The 21St Annual INDY HEMATOLOGY REVIEW® State of the Art 2024: Emerging Therapies in Hematologic Malignancies and Disorders

Ruemu Ejedafeta Birhiray, MD

Program Chair

CEO, Indy Hematology Education, Inc.,

Partner, Hematology Oncology of Indiana, American Oncology Network, PA, Indianapolis, IN

Clinical Professor of Medicine,

Marian University College of Medicine, Indianapolis, IN

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Acute Myeloid Leukemia

- **Acute Promyelocytic Leukemia:**
  - **APL: All-ORAL REGIMEN: Arsenic Trioxide/ATRA/Ascorbic Acid: Induction in ND-APL:** Phase II, N=125, Risk/Age-adapted for high-risk and age <65, DNR 50mg/M2 x 3, AAA alone (N=90), AAA+DNR (N=24): 3-yr OS: 97%; 3-yr RFS: 97%, 1 relapse/death from refractory APL, 1 death in CR1 unrelated to treatment. 7 deaths at presentation before induction
  - ORR at EoT: 95%; CR rate at EoT: 91% (primary endpoint), CR as best response: 99%, 12-mo/18-mo PFS: 100% and 97%, respectively (median f/u: 16.5 mo), 3-yr RFS: 97.9%, 3 yr-OS 99.1%, 1 relapse with PML B2 domain A216V mutation
- **MENIN/KMT2A INHIBITORS for KMT2Ar AML/ALL: Poor prognosis, <5% CR, mOS ~2.4mos**
- **AUGMENT-101: Revumenib for R/R KMT2Ar AML/ALL:** Phase I/II, N=94, CR/CRh: 22.8% at interim analysis of the pooled KMT2Ar AML and ALL cohorts (p-value = 0.0036); an additional 14% of proceeded to transplant without achieving CR/CRh; 65% (32/49), ORR in KMT2Ar AML; CR/CRh: 24.5% , DoR: 6.4mo, CRc: 43.9% (uMRD: 68.2%), 38.9% of responders proceeded to HSCT.
- **Menin-KMT2A (MLL1) Inhibitor JNJ-75276617 in Adult Patients with R/R Acute Leukemia Harboring KMT2A or NPM1 Alterations:** N=58, Phase 1, acceptable safety profile, encouraging antileukemic activity, and emerging biologic activity: In 26 (63%) of the 41 pts with disease evaluation data, there was a reduction in bone marrow (BM) disease burden
- **BEYOND VAALE-A and R/R AML**
- **FLT3-ITD with ND or R/R AML: Quizartinib, Venetoclax, and Decitabine:** Phase I/II, R/R AML, N=50, CRc rate 65%, responses similar after prior gilteritinib (78%), ND AML; N=10; CRc: 100%, RR AML N=40; CRc: 68%, OS 7.1mo
- **Selinexor in Combination with Venetoclax and Azacitidine ND AML:** Phase I/II, N=20, The CR/CRi rates and ORR across the ELN 2022 risk groups for all pts, int-risk and adverse-risk: 80% (16/20) and 90% (18/20), 75% (9/12) and 91.7% (11/12), 87.5% (7/8) and 87.5% (7/8), respectively. In comparison, the VIALE-A data showed a CR/CRi rate of 52.9% for adverse-risk pts
- **Venetoclax and Selinexor in Combination with FLAG Chemotherapy in Pediatric and Young Adult Patients with Relapsed or Refractory Acute Myeloid Leukemia: SELCLAX;** N=15, Phase I/Expansion Cohort: 41.7% (5/12) CR/Cri
- **SAVE: Phase I/II, All-Oral Combination Revumenib (SNDX-5613) with Decitabine/Cedazuridine (ASTX727) and Venetoclax in R/R AML:** N=8, Phase I/II, (65% prior VEN and HMA): Seven of 8 pts are response-evaluable, and all 7 attained a morphologic remission (ORR: 100%)

Acute Leukemias

- **ENHANCING ANTI-NEOPLASTIC IMMUNITY in AML**
  - ✓ **STIMULUS-AML2**: Sabatolimab Monotherapy in Patients With MRD+ AML After AlloSCT, novel monoclonal antibody targeting TIM-3: Enhancing GvL
  - ✓ Phase Ib/II, N=21, No GVHD, iMAEs, 30% of the pts at 400 mg still in CR at > 1 y on treatment and data may suggest a delayed onset of relapse. 1 DLT myocarditis
- **ACUTE LYMPHOBLASTIC LEUKEMIA**

○ **Risk-Adjusted Therapies in AYA compared with COG studies:** Yield equivalent outcomes for AYAs (Age 16-31) treated for Newly Diagnosed T-Cell Acute Lymphoblastic Leukemia on COG Studies AALL0434 and AALL1231.

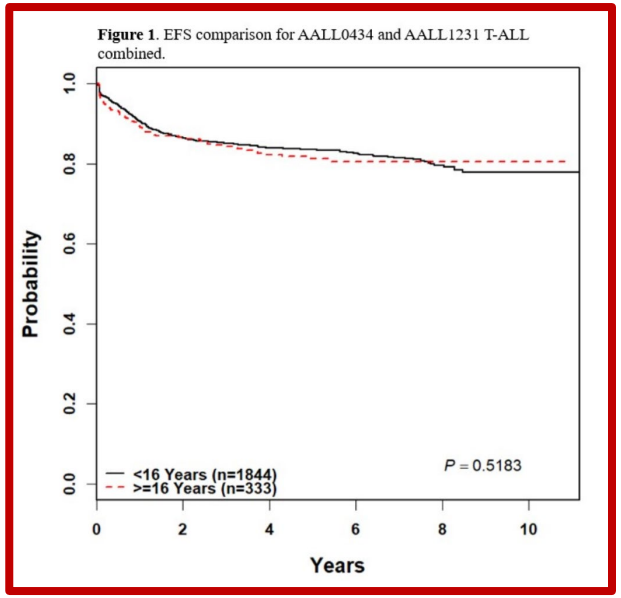
✓ Combined outcome data for AALL0434 and AAL1231; 4-year EFS for AYA (n=333): 82.2+2.4% vs 83.9+0.9% for non-AYA (n=1844) (P=0.52) and OS of 87.5+2.1% vs 90+0.8% (P=0.19), similar AES.

○ **GRAALL-2014/T ATRIALL: Frontline Consolidation with Nelarabine for Adults with High-Risk T-Cell ALL:** Phase II, N=325 (N=199 presented with HR features, N=121 in analysis); NELA did not yield an overall improved outcomes, but reduced CIR with HCST censor, but benefits were observed in favorable MRD responders and non-ETP patients.

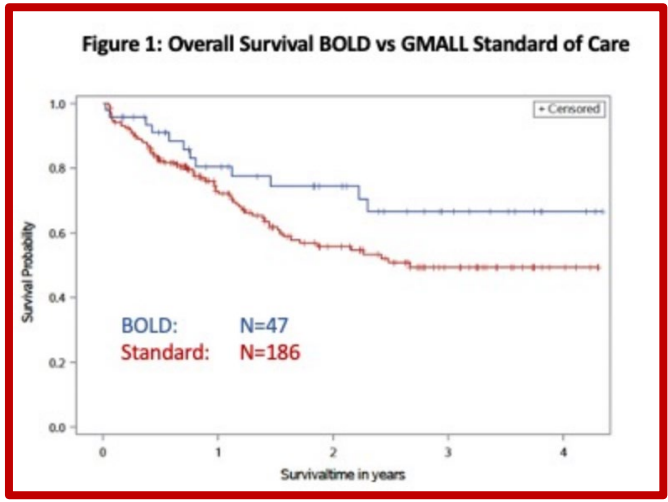
○ **Nelarabine, Pegylated Asparginase and Venetoclax + HCVAD Frontline Treatment of Adult Patients with T-ALL/T-LBL):** Phase II, N=133, 5 cohorts; 3-yr OS of 76%-88%

○ **GMALL BOLD Trial: Dose Reduced Chemotherapy in Sequence with Blinatumomab for Newly Diagnosed Older Patients with Ph/BCR::ABL Negative B-Precursor Adult ALL:** Phase II, N=50: 3 cycles of consolidation chemo omitted. 76%; CR/CRu, 33% with a molecular response, 18% MolCR. Primary Endpoint after blinatumomab1 (N=47): CR/CRu 85%; 82% MolCR. Compared to standard GMALL regimen; OS @ 3 yrs: 67% vs 49%, (p=0.08)

Risk-Adjusted Therapies in AYA



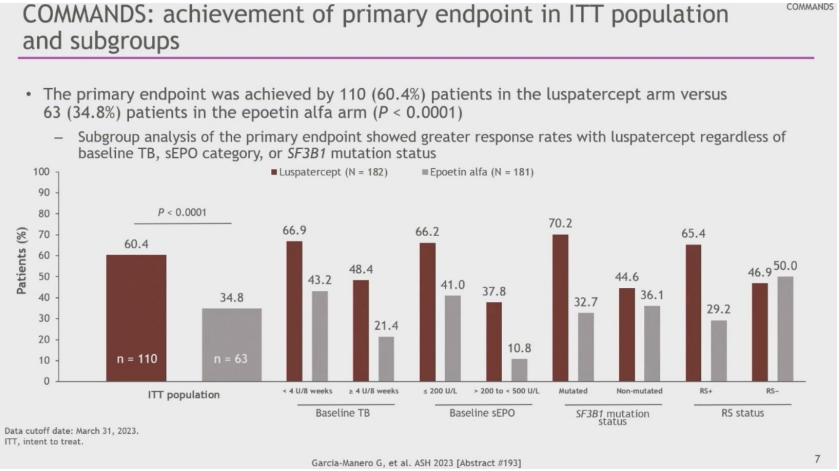
GMALL BOLD Trial



MYELODYSPLASTIC SYNDROME

- **COMMANDS: luspatercept vs ESA in ESA-naive patients with TI- Lower-risk MDS**
- N= 363, Phase III, primary endpoint (RBC-TI ≥12 wk + mean Hb increase ≥1.5 g/dL): 60.4% vs 34.8% regardless of transfusion burden, sEPO, or SF3B1 mutation (p<0.0001),
- DoR: 126.6 vs 89.7 wks (HR; 0.586)
- **IMERGE: Imetelstat versus Placebo for Achieving Transfusion Independence in ESA R/R or Ineligible Lower-Risk MDS**
- Subgroup Analysis: Phase II/III, N=105, First in class competitive telomerase inhibitor, leading to recovery of BM function
- Imetelstat significantly increased proportion of patients with RBC-TI vs placebo, irrespective of IPSS-M risk category
- For IPSS-M risk groups, the TI rates of ≥8-week, ≥24-week, and ≥1-year with imetelstat vs placebo: 47.8% vs 21.2%, 34.8% vs 3%, and 14.5% vs 0%, respectively, in patients with very low/low risk and 20.7% vs 6.3%, 10.3% vs 0%, and 6.9% vs 0%, respectively, in patients with moderate low/moderate high risk. In patients with high/very high risk, ≥8-week TI rates were 40% vs 0% with imetelstat vs placebo, with no ≥24-week or ≥1-year TI observed in either arm

COMMANDS



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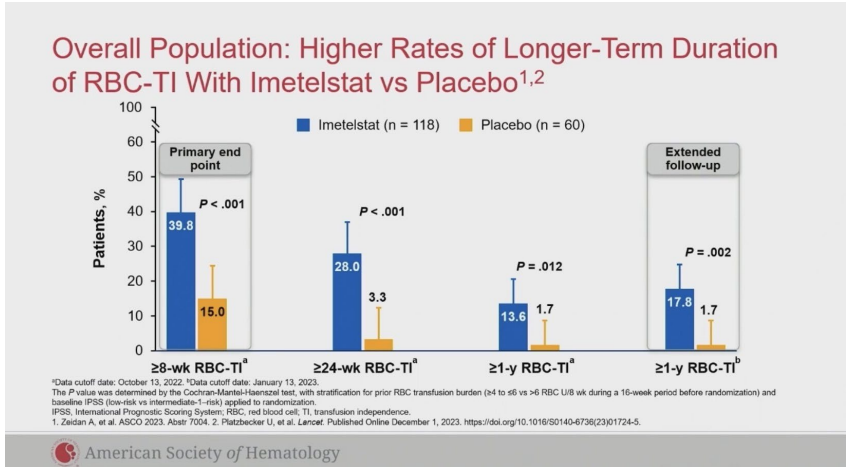
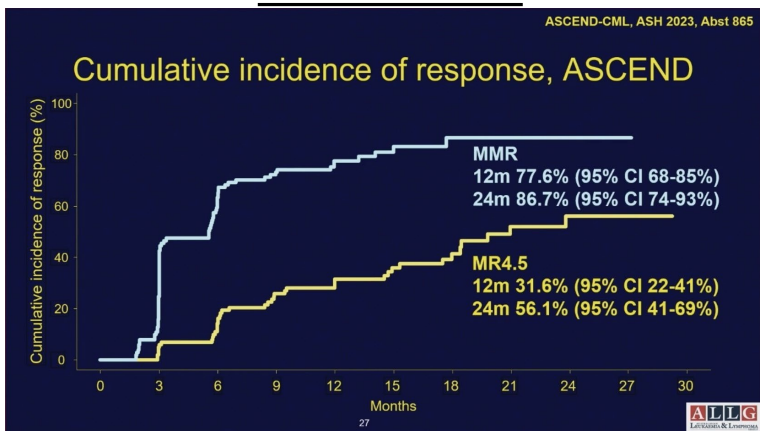


Chronic Myeloid Leukemia, Large Granular Cell Leukemia and BPDCN

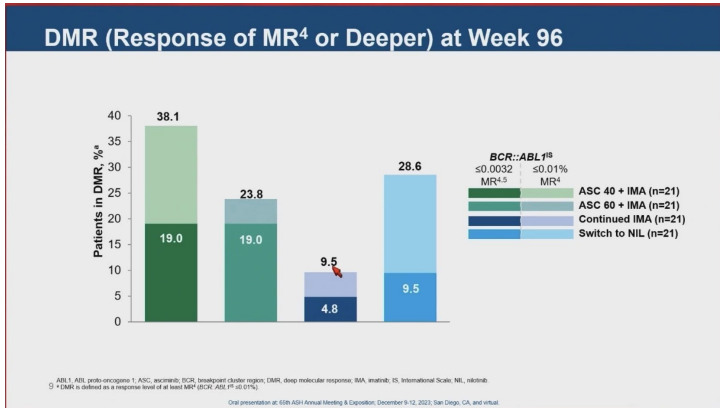
CHRONIC MYELOID LEUKEMIA

- **ASCEND-CML**: N=101, Phase II Trial of Frontline Asciminib in Patients With CP-CML
  - **Coprimary endpoints:** EMR (*BCR::ABL1* ≤10% by 3 mo): 93%, and MMR (*BCR::ABL1* ≤0.1% by 12 mo): 78.4%
  - MMR 4.5 @ 12 mo: 32% (Faster but MMR rates comparable to 2nd Generation TKIs)
- **ASC4MORE:** N=84, Phase II
  - At 96 weeks of follow-up:
  - MR $^{4.5}$ /MR ^{4} (*BCR::ABL1*^{IS} ≤.01%): 40-mg ASC add-on: 19%/28.6%, 60-mg ASC add-on 19.0%/28.6%, IMA: 4.8%/9.5%, and NIL: 9.5%/19%
  - Cumulative MR $^{4.5}$ rates at wk 96 were 28.6%, 28.6%, 9.5%, and 19.0%, respectively, with higher AE burden
- **LARGE GRANULAR CELL LEUKEMIA (LGL)**
- **Ruxolitinib Induces Responses in LGL Via Suppression of JAK/STAT-Pathway**
  - N=23, 20 pts evaluable, CR: 5 (25%) PR: 6 (30%) , SD: 4 (20%) SD. ORR/CBR: 55%/75%
  - mEFS) NR and 68% at 14 months
  - STAT3 mutation status predicted for improved EFS (14-mo EFS 100% vs 40%, p=0.007).
- **Blastic Plasmacytoid Dendritic Cell Neoplasm**
  - **Tagraxofusp for Treatment-Naive Patients with Blastic Plasmacytoid Dendritic Cell Neoplasm:** Phase II, N =22, ORR: 89%, CR: 67%, PR: 22%, mOS: 20 mos with TAG, which compares favorably to chemotherapy's shorter median OS of ~8-14 mos

ASCEND-CML



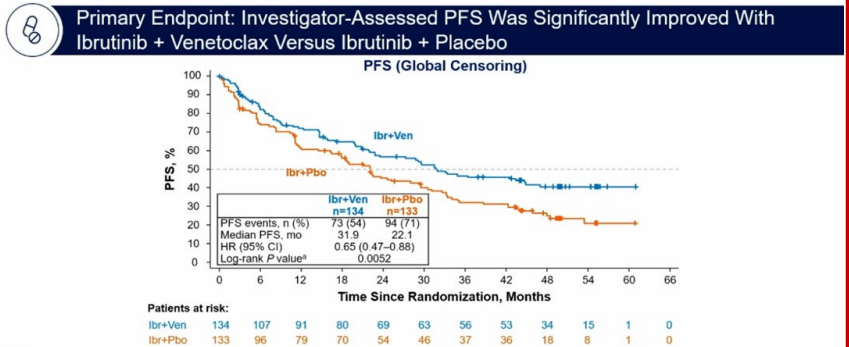
ASC4MORE



HODGKIN'S AND INDOLENT LYMPHOMAS

- **SYMPATICO (MANTLE CELL LYMPHOMA)**: Phase III Trial of Ibrutinib + Venetoclax vs Ibrutinib + PBO in R/R MCL, N=267, INV-mPFS: 31.9 vs 22.1 mo, HR; 0.65 (P=0.0052), CR: 54% vs 32%, TTNT NR vs 35.4 mo
- **BOVen (MANTLE CELL LYMPHOMA):** Zanubrutinib, Obinutuzmab, and Venetoclax in Treatment-Naive TP53-Mutated MCL, Phase II, N=25, CMR: 88%, 2-yr PFS/DFS/OS: 72%, 88%, and 75%, EOT u10^{-6}: 6/10
- **ROSEWOOD: Zanubrutinib Plus Obinutuzumab Versus Obinutuzumab in R/R Follicular Lymphoma**: Phase II, N=217, ORR by ICR: 69% (ZO) vs 46% (O; P = .001). CR: 39% (ZO) vs 19% (O); 18-month DOR: 69% (ZO) vs 42% (O). mPFS: 28.0 mos (ZO) vs 10.4 mos (O); HR; 0.50, and ZO was associated with improved HRQoL
- **Mosunetuzumab first-line therapy, Follicular Lymphoma**: Phase II, N=54. ORR: 96%; CR: 76%, including high risk disease, manageable CRS; 54%, no G3/4
- **SWOG S1826: Nivolumab + AVD vs Brentuximab Vedotin + AVD for ND Advanced Classical HL**: Phase III, N=994 (≥ 25% minorities), Nivo-AVD significantly improved PFS (HR: 0.48) and EFS (HR: 0.56) vs. BV-AVD, 1-yr PFS: 94% vs 86%; 1-yr EFS: 91% vs 84%, 25% of patients Blacks/Hispanics
- **SWOG S1826: Age ≥ 60**: Nivo-AVD improved PFS and EFS vs BV-AVD, and better tolerated with less AES, and discontinuations
- **Brentuximab Vedotin, Nivolumab, Doxorubicin, and Dacarbazine in Early-Stage Classical Hodgkin Lymphoma:** Phase II, N=154, Non-bulky, ORR at EoT: 95%; CR at EoT: 91% (primary endpoint), CR as best response: 99%, 18-mo PFS: 97%, respectively (mf/u: 16.5 mo)

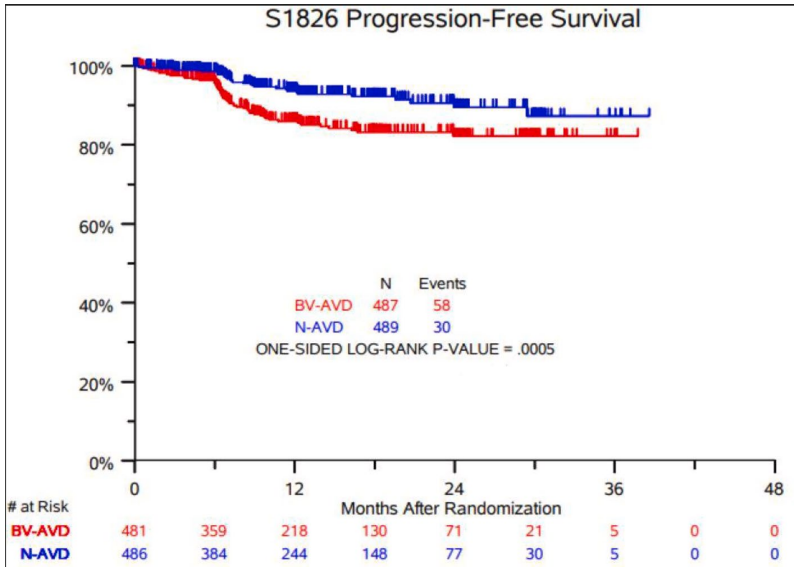
SYMPATICO (MCL)



Median PFS, mo	Global Censoring[b]				US FDA Censoring[c]			
	Ibr+Ven n=134	Ibr+Pbo n=133	HR (95% CI)	Log-rank P value[a]	Ibr+Ven n=134	Ibr+Pbo n=133	HR (95% CI)	Log-rank P value[a]
Investigator assessment	31.9	22.1	0.65 (0.47–0.88)	0.0052	42.6	22.1	0.60 (0.44–0.83)	0.0021
IRC assessment	31.8	20.9	0.67 (0.49–0.91)	0.0108	43.5	22.1	0.63 (0.45–0.87)	0.0057

HR, hazard ratio; Ibr, ibrutinib; Pbo, placebo; Ven, venetoclax.
[a]P values were determined by stratified log-rank test (stratification factors: prior lines of therapy [1–2 vs ≥3] and TLS risk category [low vs increased risk]). [b]Censoring at last non-PD assessment for patients without PD or death. [c]Patients were censored at last non-PD assessment before start of subsequent anticancer therapy or missing ≥2 consecutive visits prior to a PFS event, whichever occurred first.

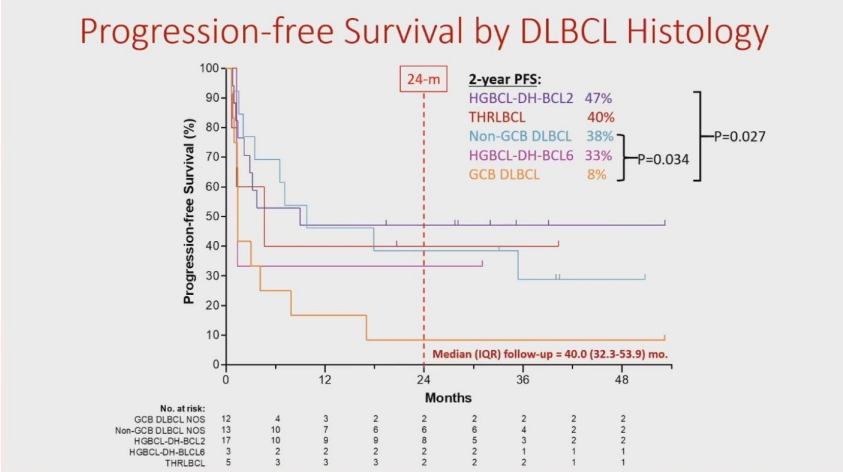
SWOG S1826 (HODGKIN'S LYMPHOMA)



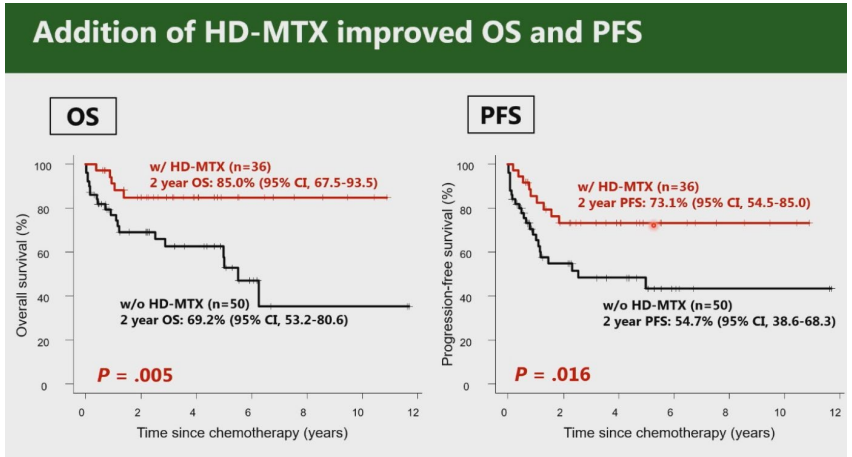
Aggressive Lymphomas

- **ViPOR: Venetoclax, Ibrutinib, Prednisone, Obinutuzumab, and Lenalidomide in R/R DLBCL:** Phase Ib/II, N=50, ORR: 54% (26/48), CR: 38%, 2-year PFS/OS: 34% and 36%
- **ELM-2: Odronextamab in R/R DLBCL:** Final Analysis, Phase II, N= 127, ORR: 52%, CR: 31%, 2-yr DoCR rate: 47%, CRS: 55.1%
- **EPCORE NHL-5: Epcoritamab + Lenalidomide in R/R DLBCL**; Phase Ib/II, N=24, ORR: 72%; CR: 53%; mDoCR: NR, CRS: 69%
- **Glofitamab+R-CHOP in untreated DLBCL:** Phase Ib, N=24, interim and EOT-ORR; 93.3% (95% CI: 68.1–99.8)
- **HD-Methotrexate + Chemotherapy in ND Intravascular Large B-Cell Lymphoma**: Retrospective, N=141, w HD-MTX 2-year PFS and OS: 73.1%/85.0% vs. w/o HD-MTX: 54.7%/69.2% (,*P* = 0.016 and *P* = 0.005)
- **VALENTINE-PTCL01, Valemetostat (EZH1/2 inhibitor) in R/R PTCL:** Phase II, N=148, ORR: 43.7%; across all disease subtypes, 8.4% proceeded to allogeneic HCT

ViPOR



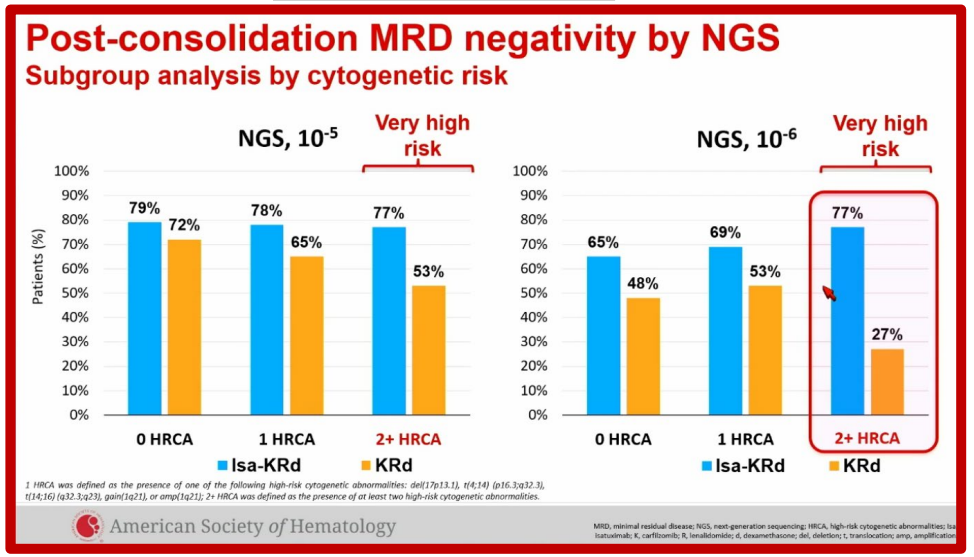
HD-Methotrexate in ND IVLCL



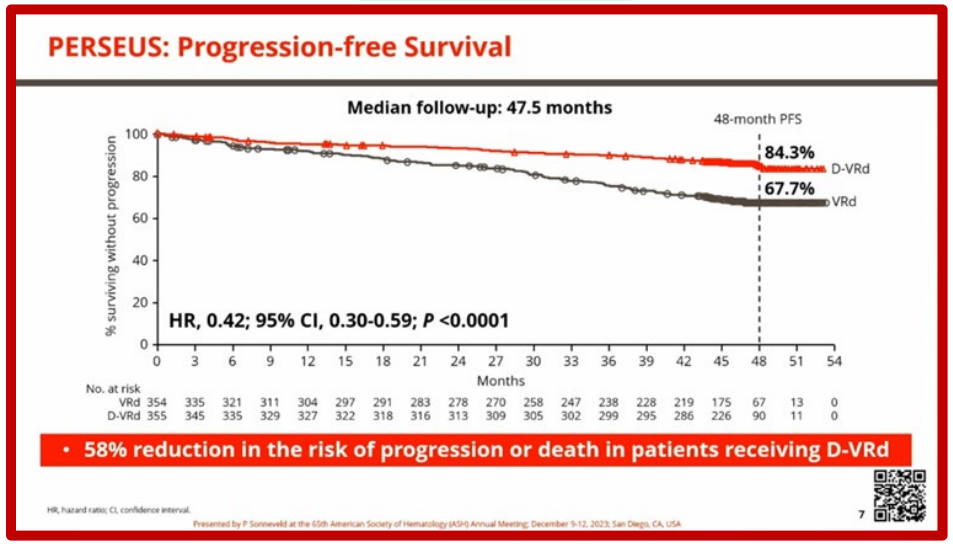
Multiple Myeloma

- **IsKia EMN24 trial: Isatuximab-KRd vs KRd for TE-NDMM with post-ASCT consolidation**;
- Phase III, N=302, MRD negativity (10^{-5}) after consolidation (primary endpoint): 77% vs 67% (OR 1.67; p=0.049); uMRD-10^{-6}: 67% vs 48% (OR 2.29; p<0.001) and in all subgroups
- **PERSEUS Trial: Daratumumab + VRd vs. VRd in TE-NDMM;**
- Phase III, N=709, 48-mo PFS: 84.3% vs 67.7% (HR, 0.42; *P* <0.0001) [crossing the prespecified stopping boundary of 0.0126], ≥CR: 87.9% vs 70.1% (*P* <.001)
- MRD negativity (10^{-5}): 75.2% vs 47.5% (*P* < .001)
- **CENTAURUS: Daratumumab Monotherapy in Intermediate or High-Risk Smoldering MM:**
- Phase II, N=123, Final analysis; ORR and ≥CR rate were higher in the Intense and Intermediate arms (≥CR rate was 8.5%.) than in the Short arm.
- mOS NR, 84-mo OS: Intense; 81.3%, Intermediate; 89.5%, and Short arms; 88.1%.
- **Venetoclax/Dara/Dex (VenDd) vs Bortezomib/Dara/Dex (DVd) in t(11;14) R/R MM:**
- N=81, Phase 1/II, ORR: 96%, ≥ VGPR: 93%, ≥ CR: 67%, and mPFS: NR, VenDd; ORR:, 39% ≥ VGPR: 39%, ≥ CR 19%, and mPFS 15.5 mos. The 33-month PFS rate: 73.4% versus 38.8% for VenDd versus DV.
- uMRD: 38% with VenDd and 8% with DVd.
- **MonumenTAL-2: Talquetamab + Pomalidomide in R/R Multiple Myeloma;**
- Phase Ib, N=35, ORR: 86.7% and 83.3% in the QW and Q2W cohorts.
- ≥CR in 60.0% and 44.4% and ≥VGPR in 86.7% and 77.8%, respectively.
- ORRs consistent across pt subgroups (>80% independent of prior pom or CAR-T exposure).

IsKia EMN24 trial

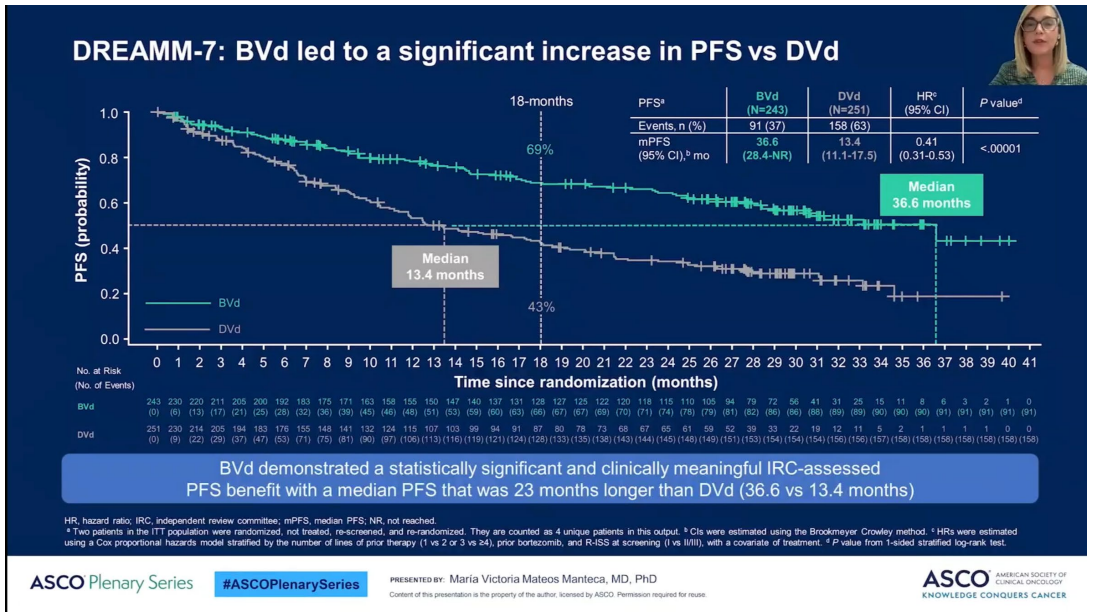


PERSEUS Trial



Multiple Myeloma

- **GEM2017FIT trial**: Phase III, Induction Therapy with Bortezomib-Melphalan and Prednisone followed By Lenalidomide and Dexamethasone versus Carfilzomib, Lenalidomide and Dexamethasone +/- Daratumumab x18 Cycles, followed By Consolidation and Maintenance Therapy with Lenalidomide and Daratumumab: N=462, Elderly, Fit, NDMM, aged 65 - 80 years:
- Primary endpoint MRD(-) rate at 10^{-5} @ EOT: VMP-Rd; 32%, KRd; 69% (p<0.0001) and D-KRd; 79% (p<0.0001).
- At 10^{-6}, the MRD(-) rate was also significantly superior for KRd (59%) and D-KRd (75%) in comparison with VMP-Rd (24%) (p values <0.0001).
- **DREAMM-7 Trial**: Phase III, N= 494, Belantamab mafodotin + Bortezomib, and Dexamethasone (BVd) vs Daratumumab, Bortezomib, and Dexamethasone (DRd) in RRMM with ≥1 prior line of therapy
- mPFS in the (BVd) 36.6 vs (DVd) 13.4 mo, HR: 0.41 OS 29% mature; mOS: NR; HR, 0.57, nominal p < 0.0005).
- ORR: BVd; 82.7% vs DVd; 71.3%.
- mDOR: BVd; 35.6 vs DVd; 17.8 mo



PFS[a]	BVd (N=243)	DVd (N=251)	HR[c] (95% CI)	P value[d]
Events, n (%)	91 (37)	158 (63)		
mPFS (95% CI),[b] mo	36.6 (28.4-NR)	13.4 (11.1-17.5)	0.41 (0.31-0.53)	<.00001

Myeloproliferative Neoplasms

- **TRANSFORM-1: Navitoclax + Ruxolitinib vs Placebo + Ruxolitinib** in Previously Untreated Myelofibrosis, BCL inhibitor, N=252, Phase III; Significantly improved SVR_{35} at Wk 24 SVR_{35} at Wk 24: 63.2% vs 31.5% (*P* <.0001).

- **MANIFEST-2: Pelabresib + Ruxolitinib vs Placebo + Ruxolitinib for JAKi–Naive Myelofibrosis:** N=431, Phase III, BET inhibitor, Significantly greater reductions in SVR_{35} (66% vs 35%; P <.001), improved TSS and TSS_{50}, 2-fold increase in proportion with both SVR35/TSS50 response.

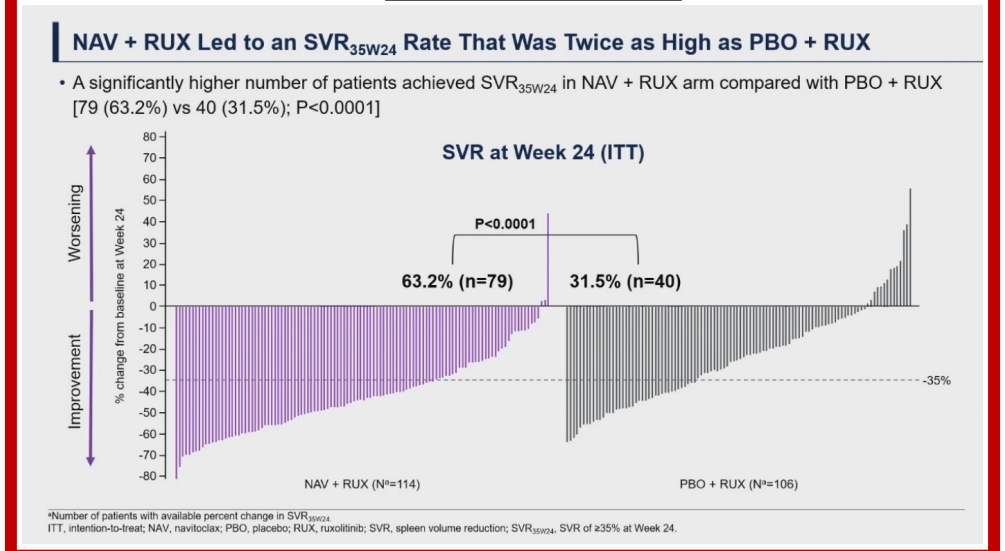
- **Bomedemstat (LSD-1 inhibitor) in Combination with Ruxolitinib in with Myelofibrosisis:** N=32, Phase II, improves splenomegaly and symptom scores, and stabilizes hemoglobin both in the frontline and second-line setting.

- **RuxoBEAT: Ruxolitinib Vs BAT as First-line Therapy in High-Risk Polycythemia Vera:** N=190, Phase IIb; First-interim analysis; Rux not superior to BAT (CR 2.3/2.9%, ORR 77.3% vs. 55.9% (p=0.054)), but greater reduction in spleen size (P <.0001) and less PV-associated pruritus (P = .002), HCT(40.8% vs 42.1%, p=0.046)

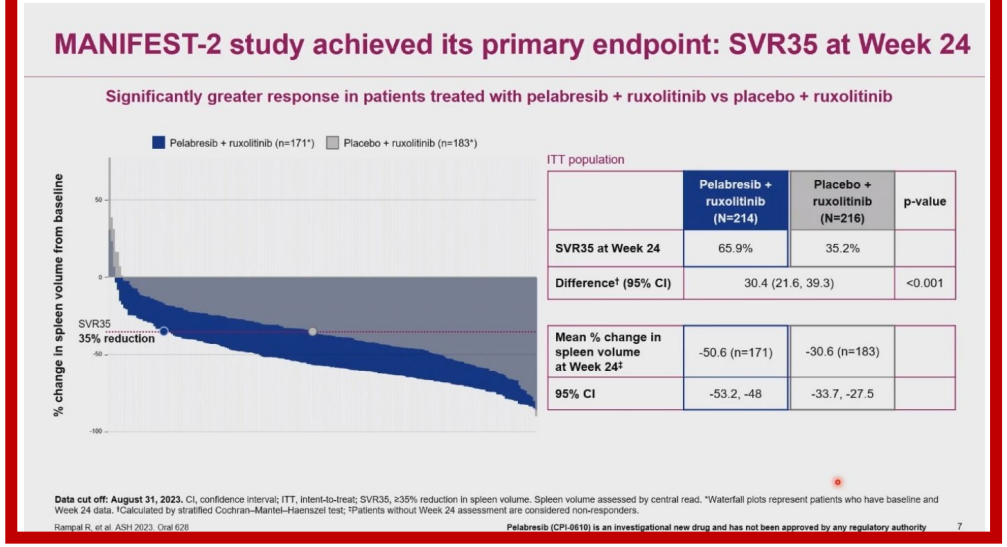
- **Bomedemstat (LSD-1 inhibitor) in Essential Thrombocythemia Resistant or Intolerant to Standard Therapy:** N= 73, Phase IIb, Response by Wk 24: 77%,

- No significant change in symptom burden (MPN-SAF TSS), with favorable response reported in Patient Global Impression of Change; 72%

TRANSFORM-1

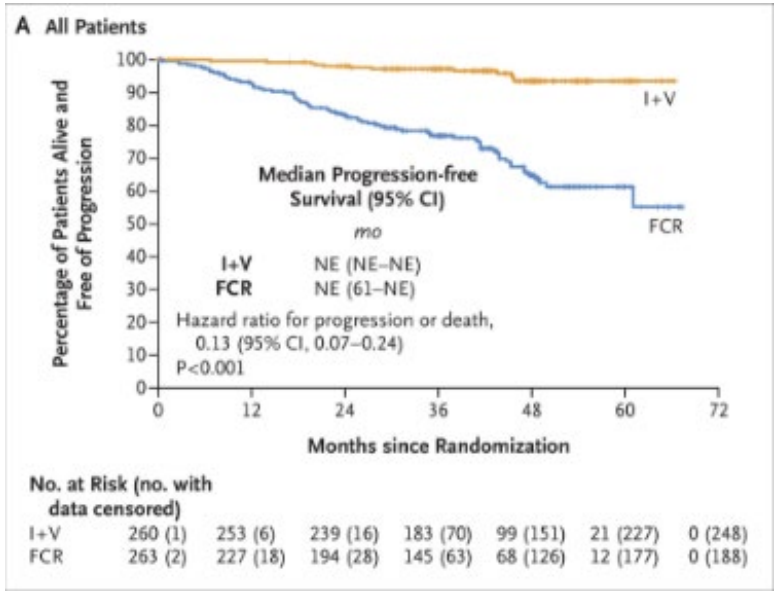


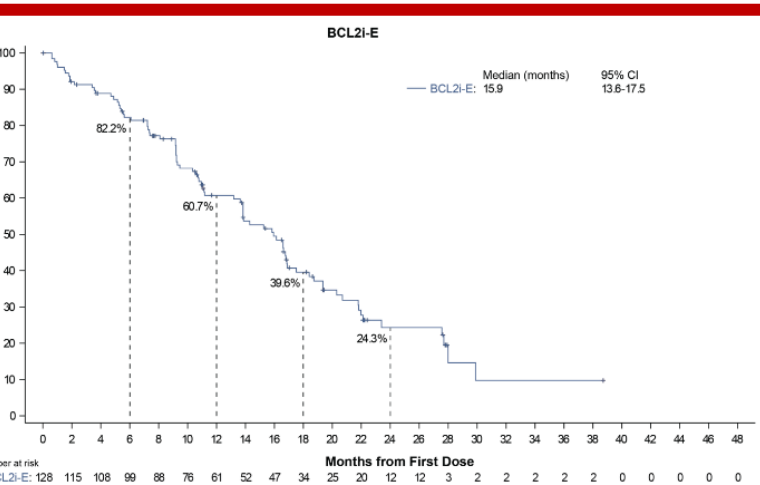
MANIFEST-2



Chronic Lymphocytic Leukemia, Waldenstrom's Macroglobulinemia and Amyloidosis

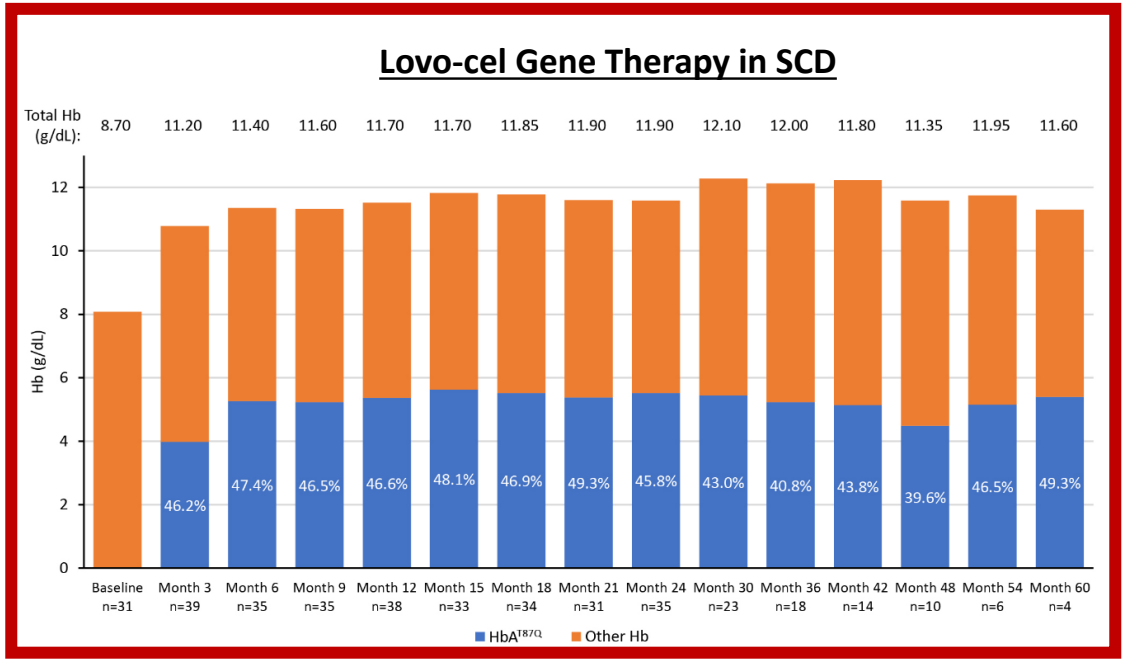
- **UK NCRI FLAIR Study: Ibrutinib Plus Venetoclax with MRD-Directed vs. FCR**; Phase III, N=523; @3yrs 58.1% stopped I+V based on uMRD
- PFS @ 4 yrs 93.5% vs. 64.8%, HR 0.13, p<0.0001; OS 94.9% vs. 87.3%, HR 0.31; p=0.0029
- **TRANSCEND CLL 004: Lisocabtagene Maraleucel in R/R CLL/SLL, N=118,**
- Phase I/II, CR/CRi 19.3%, ORR 47.7%, (PEAS: CR/CRi: 20%, ORR: 44%)
- mPFS: 11.9 mo, mOS: 30.3 mo.
- CRS: 85% (grade 3, 8%; no grade 4/5) , NE: 45% (grade 3, 18%; grade 4, 1%; no grade 5); 69% received tocilizumab and/or corticosteroids for CRS/NEs.
- **BRUIN: Pirtobrutinib in Post-cBTKi CLL/SLL:** ~30 Months Follow-up and Subgroup Analysis With/Without Prior BCL2i, N=282, Phase I/II, ORR for all post-cBTKi pts was 72% (95% CI, 66.4-77.1), and ORR including PR-L was 82% (95% CI, 76.5-85.9)
- median PFS was 19.4 months (95% CI, 16.6-22.1) among all cBTKi pre-treated pts, 23.0 months (95% CI, 19.6-28.4) for BCL2i-N, and 15.9 months (95% CI, 13.6-17.5) for BCL2i-E
- **Acalabrutinib with Rituximab in Patients with Symptomatic Anti-MAG Mediated IgM Peripheral Neuropathy**: Phase II, N=8, ORR: 86% with 57% improvement in the I-RODS score (median improvement 0.5%).
- **CD19-Targeting CAR T-Cell Therapy in Transformed Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma**: A Descar-T and US Collaborative Study: N=22, ORR/CRR 68%/68% at 6 months. CRS: 78%
- **CAEL-101, an Anti-Amyloid Monoclonal Antibody, Combined with Anti-Plasma Cell Dyscrasia Therapy in Patients with Light-Chain Amyloidosis;** N=25, Phase I/II, 27%: cardiac responders (>30% NT-proBNP decrease and more than 300 ng/L decrease, if baseline NT-proBNP ≥650 ng/L), 32%: stable, 9%: cardiac disease progression

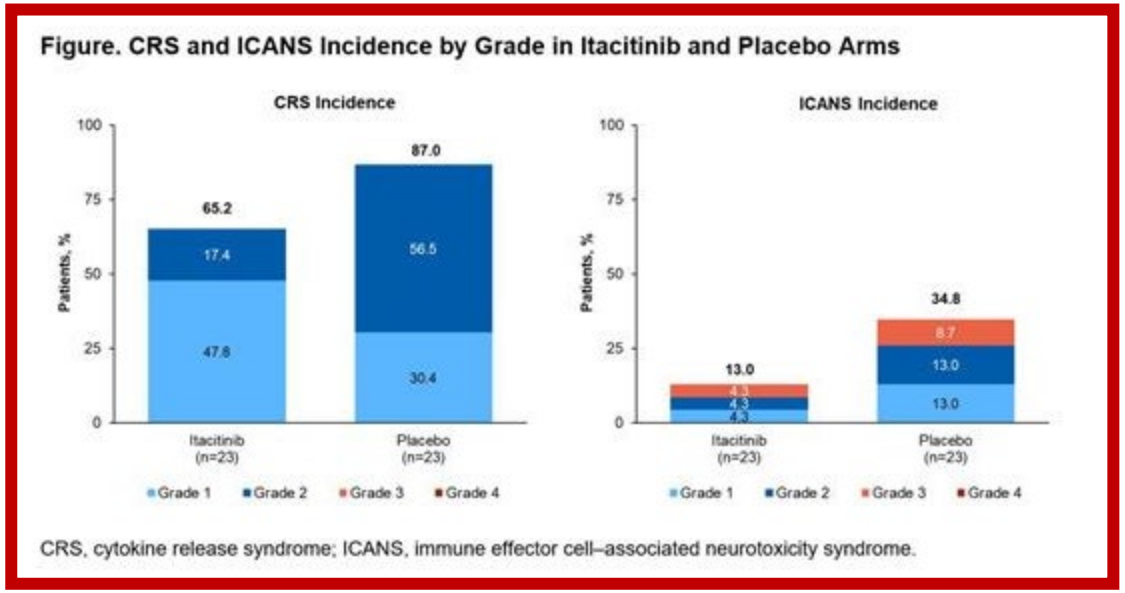




Hematopoietic Stem Cell Transplantation and Cellular Therapy

- **Lovotibeglogene Autotemcel (Lovo-cel) Gene Therapy in SCD:** N=47, Pooled analysis of HGB-206 and HGB-210 trials: complete resolution of VOEs: 88%, serious VOEs: 94%.
- Increased mHg 8.7 g/dL to 11.8 g/dL. Median HbAT87Q of non-transfused total Hb ≈40% or more.
- **CLIMB SCD-121: Exagamglogene autotemcel (exa-cel) in SCD:** Ex vivo CRISPR-Cas9 gene-edited autologous CD34+ HSPCs at the erythroid-specific enhancer region of the BCL11A gene in SSCD: N=42,
- VF12; 95%, P<0.0001), HF12: 20/20 (100%); P<0.0001), VF9: 29/30 (96.7%); P<0.0001). In pts achieving VF12, VOC free duration was 21.8 mo;
- **BMT CTN 1507: Reduced Intensity Haploidentical BMT in Adults with Severe Sickle Cell Disease:** N=54, multi-center single-arm, phase-II;
- 2-year EFS: 88%, 2-year OS post HU: 93.0%, 2-year OS post-transplant: 95.0%
- **Tandem Transplant in High-Risk ND Myeloma with Daratumumab, Carfilzomib, Lenalidomide, and Dexamethasone:** N=50, Phase II, CR 81 %, pre maintenance uMRD (NGS, 10^{-6}): 94%. 24-months PFS is 87% and OS is 94%.
- **AGVAE-201: Axatilimab (high-affinity anti–CSF-1R monoclonal antibody)** in Chronic GVHD; Phase II, N=241, ORR: 50-74%, Reduction in mLSS score: 36-55%, DoR: NR
- **Itacitinib for the Prevention of Immune Effector Cell Therapy–Associated Cytokine Release Syndrome:** N=42, Phase II, lower rate and grade of CRS and ICANS after lymphoma treatment with axicabtagene ciloleucel.
- CRS: Grade 1: 47.8% vs. 87.0%, Grade 2: 17.4% vs. 56.5% (P=0.003), 0 Gr. 3/4
- ICANS: 13% v. 34.8% (Grade ≥2: 8.6% vs. 21.7%)





Not So Benign Hematology

- **REACH: Dose-Optimized Hydroxyurea for Pediatric SSD in Sub-Saharan Africa:** Phase I/II, N=606, age ≤ 10yrs, LT-analysis (mF/u 80mos), dosed to MTD (ANC < 4 X 10^6)

✓ Improved SCD-related clinical events: VO-pain, ACS, stroke, and SAEs decreased as the dose increased.

- **ALPHA: Ravulizumab or Eculizumab with add-on Danicopan vs PBO in PNH with cs-EVH:** Phase III, N=86;

✓ Significantly improved Hgb and ARC levels and reduced need for transfusion.

- **APPLY-PNH: Factor B inhibition with Iptacopan Monotherapy in PNH Patients with Residual Anemia on Anti-C5 therapy:** Phase III, N=97,

✓ Substained improvements of increased Hb, mean normal/near-normal Hb levels, transfusion avoidance and decreased fatigue.

- **BASIS: Marstacimab (Anti-Tissue Factor Pathway Inhibitor) in Severe Hemophilia without Inhibitors:** Phase III, N=128

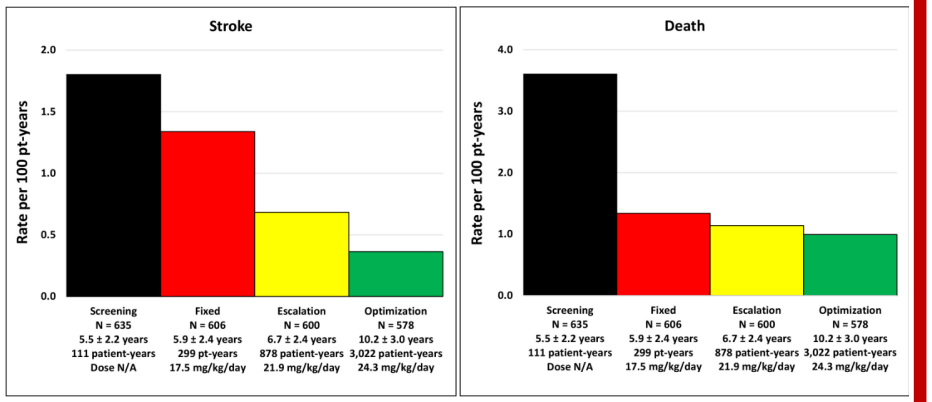
✓ Decreased bleeding events in participants with severe HA or moderately severe to severe HB without inhibitors beyond 12 months.

- **PATH-HHT: Pomalidomide vs PBO in Hereditary Hemorrhagic Telangiectasia:**

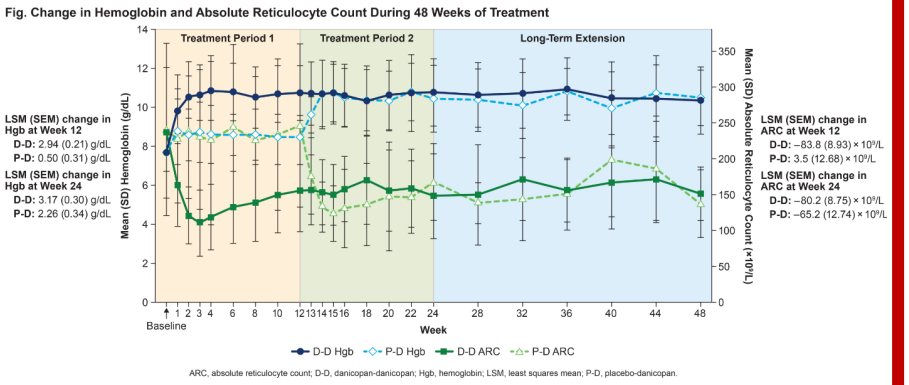
✓ Phase III, N=144, clinically relevant reduction in epistaxis and improvement in the HHT-specific QOL score vs PBO

✓ POM decreased ESS by a mean of -1.84 vs -0.89 in PBO group (p = 0.003)

REACH



APPLY-PNH



WHAT DOES IT ALL MEAN? My thoughts

- **PRACTICE Changing:**
- *MENIN INHIBITORS in R/R KMNT2r/NPM1 mutant AML; REVUMENIB*
- *NIVOLUMAB as initial therapy in HODGKINS LYMPHOMA (SWOG1836)*
- *FIRST LINE ANTI CD38 MONOCLONAL ANTIBODY THERAPY: DARATUMUMAB (PERSEUS)*
- *FIXED DURATION THERAPY IN CLL: Ibrutinib and Venetoclax; FLAIR*
- *GENE THERAPY IN SCD: Exagamglogene autotemcel (exa-cel) , and Lovotibeglogene Autotemcel (Lovo-cel)*
- *REDUCED-INTENSITY HAPLO-IDENTICAL HSC TRANSPLANTION in SCD: BMT CTN 1507*
- *DANICOPAN (APHA) and IPTACOPAN (APPLY-PNH) in PNH*
- *MPNS: BEYOND JAK INHIBITION: Navitoclax + Ruxolitinib (TRANSFORM-1:), and Pelabresib + Ruxolitinib (MANIFEST-2:)*
- *BEYOND ESAs in MDS ASSOCIATED ANEMIA: luspatercept (COMMANDS), and Imetelstat (IMERGE)*
- *Axatilimab (high-affinity anti–CSF-1R monoclonal antibody) in Chronic GVHD (AGVAE-201)*
- *Belantamab mafodotin (belamaf) + bortezomib, and dexamethasone in RRMM*

- **Potentially Practice Changing:**
- *FIRST LINE ANTI CD38 MONOCLONAL ANTIBODY THERAPY : ISATUXIMAB (IsKIA)*
- *Ibrutinib +Venetoclax for relapsed in Mantle Cell Lymphoma: SYMPATICO*
- *Marstacimab (Anti-Tissue Factor Pathway Inhibitor) in Severe Hemophilia without Inhibitors*
- *BCR/abl ALLOSTERIC INHIBITOR THERAPY IN CML: ASCIMINIB*
- *POMALIDOMIDE in Hereditary Hemorrhagic Telangiectasia*
- **Practice Confirming**
- *BISPECIFIC antibodies in lymphomas: Glofitamab, Epcoritamab, Mosunetuzumab, Odronextamab*
- *BISPECIFIC antibodies in Multiple Myeloma: Teclistimab, Elranatamab, Talquetamab*
- *BLINATUMUMAB as Initial therapy in ALL*
- **Stay Tuned**
- Selenexor in AML
- Itacitinib for the Prevention of ICANS
- CD19-Targeting CAR T-Cell Therapy in Transformed Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma
- Anti-Amyloid Monoclonal Antibody, Combined with Anti-Plasma Cell Dyscrasia Therapy in Patients with Light-Chain Amyloidosis (CAEL-101)
- Valemetostat (EZH1/2 inhibitor) in R/R PTCL

Announcements and Acknowledgments

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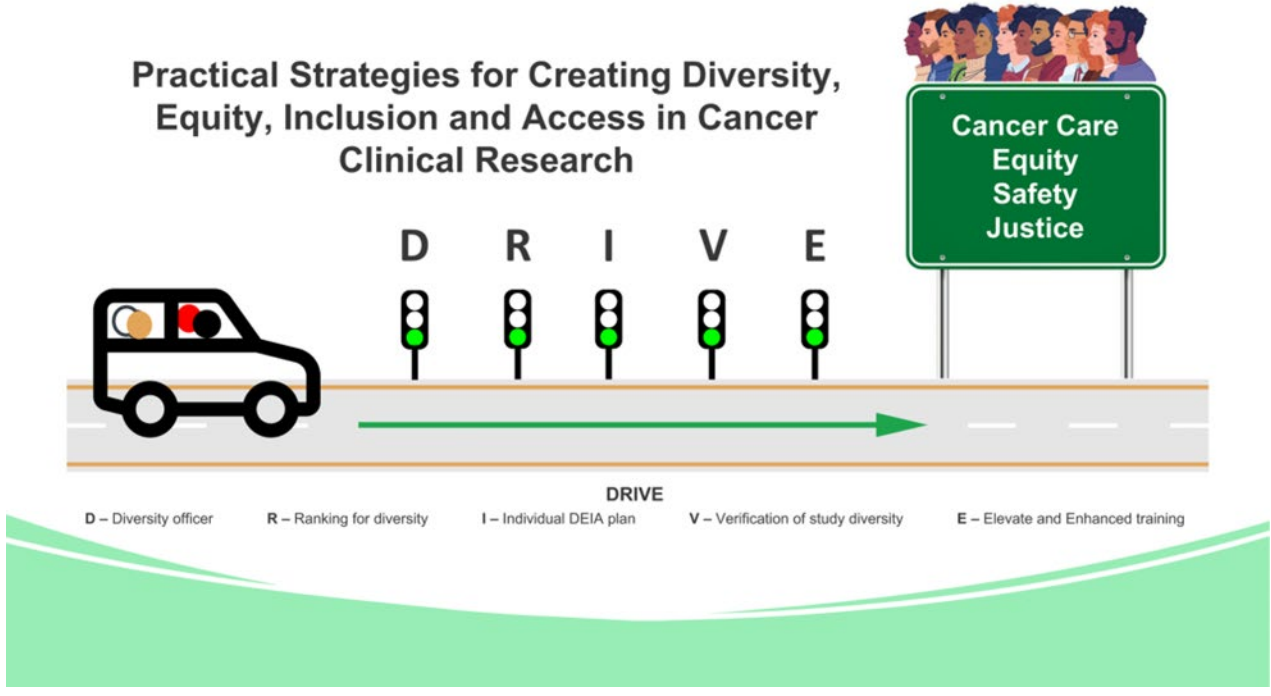

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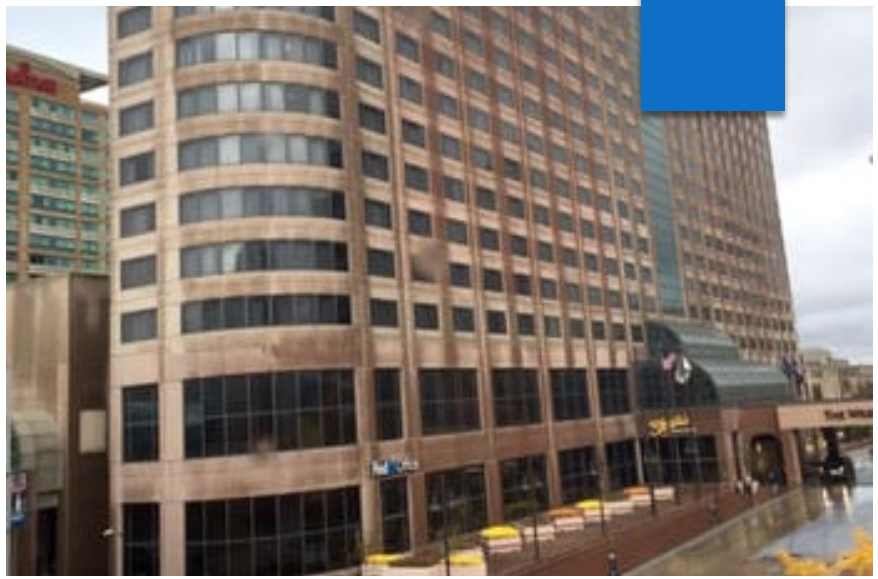

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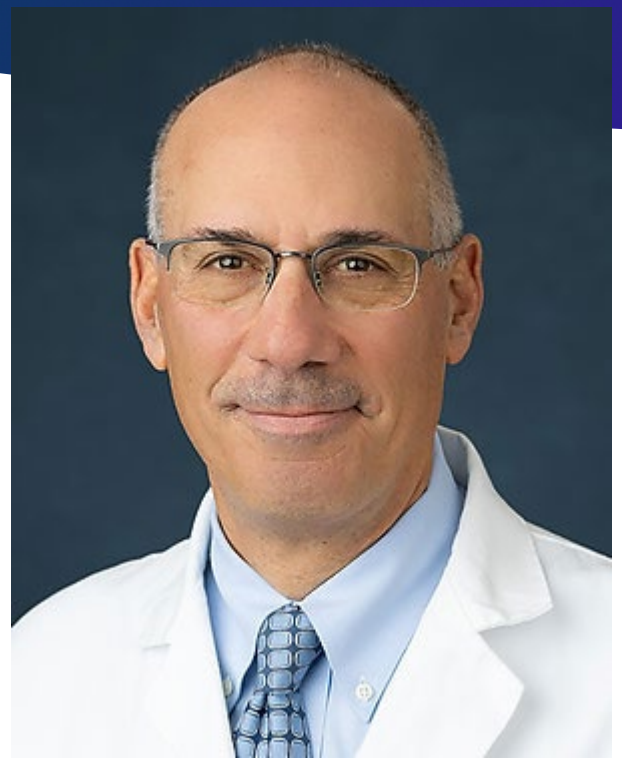
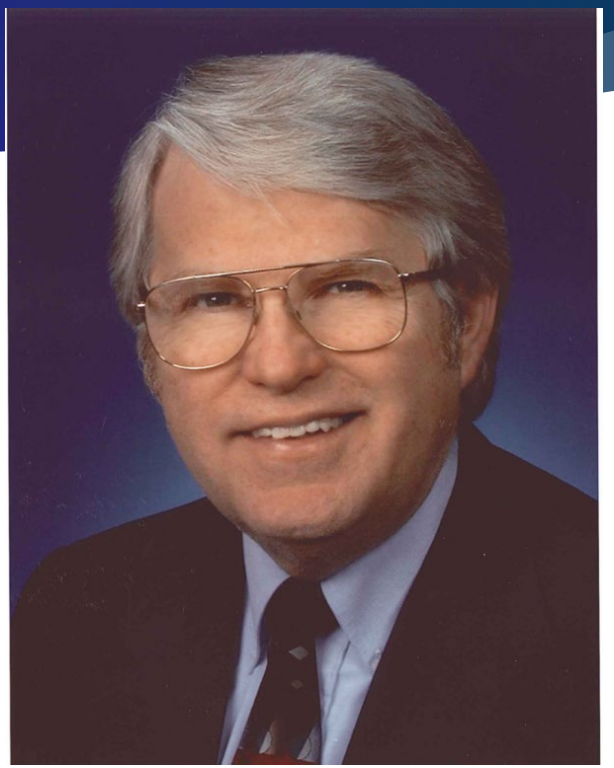
T. Howard Lee Keynote Lecture

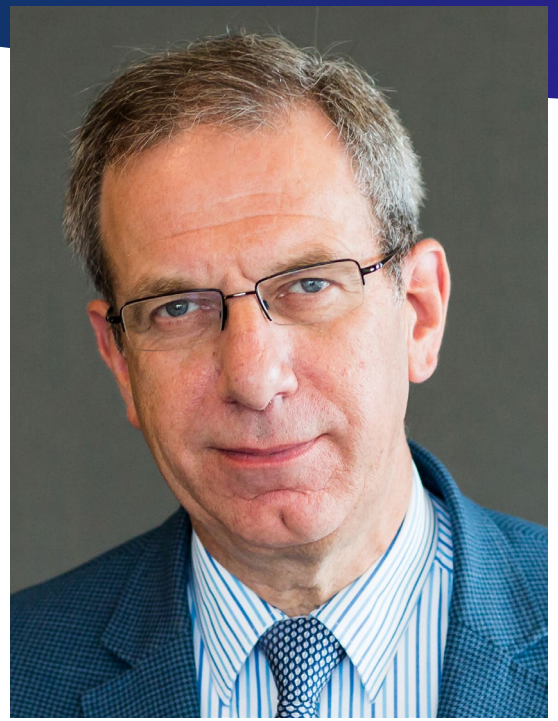


Robert Alan Brodsky, M.D.
2023 President American Society of Hematology
Director, Division of Hematology
Johns Hopkins Family Professor of Medicine and Oncology
Johns Hopkins University School of Medicine., Baltimore, MD



T. HOWARD LEE, MD
Founder and
President Emeritus,
Hematology Oncology of Indiana, PC
Indianapolis, IN

ANNUAL STEVEN COUTRE CHRONIC LYMPHOCYTIC LEUKEMIA MEMORIAL LECTURE:



Peter Hillmen, MBChB, FRCP, FRCPath, PhD,
Professor of Experimental Hematology, University of Leeds, United Kingdom

Steven Coutré, MD,
Fomerly Professor of Medicine Stanford University School of Medicine Stanford, CA

INDY HEMATOLOGY REVIEW 2024 SCHOLARSHIP RECIPIENT

HYGINUS IKECHUKWU OKEZIE OPARA, MD

CONSULTANT PAEDIATRICIAN

Consultant-in-Charge

Paediatric Haematology/ Oncology Unit

FEDERAL MEDICAL CENTRE,

ASABA, DELTA STATE, NIGERIA

INDY HEMATOLOGY REVIEW 2024 SCHOLARSHIP RECIPIENT

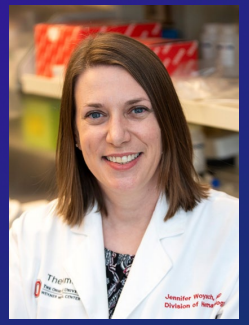
HYGINUS IKECHUKWU OKEZIE OPARA, MD

Hematologic Malignancies Town Hall

- Michael Wiemann, MD, FACP – Co-Chair
- Richard Childs, MD, Hematopoietic Stem Cell Transplantation
- Morie Gertz, MD, MACP – Plasma Cell Disorders and Amyloidosis
- Jennifer Woyach, MD – Chronic Lymphocytic Leukemia
- Rami Komrokji, MD – Acute Leukemias and Myelodysplastic Syndromes
- Matthew Lunning DO, FACP – Lymphomas
- Tycel Phillips, MD – Lymphomas
- Saad Z. Usmani, MD, MBA, FACP, FRCP – Multiple Myeloma
- Ayalew Tefferi, MD – Myeloproliferative Neoplasms



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