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Conference Coverage: EHA 2024 – Focus on AML and MDS

Saturday, 15 June 2024

Report Contents

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Meeting Snapshot

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CLOSED-DOOR ROUNDTABLE

DATE:
15 June 2024

SELECTED EHA ABSTRACT PRESENTATIONS by key experts

INSIGHTS REPORT including postmeeting analyses and actionable recommendations

PANEL: 8 US experts in leukemia

LEUKEMIA-SPECIFIC DISCUSSIONS on latest research updates, therapeutic advances, and their application in clinical decision-making

Panel Consisting of 8 US Experts in Leukemia

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Daniel Pollyea, MD, MS
University of Colorado
School of Medicine

Uma Borate, MD, MBBS
The Ohio State University
Comprehensive Cancer Center

Eytan Stein, MD
Memorial Sloan
Kettering Cancer Center

Alexander Perl, MD
University of Pennsylvania
Perelman School of Medicine

CHAIR:
Elias Jabbour, MD
University of Texas
MD Anderson Cancer Center

Tapan Kadia, MD
University of Texas
MD Anderson Cancer Center

Courtney DiNardo, MD
University of Texas
MD Anderson Cancer Center

Rami Komrokji, MD
Moffitt Cancer Center

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Meeting Agenda

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Time (CEST)	Topic	Speaker/Moderator
18.00 – 18.05	Welcome and Introductions	Elias Jabbour, MD
18.05 – 18.15	**Advances in AML: Newly Diagnosed**	Alexander Perl, MD
18.15 – 18.40	Discussion: Advances in AML – Newly Diagnosed	All
18.40 – 18.45	Key Takeaways	Alexander Perl, MD
18.45 – 19.00	**Advances in AML: R/R Disease – Monotherapies**	Courtney DiNardo, MD
19.00 – 19.10	**Advances in AML: R/R Disease – Combination Therapies**	Daniel Pollyea, MD
19.10 – 19.35	Discussion: Advances in AML – R/R Disease	All
19.35 – 19.40	Key Takeaways	Courtney DiNardo, MD, and Daniel Pollyea, MD
19.40 – 19.45	**BREAK**	
19.45 – 19.55	**New Developments in First-Line Treatment of MDS**	Rami Komrokji, MD
19.55 – 20.15	Discussion: New Developments in First-Line Treatment of MDS	All
20.15 – 20.20	Key Takeaways	Rami Komrokji, MD
20.20 – 20.30	**New Developments in Treatment of R/R MDS**	Eytan Stein, MD
20.30 – 20.50	Discussion: New Developments in Treatment of R/R MDS	All
20.50 – 20.55	Key Takeaways	Eytan Stein, MD
20.55 – 21.00	Summary and Closing Remarks	Elias Jabbour, MD

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Conference Highlights

Advances in AML: Newly Diagnosed

PHASE II: FLAG-IDA + VEN in ND OR R/R AML

Jen W-Y, et al. Abstract S136

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STUDY POPULATION

- Pts (aged ≥18 yr) with newly diagnosed (ND) or relapsed/refractory (R/R) AML/MDS-EB2 were eligible if they had no prior VEN exposure

PHASE III ENHANCE-3 STUDY: MAGROLIMAB + VEN-AZA IN PREVIOUSLY UNTREATED PTS WITH AML WHO ARE INELIGIBLE FOR INTENSIVE CHEMOTHERAPY

Daver N, et al. Abstract S138

EPICS

STUDY POPULATION

> Pts with previously untreated AML who are ineligible for intensive chemotherapy due to age ≥75 yr or documented comorbidities

randomized phase 2 study – (ICML) Zhang 408

- Experts believe the resolution of molecular phenotype is possible in real time, and these vulnerabilities can potentially be targeted

Promising tolerability and efficacy results from dose-escalation in an ongoing phase I/II study of mosunetuzumab with polatuzumab vedotin for relapsed/refractory B-cell NHL – (EHA) Ghosh #S222

- The regimen is seen as effective, exciting, safe, and broadly applicable to many patients

Mosunetuzumab (mosun) monotherapy for elderly/unfit patients with first-line DLBCL continues to show promising safety and efficacy with durable complete responses – (EHA) Oluwaseki #EP1501

- This approach is seen as a great solution for a patient population in whom giving immunochemotherapy is difficult. It is viewed as effective and safe

FIRST-MIND: a phase Ib, open-label, randomized study to assess safety of tafasitamab or tafasitamab + lenalidomide in addition to R-CHOP in patients with newly diagnosed DLBCL – (EHA) Beriada #EP1504

- Experts believe the combination of tafasitamab + lenalidomide with R-CHOP is safe. However, they would like to see phase III data to confirm its activity in this setting

Long-term analyses from L-MIND, a phase II study of tafasitamab plus lenalidomide (len) in patients with R/R DLBCL – (ICML) Duell #29

- The L-MIND regimen is seen as useful in the specific patient population with refractory disease. It was noted to be effective, very safe, and well tolerated. Some of the responses seen were clearly very durable

PHASE I/II: ORAL DECITABINE-CEDAZURIDINE WITH VEN AND GILTERITINIB IN ND AND R/R AML

Bataller A, et al. Abstract S139

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STUDY POPULATION

> ND and R/R AML or high-risk

OUTCOMES

> Between Nov 2021 and Feb 2024, 26 pts were enrolled, with 25 evaluable for response (18 R/R, 7 ND)

PHASE III QUANTUM-FIRST: EXPLORATORY ANALYSIS OF QUIZARTINIB MAINTENANCE IN *FLT3*-ITD AML

Sekeres MA, et al. Abstract S142

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BACKGROUND

> QuANTUM-First established

OUTCOMES

> 3-yr OS: 79.9% for quizartinib vs 71.1% placebo (HR 0.683; 95% CI, 0.395–1.183)

GENETIC INSIGHTS INTO ACQUIRED RESISTANCE AND CLONAL EVOLUTION IN VEN-BASED THERAPY FOR AML

Konopleva M, et al. Abstract S145

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BACKGROUND

- Molecular mechanisms of resistance to VEN-HMA are

OUTCOMES

- 66 VEN-AZA pts gave >1 sample

PHASE II: INTERIM SAFETY AND EFFICACY OF BP1001 + VEN + DECITABINE IN AML

Cortes J, et al. Abstract P536

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BACKGROUND

> BP1001 is a liposome-incorporated Grb2 antisense

STUDY POPULATION

> Unfit, ND AML including secondary AML (cohort 1) or R/R AML (cohort 2)

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Discussion Summary

Advances in AML: Newly Diagnosed

Advances in AML: Newly Diagnosed (1/3)

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Promising results with FLAG-IDA + VEN that warrant further investigation in randomized trial

S136: FLAG-IDA + VEN in ND or R/R AML (Jen W-Y, et al)

Advances in AML: Newly Diagnosed (2/3)

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Preliminary findings of novel triplet studies for ND AML

Advances in AML: Newly Diagnosed (3/3)

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Role of quizartinib maintenance post-HSCT remains unclear

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Conference Highlights

Advances in R/R AML: Monotherapies

PHASE I/II: DSP-5336 IN PTS WITH R/R AML – UPDATED RESULTS FROM DOSE ESCALATION

Daver N, et al. Abstract S132

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STUDY POPULATION

- Pts with R/R ALL or AML are eligible, with no limit

OUTCOMES

Accrual is ongoing, with 58 pts enrolled as of Jan 31, 2024

PHASE II AUGMENT-101: REVUMENIB MONOTHERAPY IN R/R *KMT2Ar* ACUTE LEUKEMIA

Aldoss I, et al. Abstract S136

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STUDY POPULATION

- Pts with R/R *KMT2Ar* ALL/MPAL (cohort A) or R/R *KMT2Ar* AML (cohort B)

PHASE II FINAL 5-YR RESULTS: OLUTASIDENIB FOR m*IDH1* AML

Cortes J, et al. Abstract S144

EPICS

STUDY POPULATION

> Pts with R/R m*IDH1* AML

PHASE II SUBGROUP ANALYSIS: OLUTASIDENIB IN m*IDH1* AML SECONDARY TO MPN

De Botton S, et al. Abstract P605

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STUDY POPULATION

- Pts with R/R m*IDH1* AML

OUTCOMES

PHASE II SUBGROUP ANALYSIS: OLUTASIDENIB IN ELDERLY PTS WITH R/R m*IDH1* AML

De Botton S, et al. Abstract P611

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STUDY POPULATION

- Pts with R/R m*IDH1* AML

PHASE II SUBGROUP ANALYSIS: OLUTASIDENIB IN PTS WITH R/R AML FOLLOWING VEN FAILURE

Cortes J, et al. Abstract P614

EPICS

STUDY POPULATION

- Pts with R/R m*IDH1* AML

PHASE II SUBGROUP ANALYSIS: OLUTASIDENIB AS BRIDGE TO TRANSPLANT IN PTS WITH R/R m*IDH1* AML

De Botton S, et al. Abstract P1373

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STUDY POPULATION

- Pts with R/R m*IDH1* AML

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Conference Highlights

Advances in R/R AML: Combination Therapies

PHASE IB: BLEXIMENIB (JNJ-75276617) + VEN-AZA IN R/R AML WITH ALTERATIONS IN *KMT2A* OR *NPM1*

Wei AH, et al. Abstract S133

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STUDY POPULATION + DESIGN

- Adult pts with R/R AML harboring *KMT2A* or *NPM1* alterations

OUTCOMES

Efficacy population (n=34; ≥50 mg BID)

PHASE I/II SAL RELAX TRIAL: UPDATED RESULTS WITH HIGH-DOSE CYTARABINE AND MITOXANTRONE (HAM) AND VEN FOR R/R AML

Ruhnke L, et al. Abstract S135

EPICS

STUDY POPULATION + DESIGN

> Pts with R/R AML, aged 18–75 yr, fit for intensive salvage

OUTCOMES

> mOS: NR

PHASE I/II: TUSPETINIB AS MONOTHERAPY AND COMBINED WITH VEN IN R/R AML

Daver N, et al. Abstract P557

EPICS

STUDY POPULATION + DESIGN

> Dose exploration was done with tuspetinib (93 pts) and tuspetinib

OUTCOMES

Tuspetinib monotherapy

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PHASE II: CLIA IN PTS WITH R/R AML

Kadia T, et al. Abstract P603

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STUDY POPULATION + TREATMENT PLAN

- Pts aged 18–65 yr, fit for intensive chemotherapy, with R/R AML

OUTCOMES

- mOS: 8.1 mo

Patient Characteristics and Response

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Discussion Summary

Advances in R/R AML

Advances in R/R AML: Monotherapies (1/2)

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More research is needed to validate single-agent efficacy and responsive patient subgroups for menin inhibitors

S131: Revumenib monotherapy in patients with R/R *KMT2Ar* acute leukemia – topline efficacy and safety results form the pivotal

Advances in R/R AML: Monotherapies (2/2)

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Dr Pogosian

We used to run out of good options and we would just register to the mean of chemotherapy plus tradusomab in the salvage setting, but now we have so many great choices that that really takes a backseat. It's really been exciting to have multiple options for patients after T-DXd — again, practice changing, unprecedented.

Advances in R/R AML: Combination Therapies

EPICS

Promising signals but no practice-changing data with combination therapies in R/R AML

S133: A phase Ib study of the menin-*KMT2A* inhibitor JNJ-75276617 in combination with VEN and AZA in R/R AML with alterations in *KMT2A* or

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Conference Highlights

New Developments in First-Line Treatment of MDS

PHASE III STIMULUS-MDS2 TRIAL: PRIMARY RESULTS OF SABATOLIMAB + AZA AS FRONTLINE THERAPY FOR PTS WITH HIGHER-RISK MDS OR CMML-2

Zeidan AM, et al. Abstract S180

EPICS

STUDY POPULATION

> Pts with higher-risk (intermediate, high, and very high risk) MDS or CMML-2

PHASE III ENHANCE TRIAL: FINAL RESULTS OF MAGROLIMAB + AZA IN PTS WITH UNTREATED HIGHER-RISK MDS

Sallman D, et al. Abstract S181

EPICS

STUDY POPULATION

> Treatment-naive adults with intermediate-, high-, or very high-risk MDS per IPSS

PHASE II: PRELIMINARY RESULTS OF ELRITERCEPT (KER-050) IN PTS WITH LR-MDS

Campelo MD, et al. Abstract S183

EPICS

BACKGROUND

> Elritercept is designed to inhibit select TGF-beta superfamily ligands, including activin

STUDY POPULATION

> Pts with very low-, low- or intermediate-risk

PHASE III COMMANDS TRIAL: LUSPATERCEPT IN TRANSFUSION-DEPENDENT, ESA-NAIVE PTS WITH VERY LOW-, LOW-, OR INTERMEDIATE-RISK MDS

Santini V, et al. Abstract P785

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STUDY POPULATION

> Transfusion-dependent, ESA-naive pts with LR-MDS (IPSS-R very low, low, or intermediate risk) with or without ring sideroblasts

PROPENSITY SCORE MATCHED ANALYSIS: ORAL DECITABINE-CEDAZURIDINE ± VEN IN HIGH-RISK MDS

Bataller A, et al. Abstract P770

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STUDY POPULATION

> Comparison of pts treated with oral decitabine-cedazuridine in the phase II/III (ASCERTAIN) clinical trials with those treated with decitabine-cedazuridine + VEN in a phase II study

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REAL-WORLD: LUSPATERCEPT IN LR-MDS WITH TRANSFUSION DEPENDENCY, POSITIVE EFFECT OF COMBINATION THERAPY WITH ERYTHROPOIETIN

Jonasova A, et al. Abstract P1886

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STUDY POPULATION

> LR-MDS pts (N=54) with median age of 74 yr were treated with luspatercept ± ESA at 2 Charles University hematology centers in Prague and

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Discussion Summary

New Developments in First-Line Treatment of MDS

New Developments in First-Line Treatment of MDS (1/2)

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Additional data support luspatercept as first-line therapy for transfusion-dependent anemia in LR-MDS

ongoing trials will help clarify the optimal sequencing of agents

- Experts are still using a [redacted] regimen (± lenalidomide and pembrolizumab) first-line, followed by "I-DAC" second-line, for most patients
- Most experts are using imetelstat-decitabine-then-line, but will prioritize the luspatercept regimen for patients with evidence of brain metastases
- The luspatercept regimen may also be used in the second-line setting, before "I-DAC," for patients with documented brain metastases
  - If luspatercept is used second-line, experts are divided on whether they would currently use "I-DAC" or imetelstat-decitabine-then-line
    - Results of the ongoing [redacted] trial comparing imetelstat-decitabine vs "I-DAC" will help to clarify the optimal sequence of these ASCs
- Imetelstat-decitabine and the luspatercept regimen may also be used earlier than third-line in patients who recur following treatment with imetelstat, pembrolizumab, and "I-DAC" in the (neo)adjuvant setting, but this represents a small fraction of patients
- Patient preferences can also factor into the sequencing of these new agents (eg, 3 drugs vs 1 drug, concern about hair loss vs diarrhea)
- The impressive efficacy of imetelstat-decitabine and the luspatercept regimen have pushed other options, such as imetelstat-chemotherapy combinations, venetoclax, and investigational, to later lines of therapy

Dr Pagano

We used to run out of good options and we would just default to the mean of chemotherapy plus imetelstat in the salvage setting, but now we have so many great choices that that really takes a backseat. It's really been exciting to have multiple options for patients after "I-DAC" — again, practice changing, unprecedented

New Developments in First-Line Treatment of MDS (2/2)

EPICS

HR-MDS remains an unmet need

ongoing trials will help clarify the optimal sequencing of agents

- Experts are still using a CLOFARA-like regimen (a taxane plus trastuzumab and pertuzumab) first-line, followed by T-DM1 second-line, for most patients
- Most experts are using trastuzumab deruxtecan third-line, but will prioritize the tucatinib triplet for patients with evidence of brain metastases
- The tucatinib triplet may also be used in the second-line setting, before T-DM1, for patients with documented brain metastases
  - If tucatinib is used second-line, experts are divided on whether they would currently use T-DM1 or trastuzumab deruxtecan third-line
    - Results of the ongoing DESTINY-Breast03 trial comparing trastuzumab deruxtecan vs T-DM1 will help to clarify the optimal sequence of these ADCs
- Trastuzumab deruxtecan and the tucatinib triplet may also be used earlier than third-line in patients who recur following treatment with trastuzumab, pertuzumab, and T-DM1 in the (neo)adjuvant setting, but this represents a small fraction of patients
- Patient preferences can also factor into the sequencing of these new agents (eg, 3 drugs vs 1 drug, concern about hair loss vs diarrhea)
- The impressive efficacy of trastuzumab deruxtecan and the tucatinib regimen have pushed other options, such as trastuzumab-chemotherapy combinations, neratinib, and margetuximab, to later lines of therapy

Dr Pegram

We used to run out of good options and we would just regress to the mean of chemotherapy plus trastuzumab in the salvage setting, but now we have so many great choices that that really takes a backseat. It's really been exciting to have multiple options for patients after T-DM1 — again, practice changing, unprecedented

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Conference Highlights

New Developments in Treatment of R/R MDS

PHASE II IDIOME TRIAL: FINAL RESULTS OF IVOSIDENIB MONOTHERAPY IN m*IDH1* MDS

Sébert M, et al. Abstract S182

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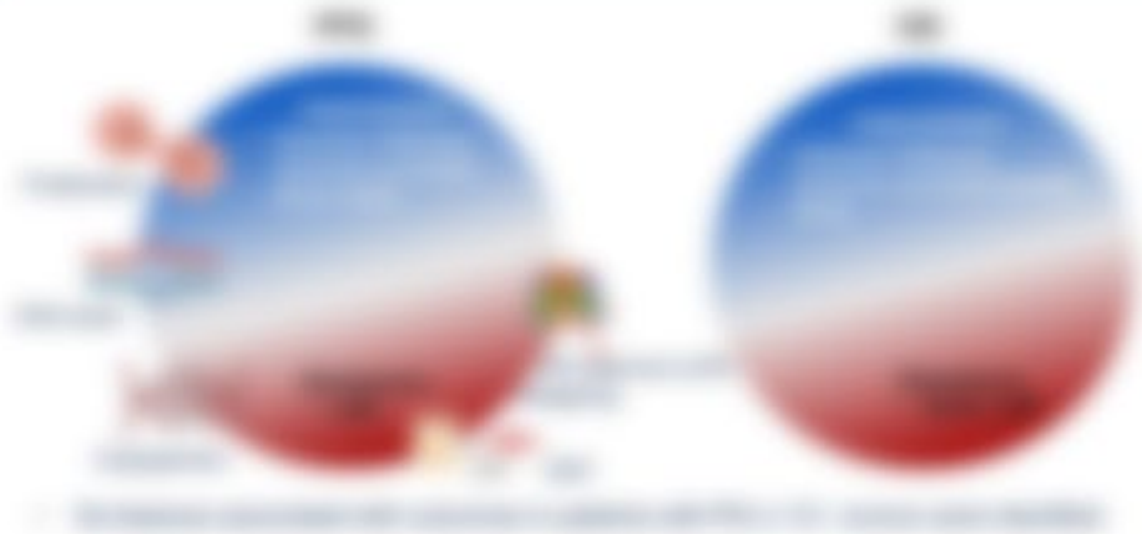
STUDY POPULATION



PHASE III IMERGE TRIAL: IMETELSTAT IN RBC-TRANSFUSION DEPENDENT LR-MDS

Santini V, et al. Abstract S184

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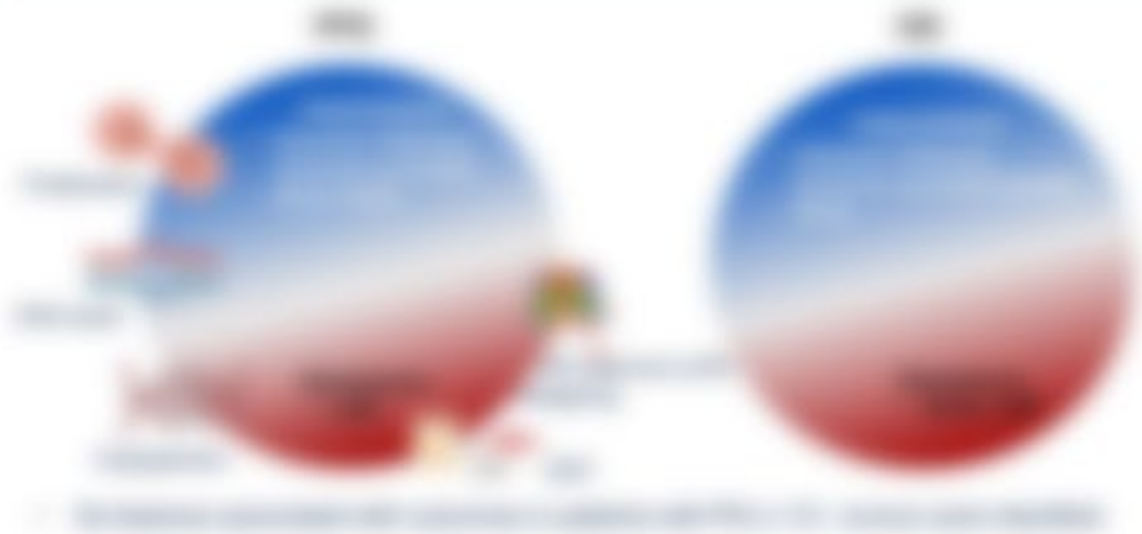
STUDY POPULATION



REAL-WORLD DATA: LUSPATERCEPT FOR LR-MDS

Patel K, et al. Abstract P768

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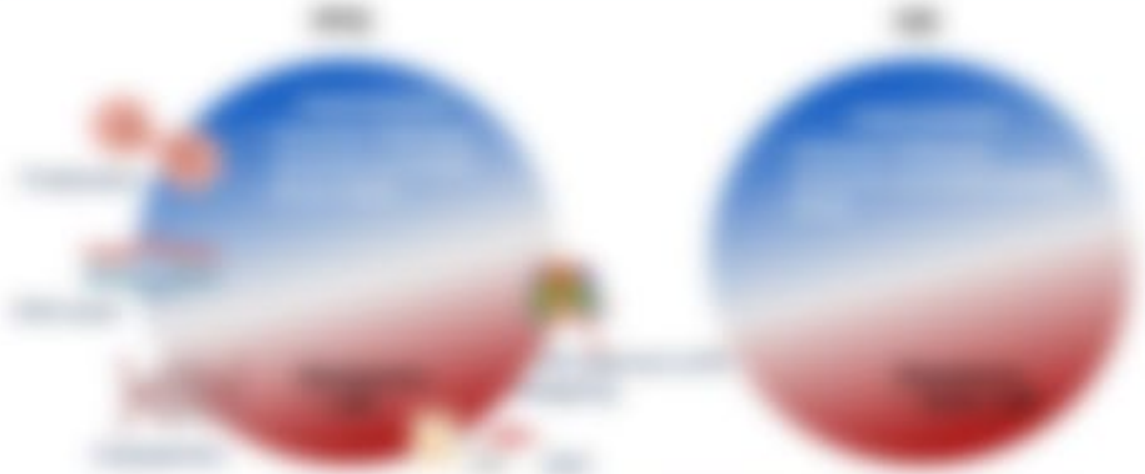
STUDY POPULATION

OUTCOMES



PHASE I/II: SECLIDEMSTAT + AZA FOR PTS WITH MDS AND CMML

Montalban-Bravo G, et al. Abstract P788

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STUDY POPULATION

> Pts with MDS or CMML with intermediate-1 or higher risk by IPSS and progression or no response to 6 prior cycles of HMA

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Discussion Summary

New Developments in Treatment of R/R MDS

New Developments in Treatment of R/R MDS

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Recent data shed further light on the treatment paradigm for R/R MDS

APTITUDE HEALTH®

US 5901-B Peachtree Dunwoody Road
Suite 415, Atlanta, GA 30328, US

EU Laan van Nieuw Oost-Indië 133 F
2593 BM The Hague, the Netherlands

UK 6th Floor, 2 Kingdom Street
London, W2 6BD, United Kingdom

aptitudehealth.com