 12,015 cases (5,015 B-NHL, 7,000 non-B-NHL). The model performed binary classification (B-NHL vs. non-B-NHL) and subtype identification. Automated visualization tools were also developed. • **Results:** The model achieved 99.3% accuracy for B-NHL detection and 98.7% for subclassification. Performance was consistent with new data, with 98.7% accuracy in routine settings. • **Conclusions:** The AI model shows exceptional performance and can be integrated into routine operations, reducing hands-on time by 75%. This approach supports further applications like minimal residual disease detection.
8 Dec 2025	Machine learning–based detection model for leukemia cells in peripheral blood smears using YOLOv11-large	Johan Diaz	• **Introduction**: Manual blood cell identification for hematological diseases is labor-intensive and prone to variability. Despite advances, automated analysis remains challenging due to variations in cell size, frequency, and imaging conditions. This study evaluates the efficacy of a YOLOv11-large model with spatial attention for simultaneous localization and classification of 13 white blood cell subtypes. • **Methodology:** The model was trained on 18,664 annotated images from the LeukemiaAttri dataset, expanded to 65,785 images through augmentation. YOLOv11l was fine-tuned for 250 epochs on a NVIDIA H200 SXM GPU. • **Results:** The model achieved 93.6% precision, 89.2% recall, and 93.8% mAP50. It showed excellent classification and localization across subtypes. • **Conclusions:** The YOLOv11l model demonstrated strong performance, offering a potential tool for hematology platforms to streamline blood cell analysis.

Notable Presentations At ASH 2025
AI / ML (20/20)

Date	Title	Author	Summary
8 Dec 2025	Automated subtype classification of acute leukemia from bone marrow smears using a cross-platform deep learning model	Guangqi Wang	• **Introduction**: Accurate morphological classification of acute leukemia (AL) subtypes from bone marrow smears (BMS) is crucial for guiding clinical decisions. Manual evaluation is labor-intensive and dependent on expert interpretation. To address this, we developed ALSNet, a deep learning model for automated, robust AL subtyping using region-of-interest images from BMSs. • **Methodology:** 1,232 digitized BMSs were collected and preprocessed using a human-in-the-loop framework. A Mask R-CNN network segmented cells, and a ResNeXt-based deep learning model (ALSNet) was trained for cell classification and AL subtyping, validated on a separate testing cohort. • **Results:** ALSNet achieved a macro-averaged accuracy of 0.912 in cell-level classification and 0.75 in case-level AL subtyping, demonstrating high accuracy and cross-platform robustness. • **Conclusions:** ALSNet offers a promising AI solution for automated leukemia subtyping, with strong real-world applicability in hematologic diagnostics.
8 Dec 2025	Clinical and technological validation of locally-installed, privacy-compliant, and hematology-tailored ambient AI platform for clinical report transcription assistance and clinical trial patient management	Mattia Delleani	• **Introduction**: Effective clinician-patient communication is essential in hematology for personalized treatment, but traditional practices are time-consuming and lack focus on patient-reported outcomes. Current AI-based solutions are costly, not specialized, and pose privacy concerns. To address this, we developed Ambient AI, a hematology-tailored platform to support medical documentation, optimize patient enrollment, and improve clinical trial management. • **Methodology:** Ambient AI records and transcribes clinician-patient conversations in real-time, extracts clinical data, and generates structured medical reports. It uses local AI models and open-source LLMs fine-tuned for hematology. The validation framework includes technological performance, clinical fidelity, and physician satisfaction. • **Results:** Preliminary analysis of 100 simulated reports showed high transcription accuracy (JS 0.85), with AI-generated reports needing minimal edits. The platform improved workflow efficiency and patient engagement, with early validation at Humanitas Research Hospital showing increased physician satisfaction. • **Conclusions:** Ambient AI enhances hematology workflows by improving communication, streamlining documentation, and integrating PROs. It supports patient selection and clinical trial management, facilitating precision medicine.

Strategic Insights and Strategy Development is our focus