EMERGING THERAPIES FOR BLOOD DISEASES, CANCERS AND LYMPHOMAS 2023

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

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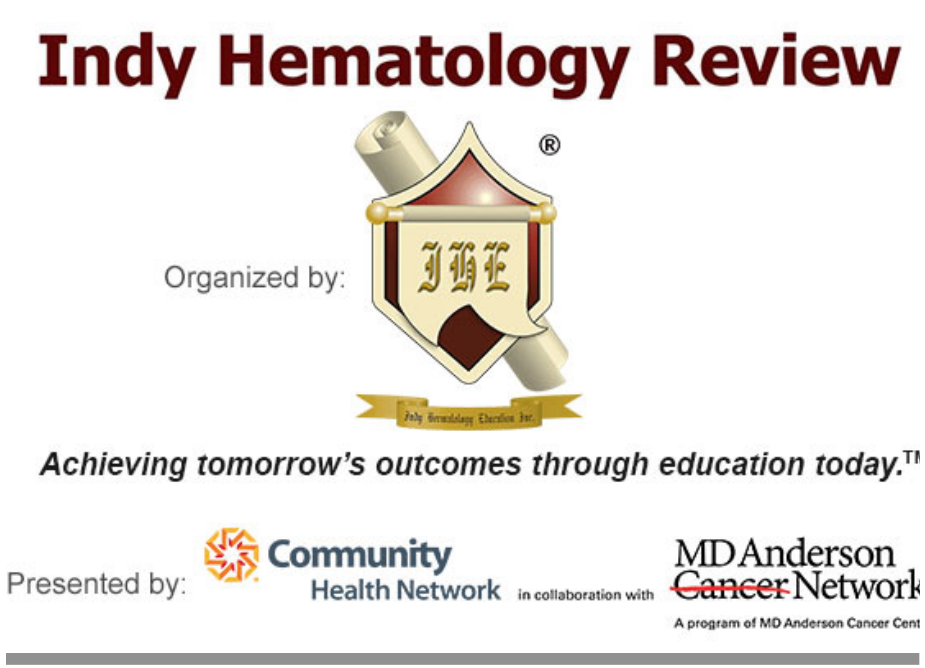

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ACHIEVING TOMMORROW'S OUTCOMES TODAY THROUGH EDUCATION™

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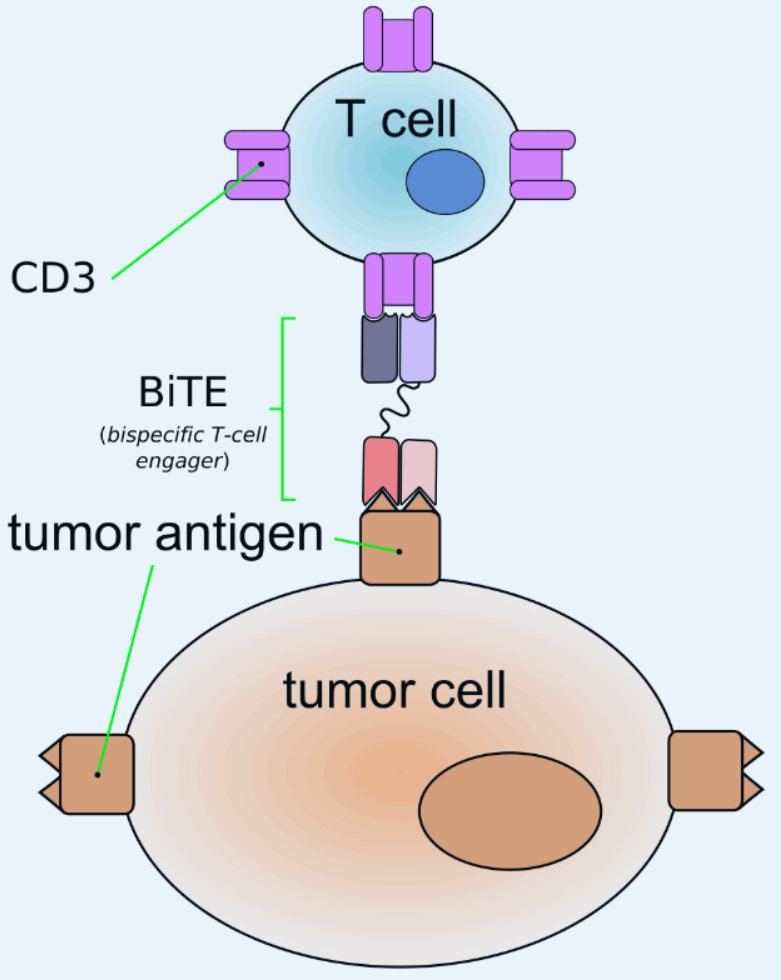
Bi-Specific Antibodies in Hematologic Malignancies

NEW DRUGS IN DEVELOPMENT

- Bi-Specific Antibodies: T-Cell Engagers in Lymphoma
- Glofitamab
- Mosunetuzumab (FDA Approved for Follicular Lymphoma)
- Odronextamab
- Epcoritamab
- Bi-Specific Antibodies: T-Cell Engagers in Myeloma
- Teclisimab (FDA Approved for Multiple Myeloma)
- Talquetamab
- Elranatamab
- Cevostamab
- Bi-Specific Antibodies: T-Cell Engagers in Leukemia
- Blinatumomab



ACUTE LEUKEMIA

- **What is Acute Leukemia ?**
- Diseases caused by the maturation arrest of bone marrow stem cells at a very early stage
- **Subtyptes:**
- Acute Lymphoblastic Leukemia(ALL)
- Acute Myeloid Leukemia (AML)

ACUTE MYELOID LEUKEMIA

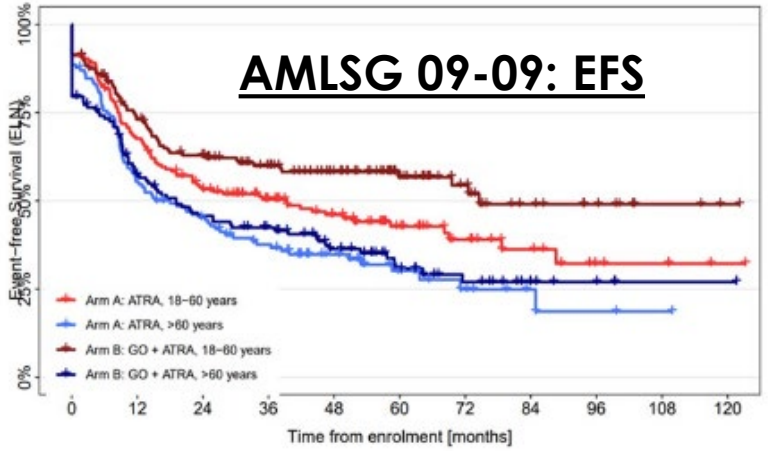
AMLSG 09-09: Phase III, Gemtuzumab Ozogamicin Plus Intensive Chemotherapy in NPM1-Mutant AML, N=588

- Similar overall survival, but event free survival (EFS) trend to benefit in favor of GO.
- Age subgroup analysis: Significant beneficial effect of GO on EFS and cumulative relapse (CIR) for ages 18 to 60 years but similar OS.

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

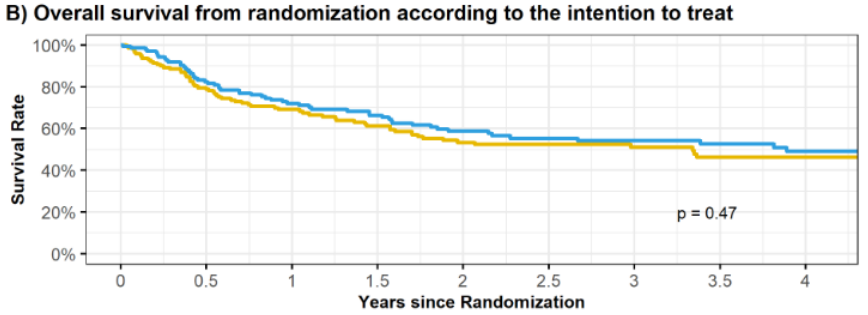
- Primary End Point: Non-Inferiority CR@day56 after alloHCT.
- Secondary End Points: OS and Leukemia free survival (LFS) from CR@day56.
- At 37 mo f/u: OS @1-year: 69.1% vs. 71.9% and 3-years OS 51.0% vs 54.2% in the DISC vs RIST arms, respectively (LR p=0.47)

AMLSG 09-09: EFS



Arm A: ATRA, 18–60 years	165	110	83	63	49	31	19	11	5	4	1
Arm A: ATRA, >60 years	131	72	56	41	27	16	8	4	2	1	0
Arm B: GO + ATRA, 18–60 years	160	110	91	74	60	37	23	12	8	3	1
Arm B: GO + ATRA, >60 years	132	70	55	47	33	21	13	6	4	1	1

ASAP TRIAL: RISC versus DISC



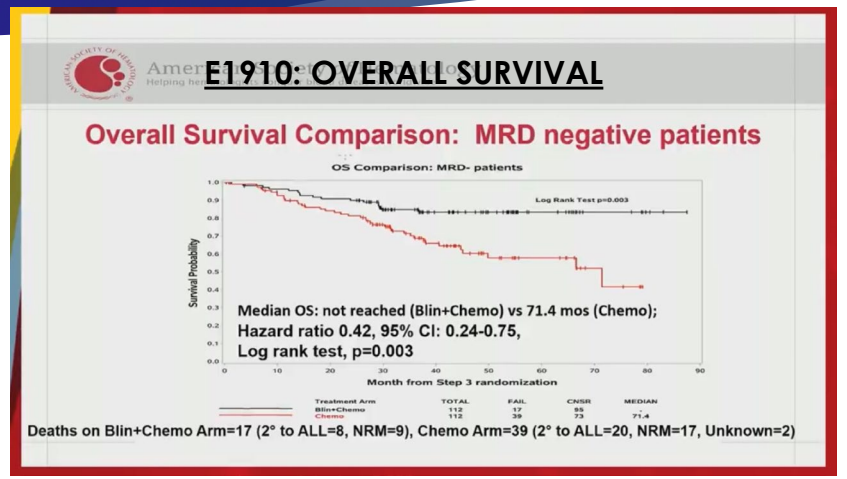
ACUTE LYMPHOBLASTIC LEUKEMIA

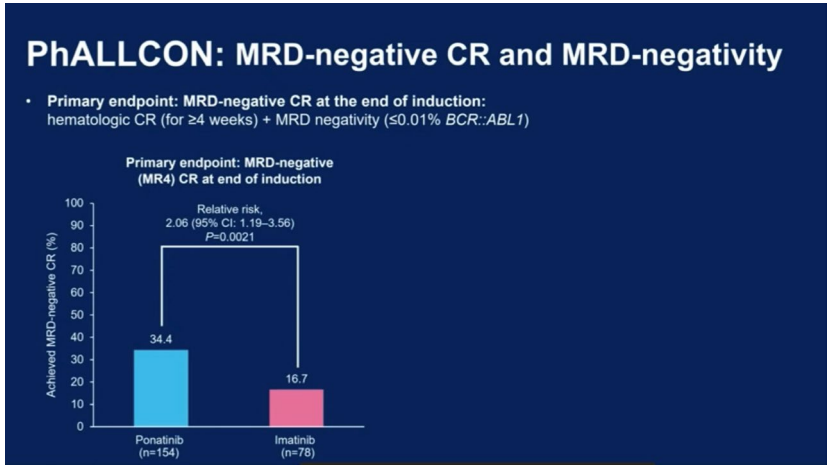
ECOG-ACRIN E1910: Phase III, Consolidation Chemo ± Blinatumomab in MRD^{-Neg}, BCR^{-Neg} B-ALL, N=488

- Median overall survival (OS): NR vs 71.4mo, HR: 0.42, p= 0.003 **(58% improvement in overall survival)**
- mRFS: NR vs 22.4mo, HR: 0.46, p=0.004 (54% improvement)
- 3.6-year OS: 83 vs 65%
- Deaths: 17 vs 39 – 50% of deaths due to relapse

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

- Composite Primary Endpoint: minimal residual disease negative complete response for 4 wks at EOI: 34.4% vs 16.7%; p=0.0021, similar toxicities.
- EFS: HR=0.652, 95% CI 0.385–1.104, TTF: HR=0.455





CHRONIC LEUKEMIA

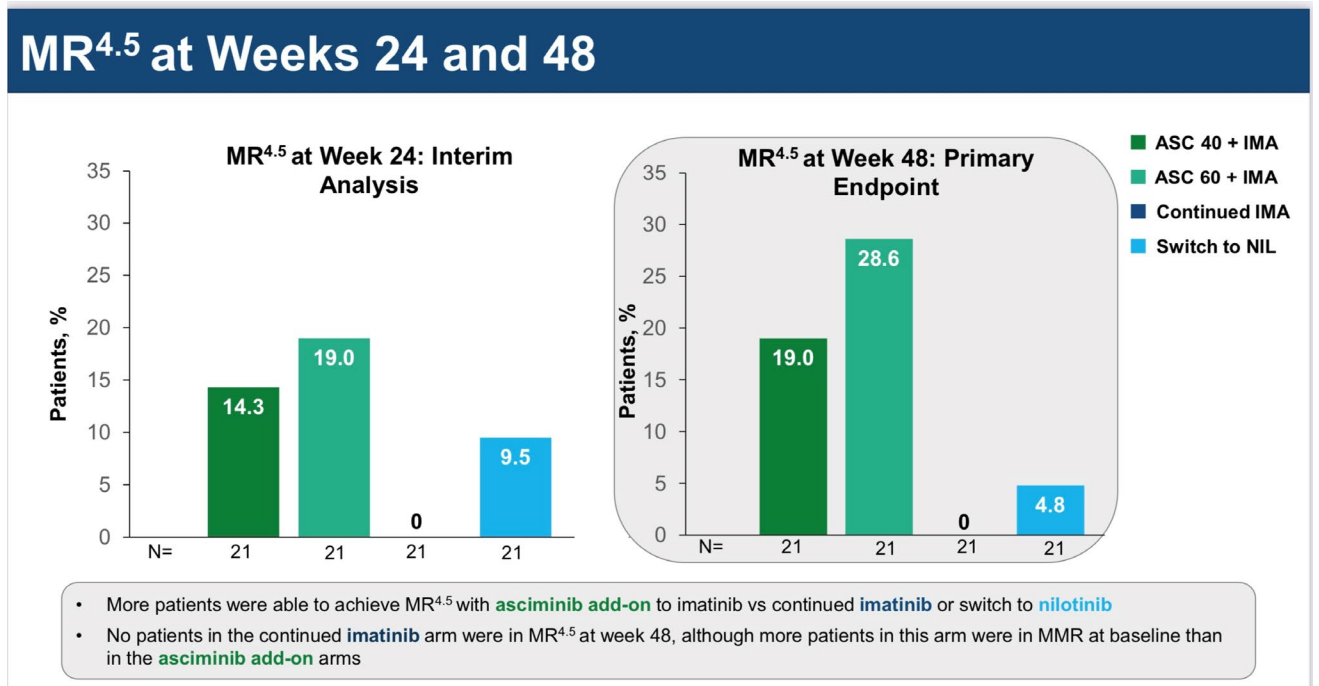
- **What is Chronic Leukemia?**
- Disease of blood and bone marrow associated with abnormal mature white blood cells.
- **2 major subtypes:**
- Chronic Myeloid Leukemia (CML)
- Chronic Lymphocytic Leukemia (CLL)

- Chronic Leukemia can transform into acute leukemia or aggressive lymphoma

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 IMATINIB 400 mg QD for ≥1 y with BCR::ABL1IS >0.01% to ≤1% at randomization
- **MR4.5 for ≥48 wks:**
- 40mg ASC Add-on; 60.0%,
- 60mg ASC Add-on: 80.0%,
- NIL Add-on; 66.7%
- **Increased AEs with Add-ons; Toxicities leading to discontinuations:** 40-mg add-on; 4.8%, 60-mg ASC add-on; 14.3%, IMA; 0, and NIL; 23.8%

ASC4MORE

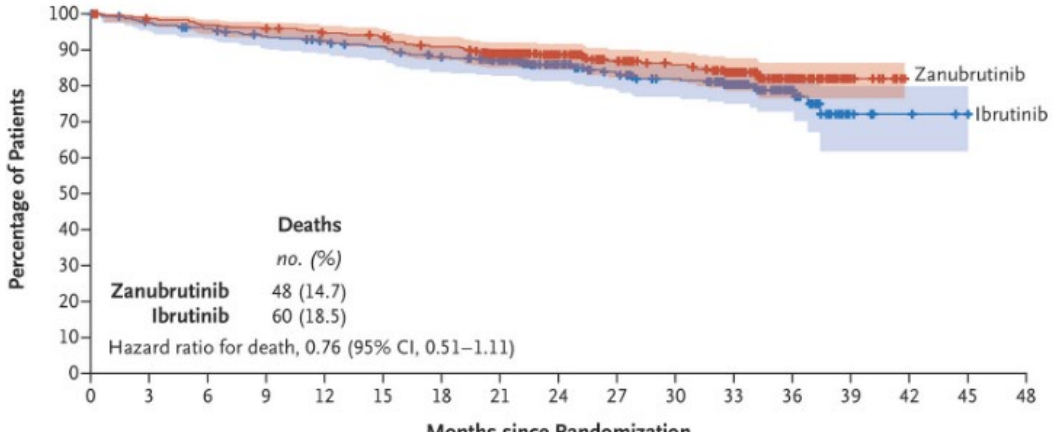


Cortes, et al. ASH. Abstr. 84

CHRONIC LYMPHOCYTIC LEUKEMIA

- **ALPINE: Zanubrutinib vs Ibrutinib for R/R CLL/SLL, Final analysis: Phase III, N=652**
- Primary End-Point: Inv-Assessed ORR; 83.5% vs. 74.2%, 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),
- I+V: uMRD rates higher and earlier in pts with uIGHV CLL vs mIGHV CLL.
- uMRD status from EOT+3 to EOT+18: Ibr+Ven; 77.6% vs 12.2% in the Clb+O.

ALPINE: OVERALL SURVIVAL and ADVERSE EVENTS



TEAE by Preferred Term, n (%)	Zanubrutinib (n=324)	Ibrutinib (n=324)
≥1 TEAE	**318 (98.1)**	**321 (99.1)**
COVID-19	75 (23.1)	58 (17.9)
Neutropenia	74 (22.8)	59 (18.2)
Hypertension	71 (21.9)	64 (19.8)
Upper respiratory tract infection	68 (21.0)	46 (14.2)
Diarrhea	52 (16.0)	78 (24.1)
Anemia	49 (15.1)	51 (15.7)
Arthralgia	47 (14.5)	53 (16.4)
Contusion	44 (13.6)	34 (10.5)
Cough	38 (11.7)	34 (10.5)
Pneumonia	34 (10.5)	40 (12.3)
Rash	33 (10.2)	40 (12.3)
Fatigue	31 (9.6)	43 (13.3)
Pyrexia	27 (8.3)	33 (10.2)
Atrial fibrillation	15 (4.6)	40 (12.3)
Muscle spasms	10 (3.1)	41 (12.7)

TEAE, treatment-emergent adverse event.

LYMPHOMA

- Cancer of the lymph nodes and lymphatic system and bone marrow that usually manifest as enlarged lymph glands
- Divided into 2 types:
- Hodgkin lymphoma, named after the British physician Sir Thomas Hodgkin, who described it 1832 and is pathologically characterized.
- Non-Hodgkin lymphoma

Lymphoma: Firstline Therapy for DLBCL

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

- Improved PFS, OS with RB-CHOP in ABC patients; PFS:54 vs 69%
- OS: 67% vs 80%: OS HR. No overall benefit on PFS or OS

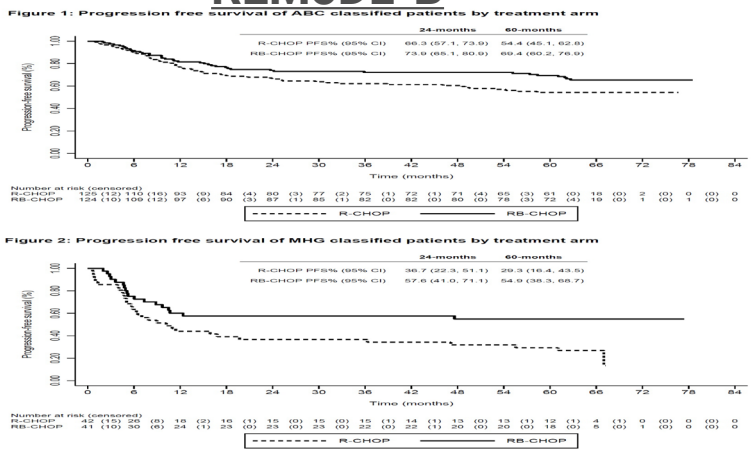
MATRix/IELSG43: HDC+ ASCT vs CIT in PCNS NHL, Phase III, N=346

- 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.

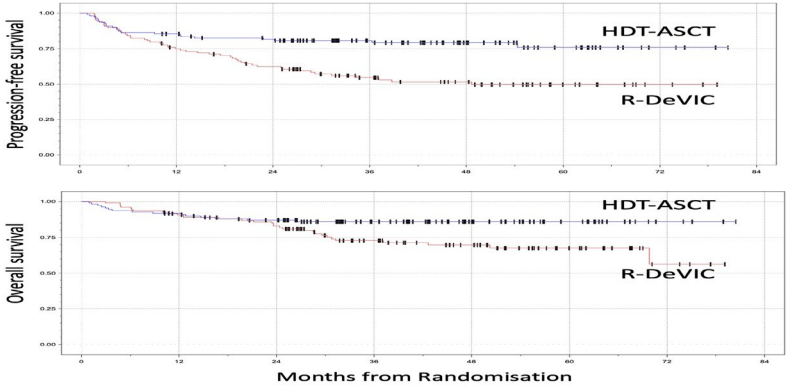
NEW DRUGS IN DEVELOPMENT

- **Bi-Specific Antibodies: T-Cell Engagers**
- **Glofitamab+R-CHOP in Untreated DLBCL: N=56:** ORR; 93.5%
- **Mosunetuzumab in Elderly/Unfit DLBCL: N=54:** ORR; 43%

REMoDL-B



MATRix/IELSG43



Hodgkin's Lymphoma and Relapsed/Refractory Lymphoma

TRIANGLE: Firstline Ibrutinib + CIT As Substitute for ASCT in Younger Patients 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)

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

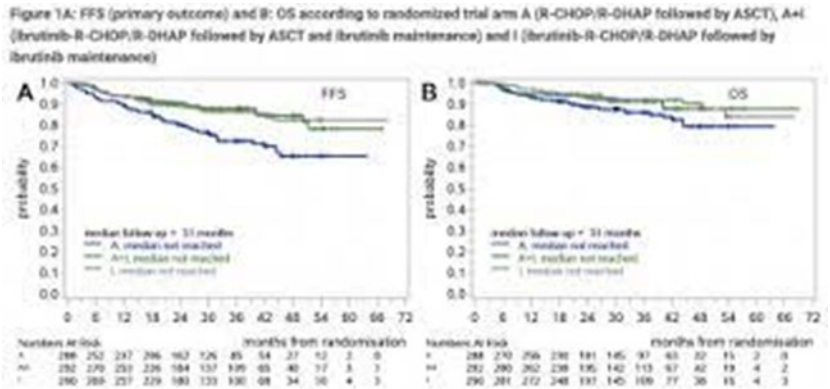
ELM-2: Odronextamab in R/R DLBCL: Pivotal Phase II N=121

- ORR: 53%, CR: 537% (33/90)

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

- ORR: 68% ,VGPR: 24%, PR: 44%

TRIANGLE: Firstline Ibrutinib + CIT



MULTIPLE MYELOMA

- What is Multiple Myeloma
- Cancer of the antibody producing cells of the bone marrow called plasma cells causing:
- Antibody production
- Increased blood calcium
- Kidney failure
- Low blood counts, particularly red blood cells
- Destruction of the bone marrow
- EMERGING THERAPIES:
- Immune Engagers: “Immune Match Markers”
- CAR-T Therapy: Re-educated T cells directed at Cancer Cell Targets
- Immunomodulators: Targeting the Myeloma microenviroment

Multiple Myeloma: NDMM

- **IFM 2017-03: Phase III, Daratumumab + Lenalidomide vs Len + Dex in Frail Patients with NDM, N=293 (NO DEX IN ELDERLY)**
- ORR: 96% with DR vs 85% with Rd, Higher MRD negativity (MRD-10^{-5}): 10% vs 3%, and rapid responses
- **DSMM XIII: Phase III Trial, Rd Induction + ASCT With MEL140 Followed by R Maintenance vs Continuous Rd in Patients 60-75 Yr of Age With NDMM, N=348:**
- 68 mo mFU: Rd + ASCT MEL140 + R: mPFS; 32mo vs. 38mo with continuous Rd, HR: 1.15; P = .32, NS.
- In the intention-to-treat population, MEL140 plus RD induction and lenalidomide maintenance was not superior to continuous lenalidomide/dexamethasone treatment, but only 66% of patients in the transplant arm received a transplant.
- **Myeloma XI: Phase III, Optimal Duration of Lenalidomide Maintenance After ASCT, N=1248**
- Continuing len maintenance for ≥3 yr beneficial. Impact of maintenance therapy decreases with time.
- Maintenance impact diminishes between 4 and 5 years in all patients, earlier in the subgroup that is MRD-ve after ASCT.
- MRD-positive patients benefit from continuing lenalidomide until disease progression
- **MM6: In-Class Transition (iCT) from Parenteral Bortezomib to Oral Ixazomib in NDMM, Phase II, N=140, (17% Black/AA)**
- Subset Analysis: Ages <75 and ≥75 Years: ORR; 60% at the end of 3 cycles of bortezomib-induction to 79% after iCT to Ird

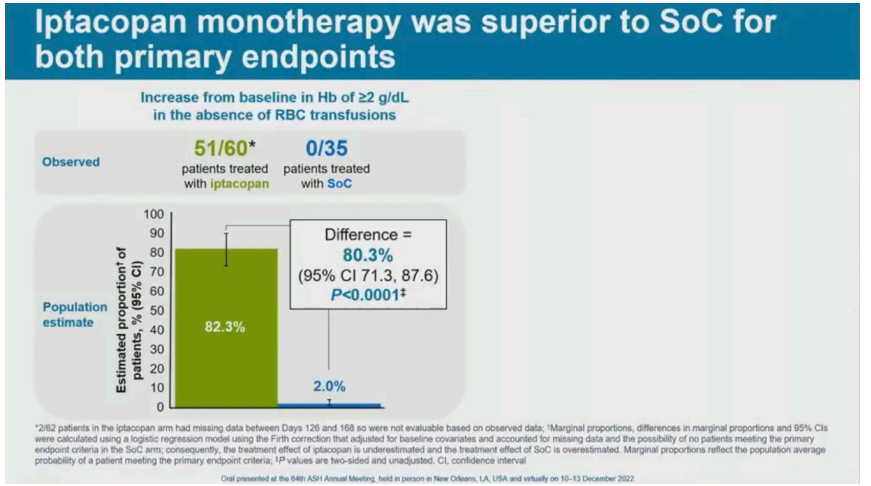
BiSpecific Antibody Therapy in R/R MM

- **MonumenTAL-1: GPCR5D 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.

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.
- **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

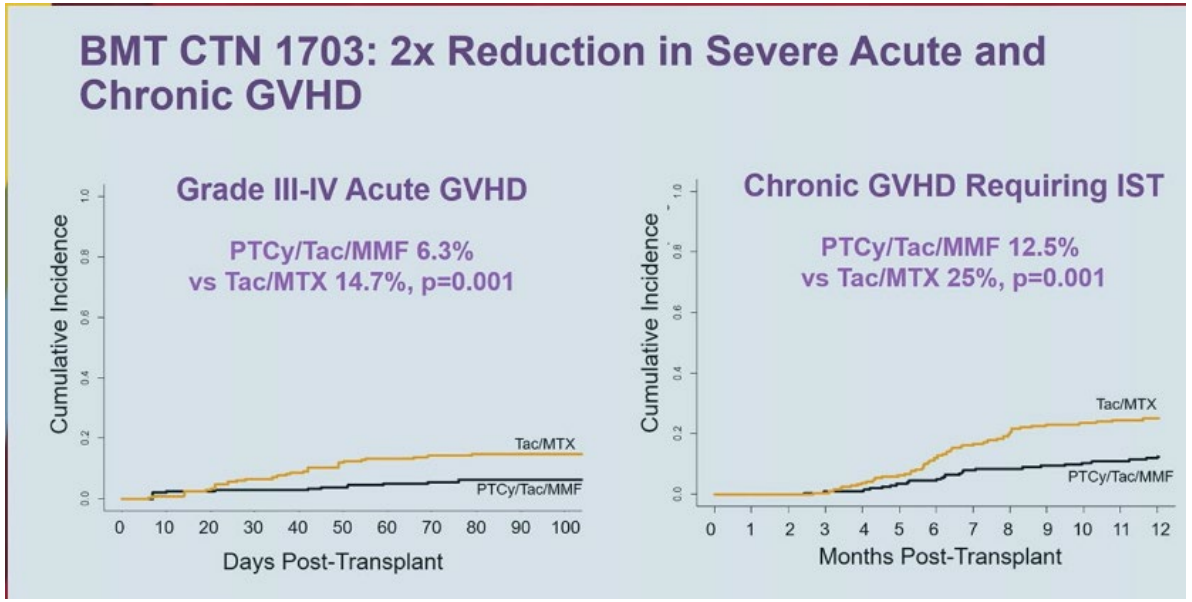


ADVANCE IV: Efgartigimod in ITP

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



EVENING WITH EXPERTS 2022: FACULTY

MULTIPLE MYELOMA

Kenneth Anderson, MD

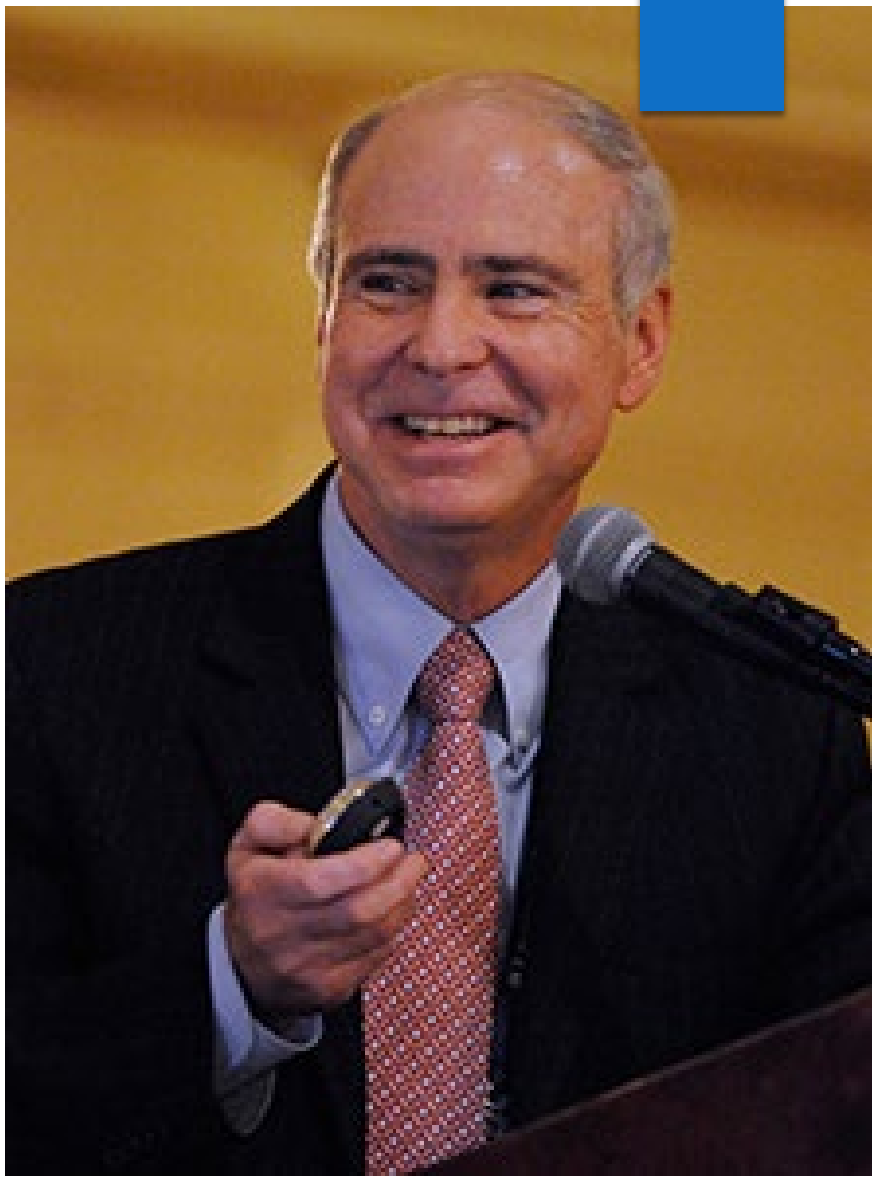
PAST PRESIDENT AMERICAN SOCIETY OF HEMATOLOGY 2017

Kraft Family Professor,

Harvard Medical School, Myeloma

Program Director and Chief, Division of Hematologic Neoplasia,

Dana Faber Cancer Institute, Boston, MA



WALDENSTRÖM'S MACROGLOBULINEMIA

Morie Gertz, MD, MACP

Roland Seidler Jr. Professor, Art of Medicine

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

LYMPHOMAS

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

MYELOPROLIFERATIVE NEOPLASMS

Angela G. Fleischman MD, PhD

Associate Professor, Division of Hematology/Oncology,

University of California, Irvine, CA

Acute Leukemias, Myelodysplastic Syndromes and Chronic Myeloid Leukemia

Charles Schiffer, MD

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

CHRONIC LYMPHOCYTIC LEUKEMIA

William G. Wierda, M.D., Ph.D.

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

Section Chief - Chronic Lymphocytic Leukemia, Department of Leukemia, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX

Evening with Experts: Surviving Cancer With Art Therapy

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

HEMATOPOIETIC STEM CELL TRANSPLANTATION AND CELLULAR THERAPY

Richard Childs, MD
Bethesda, MD

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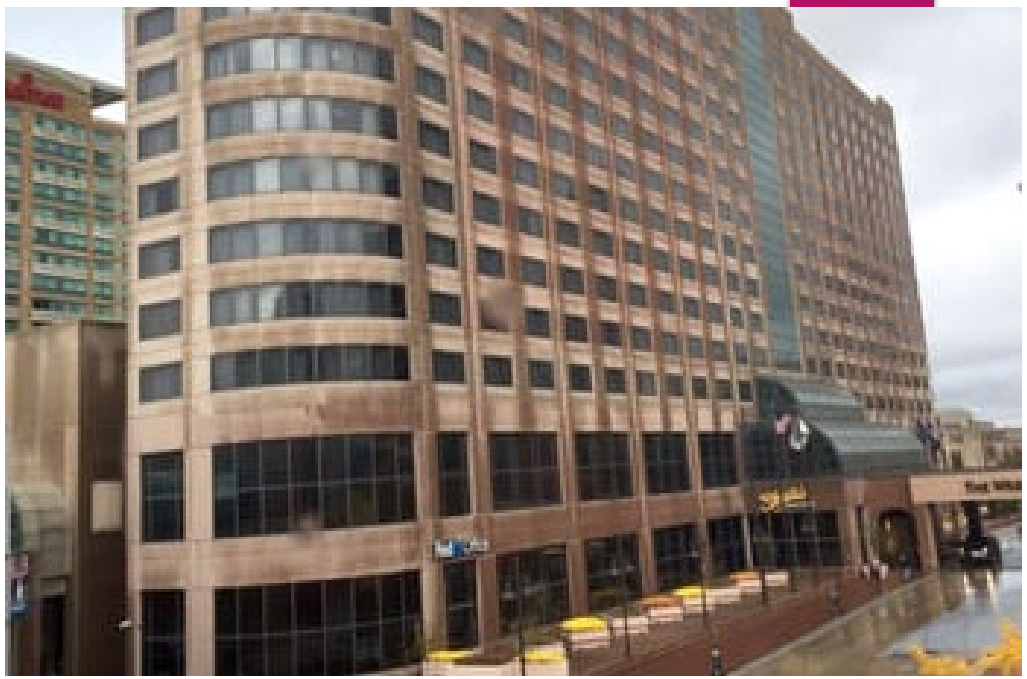

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