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# ESA- Still the 1st line for LR-MDS ?

# NO

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# LR-MDS patients suffer substantial loss of life expectancy

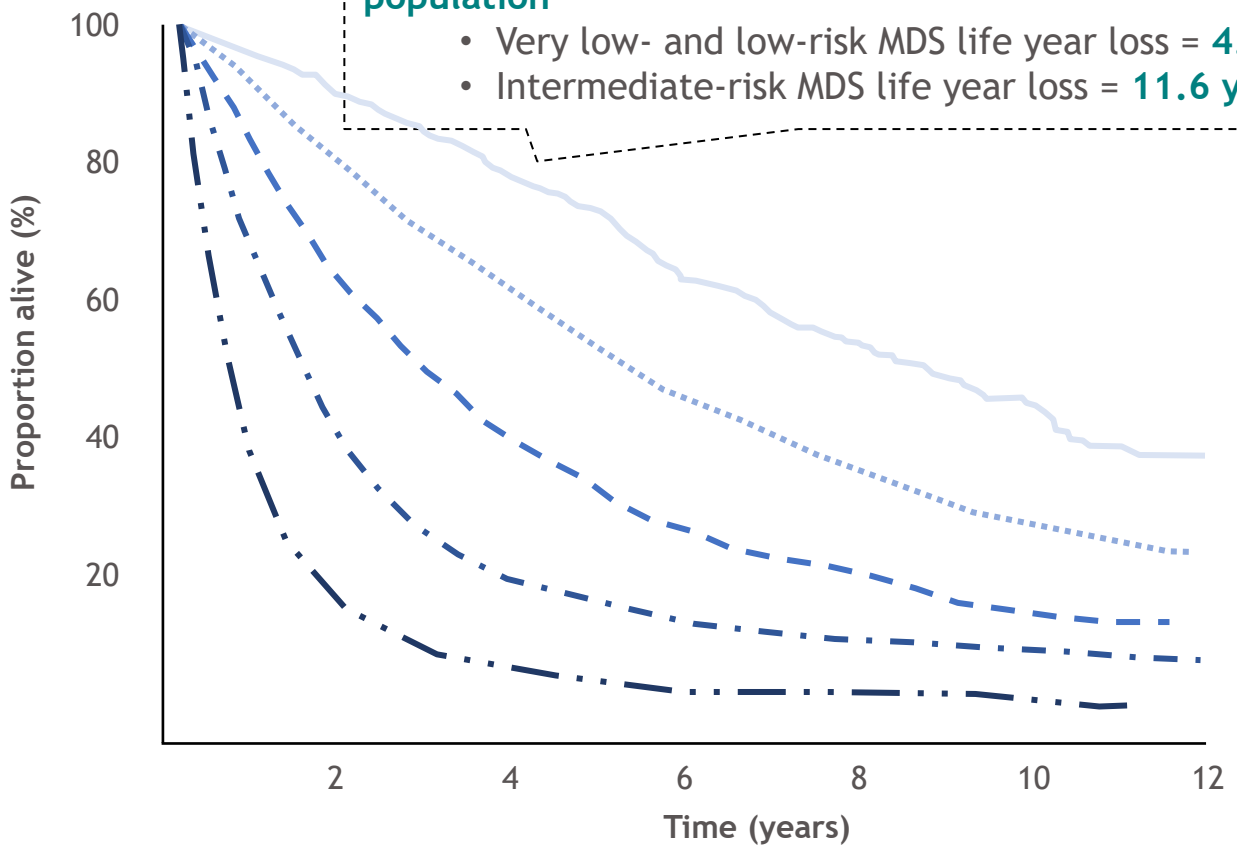
**Survival based on IPSS-R risk category[1a]**

[a]Combined international databases of untreated MDS (n=7012)

| | Risk group | mOS (years) |
|---|---|---|
| LR-MDS | Very low | 8.8 |
| LR-MDS | Low | 5.3 |
| LR-MDS | Intermediate | 3.0 |
| | High | 1.6 |
| | Very high | 0.8 |

A recent study estimated that **LR-MDS patients suffer a median life year loss of 6.8 years vs. the general population[2]**

- Very low- and low-risk MDS life year loss = **4.9 years**
- Intermediate-risk MDS life year loss = **11.6 years**




IPSS-R, Revised International Prognostic Scoring System; LR-MDS, low-risk myelodysplastic syndromes; MDS, myelodysplastic syndromes; mOS, median overall survival.

1. Greenberg PL, et al. Blood. 2012; 120(12):2454-2465. 2. Li Z, et al. HemaSphere 2019; 3(Suppl_1):693.

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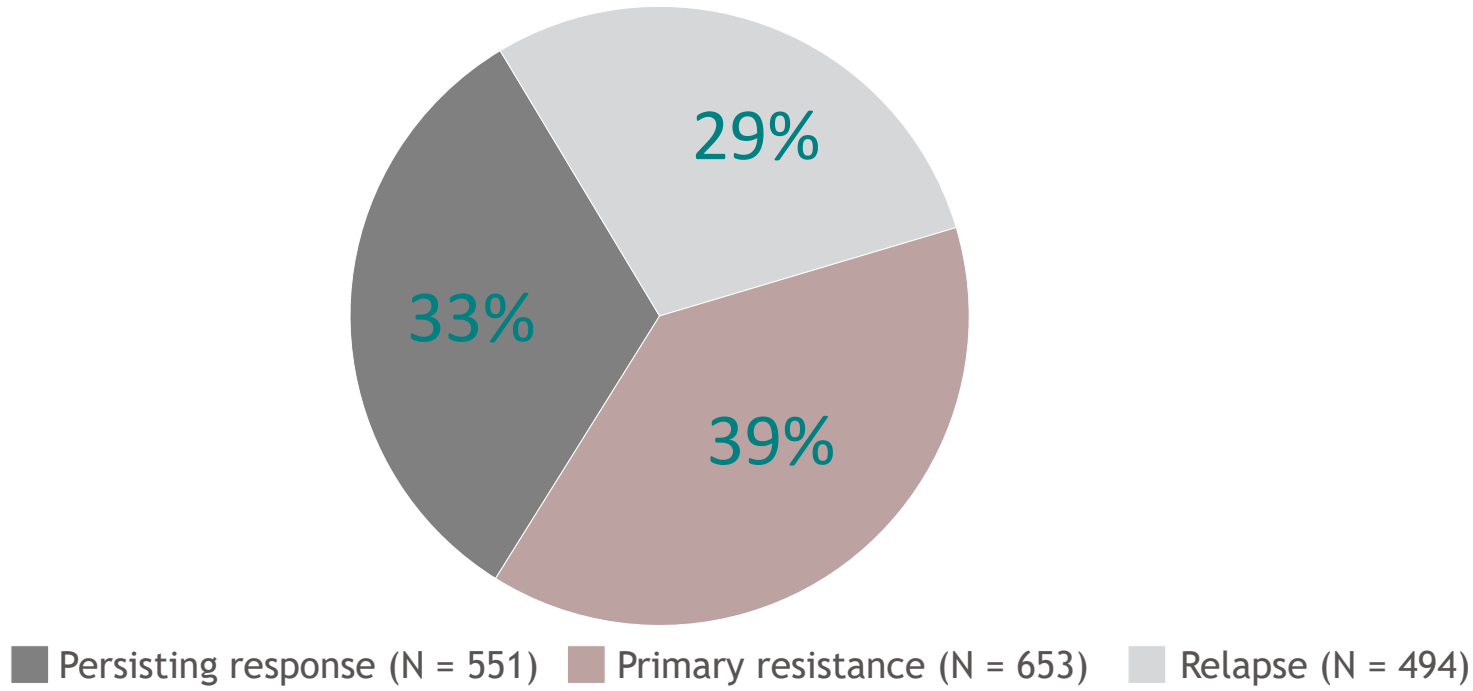
# Two-thirds of LR-MDS patients either fail to respond to ESAs or relapse, the majority of whom then receive RBCTs only

- **39%** of patients with LR-MDS fail to respond to ESAs, and **29%** of patients relapse to ESAs within 1 year [1]
- **HMAs and lenalidomide** are the most common treatments post ESAs[1]
- However, **most patients will continue to receive RBCTs only post-ESA treatment**[1,a]

## Patients with LR-MDS receiving ESA treatment[1] *(N = 1698)*




Del(5q), deletion 5q; ESA, erythropoiesis stimulating agent; HMA, hypomethylating agent; LR-MDS, low-risk myelodysplastic syndromes; MDS, myelodysplastic syndromes; RBCT, red blood cell transfusion.

1. Park S, et al. J Clin Oncol. 2017; 35(14):1591-1597.

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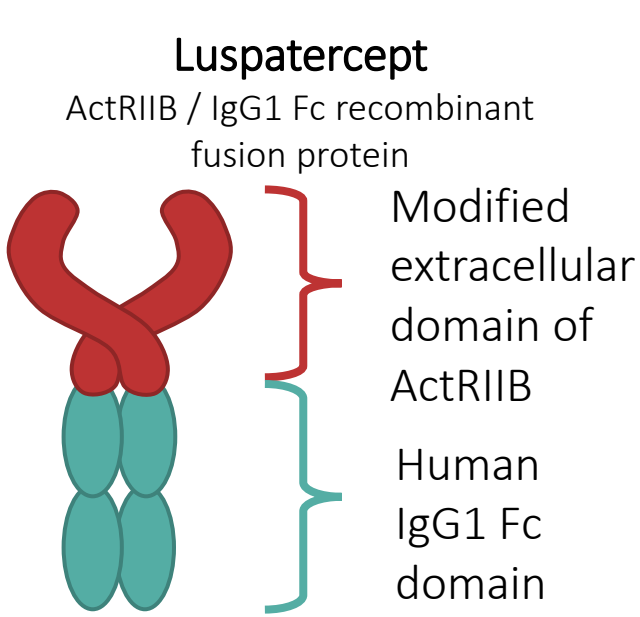
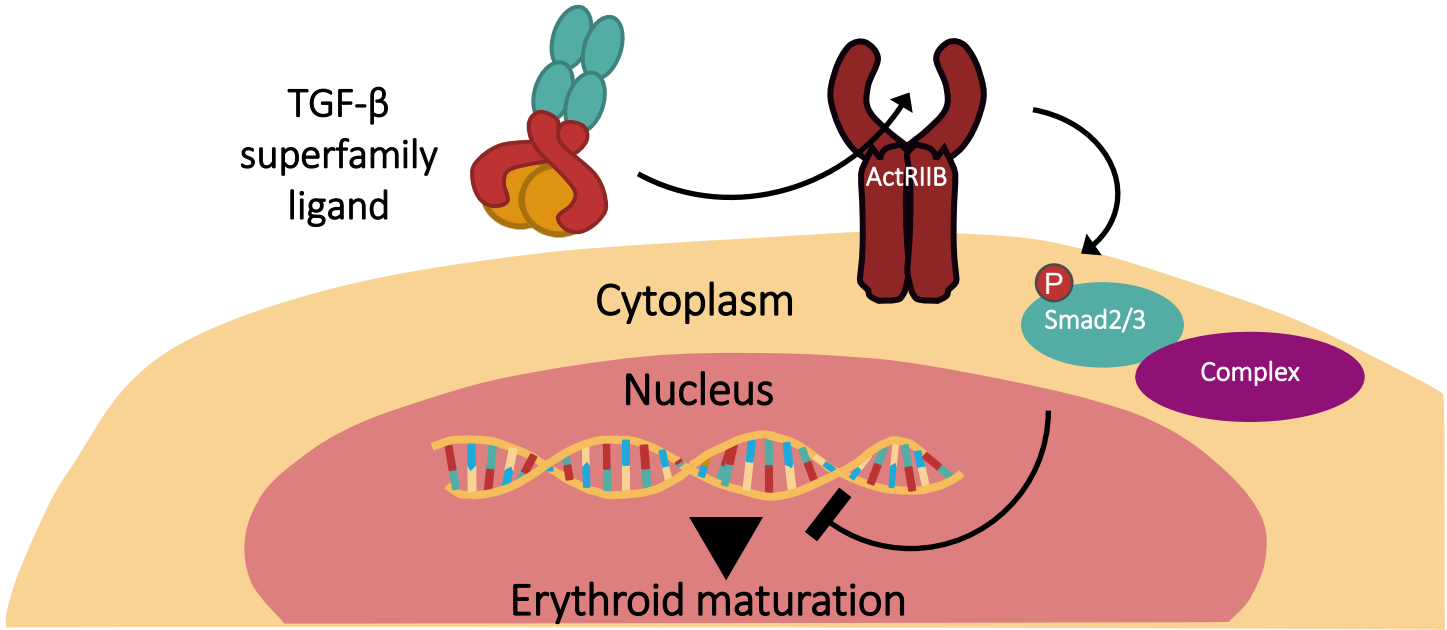
# Improving Ineffective Erythropoiesis in MDS by Luspatercept

- Luspatercept is a first-in-class erythroid maturation agent that neutralizes select TGF-β superfamily ligands to inhibit aberrant Smad2/3 signaling and enhance late-stage erythropoiesis in MDS models
- Luspatercept improves erythropoiesis in MDS-RS as shown in the MEDALIST trial




1. Suragani RN, et al. Nat Med. 2014;20:408-414;
2. Fenaux P, et al. New Engl J Med 2020;382:140–151; 2.

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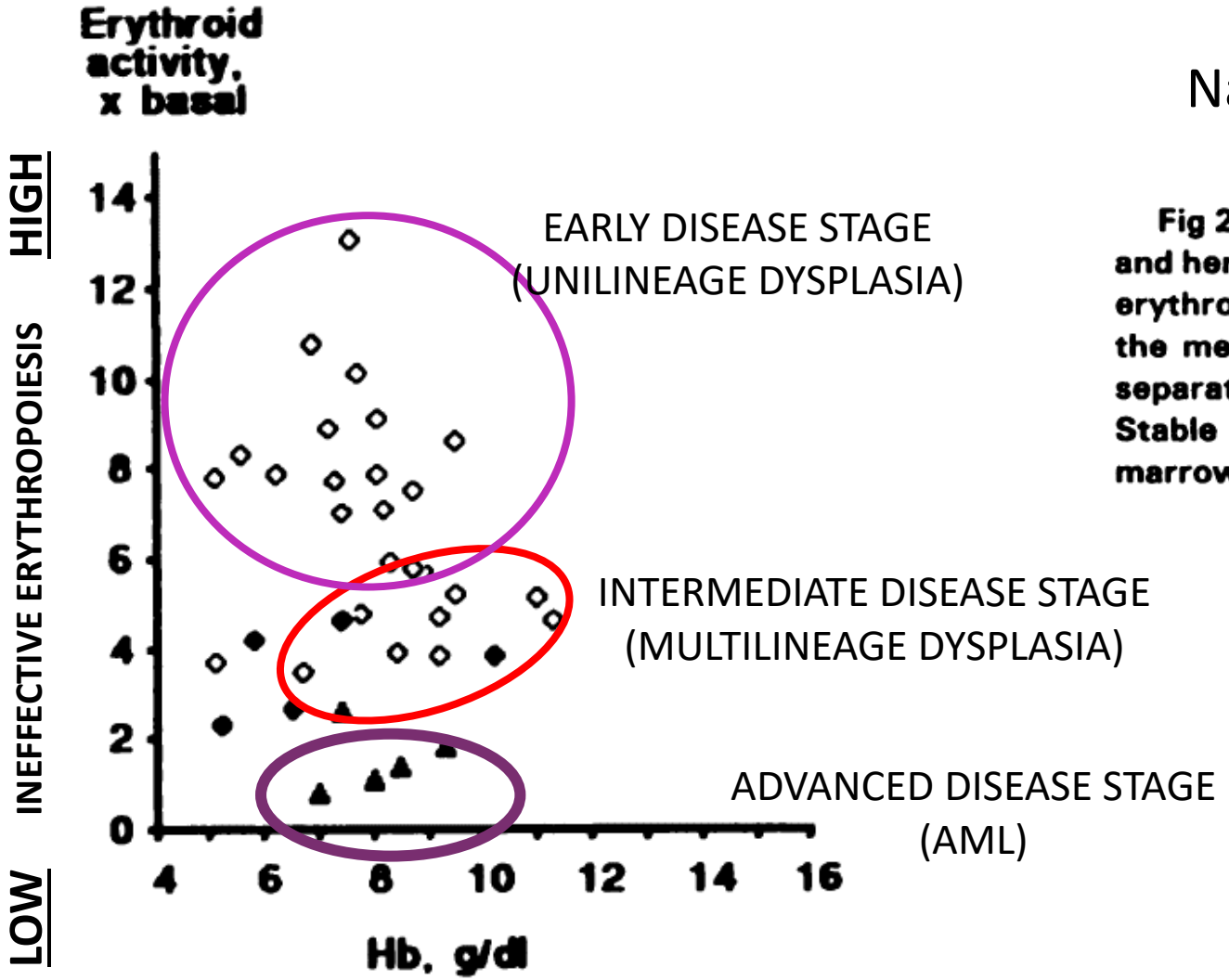
# Contribution of ineffective hematopoiesis to anemia in the natural history of MDS-RS




Natural history of idiopathic refractory sideroblastic anemia

**Fig 2. Relationship between in vivo erythroid marrow activity and hemoglobin level in 37 patients with IRSA. The relative rate of erythropoiesis was derived from the EIT in the patient divided by the mean normal EIT (0.50 mg/dL whole blood/d). Patients are separated into three groups according to the clinical evolution. ○, Stable course or worsening of anemia; ●, evolution into bone marrow failure; ▲, evolution into ANLL.**

Cazzola M et al. Blood. 1988: 108:337-45

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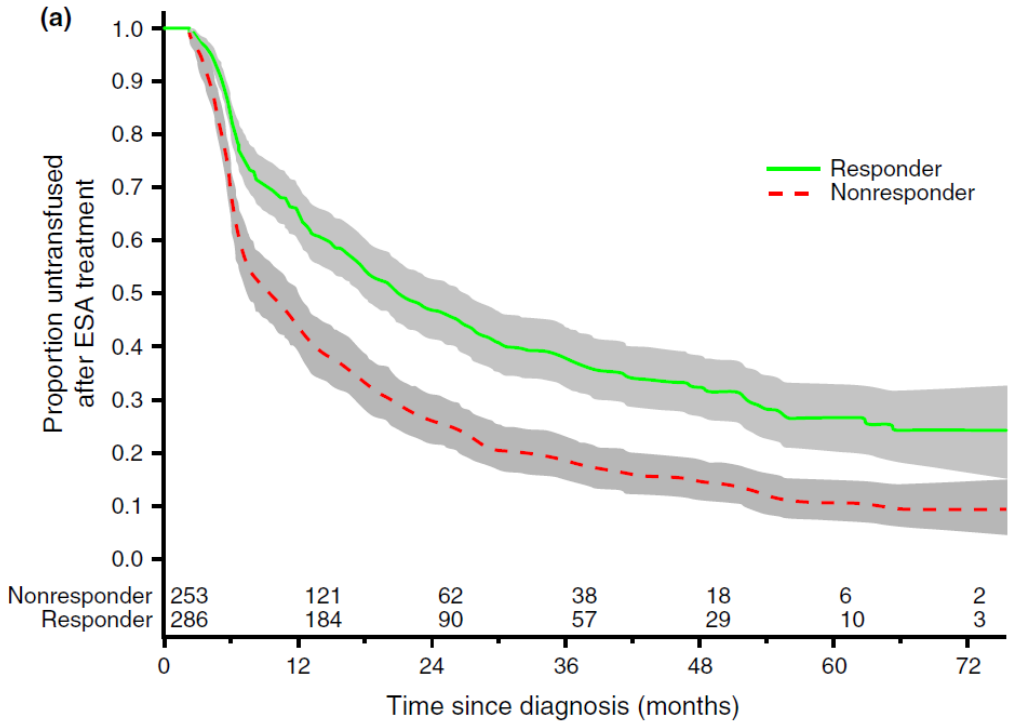
# Low-risk patients with mild anaemia treated with ESA had a significantly better response rate /duration than those treated after the onset of transfusions




Garelius H, J Intern Med . 2017 Mar;281(3):284-299

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# The COMMANDS study

The COMMANDS study (NCT03682536) is a global, phase 3, 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-naïve patients who require RBC transfusions

**Key eligibility criteria**

- Age ≥ 18 years
- IPSS-R very low-, low, or intermediate-risk MDS by WHO 2016, with < 5% blasts in bone marrow[a]
- Required RBC transfusions (2–6 pRBC U/8 wk for a minimum of 8 wk immediately prior to randomization)
- Endogenous sEPO < 500 U/L
- ESA-naïve

**Patients stratified by:**

- Baseline TB (< 4 U/8 wk vs ≥ 4 U/8 wk)
- Baseline RS status (RS+ vs RS−)
- Baseline sEPO level (≤ 200 U/L vs > 200–500 U/L)
- *Post-hoc: SF3B1* mutation status (mutated vs non-mutated)

R 1:1

**Luspatercept (N = 178) starting at 1.0 mg/kg s.c. Q3W**

**Epoetin alfa (N = 176) starting at 450 IU/kg s.c. Q1W**

**Response assessment at day 169 and every 24 weeks thereafter**

**End treatment**
Due to lack of clinical benefit[b] 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]Clinical benefit defined as transfusion reduction of ≥ 2 pRBC units/8 weeks vs baseline. ESA, erythropoiesis-stimulating agent; IPSS-R, Revised International Prognostic Scoring System; IWG, International Working Group; LR-MDS, lower-risk MDS; MDS, myelodysplastic syndromes; pRBC, packed RBC; RBC, red blood cell; RS, ring sideroblasts; s.c., subcutaneously; sEPO, serum erythropoietin; TB, transfusion burden; WHO, World Health Organization; wk, week.

Platzbecker U, Della Porta MG, et al. Lancet 2023;402:373-385

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# Study endpoints

## Composite primary endpoint (weeks 1-24)

- **RBC-TI for ≥ 12 weeks WITH CONCURRENT mean hemoglobin increase ≥ 1.5 g/dL**

## Secondary endpoints (weeks 1-24)

- HI-E response ≥ 8 weeks per IWG criteria
- RBC-TI for 24 weeks
- RBC-TI for ≥ 12 weeks

## Secondary and exploratory endpoints

- Duration of RBC-TI for ≥ 12 weeks (week 1–EOT)
- Impact of baseline mutations on response
- Subgroup analyses

- The data cutoff date for this planned interim analysis was August 31, 2022
    - This prespecified interim analysis was planned for when ~300 patients had either completed 24 weeks of treatment or discontinued prior to completing 24 weeks of treatment (at 85% of information for the primary endpoint)

## Safety

- Treatment discontinuation
- TEAE
- HR-MDS/AML progression
- Death

HI-E, hematological improvement-erythroid; RBC-TI, RBC transfusion independence; TEAE, treatment-emergent adverse event.

Platzbecker & Della Porta Lancet. 2023;402:373-385.

# Demographics and baseline patient characteristics

| | Luspatercept (N = 178) | Epoetin alfa (N = 178) |
|---|---|---|
| **Age, median (range), years** | 74.0 (46.0–93.0) | 75.0 (33.0–91.0) |
| **Female, n (%)** | 71 (39.9) | 87 (48.9) |
| **Time since original MDS diagnosis, median (range), months[a]** | 8.0 (−0.4 to 243.1) | 5.2 (−0.3 to 171.6) |
| **Baseline transfusion burden, median (range), pRBC units** | 3.0 (1–10) | 3.0 (0–14) |
| **Baseline transfusion burden category, n (%)** | | |
| < 4 pRBC units | 114 (64.0) | 109 (61.2) |
| 2 pRBC units | 80 (44.9) | 79 (44.4) |
| ≥ 4 pRBC units | 64 (36.0) | 69 (38.8) |
| **IPSS-R risk classification at baseline, n (%)** | | |
| Very low | 16 (9.0) | 17 (9.6) |
| Low | 126 (70.8) | 131 (73.6) |
| Intermediate | 34 (19.1) | 28 (15.7) |
| Other[b] | 1 (0.6) | 0 |
| Missing[c] | 1 (0.6) | 2 (1.1) |

[a]Number of months from date of original diagnosis to date of informed consent. [b]The central pathology laboratory confirmed the MDS diagnosis with an IPSS-R score of intermediate at screening for 1 patient in the luspatercept arm; at the next bone marrow assessment, the central laboratory sent the report with an IPSS-R score of high, confirmed that the score at screening was also high, and acknowledged the mistake. [c]For 3 patients (1 in the luspatercept arm and 2 in the epoetin alfa arm) the risk score could not be calculated.

Platzbecker & Della Porta Lancet. 2023;402:373-385.

# Demographics and baseline patient characteristics

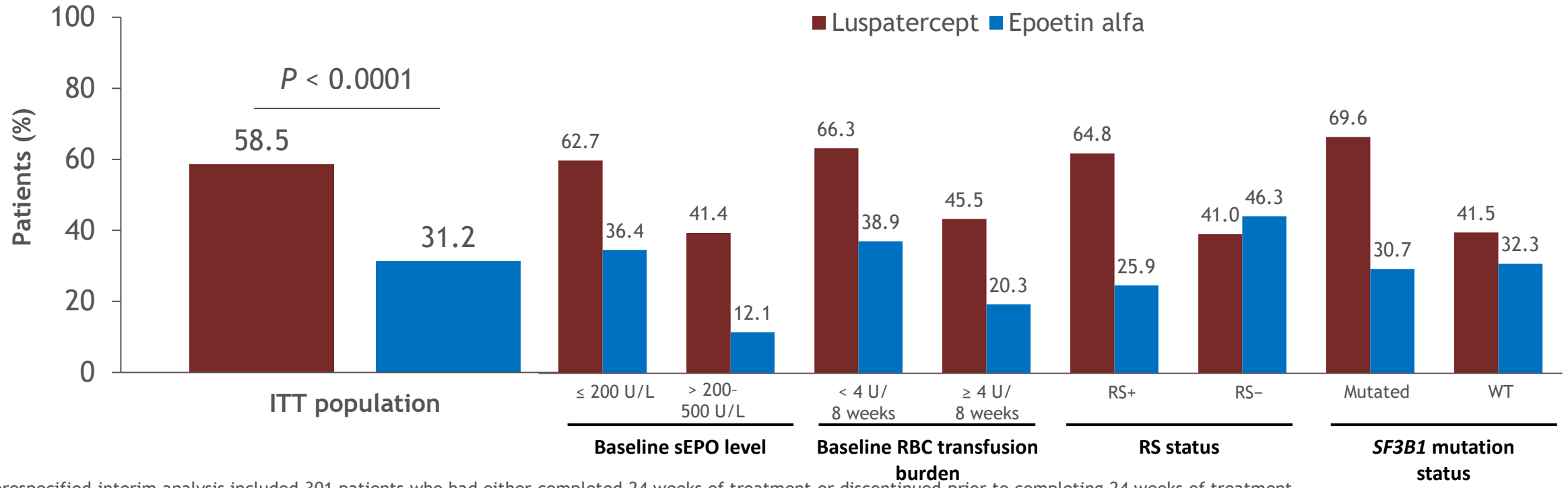
| | Luspatercept (N = 178) | Epoetin alfa (N = 178) |
|---|---|---|
| **Ring sideroblast status, n (%)** | | |
| RS+ | 130 (73.0) | 128 (71.9) |
| RS− | 48 (27.0) | 49 (27.5) |
| Missing[d] | 0 | 1 (0.6) |
| ***SF3B1* mutation status, n (%)** | | |
| Mutated | 111 (62.4) | 99 (55.6) |
| Non-mutated | 65 (36.5) | 72 (40.4) |
| Missing | 2 (1.1) | 7 (3.9) |
| **Hemoglobin, median (range), g/dL** | 7.80 (4.7–9.2) | 7.8 (4.5–10.2) |
| **Serum erythropoietin, median (range), U/L** | 78.71 (7.8–495.8) | 85.9 (4.6–462.5) |
| **Platelet count, median (range), $10^9$/L** | 230.0 (38–770) | 234.5 (47–715) |
| **Absolute neutrophil count, median (range), $10^9$/L** | 2.4 (0.4–9.1) | 2.3 (0.5–13.3) |
| **Serum ferritin, median (range), µg/L** | 626.2 (12.4–3170.0) | 651.3 (39.4–6960.5) |

[d]1 patient in the epoetin alfa arm had a bone marrow biopsy assessed by the central lab with a diagnosis of MDS with multilineage dysplasia and RS status was not provided.

Platzbecker & Della Porta Lancet. 2023;402:373-385.

# Primary endpoint: luspatercept superior to epoetin alfa

- Of 301 pts included in the efficacy analysis, **86 (58.5%) patients receiving luspatercept and 48 (31.2%) epoetin alfa achieved the primary endpoint**
    - Achievement of the primary endpoint favored luspatercept or was similar to epoetin alfa for all subgroups analyzed




This prespecified interim analysis included 301 patients who had either completed 24 weeks of treatment or discontinued prior to completing 24 weeks of treatment.

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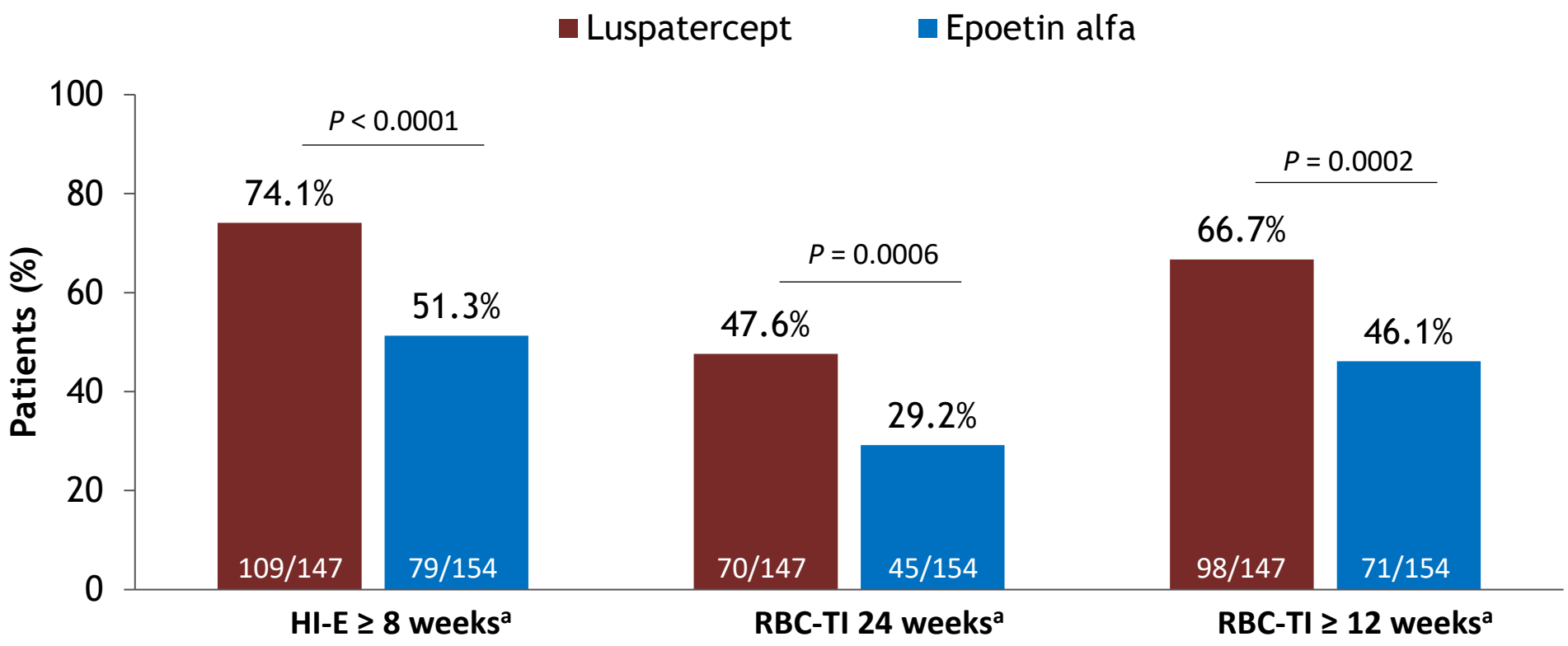
# Secondary endpoints: luspatercept superior to epoetin alfa

| | Luspatercept (N = 147) | Epoetin alfa (N = 154) |
|---|---|---|
| **Time to first RBC transfusion (week 1-EOT)** | n = 93<br>168.0 (64.0–323.0) | n = 116<br>42.0 (22.0–55.0) |




[a]During weeks 1-24.

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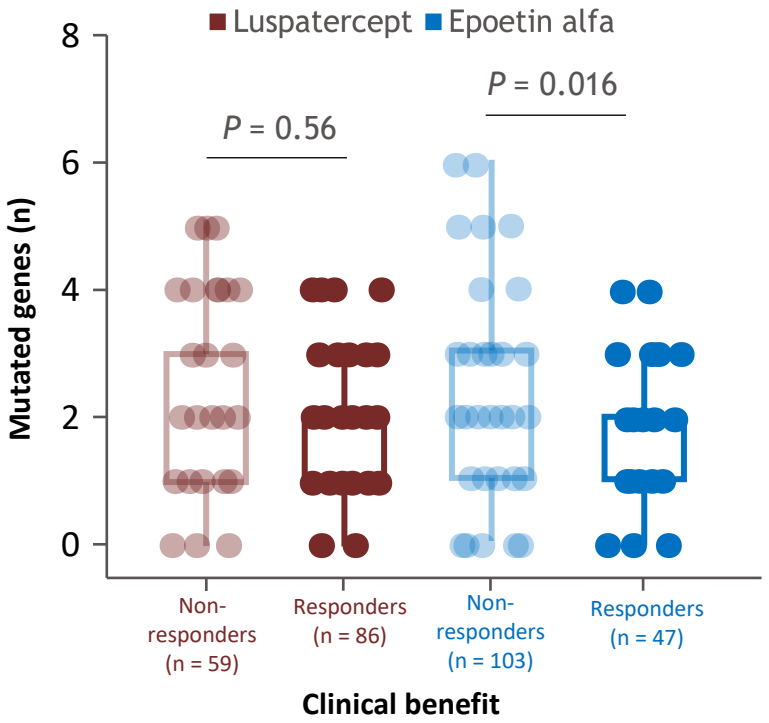
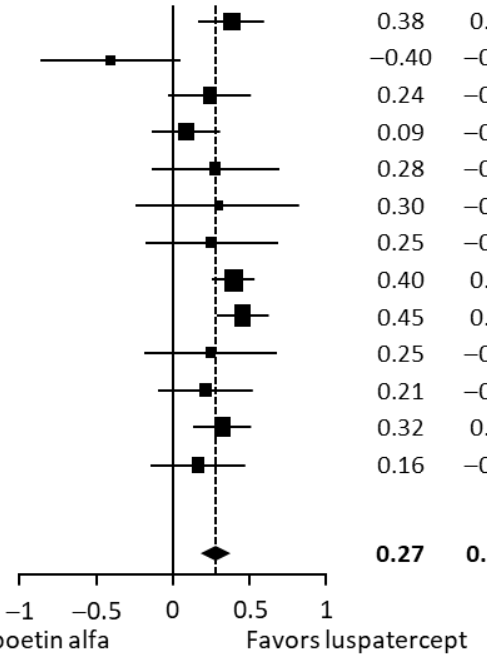
# Exploratory endpoints: mutational burden association with response and broad activity of luspatercept across various mutational burden

- Baseline mutational burden was lower in primary endpoint responders versus non-responders in the epoetin alfa arm and was significantly associated with the achievement of clinical benefit ($P$ = 0.016); but not for luspatercept ($P$ = 0.56)
- **Patients with *SF3B1*, *SF3B1α*, *ASXL1*, and *TET2* mutations were associated with favorable clinical benefit with luspatercept versus epoetin alfa**
- Luspatercept patients had a higher probability of achieving clinical benefit, regardless of overall mutational burden, versus epoetin alfa




| Marker | Luspatercept Responders | Luspatercept Total | Epoetin alfa Responders | Epoetin alfa Total | Risk difference | 95% CI | Weight (%) |
|---|---|---|---|---|---|---|---|
| *ASXL1* | 15 | 31 | 3 | 29 | 0.38 | 0.17 to 0.59 | 10.5 |
| *CBL* | 0 | 5 | 2 | 5 | −0.40 | −0.85 to 0.05 | 3.6 |
| *DNMT3A* | 19 | 28 | 11 | 25 | 0.24 | −0.02 to 0.50 | 8.1 |
| *DTA.SF3B1.n*[a] | 12 | 31 | 12 | 40 | 0.09 | −0.14 to 0.31 | 9.8 |
| *EZH2* | 5 | 10 | 2 | 9 | 0.28 | −0.13 to 0.69 | 4.2 |
| *IDH2* | 3 | 6 | 1 | 5 | 0.30 | −0.23 to 0.83 | 2.7 |
| *RUNX1* | 1 | 4 | 0 | 9 | 0.25 | −0.17 to 0.67 | 4.0 |
| *SF3B1* | 64 | 92 | 27 | 90 | 0.40 | 0.26 to 0.53 | 15.1 |
| *SF3B1*$^{alpha}$[b] | 41 | 55 | 16 | 55 | 0.45 | 0.29 to 0.62 | 12.9 |
| *SF3B1*$^{beta}$[c] | 1 | 4 | 0 | 8 | 0.25 | −0.18 to 0.68 | 3.9 |
| *SRSF2* | 5 | 14 | 2 | 14 | 0.21 | −0.10 to 0.53 | 6.4 |
| *TET2* | 30 | 48 | 16 | 53 | 0.32 | 0.14 to 0.51 | 11.8 |
| *U2AF1* | 6 | 16 | 4 | 19 | 0.16 | −0.14 to 0.46 | 6.8 |
| **Random effects model** | | **344** | | **361** | **0.27** | **0.18 to 0.37** | **100.0** |




[a]*DTA.SF3B1.n* is a wild-type *SF3B1* with concomitant mutations in *ASXL1* and/or *TET2* or *DNMT3A*. [b]*SF3B1alpha* is defined as *SF3B1* mutations with concomitant mutation of *DNMT3A* or *ASXL1* and/or *TET2*. [c]*SF3B1beta* is defined as mutated *SF3B1* with concomitant mutations in any of the listed genes *BCOR*, *BCORL1*, *NRAS*, *RUNX1*, *SRSF2* or *STAG2*.

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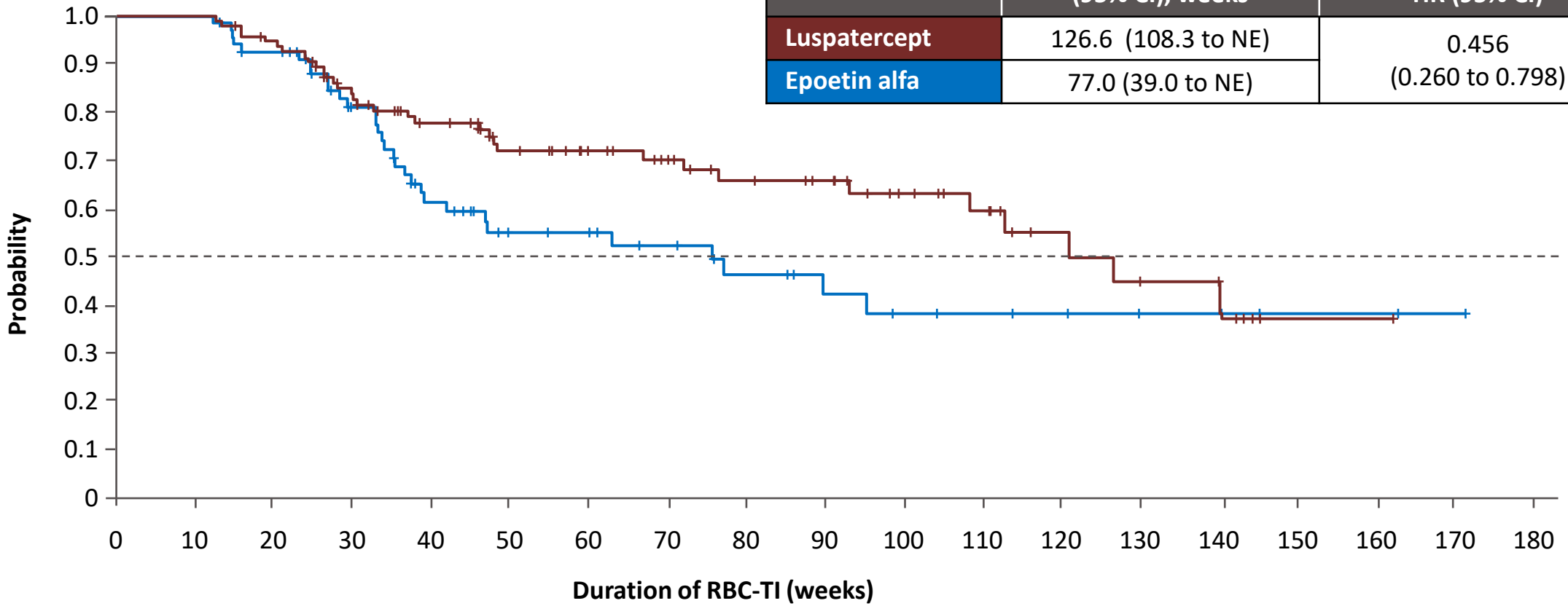
# Duration of RBC-TI ≥ 12 weeks[a]

| | Median duration (95% CI), weeks | HR (95% CI) |
|---|---|---|
| Luspatercept | 126.6 (108.3 to NE) | 0.456 (0.260 to 0.798) |
| Epoetin alfa | 77.0 (39.0 to 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 |

EOT, end of treatment; NE, not estimable; RBC-TI, red blood cell transfusion independence.
[a]In ITT responders during weeks 1–EOT.

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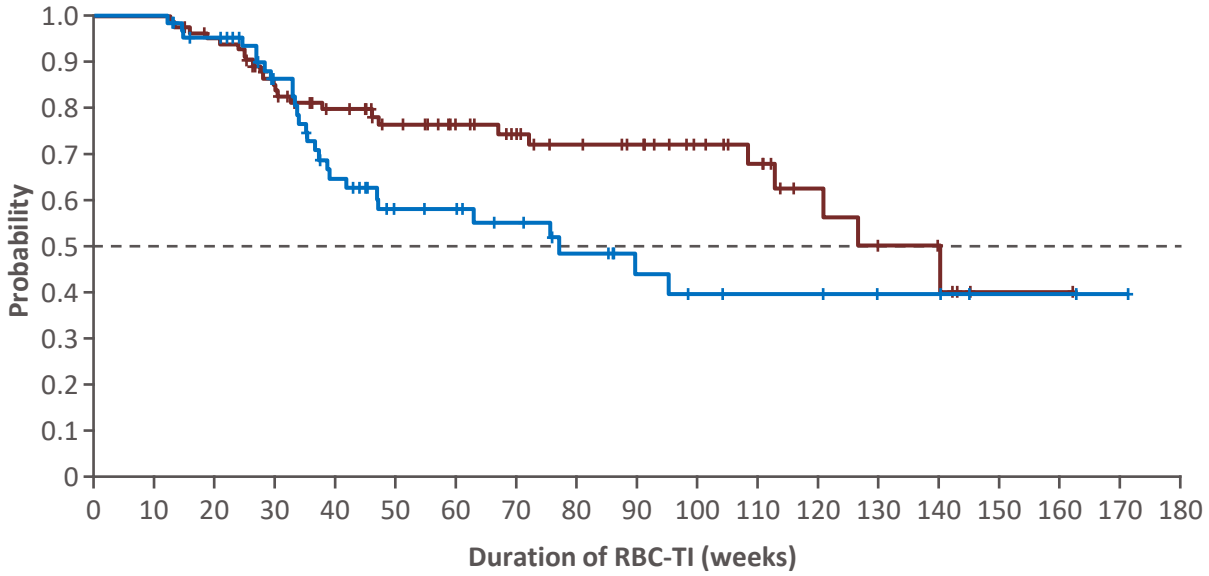
# Duration of RBC-TI ≥ 12 weeks[a]: sEPO subgroups

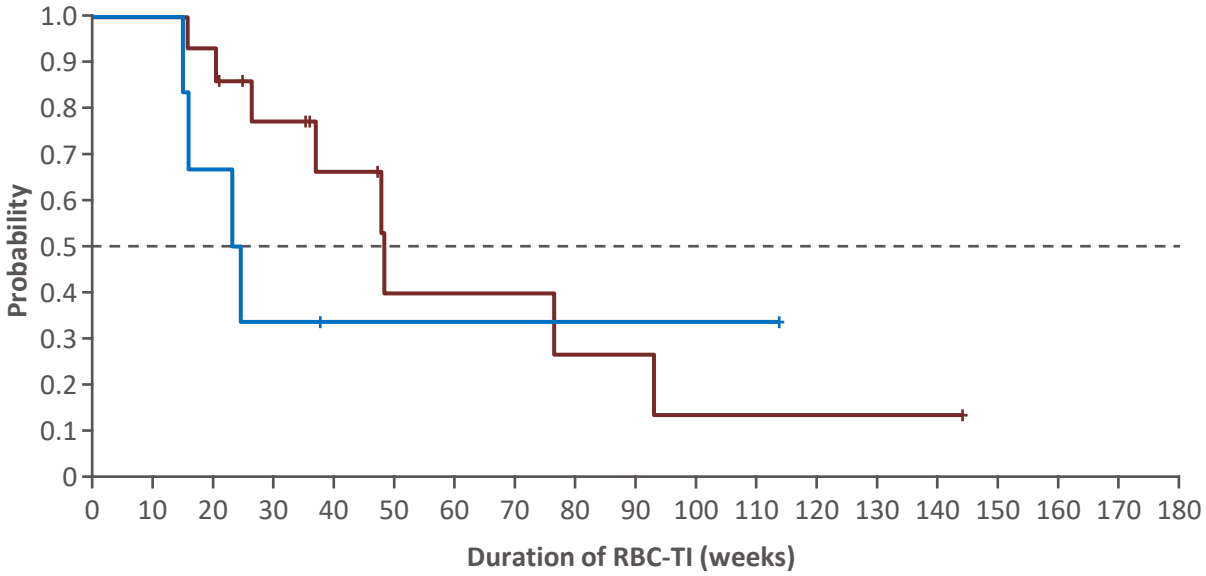
| Median duration (95% CI), weeks | Luspatercept | Epoetin alfa | HR (95% CI) |
|---|---|---|---|
| **sEPO ≤ 200 U/L** | 140.1 (112.7 to NE) | 77.0 (41.9 to NE) | **0.601 (0.348 to 1.038)** |
| **sEPO >200-500 U/L** | 48.3 (26.3 to 93.0) | 23.9 (14.9 to NE) | **0.624 (0.186 to 2.092)** |

## sEPO ≤ 200 U/L




| No. at risk | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Luspatercept | 84 | 84 | 78 | 65 | 55 | 46 | 39 | 34 | 29 | 26 | 20 | 16 | 10 | 7 | 5 | 1 | 1 | 0 | |
| Epoetin alfa | 65 | 65 | 59 | 45 | 32 | 23 | 22 | 18 | 14 | 10 | 8 | 7 | 7 | 5 | 5 | 2 | 2 | 1 | 0 |

## sEPO > 200-500 U/L




| No. at risk | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Luspatercept | 14 | 14 | 13 | 9 | 6 | 3 | 3 | 3 | 2 | 2 | 1 | 1 | 1 | 1 | 1 | 0 | | | |
| Epoetin alfa | 6 | 6 | 4 | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | | | | | | |

EOT, end of treatment; NE, not estimable; RBC-TI, red blood cell transfusion independence.
[a]In ITT responders during weeks 1–EOT.

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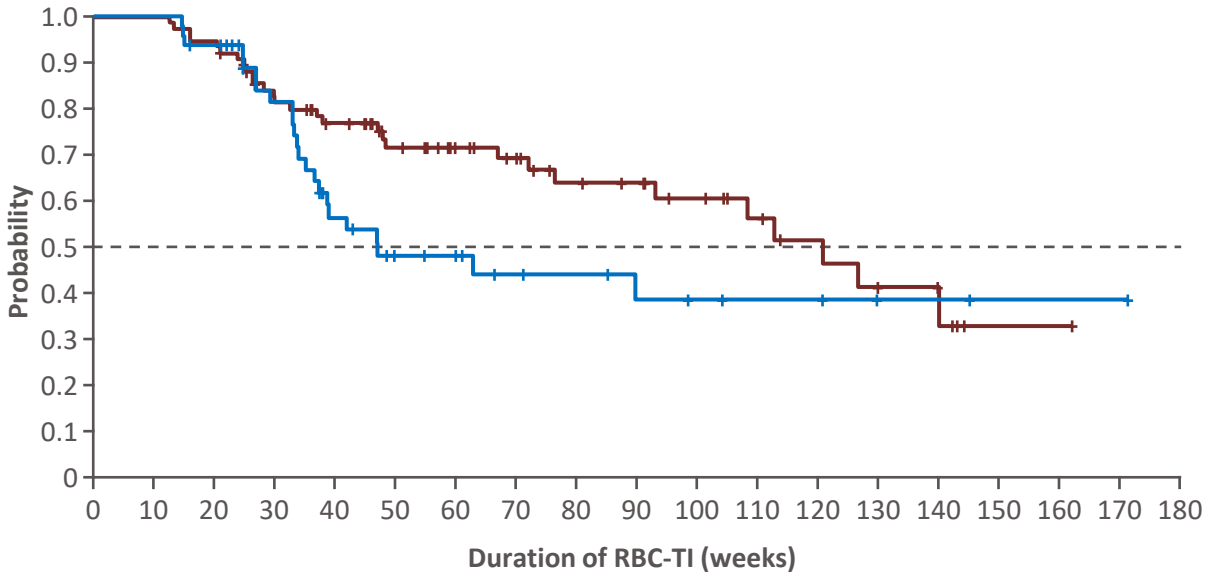
# Duration of RBC-TI ≥ 12 weeks[a]: RS subgroups

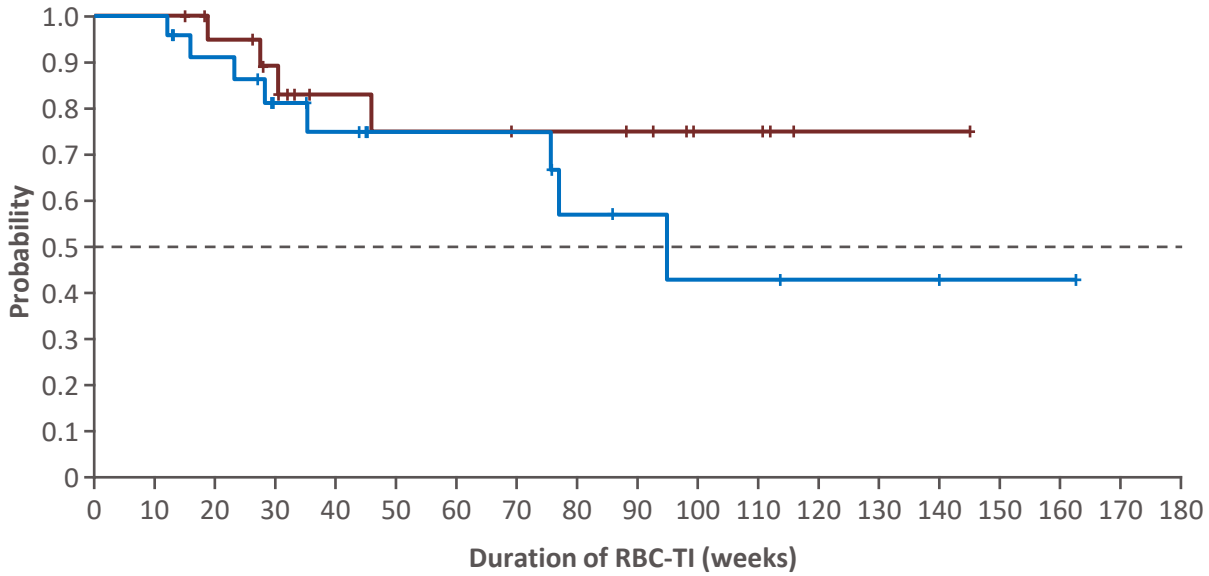
| Median duration (95% CI), weeks | Luspatercept | Epoetin alfa | HR (95% CI) |
|---|---|---|---|
| **RS+** | 120.9 (76.4 to NE) | 47.0 (36.6 to NE) | **0.626 (0.361 to 1.085)** |
| **RS–** | NE (46.0 to NE) | 95.1 (35.3 to NE) | **0.492 (0.148 to 1.638)** |

**RS+**




| No. at risk | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Luspatercept | 77 | 77 | 73 | 59 | 51 | 40 | 33 | 29 | 23 | 21 | 17 | 13 | 10 | 7 | 5 | 1 | 1 | 0 | |
| Epoetin alfa | 48 | 48 | 44 | 33 | 21 | 15 | 14 | 10 | 9 | 7 | 6 | 5 | 5 | 3 | 3 | 1 | 1 | 1 | 0 |

**RS–**




| No. at risk | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Luspatercept | 21 | 21 | 18 | 15 | 10 | 9 | 9 | 8 | 8 | 7 | 4 | 4 | 1 | 1 | 1 | 0 | | | |
| Epoetin alfa | 23 | 23 | 19 | 14 | 12 | 9 | 9 | 9 | 6 | 4 | 3 | 3 | 2 | 2 | 2 | 1 | 1 | 0 | |

EOT, end of treatment; NE, not estimable; RBC-TI, red blood cell transfusion independence.
[a]In ITT responders during weeks 1–EOT.

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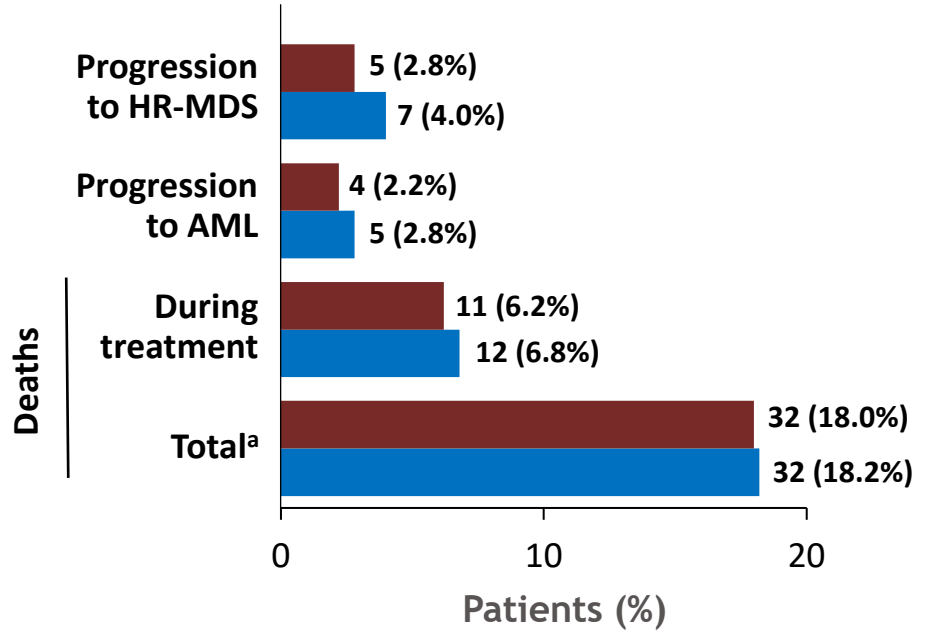
# Safety

| | Luspatercept (N = 178) | | Epoetin alfa (N = 176) | |
|---|---|---|---|---|
| **Patients, n (%)** | **Any grade** | **Grade 3/4** | **Any grade** | **Grade 3/4** |
| **Heme-related TEAEs** | | | | |
| Anemia | 17 (9.6) | 13 (7.3) | 17 (9.7) | 12 (6.8) |
| Thrombocytopenia | 11 (6.2) | 7 (3.9) | 3 (1.7) | 1 (0.6) |
| Neutropenia | 9 (5.1) | 7 (3.9) | 13 (7.4) | 10 (5.7) |
| Leukocytopenia | 2 (1.1) | 0 | 3 (1.7) | 0 |
| **TEAEs of interest** | | | | |
| Fatigue | 26 (14.6) | 1 (0.6) | 12 (6.8) | 1 (0.6) |
| Diarrhea | 26 (14.6) | 2 (1.1) | 20 (11.4) | 1 (0.6) |
| Peripheral edema | 23 (12.9) | 0 | 12 (6.8) | 0 |
| Asthenia | 22 (12.4) | 0 | 25 (14.2) | 1 (0.6) |
| Nausea | 21 (11.8) | 0 | 13 (7.4) | 0 |
| Dyspnea | 21 (11.8) | 7 (3.9) | 13 (7.4) | 2 (1.1) |
| TEE | 8 (4.5) | 5 (2.8) | 5 (2.8) | 1 (0.6) |

**TEAEs of any grade**
164 (92.1%) luspatercept
150 (85.2%) epoetin alfa

**Treatment duration, median (range), weeks**
41.6 (0–165) luspatercept
27.0 (0–171) epoetin alfa




Safety data are not exposure-adjusted.
[a]Deaths during treatment period and post-treatment period. TEE, thromboembolic event.

Platzbecker U, Della Porta MG, et al. Lancet 2023;402:373-385

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# COMMANDS trial: Summary

- COMMANDS study achieved its primary endpoint, demonstrating that luspatercept is superior to ESA in front-line transfusion-dependent LR-MDS
    - The primary endpoint was achieved in 59% of patients treated with luspatercept vs 31% with ESA
    - Median duration of response was 127 weeks vs 77 in favor of luspatercept, which is ~1 year longer than ESAs
- Luspatercept provides clinical benefit regardless of subgroups and baseline mutational burden
- Luspatercept has a manageable and predictable safety profile, consistent with previous clinical experience and convenient (Q3W) administration

**Luspatercept is the first and only therapy to demonstrate superiority in a head-to-head study against ESAs and brings a paradigm shift in the treatment of LR-MDS-associated anemia**

Platzbecker & Della Porta Lancet. 2023;402:373-385.

# Personalized (first-line) treatment of LR-MDS with severe anemia

**MDS with *SF3B1* mutations (MDS_RS)**

Luspatercept is associated with higher rate of response and longer duration of response vs ESA

**MDS without RS**

Luspatercept is associated with comparable rate of response but longer duration of response vs ESA

High baseline sEPO level
High baseline transfusion burden

Luspatercept is superior to ESA

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# ESA- Still the 1st line for LR-MDS? Yes perspective

Marien Hospital Düsseldorf

D·MDS


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# DISCLOSURES OF CONFLICT OF INTEREST

| Name of Company | Research support | Employee | Consultant | Stockholder | Speaker's Bureau | Scientific Advisory Board | Other |
|---|---|---|---|---|---|---|---|
| **BMS** | | | | | | X | |
| **AMGEN** | | | X | | | | |
| **Geron** | | | X | | | | |
| **NOVARTIS** | | | X | | | X | |
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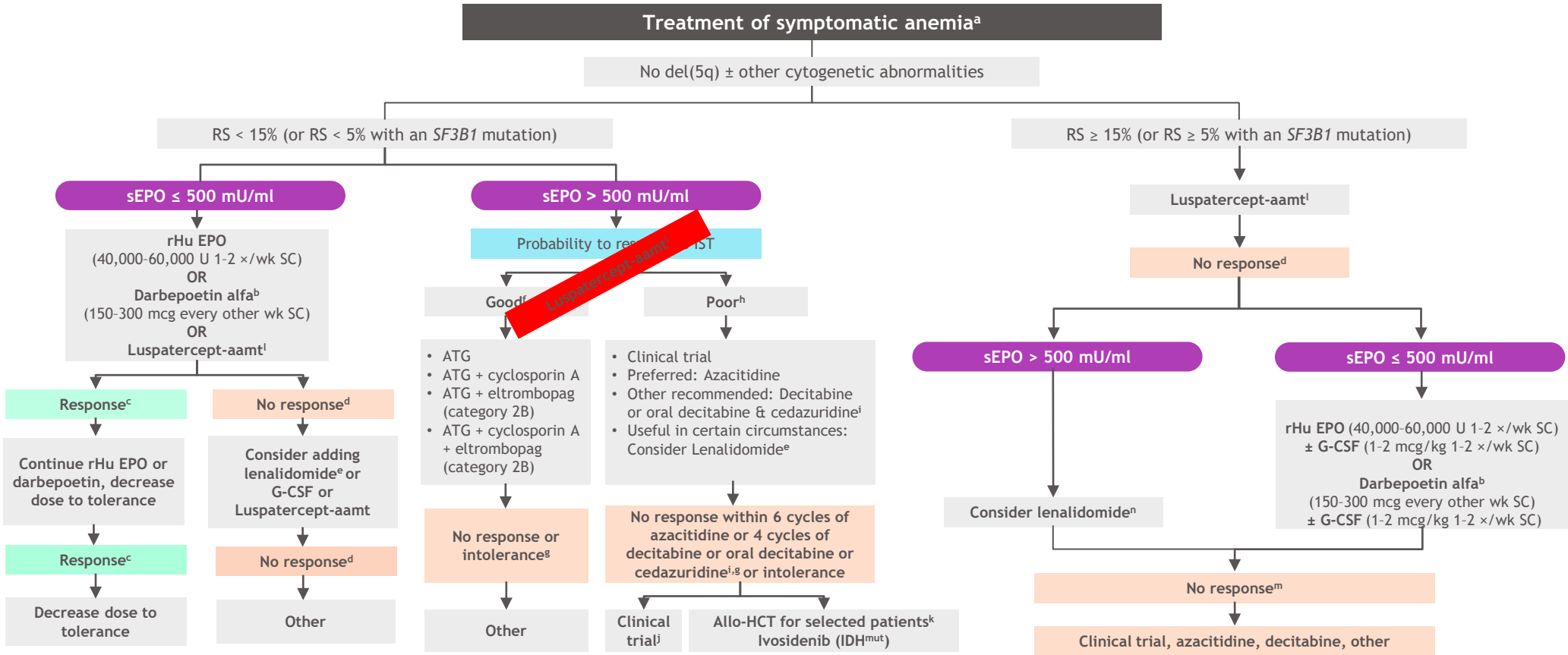
# NCCN Clinical Practice Guidelines In Oncology (NCCN Guidelines®) V3.2023: Myelodysplastic Syndromes




allo-HCT, allogeneic hematopoietic cell transplant; ATG, anti-thymocyte globulin; EPO, erythropoietin; G-CSF, granulocyte colony-stimulating factor; IST, immunosuppressive therapy; rHu, recombinant human; RS, ring sideroblasts; SC, subcutaneous; sEPO, serum EPO

# Loeb's Laws of Medicine

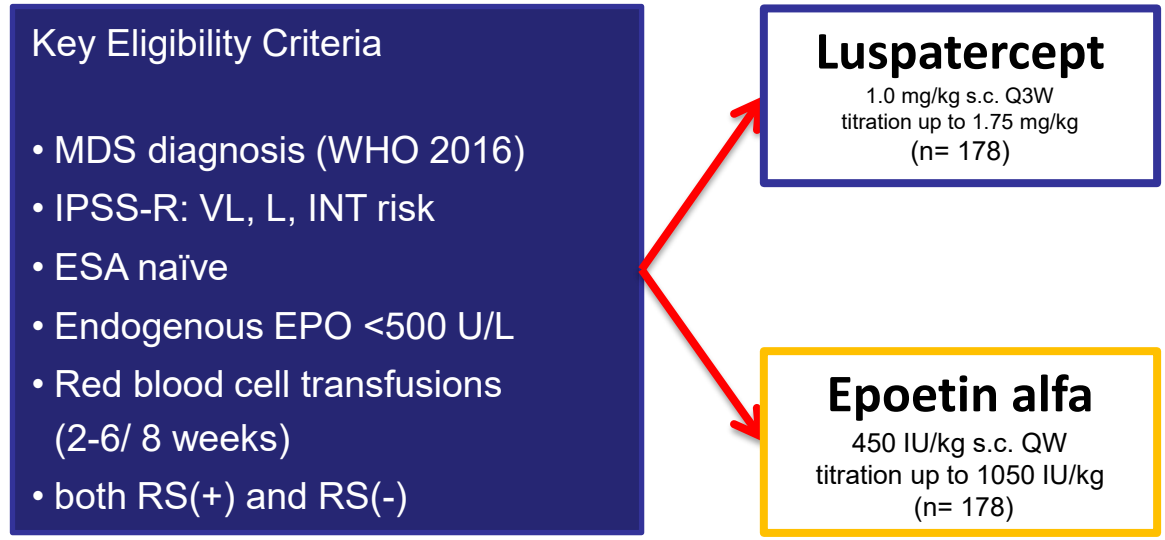
- Law No. 1: *If what you're doing works in your patient, keep doing it*
- Law No. 2: *If what you're doing doesn't work in your patient, stop doing it*
- Law No. 3: *If you do not know what to do, do nothing*
- Law No. 4: *Never let a surgeon get your patient*

**Robert Loeb** (1895 – 1973) American Physician; "Cecil and Loeb's Textbook of Medicine"

I only believe in statistics that i doctored myself

# COMMANDS Trial

Luspatercept vs EPO in RS+/RS- MDS




Platzbecker et al. Lancet 2023; 402: 373-3853

# Prediction of EPO-response in MDS

Marien Hospital Düsseldorf

D·MDS

| Variable | | Score | | Score |
|---|---|---|---|---|
| Transfusions | 0 U/month | 0 | ≤4 U/month | 1 |
| Serum-Epo | <200 U/l | 0 | ≥200 U/l | 2 |

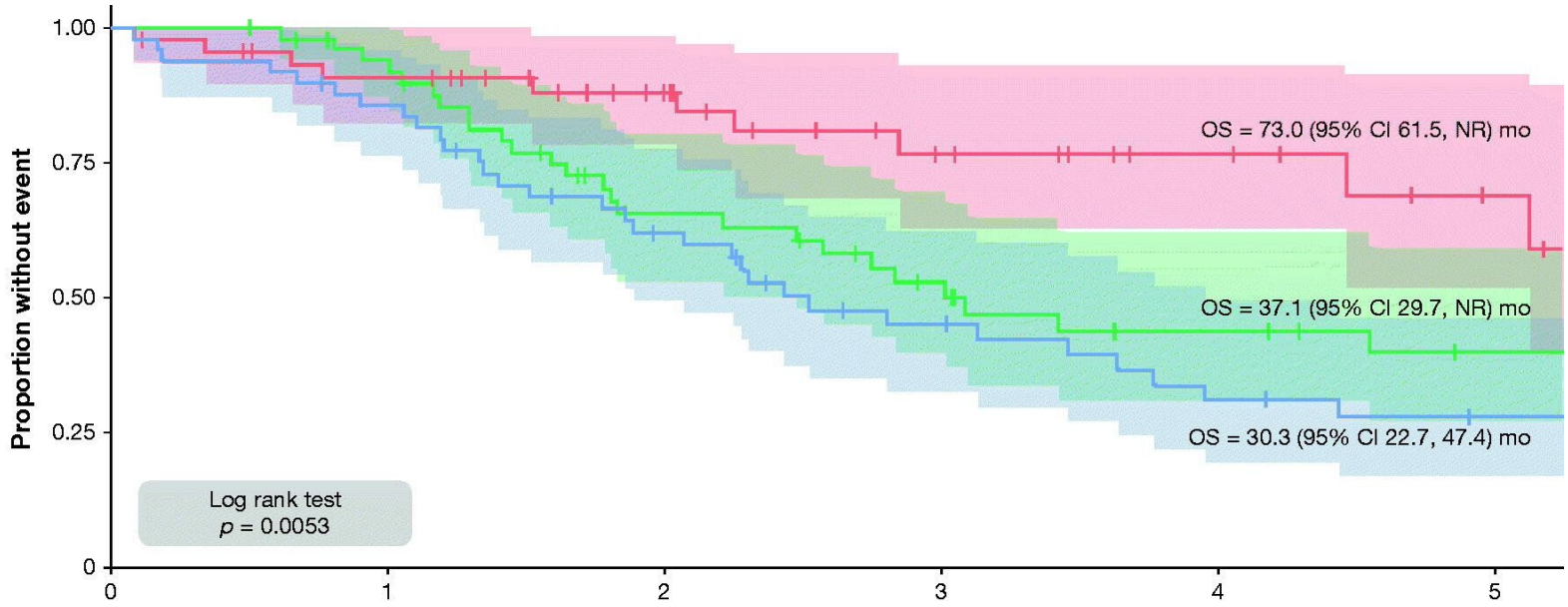
**Prediction**

**Score = 0:** **67%**
**Score 1:** **25%**
**Score ≥ 2:** **0%**

Fenaux P, Santini V, Spiriti MAA, et al. Leukemia. 2018;32:2648-2658

# RBC burden

The cumulative density of RBC transfusions is associated with significantly greater mortality, hospitalization, and inferior HRQoL

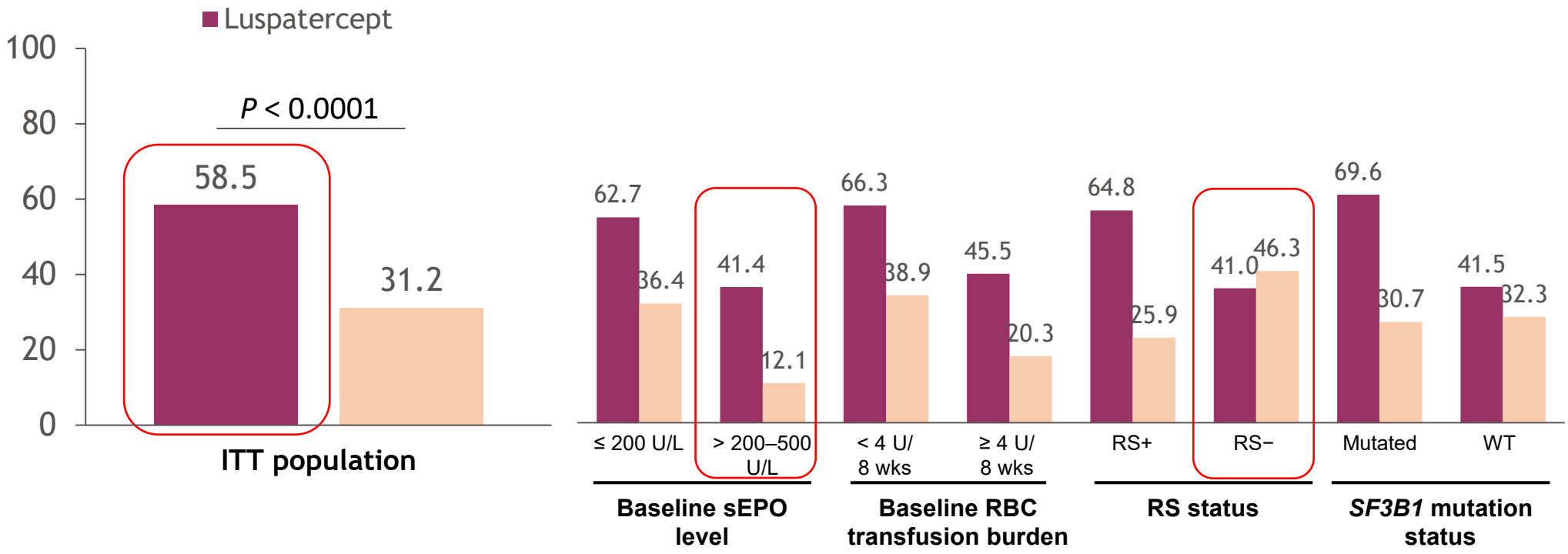



| No. at risk | | | | | | |
|---|---|---|---|---|---|---|
| TI | 45 | 38 | 27 | 17 | 12 | 7 |
| Moderate burden | 51 | 45 | 27 | 19 | 13 | 9 |
| High burden | 49 | 41 | 27 | 17 | 11 | 8 |

Buckstein R. et al. Leukemia & Lymphoma 2023

# COMMANDS: Luspatercept vs. Epoetin

Transfusion independence ≥ 12 weeks +
mean Hb increase ≥ 1.5 g/dl




Garcia-Manero G, et al. ASCO2023 ; Platzbecker et al. Lancet 2023

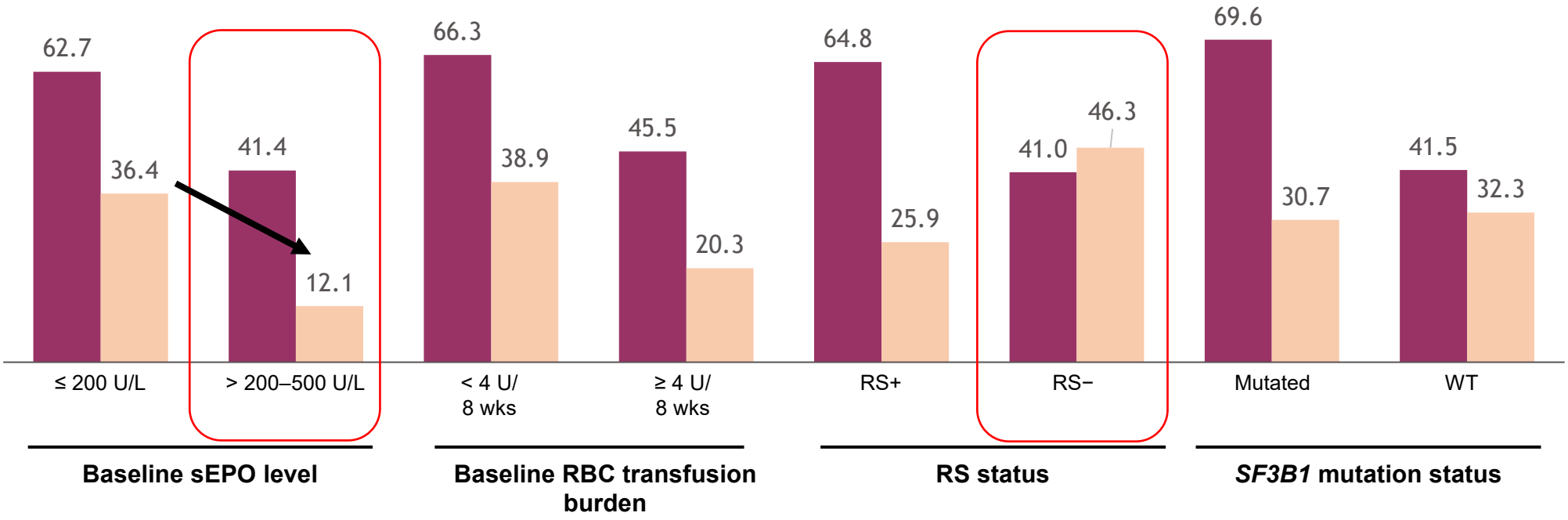
# Patient demographics and disease characteristics at baseline

| | Luspatercept (n=178) | Epoetin alfa (n=178) | Total (n=356) |
|---|---|---|---|
| Age, years | 74 (68–80) | 75 (69–80) | 74 (69–80) |
| Sex | | | |
| Male | 107 (60%) | 91 (51%) | 198 (56%) |
| Female | 71 (40%) | 87 (49%) | 158 (44%) |
| Time since original diagnosis of myelodysplastic syndromes, months* | 8·0 (2·0–28·8) | 5·2 (1·6–18·5) | 6·2 (1·8–23·6) |
| WHO 2016 classification of myelodysplastic syndromes | | | |
| Myelodysplastic syndromes with single lineage dysplasia | 1 (1%) | 4 (2%) | 5 (1%) |
| Myelodysplastic syndromes with multiple lineage dysplasia | 49 (28%) | 46 (26%) | 95 (27%) |
| Myelodysplastic syndromes with single lineage dysplasia and ring sideroblasts | 2 (1%) | 6 (3%) | 8 (2%) |
| Myelodysplastic syndromes with multiple lineage dysplasia and ring sideroblasts | 125 (70%) | 117 (66%) | 242 (68%) |
| Myelodysplastic syndromes or myeloproliferative neoplasm with ring sideroblasts and thrombocytosis | 1 (1%) | 4 (2%) | 5 (1%) |
| Missing† | 0 | 1 (1%) | 1 (<1%) |

| | Luspatercept (n=178) | Epoetin alfa (n=178) | Total (n=356) |
|---|---|---|---|
| IPSS-R myelodysplastic syndromes risk category | | | |
| Very low | 16 (9%) | 17 (10%) | 33 (9%) |
| Low | 126 (71%) | 131 (74%) | 257 (72%) |
| Intermediate | 34 (19%) | 28 (16%) | 62 (17%) |
| High‡ | 1 (1%) | 0 | 1 (<1%)† |
| Missing§ | 1 (1%) | 2 (1%) | 3 (1%) |
| Serum erythropoietin concentration, U/L | 78·7 (41·7–185·3) | 85·9 (40·5–177·8) | 84·5 (40·9–179·1) |
| Serum erythropoietin category, U/L | | | |
| ≤200 | 141 (79%) | 141 (79%) | 282 (79%) |
| ≤100 | 100 (56%) | 103 (58%) | 203 (57%) |
| >100 and ≤200 | 41 (23%) | 38 (21%) | 79 (22%) |
| >200 and <500 | 37 (21%) | 37 (21%) | 74 (21%) |
| Ring sideroblasts¶ | 130/178 (73%) | 128/177 (72%) | 258/355 (73%) |
| Mutated *SF3B1*‖ | 111/176 (63%) | 99/171 (58%) | 210/347 (61%) |
| Red blood cell transfusion burden, units per 8 weeks** | 3 (2–4) | 3 (2–4) | 3 (2–4) |
| Red blood cell transfusion burden category | | | |
| <4 units per 8 weeks | 114 (64%) | 109 (61%) | 223 (63%) |
| 2 units per 8 weeks | 80 (45%) | 79 (44%) | 159 (45%) |
| ≥4 units per 8 weeks | 64 (36%) | 69 (39%) | 133 (37%) |
| Pretransfusion haemoglobin concentration, g/dL | 7·8 (7–8) | 7·8 (7–8) | 7·8 (7–8) |
| Haemoglobin category | | | |
| <8 g/dL | 107 (60%) | 106 (60%) | 213 (60%) |
| ≥8 g/dL | 71 (40%) | 72 (40%) | 143 (40%) |
| Platelet count, $10^9$/L | 230 (155–304) | 235 (140–324) | 232 (144–310) |

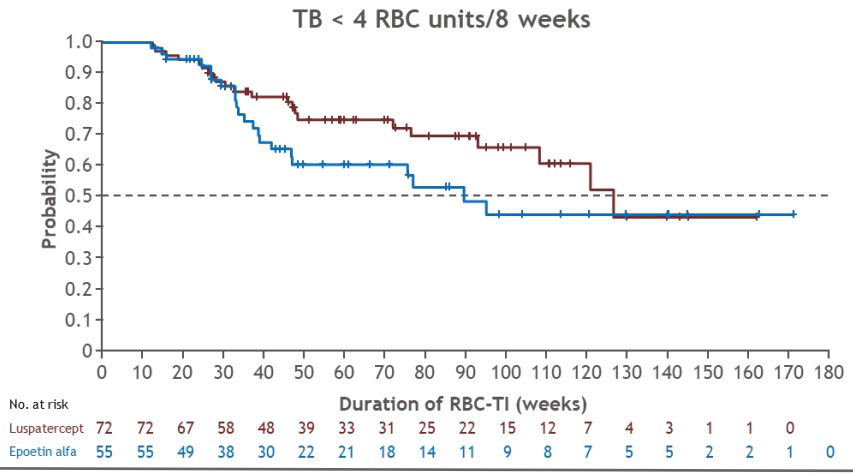
Platzbecker et al. Lancet 2023; 402: 373-3853

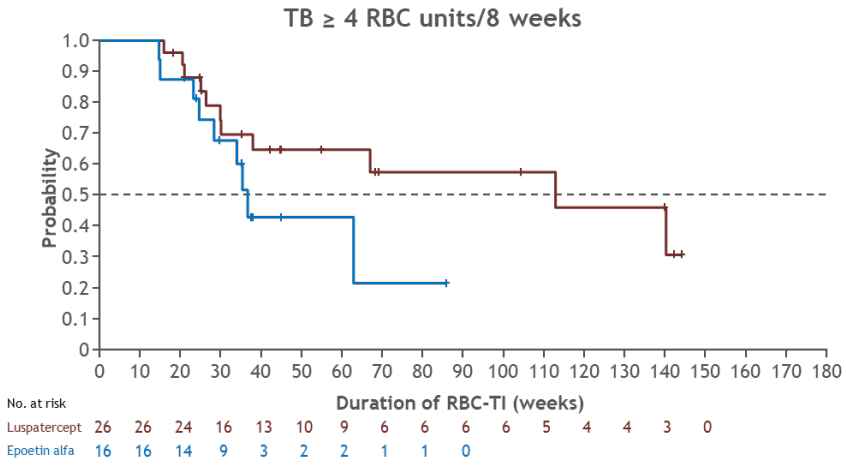
# COMMANDS: Luspatercept vs. Epoetin

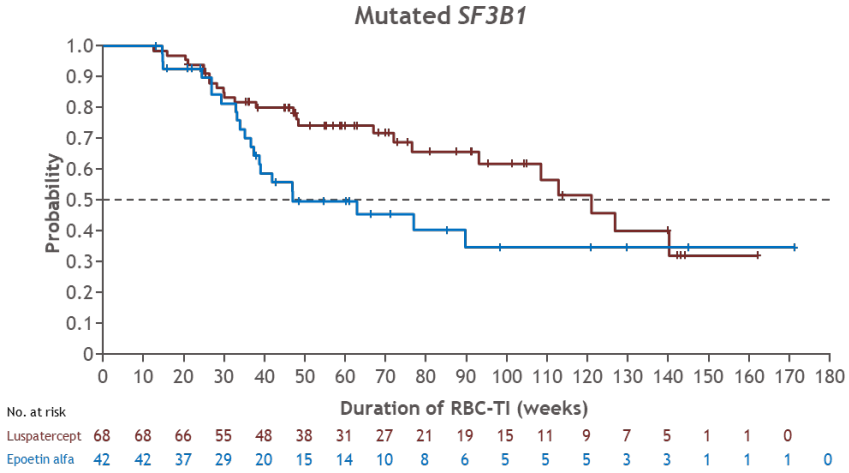


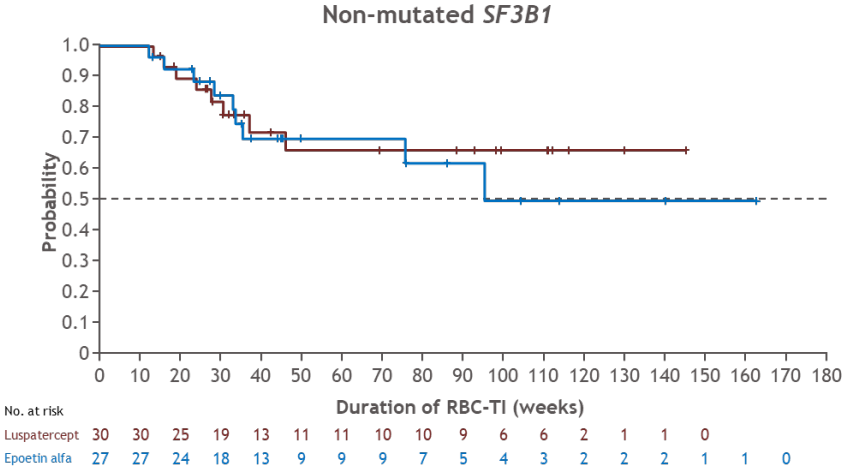

Garcia-Manero G, et al. ASCO2023 ; Platzbecker et al. Lancet 2023

# Duration of response in subgroups: Transfusion burden and SF3B1



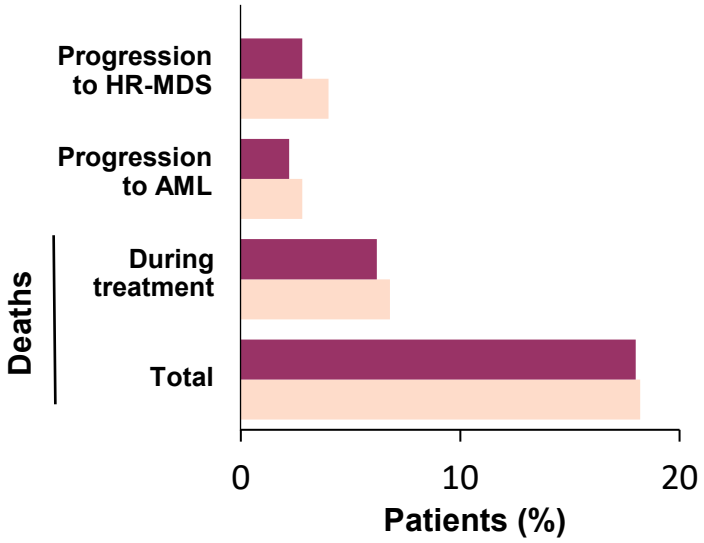

Della Porta MG, et al. EHA 2023 [Abstract #S102]

# Side effect profile: Epoetin

# Side effect profile: Luspatercept vs Epoetin

| | Luspatercept (N = 178) | | Epoetin alfa (N = 176) | |
|---|---|---|---|---|
| **Patients, n (%)** | **Any grade** | **Grade 3/4** | **Any grade** | **Grade 3/4** |
| **Heme-related TEAEs** | (%) | (%) | (%) | (%) |
| Anemia | 17 (9.6) | 13 (7.3) | 17 (9.7) | 12 (6.8) |
| Thrombocytopenia | 11 (6.2) | 7 (3.9) | 3 (1.7) | 1 (0.6) |
| Neutropenia | 9 (5.1) | 7 (3.9) | 13 (7.4) | 10 (5.7) |
| Leukocytopenia | 2 (1.1) | 0 | 3 (1.7) | 0 |
| **TEAEs of interest** | | | | |
| Fatigue | 26 (14.6) | 1 (0.6) | 12 (6.8) | 1 (0.6) |
| Diarrhea | 26 (14.6) | 2 (1.1) | 20 (11.4) | 1 (0.6) |
| Peripheral edema | 23 (12.9) | 0 | 12 (6.8) | 0 |
| Asthenia | 22 (12.4) | 0 | 25 (14.2) | 1 (0.6) |
| Nausea | 21 (11.8) | 0 | 13 (7.4) | 0 |
| Dyspnea | 21 (11.8) | 7 (3.9) | 13 (7.4) | 2 (1.1) |
| Hypertension | 23 (13) | 15 (8) | 12 (7) | 8 (5) |

**TEAEs of any grade**
164 (92.1%) luspatercept
150 (85.2%) epoetin alfa




Garcia-Manero G, et al. ASCO2023 ; Platzbecker et al. Lancet 2023

## Conclusion

- EPO remains standard of care in patients with low-risk MDS, if

  they have an EPO level of <200 U/L

  they are transfusion independent

  they don‘t have ring sideroblasts