20th Annual INDY HEMATOLOGY REVIEW® State of the Art 2023: Emerging Therapies in Hematologic Malignancies and Disorders

RUEMU E. 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

HEMATOLOGY ONCOLOGY of INDIANA
A DIVISION OF AMERICAN ONCOLOGY PARTNERS, P.A.

MARIAN UNIVERSITY Indianapolis College of Osteopathic Medicine

IHE®

CONFLICTS OF INTEREST

Speakers Bureau
Consultant,
Advisory Board

- JANSSEN BIOTECH, INC.
- AMGEN INC.
- PUMA BIOTECHNOLOGY, INC.
- LILLY USA, LLC
- NOVARTIS PHARMACEUTICALS CORPORATION
- INCYTE CORPORATION
- PHARMACYCLICS LLC, AN ABBVIE COMPANY
- SANOFF/GENZYME CORPORATION
- DOVA PHARMACEUTICALS
- TESARO, INC
- EXELIXIS INC.
- PFIZER INC.
- E.R. SQUIBB & SONS, L.L.C.
- ABBVIE, INC.
- ASTRAZENECA PHARMACEUTICALS LP
- BAYER HEALTHCARE PHARMACEUTICALS INC.
- ARRAY BIOPHARMA INC.
- GENENTECH USA, INC.
- JANSSEN SCIENTIFIC AFFAIRS, LLC
- MERCK SHARP & DOHM
- TAKEDA
- DIIACHI SANCHO
- MORPHOSYS
- REGENERON
- KITE
- IPSEN
- STEMLINE

INDY HEMATOLOGY EDUCATION, INC

Indy Hematology Review™

Organized by:

Achieving tomorrow's outcomes through education today.™

Presented by: Community Health Network MD Anderson Cancer Center Making Cancer History®

Board of Directors:

President/CEO: Ruemu E. Birhiray, MD

Vice-President: Michael C. Weimann, MD

Treasurer/COO: Donna M. Birhiray, OT, MBA

Secretary: Jennifer Terry, JD

Director of Conventions: Thalia Hammond

ACHIEVING TOMMORROW'S OUTCOMES TODAY THROUGH EDUCATION™

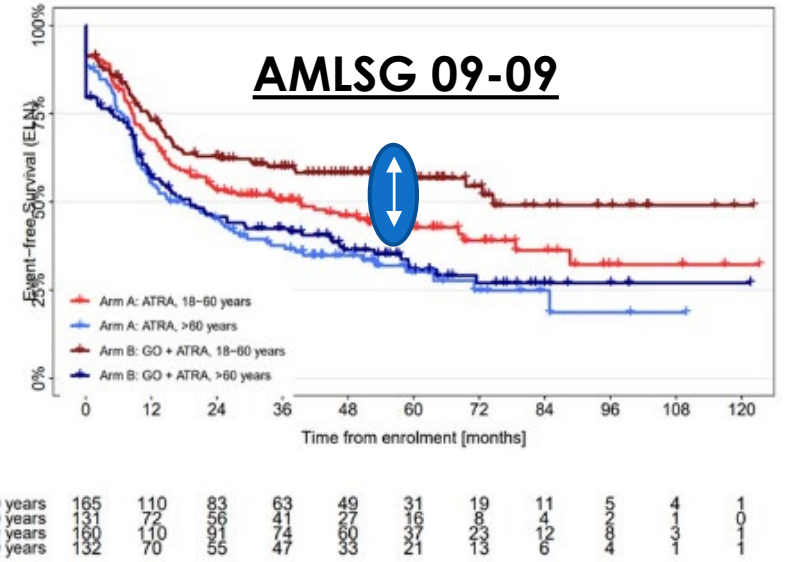
ACUTE MYELOID LEUKEMIA

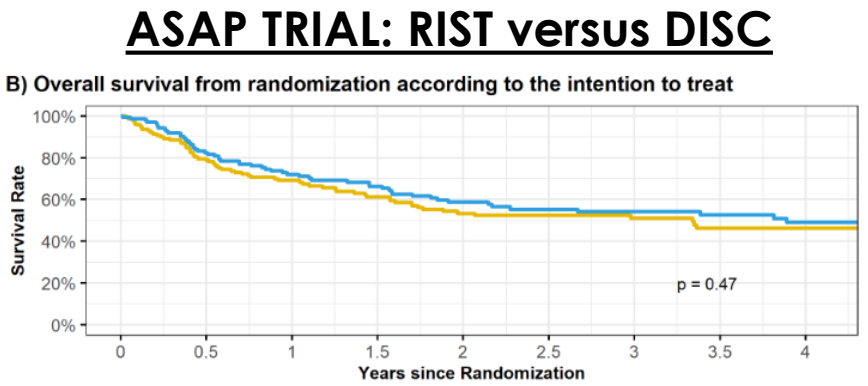
AMLSG 09-09: Phase III, Gemtuzumab Ozogamicin Plus Intensive Chemotherapy in NPM1-Mutant AML, N=588

- Similar OS, but EFS trend of benefit in favor of GO.
- **Age subgroup analysis**: Significant beneficial effect of GO on EFS and CIR for ages 18 to 60 years (HR: 0.65; p=0.003) but similar OS.

ASAP TRIAL: Remission Induction Chemotherapy (RIST) followed by AlloHSCT vs Immediate AlloHSCT (DISC) in R/R AML, Phase III, N=281

- Primary End Point: Non-Inferiority (NIF) at CR@day56 after alloHCT.
- Secondary End Points: OS and LFS from CR@day56.
- CR@day56 after alloHCT: DISC; 84.1% vs. RIST; 81.3% (NIF: p=0.047)
- At 37 mo f/u: OS @3-years: 51.0% vs 54.2% in the DISC vs RIST arms, respectively (LR p=0.47)





ACUTE MYELOID LEUKEMIA

Triplet Magrolimab Azacitidine and Venetoclax, in ND and R/R AML, Phase I/II, N=79, Age >75y

- Magrolimab: humanized monoclonal antibody targeting CD47 **("DON'T EAT ME")**
- **TP53mut AML**: 63% CR/CRi, 42% CR, **TP53wt AML**: 88% CR/CRi, 56% CR, 8-week mortality: 7%

V-FAST Master: CPX-351+Midostaurin in ND AML; FLT3 Mutant Subgroup Analysis, Phase Ib, N=23

- FLT-3 ITD: CR 82.4% (14/17), HCST 55.6% (10/18), FLT-3 TKD CR: 83.3% (5/7), HCST: 33.3% (2/6)

Gilteritinib + Azacitidine/Venetoclax in FLT3-Mutated AML: Phase I/II, N=40: Updated Results

- mCRc in frontline (100%) and R/R (70%) FLT3-mutated AML, 1-yr OS: 85%

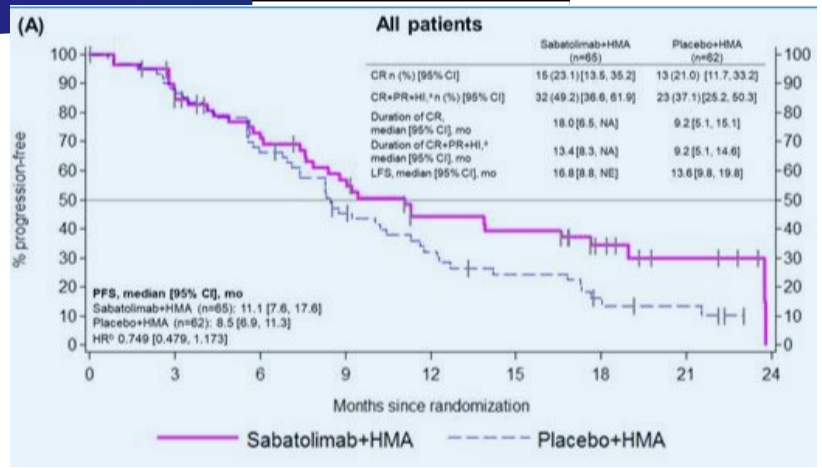
MENIN INHIBITORS: Menin is a cofactor necessary for KMT2A and NPM-1 HOX interactions

- **AUGMENT-101: Revumenib in KMT2A-Rearranged or NPM1-Mutant AML, Phase I, N=68**
- ORR: 53%, CR/CRh; 30%; MRD negativity; 78% of patients with CR/CRh
- Median DoR: 9.1 mo; median OS: 7.0 mo
- **KOMET-001: Ziftomenib in R/R AML, N=60, Phase I, First in human**
- NPM1m: ORR 8/20 (40%) and KMT2r 3/16 (16.7%) @ 600mg, No QTc prolongation, manageable differentiation syndrome

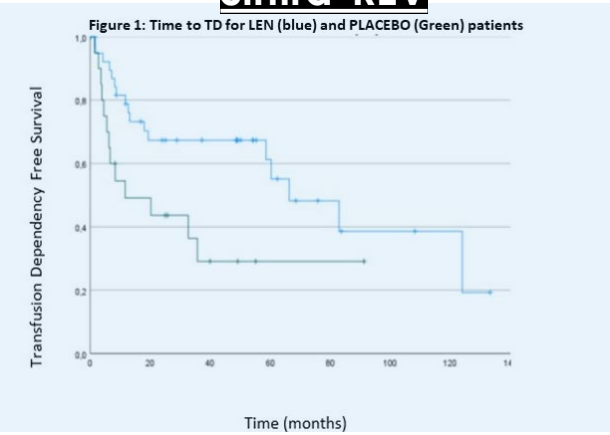
MYELODYSPLASTIC SYNDROME

- **STIMULUS-MDS1: Sabatolimab + HMA in IR/HR/vHR-MDS: Phase II, Placebo Controlled RCT, N=127**
- Monoclonal antibody to TIM-3, coinhibitory immuno-myeloid receptor overexpressed in AML/MDS.
- Updated CR: 23.1% vs 21.0% (N.S), CR+PR+HI; 49.2% vs 37.1%, mDoCR: 18.0 vs 9.2 mo, mDoR-CR+PR+HI: 13.4 vs 9.2 mo
- OS:19.0 vs. 18.0 mo (HR; 0.905 [95% CI: 0.565, 1.450])
- NS improvements in end-points but possible delayed-onset benefit.
- **Sintra-REV: LD-Lenalidomide in Non–Transfusion Dependent LR-del(5q) MDS, Phase III, PCT, N=61**
- 5-yr: Improved Primary End-Point: Time to transfusion dependence; Risk reduced by 69.8% (HR: 0.302), @mf/u of 60.6mo, no difference in OS

STIMULUS-MDS1



Sintra-REV



ACUTE LYMPHOBLASTIC LEUKEMIA

ECOG-ACRIN E1910: Phase III, Consolidation Chemo ± Blinatumomab in MRD^{-Neg}, BCR^{-Neg} B-ALL, N=488 (MRD^{-neg} 224)

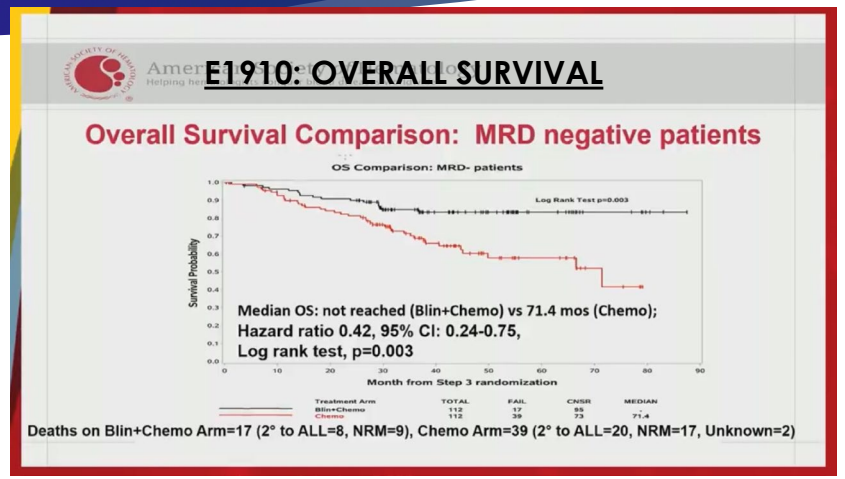
- mOS: 58% improvement in OS: NR vs 71.4mo, HR: 0.42, p= 0.003, mRFS: NR vs 22.4mo, HR: 0.46, p=0.004
- 3.6-year OS: 83 vs 65%
- Deaths: 17 vs. 39 – 50% of deaths due to relapse

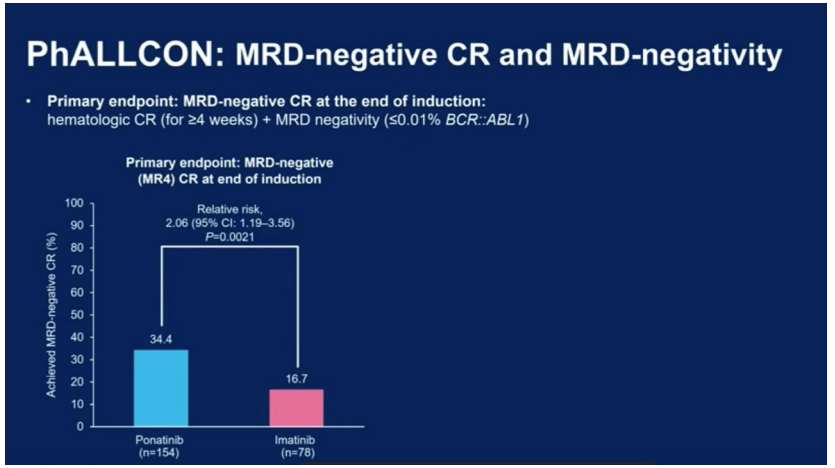
GMALL-INITIAL1: Inotuzumab Ozogamicin Induction Followed by Chemo in >55 years, B-ALL, Phase II, N=45

- Primary Endpoint: RFS @ 1year: 88%
- MRD^{-neg} CR after induction: 74%, OS @ 2 yrs: 81%

PhALLCON: Ponatinib vs imatinib plus RIC in ND Ph+ALL, Phase III, N=245,median Age 54 y, 37% ≥60 y

- Composite Primary Endpoint MRD-neg (BCR::ABL1 ≤0.01%) CR for 4 wks at EOI: 34.4% vs 16.7%; p=0.0021, similar AEs.
- EFS: HR=0.652, 95% CI 0.385–1.104, TTF: HR=0.455



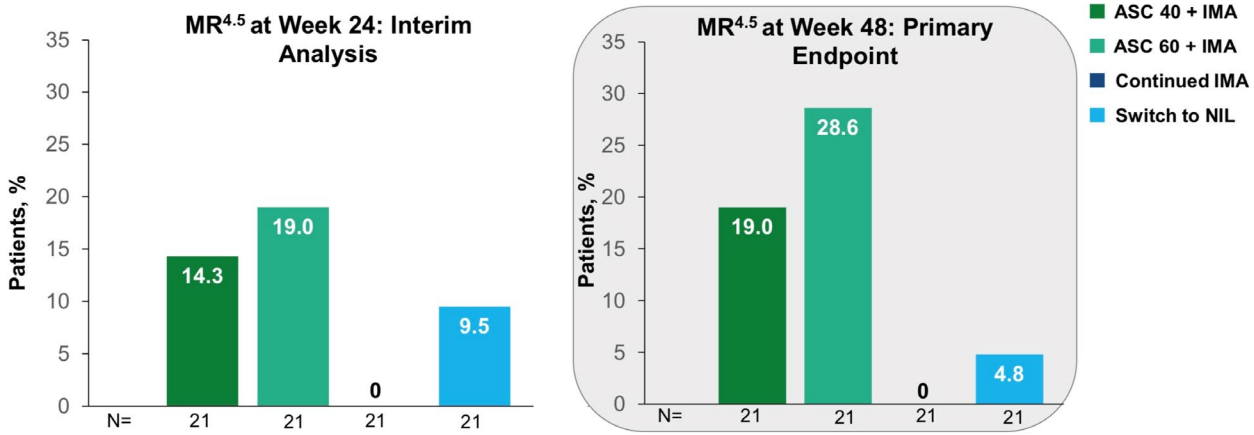


CHRONIC MYELOID LEUKEMIA

- **ASC4MORE: Imatinib+ Asciminib Add-on vs Continued Imatinib vs Switch to Nilotinib in CML Not Achieving Deep Molecular Responses With ≥1 Yr of Imatinib Therapy, Randomized Phase II, N=44**
- Asciminib: First-in-class ABL1 inhibitor to target the ABL Myristoyl Pocket (STAMP)
- Pts enrolled after 1L IMA 400 mg QD for ≥1 y with BCR::ABL1IS >0.01% to ≤1% at randomization
- **$MR^{4.5}$ at week 48:**
- 40mg ASC Add-on; 19.0%,
- 60mg ASC Add-on: 28.6%
- IMA: 0.0%
- NIL Add-on; 4.8%
- **Increased AEs with Add-ons; AEs leading to discontinuations:** 40-mg add-on; 4.8%, 60-mg ASC add-on; 14.3%, IMA; 0, and NIL; 23.8%

ASC4MORE

$MR^{4.5}$ at Weeks 24 and 48



- More patients were able to achieve $MR^{4.5}$ with **asciminib add-on** to imatinib vs continued **imatinib** or switch to **nilotinib**
- No patients in the continued **imatinib** arm were in $MR^{4.5}$ at week 48, although more patients in this arm were in MMR at baseline than in the **asciminib add-on** arms

Cortes, et al. ASH. Abstr. 84

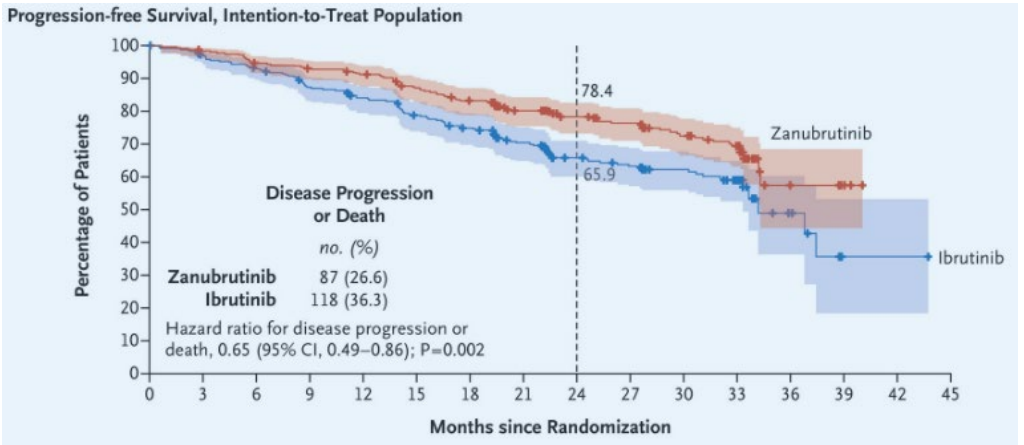
CHRONIC LYMPHOCYTIC LEUKEMIA

- **ALPINE: Zanubrutinib vs Ibrutinib for R/R CLL/SLL, Final Analysis: Phase III, N=652, (81% White,14%Asian) (RANKSCORE-2)**
- Primary End-Point: Inv-Assessed ORR; 83.5% vs. 74.2%, HR 0.65
- PFS_{IRC}: HR: 0.65 (95% CI, 0.49-0.86), 2-sided P = .0024
- OS: HR 0.76 (95% CI, 0.51 to 1.11) : Not significant
- Neutropenia: 29.3% (Z) vs 24.4% (I), Cardiac events: 21.3% (Z) vs 29.6% (I)

- **GLOW: MRD with First-line FD Ibrutinib + Venetoclax vs Chlorambucil + Obinutuzumab, Phase III, N=211**
- 3.5 yr F/U: I+V improved PFS (74.6%) vs (24.8%) Clb+O (HR: 0.214); p<0.0001.1, improved OS vs Clb+O (HR 0.487; nominal p=0.0205),
- MRD KINETICS: I+V: uMRD rates higher and earlier in pts with uIGHV CLL vs mIGHV CLL but similarly sustained after treatment.
- I+V: uMRD status from EOT+3 to EOT+18: 77.6% Ibr+Ven vs 12.2% in the Clb+O.

ALPINE: Zanubrutinib vs Ibrutinib for R/R CLL/SLL

Best Response, n (%)	ITT Population		del(17p)/*TP53* Mutation	
	Zanubrutinib (n=327)	Ibrutinib (n=325)	Zanubrutinib (n=75)	Ibrutinib (n=75)
Investigator Assessed				
ORR, % 95% CI	**83.5 79.0–87.3**	**74.2 69.0–78.8**	**81.3 70.7–89.4**	**64.0 52.1–74.8**
CR or CRi	23 (7.0)	16 (4.9)	5 (6.7)	3 (4.0)
PR or nPR	250 (76.5)	225 (69.2)	56 (74.7)	45 (60.0)
PR-L	21 (6.4)	27 (8.3)	6 (8.0)	9 (12.0)
SD	23 (7.0)	37 (11.4)	5 (6.7)	13 (17.3)
PD	1 (0.3)	6 (1.8)	0	2 (2.7)
Discontinue prior to first assessment, NA or NE	9 (2.8)	14 (4.3)	3 (4.0)	3 (4.0)



CHRONIC LYMPHOCYTIC LEUKEMIA

- **CAPTIVATE: FD Frontline, Ibrutinib + Venetoclax: uMRD then randomized to Ibrutinib vs. placebo (n=86)**
- I+V x16 cycles, 86/164 uMRD: 4-y f/u - OS 100% vs. 98%, 3-y DFS: 93% vs. 85%), 4-y PFS; 95% (95% CI, 82-99) vs. 88% (95% CI, 74-95)
- CR: 56% (95% CI, 48-64) by investigator assessment in patients without del(17p)
- Durable uMRD with FD therapy > 85%: Supports Fixed Duration therapy.
- **AVO: FD Frontline Acalabrutinib, Venetoclax, and Obinutuzumab in High-Risk CLL, Phase II, N=68**
- CR rate with undetectable MRD in BM at cycle 16: All patients: 43%, *TP53*-aberrant; 45%
- **EPCORE-CLL-1: Epcoritamab (CD3xCD20 Bispecific) in Richter's Syndrome: Phase Ib/II:** N=10: ORR 60%, CR 50% @ 6weeks evaluation

Lymphoma: Firstline Therapy for DLBCL

REMoDL-B Trial: Bortezomib+R-CHOP vs R-CHOP, Phase III, N=1077

- Primary analysis @ 30 mo: No benefit. Current analysis retrospective;
- COO:ABC subset: Improved 5-y PFS; 54 vs 69% and OS; 67 vs 80% (HR 0.58)
- MHG: Improved 5-yr PFS: 29 vs 55%, HR; 0.56, p=0.011, OS: 48 vs 60%; NS, p=0.156
- No overall benefit on PFS or OS for entire group.

MATRix/IELSG43: HDC+ ASCT vs CIT in PCNS NHL, Phase III, N=346

- 3-yr PFS: 79% HDC-ASCT vs. 53% R-DeVIC (HR 0.42; p=0.0003).
- 3-yr OS: 86 vs. 71% (HR 0.47; p=0.01). CR: 65% vs. 68%; p= 0.71.

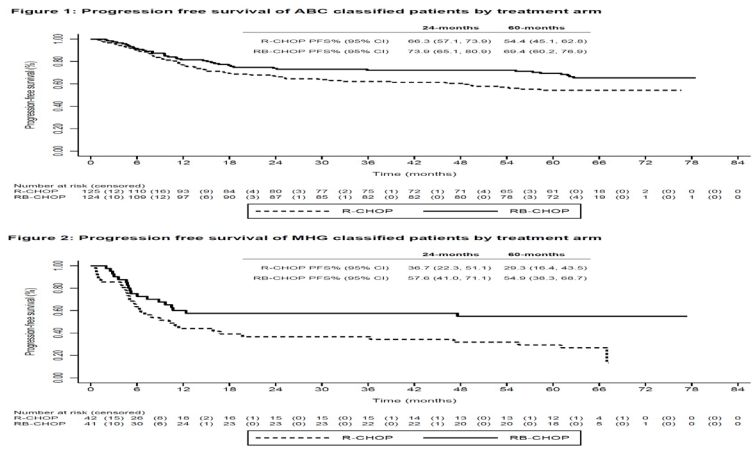
Glofitamab (Bivalent CD20xCD3) +R-CHOP in Untreated DLBCL: Phase Ib Study, N=56,

- CMR: 76.1%, ORR: 93.5% in the EOT population, mf/u 5.6 mo
- CRS: Gr 1–2:10.7%, Gr 3–5 CRS: 0, ICANS: None

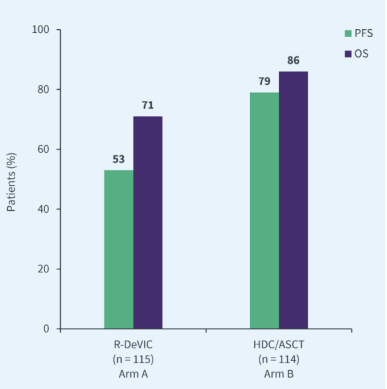
Mosunetuzumab in Elderly(≥80yrs)/Unfit (60-79yrs) DLBCL, Phase II, N=54, mAge: 83yrs

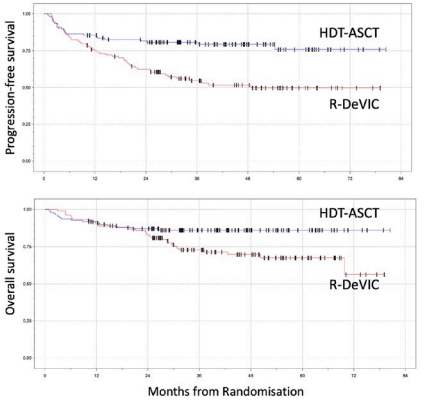
- EOT-ORR, 43% (23/54); CR, 35% (19/54); PR, 7% (4/54); SD, 2% (1/54); progressive disease, 33% (18/54). Grade 1-2 CRS 10/54, 12mo-PFS: 39%
- mDoCR: 15.8 months (95% CI: 8.5–not estimable), No G3+ CRS, ICANS: None

REMoDL-B



MATRix/IELSG43





INDOLENT AND MANTLE CELL LYMPHOMA

TRIANGLE: Firstline Ibrutinib (I) + CIT As Substitute for ASCT (A) in Younger Patients (≤ 65yrs) with MCL, Phase III, N=870

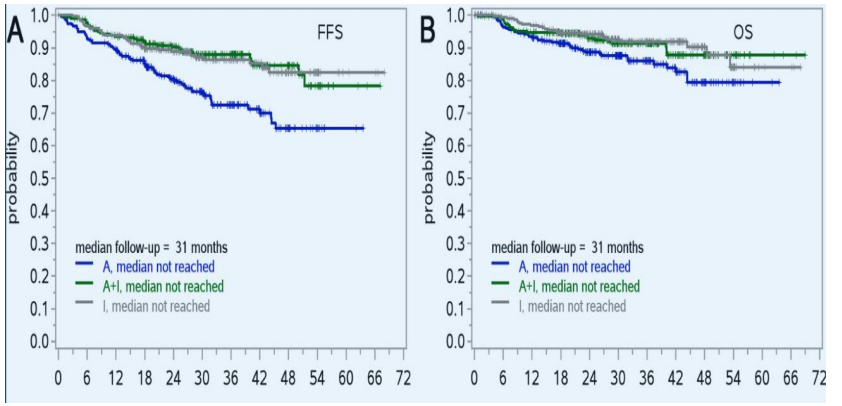
- 3-year FFS 72% (A) vs. 86% (I); p=0.9979, HR: 1.77, A+I: 88% (A+I) vs. 72% (A); p=0.0008, HR: 0.52. OS: 86% (A) vs. 91% in A+I, and 92% (I)

Acalabrutinib-Len-Rituximab in Untreated MCL: N=24, ORR; 100%

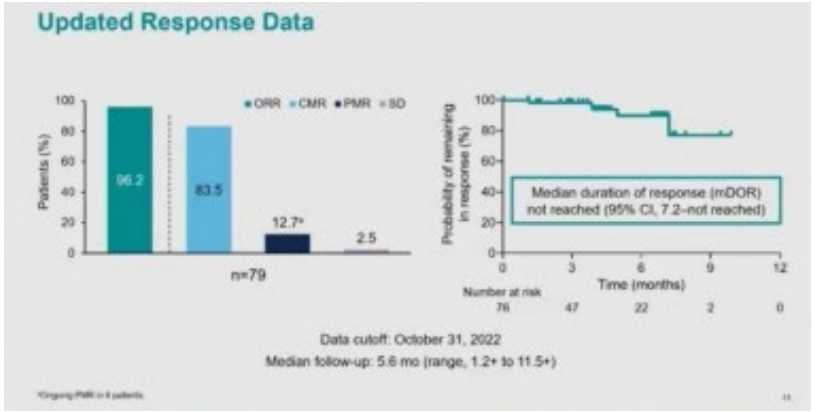
CD20 X CD3 T-Cell Engagers for R/R Indolent Lymphomas and MCL

- **Glofitamab R/R MCL: Phase I/II, N=37**
- ORR: 83.8% (31/37), CR: 73.0% (27/37), mDoR/CR: 12.6mo and 10mo
- **ELM-2: Odronextamab in R/R Follicular NHL, Gr 1–3a, N=96, Phase II**
- ORR 81% (69/85), CR 75% (64/85), mPFS: 20.2 mos
- **Epcoritamab + Rituximab + Lenalidomide for Untreated Follicular NHL, Gr 1-3a: Phase I/II, N=41 (Arm 6 EPCORE NHL-2 Trial)**
- ORR: 90% (26/29), CMR: 69% (20/29), CRS: 41%, ICANS: 0%

TRIANGLE: Outcomes



Epcoritamab + R²: Outcomes



Hodgkin's Lymphoma and Relapsed/Refractory Lymphoma

Polatuzumab Vedotin + R-ICE (PolaR-ICE) As Second-Line Therapy in R/R DLBCL, Phase II, N=42

- End of 3 cycles: ORR: 89% , CR: 61%, 21 pts proceeded to ASCT

ELM-2: Odronextamab in R/R DLBCL: Pivotal Phase II N=121

- ORR: 53%, CR: 537% (33/90), mDoCR NR (CI: 10.2 mos–NE), CR @ 9 mos: 73%. G1-2 CRS: 48%, G3/4: 0

BRUIN: Pirtobrutinib in R/R Waldenström Macroglobulinemia, Phase I/II, N=78

- ORR: 68% ,VGPR: 24%, PR: 44% mDoR NR (10mo-NE). 6-mo DoR rate: 86%, Prior BTKi 6mo DoR: 83%

VALERIA (NLG-MCL7): Venetoclax, Lenalidomide and Rituximab for R/R MCL, Phase Ib-II, N=59

- @ 6 months, ORR was 63% (29 CR, 8 PR).

SYMPHONY-1: Tazemetostat + Len and Rituximab in R/R Follicular Lymphoma, Phase Ib/+III trial, N=44

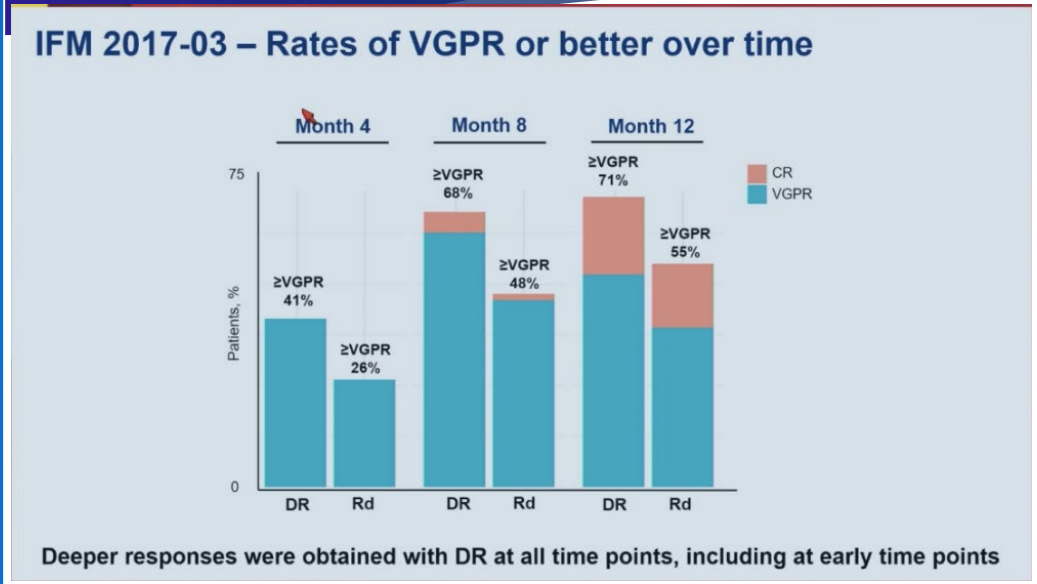
- ORR: 97.6% and 96.2% - 100% across subgroups, EZHm; 97%, EZHw; 100%, mPFS: NR

Brentuximab Vedotin + Nivolumab, Doxorubicin + DTIC for Untreated Advanced cHL, Phase II, N = 57

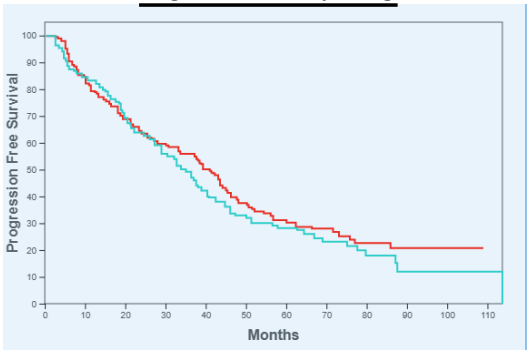
- EOT: ORR; 93% , CR; 88%, 12-mo PFS; 95%

Multiple Myeloma: NDMM

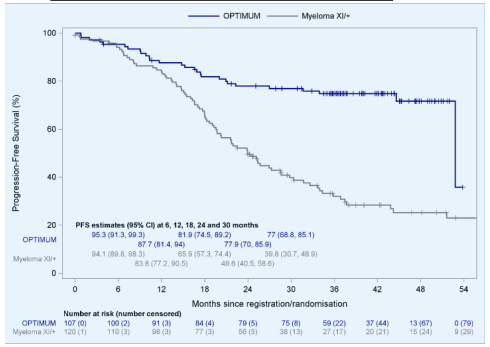
- **IFM 2017-03: Dexamethasone Sparing-Regimen with Daratumumab and Lenalidomide in Frail Patients with ND Multiple Myeloma, Phase III, N=293 (NO DEX!) vs. Rd**
- Superior ORR: DR; 89% vs Rd; 77% (p=0.025), Higher MRD negativity (MRD-10^{-5}) @12mo: 33% vs 18% and rapid responses
- **DSMM XIII: Phase III Trial, Rd Induction + ASCT With MEL140 Followed by R Maintenance vs Continuous Rd in Patients 60-75 Yrs of Age With NDMM, N=348 with 68 mo mFU:**
- Similar outcomes: Rd + ASCT MEL140 + R: mPFS; 32mo vs. 38mo with continuous Rd, HR: 1.15; P = .32, NS. ITT: 66% ASCT.
- **UK Optimum/Muknine: Extended Intensified Post-ASCT Consolidation with Dara-VRd for UHiR NDMM and pPCL:**
- PFS @ 30 mo: 77.0% (CI: 68.8-85.1)
- For context, PFS at 30 months for UHiR patients in Myeloma XI: 39.8% (CI: 30.7-48.9), and MASTER trial UHiR 24-mo-PFS: 58%



DSMM XIII: PFS



OPTIMUM/Muknine



Multiple Myeloma: NDMM

- **Myeloma XI: Phase III, Optimal Duration of Lenalidomide Maintenance After ASCT, N=1248**
- Continuing lenalidomide maintenance for ≥3 yrs beneficial for all patients.
- In MRD^{-neg} patients landmarked from 2y: HR; 0.63, p=0.025 but from 3y NS (3y HR 0.65, 4y HR 0.68), mPFS 59mo (50-NE) vs. 44mo (35-50), NS – NO BEFNEFIT BEYOND 3 years.
- MRD^{-pos} patients benefit from continuing lenalidomide until disease progression
- **ASCENT TRIAL: Fixed Duration Therapy with Daratumumab, Carfilzomib, Lenalidomide and Dexamethasone for High Risk Smoldering Multiple Myeloma, Phase II, N=87**
- ORR: 97% (37% sCR, 26% CR, 29% VGPR, 2% PR, 1% SD, and 2% NE. (61%; CR – IMWG MRDneg); PFS rate at 3 years; 89.9% (82.3-98.3%).
- **MM6: In-Class Transition (iCT) from Parenteral Bortezomib to Oral Ixazomib in NDMM, Phase IV, N=140, (17% Black/AA): iCT to IRd allows long-term, tolerable PI-based treatment**
- Subset Analysis: Ages <75 and ≥75 Years: ORR; Age <75; 60% at the end of 3 cycles of bortezomib-induction to 79% after iCT to Ird vs Age > 75; From 74% to 76%

Relapsed/Refractory Multiple Myeloma

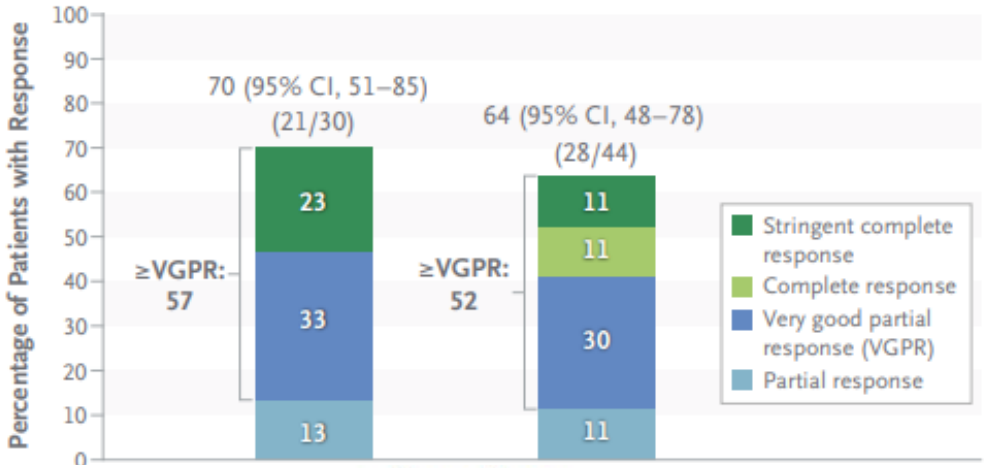
BiSpecific Antibody Therapy in R/R MM

- **MonumenTAL-1: GPRC5D x CD3 Bispecific Antibody Talquetamab in RRMM, Phase I/II, N=288**
- ORR: 73.1-74.1%, 63% after prior T-cell redirection therapy, mDoR ≥9 mo in all groups; longer DoR in ≥ CR patients.
- AEs: Grade ≥3 CRS: 0.7-2.1% 7-8% of Tocilizumab or corticosteroids , Others: skin-related/nail-related events, and dysgeusia.

CelMOD/iMID:

- **Mezigdomide + Dexamethasone in R/R MM: Phase I/II, Cereblon E3 ligase modulator (CelMOD), N=:101**
- ORR: 40.6% in triple-class–refractory R/R MM, mDoR (overall): 7.6 mo

Response to Subcutaneous Talquetamab Therapy



Adverse Events

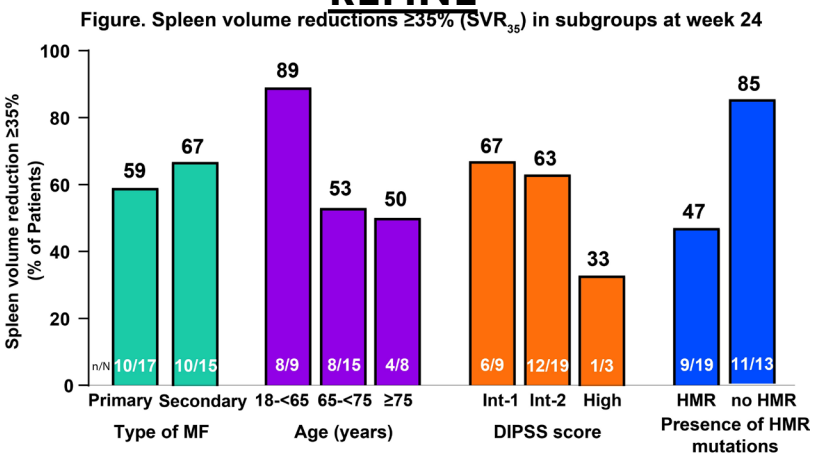
Event	Talquetamab 405 μg Weekly (N=30)		Talquetamab 800 μg Every 2 Wk (N=44)	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
	number of patients (percent)			
Any adverse event	30 (100)	26 (87)	44 (100)	38 (86)
Cytokine release syndrome	23 (77)	1 (3)	35 (80)	0
Skin-related event*	20 (67)	0	31 (70)	1 (2)
Dysgeusia	19 (63)	NA	25 (57)	NA

* Skin-related adverse events included asteatotic eczema, dry skin, eczema, pruritus, exfoliation, fissures, hyperpigmentation, lesions, skin toxic effects, and ulcers. NA denotes not available.

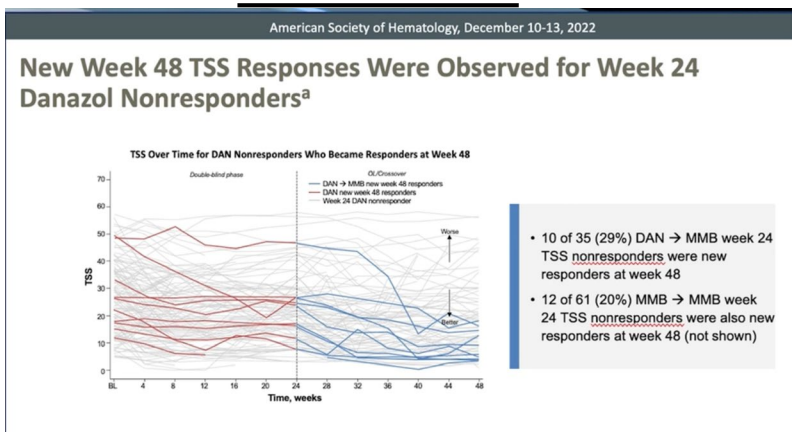
MYELOPROLIFERATIVE NEOPLASMS

- **REFINE: Navitoclax (BCL-XL/BCL-2 inhibitor) + Rux in MF: Cohort 3, N=32, JAKi Naïve, Phase II**
- SVR_{35} at week 24 : 33-89%, BMF grade improvement: 35%, Reduction in $JAK2^{V617}$ mutation VAF > 20% @ 24 weeks: 50%.
- **MOMENTUM: Momelotinib (JAK1/2,ACVRi) versus Danazol in Anemic MF after prior Ruxolitinib, Phase III, N=195, OPEN LABEL, Updated Analysis**
- MMB maintained TSS, TI, spleen responses, survival and safety in the ITT (symptomatic and anemic MF pts) and in those with low PLT @ wk 48.
- **Parsaclisib (PI3Kδ) Add-on to Ruxolitinib in MF With Suboptimal Response, N=74:** Improvement in TSS and SV with add-on parsaclisib daily dosing superior.
- **Ropeginterferon Alfa-2b for Pre-Fibrotic PMF, DIPSS Low and Int-1 MF, N=56**
- Hematologic and $JAK2^{V617F}$ molecular responses at 24 wk: 92%, 8% >50%.
- **SYSTEMIC MASTOCYTOSIS:** ASM: **Avapritinib** (PATHFINDER): ORR; 84%, **Blu-263** +/- AZA(AZURE) in AdvSM+AHN: Planned NonAdvSM: **Bezuclastinib** (SUMMIT): Planned. AdvSM: (APEX): 55% (6/11) Tryptase <20ng/mL

REFINE



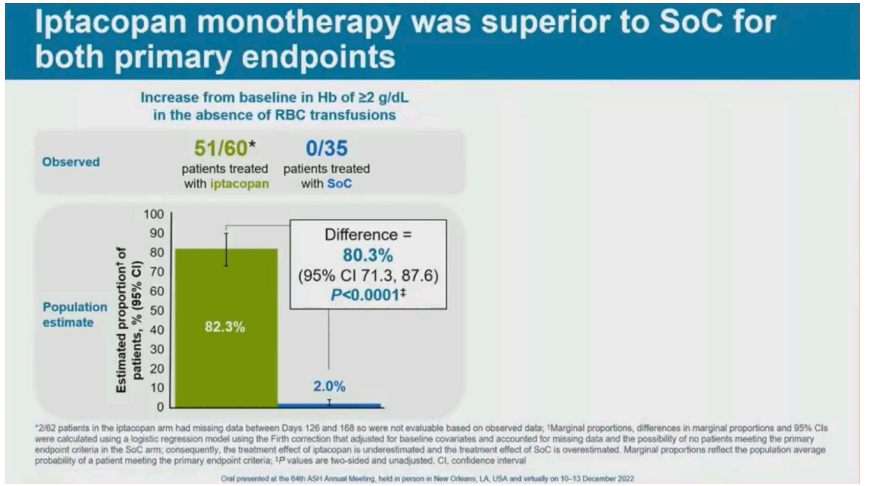
MOMENTUM



BENIGN AND NON-MALIGNANT HEMATOLOGY

- **APPLY-PNH: Phase III: Iptacopan in PNH and Residual Anemia with Anti-C5 Therapy, N=97**
- IPTACOPAN: First-in-class oral, selective inhibitor of factor B: Increased rate of Hb ≥2 g/dL and Hb ≥12 g/dL without transfusions, well tolerated, with no serious breakthrough hemolysis.
- Improved transfusion independence, fatigue, resolved extravascular hemolysis and maintained control of intravascular hemolysis.
- **Vemircopan in PNH, Phase II; Oral factor D inhibitor to prevent extravascular hemolysis, N=27, Untreated PNH**
- Increased mean Hb by 3.9 g/dL @week 12, reduced LDH/hemolysis, improved fatigue, tolerated.
- **ADVANCE IV: Phase III; Efgartigimod in Adult Primary ITP, N=131**
- Human IgG1 Fc engineered for increased affinity to FcRn; FDA approved for Myasthenia Gravis.
- Sustained PLT ≥50K: 21.8% vs 5.0% (P = .0316), Wks with PLTs ≥50K, chronic ITP: 6.1 vs 1.5 wks (P = .0009)

APPLY-PNH

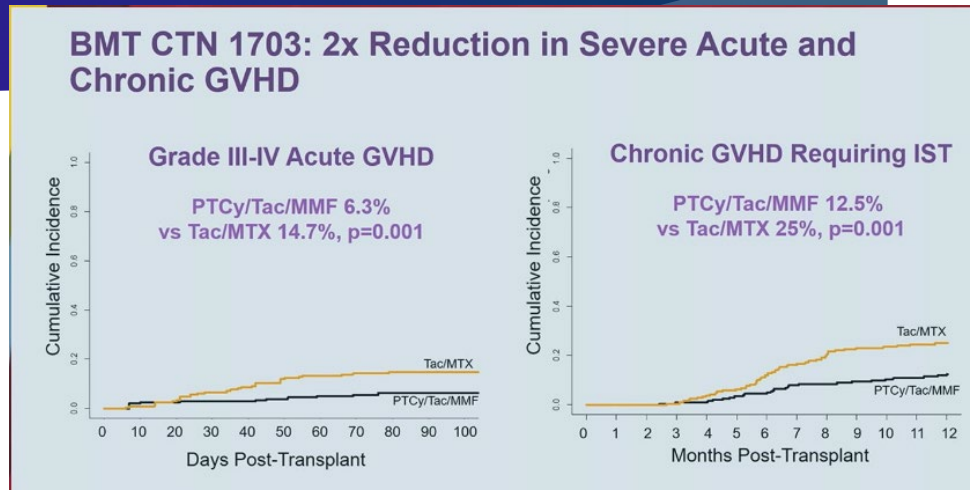


ADVANCE IV: Efgartigimod in ITP

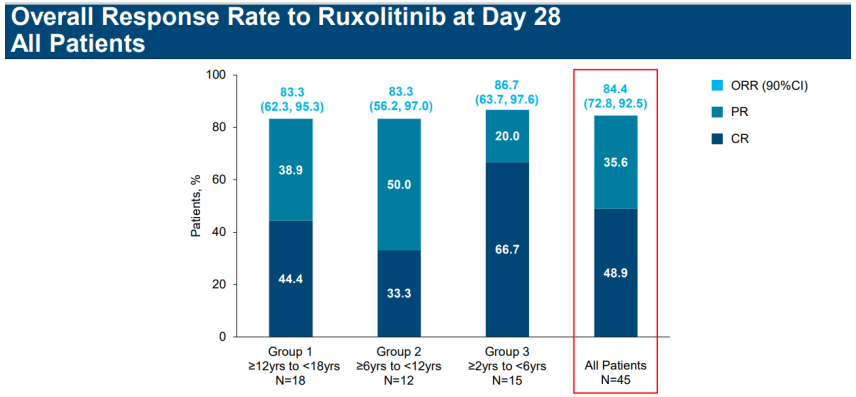
Endpoint	Population	Efgartigimod	Placebo	*P*-value
Primary endpoint				
Sustained platelet count response	Chronic	17/78 (21.8%)	2/40 (5.0%)	.0316*
Key Secondary endpoints				
Extent of disease control[a]	Chronic	6.1 (7.66), 2.0 (0.0, 11.0)	1.5 (3.23), 0.0 (0.0, 1.0)	.0009*
Sustained platelet count response	Overall	22/86 (25.6%)	3/45 (6.7%)	.0108*
Incidence of WHO bleeding events[b]	Overall	6.2 (6.39), 4.0 (1.0, 10.0)	8.3 (8.01), 5.0 (2.0, 14.0)	.8287
Durable sustained platelet count response	Overall	19/86 (22.1%)	3/45 (6.7%)	.0265

Hematopoietic Stem Cell and Cellular Therapy

- **BMT CTN 1703: Phase III; PTCy + TAC + MMF vs TAC + MTX for Prevention of GVHD Following Reduced-Intensity Conditioning AlloSCT, N=431, Primary End Point: 1-year GRFS**
- GRFS: 52.5% vs 34.9% (HR: 0.641; P <.001), Reduced severeGVHD with PTCy + TAC + MM and similar rates of relapse/progression
- Mildly delayed hematopoietic recovery and increased grade 2 but not grade 3 infections with PTCy + TAC + MM
- **REACH4: Phase I/II Study of Ruxolitinib in Pediatric Patients With Untreated or Steroid-Refractory Acute Graft-vs-Host Disease: N=45**
- • High ORR at day 28 of 84.4% (90% CI: 72.8, 92.5)
- • Durable ORR at day 56 of 66.7% (90% CI: 65.2, 89.1)
- **KarMMa-2 Cohort 2a: Idecabtagene Vicleucel in Early Relapsed Multiple Myeloma After Frontline ASCT, Phase II, N=37**
- ORR: 83.8%; CR/sCR: 45.9%, mDoR: 15.7 mo; mPFS: 11.4 mo
- Median OS: NR; 24-mo OS rate: 84.7%



REACH4



Efficacy was analyzed once all patients had completed 24 weeks of treatment or discontinued earlier; data cut-off 22 Feb 2022. ORR is defined as the proportion of patients achieving CR or PR. The two-sided 90% CI for the response rate was calculated using Clopper Pearson exact method.
CI, confidence interval; CR, complete response; n, number of patients with the specified response; N, number of patients in the treatment group; ORR, overall response rate; PR, partial response; yrs, years.

Oral presentation at: 64th ASH Annual Meeting & Exposition; December 10-13, 2022; New Orleans, LA, and virtual

What does it all mean?

My thoughts

- **PRACTICE Changing:**
- *Blinatumumab + Chemotherapy Consolidation in MRD negative Ph Negative ALL*
- *Ponatinib plus reduced intensity chemotherapy in Ph positive ALL*
- *Avoiding remission induction and proceeding with immediate allotransplantation in Relapsed/Refractory AML.*
- *MATRix chemotherapy followed by HDC/ASCT in Primary CNS lymphoma*
- *Ibrutinib + chemoimmunotherapy as substitute for ASCT in younger patients with MCL.*
- *Iptacopan in Paroxysmal Nocturnal Hemoglobinuria with residual anemia residual anemia on anti-C5 therapy.*
- **Practice Confirming**
- *Gemtuzumab Ozogomycin in in patient's aged 18-60 years with NPM-1 mutant AML*
- *Post Transplant Cyclophosphamide + TAC + MMF vs TAC + MTX for Prevention of GVHD following Reduced-Intensity conditioning allogeneic SCT.*
- *Covalent BTKi therapy in CLL: Zanabrutinib*
- **Potentially Practice Changing:**
- *Pirtobrutinib in relapsed and refractory Waldenström Macroglobulinemia*
- *Efgartigimod in Adult Primary Chronic or Persistent ITP*
- *GPRC5D x CD3 Bispecific antibody Talquetamab in RRMM*
- **Stay Tuned**
- *Asciminib in patients failing to reach molecular targets in CML after initial TKI therapy*
- *CD20 x CD3 Bispecific antibodies plus chemo-immunotherapy as initial therapy for DLBCL*
- *Bispecific antibodies in R/R lymphoma and RRMM*
- *Polatuzumab Vedotin + R-ICE (PolaR-ICE) As Second-Line Therapy in R/R DLBCL*
- *Epcoratimab after Richter's transformation in CLL*

And The Winners are ….

SAVE THIS DATE !

21th Annual Indy Hematology Review 2024

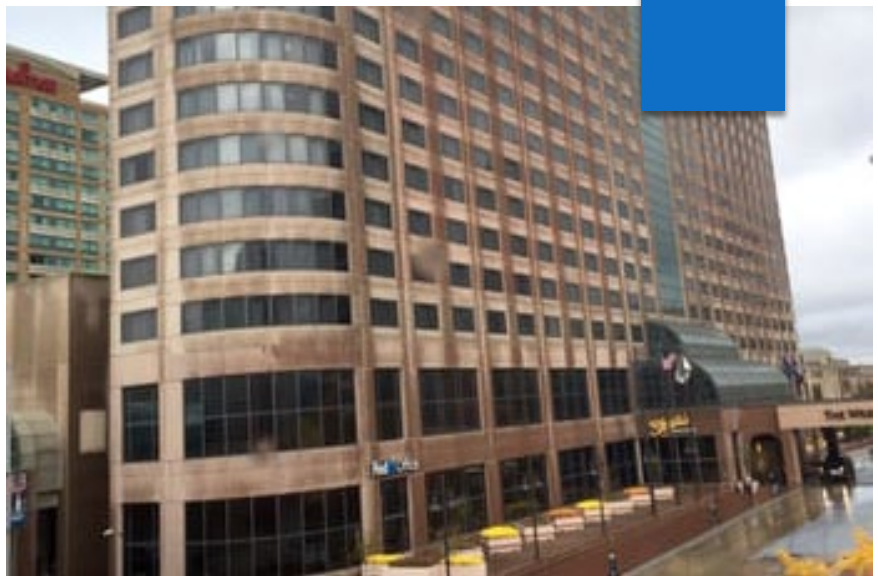
(http://www.indyhematologyreview.com)

February 24th, 2024

Westin Indianapolis,

Indianapolis,

Indiana, 46204



Indy Hematology Clinical Rounds®

Join us at our forthcoming Quarterly

Indy Hematology Clinical Rounds®: A CME education program

Present your challenging hematology cases to your peers in a live tumor board atmosphere for consensus recommendations and treatment options.

Visit: Indyhematologyreview.com for details

Next Meeting: April 19th, 2023: Focus on Chronic Lymphocytic Leukemia

Faculty: Nitin Jain, MD, MD Anderson Cancer Center

20TH INTERNATIONAL ULTMANN CHICAGO LYMPHOMA SYMPOSIUM

APRIL 21-22, 2023

Register at
ChicagoLymphoma.com

20TH ULTMANN

THE UNIVERSITY OF CHICAGO
MEDICINE &
BIOLOGICAL
SCIENCES

Co-Chair Indy Hematology Review

MICHAEL C. WIEMANN, MD, FACP

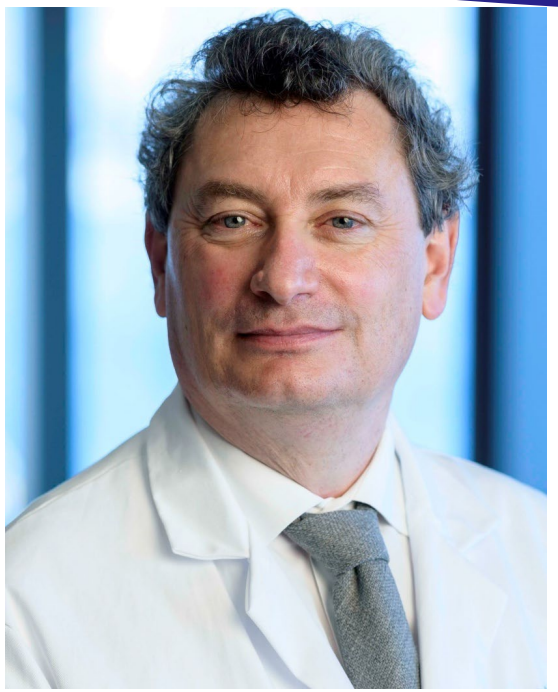
PRESIDENT, CLINICAL
ST. JOHN PROVIDENCE PHYSICIAN NETWORK

DETROIT, MICHIGAN

CLINICAL PROFESSOR OF MEDICINE, MCHIGAN STATE SCOOL OF MEDICINE, EAST LANSING, MI

T. Howard Lee Keynote Lecture

20 Years of Indy Hematology Review and The Cure is in: Managing Indolent and Mantle Cell Lymphomas with Targeted and Cellular Therapies in 2023

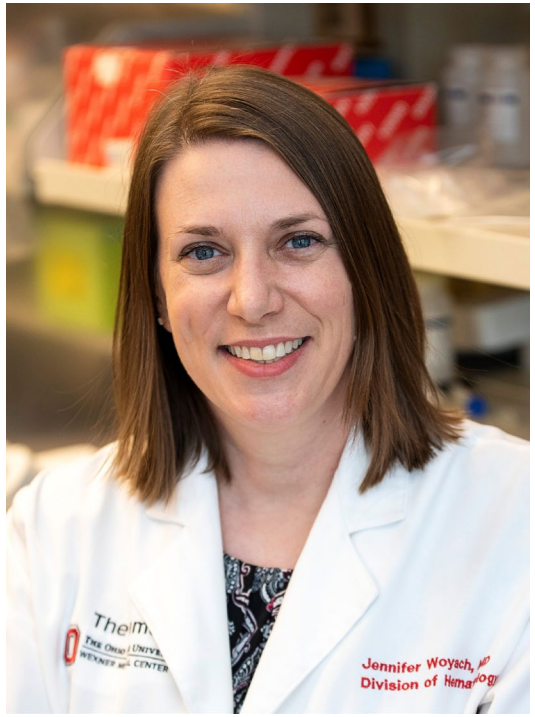


Gilles Salles, MD, PhD,
Chief of the Lymphoma Service at the Memorial Sloan Kettering Cancer Center (New York, NY)

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

ANNUAL STEVEN COUTRE CHRONIC LYMPHOCYTIC LEUKEMIA MEMORIAL LECTURE:

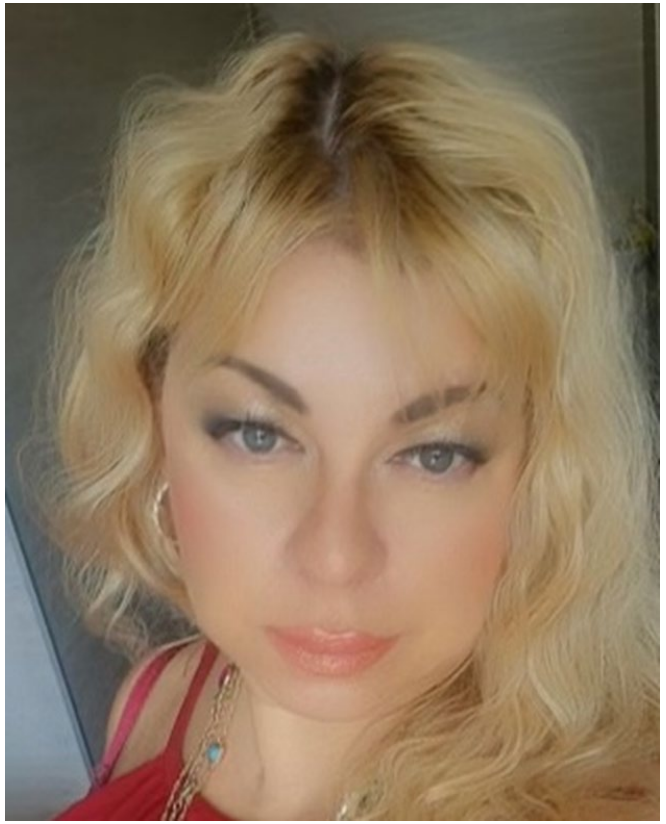
Therapeutic Options in CLL in 2023: Choosing Wisely; Initial Therapy in CLL



Jennifer Woyach, MD
Professor and Section Chair of Chronic Lymphocytic Leukemia, The Ohio State University, Columbus, OH

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

INDY HEMATOLOGY REVIEW 2023 SCHOLARSHIP RECIPIENT

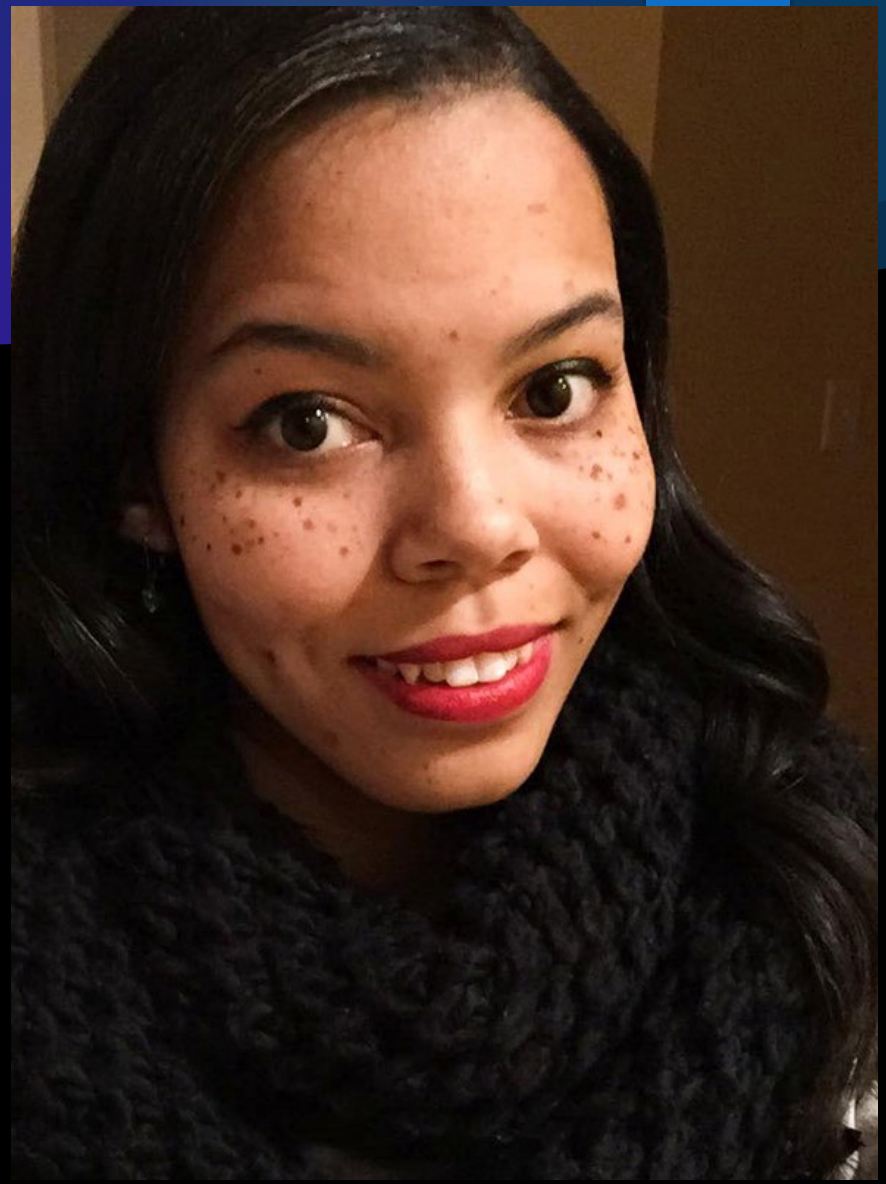


Svitlana Fomina, MD

Oncologist at the Regional Oncology Center and Director at the Doctor Alex Expert Medical Center,

Kharkiv, Ukraine

Evening with Experts: Surviving Cancer With Art Therapy



- Meaghan E. Wiggins, MA
- Art Therapist
- Clinical Hospital Coordinator,
- Cancer Support Community,
- Indianapolis, IN

Nursing and Allied Health Symposium

- **Moderators**
- Thalia Hammond
- Donna M. Birhiray, OTR, MBA

- **FACULTY**

Kristi K Orbaugh MSN, RNP, AOCN,

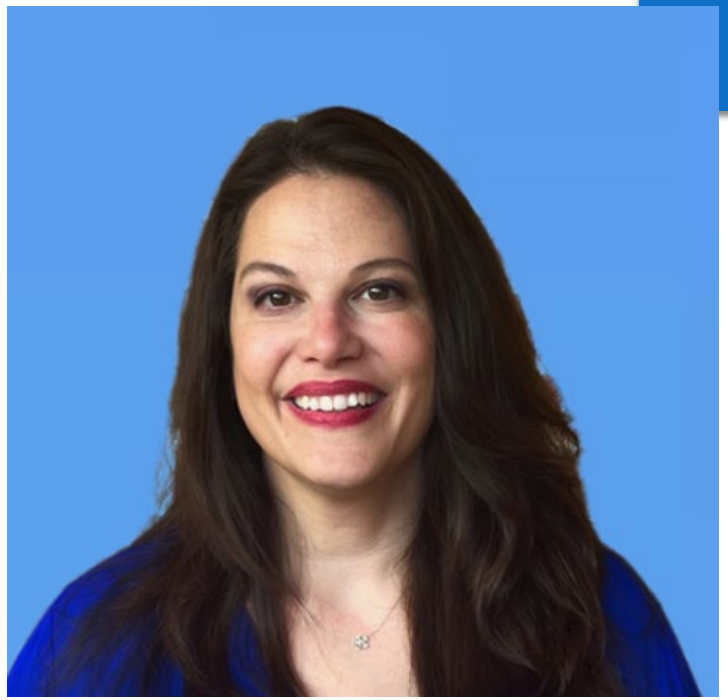
Nurse Practitioner, Community Hospital, Indianapolis, IN

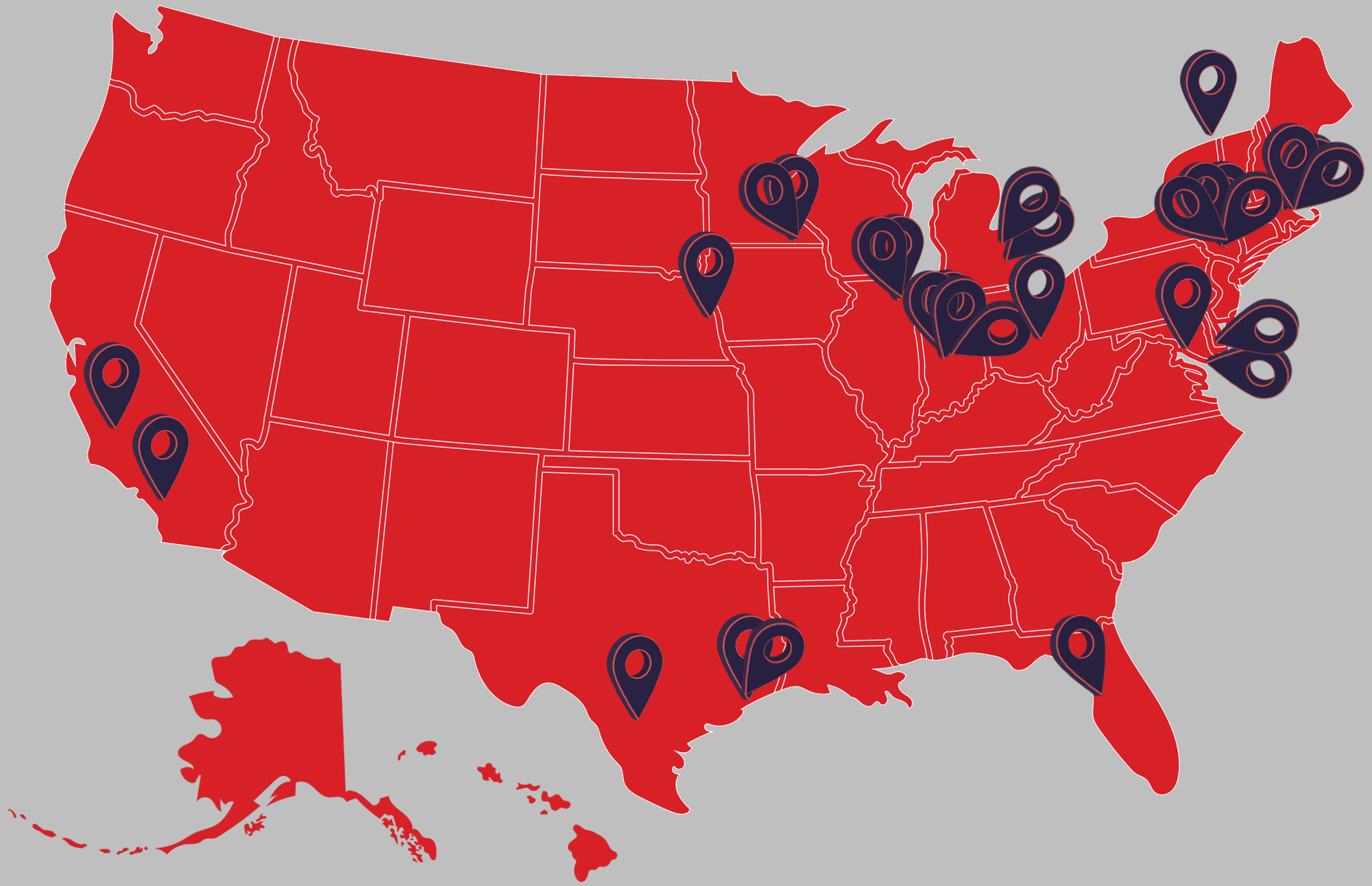
David Reeves, PharmD, BCOP

Associate Professor, Butler University and Clinical Pharmacist at Franciscan Hospital.

Sandra Garofalo, MS, APRN, AOCNP

Nurse Practitioner, Hematology Oncology of Indiana/AON, Indianapolis, IN





CONVERSATIONS WITH THE 2023 PRESIDENT OF THE AMERICAN SOCIETY OF HEMATOLOGY

Robert A. Brodsky, MD

PRESIDENT AMERICAN SOCIETY OF HEMATOLOGY 2023

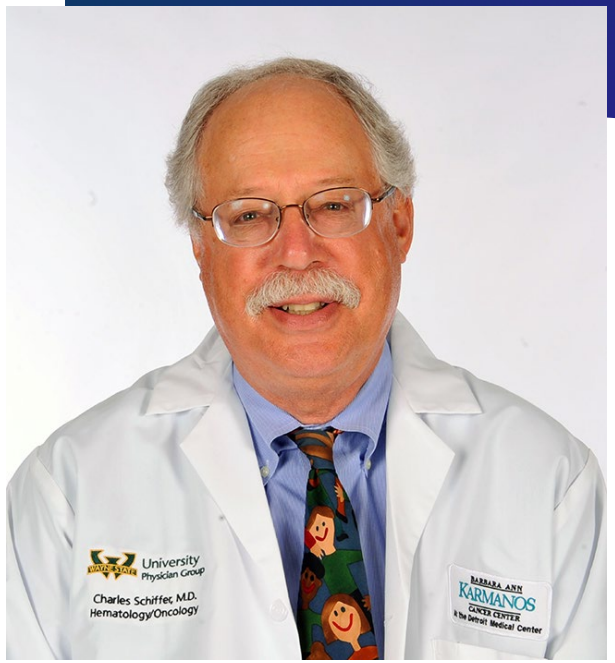
HOPKINS FAMILY PROFESSOR, DIRECTOR OF THE DIVISION OF HEMATOLOGY, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MD.

Emerging Therapy for Relapsed and Refractory Chronic Lymphocytic Leukemia

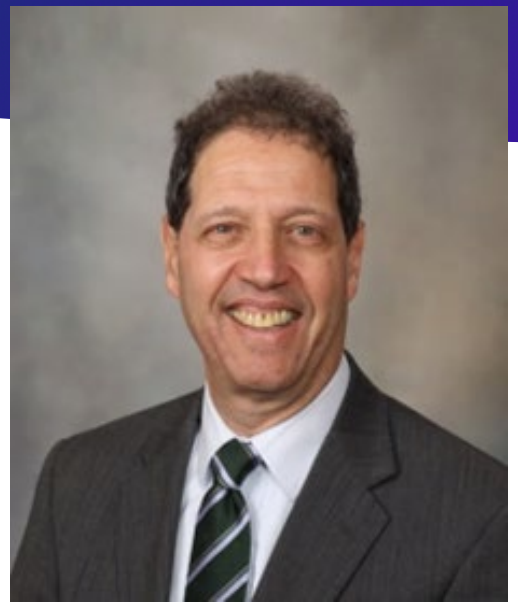
William Wierda, MD, PhD

D.B. Lane Cancer Research Distinguished Professor, Section Chief - Chronic Lymphocytic Leukemia, Department of Leukemia, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX

Hematologic Malignancies Town Hall

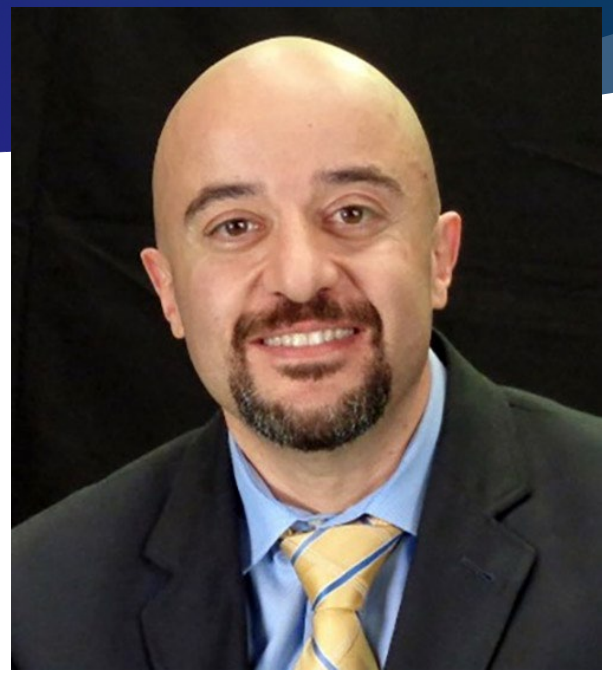


Charles Schiffer, MD
Emeritus Professor of Oncology and previously the Joseph Dresner Chair for Hematologic Malignancies Wayne State University School of Medicine Detroit, MI



Morie Gertz, MD, MACP
Roland Seidler Jr. Professor, Art of Medicine
Chair Emeritus, Department of Internal Medicine, Mayo Clinic Rochester, MN

President, Enterprise Cancer Service Line Atrium Health; Executive Director of the NCI Comprehensive Cancer based at Wake Forest Baptist (Winston-Salem, NC



Rami Komrokji, MD
Vice Chair of the Malignant Hematology and Head of the Leukemia and MDS Section at the Moffitt Cancer Center Tampa
Professor in Medicine & Oncologic Sciences at the College of Medicine, at the University of South Florida in Tampa, Florida.

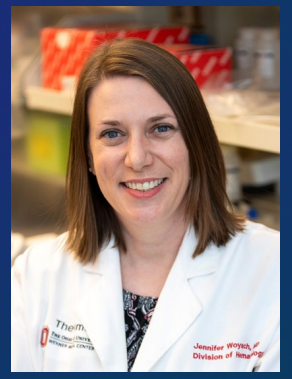
Hematologic Malignancies Town Hall

PLUS: Michael Weimann, MD, Saad Usmani, MD, Joseph Mikhael, MD, Matthew Lunning, DO, Steven Treon, MD, PhD, Tycell Phillips, Jennifer Woyach, MD,









Take Home Messages: Achieving Tomorrow's Outcomes Through Education Today

- Rami Komrokji, MD – Acute Myeloid Leukemias and MDS
- Ruben Mesa, MD, FACP – MPNs
- Charles Schiffer, MD – ALL
- Morie Gertz, MD, MACP – Plasma Cell Neoplasms and Amyloidosis
- William Wierda, MD, PhD – CLL




Emerging and Current Treatment of Multiple Myeloma: What Should We Know and What Should We Do?

Kenneth Anderson, MD

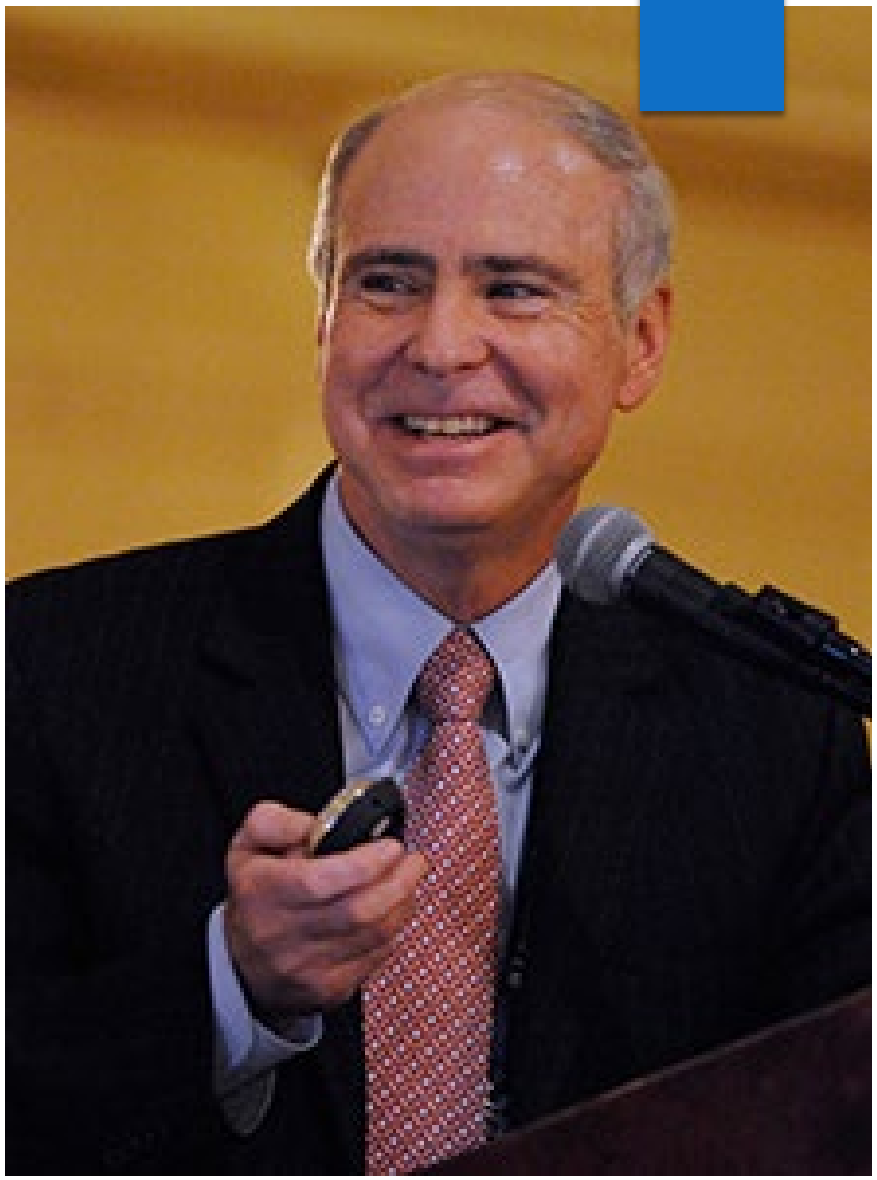
PAST PRESIDENT AMERICAN SOCIETY OF HEMATOLOGY 2017

Kraft Family Professor,

Harvard Medical School, Myeloma

Program Director and Chief, Division of Hematologic Neoplasia,

Dana Faber Cancer Institute, Boston, MA



To Transplant or Not When Minimal Residual Disease has been Achieved as Initial Therapy for Multiple Myeloma Monitoring and Rescuing the MRD Negative Patient with Multiple Myeloma After Initial Therapy

Joseph Mikhael MD, MEd, FRCPC, FACP

Professor, Applied Cancer Research and Drug Discovery

Translational Genomics Research Institute (TGen), an affiliate of City of Hope Cancer Center. Chief Medical Officer of the International Myeloma Foundation (IMF) and Director of Myeloma research at the HonorHealth Research Institute

Transplanting the MRD Negative Myeloma Patients for a Deeper Remission After Initial Therapy

Saad Usmani, MD, MBA, FACP

Chief of Myeloma Service, Memorial Sloan Kettering Cancer Center, Chief of Myeloma Service Member, Memorial Sloan Kettering Cancer Center, Attending Physician, Myeloma, Cellular Therapy and Adult BMT Services New York, NY

BEYOND HYPERVISCOSITY: 80 YEARS AND COUNTING, TREATMENT OF WALDENSTRÖM'S MACROGLOBULINEMIA

Steven P. Treon, MD, MA, PhD, FACP, FRCP

Director,

Bing Center for Waldenström's Macroglobulinemia
Professor of Medicine, Harvard Medical School,
Boston, MA

PLASMA CELL NEOPLASMS AND AMYLOIDOSIS

Morie Gertz, MD, MACP

Roland Seidler Jr. Professor, Art of Medicine

Chair Emeritus, Department of Internal Medicine,
Mayo Clinic Rochester, MN

Treatment Goals in Chronic Myeloid Leukemia: Managing Resistance, Recurrence and Discontinuation

Richard A. Larson, MD

Professor of Medicine ,

Director of the Hematologic Malignancies Clinical Research Program, University of Chicago,

Chicago, Illinois

Jumping On a Moving Train: Emerging and Current Treatment for Hodgkin's Lymphoma

Matthew Lunning D.O., FACP
Associate Professor of Medicine, University of Nebraska Medical Center, Omaha, NE.
Associate Vice Chair of Research Department of Internal Medicine, Medical Director of the Clinical Research Center (CRC), and Medical Director of Cellular Therapies.

Advancing Therapeutic Outcomes in Aggressive B and T Cell Lymphomas

Tycel Phillips, MD
Associate Professor, Division of Lymphoma, Department of Hematology and Hematopoietic Cell Transplantation, City of Hope Comprehensive Cancer Center, Duarte, CA

Current Controversies and Recommendations for the Treatment of Acute Lymphoblastic Leukemia and Lymphoblastic Lymphoma: The Indy Hematology Review Recommendations for 2023

Wendy Stock, MD, MA

Professor of Leukemia Research at the University of Chicago. Anjuli Seth Nayak Professor of Leukemia Research at the University of Chicago. Co-leader for Clinical and Experimental Therapeutics in the University of Chicago Comprehensive Cancer Center , Chicago, IL

Managing the Benign Hematology Consult: Treatment Recommendations for Coagulopathy, Cytosis and Cytopenia

Craig Kessler, MD

Professor of Medicine and Pathology,

Attending Physician, Division of Hematology-Oncology, Georgetown University Medical Center, Director, Division of Coagulation, Department of Laboratory Medicine and Director of the Therapeutic and Cellular Apheresis Unit. Washington, DC

Polycythemia Vera, Philadelphia Chromosome Negative Myeloproliferative and FGFR Mutant Myeloid Neoplasms

Angela G. Fleischman MD, PhD

Associate Professor, Division of Hematology/Oncology,

University of California, Irvine, CA

Myelofibrosis Chronic and Blast Phase: 2023 Algorithms for risk Stratification and Treatment

Ayalew Tefferi, MD

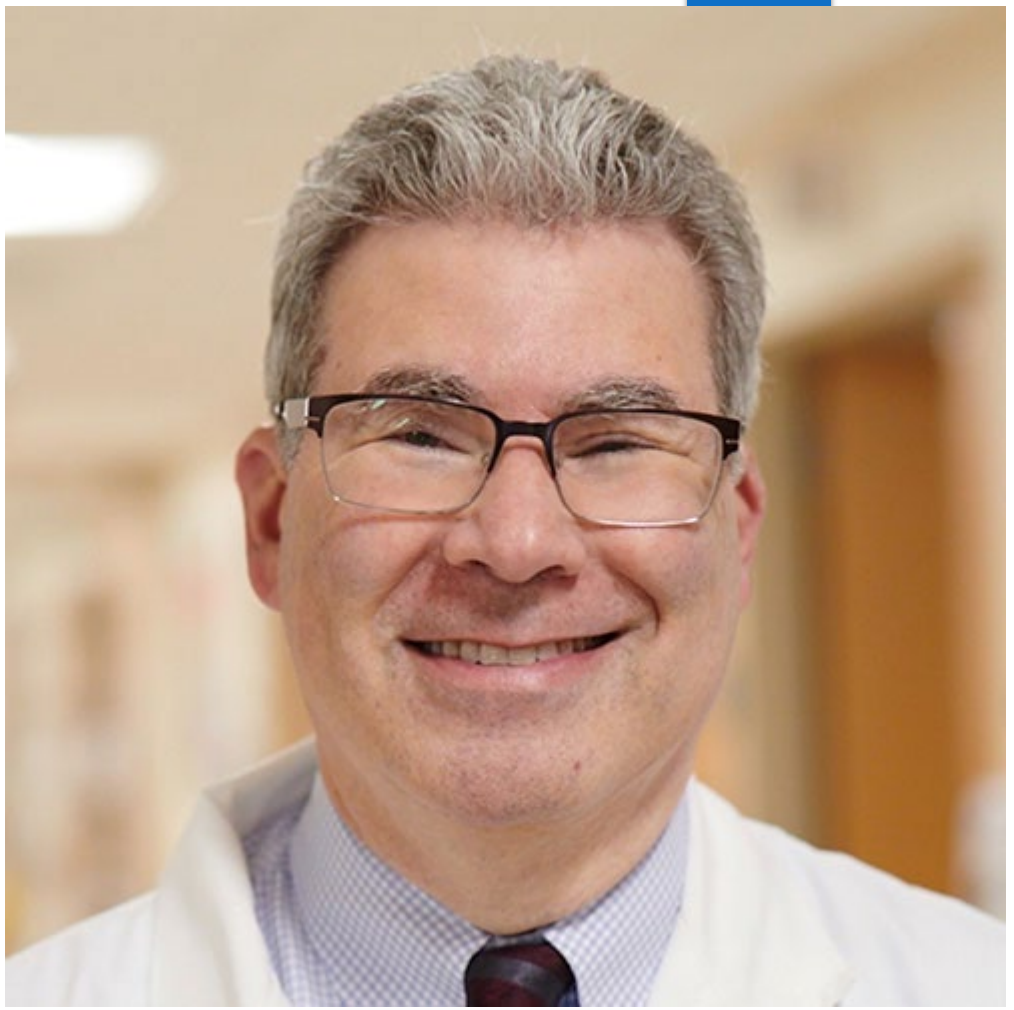
Barbara Woodward Lips II Professor of Medicine at the Mayo Clinic (Rochester, MN)

Improving Outcomes with Current Therapies in Acute Myeloid Leukemia and Acute Promyelocytic Leukemia: What we Recommend in 2023

Martin Tallman, MD

Director of Faculty Mentorship and Career Development at Lurie Cancer Center of Northwestern University

2021 PRESIDENT, AMERICAN SOCIETY OF HEMATOLOGY



Improving Outcomes with Current Therapies in Acute Myeloid Leukemia and Acute Promyelocytic Leukemia: What we Recommend in 2023

Richard Stone, MD

Professor of Medicine

Chair Leukemia Committee ALLIANCE

Chief of Staff and Director of Translational Research for the Adult Leukemia Program at Dana-Farber, and Harvard Medical School, Boston, MA

Hematopoietic Transplantation and Cellular Therapies

Richard Childs, MD
Clinical Director, National Heart, Lung, and Blood Institute (NHLBI) at the National Institutes of Health (NIH)
Bethesda, MD

REFERENCES

- **Acute Myelogenous Leukemia**
- Döhner. ASH 2022. Abstr 832.
- Stelljes. ASH 2022. Abstr 4.
- Daver. ASH 2022. Abstr 61.
- McCloskey. ASH 2022. Abstr 1436
- Short. ASH 2022. Abstr 831.
- Issa. ASH 2022. Abstr 63
- Erba. ASH 2022. Abstr 64.

- **Myelodysplastic Syndrome**
- Zeidan. ASH 2022. Abstr 853., Brunner. ASH 2021. Abstr 244
- Cadenas. ASH 2022. Abstr 460

- **Acute Lymphoblastic Leukemia**
- Litzow. ASH 2022. Abstr LBA1.
- Stelljes. ASH 2022. Abstr 212.
- Jabbour et al. ASCO 2023 Monthly Plenary Series, Journal of Clinical Oncology 41, no. 36_suppl (January 20, 2023) 398868-398868. Published online February 17, 2023.

- **Chronic Myeloid Leukemia**
- Cortes. ASH 2022. Abstr 80

REFERENCES

- **Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma**
- Brown. ASH 2022. Abstr LBA-6. Brown. NEJM. 2022;[Epub].
- Neimann. ASH 2022. Abstr 93.
- Allen. ASH 2022. Abstr 92.
- Ryan. ASH 2022. Abstr 344.
- Kater, ASH 2022. Absr 348.

- **Firstline Therapy for DLBCL**
- Davies. ASH 2022. Abstr 735
- Illerhaus. ASH 2022. Abstr LBA-3.
- Topp. ASH 2022. Abstr 737
- Olszewski. ASH 2022. Abstr 738

- **Indolent Lymphoma and Mantle Cell Lymphoma**
- Dreyling. ASH 2022. Abstr 1.
- Ruan. ASH 2022. Abstr 73.
- Phillips ASH 2022. Abstr 74.
- Kim ASH 2022. Abstr 949.
- Falchi ASH 2922. Abstr 611

REFERENCES

- **Hodgkin's Lymphoma and Relapsed/Refractory Lymphoma**
- Herrera. ASH 2022. Abstr 442
- Kim ASH 2022. Abstr 444.
- Palomba. ASH 2022. Abstr. 229.
- Jerkeman. ASH 2022. Abstr. 76.
- Batlevi. ASH 2022. Abstr 954.
- Lee. ASH 2022. Abstr 314.

- **Newly Diagnosed Multiple Myeloma**
- Manier. ASH 2022. Abstr 569.
- Straka. ASH 2022. Abstr 116.
- Kaiser. ASH 2022. Abstr 758.
- Pawlyn. ASH 2022. Abstr 570
- Kumar. ASH 2022. Abstr 757.
- Birhiray, ASH Abstr 3255.
-
- **Relapsed/Refractory Multiple Myeloma**
- Chari. ASH 2022. Abstr 157 and Chari A et al. DOI: 10.1056/NEJMoa2204591
- Richardson. ASH 2022. Abstr 568.

REFERENCES

- **Myeloproliferative Neoplasms**
- Passamonti. ASH 2022. Abstr 237.
- Gerds. ASH 2022. Abstr 627.
- Yacoub. ASH 2022. Abstr 236.
- Gill. ASH 2022. Abstr 629.
- Radia, ASH 2022, Abstr 625,
- DeAngelo, ASH 2022, Abstr. 3058 ,
- Akim ASH 2022, Abstr 3041,
- DeAngelo, ASH 2022, Abstr. 626

- **BENIGN/CLASSICAL HEMATOLOGY**
- De Latour. ASH 2022. Abstr LBA-2
- Browett. ASH 2022. Abstr 294. NCT04170023.
- Broome. ASH 2022. Abstr 3

- **Hematopoietic Stem Cell and Cellular Therapy**
- Holtan. ASH 2022. Abstr LBA-4.
- Locatelli. ASH 2022. Abstr 572.
- Usmani. ASH 2022. Abstr 361.