Supplementary Material: Long-Term Transfusion Independence with Luspatercept Versus Epoetin Alfa in Erythropoiesis-Stimulating Agent-Naive, Lower-Risk Myelodysplastic Syndromes in the COMMANDS Trial

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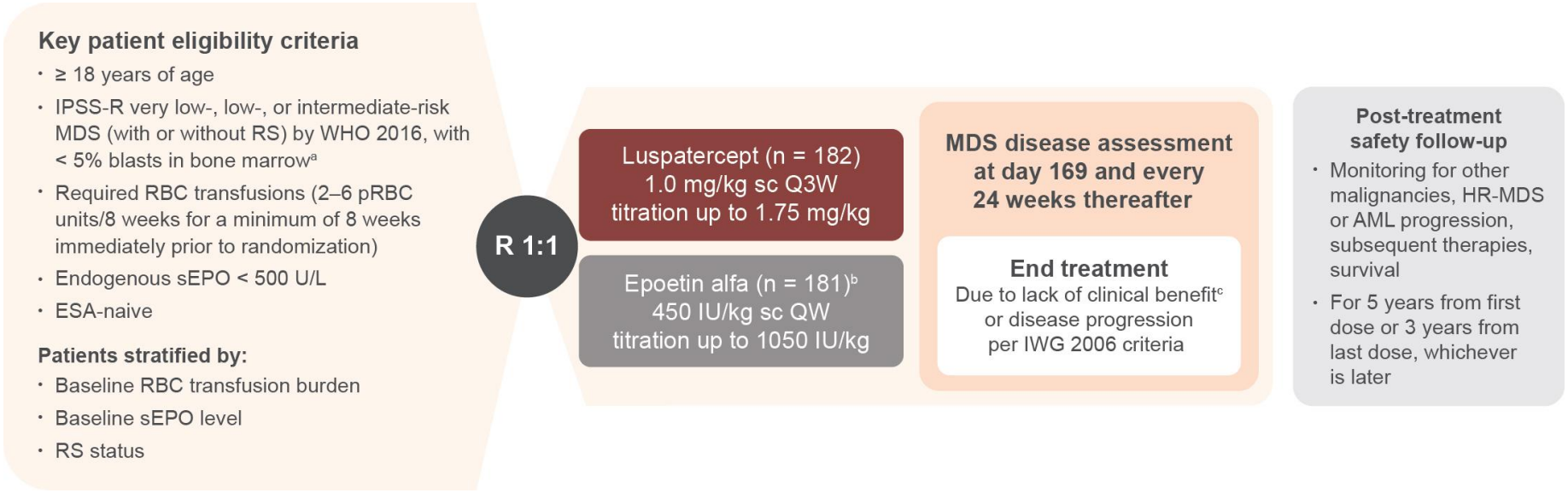
Supplementary figures

Supplementary figure 1 COMMANDS trial design



[a]MDS patients 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

Platzbecker U, et al. *Lancet* 2023;402:373–85; 2. Della Porta MG, et al. *Lancet Haem* 2024;11:E646–E648.

AML acute myeloid leukemia, *HR-MDS* higher-risk MDS, *IPSS-R* Revised International Prognostic Scoring System, *IWG* International Working Group, *MDS* myelodysplastic syndrome, *pRBC* packed red blood cells, *QW* once weekly, *Q3W* every 3 weeks, *R* randomized, *RBC* red blood cell, *RS* ring sideroblasts, *sc* subcutaneous, *sEPO* serum erythropoietin, *WHO* World Health Organization

Supplementary tables

Supplementary table 1 Dose titration criteria for maintenance of Hb concentrations within target range (10 g/dL–12g/dL) in the COMMANDS trial[a]

Appropriate dose escalations should be made to maintain Hb concentrations within the target range of 10 g/dL–12 g/dL independent of transfusions. Dose should be increased in a stepwise manner from the starting dose of 1.0 mg/kg to 1.33 mg/kg, and up to a maximum of 1.75 mg/kg, if all of the following criteria are met:	
Criteria	**Dose increase**
Patient Hb levels are below the target range of 10 g/dL–12 g/dL. If the Hb levels are within 10 g/dL–12 g/dL due to the influence of transfusions, the dose may still be adjusted (please consider the other three criteria noted below)	Increase dose in a stepwise manner by 1 level up to a maximum of 1.75 mg/kg
Patient Hb level increase compared to the Hb sample taken prior to the previous luspatercept dose is ≤ 1 g/dL. If the Hb level increase is > 1 g/dL due to the influence of transfusions, the dose may still be adjusted	
The two most recent prior luspatercept administrations assessed must be at the same dose level	
The patient must not have met dose delay and/or reduction criteria in the two most recent luspatercept administrations (with the exception of dose delay required due to influence of RBC transfusions)	
Dose reductions in a stepwise manner from the starting dose of 1.0 mg/kg to 0.8 mg/kg, from 0.8 mg/kg to 0.6 mg/kg, and down to 0.45 mg/kg can be considered in response to Hb increase as follows[a]:	
Condition	**Dose reduction**
If > 2.0 g/dL increased in Hb compared with previous dose level, when not influenced by RBC transfusions (ie, Hb result > 14 days after last RBC transfusion or within 3 days from next RBC transfusion)	Reduce dose by 1 level

If pre-dose Hb ≥ 12.0 g/dL	Delay dose until Hb < 11.0 g/dL; Hb should be rechecked weekly during dose delay

[a]This table only includes target Hb-guided dose modifications. Please see the REBLOZYL (luspatercept-aamt) prescribing information for full dose modification guidelines, including in the instance of an AE.

Hb hemoglobin, *RBC* red blood cell