ASH 2023 update on AML and MDS

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City of Hope Phoenix

Disclosures

- Research funding: Abbvie, Gilead, Glycomimetics, Novartis, Syndax
- Honoraria: Rigel, Servier

Outline

- AML
  - FLT3 mutated AML: Quizartinib
  - Menin inhibitors

- MDS
  - high risk MDS: Ivosidenib
  - low risk MDS: Luspatercept, Imetelsat

QuANTUM-First Phase 3 Trial: Quizartinib Plus Standard Induction Chemotherapy and Consolidation Followed by Single-Agent Quizartinib

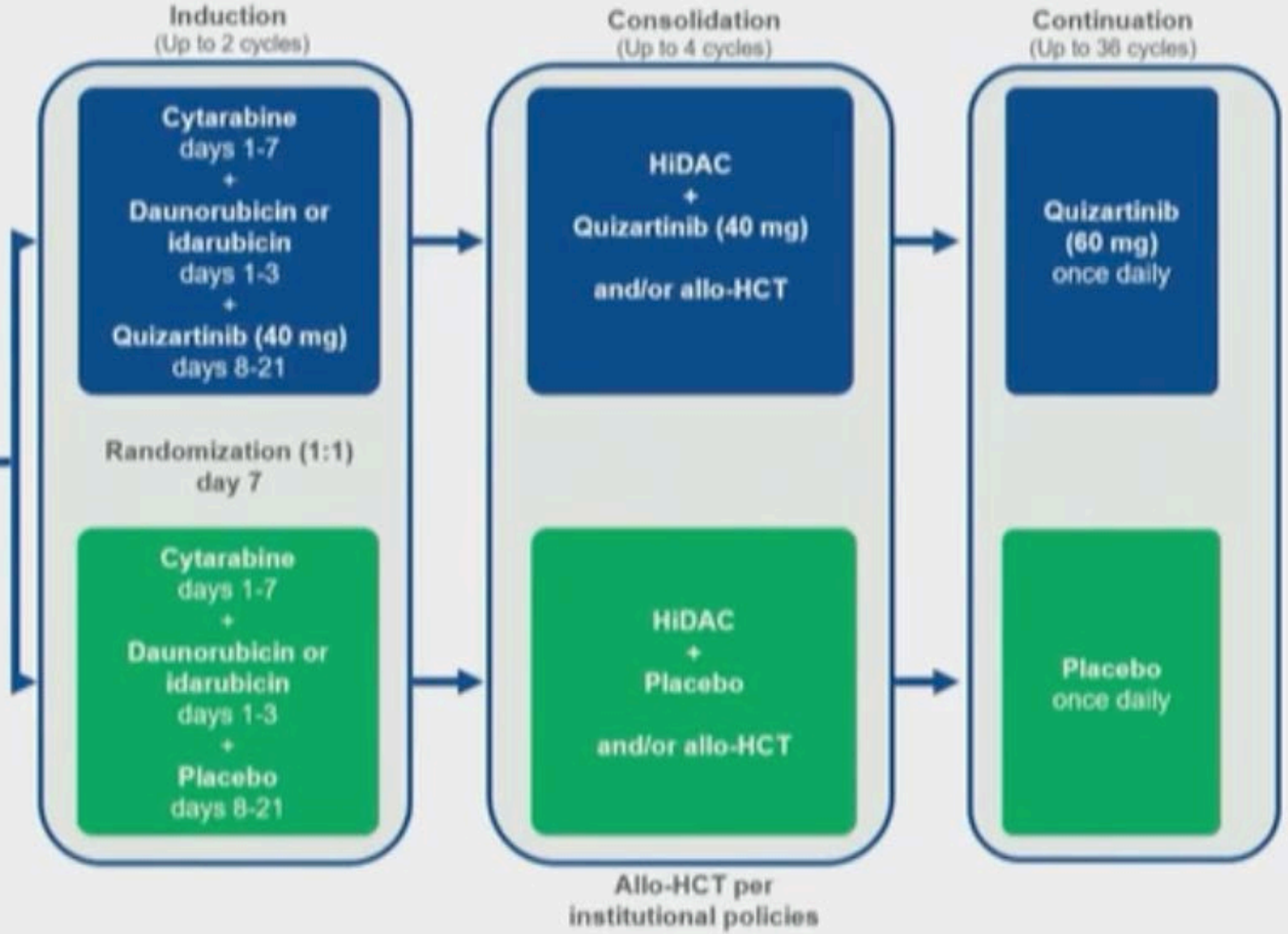
Enrollment dates: September 2016 to August 2019
Data cutoff: August 13, 2021

Stratification factors
- **Region**: NA, EU, and Asia/other regions
- **Patient age**: <60 years, ≥60 years
- **WBC**[a]: <40×10⁹/L, ≥40×10⁹/L

- Newly diagnosed *FLT3*-ITD+ AML
- 18-75 years of age
- ≥3% *FLT3*-ITD allelic frequency
- Patients begin 7+3 chemotherapy during screening

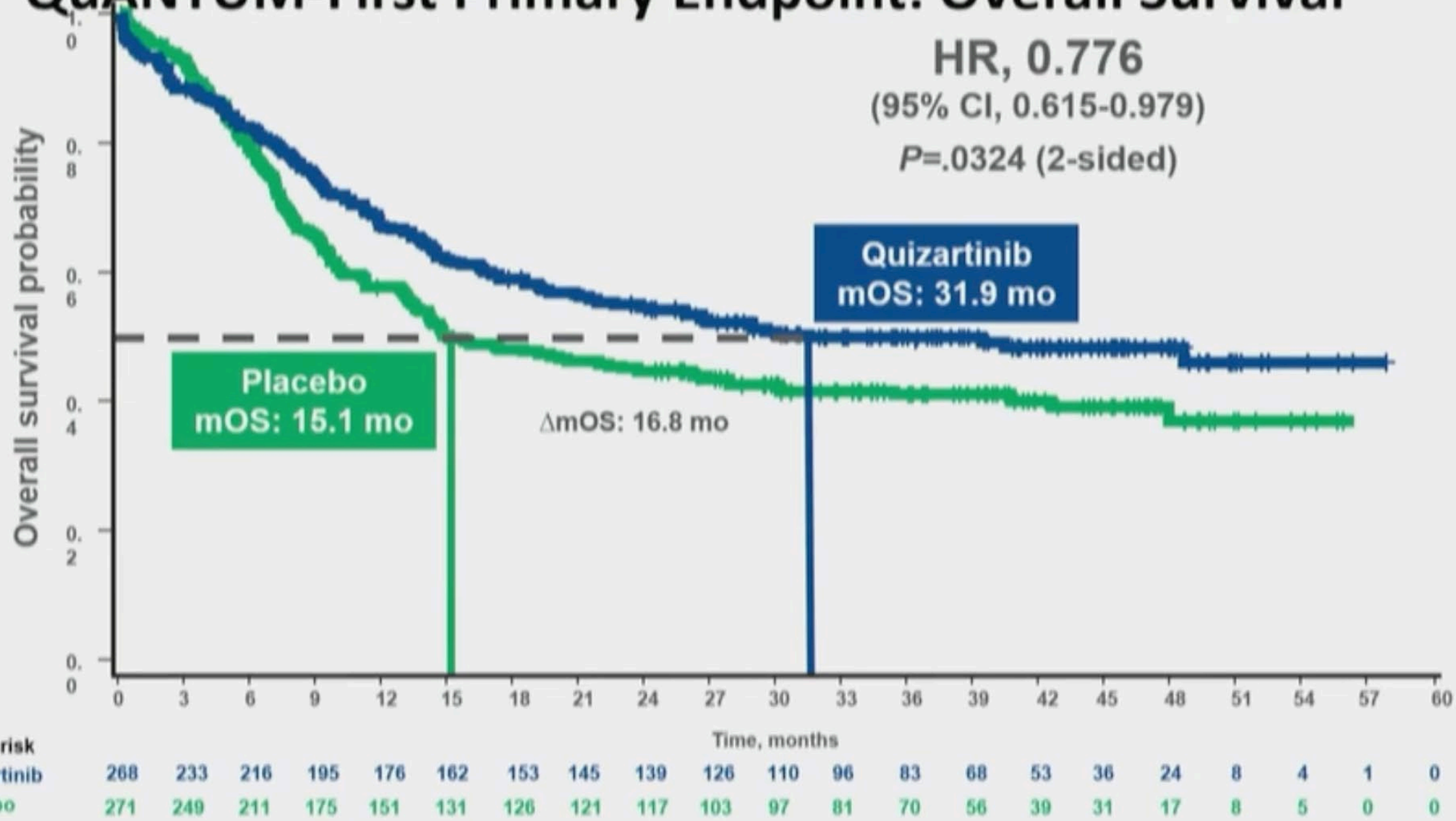
Selected endpoints
- **Primary endpoint**: OS
- **Secondary endpoints**: EFS, CR/CRc, Safety
- **Exploratory endpoints**: RFS, DoCR

A hierarchical testing procedure was used to test the primary endpoint of OS, followed by EFS, CR and CRc.



Erba HP, et al. *Lancet* 2023; 401(10388): 1571-1583

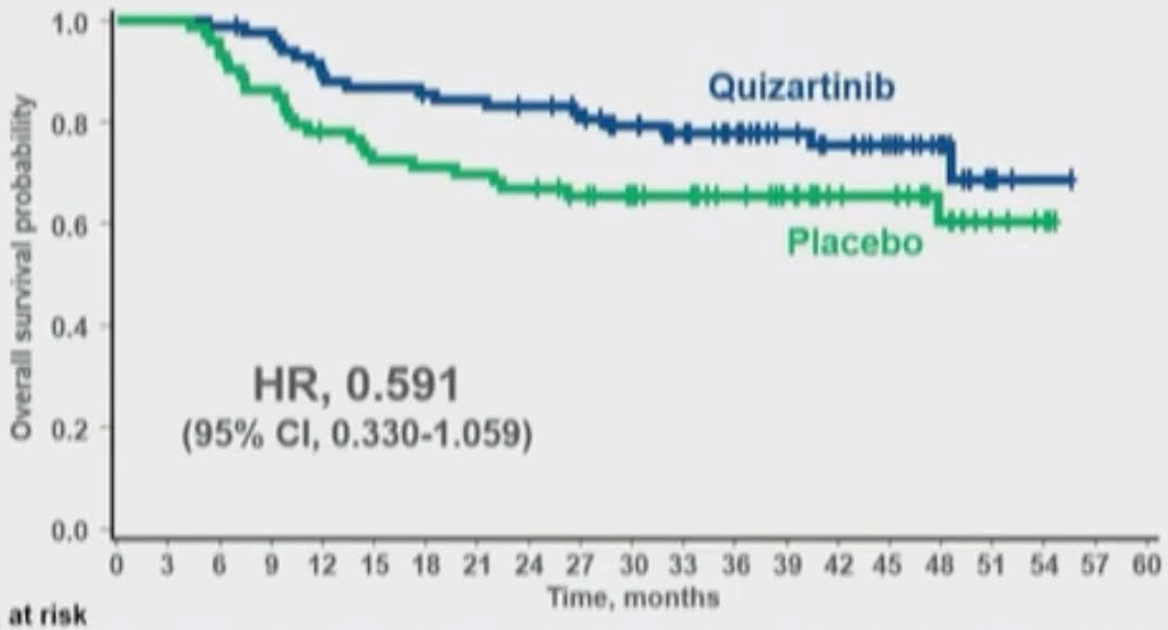
QuANTUM-First Primary Endpoint: Overall Survival



Erba HP, et al. *Lancet* 2023; 401(10388): 1571-1583

QuANTUM-First: Overall Survival in Patients Who Achieved CR

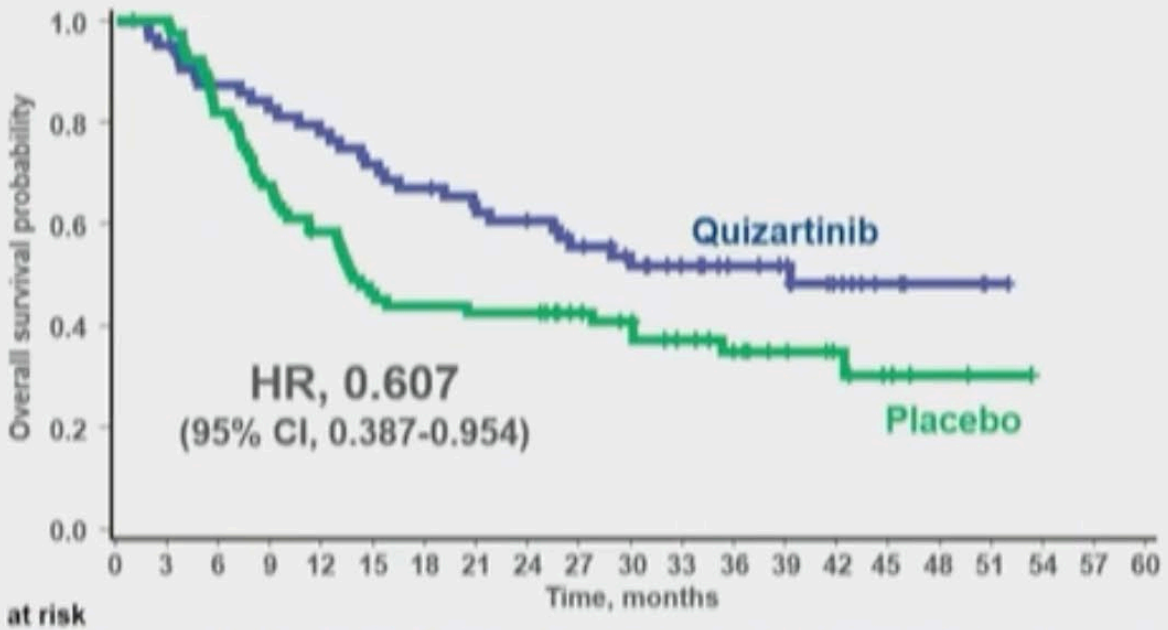
Patients With CR Who Received Allo-HCT in CR1



No. at risk

Quizartinib	84	84	83	81	74	72	70	69	67	63	57	50	42	34	29	22	14	3	1	0	0
Placebo	73	73	68	63	56	52	51	50	48	43	39	37	32	27	21	20	12	5	3	0	0

Patients With CR NOT Receiving Allo-HCT in CR1



No. at risk

Quizartinib	63	60	54	51	48	44	41	37	35	30	25	21	17	15	9	5	3	1	0	0	0
Placebo	77	76	61	50	42	33	31	30	30	25	22	17	14	10	7	4	2	1	0	0	0

Erba HP, et al. *Lancet* 2023; 401(10388): 1571-1583

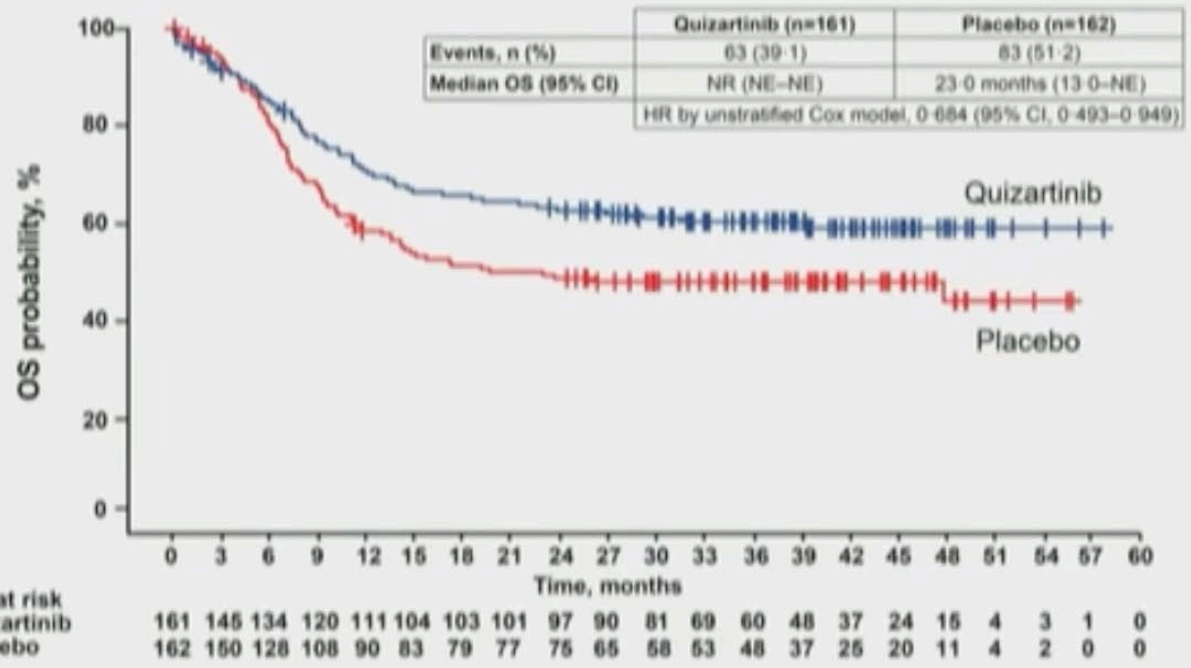
QuANTUM-First: Response and Duration of Complete Remission

Parameter	Quizartinib (N=268)	Placebo (N=271)
CRc		
%	71.6	64.9
95% CI	(65.8-77.0)	(58.9-70.6)
CR		
%	54.9	55.4
95% CI	(48.7-60.9)	(49.2-61.4)
CRi		
%	16.8	9.6
95% CI	(12.5-21.8)	(6.4-13.7)
Duration of CR		
Median, months	38.6	12.4
95% CI	(21.9-NE)	(8.8-22.7)

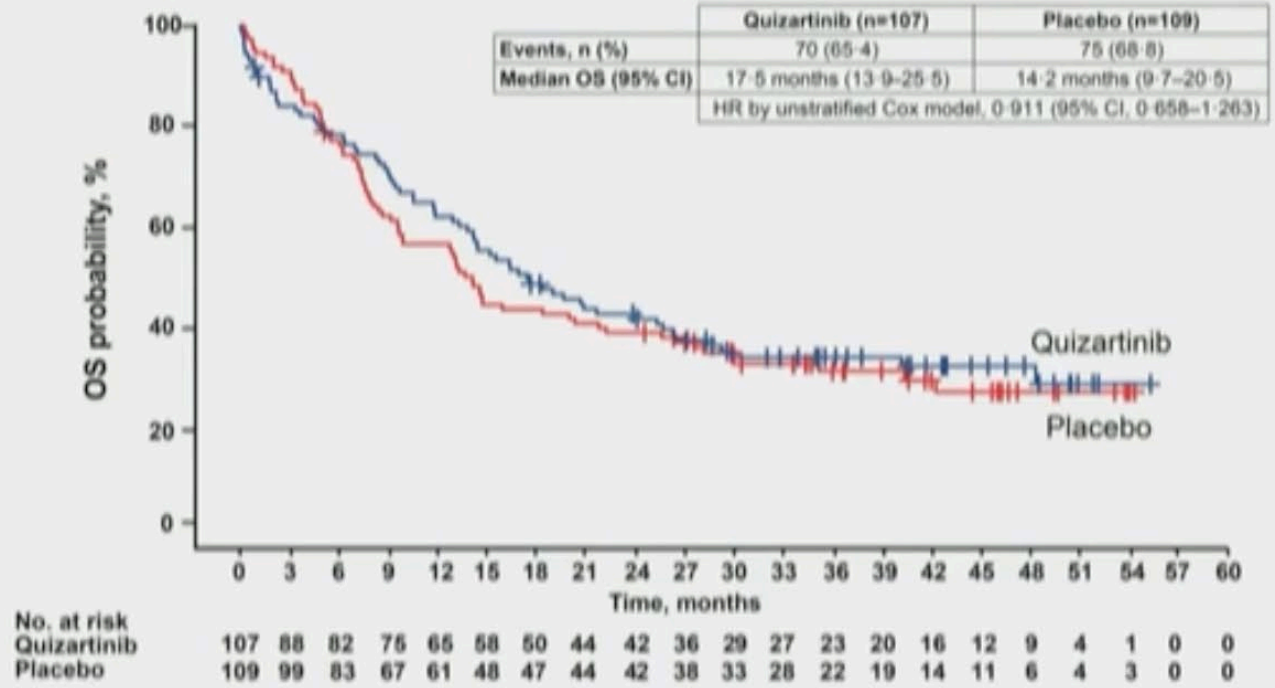
Erba HP, et al. *Lancet* 2023; 401(10388): 1571-1583

QuANTUM-First: Overall Survival by Age

A. Overall survival in patients <60 years old



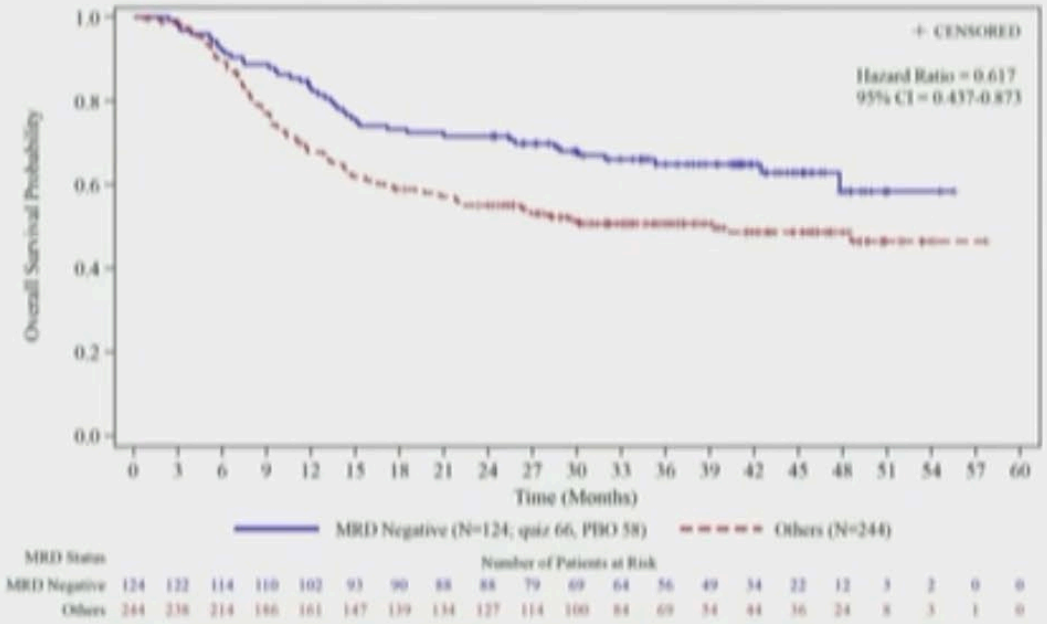
B. Overall survival in patients ≥60 years old



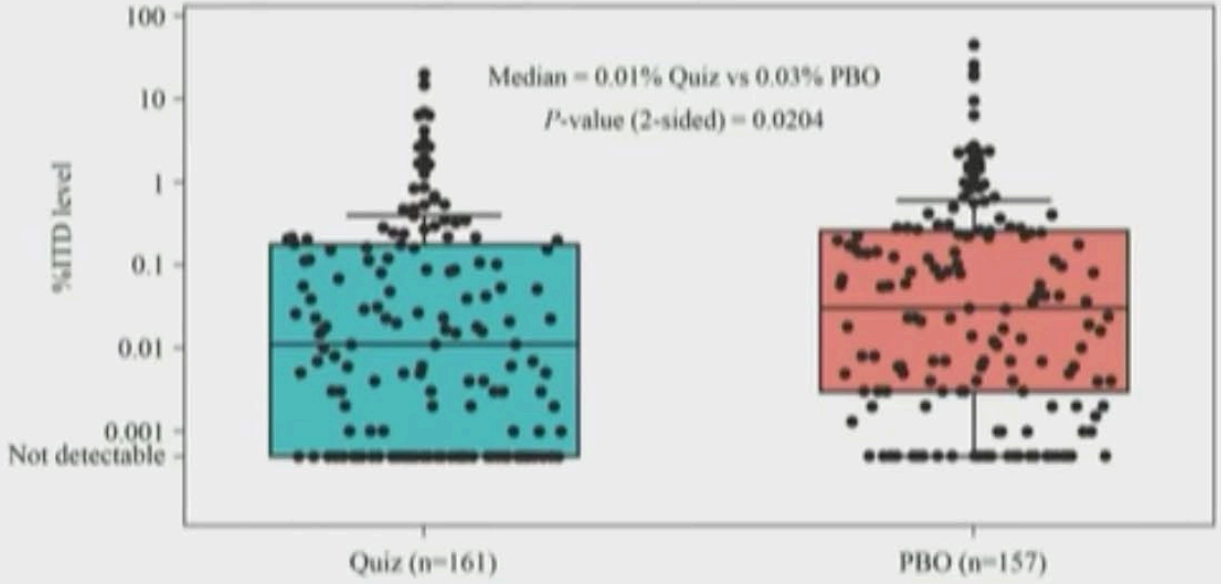
Erba HP, et al. *Lancet* 2023; 401(10388): 1571-1583

QuANTUM-First: *FLT3*-ITD–Specific MRD Clearance Is Associated With Improved OS

Percentage of patients in CRc with *FLT3*-ITD MRD of $<10^{-4}$ was similar across study arms (24.6% quiz vs 21.4% PBO, $P = 0.385$)



Percentage of patients in CRc with undetectable MRD ($< 1x10^{-5}$) was greater with quizartinib (13.8% vs 7.4%, $P = 0.017$).

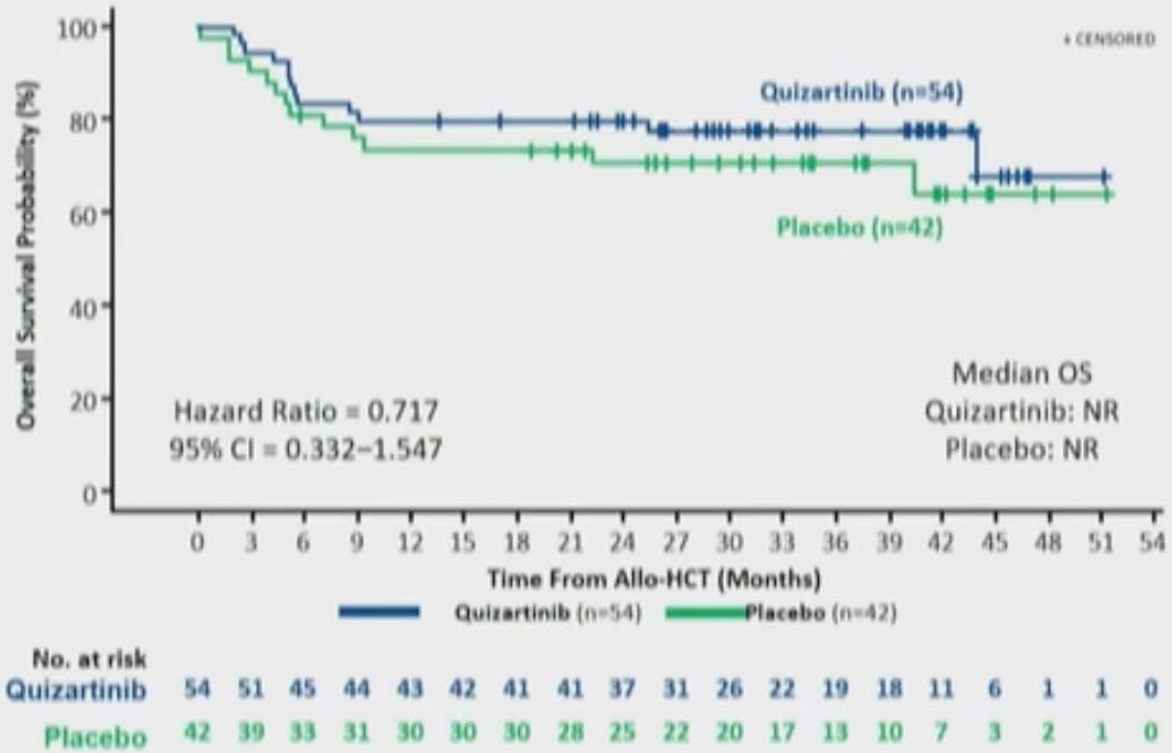


Long-term survival benefits conferred by quizartinib in the QuANTUM-First may in part derive from an early and deep reduction of the *FLT3*-ITD+ leukemia burden

Erba HP, et al. *Lancet* 2023; 401(10388): 1571-1583

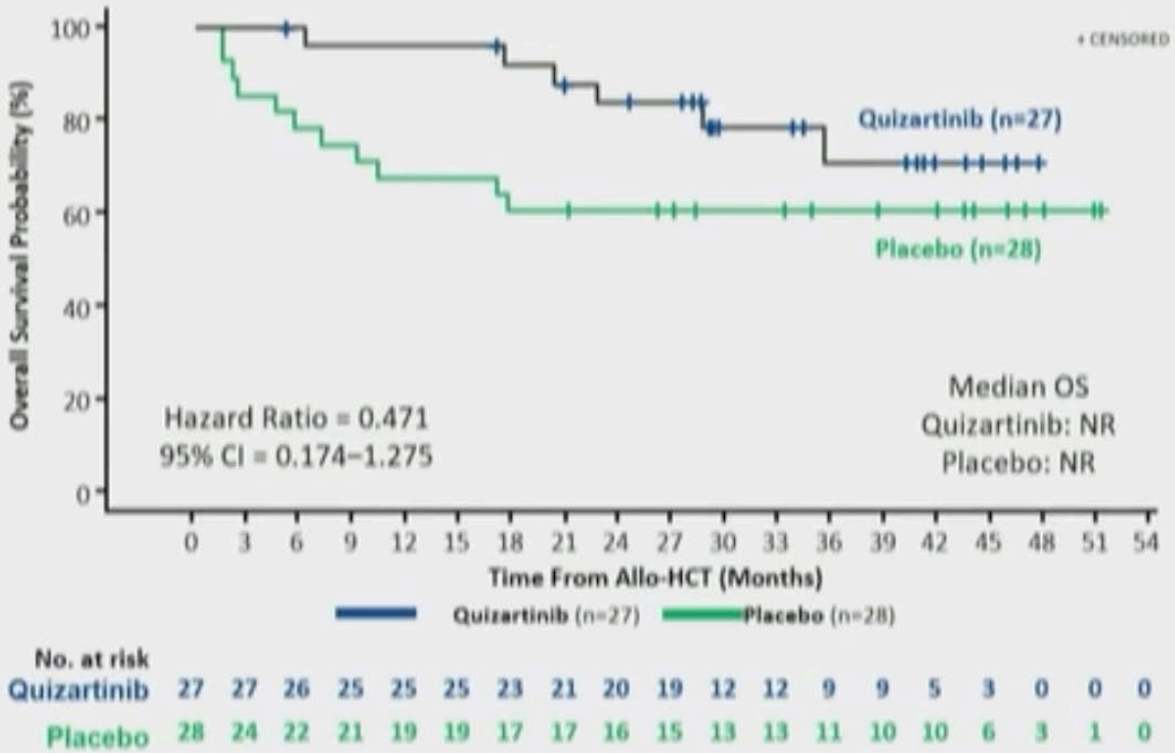
OS in Patients Undergoing Allo-HCT in CR1, From the Time of Allo-HCT, by Latest Pre-HCT MRD Status (Cut-off 10^{-4}), and by Treatment Arm

MRD Negative (n=96)



No. at risk																			
Quizartinib	54	51	45	44	43	42	41	41	37	31	26	22	19	18	11	6	1	1	0
Placebo	42	39	33	31	30	30	30	28	25	22	20	17	13	10	7	3	2	1	0

MRD Positive (n=55)

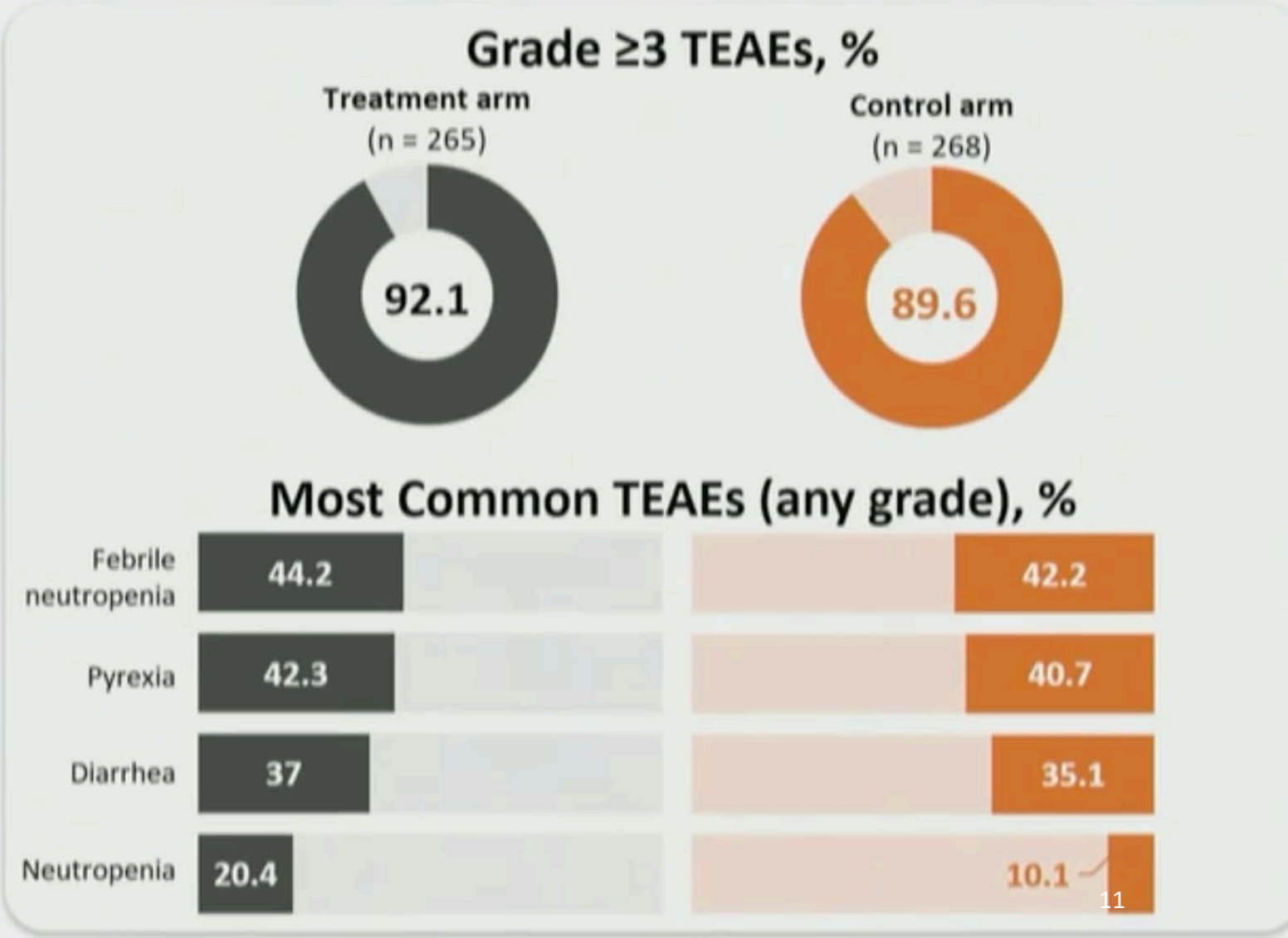


No. at risk																			
Quizartinib	27	27	26	25	25	25	23	21	20	19	12	12	9	9	5	3	0	0	0
Placebo	28	24	22	21	19	19	17	17	16	15	13	13	11	10	10	6	3	1	0

Levis M, et al. ASH 2022

QuANTUM-First: Safety and Tolerability

- Overall, combining quizartinib with intensive chemotherapy and as continuation monotherapy was found to be manageable
- No new safety signals were reported
- 30-day mortality: Q 5.7%, P 3.4%
- 60-day mortality: Q 7.5%, P 4.9%
- Grade 3 QT incr: Q 2.3%, P 0.7%



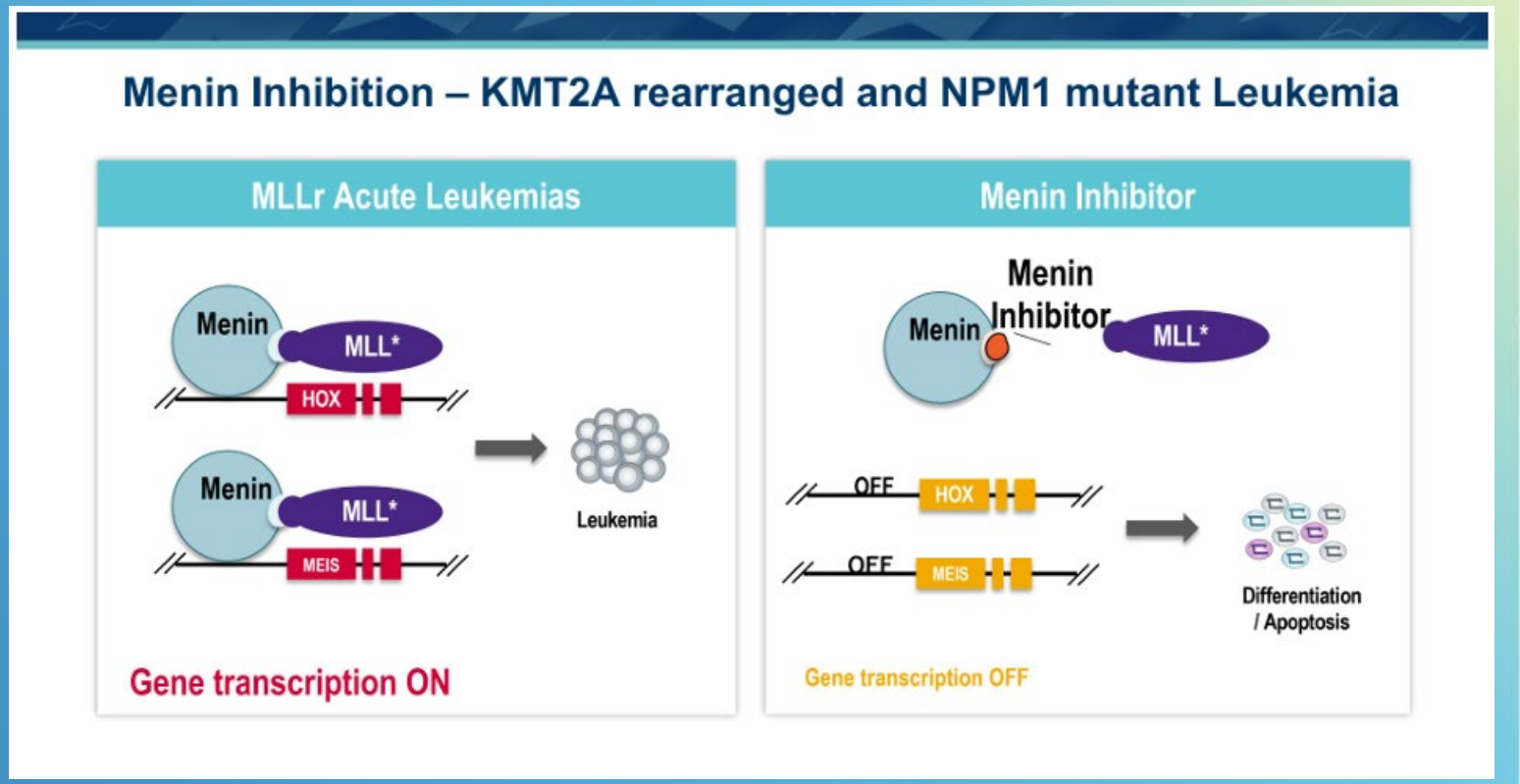
Erba HP, et al. *Lancet 2023*; 401(10388): 1571

Quizartinib

- Second FLT3 inhibitor approved in front line therapy
- Compared to Midostaurin, the use of Quizartinib is limited to FLT3-ITD and to patients with a QTc <450 msec
- Emerging use of FLT3 ITD MRD testing using a PCR test followed by next generation sequencing (Invivoscribe)

Menin inhibitors

- Novel agents, blocking the interaction between menin and mutated KMT2A or NPM1
- Several inhibitors are in clinical development



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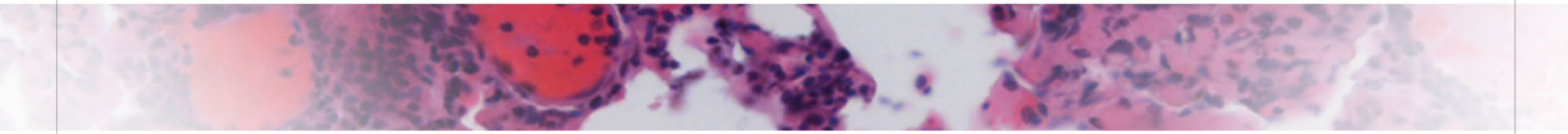
American Society *of* Hematology

Helping hematologists conquer blood diseases worldwide



Revumenib Monotherapy in Patients with Relapsed/Refractory *KMT2Ar* Acute Leukemia: Topline Efficacy and Safety Results from the Pivotal AUGMENT-101 Phase 2 Study

Ibrahim Aldoss, Ghayas C. Issa, Michael Thirman, John DiPersio, Martha Arellano, James S. Blachly, Gabriel N. Mannis, Alexander Perl, David S. Dickens, Christine M. McMahon, Elie Traer, C. Michel Zwaan, Carolyn Grove, Richard Stone, Paul J. Shami, Ioannis Mantzaris, Matthew Greenwood, Neerav Shukla, Branko Cuglievan, Yu Gu, Rebecca G. Bagley, Kate Madigan, Soujanya Sunkaraneni, Huy Van Nguyen, Nicole McNeer, Eytan M. Stein

Aldoss et al, ASH 2023 meeting, abstract 2907

City of Hope

AUGMENT-101 Phase 2 Study Design

Patients aged ≥30 days with R/R acute leukemia

Revumenib RP2D

163 mg (95 mg/m^2 if body weight <40 kg) q12h oral
+ a strong CYP3A4i in 28-day cycles

→ ***KMT2Ar* acute leukemia**

→ ***NPM1m* AML**

Still enrolling, not included in this analysis

- **Primary endpoint**
  - CR+CRh rate*
- **Key secondary efficacy endpoints**
  - CRc
  - ORR

A planned interim analysis of patients with *KMT2Ar* acute leukemia was conducted

*CR+CRh rate >10% in adult evaluable population considered lower efficacy bound

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AML, acute myeloid leukemia; CR, complete remission; CRc, CR composite (CR+CRh+CRp+CRi); CRh, CR with partial hematologic recovery; CRi, CR with incomplete hematologic recovery; CRp, CR with incomplete platelet recovery; CYP3A4i, cytochrome P450 3A4 inhibitor; *KMT2Ar*, histone-lysine N-methyltransferase 2A rearrangements; *NPM1m*, nucleophosmin 1–mutated; ORR, overall response rate; q12h, every 12 hours; RP2D, recommended phase 2 dose; R/R, relapsed/refractory.

Baseline Characteristics

Parameter	Efficacy population (n=57)	Safety population (n=94)[a]
Leukemia type, n (%)		
AML	49 (86)	78 (83)
ALL	7 (12)	14 (15)
MPAL/Other	1 (2)	2 (2)
Co-mutations[b], n (%)		
FLT3	5 (9)	7 (7)
RAS	9 (16)	12 (13)
p53	4 (7)	5 (5)
Primary refractory, n (%)	14 (25)	18 (19)
Number of prior lines of therapy, median (range)	2 (1–11)	2 (1–11)
1, n (%)	17 (30)	25 (27)
2, n (%)	14 (25)	28 (30)
≥3, n (%)	26 (46)	41 (44)
Prior venetoclax, n (%)	41 (72)	61 (65)
Prior HSCT, n (%)	26 (46)	47 (50)

Data cutoff: July 24, 2023. [a]Defined as patients with *KMT2Ar* acute leukemia having received at least 1 dose of revumenib. [b]In patients that had co-mutation status reported.

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ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; *FLT3*, fms-related tyrosine kinase 3; HSCT, hematopoietic stem cell transplant; *KMT2Ar*, histone-lysine N-methyltransferase 2A rearrangements; MPAL, mixed phenotype acute leukemia; *RAS*, rat sarcoma virus.

Response

Parameter	Efficacy population (n=57)
ORR, n (%)	**36 (63)**
CR+CRh rate, n (%)	13 (23)
95% CI	12.7–35.8
P value, 1-sided	0.0036
CRc	25 (44)
95% CI	30.7–57.6
Negative MRD status[a]	
CR+CRh	7/10 (70)
CRc	15/22 (68)

Parameter	Efficacy population (n=57)
Best response, n (%)	
CR	10 (18)
CRh	3 (5)
CRi	1 (1.8)
CRp	11 (19)
MLFS	10 (18)
PR	1 (1.8)
PD	4 (7)
No response	14 (25)
Other[b]	3 (5)

Data cutoff: July 24, 2023. [a]MRD done locally; not all patients had MRD status reported. [b]Includes patients without postbaseline disease assessment.

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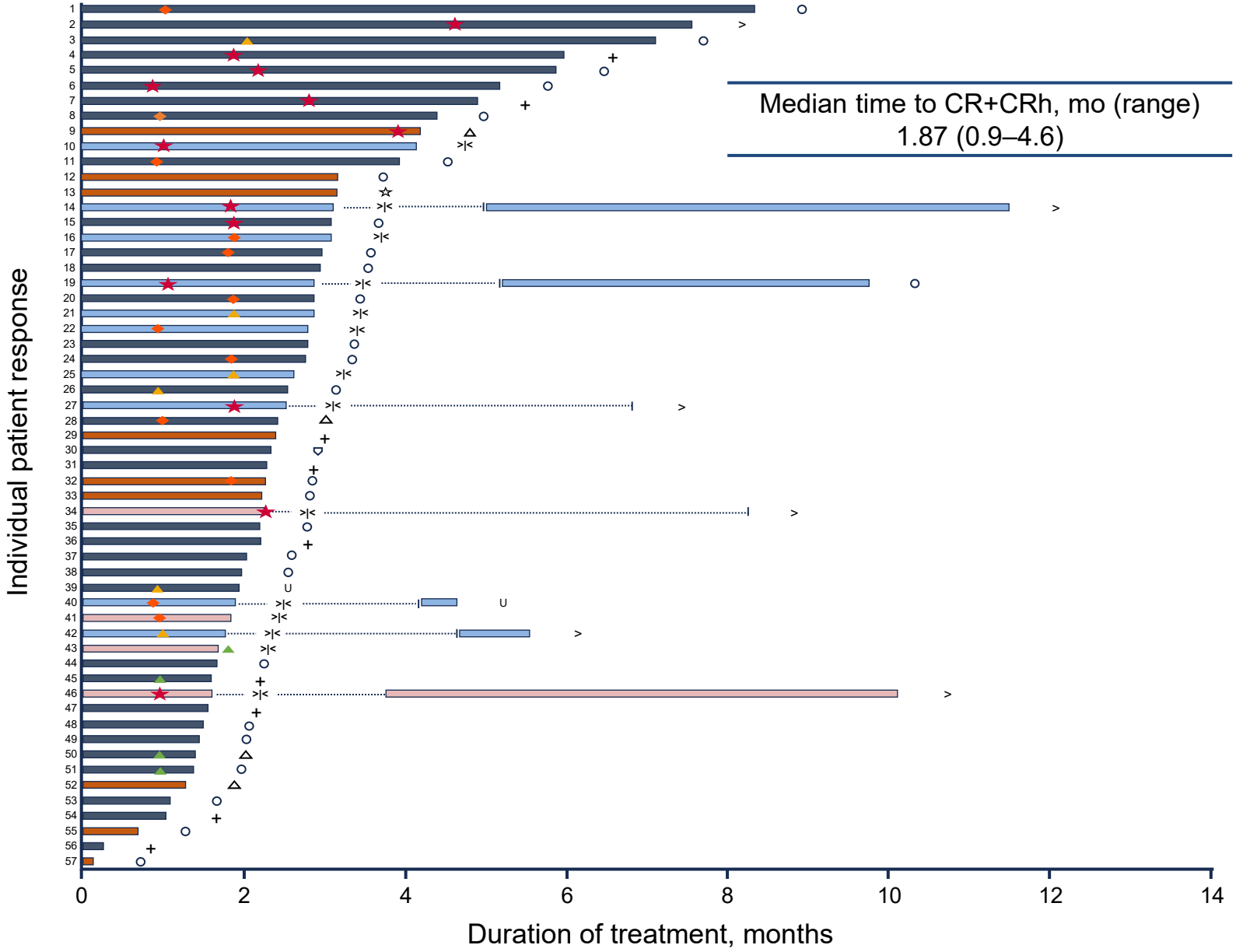
CR, complete remission; CRc, composite CR (CR+CRh+CRp+CRi); CRh, CR with partial hematologic recovery; CRi, CR with incomplete hematologic recovery; CRp, CR with incomplete platelet recovery; MLFS, morphological leukemia-free state; MRD, minimal residual disease; ORR, overall response rate (CRc+MLFS+PR); PD, progressive disease; PR, partial remission.

Duration of Treatment

- Adult
- Adult, underwent HSCT
- Pediatric
- Pediatric, underwent HSCT
- ★ CR/CRh
- ◆ CRp/CRi
- ▲ MLFS
- ○ Progressive disease
- > Ongoing at data cutoff
- \+ Adverse event
- △ Subject withdrew consent for treatment
- >|< HSCT
- ☆ Noncompliance
- ▯ Patient did not achieve at least a PR after 4 cycles
- U Prohibited concomitant medication



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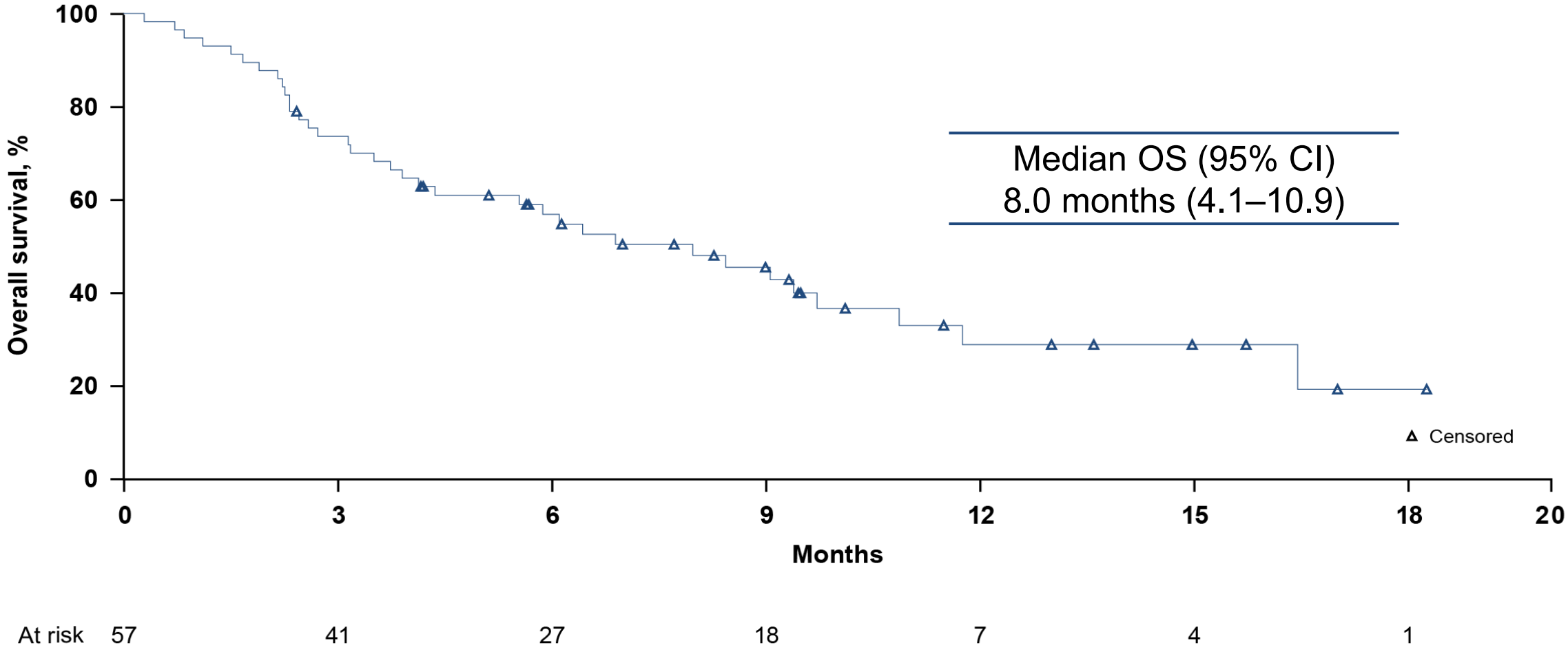
CR, complete remission; CRh, CR with partial hematologic recovery; CRi, CR with incomplete hematologic recovery; CRp, CR with incomplete platelet recovery; HSCT, hematopoietic stem cell transplant; MLFS, morphological leukemia-free state; PR, partial remission.

Overall Survival



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Activity, tolerability and resistance profile of the menin inhibitor ziftomenib in adults with relapsed or refractory *NPM1*-mutated AML

Amir T. Fathi[1], Eunice S. Wang[2], Ghayas C. Issa[3], Jessica K. Altman[4], Pau Montesinos[5], Stephane DeBotton[6], Roland Walter[7], Kristen Pettit[8], Stephen Strickland[9], Mrinal Patnaik[10], Marina Kremyanskaya[11], Maria R. Baer[12], James Foran[13], Gary Schiller[14], Lionel Ades[15], Mael Heiblig[16], Celine Berthon[17], Jolanta Grembecka[8], Tomasz Cierpicki[8], Bradley Clegg[8], Pierre Peterlin[18], Eduardo Rodriguez Arboli[19], Olga Salamero Garcia[20], Cristina Papayannidis[21], Kun Nie[22], Julie Mackey[22], Marilyn Tabachri[22], Daniel Corum[22], Mollie Leoni[22], Stephen Dale[22], Harry P. Erba[23]

[1]Massachusetts General Hospital, Boston, MA; [2]Roswell Park Comprehensive Cancer Center, Buffalo, NY; [3]MD Anderson Cancer Center, Houston, TX; [4]Northwestern University Robert H. Lurie Comprehensive Cancer Center, Chicago IL; [5]Hospital Universitari i Politècnic La Fe, Valencia, Spain; [6]Institut Gustave Roussy Service d'Hématologie Clinique, Paris, France; [7]Fred Hutchinson Cancer Research Center, Seattle, WA; [8]University of Michigan, Ann Arbor, MI; [9]Sarah Cannon Research Institute, Nashville, TN; [10]Mayo Clinic-Minnesota, Rochester, MN; [11]Mount Sinai PRIME, New York, NY; [12]University of Maryland Marlene and Stewart Greenebaum Cancer Center, Baltimore, MD; [13]Mayo Clinic Florida, Jacksonville, FL; [14]UCLA Medical Center, Los Angeles, CA; [15]Hospital Saint-Louis, Paris, France; [16]Centre Hospitalier Lyon Sud, Lyon, France; [17]Centre Hospitalo-Universitaire Lille, Lille, France; [18]CHU de Nantes-Hôtel-Dieu, Nantes, France; [19]Hospitales Universitarios Virgen del Rocio, Sevilla, Spain; [20]Hospital Universitari Vall d'Hebron-Institut de Recerca (VHIR), Barcelona, Spain; [21]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy; [22]Kura Oncology, Inc., San Diego, CA; [23]Duke Cancer Institute, Durham, NC

Fathi et al, EHA 2023 meeting, abstract LB2713

KOMET-001 Phase 1/2 Study of Ziftomenib in R/R AML

Phase 1a Dose Escalation	Phase 1b Validation Cohorts	Phase 1b Expansion	Phase 2 Registration-Enabling
Completed	*Completed*	*Completed*	*Ongoing*
50 mg QD — 100 mg QD — 1000 mg QD	Cohort 1: 200 mg QD Cohort 2: 600 mg QD	Expansion of 600 mg QD	600 mg QD
NPM1-m, KMT2A-r, Other	*NPM1-m or KMT2A-r*	*NPM1-m*	*NPM1-m*
OBJECTIVES			

• Safety and tolerability
• Pharmacokinetics
• Early evidence of clinical activity
	• Safety and tolerability
	• Pharmacokinetics
	• Clinical activity
		Continue enrollment of Phase 1b validation cohort(s) consistent with FDA's Project Optimus
		• Safety and tolerability
		• Pharmacokinetics
		• Clinical activity
			• Primary endpoint:
			  • CR/CRh
			• Secondary endpoints:
			  • Duration of CR/CRh
			  • Transfusion independence
			  • CR/CRh MRD negativity
			  • Adverse events

Fathi et al, EHA 2023 meeting, abstract LB2713

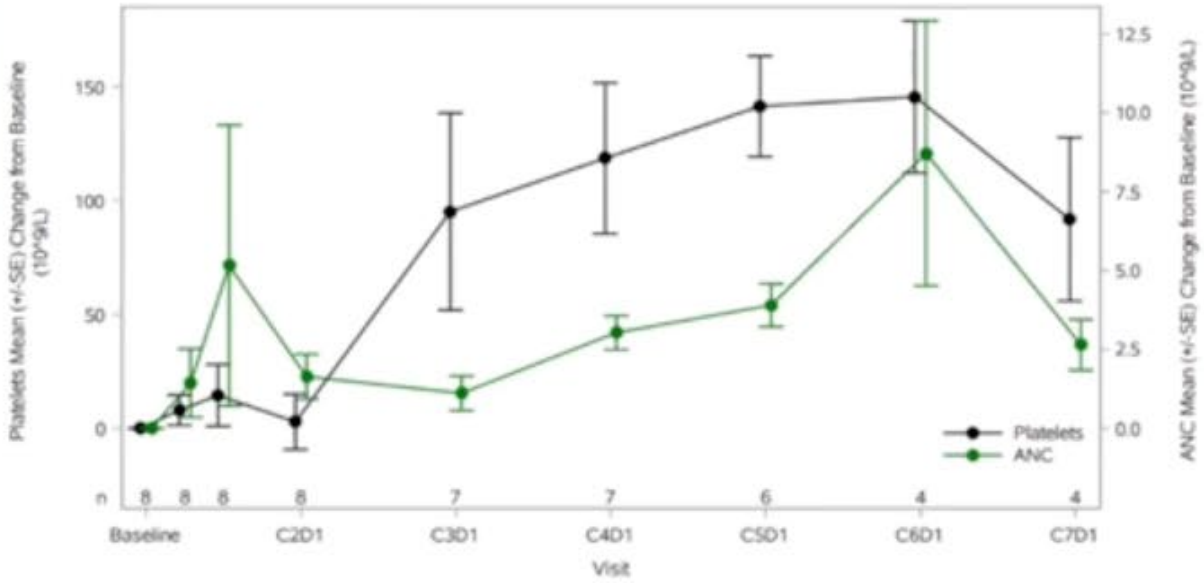
CR, complete remission; CRh, complete remission with partial hematological recovery; FDA, United States Food and Drug Administration; MRD, measurable residual disease; R/R, relapsed/refractory; RP2D, recommended phase 2 dose.

Ziftomenib Demonstrates Encouraging Clinical Activity

Best Overall Response	n (%)
Complete remission rate (CR)	**7 (35)**
CRc rate (CR+CRh+CRi)	8 (40)
Overall response rate (CR+CRh+CRi+MLFS)	9 (45)
CR	7 (35)
CRh	0
CRi	1 (5)
MLFS	1 (5)

33% CR co-*FLT3*m (N=6)
50% CR co-*IDH*m (N=8)

Mean Change in Platelets and ANC for CRc up to C7D1



- Co-mutations in *FLT3* and *IDH1/2* did not affect chances of response to single agent ziftomenib
- 1 patient achieved CRi, proceeded to HSCT, and achieved and remains in CR
- Median time to first response: 51 days

HSCT, hematopoietic stem cell transplantation; MLFS, morphological leukemia-free state

12-April-2023 Data Cut

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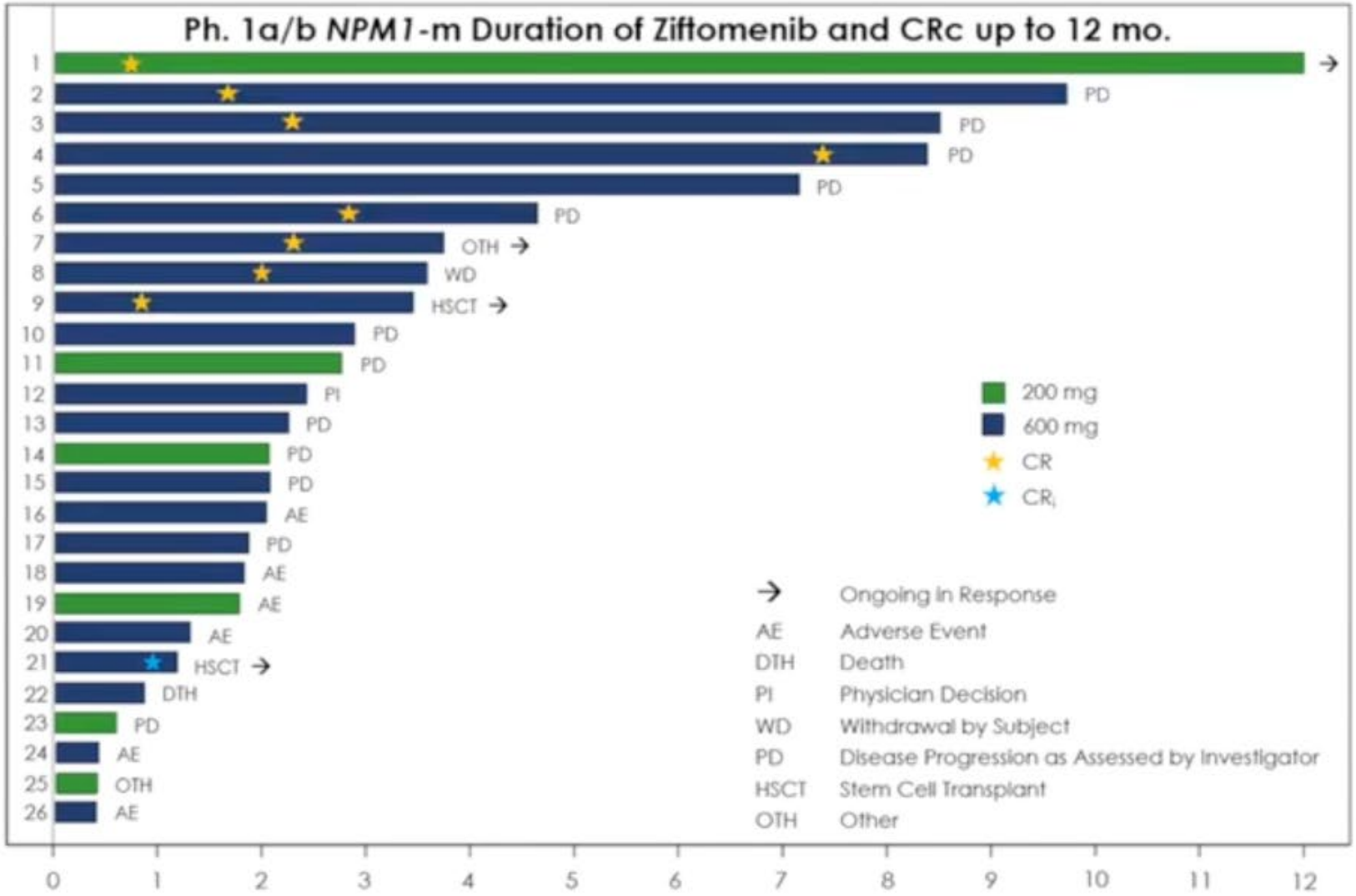
Ziftomenib Monotherapy Drives Durable Responses

- Median DoR **8.2 months** (95% CI: 1.0 to Not Evaluable) with a median follow up time of 8.8 months

- Patient 1 remained on ziftomenib in CR (MRD-) into Cycle 36
- Patients 9 and 21 proceeded to HSCT
  - Patient 9 remains in complete response on ziftomenib for post-HSCT maintenance
  - Patient 21 remains in complete response



12-April-2023 Data Cut

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Menin inhibitors

- Novel agents showing activity as single agents in KMT2A- and NPM1 mutated AML
- Several agents being tested in clinical trials (Syndax, Kura, Sumimoto, Janssen)
- The first approval of a menin inhibitor is expected later this year
- Combination therapies are being developed

MDS

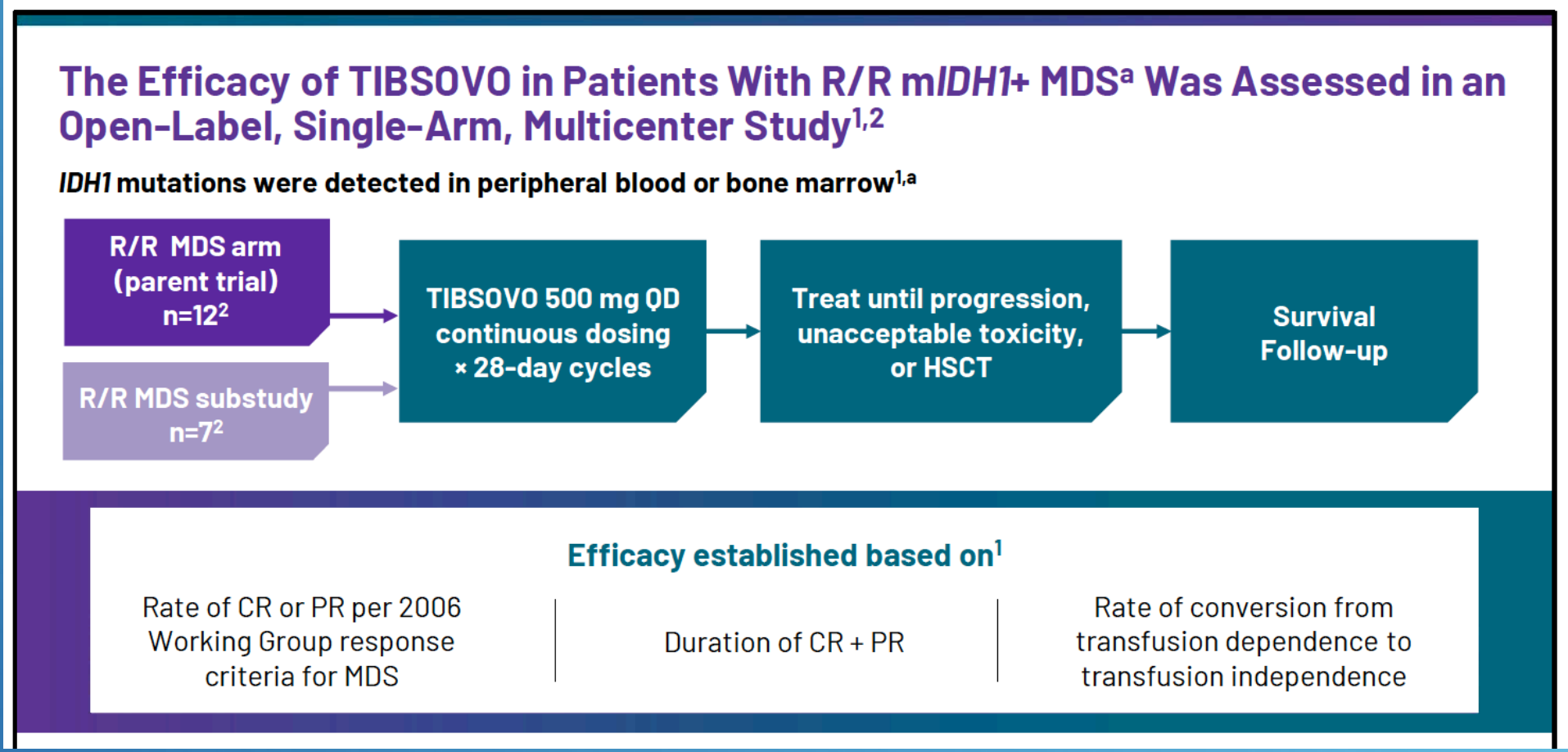
HR MDS

- Disappointing year for HR MDS, with negative anti-CD47 and anti-TIM3 antibody (Sabatolimab) trials
- The results of the Verona trial (Vidaza vs Vidaza/Ven) are still pending
- Ivosidenib approval

LR MDS

- Luspaterecept
- Imetelstat

Ivosidenib in MDS: study design



Servier, unpublished data

Ivosidenib in MDS: patient characteristics

Demographics and Disease Characteristics	TIBSOVO (500 mg Daily) (N=18)
Age, years, median (min, max)[1]	74 (61, 82)
Sex, %[1]	
Male	78
Race, %[1]	
White	78
Black or African American	6
Not reported	17
IPSS-R score at screening, %[2]	
≤1.5 (Very Low)	0
>1.5 to 3 (Low)	22
>3 to 4.5 (Intermediate)	39
>4.5 to 6 (High)	17
>6 (Very High)	17
Unknown	6
Baseline bone marrow blasts, %, median (min, max)[2]	6 (0, 19)

Disease Characteristics	TIBSOVO (500 mg Daily) (N=18)
ECOG PS, %[1]	
0	28
1	56
2	17
Cytogenetic risk status, %[1]	
Good	22
Intermediate	44
Poor	28
Missing	6
Prior therapies, %[1]	
Intensive chemotherapy	17
Non-intensive chemotherapy	83
1 line of HMA-based therapy	78
2 lines of HMA-based therapy	6

Servier, unpublished data

Ivosidenib in MDS: study results

Primary endpoint: CR+PR[1]
All observed responses were CRs with no PRs

	TIBSOVO (500 mg Daily) (N=18)
CR, %[a]	**38.9**
95% CI	17.3-64.3

Secondary endpoint: DOCR+PR[1]
All observed responses were CRs with no PRs

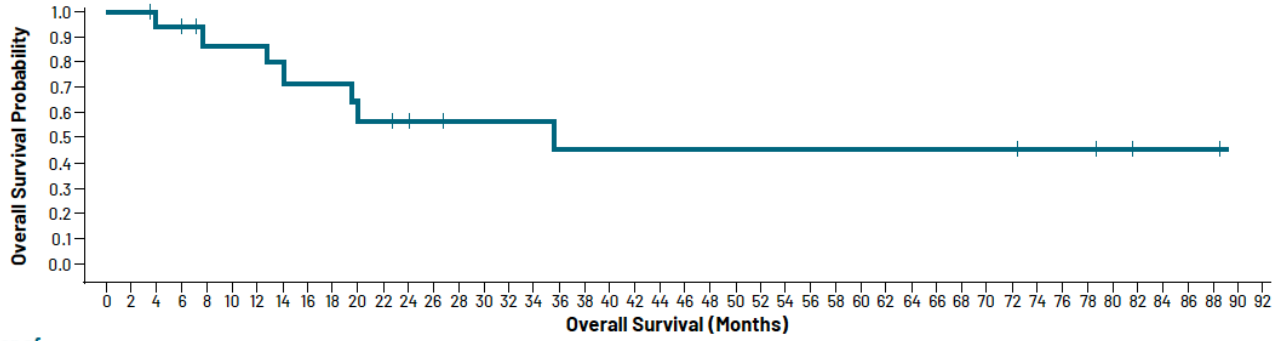
	TIBSOVO (500 mg Daily) (N=18)
Median DOCR,[b] months (range)	NE (1.9, 80.8+)

- The **median time to CR** was **1.9 months** (range, 1.0-5.6)[1]

	TIBSOVO (500 mg Daily) (N=18)
mOS, months (range)	**35.7 (3.7-88.7)**
95% CI	13.1-NE

- **Median OS follow-up** was **27.1 months**
- **87% survival rate at 12 months** per Kaplan-Meier estimation
- **Because there was no control arm in this study, OS results should be interpreted cautiously**

mOS, Kaplan Meier Estimate



In the absence of a control arm, the exact treatment effect is not known.

Servier, unpublished data

Luspatercept versus epoetin alfa for treatment of anemia in patients with erythropoiesis-stimulating agent-naive lower-risk myelodysplastic syndromes requiring red blood cell transfusions: data from the phase 3 COMMANDS study

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*At the time of the study.

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The COMMANDS study design

The COMMANDS study (NCT03682536) is a phase 3, global, open-label, randomized trial comparing the efficacy and safety of luspatercept versus epoetin alfa for the treatment of anemia due to IPSS-R LR-MDS in ESA-naive patients who require RBC transfusions

Key eligibility criteria

- ≥ 18 years of age
- IPSS-R Very low-, Low, or Intermediate-risk MDS (with or without RS) by WHO 2016, with < 5% blasts in bone marrow[a]
- Required RBC transfusions (2-6 pRBC units/8 weeks for a minimum of 8 weeks immediately prior to randomization)
- Endogenous sEPO < 500 U/L
- ESA-naive

Patients stratified by:

- Baseline sEPO level
- Baseline RBC transfusion burden
- RS status

Randomized 1:1

Luspatercept (N = 178)
1.0 mg/kg s.c. Q3W
titration up to 1.75 mg/kg

Epoetin alfa (N = 178)[b]
450 IU/kg s.c. QW
titration up to 1050 IU/kg

Response assessment at day 169 and every 24 weeks thereafter

End treatment
Due to lack of clinical benefit[c] or disease progression per IWG criteria

Post-treatment safety follow-up

- Monitoring for other malignancies, HR-MDS or AML progression, subsequent therapies, survival
- For 5 years from first dose or 3 years from last dose, whichever is later

[a]MDS with del(5q) were excluded; [b]2 patients randomized to the epoetin alfa arm withdrew consent prior to receiving their first dose; [c]Clinical benefit defined as transfusion reduction of ≥ 2 pRBC units/8 weeks versus baseline. AML, acute myeloid leukemia; del(5q), deletion 5q; HR-MDS, higher-risk MDS; IPSS-R, Revised International Prognostic Scoring System; IWG, International Working Group; MDS, myelodysplastic syndromes; pRBC, packed RBC; Q3W, every 3 weeks; QW, once weekly; RBC, red blood cell; RS, ring sideroblasts; SC, subcutaneously; sEPO, serum erythropoietin; WHO, World Health Organization.

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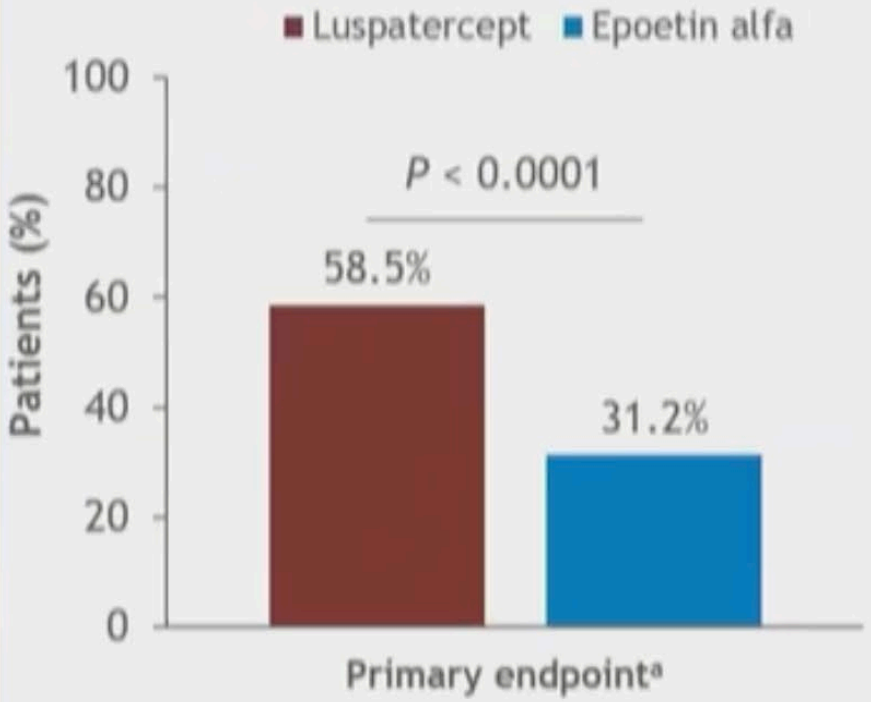
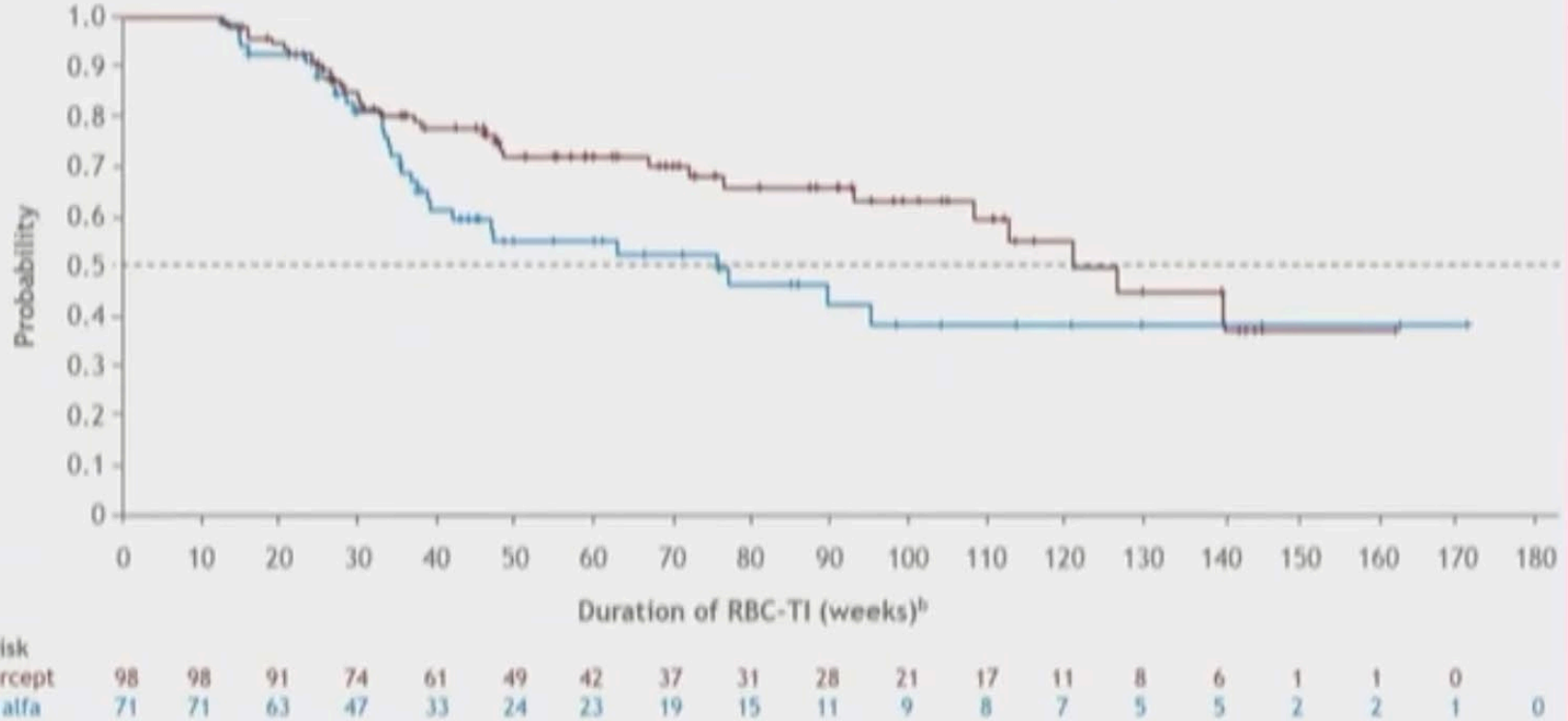
Key responses from the COMMANDS: luspatercept superior to epoetin alfa

	Duration, median (95% CI), weeks	HR (95% CI)
Luspatercept	126.6 (108.3-NE)	0.456 (0.260-0.798)
Epoetin alfa	77.0 (39.0-NE)	





No. at risk																			
Luspatercept	98	98	91	74	61	49	42	37	31	28	21	17	11	8	6	1	1	0	
Epoetin alfa	71	71	63	47	33	24	23	19	15	11	9	8	7	5	5	2	2	1	0

From Platzbecker U, et al. *Lancet* 2023;402:373-385. Used with permission.
This prespecified interim analysis included 301 patients who had either completed 24 weeks of treatment or discontinued prior to completing 24 weeks of treatment; [a]During weeks 1-24; [b]In ITT responders during week 1-EOT.

Imetelstat: IMerge Subgroup Analysis: Study Design

- International, double-blind, randomized phase III trial

Stratified by transfusion burden (4-6 vs >6 U) and IPSS-R category (low vs intermediate-1)

Patients with low-risk or intermediate-1–risk MDS (IPSS-R); R/R* to ESA or EPO >500 mU/mL (ESA ineligible); RBC transfusion dependent (≥4 U/8 wk over 16 wk prestudy); non-del(5q); no prior lenalidomide or HMAs
(N = 178)

2:1

Imetelstat
7.5 mg/kg IV Q4W
(n = 118)

Placebo
(n = 60)

Supportive Care
RBC and platelet transfusions, myeloid growth factors (eg, G-CSF), and iron chelation therapy as needed at discretion of investigator

Primary endpoint: 8-wk RBC-TI

Secondary endpoints: 24-wk RBC-TI, TI duration, HI-E, safety

This analysis

Subgroup analysis: rates of RBC-TI vs placebo across IPSS, IPSS-R, IPSS R cytogenetic, and IPSS-M risk categories

*Received ≥8 wk of ESA treatment (epoetin alfa ≥40,000 U, epoetin beta ≥30,000 U, darbepoetin alfa 150 µg, or equivalent per wk) without Hgb rise ≥1.5 g/dL or decrease in RBC transfusion requirement ≥4 U/8 wk, transfusion dependence, or reduction of Hgb by ≥1.5 g/dL after hematopoietic improvement from ≥8 wk of ESA treatment.

NCT02598661. Platzbecker. Lancet. 2023;[Epub]. Komrokji. ASH 2023. Abstr 194.

IMerge Subgroup Analysis: Rates of Durable Transfusion Independence

RBC-TI Response, %	Rates of Durable RBC-TI Over Time		
	Imetelstat	Placebo	*P* Value
≥ 8-Wk RBC-TI*	40	15	<.0008
≥ 16-Wk RBC-TI	31	7	<.0002
≥ 24-Wk RBC-TI	28	3	<.0001
≥ 1-Yr RBC-TI	18	2	<.0023

*Primary endpoint.

- Single continuous RBC-TI period was achieved by most 8-wk responders to imetelstat (83%)

Platzbecker. Lancet. 2023;[Epub]. Komrokji. ASH 2023. Abstr 194.

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IMerge Subgroup Analysis: RBC-TI by IPPS-M Risk Category

RBC-TI Response, n/N (%)	IPSS-M Very Low/Low/Moderate Low			IPSS-M Moderate High/High/Very High		
	Imetelstat	Placebo	*P* Value	Imetelstat	Placebo	*P* Value
≥8 wk	37/91 (40.7)	7/43 (16.3)	.007	4/12 (33.3)	1/9 (11.1)	.257
≥24 wk	26/91 (28.6)	1/43 (2.3)	<.001	1/12 (8.3)	0/9 (0)	.414
≥1 yr	11/91 (12.1)	0/43 (0)	.020	1/12 (8.3)	0/9 (0)	.414

- Imetelstat significantly increased proportion of patients with RBC-TI vs placebo, irrespective of IPSS-M risk category
- ≥8-wk RBC-TI observed in 4 of 12 (33.3%) patients with MDS recategorized as higher risk by IPSS-M who were treated with imetelstat

Komrokji. ASH 2023. Abstr 194.

Slide credit: clinicaloptions.com

MDS

- Two new agents approved in 2023: Luspatercept and Ivosidenib
- Imetelstat expected to be approved later this year
- The use of ESAs in low risk MDS will become more limited over time
-

Thank you

Questions?