Elritercept vs epoetin alfa in erythropoiesis-stimulating agent (ESA)-naïve adults with lower-risk myelodysplastic syndromes (MDS) and transfusion-dependent anemia: The ELRiSE MDS phase 3 study

MDS-824

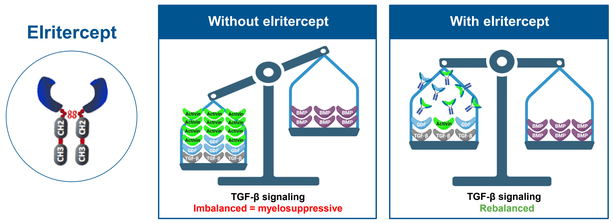
Valeria Santini,[1] Rami Komrokji,[2] Guillermo Garcia-Manero,[3] Hetty E. Carraway,[4] Matteo Giovanni Della Porta,[5] Thomas Cluzeau,[6] Aristoteles Giagounidis,[7] María Díez Campelo,[8] John F. Seymour,[9] Phillip Scheinberg,[10] Amer M. Zeidan,[11] Cong Li,[12] Meliessa Hennessy,[12] Leopold Sellner,[12] Alexander Vorog,[12] Mikkael A. Sekeres[13]

[1]MDS Unit, AOU Careggi, DMSC, University of Florence, Florence, Italy; [2]Department of Malignant Hematology, Moffitt Cancer Center, Tampa, FL, USA; [3]Department of Leukemia, Division of Cancer Medicine, MD Anderson Cancer Center, University of Texas, Houston, TX, USA; [4]Leukemia Program, Taussig Cancer Institute, Cleveland Clinic, Cleveland, OH, USA; [5]Humanitas Clinical and Research Center, IRCCS, Rozzano, Milan, Italy & Humanitas University Pieve Emanuele, Milan Italy; [6]Hematology Department, Côte d'Azur University, Centre Hospitalier Universitaire de Nice, Nice, France; [7]Hematology Oncology and Palliative Medicine Clinic, Marien Hospital Düsseldorf, Düsseldorf, Germany; [8]Department of Hematology, Hospital Universitario de Salamanca, Salamanca, Spain; [9]Clinical Haematology, Peter MacCallum Cancer Centre and Royal Melbourne Hospital, Melbourne, Vic, Australia; [10]Division of Hematology, Hospital A Beneficência Portuguesa, São Paulo, Brazil; [11]Yale University and Yale Comprehensive Cancer Center, New Haven, CT, USA; [12]Takeda Development Center Americas, Inc. (TDCA), Cambridge, MA, USA; [13]Divison of Hematology, Sylvester Comprehensive Cancer Center, Miller School of Medicine, University of Miami, FL, USA

Background

- Anemia is a key clinical consequence of MDS, with approximately 80% of patients developing clinically significant anemia over the course of their disease[1]
- Long-term red blood cell (RBC) transfusions can result in decreased overall survival, reduced quality of life (QoL), and iron overload, which can be associated with end-organ damage[2,3]
- Treatment with ESAs can lessen transfusion needs, but most patients either do not respond or become unresponsive over time[4-6]
- Identifying new treatments for patients with MDS that can achieve sustained RBC-transfusion independence (TI), decrease symptoms due to anemia, and provide rapid and durable responses remains crucial[7-9]
- Elritercept is an investigational TGF-β superfamily ligand trap designed to block activin A/B and growth differentiation factor 8/11 signaling and restore effective hematopoiesis beyond erythroid maturation(**Figure 1**).[10] Elritercept is being evaluated in diseases with dysfunctional hematopoiesis, such as MDS[11-13]
- In a phase 2 study, elritercept led to durable transfusion independence (TI) and clinically meaningful improvements in QoL (such as reducing fatigue) in patients with very low-, low- and intermediate-risk (lower risk) MDS (LR-MDS), including those with packed RBC transfusion dependence (TD)[12,13]

Figure 1: Elritercept proposed mechanism of action



BMP, bone morphogenic protein; CH2/3, constant heavy-chain domain 2/3; TGF-β, transforming growth factor β.

Methods

Patients

- Key study inclusion criteria are shown in the **Summary Panel**

Key exclusion criteria

- Presence of Del5q mutation
- History of thromboembolic events <6 months prior to screening
- Clinically significant cardiovascular, hepatic, or renal issues
- Body mass index ≥40 kg/m^2
- Prior therapy with immunomodulatory/suppressive agents or procedures
- Anemia due to any other known cause

Objective

This open-label, randomized phase 3 study will evaluate the efficacy and safety of elritercept versus epoetin alfa for the treatment of anemia in patients with LR-MDS

Study design

ClinicalTrials.gov identifier: NCT07422480

Key inclusion criteria

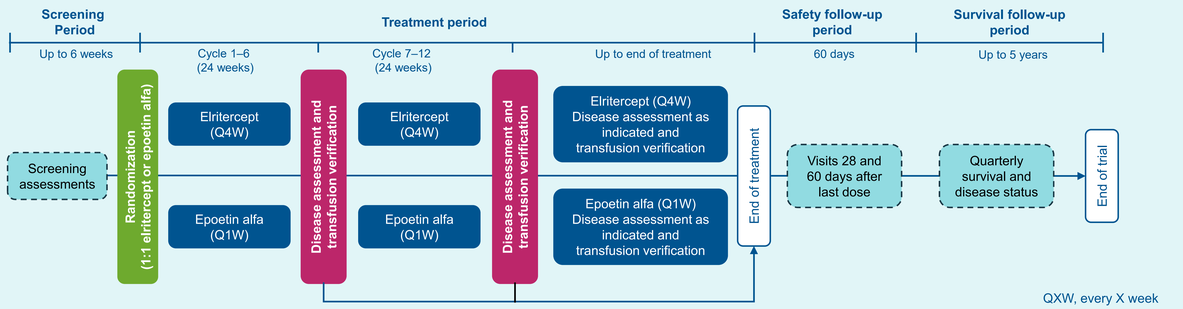
- Adults ≥18 years
- ESA-naïve with anemia due to LR-MDS (per Revised International Prognostic Scoring System)
- TD (2–6 RBC units/8 weeks)
- <500 U/L serum erythropoietin >2 weeks post-transfusion
- <5% bone marrow blast count
- <11.0 g/dL hemoglobin
- Eastern Cooperative Oncology Group performance status of 0, 1, or 2

N~210–300 patients

N~150–175 global sites

Primary endpoint

Proportion of patients achieving TI ≥12 weeks from first dose through Week 24 with concurrent mean Hgb increase ≥1.5 g/dL from baseline



Summary

ELRISE is an actively recruiting phase 3 study evaluating elritercept for the treatment of anemia in patients with TD LR-MDS

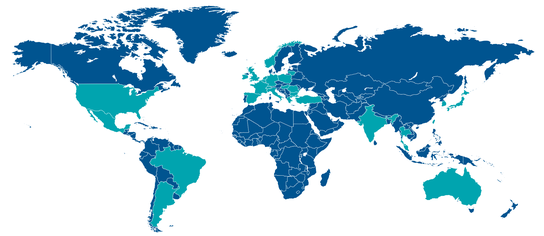
Study design

- The full study design is shown in the **Summary Panel**
- Patients are randomized 1:1 to receive subcutaneous elritercept 3.75 mg/kg once every 4 weeks (with possible up-titration to 5 mg/kg after ≥8 weeks) or epoetin alfa 450 IU/kg weekly (with possible up-titration to 1050 IU/kg after ≥8 weeks, with a maximum total dose of 80,000 IU)
- Randomization is stratified by ringed-sideroblast (RS) status (RS+ vs RS-), baseline erythropoietin levels (≤200 vs >200 U/L) and RBC transfusion burden (low vs high [2–3 vs 4–6 units/8 weeks])
- RBC transfusions are allowed at the investigators' discretion for low hemoglobin
- Transfusion verification and disease assessments will be performed periodically and as clinically indicated until the end of treatment
- The survival follow-up period will be up to 5 years

Enrollment and study locations

- This study will enroll ~210–300 patients across ~150–175 sites (**Figure 2**)

Figure 2: Map of global study sites



Key study objectives

Primary objective	• To evaluate the efficacy of elritercept on RBC-TI for ≥12 consecutive weeks from first dose through Week 24 with concurrent mean hemoglobin increase ≥1.5 g/dL versus epoetin alfa
Key secondary objective	• To compare the effect of elritercept on RBC-TI for consecutive ≥12-week, ≥16-week, and ≥24-week periods from first dose through Week 24 versus epoetin alfa
Other secondary objectives*	• To compare the effect of elritercept vs epoetin alfa on patient-reported fatigue response (measured by the FACIT-fatigue scale) in the absence of RBC transfusions between Weeks 12 and 24 • To compare the effect of elritercept versus epoetin alfa on erythroid hematologic improvement, including achievement and durability of hematological improvement-erythroid responses (≥8 and ≥12 weeks) from first dose through Weeks 24 and 48 • To compare the effect of elritercept vs epoetin alfa on achievement, durability, and time to RBC-TI, including RBC-TI responses of varying durations (≥8, ≥12, ≥16, and ≥24 weeks) from first dose through Weeks 24 and 48 • To compare the effect of elritercept vs epoetin alfa on changes in hemoglobin levels through Weeks 24 and 48 • To evaluate the safety of elritercept versus epoetin alfa
Exploratory objectives*	• To assess the broader hematologic and biologic effects of elritercept vs epoetin alfa through Weeks 24 and 48, including effects on neutrophils, thrombopoiesis and platelet parameters, erythropoiesis-related biomarkers, and iron homeostasis

*List is not comprehensive. FACIT, Functional Assessment of Chronic Illness Therapy.

Europe
68 sites

Asia
37 sites

North America
29 sites

South America
12 sites

Australia
10 sites

Countries (number of sites): Argentina (4), Australia (10), Belgium (3), Brazil (8), Bulgaria (2), France (5), Germany (5), Greece (6), Hungary (2), India (7), Ireland (4), Italy (11), Japan (8), Lithuania (2), Malaysia (3), Mexico (4), Netherlands (1), Norway (3), Poland (5), Romania (2), South Korea (6), Spain (7), Switzerland (3), Taiwan (6), Thailand (3), Turkey (5), United Kingdom (6), and United States (25).

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Disclosures

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