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Torino
Centro Congressi Lingotto
19-21 febbraio 2026

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Terapia delle sindromi mielodisplastiche a basso rischio

Humanitas - Milano

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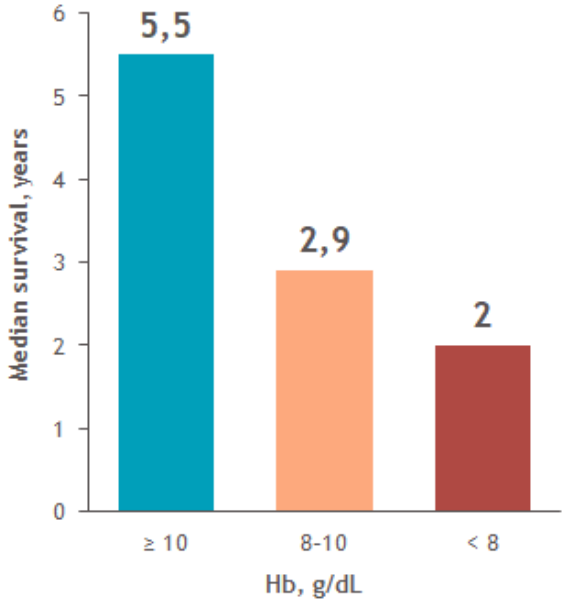
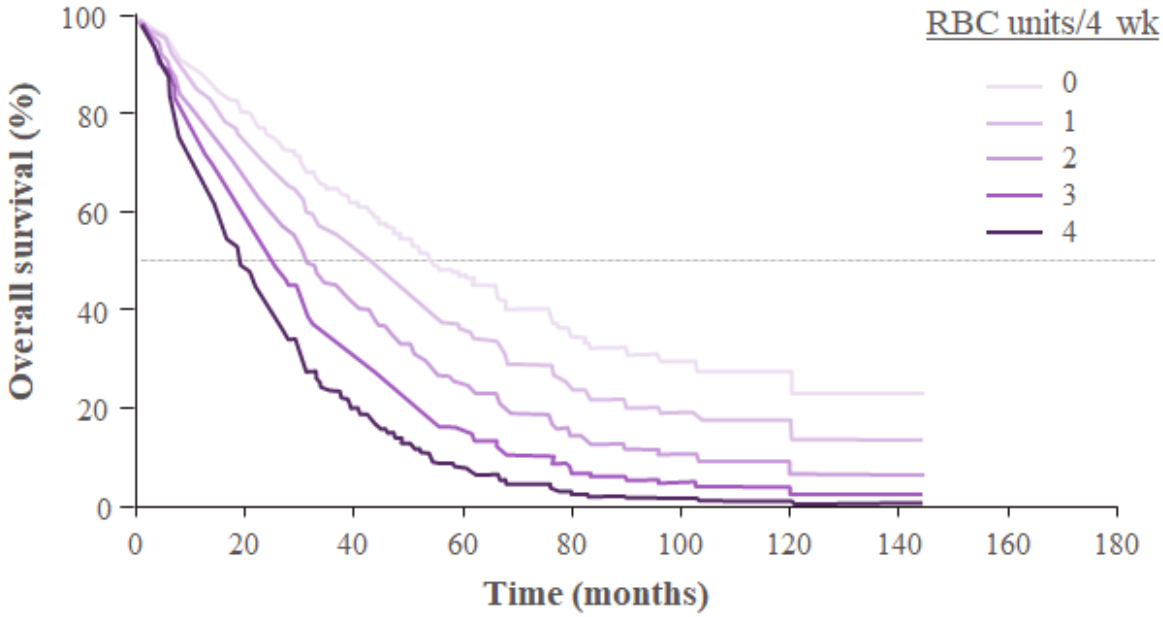
Anemia results in significantly increased risk of mortality in low-risk MDS

Severity of anemia and OS (n 7,012)



OS in MDS with transfusion-dependent anemia (n 426)



The detrimental effect of anemia in low-risk MDS is associated to

- Increased risk of cardiovascular morbidity and mortality
- Transfusional iron overload
- Increased risk of leukemic evolution

Zeidan AM, et al. Blood Rev. 2019;34:1-15
Malcovati L, et al. Haematologica. 2011;96:1433-1440
Greenberg PL, et al. Blood. 2012;120:2454-2465

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Luspatercept initiated at the maximum-approved dose in transfusion-dependent lower-risk myelodysplastic syndromes: interim analysis from MAXILUS

Amer M. Zeidan,[1] *Maria Diez Campelo,*[2] *Valeria Santini,*[3] *Rena Buckstein,*[4] *Lionel Adès,*[5] *Lea Sahagun,*[6] *Gitanjali Das,*[6] *Tatiana Zelinsky,*[6] *Yinzhi Lai,*[6] *Dimana Miteva,*[7] *Ali McBride,*[6] *Jose Alberto Nadal,*[7] *Krzysztof Madry,*[8] *David Valcarcel,*[9] *Jose Miguel Torregrosa-Diaz,*[10] *Dries Deeren,*[11] *Sebastian Grosicki,*[12] *Sangeetha Venugopal,*[13] *Uwe Platzbecker,*[14] *Luke Fletcher,*[15] *Thomas Cluzeau,*[16] *Matteo Giovanni Della Porta*[17]

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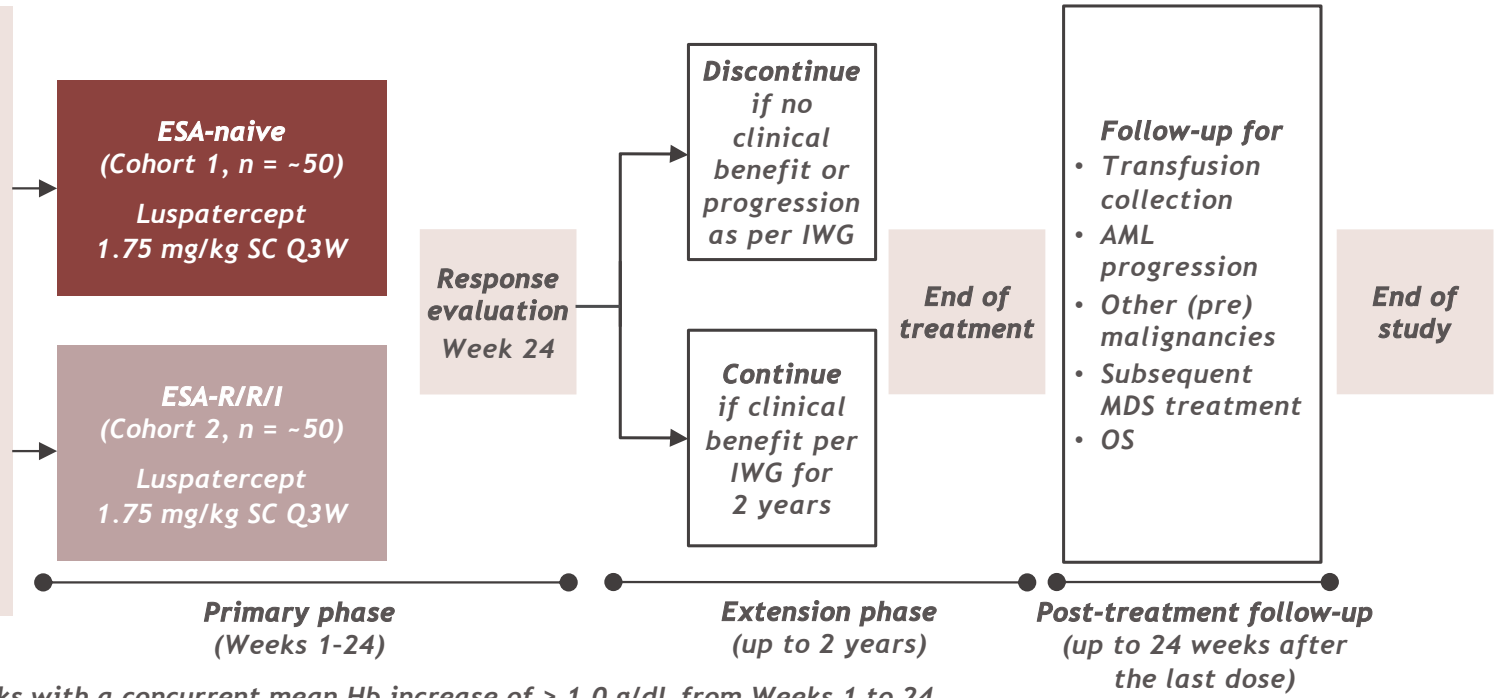
Key patient eligibility criteria

- ≥ 18 years of age
- MDS diagnosis (WHO 2018 criteria)
- IPSS-R very low-, low-, or intermediate-risk MDS
- ESA-naive[a] and ESA-R/R/I allowed
- RS+ and RS−
- Hb ≤ 10 g/dL
- ECOG PS score of 0-2
- ≥ 1 U of RBCs within 8 weeks prior to treatment

TB central enrollment control

- ≥ 20% of patients with baseline low TB (< 4 U/8 weeks) and high TB (≥ 4 U/8 weeks) per cohort



- Primary endpoint: RBC-TI for ≥ 8 weeks with a concurrent mean Hb increase of ≥ 1.0 g/dL from Weeks 1 to 24
- Secondary endpoints: RBC-TI for ≥ 8 weeks from Weeks 1 to 24, RBC-TI for ≥ 12 weeks from Weeks 1 to 24, disease progression to AML, and safety
- At this preplanned interim analysis (data cutoff date: April 14, 2025), ~40% of the ESA-naive cohort and ~80% of the ESA-R/R/I cohort were expected to be eligible for the primary efficacy analysis
- At the primary analysis, ~90% of patients in both cohorts are expected to be eligible for the primary efficacy analysis

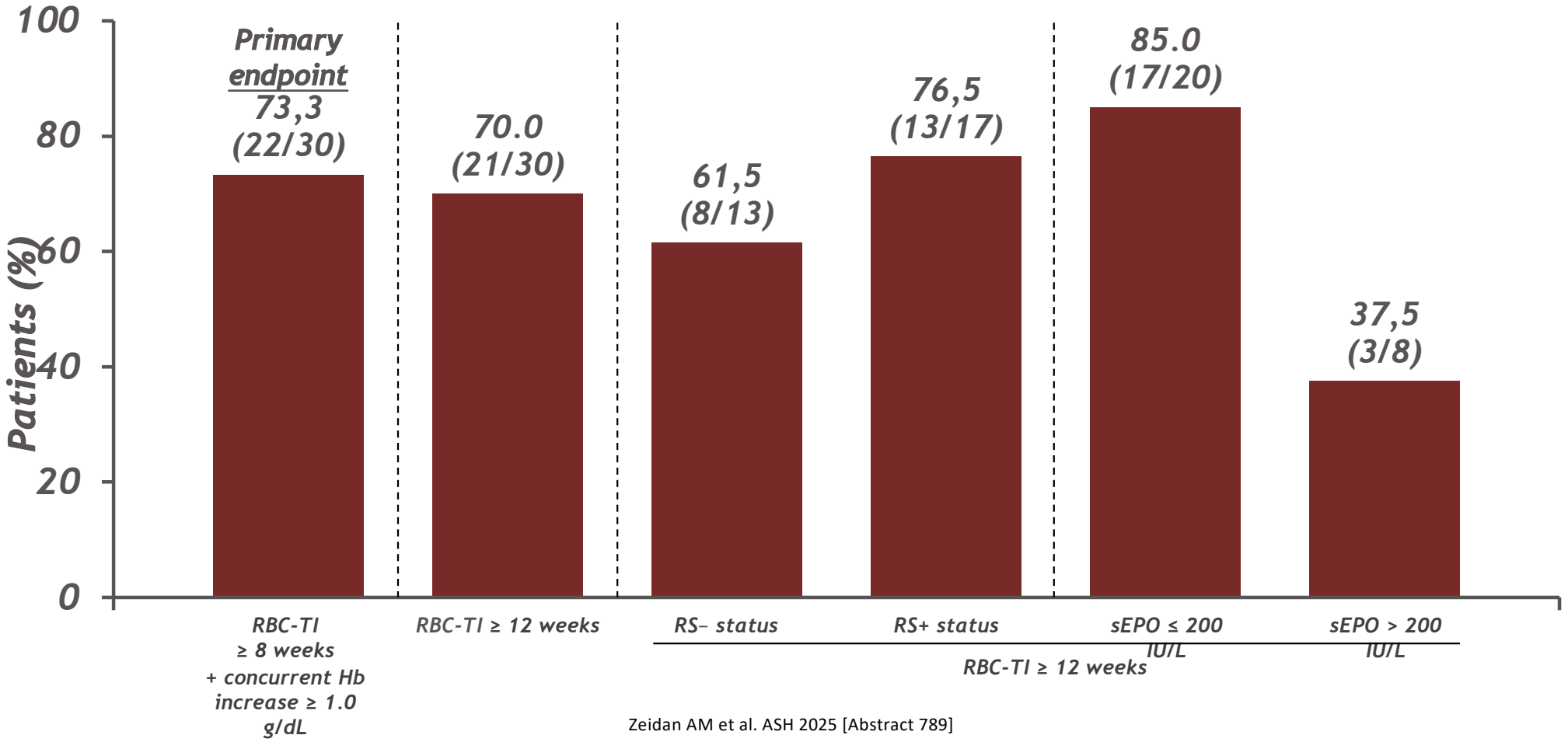
Zeidan AM et al. ASH 2025 [Abstract 789]

MAXILUS: patient demographics and disease characteristics

Characteristic	ESA-naive (n = 52)	ESA-R/R/I (n = 53)
Age, median (IQR), years	76.0 (70.5-81.0)	76.0 (71.0-81.0)
Sex, female, n (%)	15 (28.8)	19 (35.8)
Region, n (%)		
Europe	38 (73.1)	48 (90.6)
North America	14 (26.9)	5 (9.4)
Time since original MDS diagnosis,[b] median (IQR), months	1.9 (0.1-9.5)	24.8 (7.8-64.5)
Baseline TB, median (IQR), RBC U/8 weeks	2.0 (1.0-4.0)	3.0 (2.0-6.0)
Baseline TB category, n (%), RBC U/8 weeks		
< 4	38 (73.1)	27 (50.9)
4 to < 6	11 (21.2)	7 (13.2)
≥ 6	3 (5.8)	19 (35.8)
Baseline Hb, median (IQR), g/dL	8.1 (7.1-8.5)	7.5 (6.8-7.7)
Baseline sEPO category,[c] n (%), IU/L		
≤ 200	38 (73.1)	23 (43.4)
> 200	12 (23.1)	27 (50.9)
> 500	4 (7.7)	15 (28.3)
IPSS-R risk classification,[d] n (%)		
Very low	1 (1.9)	5 (9.4)
Low	38 (73.1)	36 (67.9)
Intermediate	12 (23.1)	12 (22.6)
RS status, n (%)		
RS+	31 (59.6)	32 (60.4)
RS−	21 (40.4)	21 (39.6)
SF3B1 mutation status,[e] n (%)		
Mutated	27 (51.9)	30 (56.6)
Non-mutated	23 (44.2)	23 (43.4)

Zeidan AM et al. ASH 2025 [Abstract 789]

MAXILUS: ***RBC-TI (Weeks 1-24)*** in the ESA-naive cohort



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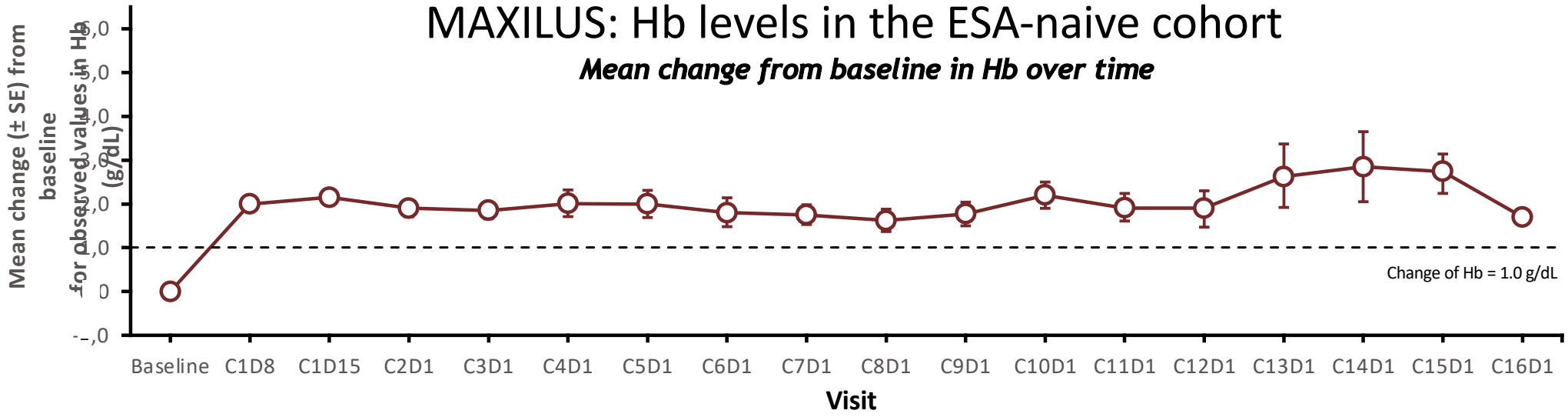
MAXILUS: Hb levels in the ESA-naive cohort

Mean change from baseline in Hb over time



No. of patients	52	41	43	46	43	39	35	35	31	28	24	20	14	12	9	6	3	1

	Median (IQR), g/dL
Baseline Hb,[a] (n = 52)[b]	*8.1 (7.1-8.5)*
Baseline Hb,[c] primary endpoint responders (n = 22)[d]	*8.0 (7.1-8.4)*
Change from baseline to maximum Hb value,[c] (n = 30)[e]	*3.0 (2.0-3.8)*
Change from baseline to maximum Hb value,[c] primary endpoint responders (n = 22)[d]	*3.2 (2.3-4.1)*

Data cutoff date: April 14, 2025. Median (IQR) follow-up was 5.8 (3.3, 8.2) months for the ESA-naive cohort.

C, cycle; D, day.

[a]After applying the 14/3-day rule, the baseline Hb value is defined as the lowest Hb value from the central, local laboratory, or pretransfusion Hb value from transfusion records that is within 56 days on or prior to the first dose of investigational product. If a patient is missing Hb records after the 14/3-day rule, a 7/3-day rule is applied. [b]Data are among the all-treated population, defined as all patients who received ≥ 1 dose of study intervention (ESA-naive, n = 52). [c]Only Hb values that are ≤ 14 days after a transfusion may be used unless there is another transfusion ≤ 3 days after the Hb assessment. Only patients with both baseline and post-baseline values are included. [d]Data are among patients who achieved RBC-TI ≥ 8 weeks (Weeks 1-24) with a concurrent mean Hb increase of ≥ 1.0 g/dL (ESA-naive, n = 22). [e]Data are among the efficacy-evaluable population who had both baseline and post-baseline values (ESA-naive, n = 30).

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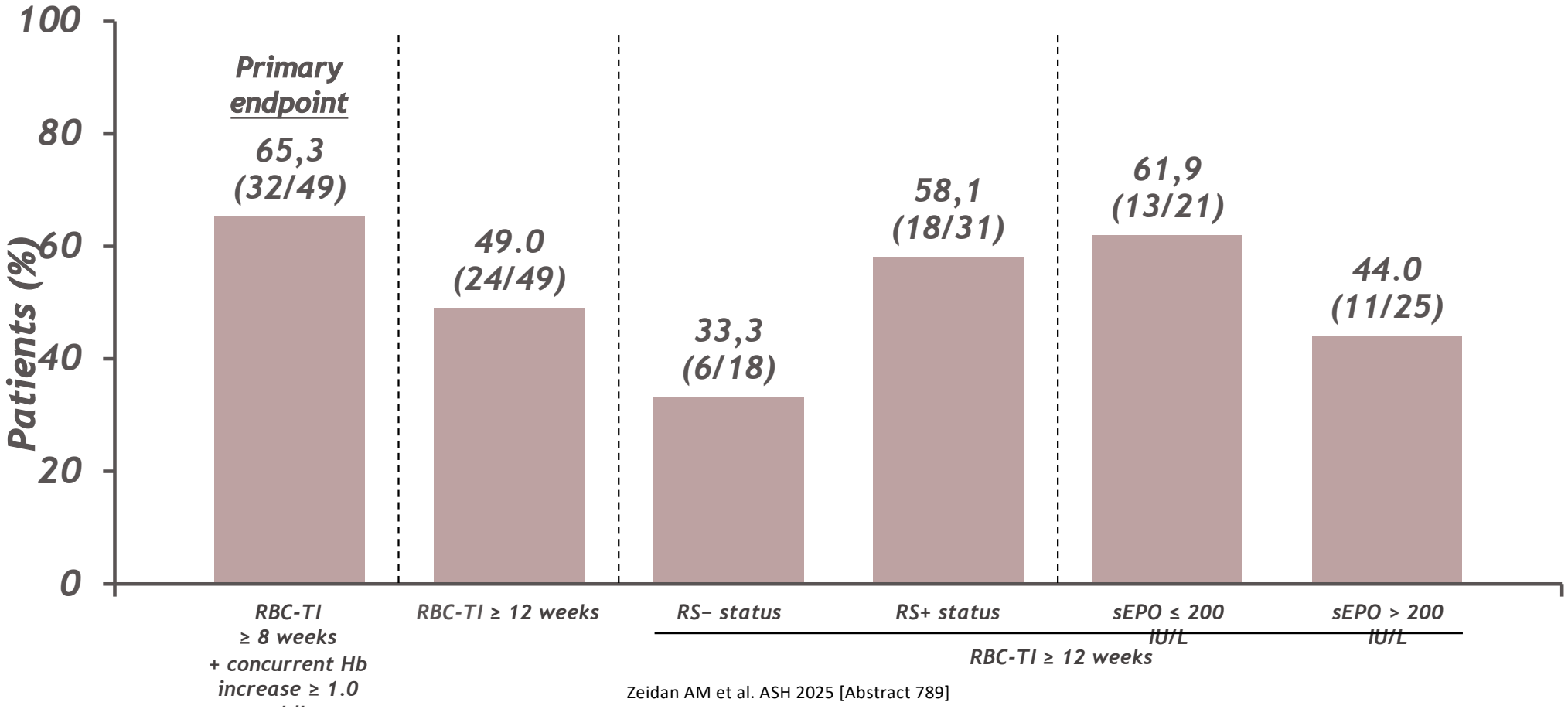
MAXILUS: ***RBC-TI (Weeks 1-24)[a]*** in the ESA-R/R/I cohort



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Clinical benefit of luspatercept in erythropoiesis-stimulating agent-naive patients with early disease characteristics and very low-, low-, or intermediate-risk myelodysplastic syndromes: a post-hoc analysis from the COMMANDS trial

***Valeria Santini*,[1] *Matteo Giovanni Della Porta*,[2] *Rami S. Komrokji*,[3] *Veronika Pozharskaya*,[4] *Thalia Farazi*,[4] *Karen L. Keeperman*,[4] *Yinzhi Lai*,[4] *Dimana Miteva*,[5] *Tracy Krimmel*,[4]**
***Barkha Aggarwal*,[4] *David Valcárcel*,[6] *Pierre Fenaux*,[7] *Jake Shortt*,[8] *Uwe Platzbecker*,[9] *Guillermo Garcia-Manero*,[10] *Amer M. Zeidan*[11]**

[1]MDS Unit, Hematology, University of Florence, Florence, Italy; [2]Cancer Center IRCCS Humanitas Research Hospital, Milan, Italy; Humanitas University, Milan, Italy; [3]Moffitt Cancer Center, Tampa, FL, USA; [4]Bristol Myers Squibb, Princeton, NJ, USA; [5]Bristol Myers Squibb, Boudry, Switzerland; [6]Hospital Universitari Vall d'Hebron, Barcelona, Spain; [7]Hôpital Saint-Louis, Université Paris 7, Paris, France; [8]Monash University and Monash Health, Melbourne, VIC, Australia; [9]University Hospital Leipzig, Leipzig, Germany; [10]University of Texas M.D. Anderson Cancer Center, Houston, TX, USA; [11]Yale University School of Medicine, New Haven, CT, USA

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Study design

- COMMANDS (NCT03682536) is a global, phase 3, open-label, randomized controlled trial

Key patient eligibility criteria

- ≥ 18 years of age
- IPSS-R very low-, low-, or intermediate-risk MDS (with or without RS) by WHO 2016 classification, with < 5% BM blasts[a]
- Required RBC transfusions (2–6 pRBC U/8 weeks, minimum of 8 weeks prior to randomization)
- ESA-naive
- Endogenous sEPO < 500 U/L

R 1:1

Luspatercept
1.0 mg/kg SC Q3W
titration up to 1.75 mg/kg
(n = 182)

Epoetin alfa[b]
450 IU/kg SC QW
titration up to 1050 IU/kg
(n = 181)

Response assessments at Day 169 and then every 24 weeks thereafter

End of treatment

- *Due to lack of clinical benefit[c] or disease progression per IWG 2006 criteria*

Post-treatment safety follow-up

- *Monitoring for other malignancies, HR-MDS or AML progression, subsequent therapies, and survival for 5 years from first dose*

Primary endpoint

- RBC-TI for ≥ 12 weeks with concurrent mean Hb increase ≥ 1.5 g/dL (Weeks 1-24)

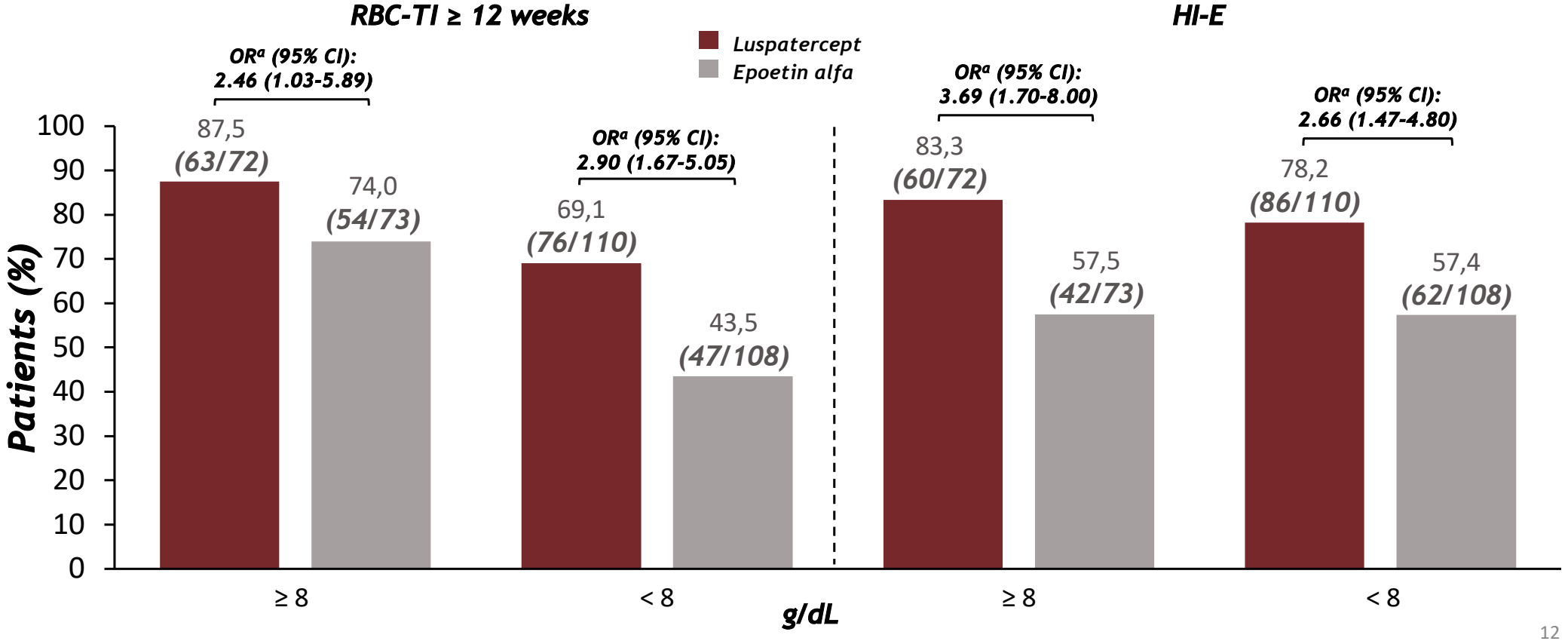
Select secondary endpoints

- RBC-TI for ≥ 12 weeks (Weeks 1-24)
- Duration of RBC-TI ≥ 12 weeks (Week 1-EOT)
- OS
- Progression to AML
- Safety

Post-hoc efficacy outcomes (data cutoff: February 7, 2025)

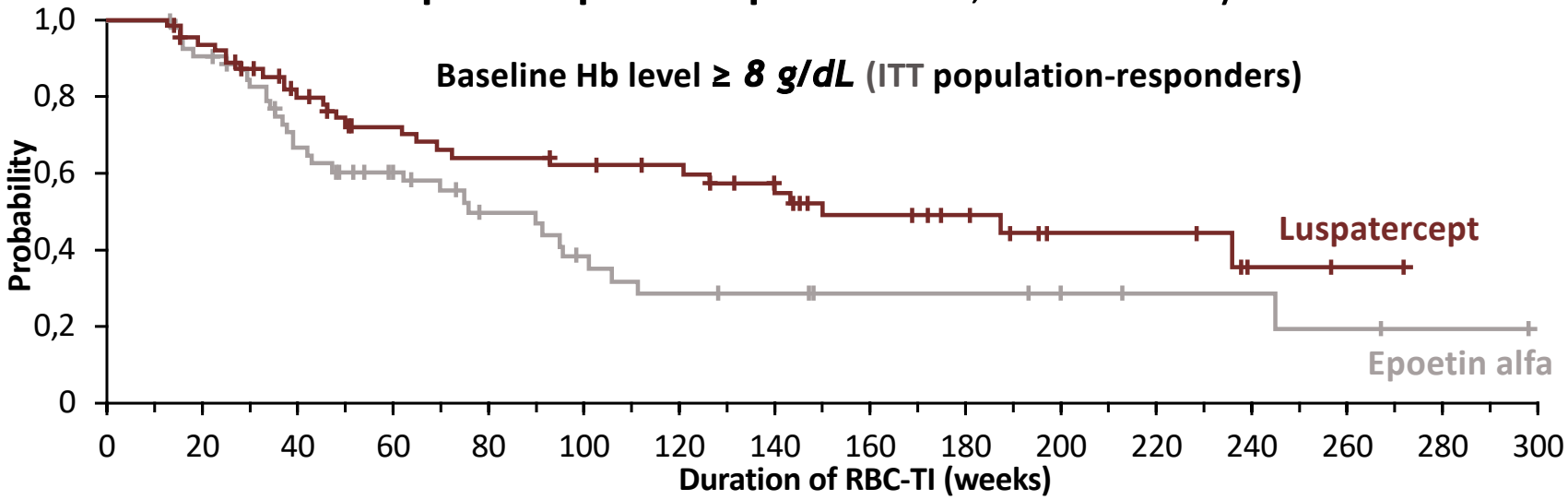
- *RBC-TI ≥ 12 weeks (Week 1-EOT)*
- *Duration of RBC-TI ≥ 12 weeks (Week 1-EOT)*
- *HI-E[d] (Week 1-EOT)*

Achievement of RBC-TI ≥ 12 weeks and HI-E (Week 1-EOT) with **luspatercept and epoetin alfa**, stratified by baseline Hb



Santini V et al. ASH 2025 [Abstract 792]

Duration of RBC-TI ≥ 12 weeks (Week 1-EOT) with **luspatercept and epoetin alfa**, stratified by baseline Hb



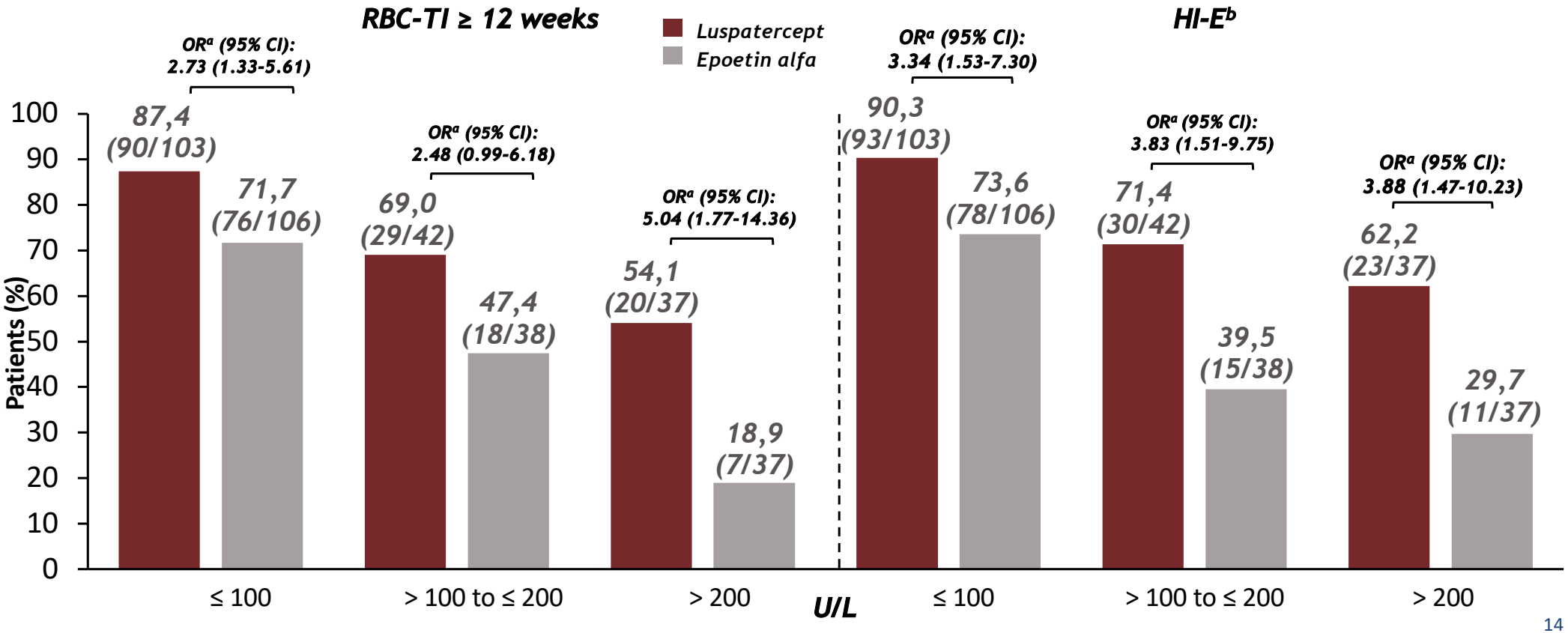
No. at risk

Luspatercept	63	63	57	50	43	37	35	32	31	31	29	28	27	24	23	16	15	14	11	8	6	6	6	5	2	2	1	1	0
Epoetin alfa	54	54	48	42	33	28	25	21	17	16	12	10	9	8	8	6	6	6	6	6	5	4	3	3	3	2	2	1	1	1	0

Median (95% CI) duration,[a] weeks	*Luspatercept*	*Epoetin alfa*	*HR[b] (95% CI)*
Hb, g/dL			
≥ 8	*150.0 (72.0-NE)*	*75.6 (41.9-101.1)*	*0.600 (0.359-1.002)*
< 8	*108.3 (53.7-132.6)*	*86.7 (37.3-186.1)*	*1.042 (0.636-1.706)*

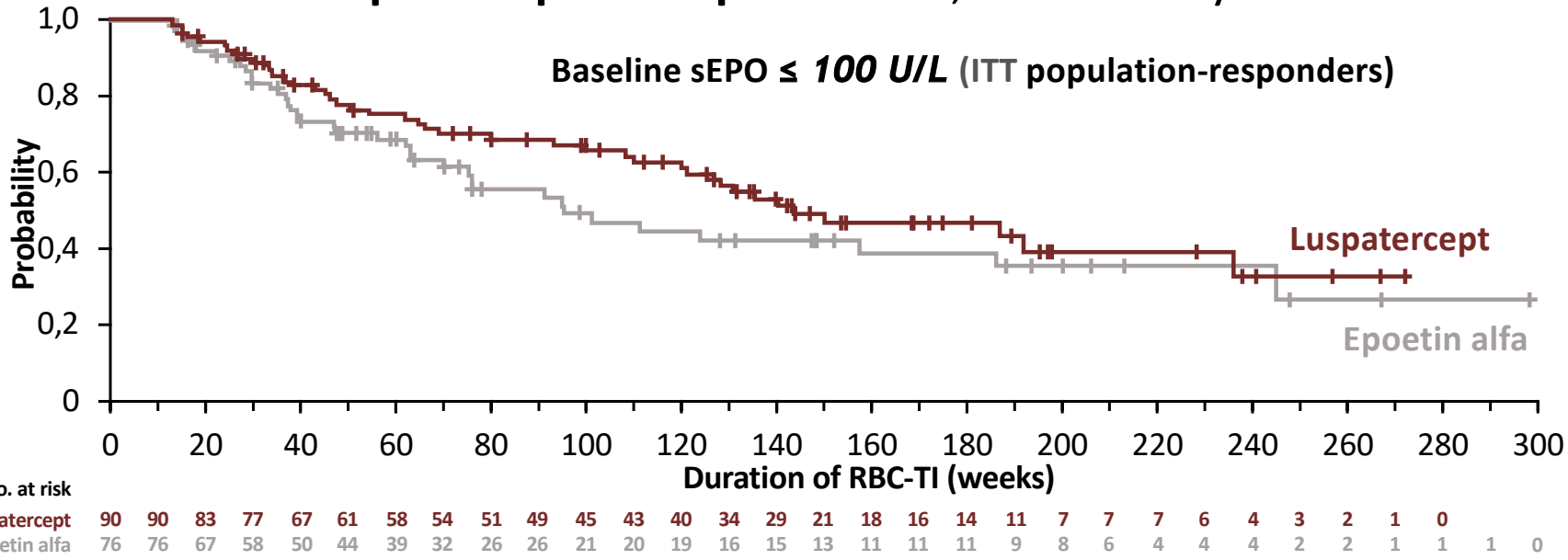
Santini V et al. ASH 2025 [Abstract 792]

Achievement of RBC-TI ≥ 12 weeks and HI-E (Week 1-EOT) with **luspatercept and epoetin alfa**, stratified by baseline sEPO



Santini V et al. ASH 2025 [Abstract 792]

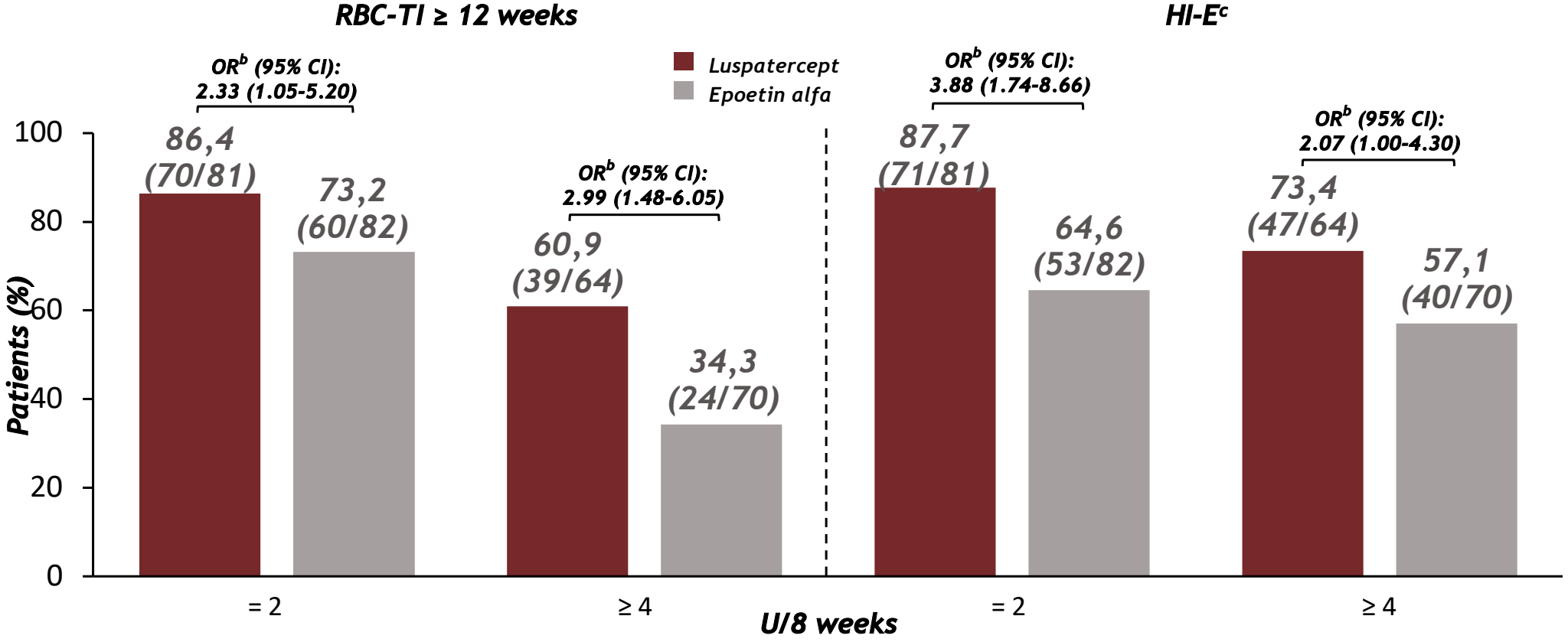
Duration of RBC-TI ≥ 12 weeks (Week 1-EOT) with **luspatercept and epoetin alfa**, stratified by baseline sEPO



Median (95% CI) duration,[a] weeks	*Luspatercept*	*Epoetin alfa*	*HR[b] (95% CI)*
sEPO, U/L			
≤ 100	*143.3 (120.1-235.9)*	*95.1 (69.7-186.1)*	*0.753 (0.484-1.171)*
> 100 to ≤ 200	*66.9 (31.1-154.1)*	*33.1 (26.9-89.7)*	*0.512 (0.246-1.067)*
> 200	*48.3 (26.3-132.6)*	*24.6 (14.9-NE)*	*0.848 (0.300-2.394)*

Santini V et al. ASH 2025 [Abstract 792]

Achievement of RBC-TI ≥ 12 weeks and HI-E (Week 1-EOT) with **luspatercept and epoetin alfa**, stratified by baseline TB[a]



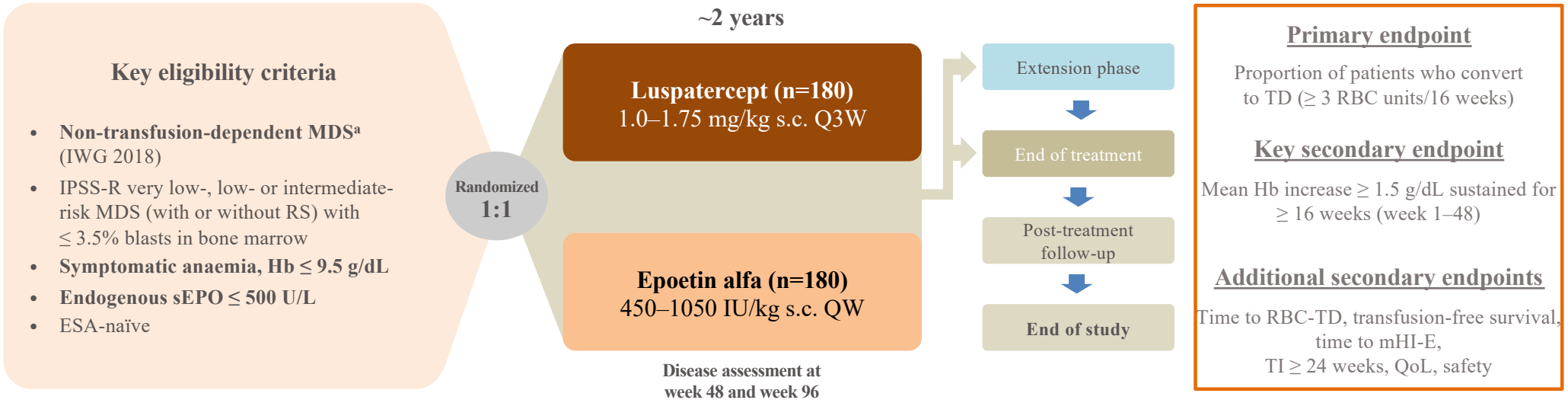
Santini V et al. ASH 2025 [Abstract 792]

- In the COMMANDS trial, luspatercept consistently yielded higher response rates and longer response duration than epoetin alfa across all clinically relevant subgroups (Hb, sEPO, and TB), supporting luspatercept as a preferred first-line therapy in TD LR-MDS
- Patients with higher Hb, lower sEPO, and lower TB, indicative of less advanced disease, achieved greater clinical benefit with luspatercept than those with more advanced disease
- Given these results, initiation of luspatercept early in the disease course of LR-MDS may lead to higher rates and a longer duration of transfusion independence

This COMMANDS post-hoc analysis supports early luspatercept use in TD LR-MDS, including in patients with less advanced disease characteristics

Luspatercept: Wait for transfusion dependency?

Ongoing: ELEMENT-MDS Phase 3 trial



Luspatercept is not approved in Europe for patients with NTD anemia caused by lower-risk MDS

[a] 0 RBC units over 16 weeks prior to randomization; 1–2 RBC units within the 16 weeks prior to enrollment are allowed provided transfusion was administered for an acute event/illness (i.e. surgical procedure, bleeding, infection) or presence of comorbidity, and not for the treatment of low haemoglobin (with or without symptoms) alone.

ESA: erythropoiesis-stimulating agent; Hb: haemoglobin; IPSS-R: International Prognostic Scoring System-Revised; IWG: International Working Group; MDS: myelodysplastic syndromes; mHI-E: modified haematological improvement – erythroid response; QoL, quality of life; QW: once a week; Q3W: once every 3 weeks; RBC: red blood cell; s.c.: subcutaneous; sEPO: serum erythropoietin; TD: transfusion dependency, TI: transfusion independence.

1. ClinicalTrials.gov. https://clinicaltrials.gov/study/NCT05949684 (Accessed Jun 2024). 2. Zeidan AM, et al. *Blood* 2023;142(suppl.1):6503.

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Elritercept shows durable responses in lower-risk myelodysplastic neoplasms (LR-MDS) with transfusion dependence: Updated Results from an ongoing Phase 2 trial

Lynette Chee, Shuhying Tan, David Valcarcel, Anish Puliyayil, Alejandro Arbelaez, Montserrat Arnan, David Ross, Devendra Hiwase, Teresa Bernal, Thomas Cluzeau, Aristoteles Giagounidis, Jen Salstrom, Radha Ramesh, Camden Bay, Kevin Galinsky, Leopold Sellner, Kaveri Suryanarayan, Maria Diez-Campelo

- Elritercept is an investigational, modified activin receptor type IIA/IgG1 fusion protein designed to bind and block select TGF-β superfamily ligands (activins A & B, GDF 8 & 11)

- 78 pts with transfusion-dependent LR-MDS were treated with elritercept starting at the recommended Part 2 dose (RP2D; 3.75 mg/kg).

- In the first 24 weeks of treatment, 38.5% of pts achieved TI ≥8 weeks. In the first 48 weeks, 26.9% achieved TI ≥24 weeks (15.5% in patients with HTB) with 75.9% maintaining TI at 48 weeks. TI ≥48 weeks was achieved in 20.5% (prior ESA: 13.6%, ESA naïve: 23.2%) of patients over the course of the study.

- A median duration of response of 110.9 weeks among patients who had TI ≥8 weeks in the first 24 weeks was observed

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A randomized, multicenter trial of shorter durations of hypomethylating agents in lower-risk Myelodysplastic Syndromes

Ian Bouligny, Hetty Carraway, Mikkael Sekeres, Amy DeZern, Rami Komrokji, Richard Stone, Gail Roboz, Koji Sasaki, Guillermo Montalban-Bravo, Alex Bataller, Alexandre Bazinet, Danielle Hammond, Kelly Chien, Courtney DiNardo, Gautam Borthakur, Yesid Alvarado Valero, Farhad Ravandi, Naval Daver, Tapan Kadia, Naveen Pemmaraju, Nicholas Short, Jane Waukau, Matthew Rump, Colin Huck, Wei Qiao, Xuelin Huang, Elias Jabbour, Guillermo Garcia-Manero

- Randomized, multicenter study of 3-day decitabine, 3-day azacitidine, and 5-day azacitidine in low- or intermediate-1-risk MDS or CMML (n=247)

- Among transfusion-dependent patients, the ORR was 53% (95% CI, 40% to 65%) for 3-day decitabine, 53% (95% CI, 36% to 69%) for 3-day azacitidine, and 48% (95% CI, 35% to 61%) for 5-day azacitidine (P = 0.89). The proportion of red blood cell or platelet transfusion-dependent patients who became transfusion-independent was 44% (95% CI, 31% to 57%) among patients treated with 3-day decitabine, 42% (95% CI, 26% to 59%) with 3-day azacitidine, and 40% (95% CI, 28% to 54%) with 5-day azacitidine (P = 0.97).

- In a multivariate Cox model of transfusion-dependent patients controlling for age, performance status, disease risk, and molecular characteristics, the EFS of 5-day azacitidine was better than 3-day azacitidine (hazard ratio [HR], 0.41; 95% CI, 0.19 to 0.90; P = 0.03); there was no difference between 5-day azacitidine and 3-day decitabine (HR, 0.74; 95% CI, 0.41 to 1.33; P = 0.31).