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Conference Coverage: EHA 2023 – Focus on AML and MDS

Syndicated Report

June 10, 2023

Report Contents

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Meeting Snapshot

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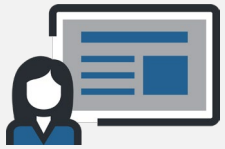
LIVE ROUNDTABLE MEETING

DATE:
June 10, 2023



DISEASE-STATE AND DATA PRESENTATIONS by key experts

INSIGHTS REPORT including postmeeting analyses and actionable recommendations

PANEL: Key experts in leukemia

> 6 from the US

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

Panel Consisting of 6 US Leukemia Experts

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Jessica K. Altman, MD
Robert H. Lurie Comprehensive Cancer Center of Northwestern University

Alexander Perl, MD
Abramson Cancer Center, University of Pennsylvania

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

Naval Daver, MD
University of Texas MD Anderson Cancer Center

Guillermo Garcia-Manero, 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
18.30 – 18.35	Welcome and Introductions	Elias Jabbour, MD
18.35 – 18.45	**New Developments in First-Line Treatment of Myelodysplastic Syndromes (MDS)**	Guillermo Garcia-Manero, MD
18.45 – 19.05	Discussion	All
19.05 – 19.15	**New Developments in Treatment of Relapsed/Refractory (R/R) MDS**	Rami Komrokji, MD
19.15 – 19.35	Discussion	All
19.35 – 19.40	Key Takeaways for MDS	Rami Komrokji, MD, and Guillermo Garcia-Manero, MD
19.40 – 19.50	**Advances in Acute Myeloid Leukemia (AML): Newly Diagnosed**	Naval Daver, MD
19.50 – 20.15	Discussion	All
20.15 – 20.20	BREAK	
20.20 – 20.30	**Advances in AML: Newly Diagnosed Elderly and/or Unfit**	Alexander Perl, MD
20.30 – 20.50	Discussion	All
20.50 – 20.55	**Advances in AML: R/R AML**	Jessica K. Altman, MD
20.55 – 21.20	Discussion	All
21.20 – 21.25	Key Takeaways	Naval Daver, MD; Alexander Perl, MD; and Jessica K. Altman, MD
21.25 – 21.30	**Summary and Closing Remarks**	Elias Jabbour, MD

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Conference Highlights

New Developments in First-Line Treatment of MDS

KER-050 TREATMENT IMPROVED MARKERS OF ERYTHROPOIETIC ACTIVITY AND HEMATOPOIESIS OVER SIX MONTHS WHICH RESULTED IN HEMATOLOGICAL RESPONSES ACROSS A BROAD, LOWER-RISK MDS POPULATION

Aristoteles Giagounidis, et al. S166

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STUDY POPULATION

> Ongoing phase II study evaluating safety and tolerability of KER-050 in pts with

Hematologic response in LR MDS

Response Endpoint	RP2D Participants[a]	
	All Evaluable	HTB Evaluable
Overall Response[b]	19/37 (51.4)	11/22 (50)

LUSPATERCEPT VERSUS EPOETIN ALFA FOR TREATMENT OF ANEMIA IN ESA-NAÏVE LOWER-RISK MYELODYSPLASTIC SYNDROME (LR-MDS) PATIENTS (PTS) REQUIRING RBC TRANSFUSIONS: DATA FROM THE PHASE-3 COMMANDS STUDY

Matteo Giovanni Della Porta, et al. S102

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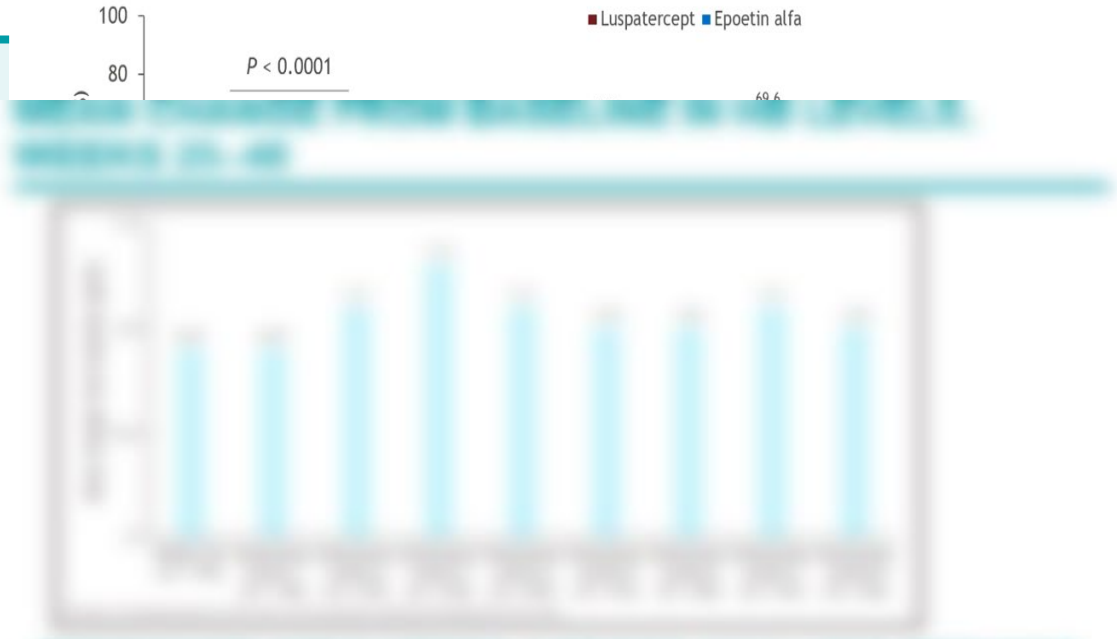
STUDY POPULATION

> Pts aged ≥18 yr with IPSS-R very low-, low-, or intermediate-risk MDS by

A. Primary endpoint: luspatercept superior to epoetin alfa



LUSPATERCEPT RESTORES EFFECTIVE ERYTHROPOIESIS AND PROVIDES SUPERIOR AND SUSTAINED CLINICAL BENEFIT VS EPOETIN ALFA: BIOMARKER ANALYSIS FROM THE PHASE 3 COMMANDS STUDY

Uwe Platzbecker, et al. P693

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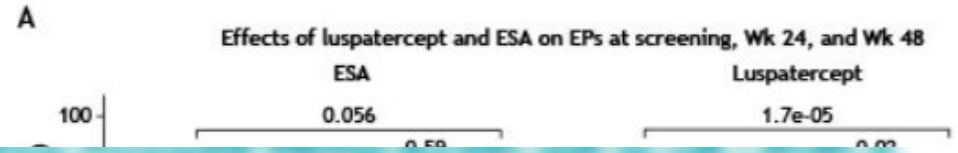
STUDY POPULATION

> Erythropoiesis-stimulating agent (ESA)-naive pts with LR MDS from the



PHASE 1/2 STUDY OF ORAL DECITABINE/CEDAZURIDINE IN COMBINATION WITH VENETOCLAX IN TREATMENT-NAÏVE HIGHER-RISK MYELODYSPLASTIC SYNDROMES OR CHRONIC MYELOMONOCYTIC LEUKEMIA

Alex Bataller, et al. S172

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STUDY POPULATION

> Pts aged 27–94 yr with confirmed diagnosis of treatment-naive HR MDS or

Efficacy

	Full cohort (n=39)	Phase 1 (n=9)	Phase 2 (n=30)
ORR, n (%)	37 (94.9)	9 (100)	28 (93.3)
CR	14 (35.9)	6 (66.7)	8 (26.7)
mCR	23 (59)	3 (33.3)	20 (66.7)

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Discussion Summary

New Developments in First-Line Treatment of MDS

New Developments in First-Line Treatment of MDS (1/4)

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LR MDS

KER-050

> KER-050 is mechanistically very similar to sotatercept, with some variation in structure. Dr Garcia-Manero confirmed that it is becoming

New Developments in First-Line Treatment of MDS (2/4)

EPICS

LR MDS

Luspatercept (cont.)

> Dr Komrokji noted that luspatercept will become the new erythropoietin, and he assumes that the intention is to get it as up-front therapy for

New Developments in First-Line Treatment of MDS (3/4)

EPICS

HR MDS

Total oral therapy: oral decitabine-cedazuridine in combination with VEN

> Dr Garcia-Manero commented that while this is a pilot phase I/II study, the data are positive, and while the combination does not look better

New Developments in First-Line Treatment of MDS (4/4)

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HR MDS

TP53 mutation

> Patients with *TP53* mutations had a high rate of response, but the response was not long-lasting. In wildtype *TP53*, Dr Garcia-Manero

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Conference Highlights

New Developments in Treatment of R/R MDS

CONTINUOUS TRANSFUSION INDEPENDENCE WITH IMETELSTAT IN HEAVILY TRANSFUSED NON-DEL (5Q) LOWER-RISK MYELODYSPLASTIC SYNDROMES RELAPSED/REFRACTORY TO ERYTHROPOIESIS STIMULATING AGENTS IN IMERGE PHASE 3

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Uwe Platzbecker, et al. S165

STUDY POPULATION

> Heavily red blood cell (RBC) transfusion-dependent (TD), ESA R/R or ESA

Background

- Phase 1 dose-escalation study of VLS-101, a ROR1-targeting ADC, in patients with heavily pretreated MCL and DLBCL
- Primary objective was to refine estimates of MTD and recommended dosing regimen

Results

- 32 patients were enrolled, including 15 patients with MCL
- DLTs were G4 neutropenia and G3 diarrhea
- G4 neutropenia occurred in 28% of patients; G-CSF successfully ameliorated neutropenia
- On-study reversible G3 neuropathy occurred in 9% of patients; no G4 neuropathy occurred
- ORR was 47% (3 CR, 4 PR) for MCL cohort and 80% (2 CR, 2 PR) for DLBCL cohort
- 8 responding patients have ongoing responses ranging from 27 weeks to 58 weeks

Key takeaways: VLS-101 demonstrated a manageable and predictable safety profile and encouraging efficacy, with durable responses in advanced MCL and DLBCL. Experts mentioned neuropathy as a potential concern and the need to identify the best histologies in which to test this agent.

A. Long-term duration of RBC TI observed with imetelstat vs PBO

DISEASE MODIFYING ACTIVITY OF IMETELSTAT IN PATIENTS WITH HEAVILY TRANSFUSED NON-DEL (5Q) LOWER-RISK MYELODYSPLASTIC SYNDROMES RELAPSED/REFRACTORY TO ERYTHROPOIESIS STIMULATING AGENTS IN IMERGE PHASE 3

Valeria Santini, et al. S164

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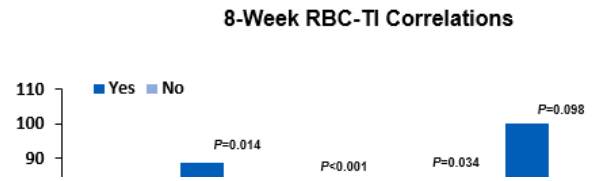
STUDY POPULATION

> Heavily RBC TD, ESA R/R or ineligible non-del(5q) LR-MDS pts naive to len-HMA were



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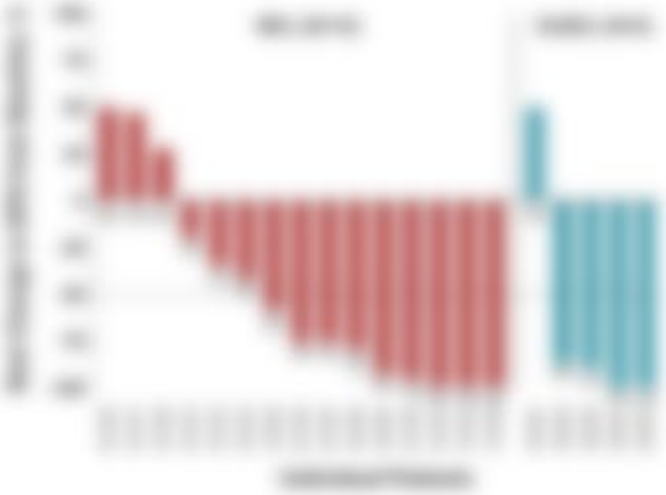

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HIGHER *MDMX* EXPRESSION WAS ASSOCIATED WITH HYPOMETHYLATING AGENT RESISTANCE AND WORSE SURVIVAL IN MYELODYSPLASTIC SYNDROME PATIENTS, INFERRING IT A POTENTIAL THERAPEUTIC TARGET

Yu-Hung Wang, et al. S171

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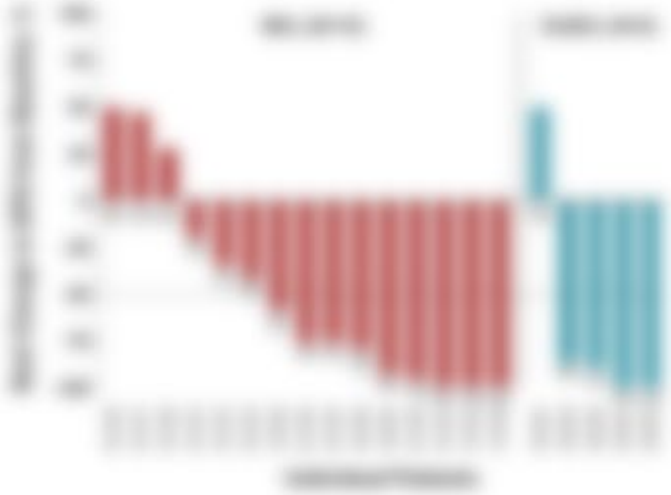
STUDY POPULATION

> MDS pts (N=340) treated at the National Taiwan University Hospital from

Pharmacologic inhibition of *MDMX* synergizes with azacitidine



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MYELODYSPLASTIC NEOPLASMS (MDS) CLASSIFICATION FROM WHO 2017 TO WHO 2022 AND ICC 2022: AN EXPANDED ANALYSIS OF 7017 PATIENTS ON BEHALF OF THE INTERNATIONAL CONSORTIUM FOR MDS (ICMDS)

Rami S. Komrokji, et al. S170

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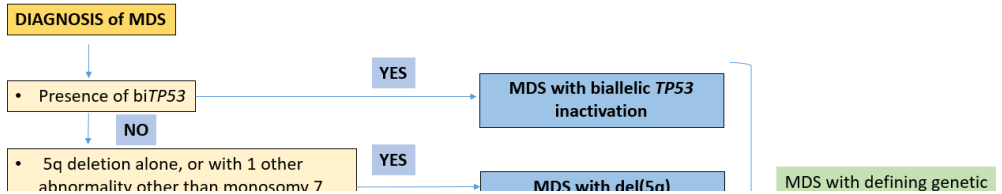
BACKGROUND AND AIMS

> In 2022, two new classifications for myeloid neoplasms were published: the



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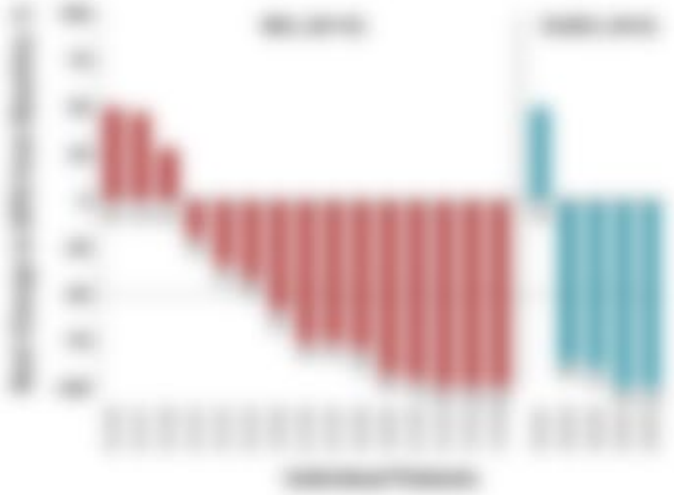

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Discussion Summary

New Developments in Treatment of R/R MDS

New Developments in Treatment of R/R MDS (1/3)

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R/R MDS

Inclusion of RS-positive patients in the IMERGE (and COMMANDS) trial

New Developments in Treatment of R/R MDS (2/3)

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R/R MDS

Imetelstat in LR MDS R/R to ESA (cont.)

> The experts believe that once approved, imetelstat will be positioned as second line after luspatercept failure in LR MDS patients, and will be

New Developments in Treatment of R/R MDS (3/3)

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R/R MDS

Promising new agents

> Dr Komrokji highlighted 2 agents, post-HMA failure, that are worth following in spliceosome and splicing mutation subsets:

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Conference Highlights

Advances in AML: Newly Diagnosed

FLAG-IDA COMBINED WITH GEMTUZUMAB OZOGAMICIN (GO) REDUCED MRD LEVELS AND IMPROVED OVERALL SURVIVAL IN *NPM1* MUT AML INDEPENDENT OF *FLT3* AND MRD STATUS, RESULTS FROM THE AML19 TRIAL

Nigel Russell, et al. S134

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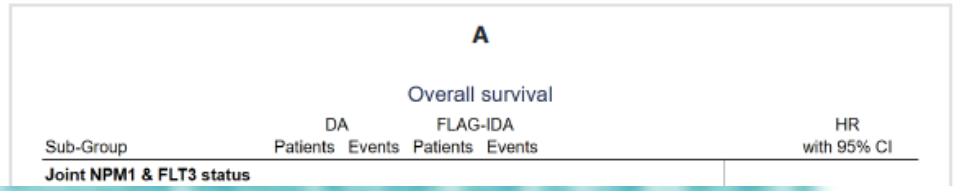
STUDY POPULATION

> The NCRI AML19 trial randomized pts (n=1475; median age 51.5 yr) with newly



PRELIMINARY RESULTS OF QUIWI: A DOUBLE BLINDED, RANDOMIZED CLINICAL TRIAL COMPARING STANDARD CHEMOTHERAPY PLUS QUIZARTINIB VERSUS PLACEBO IN ADULT PATIENTS WITH NEWLY DIAGNOSED FLT3-ITD WILD-TYPE AML

Pau Montesinos, et al. S130

EPICS

STUDY POPULATION

- Pts aged 18–70 yr (median: 57 yr) with newly diagnosed *FLT3*-ITD–wt AML, and fit for

1A. Event-free survival

BMT-CTN 1506 (MORPHO): A RANDOMIZED TRIAL OF THE FLT3 INHIBITOR GILTERITINIB AS POST-TRANSPLANT MAINTENANCE FOR FLT3-ITD AML

Mark J. Levis, et al. LBA2711

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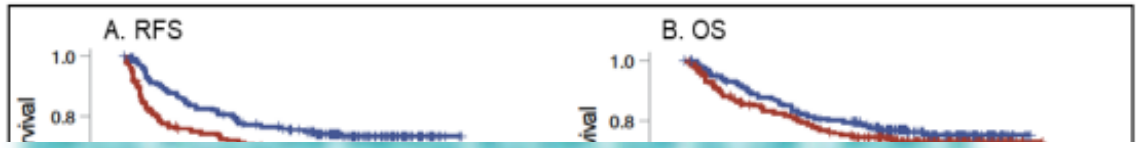
STUDY POPULATION

- Pts with *FLT3*-ITD AML in first remission after receiving no more than 2 cycles of induction therapy with HCT planned within 12 mo of achieving



IMPACT OF ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION IN FIRST COMPLETE REMISSION PLUS FLT3 INHIBITION WITH QUIZARTINIB IN ACUTE MYELOID LEUKEMIA WITH FLT3-ITD: RESULTS FROM QUANTUM-FIRST

Richard Schlenk, et al. S137

EPICS

STUDY POPULATION

- Pts aged 18–75 yr with newly diagnosed AML screened for *FLT3*-ITD prior to starting

Figure 1. Post Hoc Analysis of OS with Allo-HCT in CR1 as Time Dependent Variable in All Randomized Patients

	Hazard ratio (95% CI)	*P*-value
Treatment (quizartinib vs placebo)	0.770 (0.609-0.973)	0.0284

GEMTUZUMAB-BASED INDUCTION CHEMOTHERAPY COMBINED WITH MIDOSTAURIN FOR FLT3 MUTATED AML. UPDATED TOXICITY AND INTERIM SURVIVAL ANALYSIS FROM THE NCRI AML19V2 "MIDOTARG" PILOT TRIAL*

Nigel Russell, et al. P484

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STUDY POPULATION

- In the NCRI AML19 v2 trial, pts aged 18–60 yr with newly diagnosed AML were randomized to

1A. Overall survival

NEXT-GENERATION SEQUENCING-BASED MEASURABLE RESIDUAL DISEASE MONITORING IN ACUTE MYELOID LEUKEMIA WITH FLT3 INTERNAL TANDEM DUPLICATION TREATED WITH INTENSIVE CHEMOTHERAPY PLUS MIDOSTAURIN*

Frank G. Rücker, et al. S135

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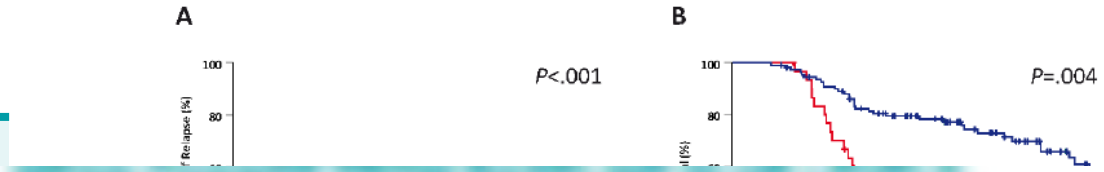
STUDY POPULATION

> Pts aged 18–70 yr with *FLT3*-ITD–positive AML enrolled on the AMLSG 16-



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Discussion Summary

Advances in AML: Newly Diagnosed

Advances in AML: Newly Diagnosed (1/3)

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Latest Updates

FLAG-IDA combined with gemtuzumab ozogamicin (GO) in isolated *NPM1*-mutated AML

> Experts agreed that FLAG-IDA + GO is the way forward for patients with isolated *NPM1*-mutated AML

[redacted]

Advances in AML: Newly Diagnosed (2/3)

EPICS

Latest Updates

Gilteritinib as posttransplant maintenance for *FLT3*-ITD–mutated AML: MORPHO

> Experts noted that data from the phase III MORPHO trial are among the first to support the effectiveness of measurable residual disease

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Conference Highlights

Advances in AML: Newly Diagnosed Elderly and/or Unfit

PHASE II STUDY ON VENETOCLAX PLUS DECITABINE FOR ELDERLY (≥60 <75YEARS) PATIENTS WITH NEWLY DIAGNOSED HIGH-INTERMEDIATE RISK AML ELIGIBLE FOR ALLO-SCT: MIDTERM UPDATE OF VEN-DEC GITMO STUDY

Domenico Russo, et al. P502

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STUDY POPULATION

> Elderly (≥60 to <75 yr), fit AML pts (N=94)

UPDATED RESULTS OF VEN-A-QUI STUDY: A PHASE 1-2 TRIAL TO ASSESS THE SAFETY AND EFFICACY OF TRIPLETS FOR NEWLY DIAGNOSED UNFIT AML PATIENTS: AZACITIDINE OR LOW-DOSE CYTARABINE WITH VENETOCLAX AND QUIZARTINIB

Bergua Burgues, et al. S132

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STUDY POPULATION

> Newly diagnosed AML pts >70 yr or unfit pts >65 yr

A RANDOMISED ASSESSMENT OF THE SEQUENTIAL ADDITION OF THE KINASE INHIBITOR QUIZARTINIB TO INTENSIVE CHEMOTHERAPY IN OLDER ACUTE MYELOID LEUKAEMIA (AML) PATIENTS: RESULTS FROM THE NCRI AML18 TRIAL

Steven Knapper, et al. S131

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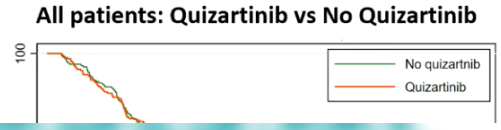
STUDY POPULATION

> Pts from NCRI AML18 ≥60 yr fit for intensive therapy (N=464), received a first course that was DA

Primary endpoint: Overall survival



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Discussion Summary

Advances in AML: Newly Diagnosed Elderly and/or Unfit

Advances in AML: Newly Diagnosed Elderly and/or Unfit (1/5)

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Latest Updates

VEN-decitabine: phase II GITMO study – midterm update

> High-intensity chemotherapy is the current standard pretransplant induction strategy for elderly, fit patients (60–75 years) with newly

[redacted]

Advances in AML: Newly Diagnosed Elderly and/or Unfit (2/5)

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Latest Updates

VEN-decitabine: phase II GITMO study – midterm update (cont.)

> The experts discussed the pros and cons of intensive therapy for newly-diagnosed elderly patients and the importance of patient fitness for

[redacted]

Advances in AML: Newly Diagnosed Elderly and/or Unfit (3/5)

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Latest Updates

Quizartinib + VEN-AZA or VEN-LDAC: VEN-A-QUI phase I/II trial

> Dr Perl highlighted that quizartinib is currently investigational; however, in Japan the label has been expanded to include both R/R and front

Advances in AML: Newly Diagnosed Elderly and/or Unfit (4/5)

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Latest Updates

Quizartinib + intensive chemotherapy in older AML patients: NCRI AML18 trial

> Experts agreed that the data are similar to those from QuANTUM-First, at least in the *FLT3*-ITD–positive population, and there was also an

Advances in AML: Newly Diagnosed Elderly and/or Unfit (5/5)

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Latest Updates

Gilteritinib + HMA-VEN in older patients with *FLT3* mutation

> Dr Daver confirmed that his practice of giving 7 days of AZA, 14 days of VEN, and 14 days of concomitant gilteritinib in the first cycle works

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Conference Highlights

Advances in AML: Relapsed/Refractory

VENETOCLAX (VEN) COMBINED WITH FLAG-IDA IS AN EFFECTIVE REGIMEN FOR PATIENTS (PTS) WITH NEWLY DIAGNOSED (ND) AND RELAPSED/REFRACTORY (R/R) ACUTE MYELOID LEUKEMIA (AML)

Madelyn Burkart, et al. P545

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STUDY POPULATION

> Single-center, retrospective study to assess the clinical activity of FLAG-

Figure 1: Overall Survival of ND and R/R AML Patients Treated with FLAG-IDA+VEN

OLUTASIDENIB IN POST-VENETOCLAX PATIENTS WITH MUTANT IDH1 AML

Jorge Cortes, et al. P555

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STUDY POPULATION

> Olutasidenib is approved for R/R AML on the basis of the registrational cohort (n=153) of a phase II trial, with a CR/CRh of 35%, and DOR of

Duration of Response to Olutasidenib in Overall Responders R/R to VEN

ACTIVITY, TOLERABILITY, AND RESISTANCE PROFILE OF THE MENIN INHIBITOR ZIFTOMENIB IN ADULTS WITH RELAPSED/REFRACTORY NPM1-MUTATED AML

Amir Fathi, et al. P504/LBA2713

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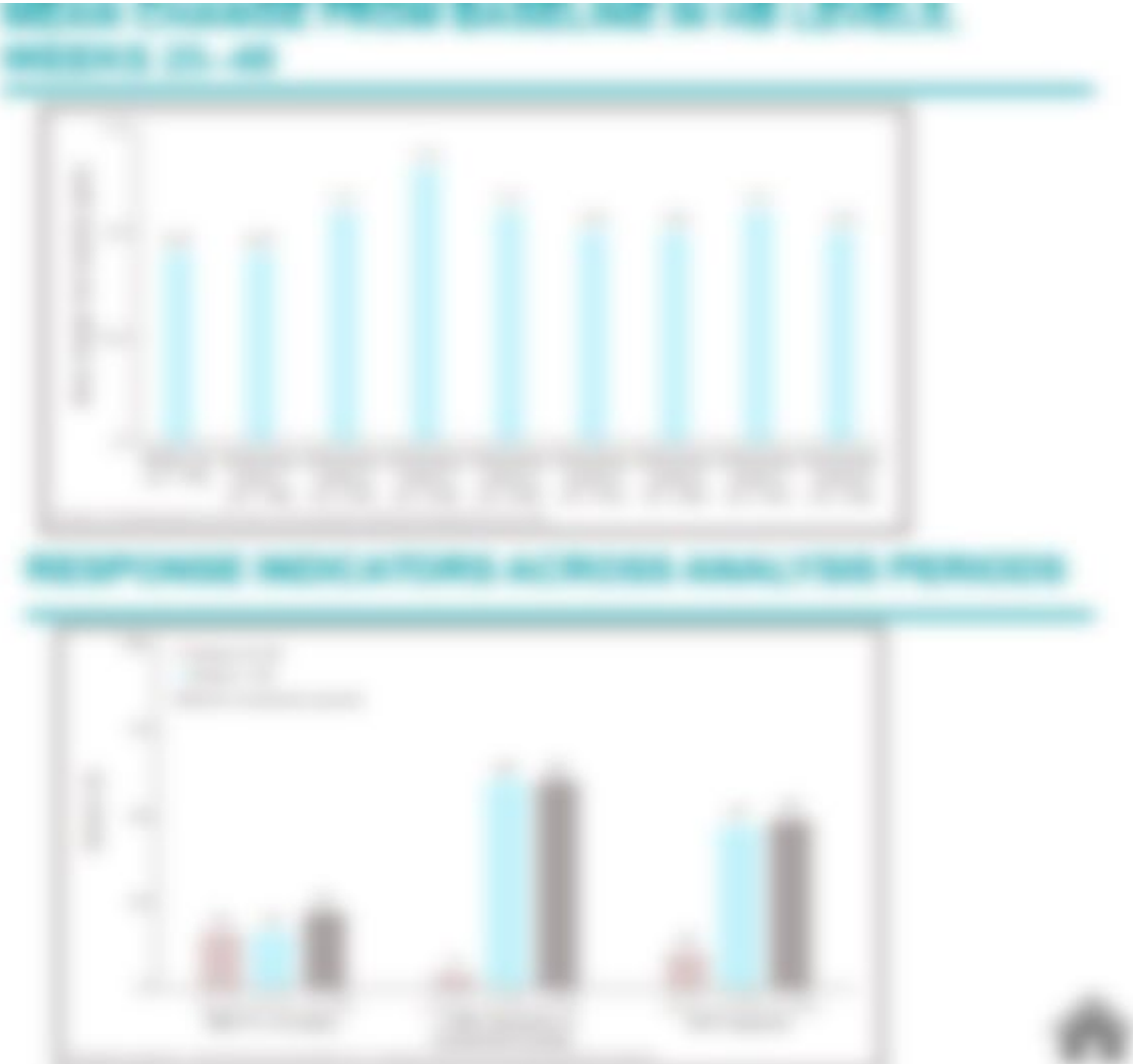
STUDY POPULATION

- Pts (median age: 70.5 yr [22–86 yr]) with R/R AML treated in the global, open-label phase I/II study of ziftomenib: 35% *FLT3*, 40% *IDH1/2*

Responses to treatment with ziftomenib



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Discussion Summary

Advances in AML: Relapsed/Refractory

Advances in AML: Relapsed/Refractory (1/2)

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Latest Updates

Venetoclax + FLAG-IDA in newly diagnosed and R/R AML

> Recent results from a phase Ib/II trial from MD Anderson were considered for the combination FLAG-IDA–VEN in newly diagnosed and R/R AML

[redacted]

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Advances in AML: Relapsed/Refractory (2/2)

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Latest Updates

Ziftomenib in patients with *NPM1*-mutated R/R AML

> The experts are encouraged by the data with ziftomenib but agreed that longer follow-up is needed. Dr Altman noted, *"My takeaway is that*

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Overall Conclusions

CHAIR:
Elias Jabbour, MD

Conference Coverage: EHA 2023 – Focus on AML and MDS

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Overall Conclusions: Dr Jabbour

MDS

> *"I am excited about the COMMANDS trial and luspatercept as a 'newborn' in the frontline"*

> *"HMA-VEN is promising in MDS… but I think 14 days is a lot, it should be 7 days"*

> *"[illegible]"*

[redacted]

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