Promising Clinical Trials and the Future Clinical Landscape of MDS

MDS Foundation Patient and Family Forum Agenda

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- Consultant and/or advisory board member for Karyopharm, MEI, OncoVerity, Rigel, Abbvie, Syndax, Treadwell, Bivictrix, Qihan, Bristol Myers Squibb, Sanofi, Beigene, Ryvu, Refined Science

MDS Clinical Trials Landscape

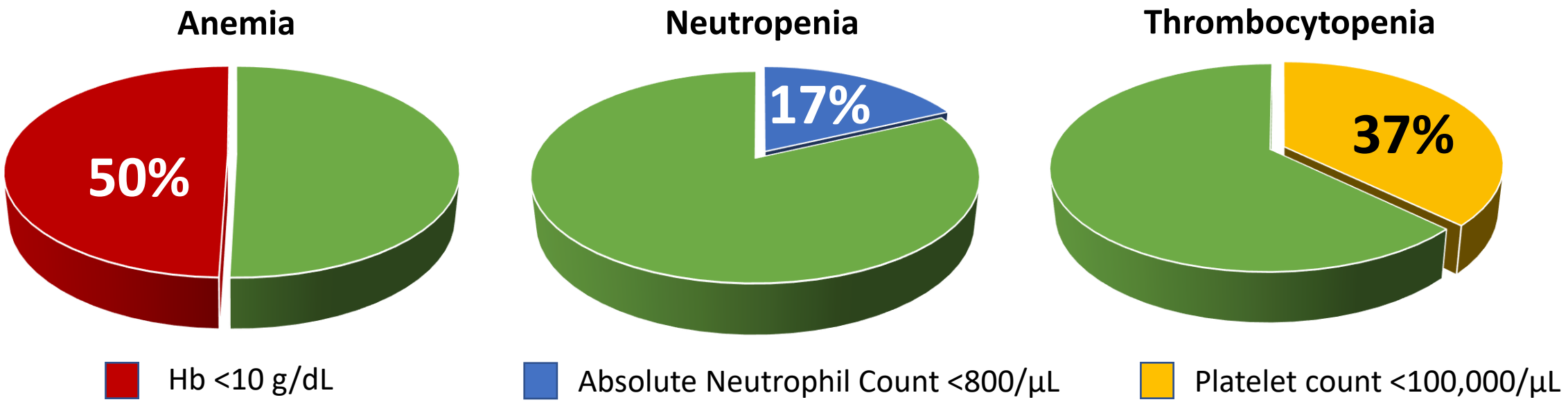
Clinical trials divided into four buckets

- Lower risk
  - Newly diagnosed
  - Previously treated
- Higher risk
  - Newly Diagnosed
  - Previously Treated

Anemia is the Hallmark of Lower Risk MDS

- Lower-risk MDS is characterized foremost by anemia[1]
- 50% of MDS patients will need RBC transfusions during the course of their disease[2]

Frequency of cytopenias in patients with Lower-risk MDS:[3,4]



1. Fenaux P, et al. *Br J Haematol*. 2019;189(6):1016-1027; 2. Germing U, et al. *Hemasphere*. 2019;3(6):e314;
3. Lanino L, et al. *Am J Hematol*. 2023; 10.1002/ajh.26960; 4. Santini V. *Hemato*. 2022;3(1):153-162

New Therapies in Lower Risk MDS

- Luspatercept
- Imetelstat

Luspatercept: Phase 3 Study

Patient Population

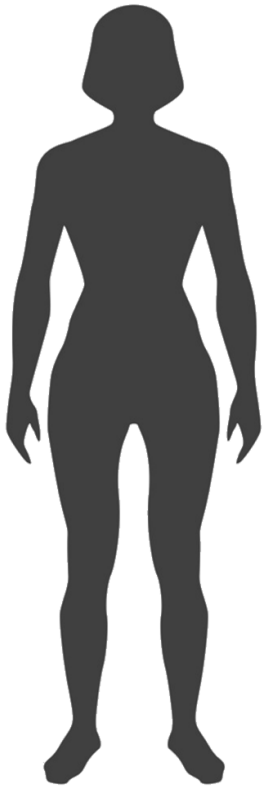
- ✓ *Very-low-risk, low-risk, or intermediate-risk MDS (IPSS-R) with ring sideroblasts*
- ✓ *Receiving regular RBC transfusions*

Most Common Grade 3–4 AEs with Luspatercept

- *Fatigue (5%)*
- *Asthenia (3%)*
- *Back pain (2%)*
- *Nausea (1%), headache (1%), arthralgia (1%), dyspnea (1%), bronchitis (1%), UTI (1%)*

FDA Approval: 04/06/2020

Luspatercept N = 153		Placebo N = 76
38%	Transfusion Independence ≥ 8 Weeks (Weeks 1–24)	13%
28%	Transfusion Independence ≥ 12 Weeks (Weeks 1–24)	8%
33%	Transfusion Independence ≥ 12 Weeks (Weeks 1–48)	12%



***P* < .001 For All Comparisons**

IPSS-R = Revised International Prognostic Scoring System; RBC = Red Blood Cell; UTI = Urinary Tra

Fenaux P, et al. *New Engl J Med*. 2020;82:140-151.

IMerge Phase 3 Trial Design (MDS3001; NCT02598661)

Phase 3
Double blind, randomized
118 Clinical sites in 17 countries

Patient Population (ITT N = 178)

- IPSS low- or intermediate 1- risk MDS
- relapsed/refractory[a] to ESA or EPO >500 mU/mL (ESA ineligible)
- **Transfusion dependent: ≥4 units RBCs/8 weeks over 16-week pre-study**
- Non-deletion 5q
- No prior treatment with lenalidomide or HMAs

R 2:1

Imetelstat
7.5 mg/kg IV/4 weeks
(N = 118)

Stratification:

- Transfusion burden (4-6 vs >6 units)
- IPSS risk category (low vs Intermediate 1)

Supportive care, including RBC and platelet transfusions, myeloid growth factors (e.g., G-CSF), and iron chelation therapy administered as needed on study per investigator discretion

Placebo
(N = 60)

Safety population (treated) N = 177

Imetelstat N = 118

Placebo N = 59

Primary endpoint:

- 8-week RBC-TI[b]

Key secondary endpoints:

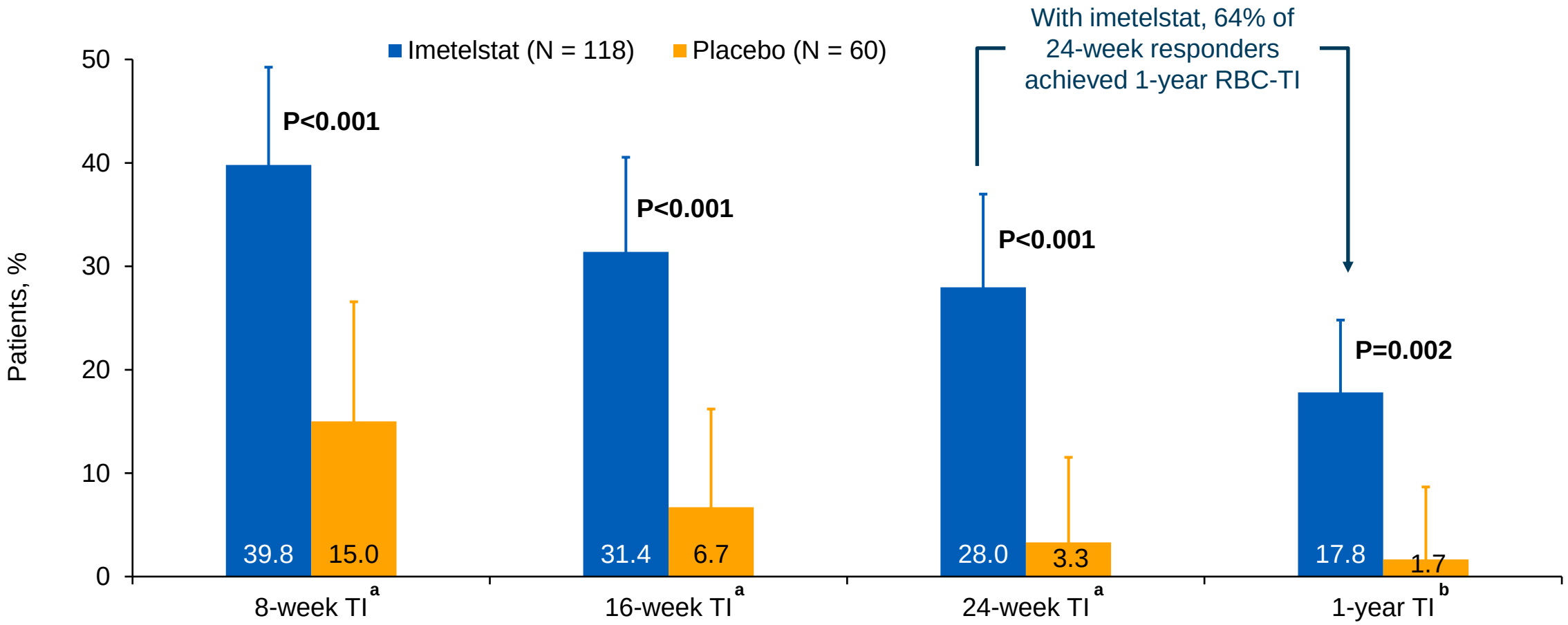
- 24-week RBC-TI[b]
- Duration of TI
- Hematologic improvement-erythroid
- Safety

Key exploratory endpoints:

- VAF changes
- Cytogenetic response
- PRO: fatigue measured by FACIT-Fatigue

[a]Received ≥8 weeks of ESA treatment (epoetin alfa ≥40,000 units, epoetin beta ≥30,000 units or darbepoetin alfa 150 µg or equivalent per week) without Hgb rise ≥1.5 g/dL or decreased RBC transfusion requirement ≥4 units/8 weeks or transfusion dependence or reduction in Hgb by ≥1.5 g/dL after hematologic improvement from ≥8 weeks of ESA treatment. [b]Proportion of patients without any RBC transfusion for ≥8 consecutive weeks since entry to the trial (8-week TI); proportion of patients without any RBC transfusion for ≥24 consecutive weeks since entry to the trial (24-week TI)
EPO, erythropoietin; ESA, erythropoiesis stimulating agent; G-CSF, granulocyte colony-stimulating factor; Hgb, hemoglobin; HMA, hypomethylating agent; IPSS, International Prognostic Scoring System; ITT, intent-to-treat; IV, intravenous; MDS, myelodysplastic syndromes; R, randomization; RBC, red blood cell; TI, transfusion independence, VAF, variant allele frequency.

Higher Rates of Longer-Term Duration of RBC TI Observed With Imetelstat vs Placebo, Including 1-year RBC TI With Additional 3 Month Follow-up



[a]Data cutoff: October 13, 2022. [b]Data cutoff: January 13, 2023.
P-values were determined by the Cochran-Mantel-Haenszel test, with stratification for prior RBC transfusion burden (≥4 to ≤6 vs. >6 RBC units/8-weeks during a 16-week period prior to randomization) and baseline International Prognostic Scoring System risk category (low vs. intermediate-1) applied to randomization.
RBC, red blood cell; TI, transfusion independence.

Recent Disappointments in the Newly Diagnosed, Higher Risk Category

- Pevonidostat (NEDD8 inhibitor)
  - Failed to meet primary endpoint of event free survival

- APR-246 (Targeted therapy for TP53 mutations)
  - Failed to meet primary endpoint of complete response rate

Two more recent large randomized studies reported this spring…

Sabatolimab

- Targets TIM-3, immunotherapy/stem cell target
- Randomized phase 2 study showed trend toward improved progression-free survival
- Improved duration of complete remission (18 vs 9.2 months)
- Definitive phase 3 study with overall survival as primary endpoint conducted

STIMULUS-MDS2 design

Randomized, double-blind, placebo-controlled, multi-centered Phase III study

530 Patients

- Aged ≥18 years with morphologically confirmed intermediate-, high- or very high-risk MDS[a], or CMML-2[b]
- Not eligible for HSCT or intensive chemotherapy

1:1 Randomization

Stratified by IPSS-R[c] and CMML

Sabatolimab IV Q4W
(800 mg on day 8 of each cycle)
+
Azacitidine SC or IV
(75 mg/m^2/day on days 1-7 or 1-5 and 8-9 of each cycle)
N=265

Placebo IV Q4W
(800 mg on day 8 of each cycle)
+
Azacitidine SC or IV
(75 mg/m^2/day on days 1-7 or 1-5 and 8-9 of each cycle)
N=265

28-day cycles until disease progression

Target enrolment was 500 but patients who were in screening when the target was reached were randomized if they met the inclusion/exclusion criteria

36 countries

151 study centers

Primary Endpoint:
Overall Survival

Key secondary endpoints:[d]
- Time to definitive deterioration of fatigue
- RBC transfusion-free intervals
- Improvement of fatigue
- Improvement of physical functioning
- Improvement of emotional functioning

Secondary endpoints included:
PFS, LFS and response rates

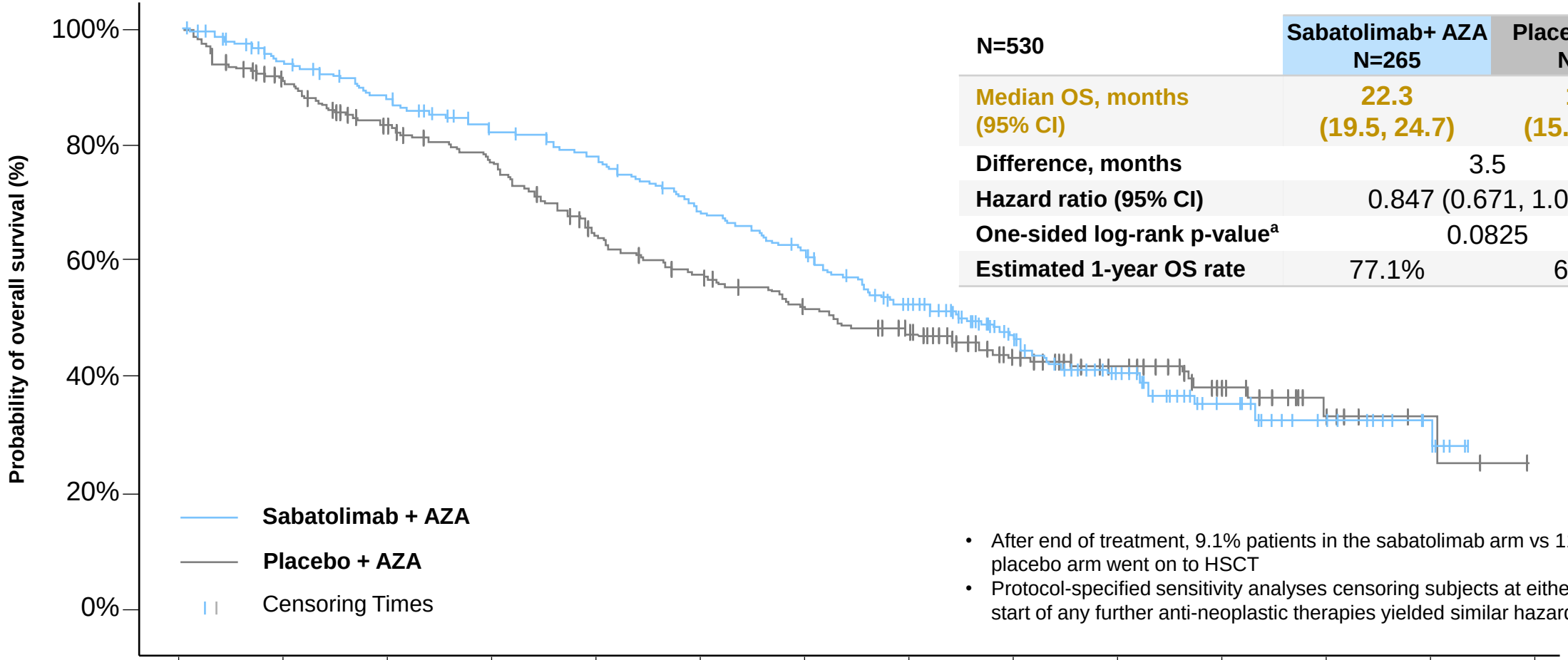
Randomization: Jun 15, 2020 - Jan 17, 2022
Primary analysis data cut-off: Sept 15, 2023
Median duration of follow-up (randomization to cut-off): 27.8 months

NCT04266301. CMML-2, chronic myelomonocytic leukemia 2; CR, complete response; HSCT, hematopoietic stem cell transplantation; IPSS-R, Revised International Prognostic Scoring System; IV, intravenous; LFS, leukemia-free survival; MDS, myelodysplastic syndromes; OS, overall survival; PFS, progression-free survival; Q4W, every 4 weeks; RBC, red blood cell; SC, subcutaneous; WBC, white blood cell.
[a]Defined according to the IPSS-R criteria: very high risk (>6 points), high risk (>4.5–≤6 points), or intermediate risk (>3–≤4.5 points). [b]WBC <13 x 10^9/L at time of initial diagnosis. [c]IPSS-R prognostic risk score (intermediate, high, very high). [d]If the primary endpoint was significant at the primary analysis, the first two key secondary endpoints were tested and if at least one of the first two key secondary endpoints was statistically [illegible] endpoints were tested in a sequence.

Zeidan et al, EHA 2024

Oral presentation at: EHA 2024 Hybrid Congress; June 13-16, 2024; Madrid, Spain, and online.

Overall survival (primary endpoint) (N=530)



N=530	Sabatolimab+ AZA N=265	Placebo + AZA N=265
Median OS, months (95% CI)	22.3 (19.5, 24.7)	18.8 (15.4, 23.7)
Difference, months	3.5	
Hazard ratio (95% CI)	0.847 (0.671, 1.070)	
One-sided log-rank p-value[a]	0.0825	
Estimated 1-year OS rate	77.1%	63.9%

- After end of treatment, 9.1% patients in the sabatolimab arm vs 11.3% in the placebo arm went on to HSCT
- Protocol-specified sensitivity analyses censoring subjects at either HSCT or start of any further anti-neoplastic therapies yielded similar hazard ratios

No. of participants still at risk	0	3	6	9	12	15	18	21	24	27	30	33	36	39	Time (months)
Sabatolimab + AZA	265	241	221	198	184	161	142	108	73	47	25	12	6	0	
Placebo + AZA	265	233	205	186	151	132	117	92	62	46	26	8	4	0	

AZA, azacitidine; CI, confidence interval; CMML-2, chronic myelomonocytic leukemia 2; HSCT, hematopoietic stem cell transplantation; IPSS-R, Revised International Prognostic Scoring System; MDS, myelodysplastic syndromes; OS, overall survival. Full analysis set. Cox-model are stratified by randomization stratification factor (Intermediate-risk MDS, High-risk MDS, Very high-risk MDS, CMML-2) as per interactive :ratified by the randomization stratification factor (IPSS-R very high, IPSS-R high, IPSS-R intermediate, CMML-2) with critical alpha level 0.0246.

Zeidan et al, EHA 2024

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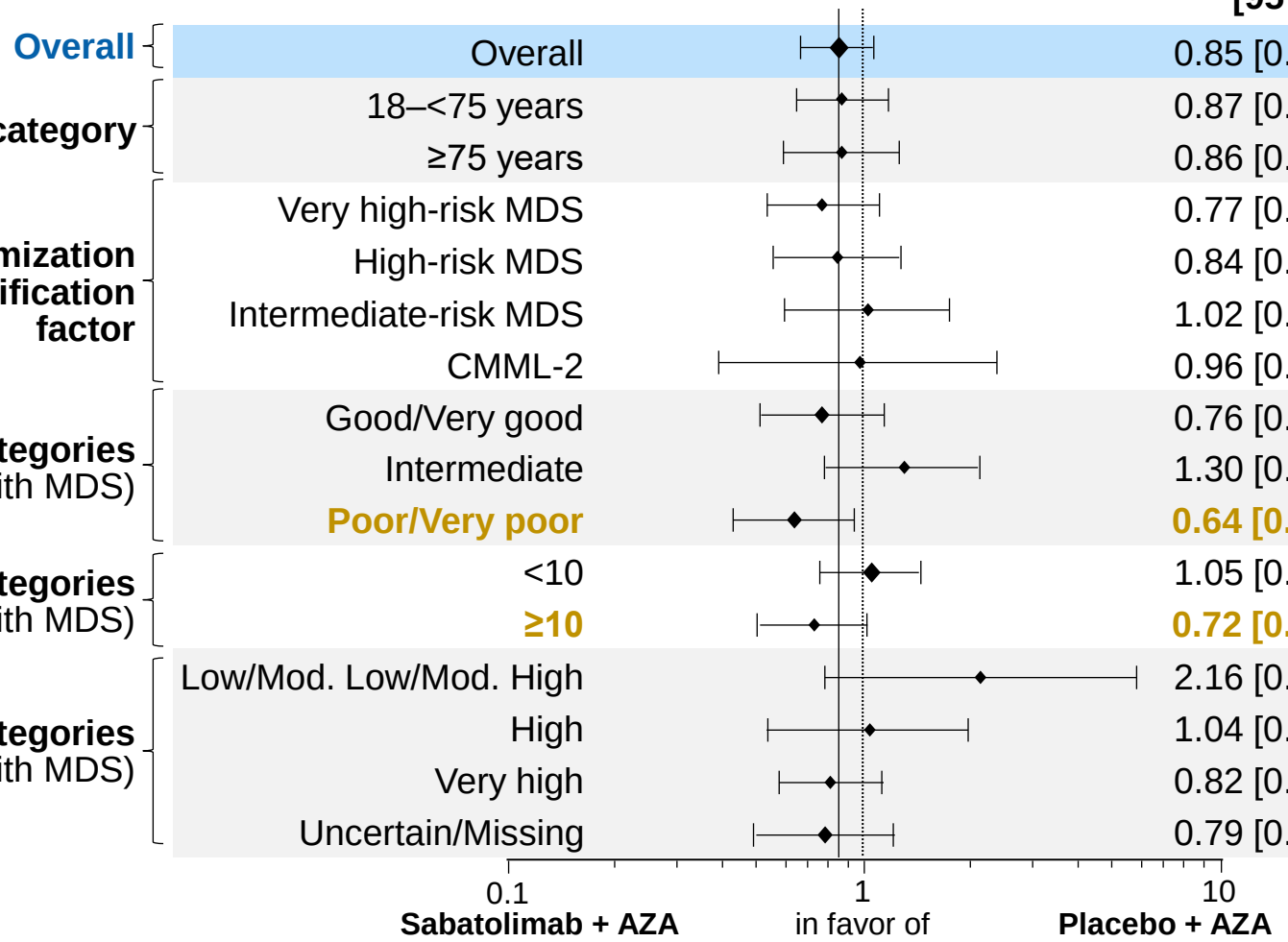
Overall survival by subgroups



		Hazard Ratio [95% CI]	Sabatolimab + AZA events n/N (%)	Placebo + AZA events n/N (%)
Overall	Overall	0.85 [0.67, 1.07]	143 / 265 (54)	143 / 265 (54)
Age category	18–<75 years	0.87 [0.64, 1.17]	78 / 160 (49)	95 / 181 (52)
	≥75 years	0.86 [0.59, 1.24]	65 / 105 (62)	48 / 84 (57)
Randomization stratification factor	Very high-risk MDS	0.77 [0.53, 1.10]	60 / 85 (71)	61 / 86 (71)
	High-risk MDS	0.84 [0.56, 1.27]	45 / 89 (51)	46 / 88 (52)
	Intermediate-risk MDS	1.02 [0.60, 1.73]	28 / 72 (39)	27 / 72 (38)
	CMML-2	0.96 [0.39, 2.38]	10 / 19 (53)	9 / 19 (47)
Cytogenetic categories (in patients with MDS)	Good/Very good	0.76 [0.51, 1.13]	44 / 112 (39)	55 / 115 (48)
	Intermediate	1.30 [0.78, 2.16]	32 / 56 (57)	29 / 64 (45)
	Poor/Very poor	**0.64 [0.44, 0.94]**	**57 / 78 (73)**	**50 / 67 (75)**
BM blast (%) categories (in patients with MDS)	<10	1.05 [0.76, 1.46]	78 / 148 (53)	66 / 138 (48)
	≥10	**0.72 [0.51, 1.04]**	**55 / 98 (56)**	**68 / 108 (63)**
IPSS-M categories (in patients with MDS)	Low/Mod. Low/Mod. High	2.16 [0.78, 6.01]	14 / 38 (37)	5 / 30 (17)
	High	1.04 [0.54, 2.01]	21 / 41 (51)	16 / 40 (40)
	Very high	0.82 [0.59, 1.13]	70 / 109 (64)	75 / 112 (67)
	Uncertain/Missing	0.79 [0.48, 1.29]	28 / 58 (48)	38 / 64 (59)

AZA, azacitidine; BM, bone marrow; CI, confidence interval; CMML-2, chronic myelomonocytic leukemia; IPSS-M, Molecular International Prognostic Scoring System; MDS, myelodysplastic syndromes; OS, overall survival. Full analysis set. Dotted line shows no effect point. Bold line shows overall treatment effect point (for all patients). Hazard ratio of sabatolimab versus placebo is calculated by using unstratified cox model except for 'Overall'. Hazard Ratio of sabatolimab versus placebo for 'Overall' is obtained from Cox model stratified by randomization stratification factor (Intermediate-risk MDS, High-risk MDS, Very high-risk MDS, CMML-2) as per interactive response technology. Only subgroup categories having at least one patient with OS event in sabatolimab and placebo are displayed. Cytogenetic categories, BM blast (%) categories and IDS only. Please note this forest plot was included in the published abstract with errors in cytogenetic and IPSS-M categories, which have been corrected here.

Zeidan et al, EHA 2024

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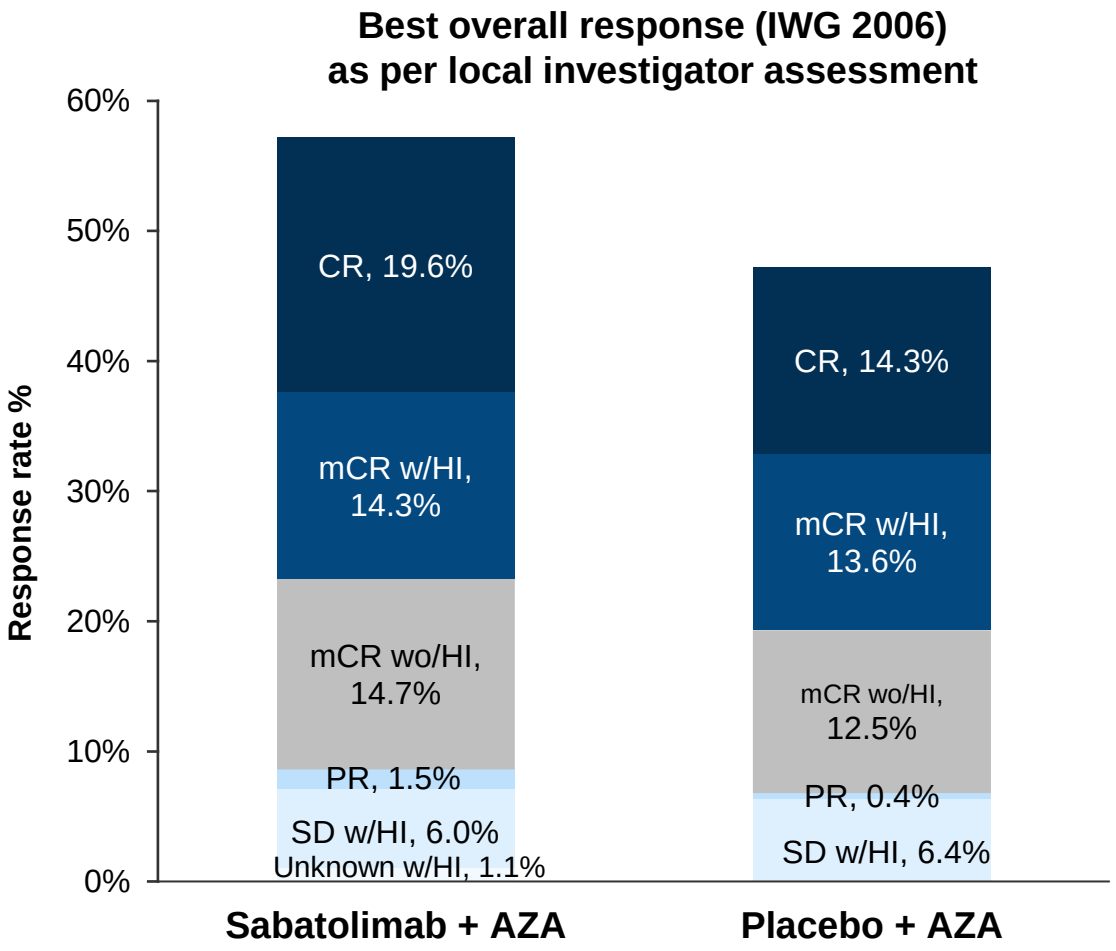
Best overall response



	Sabatolimab + AZA N=265	Placebo + AZA N=265
CR[a], % (95% CI)	**19.6** (15.0, 24.9)	**14.3** (10.4, 19.1)
CR+PR+HI[b], % (95% CI)	**42.6** (36.6, 48.8)	**34.7** (29.0, 40.8)

AZA, azacitidine; CI, confidence interval; CR, complete remission; (w/wo) HI, (with/without) hematological improvement; IWG, International Working Group; mCR, marrow CR; PD, progressive disease; PR, partial remission; SD, stable disease; w/wo, with/without. Full analysis set. [a]CR bone marrow assessments were performed less frequently than in the STIMULUS-MDS1 study and therefore CRs are not directly comparable; first assessment performed after 6 cycles. [b]HI must be concurrent with best overall response.

Zeidan et al, EHA 2024

Oral presentation at: EHA 2024 Hybrid Congress; June 13-16, 2024; Madrid, Spain, and online.

Sabatolimab Conclusions

- Did not improve overall survival, the primary endpoint

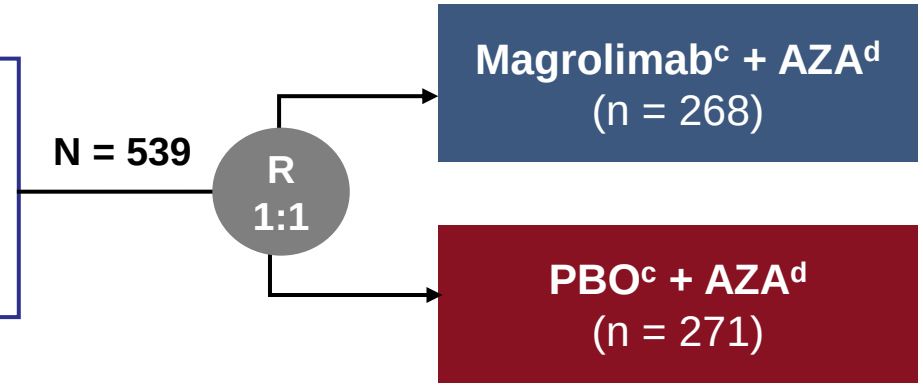
Magrolimab

- CD47 antibody
- Promising early phase data
- Potential activity in those with TP53 mutations

ENHANCE: Randomized, Double-Blind, Phase 3 Study

Key eligibility criteria
- Untreated intermediate to very high risk MDS[a]
- ECOG PS 0-2

Stratification factors
- Geography (US vs ex-US)
- Cytogenetic risk[b]
- BM blasts (≥ 10% vs < 10%)



Dual primary end points:
- CR rate[e]
- OS

Key secondary end points:
- ORR
- Duration of CR
- RBC TI rate
- EFS
- PFS
- CR rate in *TP53m* MDS
- MRD-negative response rate
- Time to transformation to AML
- Safety

- Study stopped early at prespecified interim analysis due to futility

[a]Per IPSS-R[1]: intermediate, > 3-4.5; high, > 4.5-6; very high, > 6. [b]Per IPSS-R[1]: very good/good/intermediate vs poor/very poor vs unknown. [c]Magrolimab priming doses given at 1 mg/kg IV on days 1 and 4, 15 mg/kg on day 8, and 30 mg/kg on days 11 and 15, then weekly for 5 doses, and then maintenance doses of 30 mg/kg every 2 weeks beginning 1 week after the fifth weekly dose. PBO mirrored the magrolimab dosing schedule. [d]All patients received subcutaneous or IV AZA 75 mg/m^2 on Days 1–7 or Days 1–5, 8, and 9 every 28-day cycle (6-cycle minimum). One cycle was 28 days. [e]Primary analysis of CR rate was conducted 8 months after 348 participants had been randomized.

AML, acute myeloid leukemia; **AZA**, azacitidine; **BM**, bone marrow; **CR**, complete remission; **ECOG PS**, Eastern Cooperative Oncology Group performance score; **EFS**, event-free survival; **HR**, high risk; **IPSS-R**, Revised International Prognostic Scoring System; **IV**, intravenous; **MDS**, myelodysplastic syndrome; **MRD**, minimal residual disease; **ORR**, objective response rate; **OS**, overall survival; **PBO**, placebo; **PFS**, sion; **R**, randomization; **RBC**, red blood cell; **SCT**, stem cell transplant; **TI**, transfusion independence; ***TP53m***, *TP53*-mutated; **US**, United States.

454-65.

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Response and Other Selected Efficacy Outcomes

Outcome	Magrolimab + AZA (n = 268)[a]	PBO + AZA (n = 271)[a]
Best response of CR at primary analysis (n = 348),[b] % (95% CI)	**20.5 (14.8–27.2)**	**25.0 (18.7–32.2)**
Odds ratio (95% CI),[c] *P*-value	**0.779 (0.471–1.288)**	
Final analysis (ITT)		
Best response of CR, % (95% CI)	**21.3 (16.5–26.7)**	**23.6 (18.7–29.1)**
Median[d] duration of CR (95% CI),[b,e] months	10.9 (8.9–16.7)	11.1 (8.1–NE)
ORR,[f] % (95% CI)	53.7 (47.6–59.8)	58.7 (52.6–64.6)
CR rate in *TP53m* population, % (95% CI)[g]	17.7 (10.0–27.9)	32.8 (21.6-45.7)
TI rate, % (95% CI)[h]	27.9 (20.6–36.1)	35.2 (26.9-44.2)
Median[d] duration of TI (95% CI),[i] months	11.8 (6.1–17.2)	8.2 (4.9-10.4)
MRD-negative status, % (95% CI)[j]	21.6 (16.9–27.1)	22.5 (17.7–28.0)
Transformed to AML, n (%)	34 (12.7)	43 (15.9)
Median[d] time to transformation (95% CI),[k] months	NE (21.2–NE)	25.5 (25.5–NE)
SCT rate,[l] % (95% CI)	20.9 (16.2–26.3)	35.4 (29.7–41.4)
Median[d] time to SCT (range), months	6.05 (2.66–16.85)	5.85 (2.76–19.12)

- There was no significant difference in CR rate or ORR between treatments
- The CR rate in the *TP53m* population was lower with magrolimab + AZA
- Fewer patients in the magrolimab + AZA arm proceeded to SCT (*P* = 0.0001)

[a]ITT. [b]Patients who discontinued study treatment and received SCT and patients who achieved a response and then proceeded to SCT were not censored at the time of SCT, but followed until disease progression, transformation to AML, or start of new anticancer therapy. [c]Stratified Cochran-Mantel-Haenszel test. [d]Kaplan-Meier estimate. [e]Calculated based on patients who achieved CR. [f]Investigator-assessed best response of CR, PR, marrow CR, or any hematologic improvement prior to initiation of any new anticancer therapy for MDS per IWG 2006. [g]*TP53m* testing results available in 64.0% of patients at time of report; 41.4% were *TP53m*. Denominator for CR rate in *TP53m* population was the number of patients who were *TP53m*. [h]Denominator of post-baseline TI rate was the number of patients who were transfusion dependent at baseline. [i]Calculated on the basis of patients who achieved TI. [j]Denominator for MRD-negativity rate was the ITT. [k]Calculated on the basis of patients who transformed to AML. [l]Two-sided *P*-value between treatment arms was 0.0001.

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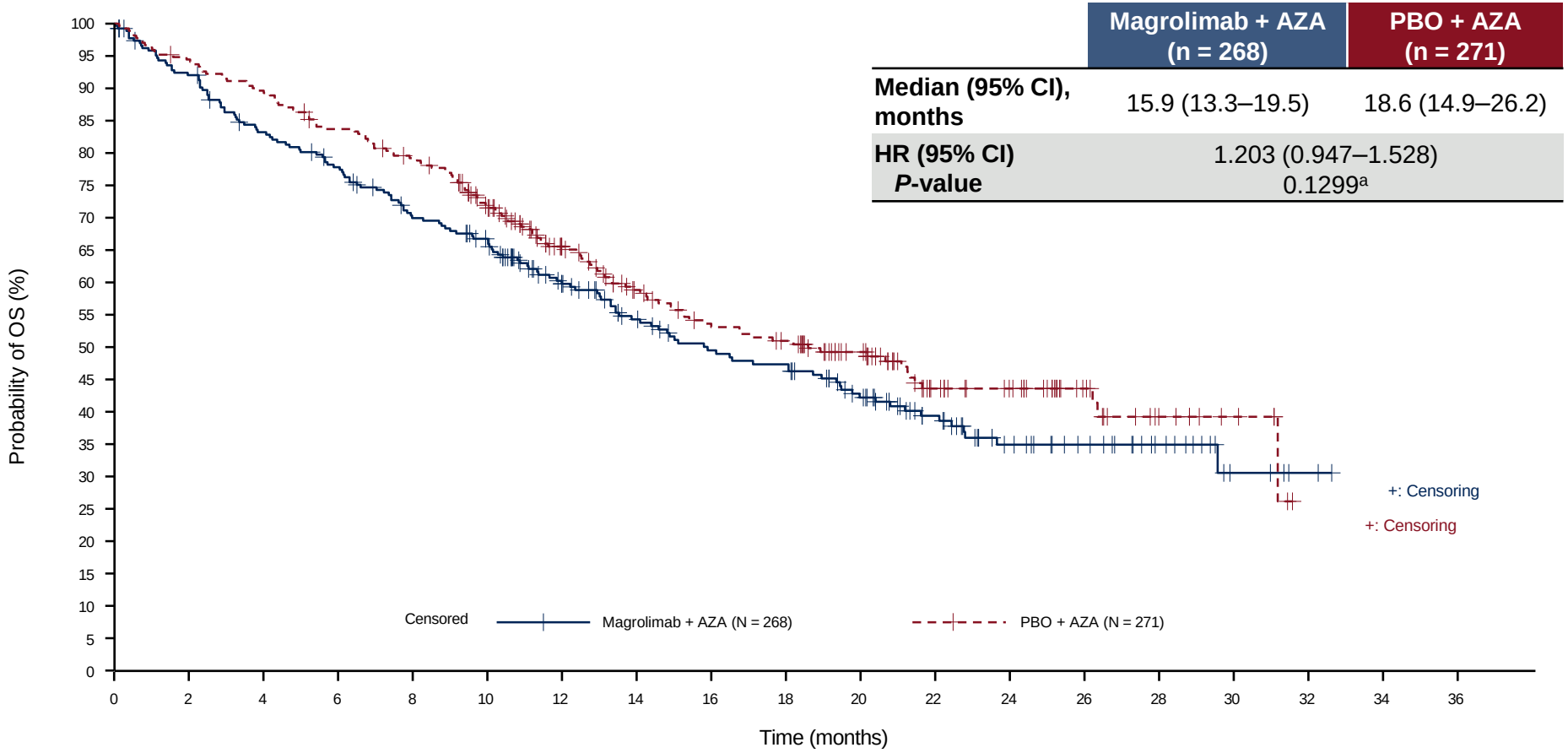
idine; **CR**, complete remission; **ITT**, intent-to-treat; **IWG**, International Working Group; **MRD**, minimal residual disease; **NE**, not estimable; **ORR**, objective response rate; **I,** transfusion independence; ***TP53m***, *TP53*-mutant.

OS at Final Analysis

	Magrolimab + AZA (n = 268)	PBO + AZA (n = 271)
Median (95% CI), months	15.9 (13.3–19.5)	18.6 (14.9–26.2)
HR (95% CI)	1.203 (0.947–1.528)	
***P*-value**	0.1299[a]	



N at risk (events)

Magrolimab + AZA	288 (0)	242 (21)	216 (44)	200 (58)	176 (78)	163 (86)	126 (102)	105 (113)	92 (122)	88 (126)	70 (135)	50 (139)	32 (144)	21 (144)	15 (144)	5 (145)	2 (145)	0 (145)
PBO + AZA	271 (0)	255 (15)	242 (28)	224 (44)	210 (56)	179 (76)	141 (90)	115 (104)	101 (115)	94 (119)	74 (122)	46 (149)	38 (129)	22 (129)	11 (131)	6 (131)	0 (132)	

Median follow-up for OS: magrolimab + AZA, 11.37 months; PBO + AZA, 12.52 months.
[a]Cox regression model utilized to estimate HRs and corresponding 95% CIs; log-rank test 2-sided *P*-values presented. Medians estimated by Kaplan-Meier method.
OS, overall survival; **PBO**, placebo.

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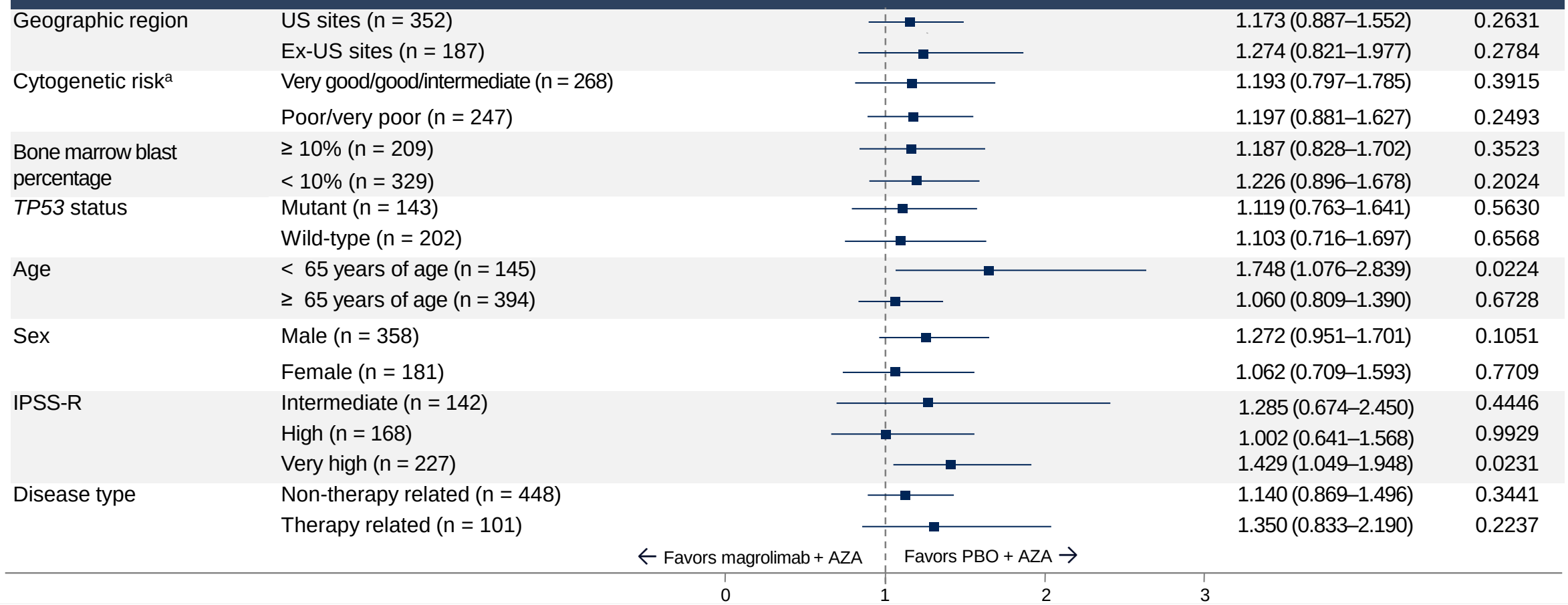
OS in Key Subgroups

- OS results in key subgroups were consistent with those in the overall population

Category	Subgroup	HR (95% CI)	*P*-value
Geographic region	US sites (n = 352)	1.173 (0.887–1.552)	0.2631
	Ex-US sites (n = 187)	1.274 (0.821–1.977)	0.2784
Cytogenetic risk[a]	Very good/good/intermediate (n = 268)	1.193 (0.797–1.785)	0.3915
	Poor/very poor (n = 247)	1.197 (0.881–1.627)	0.2493
Bone marrow blast percentage	≥ 10% (n = 209)	1.187 (0.828–1.702)	0.3523
	< 10% (n = 329)	1.226 (0.896–1.678)	0.2024
TP53 status	Mutant (n = 143)	1.119 (0.763–1.641)	0.5630
	Wild-type (n = 202)	1.103 (0.716–1.697)	0.6568
Age	< 65 years of age (n = 145)	1.748 (1.076–2.839)	0.0224
	≥ 65 years of age (n = 394)	1.060 (0.809–1.390)	0.6728
Sex	Male (n = 358)	1.272 (0.951–1.701)	0.1051
	Female (n = 181)	1.062 (0.709–1.593)	0.7709
IPSS-R	Intermediate (n = 142)	1.285 (0.674–2.450)	0.4446
	High (n = 168)	1.002 (0.641–1.568)	0.9929
	Very high (n = 227)	1.429 (1.049–1.948)	0.0231
Disease type	Non-therapy related (n = 448)	1.140 (0.869–1.496)	0.3441
	Therapy related (n = 101)	1.350 (0.833–2.190)	0.2237



arm and 9 patients in the PBO + AZA arm had unknown cytogenetic risk status.
, Revised International Prognostic Scoring System; **OS**, overall survival; **PBO**, placebo; **US**, United States.

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Magrolimab Conclusions

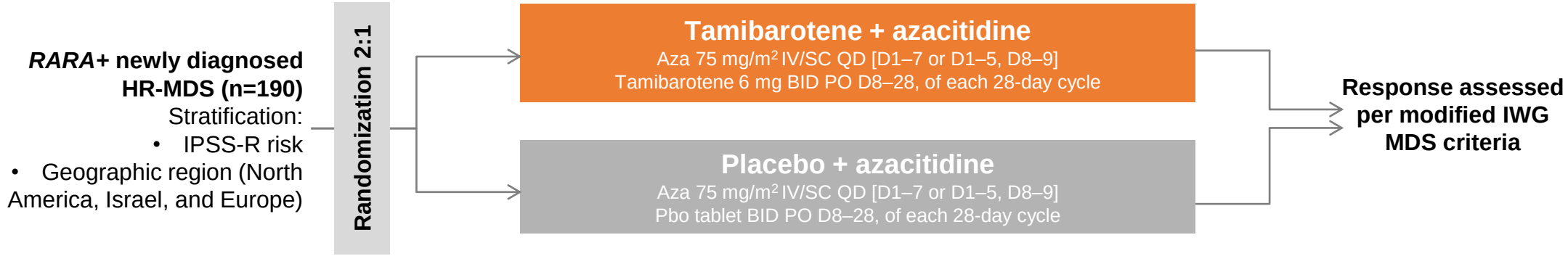
- Did not meet primary end points of CR and OS
- Trend toward worse OS in the magrolimab arm
- Resulted in more adverse events

Ongoing Studies

- Tamibarotene
- Venetoclax

Tamibarotene + Aza vs Pbo+Aza

Phase 3, double-blind, randomized trial in patients with *RARA*+ newly diagnosed HR-MDS



Key inclusion criteria

- Adults ≥18 years old
- *RARA*+ based on the investigational biomarker test
- Newly diagnosed with HR-MDS by 2016 WHO classification and classified by IPSS-R as very high, high, or intermediate risk
- Blast count >5% at study entry

Key exclusion criteria

- Patients suitable for transplant at the time of screening

Primary endpoint

- Proportion of participants with CR [Timeframe: up to 5 years]

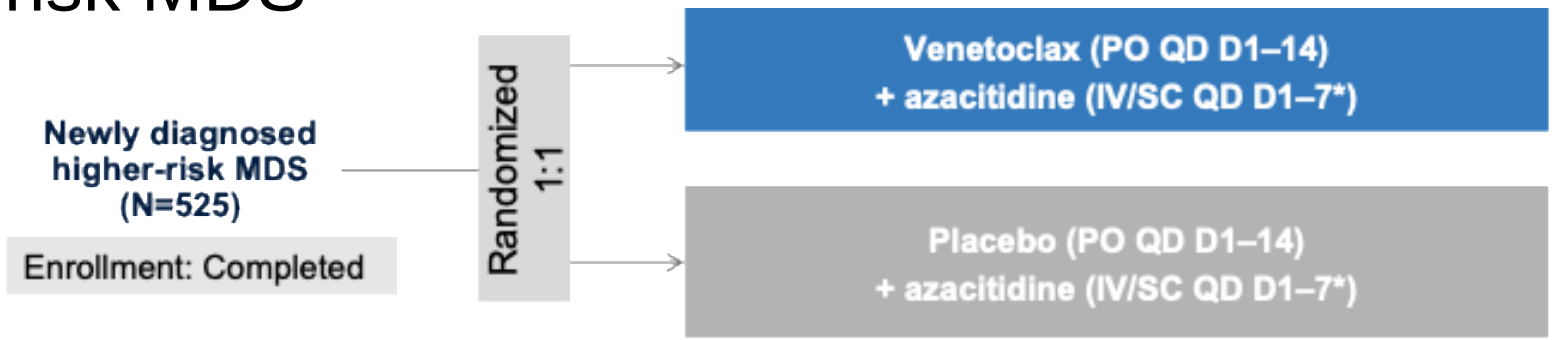
Key secondary endpoints

- ORR
- EFS, OS
- Transfusion independence

Adapted from Dezern AE, *et al. J Clin Oncol* 2022; 40(Suppl):TPS7075 (Poster)

Venetoclax

- BCL-2 inhibitor, revolutionized AML
- Subject of a registrational phase 3 study in newly diagnosed higher risk MDS



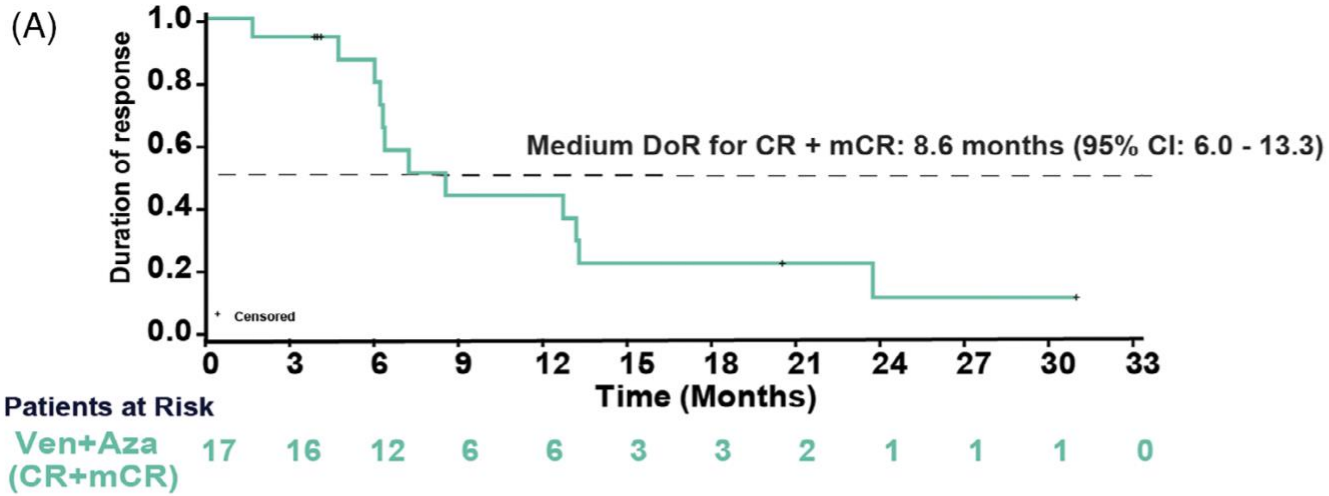
Key inclusion criteria
- ≥18 years old with newly diagnosed MDS according to 2016 WHO classification
- <20% BM blasts
- ECOG PS 0–2
- IPSS-R score of >3 (Intermediate, high, very high)
- No planned HSCT at the time of C1D1

Primary endpoints
- CR
- OS

Secondary endpoints
- Modified overall response (mOR)
- Transfusion independence (TI)
- ORR
- QoL

Higher Risk, Previously Treated

- No large phase 3 studies
- Frequently use venetoclax-based regimens off label if patients have increased blasts



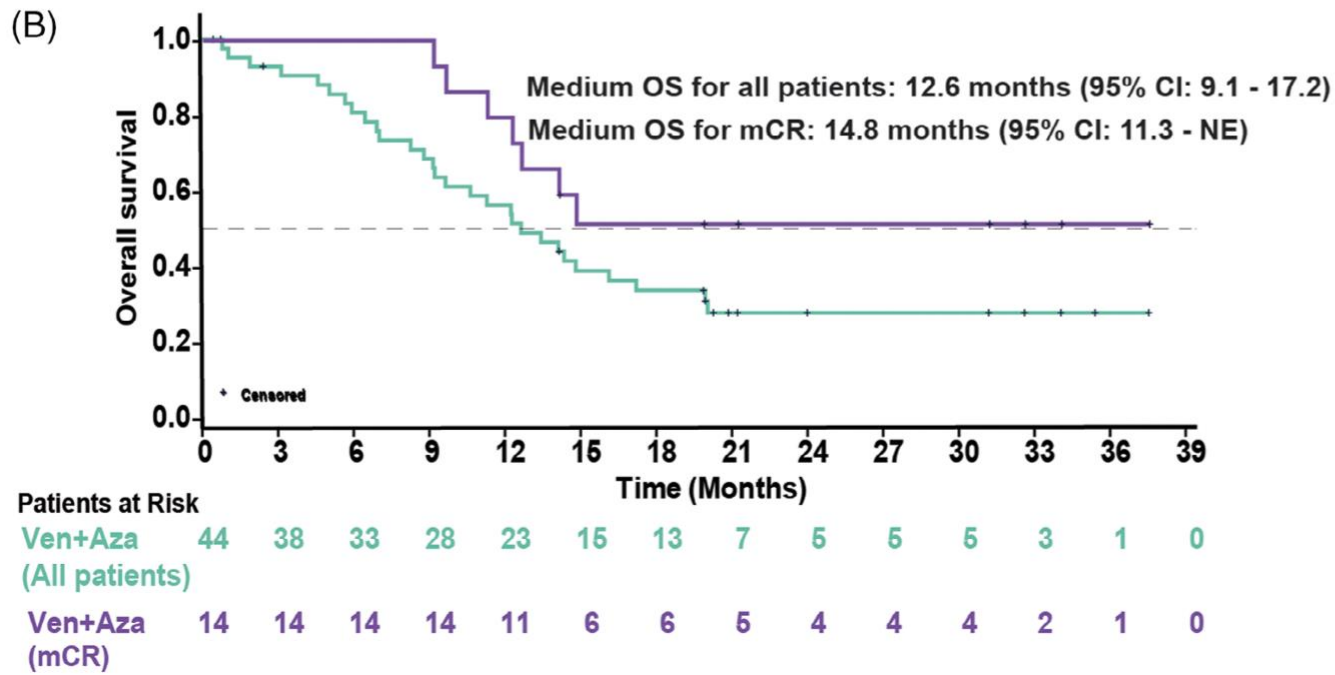


FIGURE 1 (A) Duration of response (DoR). (B) Overall survival (OS) in patients treated with venetoclax (Ven) and azacitidine (Aza). [Color figure can be viewed at wileyonlinelibrary.com]

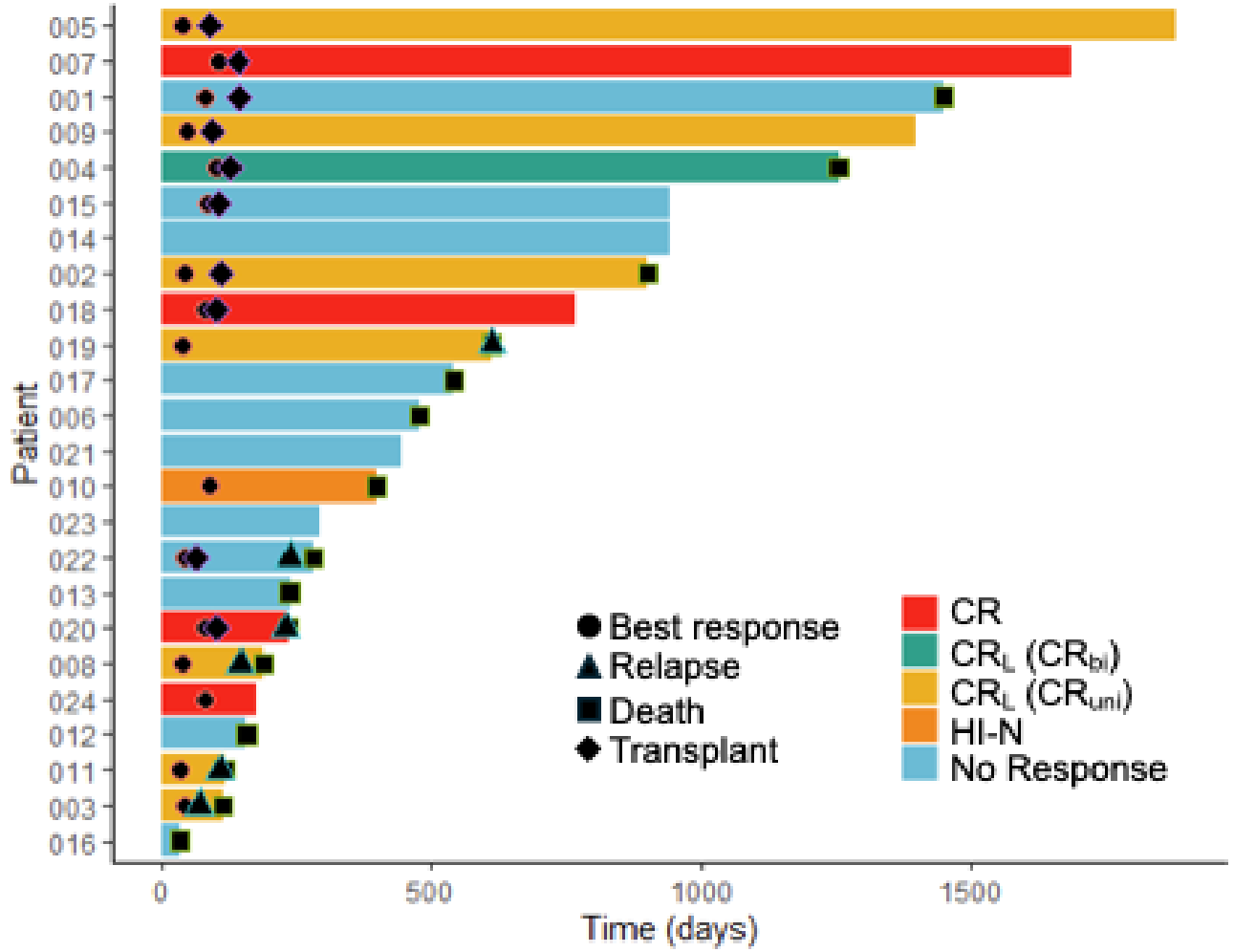
Zeidan et al, AJH 2022

Another Approach

- Can we target the root cause of MDS, the stem cell population?
- Omacetaxine with azacitidine for newly diagnosed high-risk MDS patients
- University of Colorado clinical trial

Trial Results

- 24 patients
- 54% response rate
- Median OS of 541 days



Conclusions

- Lower risk MDS has some new therapies but may not modify the disease
- Higher risk MDS sorely in need of new/improved therapies
- Near future holds promise

Alpenglow
Maroon Bells
Western Colorado