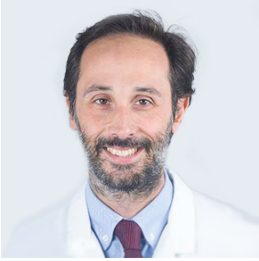

The COMMANDS trial: a phase 3 study of the efficacy and safety of luspatercept versus epoetin alfa for the treatment of anemia due to Revised International Prognostic Scoring System Very Low-, Low-, or Intermediate-risk myelodysplastic syndromes in erythropoiesis stimulating agent-naive patients who require red blood cell transfusions

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Presenting author disclosures

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Introduction and objectives

Introduction

- Studies of epoetin alfa and darbepoetin alfa have demonstrated efficacy among patients with LR-MDS, but the patient population in which a clinically significant effect is observed may be limited[1,2]
- Luspatercept, a first-in-class erythroid maturation agent with a mechanism of action distinct from ESAs,[3] is approved by the US FDA for the treatment of anemia failing an ESA and requiring 2 or more RBC units over 8 weeks in adult patients with Very Low- to Intermediate-risk MDS with RS or with MDS/MPN-RS-T
- Luspatercept may also be beneficial in treating anemia in patients with ESA-naive LR-MDS who require RBC transfusions

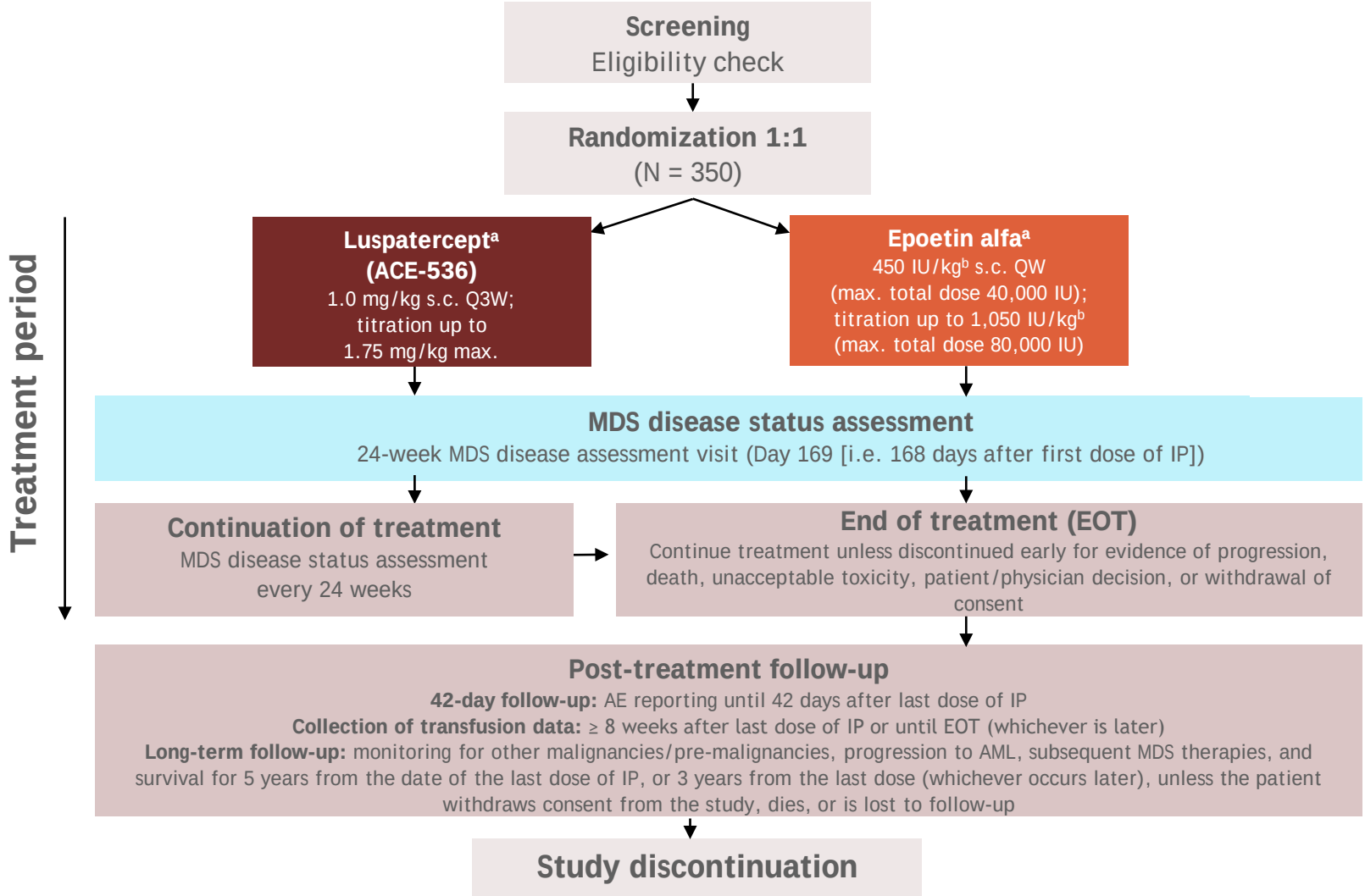
Study objectives

- COMMANDS is a randomized, open-label, phase 3 trial to evaluate the efficacy and safety of luspatercept versus epoetin alfa in anemic patients with IPSS-R–defined LR-MDS, either with or without ≥ 15% RS, who are ESA naive, and who require regular RBC transfusions

ESA, erythropoiesis-stimulating agent; FDA, US Food and Drug Administration; IPSS-R, Revised International Prognostic Scoring System; LR-MDS, lower-risk myelodysplastic syndromes; MDS/MPN-RS-T, myelodysplastic syndromes/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis; RBC, red blood cell; RS, ring sideroblasts.

1. Fenaux P, et al. *Leukemia* 2018;32:2648–2658. 2. Platzbecker U, et al. *Leukemia* 2017;31:1944–1950. 3. Suragani RNVS, et al. *Nat Med* 2014;20:408–414.

The COMMANDS trial study design



[a]Crossover between the treatment arms is not permitted during the study treatment period.
[b]Individual epoetin alfa doses according to body weight will be rounded up to the next 2,000 IU dose level for starting dose level and dose level −1, and up to the next 4,000 IU for dose level +1 and dose level +2 for doses exceeding a calculated dosing of 56,000 IU according to body weight.
AE, adverse event; AML, acute myeloid leukemia; EOT, end of treatment; IP, investigational product; IU, international units; MDS, myelodysplastic syndromes; QW, once every week; Q3W, once every 3 weeks; s.c., subcutaneous.

Methods – patient main eligibility criteria

- Inclusion criteria
  - Age ≥ 18 years at time of consent
  - Documented diagnosis of IPSS-R–defined LR-MDS with < 5% blasts in the bone marrow
  - Serum EPO levels < 500 U/L
  - An average RBC transfusion requirement of 2–6 units RBCs/8 weeks for ≥ 8 weeks immediately prior to randomization
- Exclusion criteria
  - Prior use of ESAs (≤ 2 doses of prior epoetin alfa permitted if ≥ 8 weeks from randomization date and serum EPO confirmed as ≤ 500 U/L)
  - Prior use of G-CSF or GM-CSF, unless given for the treatment of febrile neutropenia
  - Prior use of disease-modifying agents (e.g. lenalidomide) or hypomethylating agents
  - Presence of del(5q) cytogenetic abnormality

EPO, erythropoietin; G-CSF, granulocyte colony-stimulating factor; GM-CSF, granulocyte-macrophage colony-stimulating factor; U, units.

Methods – randomization and treatment

- Approximately 350 eligible patients will be randomized in a 1:1 ratio to receive either luspatercept (starting dose 1.0 mg/kg with titration up to 1.75 mg/kg) subcutaneously once every 3 weeks or epoetin alfa (starting dose 450 IU/kg with titration up to 1,050 IU/kg) subcutaneously once every week, for a minimum of 24 weeks
- Best supportive care, including RBC transfusions, may be used in combination with study treatment in both arms
- Randomization stratification factors
  - Baseline RBC transfusion burden (< 4 vs ≥ 4 units RBCs per 8 weeks)
  - RS status (with RS+ defined as RS ≥ 15%, or ≥ 5% if *SF3B1* mutation is present)
  - Baseline serum EPO level (≤ 200 U/L vs > 200 U/L)
  - In addition, ≥ 40% and ≤ 60% of randomized patients will be RS+, and ≥ 25% will have serum EPO > 200 U/L

SF3B1, splicing factor 3B subunit 1.

Methods - study endpoints

Endpoints	
Primary	• Proportion of patients who achieve RBC-TI for ≥ 12 weeks within the first 24 weeks on study, with a concurrent mean Hb increase of ≥ 1.5 g/dL compared with baseline
Secondary	• RBC-TI for 24 weeks • Mean Hb change over 24 weeks • Achievement of HI-E response per IWG 2006 criteria • Time to achieve HI-E • Safety (type, frequency, severity of AEs) • Progression to AML

Hb, hemoglobin; HI-E, hematologic improvement–erythroid; IWG, International Working Group; RBC-TI, red blood cell transfusion independence.

Clinical trial information

- This trial is currently recruiting patients. If you have a patient who could benefit from participation in this trial, please contact:
  - Dr Rodrigo Ito, MD, 86 Morris Avenue, Building A 146, Summit, NJ 08543, USA
  - Office phone: +1 (908) 673-2936
  - E-mail: Rodrigo.Ito@bms.com
- The COMMANDS trial is registered at ClinicalTrials.gov (NCT03682536) and EudraCT (number 2017-003190-34)

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