14th Annual INDY HEMATOLOGY REVIEW 2017

State of Hematology 2017
Emerging Therapies

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DISCLOSURES

SPEAKERS BUREAU

• EISAI, HELSIN, JANSSEN BIONCOLOGY, PFIZER, BMS, TAKEDA, PHARMACYCLICS, ASTRAZENECA, GENOMIC HEALTH, NORVATIS, INCYTE, SANOFI ONCOLOGY, CLOVIS ONCOLOGY

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Hematology and Hematopoietic Stem Cell Transplantation

- **SUSTAIN**: Double blind, placebo controlled, Phase II trial of Crizanlizumab with or without hydroxyurea in SCD: Significantly lower rate of annual sickle cell–related pain crises (45.3% reduction with high-dose, P=0.01) and low Aes

- **ALXN1210**: longer-acting anti-C5 antibody given q 24wks active in PNH

- **CALLISTO**: Rivaroxiban safe and effective in Cancer associated VTE?

- Waldenström macroglobulinemia: Ixazomib, dex and rituximab (IDR): ORR 80% (VGPR 5%, PR 45%, MR 30%) active, neuropathy sparing regimen in symptomatic untreated WM patients

- **ASCT in Myeloma Therapy**: “More is not always better”
  - Phase III STaMINA: single ASCT, single ASCT followed by RVD consolidation, vs tandem ASCT: No difference in PFS, OS after 38 mos

- **Ibrutinib in Steroid refractory GVHD**: n = 42, 67% response, and 71% sustained improvement.
Acute Leukemia

AML

- **SWOG S1203**: Vorinostat plus Ida/Cytarabine in Untreated AML: RCT, Phase III superiority trial vs 7 + 3, n=738, Primary end points: EFS and rate of alloSCT
  - No significant survival differences between study arms for EFS, OS in all pts

- **Vadastuximab Talirine**: Anti CD33 immunotoxin plus 7 +3 in Newly diagnosed AML: Phase 1b dose escalation study, n=42, aged 18-65yrs
  - CRc 76% (compared with GO+chemo: 72.8%), MRD 78%. No VOD/SOS, 50% alloSCT.

- **Frontline Vadastuximab Talirine + HMA** in Older pts with AML: Phase I, n=53
  - Safety profile, including myelosuppression, consistent with on-target effects
  - 73% CR + CRi rate and MRD 50%, higher than expected for HMA alone.

- **Venetoclax + LDAC Therapy** in older pts with untreated AML: Phase I/II trial, > 65 yrs, unfit for chemo, n= 61
  - ORR: 37/61 (CR + CRi + PR), CRc = 54%, is highly correlated with OS.
  - No TLS observed
Acute Leukemia

ALL

- Frontline Ponatinib + Hyper-CVAD in Ph+ ALL: 100% CR, 100% CCyR, 79% CMR, 78% 3-yr CRD, 75% 3-yr OS, n=58 (dose reduction of ponatinib to 30 mg after induction and to 15 mg in CMR resulted in reduction of vascular AEs)

- Frontline Inotuzumab Ozogamicin + Mini-HCVD in Older Pts With ALL, N=47
  - ORR: 98%, 3-yr OS 54% compares favorably with 31% 3-yr OS reported with HCVAD ± rituximab, VOD/SOS 4 pts, resulting in INO dose reduction

- TOWER: Blinatumomab vs Chemotherapy - Superior OS: 7.7 vs 4 mo (HR 0.71)
  - QoL in R/R Ph- B-Precursor ALL: Blinatumomab delays time to deterioration in HRQoL or EFS vs SoC chemotherapy

- ELIANA: CTL019 in Pediatric/Young Adult Patients With R/R B-Cell ALL: Multicenter, open-label, worldwide single-arm phase II study: n=81
  - Study met primary endpoint with CR/CRi of 82%
  - Durable CRs were observed, all CRs were MRD negative
  - 6 deaths, 3 A/Es and 5 manufacturing failures: prior to CTL019 administration, CTLs INF, n=62
  - Cytokine release syndrome managed, no CRS-related deaths observed
Chronic Myeloid Leukemia

- ABL001X2101: Allosteric BCR-ABL1 Inhibitor, ABL001 in TKI-Resistant CP CML: Phase I, dose escalation study: High RR within 6 and 12 mos on treatment.
  - Only 1 pt with relapsed/progressive disease had detectable mutations
- Phase III EURO-SKI: Cessation of TKI therapy in Deep Response: pts on TKIs ≥ 3 yrs with DMR for ≥ 1 yr 61% were free of MR at 6 mos and 55% were free of MR at 12 mos after TKI cessation
  - Restarting TKI therapy after cessation and loss of MMR, 86% achieved MMR and 80.1% achieved MR^4 at last assessment

Chronic Lymphocytic Leukemia

- VENETOCLAX: CLL After Failure of Ibrutinib or Idelalisib or both:
  - IRC-assessed ORR (pts R/R on ibrutinib: 70%; pts R/R on idelalisib: 62%)
  - MRD negativity observed in 45% of pts evaluated
- CONTINUUM Trial: Lenalidomide maintenance after 2nd line Rx
  - Median PFS: lenalidomide 33.9 mos versus 9.2 mos placebo HR 0.40 [95% CI 0.29–0.55]; P< 0.001 –Median follow-up 31.5 mos
  - OS: Similar
Diffuse Large B-Cell Lymphoma

- **R-CHOP Remains the Standard of Care in Diffuse Large B-Cell Lymphoma**
  - CALGB/Alliance 50303: DA-EPOCH-R vs R-CHOP: No differences between R-CHOP vs DA-EPOCH-R for EFS and OS with 5-yr follow-up
  - No benefit with DA-EPOCH-R identified among clinical subgroups defined by age and IPI criteria
  - Phase III GOYA Trial: Obinutuzumab versus Rituximab Plus CHOP: After a median follow-up of 29 months, no difference in investigator-assessed PFS (HR, 0.92; 95% CI, 0.76-1.11; p = .3868). DFS, EFS, and TTNT were also similar in both treatment groups
  - REMARC: Phase III, RCT, Lenalidomide Maintenance After First-line (elderly) R-CHOP: Significantly prolonged median PFS vs placebo (NR vs 58.8 mos, P = .0135) No significant effect on OS
  - **ZUMA-1: KTE-C19 CAR-T cells in Refractory Disease:** Phase II interim analysis of ZUMA-1 reports significantly higher ORR vs historical control rate in pts with DLBCL (76% vs 20%, respectively; P < .0001)
  - **PRIMARY CNS LYMPHOMA: R/R:** Single agent Ibrutinib active ORR; 75%
Lymphomas

• Follicular Lymphoma:
  - **GALLIUM**: Phase III, RCT, First-line Obinutuzumab-based vs Rituximab-Based
    CIT: Improved PFS by 34% (3 yr PFS %: 80.0 vs 73.3, HR 0.66, p = 0.0012)
  - **GADOLIN**: O-B-O improved PFS vs B: 25.8 vs. 14.1 mo (HR 0.57, p<0.0001)
  - **SAKK 35/10**: Phase II, First-line Rituximab/Lenalidomide: Improved CR/CRu @Wk 23, maintained through 30mos (42% vs 19% for rituximab alone, P = .001)
  - **ASSIST-FL**: First-line Rituximab biosimilar/CVP vs R/CVP: No difference
  - **DYNAMO**: Duvelisib (PI3K-δ,γ inhibitor) R/R iNHL; ORR 48%, PFS 8.4 mo
  - **MZL**: Ibrutinib in R/R MZL: ORR (IRC assessment): 48%, DoR at 18 mos: 62%,
  - **MCL**: CDK4/6 inhibitor, Palbociclib overcomes Ibrutinib resistance in R/R MCL; ORR - 64% (19 of 21 pts) and CR rate 43%, 1-year PFS 61%
  - **MCL**: LyMa; Phase III, RCT: 3 yr Rituximab maintenance after ASCT; Improved EFS, PFS, and OS (50% reduction of risk of death (HR = 0.5; 95%; P = .0454)).
  - **CD30+ CTCL CD30+ MF and pcALCL**: ALCANZA; Brentuximab Vedotin
    Significantly longer ORR4 vs methotrexate/bexarotene - 56.3% vs 12.5%; P < .0001
  - **Relapsed Hodgkin’s Lymphoma**: Brentuximab Vedotin and Nivolumab; n=42, ORR 90%, CR 62%, PR28%. iRR toxicities largely grade 1/2; 38%
Multiple Myeloma

- Newly Diagnosed MM
  - Phase II Ixazomib/Len/Dex: all-oral triplet as induction and consolidation following ASCT 80% >VGPR and 44% CR before maintenance treatment
  - Phase II IFM: KRd: 70% MRD, no peripheral neuropathy but cardiotoxicity
- High Risk Asymptomatic MM: Elotuzumab/Len/dex: ORR 82.6%. CBR 100%
- R/R MM: MRD
  - DARATUMUMAB: Addition of daratumumab to Rd or Vd significantly increased MRD negativity over doublets in POLLUX and CASTOR trials
  - PAVO Phase 1b: SC daratumumab + rHuPH20 effective, less infusion rxns
- New Agents in MM
  - Venetoclax monotherapy safe and tolerable: ORR: 21%
  - Pembrolizumab/Pomalidomide/Dexamethasone for R/R MM: ORR 60%, sCR 7%, CR 2%, VGPR 20%
  - CAR-BCMA T cells and Anti-BCMA immunotoxin: Active in R/R MM
  - Anti-HIV drug, NELFINAVIR overcomes Proteosome resistance in R/R MM
  - STORM Trial: Selinexor (XPO-1 inhibitor) + low-dose dex (quad-refractory and penta-refractory) MM: ORR: 21%, DoR: 5mo, OS: 9.3mo, PFS: 2.3mo
MDS/Myeloproliferative Neoplasms

- **MDS**
  - **E2905**: lenalidomide + EA in low/int-risk MDS with prior erythroid failure/low response (n = 163): Overall erythroid response 41.5 vs 29.6%: Low ratio of large CD45 isoforms by flow cytometry is predictive of MER
  - **Enasidenib (AG221)** potent oral inhibitor of mIDH2 in R/R: RR; 10 of 17 pts

- **Polycythemia vera and Essential thrombocythemia**: The role of Interferon
  - Phase III PROUD-PV: Ropeginterferon α-2b noninferior to Hydroxyurea in Polycythemia Vera: CHR at Mo 12: 43.1% vs 45.6%, No SPMs vs. 5 of 127
  - MPD-RC 112: Frontline Peginterferon α-2a vs Hydroxyurea in High-Risk PV and ET: CR at 12 mos similar. Increased toxicities with IFN

- **Myelofibrosis**
  - **Ruxolitinib + Azacitidine**: Initial therapy or R/R, Int /High-Risk MF: ORR by IWG-MRT criteria: 69% (5/16 splenic improvement after adding Azacitidine)
  - **Sotatercept** in MPN-associated MF and Anemia: 40% and 25% of evaluable patients responded @ 0.75 mg/kg and 1 mg/kg dose cohorts, respectively
  - **Pacritinib**: Phase III, PERSIST-2 study superior to BAT, including ruxolitinib in patients with MF and platelet counts < 100,000/μL: 18 vs. 3%
What does it all mean? My thoughts

- **PRACTICE changing:**
  - Crizanlizumab in SSD
  - Ibrutinib in GVHD and MZL
  - Rituximab maintenance x 3 years in MCL in younger patients

- **Potentially Practice changing:**
  - Obinutuzumab + CIT as First-Line therapy in CLL
  - Venetoclax in idelalisib and ibrutinib refractory CLL
  - TKI discontinuation in CML
  - Lenalidomide + ESA in Low/Intermediate risk MDS with low CD45 erythroid isoforms

- **PRACTICE confirming:**
  - RCHOP in DLBC NHL
  - 7+3 in AML
  - Antibody therapy in Myeloma
  - Blinatumumab in R/R ALL
  - Single ASCT/maintenance in Myeloma

- **Questions**
  - Lenalidomide maintenance in CLL?
  - Pacritinib?

- **Stay tuned**
  - Elotuzumab in High Risk SMM,
  - Ibrutinib in PCNS NHL
  - All oral Myeloma induction regimen and maintenance?
  - Elderly AML and ALL: Venetoclax + LDAC, Inotuzumab Ozogomycin + Mini-HCVAD
Co-Chair Indy Hematology Review
Challenging Cases

Michael C. Wiemann, MD
President, Clinical
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Detroit, Michigan
MULTIPLE MYELOMA

Paul G. Richardson, MD
Clinical Program Leader and Director of Clinical Research,
Jerome Lipper Multiple Myeloma Center
Professor of Medicine, Harvard Medical School,
Dana Faber Cancer Institute, Boston, MA
Robert Brodsky, MD
Director, Division of Hematology
Professor of Medicine and Oncology
The Johns Hopkins Family Professor,
Johns Hopkins University,
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MYELODYSPLASTIC SYNDROMES

Charles A. Schiffer, MD
Professor of Medicine and Oncology
Director of the Leukemia/Lymphoma
Multidisciplinary Program
Wayne State University School of Medicine
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Chronic Lymphocytic Leukemia: State of the Art

Adrian Wiestner, M.D., Ph.D.
Senior Investigator
Laboratory of Lymphoid Malignancies
National Heart, Lung, and Blood Institute (NHLBI)
National Institutes of Health, Bethesda, MD
Waldenström's Macroglobulinemia: How I treat; Emerging and current therapies

Steven P. Treon, MD, PhD
Director, Bing Center for Waldenström's Macroglobulinemia
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MYELOPROLIFERATIVE DISORDERS

Ayalew Tefferi, MD
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Mayo Clinic,
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Acute Lymphoblastic Leukemia: Beyond Adolescence

Richard Stone, MD
Professor, Department of Medicine,
Harvard Medical School
Clinical Director, Adult Leukemia Program,
Dana-Farber Cancer Institute,
Boston, MA
Acute Promyelocytic and other Acute Myeloid Leukemias: Slaying of the Old Dragon

Martin S. Tallman
Chief, Leukemia Service
Memorial Sloan Kettering Cancer Center, New York
Chair of the Leukemia Committee of the Eastern Cooperative Oncology Group (ECOG)
Hematopoietic Stem Cell Transplantation: When to offer and when to treat?

Richard Childs, MD
Clinical Director, National Heart, Lung, and Blood Institute (NHLBI),
Section Chief and Senior Investigator,
Laboratory of Transplantation Immunotherapy,
Rear Admiral, United States Public Health Service,
National Institutes of Health, Bethesda, MD
Nursing Symposium: Survivorship

Linda Nielson, DNP, APN
Hematology Oncology of Indiana PC.
St Vincent Hospital Indianapolis, Indiana
T. Howard Lee Keynote Lecture
FOLLICULAR LYMPHOMA: TARGETED, MAINTAINED AND CURED?

T. HOWARD LEE, MD
Founder and President Emeritus, Hematology Oncology of Indiana, PC
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B. CHESON, MD
Professor of Medicine, Head of Hematology and Director of Hematology Research, Deputy Chief, Division of Hematology/Oncology, Lombardi Comprehensive Cancer Center.
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T. HOWARD LEE, MD
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Crizanlizumab for the Prevention of Pain Crises in Sickle Cell Disease

SAVE THIS DATE!

15th Annual Indy Hematology Review 2018
(http://www.indyhematologyreview.com)

March 10th, 2018
JW Marriott,
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Announcements