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Conference Coverage: ASH 2024 – Focus on Leukemia

December 13, 2024

Full Report

Report Contents

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Meeting Snapshot

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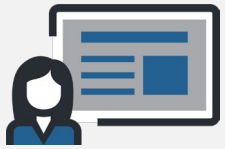
VIRTUAL CLOSED-DOOR ROUNDTABLE

DATE:
December 13, 2024



DISEASE STATE AND DATA PRESENTATIONS by key experts

INSIGHTS REPORT including postmeeting analyses and actionable recommendations

PANEL: Key experts in leukemia

- > 4 from US
- > 3 from Europe

MDS AND LEUKEMIA-SPECIFIC DISCUSSIONS on therapeutic advances and their application in clinical decision-making

Panel Consisting of 4 US and 3 European/UK Leukemia Experts

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Aaron Logan, MD, PhD
University of California
San Francisco

CHAIR:
Elias Jabbour, MD
MD Anderson Cancer Center

Naval Daver, MD
MD Anderson Cancer Center

Rami Komrokji, MD
Moffitt Cancer Center

Charles Craddock, CBE, FRCP (UK), FRCPath, DPhil
University of Birmingham

Valeria Santini, MD
University of Florence

Josep-María Ribera, MD, PhD
Catalan Institute of Oncology

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Meeting Agenda

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Time (CT/CET)	Topic	Speaker/Moderator
9.00 AM – 9.05 AM/16.00 – 16.05	Welcome, Introductions, and Meeting Objectives	Elias Jabbour, MD
9.05 AM – 9.10 AM/16.05 – 16.10	**New Developments in Low-Risk MDS**	Rami Komrokji, MD
9.10 AM – 9.20 AM/16.10 – 16.20	Discussion	Elias Jabbour, MD
9.20 AM – 9.25 AM/16.20 – 16.25	**New Developments in High-Risk MDS**	Valeria Santini, MD
9.25 AM – 9.40 AM/16.25 – 16.40	Discussion and Key Takeaways for MDS	Elias Jabbour, MD; Rami Komrokji, MD; Valeria Santini, MD
9.40 AM – 9.55 AM/16.40 – 16.55	**Advances in Newly Diagnosed AML**	Naval Daver, MD
9.55 AM – 10.20 AM/16.55 – 17.20	Discussion and Key Takeaways	Elias Jabbour, MD; Naval Daver, MD
10.20 AM – 10.35 AM/17.20 – 17.35	**Advances in R/R AML**	Charles Craddock, CBE, FRCP (UK), FRCPath, DPhil
10.35 AM – 10.55 AM/17.35 – 17.55	Discussion and Key Takeaways	Elias Jabbour, MD; Charles Craddock, CBE, FRCP (UK), FRCPath, DPhil
10.55 AM – 11.00 AM/17.55 – 18.00	*Break*	
11.00 AM – 11.10 AM/18.00 – 18.10	**Advances in Newly Diagnosed ALL**	Aaron Logan, MD, PhD
11.10 AM – 11.30 AM/18.10 – 18.30	Discussion and Key Takeaways	Elias Jabbour, MD; Aaron Logan, MD, PhD
11.30 AM – 11.35 AM/18.30 – 18.35	**Advances in R/R ALL**	Josep-María Ribera, MD, PhD
11.35 AM – 11.55 AM/18.35 – 18.55	Discussion and Key Takeaways	Elias Jabbour, MD; Josep-María Ribera, MD, PhD
11.55 AM – 12.00 PM/18.55 – 19.00	Summary and Closing Remarks	Elias Jabbour, MD

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Conference Highlights

New Developments in Low-Risk MDS

Early Versus Late Onset of ESA in Lower Risk Anemic MDS Patients: Results of the GFM Randomized Phase III EPO-Pretar Trial

Park S, et al. Abstract 349

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STUDY POPULATION

> Phase III EPO-PRETAR trial (NCT03223961) prospectively compared early (n=40) vs late (n=23) ESA initiation in non-RBC transfusion-

Improvements in Hematological Parameters and Quality of Life (QOL) with Elritercept (KER-050): Results from an Ongoing Phase 2 Trial in Participants with LR-MDS (1/2)

Giagounidis A, et al. Abstract 1825

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ANALYSIS POPULATION

- Baseline and safety data include participants with MDS treated at the

Category	RP2D (N=95) n (%)
Any TEAE	93 (97.9)

Improvements in Hematological Parameters and Quality of Life (QOL) with Elritercept (KER-050): Results from an Ongoing Phase 2 Trial in Participants with LR-MDS (2/2)

Giagounidis A, et al. Abstract 1825

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OUTCOME

> Hematologic responses were observed in 55%, and TI ≥8 weeks was achieved in 39% of the mITT$_{24}$ population, including those with RS-

Effect of Prior Treatments on the Clinical Activity of Imetelstat in Transfusion-Dependent Patients with Erythropoiesis-Stimulating Agent, Relapsed or Refractory/Ineligible Lower-Risk Myelodysplastic Syndromes

Platzbecker U, et al. Abstract 352

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STUDY POPULATION

Results: Imetelstat Shows Clinical Activity in Patients With Prior LUSP (n=36)

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Discussion Summary

New Developments in Low-Risk MDS

New Developments in Low-Risk MDS (1/2)

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New Developments in Low-Risk MDS (2/2)

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Conference Highlights

New Developments in High-Risk MDS

Decitabine Plus All-*Trans* Retinoic Acid Versus Decitabine Monotherapy for Myelodysplastic Syndromes with Excess Blasts: A Multicentre, Randomized Controlled Trial

Zhou X, et al. Abstract 663

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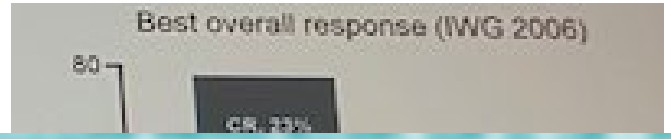
STUDY POPULATION

> This multicenter, open-label, randomized controlled trial enrolled 227



Clinical Utilization and Outcomes of Hypomethylating Agents and Venetoclax in Patients with Myelodysplastic Syndrome – a Multicenter Retrospective Analysis

Guru Murthy GS, et al. Abstract 3206

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STUDY POPULATION

> This multicenter, retrospective study across 13 US academic centers included adults (aged ≥18 years) with MDS treated with up-front HMA +

A Retrospective Cohort Study Evaluating Outcomes of Higher Risk MDS Treated with HMA with or without Venetoclax Using International Working Group 2023 Response Criteria

Shukla M, et al. Abstract 4602

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STUDY POPULATION

> Single-institution retrospective study comparing outcomes of HMA + VEN vs HMA alone in HR-MDS using IWG 2023 criteria

Olutasidenib Alone or in Combination with Azacitidine in Patients with m*IDH1* Myelodysplastic Syndromes/Neoplasms: Final 5-Year Data

Cortes JE, et al. Abstract 4600

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STUDY POPULATION

> 5-year results of olutasidenib from a pivotal cohort of a registrational phase I/II trial

	OLU Monotherapy (n=6)	Combination OLU+AZA (n=16)	Pooled (n=22)

Enasidenib (ENA) Monotherapy in Patients with *IDH2* mutated Myelodysplastic Syndrome (MDS), the Ideal Phase 2 Study By the GFM and Emsco Groups

Ades L, et al. Abstract 1839

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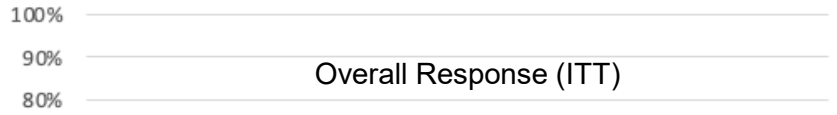
STUDY POPULATION

> Phase II trial evaluating the safety and efficacy of ENA in 3 MDS cohorts (n=69)



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Discussion Summary

New Developments in High-Risk MDS

New Developments in High-Risk MDS (1/2)

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ongoing trials will help clarify the optimal sequencing of agents

- Experts are still using a CLOFAV/7+3-like regimen (± lenvo plus tras/cyt/mab and ven/cyt/mab) first-line, followed by 7+3/IA* second-line, for most patients.
- Most experts are using tras/cyt/mab deruxtecan third-line, but will prioritize the luca/dnb triplet for patients with evidence of brain metastases.
- The luca/dnb triplet may also be used in the second-line setting, before 7+3/IA*, for patients with documented brain metastases.
  - If luca/dnb is used second-line, experts are divided on whether they would currently use 7+3/IA* or tras/cyt/mab deruxtecan third-line.
    - Results of the ongoing DESTINY-Breast03 trial comparing tras/cyt/mab deruxtecan vs 7+3/IA* will help to clarify the optimal sequence of these ADCs.
- Tras/cyt/mab deruxtecan and the luca/dnb triplet may also be used earlier than third-line in patients who recur following treatment with tras/cyt/mab, pem/cyt/mab, and 7+3/IA* 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 tras/cyt/mab deruxtecan and the luca/dnb regimen have pushed other options, such as tras/cyt/mab-chemotherapy combinations, ven/dnb, and mag/cyt/mab, 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 tras/cyt/mab in the salvage setting, but now we have so many great choices that that really feels a backseat. It's really been exciting to have multiple options for patients after 7+3/IA — again, practice changing, unprecedented.*

New Developments in High-Risk MDS (2/2)

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Conference Highlights

Advances in AML: Newly Diagnosed

Gemtuzumab Ozogamicin Added to Fludarabine, Cytarabine and G-CSF (FLAG-GO) Leads to Superior Molecular Response and Survival Outcomes Than Idarubicin (FLAG-IDA): 200 Patients Long-Term Follow up

Senapati J, et al. Abstract 1513

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STUDY POPULATION

Gilteritinib Results in Higher Remission and Transplant Rates Than Midostaurin but Does Not Increase the Post-Induction Mutational MRD Negative Rate: Results of the Phase 2 Randomized Precog 0905 Study in Newly Diagnosed *FLT3* Mutated AML

Luger S, et al. Abstract 221

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STUDY POPULATION

Final Results of Quiwi: A Double Blinded, Randomized Pethema Trial Comparing Standard Chemotherapy Plus Quizartinib Versus Placebo in Adult Patients with Newly Diagnosed *FLT3*-ITD Negative AML

Montesinos P, et al. Abstract 1512

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STUDY POPULATION

> Multicenter, randomized, double-blind, placebo-controlled phase II trial; pts with *FLT3*-ITD–negative AML (aged 18–70 years) fit for intensive

A Phase II Trial of Venetoclax in Combination with Cladribine, Idarubicin, and Cytarabine in Newly Diagnosed Acute Myeloid Leukemia and High-Risk Myelodysplastic Syndrome

Kadia T, et al. Abstract 734

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STUDY POPULATION

Category, N (%)	Overall (N = 95/96 evaluable)
ORR (CR + CRi + MLFS)	91 (96)

Phase II Study of Cladribine with Low Dose Cytarabine and Venetoclax Alternating with Azacytidine and Venetoclax for Newly Diagnosed Acute Myeloid Leukemia

Bazinet A, et al. Abstract 56

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STUDY POPULATION

- Prospective phase II clinical trial (NCT03586609) for pts with newly diagnosed AML

Group	ORR (CR+CRi)
[illegible]	[illegible]

Long-Term Survival Outcomes and Cytogenetic/Molecular Patterns of Relapse in Adults with *FLT3*-Mutated AML Receiving Frontline Triplet Therapy with a Hypomethylating Agent, Venetoclax and FLT3 Inhibitor

Short N, et al. Abstract 220

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STUDY POPULATION

- Retrospective study with 88 pts with newly diagnosed *FLT3*-mutated AML treated with frontline triplet therapy at a single center

Clinical Outcomes Using Frontline "Triplet" Regimens for Newly Diagnosed *IDH*-Mutated Acute Myeloid Leukemia (AML): A Pooled Analysis of Two Phase Ib/2 Clinical Trials

Marvin-Peek J, et al. Abstract 2883

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STUDY POPULATION

Ziftomenib Combined with Intensive Induction (7+3) in Newly Diagnosed *NPM1*-m or *KMT2A*-r Acute Myeloid Leukemia: Interim Phase 1a Results from KOMET-007

Zeidan A, et al. Abstract 214

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STUDY POPULATION

> Ongoing open-label, dose-escalation (phase Ia) study (NCT05735184) of ziftomenib combined with standard chemotherapies for newly

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Discussion Summary

Advances in AML: Newly Diagnosed

Advances in AML: Newly Diagnosed (1/7)

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Advances in AML: Newly Diagnosed (2/7)

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Advances in AML: Newly Diagnosed (3/7)

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Advances in AML: Newly Diagnosed (4/7)

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Advances in AML: Newly Diagnosed (5/7)

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Advances in AML: Newly Diagnosed (6/7)

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Advances in AML: Newly Diagnosed (7/7)

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Conference Highlights

Advances in AML: R/R

Time to Response and Overall Survival in Patients with m*IDH1* Relapsed/Refractory Acute Myeloid Leukemia Treated with Olutasidenib

Botton S, et al. Abstract 1514

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STUDY POPULATION

> Open-label, multicenter, registrational global phase II trial

Phase I/II Study of Quizartinib, Venetoclax, and Decitabine Triple Combination in FLT3-ITD Mutated AML

Yilmaz M, et al. Abstract 4263

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STUDY POPULATION

> Phase I/II study (NCT03661307) evaluating quizartinib, venetoclax, and decitabine in pts with *FLT3*-ITD–positive AML

Updated Results and Longer Follow-up from the AUGMENT-101 Phase 2 Study of Revumenib in All Patients with Relapsed or Refractory (R/R) *KMT2A*r Acute Leukemia

Aldoss I, et al. Abstract 211

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STUDY POPULATION

> A phase II study assessed revumenib in 116 pts with R/R *KMT2A*-rearranged acute leukemia

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Discussion Summary

Advances in AML: R/R

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

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ivosidenib right at the top of the pecking order for me.

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

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Conference Highlights

Advances in ALL: Newly Diagnosed

Blinatumomab and Ponatinib for Adults with Newly Diagnosed Philadelphia Chromosome-Positive Acute Lymphoblastic Leukemia: Updated Results and Predictors of Relapse

Short N, et al. Abstract 837

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STUDY POPULATION

- [redacted]

OUTCOMES

- [redacted]

EXPERT CONCLUSIONS

[redacted]

Efficacy and Toxicity of Frontline Ponatinib Plus Blinatumomab for Adult Ph+ ALL Patients of All Ages. Intermediate Analysis of the Gimema ALL2820

Chiaretti S, et al. Abstract 835

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Updated Results from a Phase II Study Hyper-CVAD, with or without Inotuzumab Ozogamicin, and Sequential Blinatumomab in Patients with Newly Diagnosed B-Cell Acute Lymphoblastic Leukemia

Nguyen D, et al. Abstract 1439

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STUDY POPULATION

Relapse Free Survival

Blinatumomab Added to Chemotherapy Improves Disease-Free Survival in Newly Diagnosed NCI Standard Risk Pediatric B-Acute Lymphoblastic Leukemia: Results from the Randomized Children's Oncology Group Study AALL1731

Rau R, et al. Abstract 1

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STUDY POPULATION

- [illegible]

OUTCOMES

- [illegible]

EXPERT CONCLUSIONS

[illegible]

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Discussion Summary

Advances in ALL: Newly Diagnosed

Advances in ALL: Newly Diagnosed (1/5)

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Advances in ALL: Newly Diagnosed (2/5)

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Advances in ALL: Newly Diagnosed (3/5)

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Advances in ALL: Newly Diagnosed (4/5)

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Advances in ALL: Newly Diagnosed (5/5)

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Conference Highlights

Advances in ALL: R/R

Updated Results of the Combination of Mini-Hyper-CVD with Inotuzumab Ozogamicin and Blinatumomab in Patients with Relapsed/Refractory B-Cell ALL

Haddad F, et al. Abstract 2811

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STUDY POPULATION

- Adult pts aged ≥18 years with R/R B-ALL; phase II trial including the “dose-dense” (D-D)

Second Infusion of CAR T-Cells in Patients with Relapsed /Refractory B-Cell Acute Lymphoblastic Leukemia: Results from a Gocart Coalition Analysis on Behalf of the PDWP, ALWP, and Ctiwp of the EBMT

Rives S, et al. Abstract 965

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STUDY POPULATION

> A multicenter, retrospective study evaluated pediatric and adult pts with R/R B-ALL treated

Outcomes At 2y	Whole series	CR at CART2	Overt relapse	CART2 for B cell recovery

Obecabtagene autoleucel (obe-cel) for Adult Relapsed/Refractory B-Cell Acute Lymphoblastic Leukemia (R/R B-ALL): Deep Molecular Remission May Predict Better Outcomes

Jabbour E, et al. Abstract 963

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STUDY POPULATION

- [redacted]

OUTCOMES

- [redacted]

EXPERT CONCLUSIONS

[redacted]

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Discussion Summary

Advances in ALL: R/R

Advances in ALL: R/R (1/3)

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disease prior to administration of the CAR T cells.

Advances in ALL: R/R (2/3)

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Dr Pagano

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

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Advances in ALL: R/R (3/3)

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