



EPICS

Conference Coverage: EHA 2023 – Focus on AML and MDS

Syndicated Report

June 10, 2023

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Advances in AML: Newly Diagnosed Elderly and/or Unfit	35 →
Advances in AML: Relapsed/Refractory	45 →

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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



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

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

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)

STUDY POPULATION

1. 100% of pts were... 2. 100% of pts were... 3. 100% of pts were... 4. 100% of pts were... 5. 100% of pts were... 6. 100% of pts were... 7. 100% of pts were... 8. 100% of pts were... 9. 100% of pts were... 10. 100% of pts were...

RESULTS

1. 100% of pts were... 2. 100% of pts were... 3. 100% of pts were...

CONCLUSIONS

1. 100% of pts were... 2. 100% of pts were... 3. 100% of pts were...

HEMATOLOGIC RESPONSE OVER TIME



RESPONSE INDICATORS ACROSS ANALYSED PARAMETERS



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

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



SECONDARY ENDPOINTS: RBC TRANSFUSION-RELATED EVENTS



RESPONSE: HEMATOLOGICAL AND CLINICAL OUTCOMES



STUDY POPULATION

1. 1000 pts aged ≥ 18 yr with IPSS-R very low-, low-, or intermediate-risk MDS by WHO criteria. 500 pts were randomized to luspatercept and 500 pts to epoetin alfa. The primary endpoint was the proportion of pts achieving a transfusion-free interval (TFI) of ≥ 12 weeks. The secondary endpoint was the proportion of pts achieving a TFI of ≥ 12 weeks with a transfusion-free interval (TFI) of ≥ 12 weeks. The primary endpoint was achieved by 85% of pts in the luspatercept group and 69.6% of pts in the epoetin alfa group. The secondary endpoint was achieved by 85% of pts in the luspatercept group and 69.6% of pts in the epoetin alfa group.

RESULTS

1. 1000 pts aged ≥ 18 yr with IPSS-R very low-, low-, or intermediate-risk MDS by WHO criteria. 500 pts were randomized to luspatercept and 500 pts to epoetin alfa. The primary endpoint was the proportion of pts achieving a TFI of ≥ 12 weeks. The secondary endpoint was the proportion of pts achieving a TFI of ≥ 12 weeks with a transfusion-free interval (TFI) of ≥ 12 weeks.

CONCLUSIONS

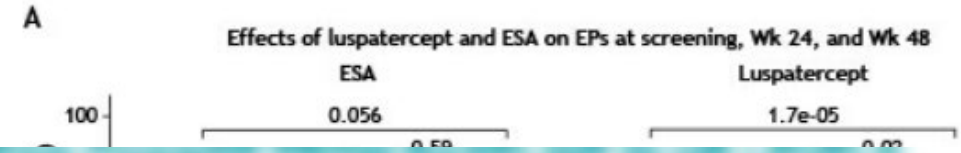
1. Luspatercept is superior to epoetin alfa for the treatment of anemia in ESA-naïve LR-MDS pts requiring RBC transfusions. Luspatercept significantly increases the proportion of pts achieving a TFI of ≥ 12 weeks.

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

STUDY POPULATION

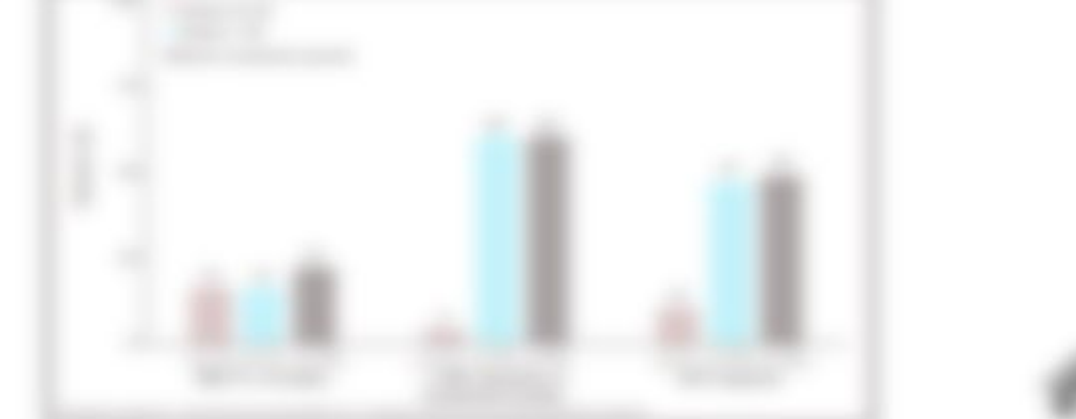
> Erythropoiesis-stimulating agent (ESA)-naive pts with LR MDS from the



RESPONSE RATES AT SCREENING AND Wk 24



RESPONSE RATES AT Wk 48 AND Wk 72



STUDY POPULATION

1. 100% of pts were ESA-naive with LR MDS, including 100% of pts with 1-2% blasts, 100% of pts with 3-5% blasts, and 100% of pts with 6-10% blasts. The median age was 70 years (range 55-85). The median duration of disease was 1.5 years (range 0.1-10.5). The median hemoglobin level was 10.5 g/dL (range 7.5-13.5). The median platelet count was 100 x 10⁹/L (range 50-150). The median neutrophil count was 1.5 x 10⁹/L (range 0.5-3.5). The median transfusion requirement was 1.5 units of RBCs per month (range 0-5). The median transfusion requirement was 1.5 units of RBCs per month (range 0-5). The median transfusion requirement was 1.5 units of RBCs per month (range 0-5).

STUDY POPULATION

2. 100% of pts were ESA-naive with LR MDS, including 100% of pts with 1-2% blasts, 100% of pts with 3-5% blasts, and 100% of pts with 6-10% blasts. The median age was 70 years (range 55-85). The median duration of disease was 1.5 years (range 0.1-10.5). The median hemoglobin level was 10.5 g/dL (range 7.5-13.5). The median platelet count was 100 x 10⁹/L (range 50-150). The median neutrophil count was 1.5 x 10⁹/L (range 0.5-3.5). The median transfusion requirement was 1.5 units of RBCs per month (range 0-5). The median transfusion requirement was 1.5 units of RBCs per month (range 0-5). The median transfusion requirement was 1.5 units of RBCs per month (range 0-5).

STUDY POPULATION

3. 100% of pts were ESA-naive with LR MDS, including 100% of pts with 1-2% blasts, 100% of pts with 3-5% blasts, and 100% of pts with 6-10% blasts. The median age was 70 years (range 55-85). The median duration of disease was 1.5 years (range 0.1-10.5). The median hemoglobin level was 10.5 g/dL (range 7.5-13.5). The median platelet count was 100 x 10⁹/L (range 50-150). The median neutrophil count was 1.5 x 10⁹/L (range 0.5-3.5). The median transfusion requirement was 1.5 units of RBCs per month (range 0-5). The median transfusion requirement was 1.5 units of RBCs per month (range 0-5). The median transfusion requirement was 1.5 units of RBCs per month (range 0-5).

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

Alex Bataller, et al. S172

STUDY POPULATION

> Pts aged 27–94 yr with confirmed diagnosis of treatment-naïve 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)

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

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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

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

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

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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

Uwe Platzbecker, et al. S165

STUDY POPULATION

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

Background

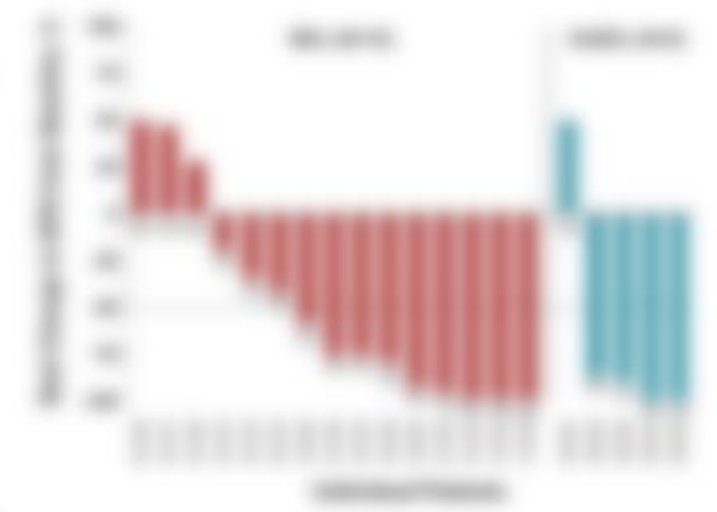
- Phase 3, randomized, controlled study of IMETELSTAT vs PBO in patients with heavily transfused MDS and tMDS.
- Primary objective was to define population of MDS and tMDS requiring regular transfusions.

Results

- 11 patients were excluded, including 10 patients with MDS.
- 26.7% were not transfused and 100 transfused.
- 100 transfused occurred in 20% of patients, 100 transfused occurred in 20% of patients.
- 100 transfused occurred in 20% of patients, 100 transfused occurred in 20% of patients.
- 100 transfused occurred in 20% of patients, 100 transfused occurred in 20% of patients.
- 100 transfused occurred in 20% of patients, 100 transfused occurred in 20% of patients.
- 100 transfused occurred in 20% of patients, 100 transfused occurred in 20% of patients.
- 100 transfused occurred in 20% of patients, 100 transfused occurred in 20% of patients.

Key findings: IMETELSTAT demonstrated a comparable and favorable safety profile and encouraging efficacy with longer transfusion independence in advanced MDS and tMDS. Experts mentioned transfusion as a potential concern and the need to identify the best strategies in which to use this agent.

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



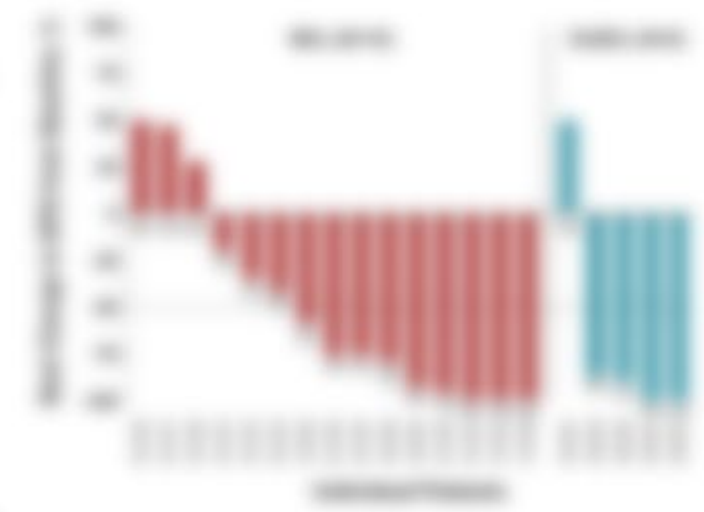
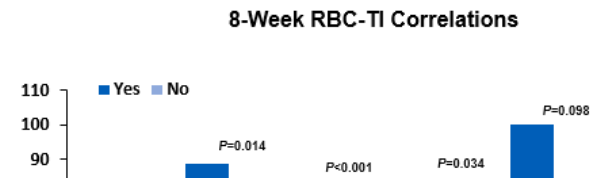
DISEASE MODIFYING ACTIVITY OF IMETELSTAT IN PATIENTS WITH HEAVILY TRANSFUSED NON-DEL (5Q) LOWER-RISK MYELODYSPLASTIC SYNDROMES RELAPSED/REFRACTORY TO ERYTHROPOIESIS STIMULATING AGENTS IN IMERGE PHASE 3

Valeria Santini, et al. S164

STUDY POPULATION

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

- Background**
- Phase 3, double-blind, randomized study of IME vs len-HMA in patients with heavily transfused MDS and tMDS.
 - Primary objective was to confirm superiority of IME vs len-HMA in heavily transfused patients.
- Results**
- 27 patients were enrolled, including 15 patients with MDS.
 - 26.7% were len-HMA resistant and 12.7% MDS.
 - 12.7% transfusion occurred in 20% of patients, 12.7% transfusion occurred in 20% of patients.
 - 12.7% transfusion occurred in 20% of patients, 12.7% transfusion occurred in 20% of patients.
 - 12.7% transfusion occurred in 20% of patients, 12.7% transfusion occurred in 20% of patients.
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 - 12.7% transfusion occurred in 20% of patients, 12.7% transfusion occurred in 20% of patients.
 - 12.7% transfusion occurred in 20% of patients, 12.7% transfusion occurred in 20% of patients.



Key takeaway: IME vs len-HMA demonstrated a comparable and predictable safety profile and encouraging efficacy with durable responses in advanced MDS and tMDS. Experts mentioned transfusion as a potential concern and the need to identify the best strategies in which to use this agent.

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

STUDY POPULATION

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

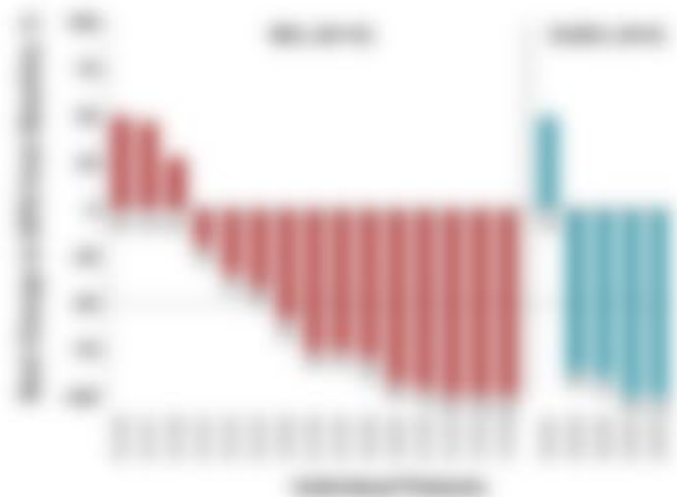
Pharmacologic inhibition of *MDMX* synergizes with azacitidine

Background

- Phase I dose-toxicity study of U.S. 501, a *MDMX*-targeting AICL, in patients with newly diagnosed MDS and t(8,21)
- Primary objective was to define maximum tolerated dose and recommended starting regimen

Results

- 37 patients were enrolled, including 19 patients with MDS
- 28.7% were 1st relapse and 12.7% 2nd
- CR remission occurred in 28% of patients, 15.8% successfully engrafted
- CR remission 12 months post-remission occurred in 8% of patients, no CR remission observed
- CRP was 47% (2/4), 47% (2/4) for MDS cohort and 80% (2/3), 27% (1/4) for t(8,21) cohort
- 8 responding patients have ongoing responses ranging from 27 weeks to 58 weeks



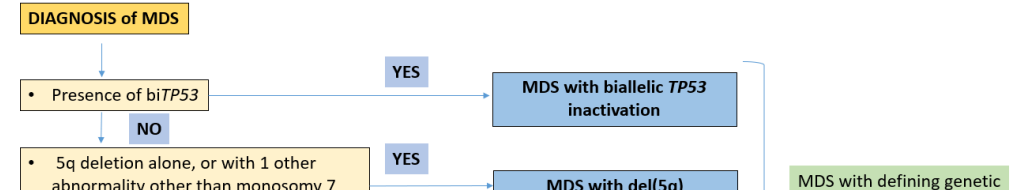
Key takeaway: U.S. 501 demonstrated a manageable and predictable safety profile and encouraging efficacy with durable responses in advanced MDS and t(8,21). Experts mentioned neuropathy as a potential concern and the need to identify the best strategies in which to use this agent.

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

BACKGROUND AND AIMS

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

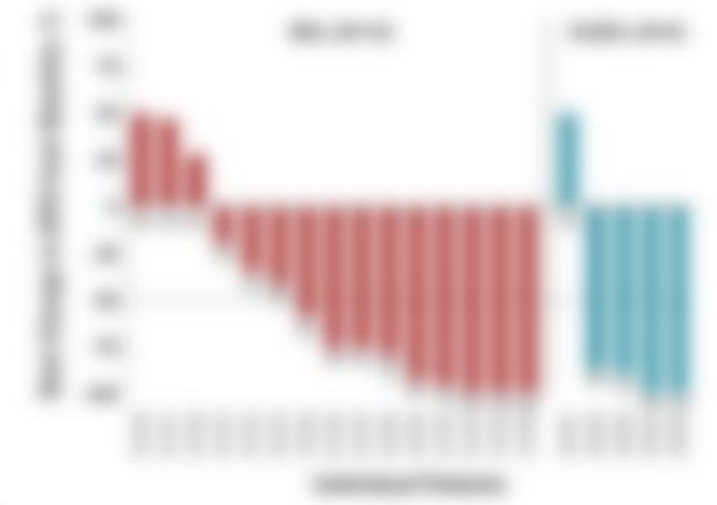


Background

- 1. There is a need for a more refined classification of MDS, including MDS, in patients with newly diagnosed MDS, and CMDS.
- 2. Primary objective was to define subtypes of MDS and associated defining genetic features.

Results

- 1. 7017 patients were included, including 10 patients with CMDS.
- 2. 58.7% were CMDS, 31.3% were MDS, and 9.0% were CMDS.
- 3. CMDS were associated with 28% of patients, 10.1% with MDS, and 1.1% with CMDS.
- 4. CMDS were associated with 10% of patients, 10.1% with MDS, and 1.1% with CMDS.
- 5. CMDS were 47% of CMDS, 4.1% for MDS, and 0.1% for CMDS, and 0.1% for CMDS.
- 6. 8 responding patients have ongoing responses ranging from 20 weeks to 58 weeks.



Key findings: The 2022 classification of myeloid neoplasms and associated genetic profile and prognostic efficacy, with focus on patients with newly diagnosed MDS, and CMDS. Experts considered secondary as a potential concern and the need to identify the best strategies in which to use this agent.

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Discussion Summary

New Developments in Treatment of R/R MDS

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

R/R MDS

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

Background: The inclusion of RS-positive patients in the IMERGE (and COMMANDS) trial is a significant development in the treatment of R/R MDS. This trial is designed to evaluate the efficacy and safety of a novel treatment approach in patients with R/R MDS, including those who are RS-positive. The inclusion of RS-positive patients is based on the understanding that these patients may have a different clinical course and may benefit from a more aggressive treatment approach. The trial is currently ongoing, and preliminary results are expected to be published in the near future.

Background: The inclusion of RS-positive patients in the IMERGE (and COMMANDS) trial is a significant development in the treatment of R/R MDS. This trial is designed to evaluate the efficacy and safety of a novel treatment approach in patients with R/R MDS, including those who are RS-positive. The inclusion of RS-positive patients is based on the understanding that these patients may have a different clinical course and may benefit from a more aggressive treatment approach. The trial is currently ongoing, and preliminary results are expected to be published in the near future.

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

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

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

STUDY POPULATION

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

Sub-Group	Overall survival				HR with 95% CI
	DA		FLAG-IDA		
	Patients	Events	Patients	Events	
Joint <i>NPM1</i> & <i>FLT3</i> status					

STUDY POPULATION

1475 patients were randomized to either FLAG-IDA (n=737) or DA (n=738). The median age was 51.5 years (range 18-82). 60% of patients had *NPM1* mutation, 30% had *FLT3* mutation, and 10% had both. The majority of patients were in the *NPM1* mutant and *FLT3* wild-type group. The majority of patients were in the *NPM1* mutant and *FLT3* wild-type group. The majority of patients were in the *NPM1* mutant and *FLT3* wild-type group.

RESULTS

Overall survival was significantly improved in the FLAG-IDA group compared to the DA group (HR 0.78, 95% CI 0.65-0.94, p=0.01). This improvement was seen in all subgroups, including those with *NPM1* mutant and *FLT3* wild-type status.

CONCLUSIONS

Combining FLAG-IDA with GO significantly improved overall survival in newly diagnosed *NPM1* mutant AML, independent of *FLT3* status.



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

1A. Event-free survival

STUDY POPULATION

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



STUDY POPULATION

180 patients were randomized to receive either standard chemotherapy plus quizartinib (n=90) or standard chemotherapy plus placebo (n=90). The median age was 57 years (range 18–70). All patients were newly diagnosed with FLT3-ITD wild-type AML. The median duration of follow-up was 12.5 months. The primary endpoint was event-free survival (EFS), defined as the time from randomization to the first occurrence of death due to any cause, relapse, or progression, or death due to unknown cause. The secondary endpoint was overall survival (OS), defined as the time from randomization to death due to any cause. The analysis was performed on an intention-to-treat basis.

RESULTS

The median EFS was 12.5 months in the quizartinib group and 10.5 months in the placebo group. The hazard ratio for EFS was 0.741 (95% CI, 0.535–1.026; P=0.059). The median OS was 18.5 months in the quizartinib group and 17.5 months in the placebo group. The hazard ratio for OS was 0.85 (95% CI, 0.65–1.10; P=0.25).

CONCLUSIONS

Quizartinib did not significantly improve EFS compared with placebo in patients with newly diagnosed FLT3-ITD wild-type AML. OS was also not significantly improved with quizartinib. Further studies are needed to evaluate the role of FLT3 inhibitors in this population.

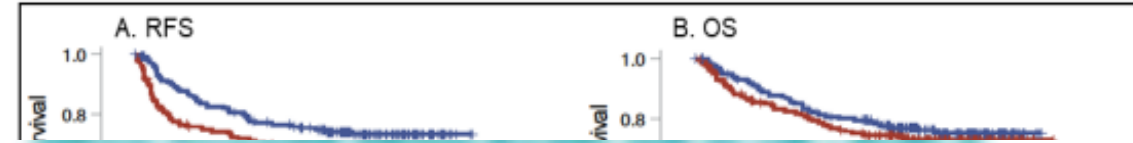


BMT-CTN 1506 (MORPHO): A RANDOMIZED TRIAL OF THE FLT3 INHIBITOR GILTERITINIB AS POST-TRANSPLANT MAINTENANCE FOR FLT3-ITD AML

Mark J. Levis, et al. LBA2711

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



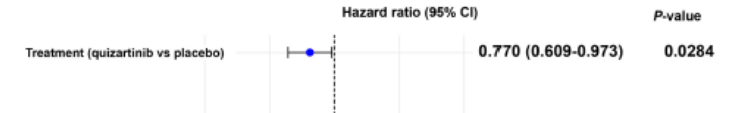
IMPACT OF ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION IN FIRST COMPLETE REMISSION PLUS FLT3 INHIBITION WITH QUIZARTINIB IN ACUTE MYELOID LEUKEMIA WITH FLT3-ITD: RESULTS FROM QUANTUM-FIRST

Richard Schlenk, et al. S137

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



STUDY POPULATION

1. 1000 patients with newly diagnosed AML, screened for FLT3-ITD prior to starting treatment. 500 patients were FLT3-ITD positive and 500 were FLT3-ITD negative. The median age was 60 years (range 18-75). The median time from diagnosis to randomization was 12 days (range 0-100). The median time from randomization to start of treatment was 10 days (range 0-100). The median time from start of treatment to death was 10 months (range 0-100).

RESULTS

1. The median overall survival (OS) was 10 months (95% CI, 9-11) in the quizartinib group and 8 months (95% CI, 7-9) in the placebo group. The median time to death was 10 months (95% CI, 9-11) in the quizartinib group and 8 months (95% CI, 7-9) in the placebo group.

CONCLUSIONS

Quizartinib significantly improved OS compared with placebo in patients with newly diagnosed AML and FLT3-ITD. The median OS was 10 months in the quizartinib group and 8 months in the placebo group.



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

1A. Overall survival

STUDY POPULATION

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



STUDY POPULATION

1. 100 pts aged 18–60 yr with newly diagnosed AML were randomized to either gemtuzumab-based induction chemotherapy (G01) or gemtuzumab-based induction chemotherapy plus midostaurin (G02). The G01 group received gemtuzumab 1.25 mg/kg on days 1, 8, and 15 of induction chemotherapy. The G02 group received gemtuzumab 1.25 mg/kg on days 1, 8, and 15 of induction chemotherapy plus midostaurin 50 mg bid on days 1–28. The primary endpoint was overall survival at 12 weeks. The secondary endpoint was overall survival at 24 weeks. The trial was stopped early due to a statistically significant difference in overall survival between the two groups at 12 weeks.

RESULTS

1. 100 pts were randomized to either G01 (n=50) or G02 (n=50). The median age was 55 years (range 18–60). The majority of pts were male (n=65). The majority of pts were white (n=85). The majority of pts were newly diagnosed AML (n=95). The majority of pts were in the G01 group (n=50).

CONCLUSIONS

Combining gemtuzumab-based induction therapy with 28 days of oral midostaurin during induction is safe and increases the proportion of pts in remission.

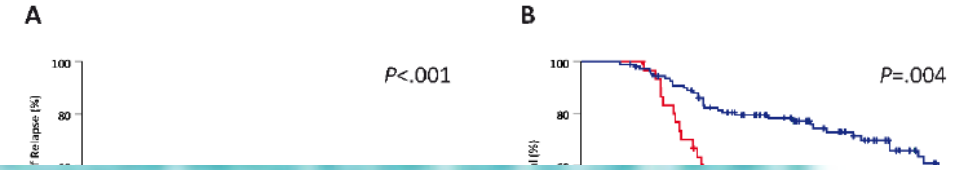


NEXT-GENERATION SEQUENCING-BASED MEASURABLE RESIDUAL DISEASE MONITORING IN ACUTE MYELOID LEUKEMIA WITH FLT3 INTERNAL TANDEM DUPLICATION TREATED WITH INTENSIVE CHEMOTHERAPY PLUS MIDOSTAURIN*

Frank G. Rücker, et al. S135

STUDY POPULATION

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



STUDY POPULATION

1. 100 pts aged 18–70 yr with *FLT3*-ITD–positive AML enrolled on the AMLSG 16-001 trial. 50 pts received intensive chemotherapy (IC) plus midostaurin (MID) and 50 pts received IC alone. The primary endpoint was relapse-free survival (RFS) at 12 months. The secondary endpoint was overall survival (OS) at 12 months. The study was prospectively registered on ClinicalTrials.gov (NCT01023705).

RESULTS

1. The 12-month RFS was significantly higher in the MID group (58%) compared with the IC group (42%) ($P = .001$). The 12-month OS was also significantly higher in the MID group (65%) compared with the IC group (55%) ($P = .004$).

CONCLUSIONS

Adding midostaurin to intensive chemotherapy significantly improves RFS and OS in *FLT3*-ITD–positive AML patients.



EPICS

Discussion Summary

Advances in AML: Newly Diagnosed

Advances in AML: Newly Diagnosed (1/3)

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

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

EPICS

Conference Highlights

Advances in AML: Newly Diagnosed Elderly
and/or Unfit

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

Domenico Russo, et al. P502

STUDY POPULATION

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

STUDY POPULATION

94 elderly patients with newly diagnosed high-intermediate risk AML, fit for allo-SCT, were enrolled in this study. The median age was 68 years (range 60-74). All patients were eligible for allo-SCT. The study was conducted in accordance with the Declaration of Helsinki and approved by the local ethics committees. All patients gave their informed consent before starting treatment.

RESULTS

The overall response rate (ORR) was 78% (73/94). The complete response (CR) rate was 55% (52/94). The median duration of response (DOR) was 12 months. The median overall survival (OS) was 18 months.

CONCLUSIONS

Combining venetoclax and decitabine showed promising activity in elderly patients with high-intermediate risk AML, supporting the use of this combination in this population.

ORR AND CR RATES BY RISK STRATIFICATION



RESPONSE, DOR, AND OS BY RISK STRATIFICATION



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

STUDY POPULATION

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

TOXICITY PROFILE (GRADE 3-4)



RESPONSE RATES (CR, CRi, CR+MR)



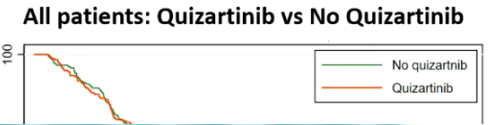
A RANDOMISED ASSESSMENT OF THE SEQUENTIAL ADDITION OF THE KINASE INHIBITOR QUIZARTINIB TO INTENSIVE CHEMOTHERAPY IN OLDER ACUTE MYELOID LEUKAEMIA (AML) PATIENTS: RESULTS FROM THE NCRI AML18 TRIAL

Steven Knapper, et al. S131

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



STUDY POPULATION

464 patients were included in the primary endpoint analysis. The median age was 70 years (range 60-89). 46% were male. The median duration of illness was 1.5 years (range 0-10). The median time from diagnosis to randomisation was 1.5 years (range 0-10). The median time from randomisation to start of treatment was 1.5 days (range 0-10). The median time from start of treatment to death was 1.5 months (range 0-10). The median time from start of treatment to last follow-up was 1.5 months (range 0-10).

RESULTS

Overall survival was significantly better in the Quizartinib group compared to the No Quizartinib group (p < 0.001). The median overall survival was 1.5 months (95% CI 1.2-1.8) in the Quizartinib group versus 1.0 months (95% CI 0.8-1.2) in the No Quizartinib group.

CONCLUSIONS

The addition of Quizartinib to intensive chemotherapy significantly improved overall survival in older AML patients. This finding supports the use of Quizartinib in this patient population.



EPICS

Discussion Summary

Advances in AML: Newly Diagnosed Elderly
and/or Unfit

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

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

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

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

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

EPICS

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

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



RESPONSE, TOXICITY, AND QUALITY OF LIFE (QOL) RESULTS



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



Response Evaluation 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



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: 25% / 51.7% / 40% / 10/14/9

Responses to treatment with ziftomenib



EPICS

Discussion Summary

Advances in AML: Relapsed/Refractory

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

[The following text is extremely faint and largely illegible. It appears to be a list of bullet points or a detailed summary of clinical trial results related to the Venetoclax + FLAG-IDA combination in AML.]

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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EPICS

Overall Conclusions

CHAIR:


Elias Jabbour, MD

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”*





US 5901-C Peachtree Dunwoody Road NE
Suite 200, Atlanta, GA 30328, US

EU Wilhelmina van Pruysenweg 104
2595 AN The Hague, the Netherlands

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

[aptitudehealth.com](https://www.aptitudehealth.com)

