Updated phase 2 results of elritercept in patients with transfusion-dependent lower-risk myelodysplastic neoplasms

MDS-838

Rami Komrokji,[1] Maria Diez Campelo,[2] Shuh Ying Tan,[3] David Valcarcel Ferreiras,[4] Anish Puliyayil,[5] Alejandro Arbelaez,[6] Montserrat Arnan,[7] David M. Ross,[8] Devendra Hiwase,[9] Teresa Bernal del Castillo,[10] Thomas Cluzeau,[11] Aristoteles Giagounidis,[12] Mikkael A. Sekeres,[13] Andrew S. Artz,[14] Radha Ramesh,[15] Camden Bay,[15] Kevin Galinsky,[15] Leopold Sellner,[15] Kaveri Suryanarayan,[15] Lynette Chee[16]

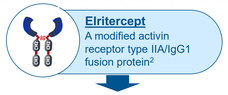
[1]Moffit Cancer Center, Tampa, FL, USA; [2]Servicio de Hematología, Hospital Universitario de Salamanca, IBSAL, Salamanca, Spain; [3]St. Vincent's Hospital Melbourne, Fitzroy, Australia; [4]Vall d'Hebron University Hospital, Barcelona, Spain; [5]Border Medical Oncology and Haematology, Albury, NSW, Australia; [6]Tweed Valley Hospital, Cancer Care Services, Tweed Heads, NSW, Australia; [7]Institut Català d'Oncologia, IDIBELL, Hospitalet de Llobregat, Barcelona, Spain; [8]Flinders Medical Centre, Adelaide, SA, Australia; [9]The Royal Adelaide Hospital, Adelaide, SA, Australia; [10]Hospital Universitario Central de Asturias, ISPA, IUOPA, Oviedo, Asturias, Spain; [11]CHU de Nice, Nice, France; [12]Marien Hospital Düsseldorf, Düsseldorf, Germany; [13]Sylvester Comprehensive Cancer Center, Miller School of Medicine, University of Miami, FL, USA; [14]City of Hope, Duarte Cancer Center, Duarte, CA, USA; [15]Takeda Development Center Americas, Inc. (TDCA), Cambridge, MA, USA; [16]The Royal Melbourne Hospital and Peter MacCallum Cancer Centre, Melbourne, VIC, Australia

Background

- Patients with myelodysplastic neoplasms (MDS)-associated anemia often become dependent on regular red blood cell (RBC) transfusions, which has a substantial impact on quality of life, particularly in patients with lower risk (LR)-MDS and high transfusion burden (HTB)[1,2]
- Erythropoiesis-stimulating agents (ESAs) are generally given as first-line therapy; however, patients may become ESA resistant, and require supportive RBC transfusions[3,4]
- Luspatercept, an erythroid maturation agent, is currently approved for the treatment of anemia in patients with LR-MDS[5]
  - Despite allowing some patients to become transfusion independent (TI), not all maintain long-term benefit, or disease response may be limited[5,6]
  - In the MEDALIST phase 3 trial, of all patients with MDS who were ring sideroblast (RS) positive, ESA-refractory or responded poorly to ESAs, 38% had TI for ≥8 weeks; 33–42% of patients with somatic baseline mutations achieved TI for ≥8 weeks[7]
  - In the COMMANDS trial, TI responses were notably higher in biologically favorable subgroups, including patients with RS and *SF3B1* mutations, compared with patients with non-RS disease or those without *SF3B1* mutations[8]
- There remains an unmet need for novel treatment options that can improve symptoms of anemia, lessen the transfusion burden, and provide rapid and durable responses for this population[8–11]

Elritercept

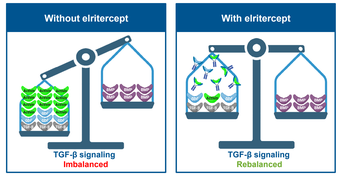
- Dysregulated transforming growth factor beta (TGF-β) superfamily signaling in LR-MDS suppresses erythroid differentiation and leads to ineffective hematopoiesis, contributing to persistent anemia[12,13]



Elritercept
A modified activin receptor type IIA/IgG1 fusion protein[2]

Elritercept selectively binds and **potently blocks downstream signaling** of the TGF-β superfamily ligands **activin A and B**, and **growth differentiation factors (GDF) 8 and 11**[13,14]

This can potentially provide therapeutic benefit to a broad and heterogeneous subset of patients with MDS[13,14]



BMP, bone morphogenetic protein.

- Here, we present the results from the elritercept phase 2 study (NCT04419649) in patients with transfusion dependent LR-MDS (**Summary Panel**)

Results

- As of data cutoff (April 3, 2025), 96 patients were enrolled in the recommended part 2 dose (RP2D) group
- At baseline, median age was 74 years, and 63.5% of patients were male
- A third of patients (32.3%) were classified as non-RS and two thirds (60.4%) had HTB
- More than half of the patients (54.2%) had *SF3B1* mutations and 81.3% of patients had baseline erythropoietin (EPO) <500 U/L

Characteristic	N=96*
Age in years, median (range)	74 (53–89)
Male, n (%)	61 (63.5)
Ring sideroblast status, n (%)	
Ring sideroblast positive	64 (66.7)
Non-ring sideroblast†	31 (32.3)
Transfusion burden, n (%)	
Non-transfused	15 (15.6)
Low transfusion burden (LTB)	23 (24.0)
HTB	58 (60.4)
Dysplasia category, n (%)	
Multi-lineage	56 (58.3)
Single-lineage	7 (7.3)
Unknown/missing	33 (34.4)
Prior erythropoietin stimulating agent, n (%)	
Yes	25 (26.0)
No	71 (74.0)
Baseline erythropoietin, n (%)	
Median (range), U/L	138.0 (1.1–4000)
<500 U/L, n (%)‡	78 (81.3)
≥500 U/L, n (%)	18 (18.8)
IPSS-R, n (%)	
Very low	11 (11.5)
Low	61 (63.5)
Intermediate	23 (24.0)
Missing	1 (1.0)
Frequent mutations (in ≥10% patients, n[%])	
SF3B1	52 (54.2)
TET2	33 (34.4)
ASXL1	22 (22.9)
EZH2	13 (13.5)
DNMT3A	12 (12.5)

*MDS RP2PD population includes all patients with MDS who received ≥1 dose of elritercept with dose level ≥3.75 mg/kg. †Non-ring sideroblast as defined by World Health Organization 2016 criteria. ‡Includes nine patients with missing data.
IPSS-R, International Prognostic Scoring System-Revised.

Key eligibility criteria

- Transfusion-dependent adult patients with a diagnosis of MDS that meet IPSS-R classification of **very low-, low-, or intermediate-risk MDS***
- **Anemia**, defined as†:

1. LTB: Having received **1–3 RBC units** for **Hgb ≤9.0 g/dL** within the 8-week pretreatment period OR,
2. HTB: Having received **≥4 RBC units** for **Hgb ≤9.0 g/dL** within the 8-week pretreatment period

Study design: a phase 2, open label study (NCT04419649)

Part 1: Dose escalation (n=31)

Pretreatment period (8 weeks) → Treatment period 4 or 24 cycles (Up to 96 weeks) → Safety follow-up period (8 weeks)

Part 2: Dose expansion (n=71)

Pretreatment period (6 weeks) → Treatment period 24 cycles (96 weeks) → Follow-up period (8 weeks)

Starting dose was 3.75 mg/kg with up titration to 5.0 mg/kg if the investigator believed the patient would derive benefit

Long-term study (Part 1 and Part 2): all cohorts (n=96)

Includes patients who may have potential benefit from continued elritercept treatment after 24 cycles, received ≥1 dose of elritercept with dose level ≥3.75 mg/kg every 4 weeks

Treatment period (Monthly visits) → Safety follow-up period (8 weeks) → Survival follow-up period (Quarterly)

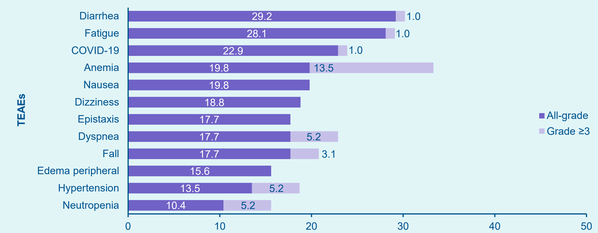
Endpoints

- **Primary:**
  - Safety/tolerability‡
- **Secondary:**
  - RBC TI ≥8 weeks
  - Modified 2006 IWG HI-E response§
  - Overall erythroid response
  - Time to and duration of HI-E and TI response
- **Exploratory:**
  - Platelet and neutrophil count

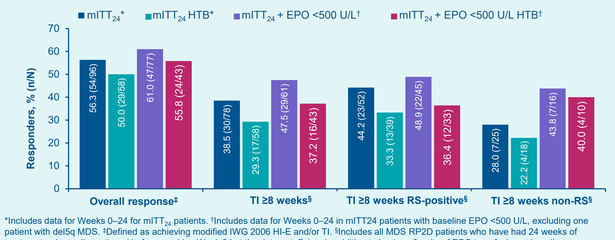
*Based on the International Prognostic Scoring System-Revised. †Some non-transfused patients were enrolled to this study (data not shown in this presentation); ‡Adverse events measured by Common Terminology Criteria for Adverse Events v5.0. §For patients with LTB, response was defined as a mean hemoglobin increase ≥1.5 g/dL during any 8-week treatment period. For patients with HTB, response was defined as a reduction in ≥4 units of RBC transfused during any 8-week study period compared with the 8-week period before cycle 1 Day 1.

Key results

Most frequent TEAEs (≥10% of patients, all grades)



TI for ≥8 weeks by Week 24



*Includes data for Weeks 0–24 for $mITT_{24}$ patients. †Includes data for Weeks 0–24 in $mITT_{24}$ patients with baseline EPO <500 U/L, excluding one patient with del5q MDS. ‡Defined as achieving modified IWG 2006 HI-E and/or TI. §Includes all MDS RP2D patients who have had 24 weeks of treatment or have discontinued before reaching Week 24 at the data cutoff date in addition to having ≥2 units of RBC transfusion at baseline.

Key take aways — **Elritercept was well tolerated and showed durable and rapid responses in transfusion-dependent patients with LR-MDS**

Safety overview

- Over the entire study period, the median exposure to elritercept was 13.8 months (range: 1.4–45.3)
- The most common treatment-emergent adverse events (TEAEs) are presented in the **Summary Panel**
- At data cutoff, elritercept treatment was ongoing in 39 (40.6%) patients: main reasons for discontinuation were lack of efficacy (n=19, 19.8%), TEAEs (n=16, 16.7%), withdrawal of consent (n=8, 8.3%) and progressive disease (n=5, 5.2%)
- Overall, six deaths were reported, with five due to TEAEs; none were considered elritercept-related

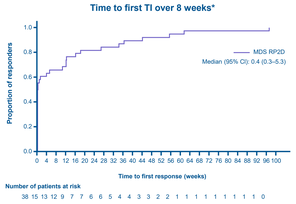
n (%)	N=96*
Any TEAEs	95 (99.0)
Elritercept-related	44 (45.8)
Grade ≥3 TEAEs	57 (59.4)
Elritercept-related†	5 (5.2)
SAEs	49 (51.0)
Elritercept-related‡	4 (4.2)
TEAEs resulting in discontinuation of elritercept	17 (17.7)
TEAEs resulting in dose modification	25 (26.0)

*Safety population includes all MDS RP2D patients who received ≥1 dose of elritercept. †Includes anemia, neutropenia, headache, syncope, neutrophil count decreased, gastric adenocarcinoma, dyspnea, and hypertension. Each event occurred once, although some patients may have experienced more than one AE considered related to elritercept. ‡Includes injection site reaction, gastric adenocarcinoma, syncope, and dyspnea (n=1 for each).
SAE, serious adverse event.

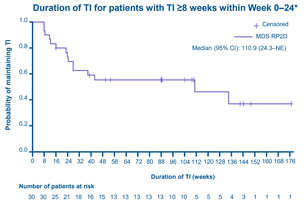
Transfusion independence

- TI for ≥8 weeks was achieved by Week 24 across a range of patient subgroups **(Summary Panel)**
- The median time to first TI was 0.4 weeks (95% confidence interval [CI]: 0.3–5.3). In the first 48 weeks, 26.9% achieved TI ≥24 weeks (15.5% in patients with HTB)
- The median duration of TI was 110.9 weeks (95% CI: 24.3–not estimated) among patients who had TI ≥8 weeks in the first 24 weeks. Sustained TI ≥24 weeks was observed in 67.3% of patients with TI ≥8 weeks

Time to first TI over 8 weeks*



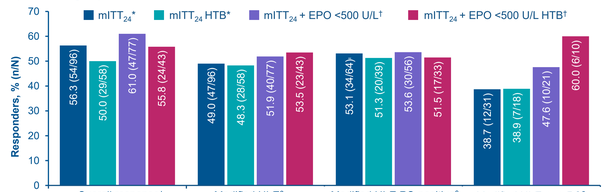
Duration of TI for patients with TI ≥8 weeks within Week 0–24*



*Population includes all MDS RP2D patients who have had 24 weeks of treatment or have discontinued before reaching Week 24 at the data cutoff ($mITT_{24}$) in addition to having at least two units of RBC transfusion at baseline.

Hematologic improvement-erythroid

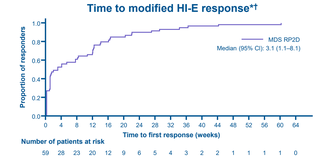
- Modified hematologic improvement-erythroid (HI-E) responses were achieved by Week 24 across a range of patient subgroups



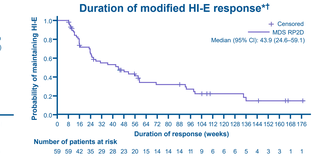
*Includes data for Weeks 0–24 for $mITT_{24}$ patients. †Includes data for Weeks 0–24 in $mITT_{24}$ patients with baseline EPO <500 U/L, excluding one patient with del5q MDS. ‡Defined as achieving modified International Working Group (IWG) 2006 HI-E and/or TI. §In patients with LTB, response was defined as a mean Hgb increase ≥1.5 g/dL during any 8-week treatment period. For patients with HTB, response was defined as a reduction in ≥4 units of RBC transfused during any 8-week study period compared with the 8-week period before cycle 1 Day 1; ‖RS status missing in one patient.

- The median time to modified HI-E response was 3.1 weeks (95% CI: 1.1–8.1)
  - The median time to modified HI-E response was 1.4 weeks (95% CI: 0.3–12.4) in patients that had prior ESA; and 4.1 weeks (95% CI: 1.1–8.4) in those who were ESA naïve
- Most patients achieved an initial response within 8 weeks
- The median duration of modified HI-E was **43.9 weeks** (95% CI: 24.6–59.1)

Time to modified HI-E response*†



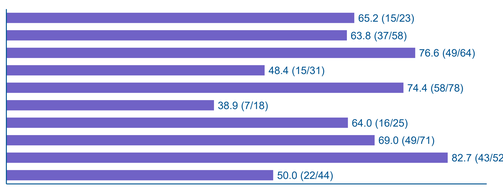
Duration of modified HI-E response*†



*MITT$_{24}$ population includes all MDS RP2D patients who have had 24 weeks of treatment or have discontinued before reaching Week 24 at the data cutoff. †HI-E response is defined per Modified IWG 2006 criteria response. In patients with LTB, response was defined as a mean Hgb increase ≥1.5 g/dL during any 8-week treatment period. For patients with HTB, response was defined as a reduction in ≥4 units of RBC transfused during any 8-week study period compared with the 8-week period before cycle 1 Day 1.

Overall erythroid response rates

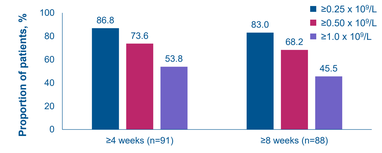
- Response rates were similar across patients with LTB or HTB
- The highest response was seen in patients who were either RS-positive or had a *SF3B1* mutation
- Most patients had lower baseline EPO levels, which were associated with higher response
- Response rates were comparable regardless of prior ESA use



*Population includes all MDS RP2D patients who have had 24 weeks of treatment or have discontinued before reaching Week 24 at the data cutoff ($mITT_{24}$) in addition to having at least two units of RBC transfusion at baseline.

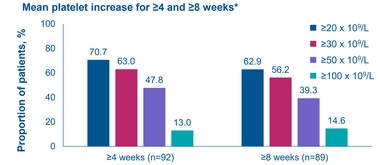
Mean absolute neutrophil count (ANC) and platelets increase

Mean ANC increase for ≥4 and ≥8 weeks*



- 7/22 (31.8%) patients with baseline ANC <1.5 x 10^9/L achieved an ANC ≥1.5 x 10^9/L (sustained for ≥8 weeks)
- Of three patients with baseline neutrophil count <1.0 x 10^9/L, one had a sustained modified 2006 IWG HI-neutrophil response† for ≥4 weeks

Mean platelet increase for ≥4 and ≥8 weeks*



- 8/24 (33.3%) patients with baseline platelet count <150 x 10^9/L achieved a platelet count ≥150 x 10^9/L (sustained for ≥8 weeks)
- In patients with pretreatment platelets <100 x 10^9/L, 2/7 (28.6%) achieved a sustained modified HI-platelet response‡ for ≥4 weeks and 1/7 (14.3%) had a sustained modified HI-platelet response for ≥8 weeks

*MDS RP2D population included all patients with MDS who received ≥1 dose of elritercept with dose level ≥3.75 mg/kg. †Defined as an increase of ≥100% and an absolute increase >500/μL from baseline neutrophil count. ‡Defined as an increase of ≥30 x 10^9/L for those with baseline starting platelet value of >20x10^9/L, or an increase from ≥20 x10^9/L to >20 x10^9/L, and by at least 100%.

Conclusions

- Elritercept was well tolerated and showed durable and rapid responses in transfusion-dependent patients with LR-MDS
  - Efficacy was observed in patients with LTB and HTB, prior exposure to ESAs, RS-positive and non-RS MDS, EPO <500 U/L, including those with a *SF3B1* mutation
  - Improvements were also observed in ANC and platelet counts
- These updated findings further consolidate the potential for elritercept as a treatment for transfusion dependent anemia and support its further development to address the high unmet medical needs in this heterogeneous patient population
- A phase 3 randomized controlled study (RENEW, NCT06499285) is ongoing and currently recruiting to confirm these results

References

1. Wan BA, et al. *Leuk Lymphoma*. 2025;66:279–88
2. D'Aveni M, et al. *Clin Lymph Myel Leuk*. 2025;25(11):e933–41
3. Szuber N, Busque L. *Blood*. 2025;146(14):1636–8
4. Boccia R, et al. *J Clin Med*. 2024;13(9):2702
5. Reblozyl (luspatercept) summary of product characteristics. Accessed May 20, 2026
6. Volpe VO, Komrokji RS. *Ther Adv Hematol*. 2021;12:2040620720986641
7. Fenaux P, et al. *NEJM*. 2020;382:140–51
8. Della Porta MG, et al. *Lancet Haematol*. 2024;11(9):e646–58
9. Oliva EN, et al. *J Clin Med*. 2022;11:27
10. Oliva EN, et al. *Blood*. 2024;144(Suppl 1):3216
11. Hoff FW, et al. *JCO Oncol Pract*. 2025:1–7
12. Bewersdorf JP, Zeidan AM. *Leukemia*. 2019;33:1303–12
13. Lachey J, et al. *Blood Adv*. 2025;9:193–201
14. Verma A, et al. *J Clin Invest*. 2020;130:582–9

Acknowledgments

This study was funded by Takeda Development Center Americas, Inc. (TDCA), Cambridge, MA, USA. The authors would like to thank all patients and their families and caregivers, as well as all investigators for their valuable contributions to this study. Medical writing support for the development of this presentation, under the direction of the authors, was provided by Advaitaa Haripershad, MSc of Ashfield MedComms, an Inizio Company, funded by Takeda Pharmaceuticals U.S.A., Inc., Cambridge, MA, and complied with the Good Publication Practice (GPP) guidelines (DeTora LM, et al. *Ann Intern Med*. 2022;175:1298–304).

Disclosures

RK: none. **MDC:** honoraria from and speaker for Bristol Myers Squibb, Novartis, Keros, and AbbVie; advisory board for Bristol Myers Squibb, Novartis, GlaxoSmithKline, Agios, Hemavant, Syros, Keros, Curis, Astex/Otsuka, Ascentage, Fortrea, AstraZeneca; and data safety monitoring data/steering committee for Fortrea, and AstraZeneca. **SYT:** honoraria from Pfizer and Otsuka. DVF: consultancy, including paid expert testimony for AbbVie, Amgen, Astellas, BMS/Celgene, Jazz Pharmaceuticals, Kite/Gilead, Merck Sharp & Dohme (MSD), Novartis, Sanofi, Sobi, Syros, and Takeda; research funding from Agios and BMS/Celgene; honoraria from Agios, Amgen, Astellas, BMS/Celgene, Gebro, Grifols, Janssen, Jazz Pharmaceuticals, Kite/Gilead, MSD, Novartis, Pfizer, Sanofi, Sobi, and Takeda. **DVF:** participated in advisory boards, consulted, participated in clinical trial committees, and/or received honoraria from AbbVie, Agios, Amgen, Asofarma, Astellas, Celgene/ Bristol Myers Squibb, Grifols, Janssen, Jazz, MSD, Novartis, Pfizer, Sanofy, Servier, Sobi, Syros and Takeda. **AP, AA:** none. **MA:** consultancy for Abbvie, Jazz, Astellas, Bristol Myers Squibb. **DH:** none. **TB:** consultancy, including paid expert testimony for AbbVie, Jazz, and Astellas. **TC:** advisory council or committee for and consulting fees from BMS, AbbVie, Jazz Pharma, Novartis, Servier, and Arog; and non-financial conflicts with Novartis, BMS, Jazz Pharma, Servier, and Incyte. **AG:** advisory role or expert testimony for Keros, Takeda, Alexion, and AstraZeneca; honoraria from BMS; and other financial relationships with AstraZeneca. **MAS:** consultancy, including paid expert testimony for AbbVie, Jazz, Astellas, and BMS. **DMR**: consultancy for Keros, Novartis, Menarini, Merck, and Takeda; research funding from Protagonist Therapeutics and Novartis, and honoraria from Novartis and Merck. **ASA:** consultancy for Daichii Sanyko, AstraZeneca, AbbVie. **RR, CB, KG**: employment with Takeda. **LS, KS**: employment and stock with Takeda. **LC**: consultancy for Novartis, Takeda, and Keros Therapeutics; honoraria from Novartis and Otsuka; and research funding from Novartis.

To view an electronic version of this poster, scan this Quick Response (QR) code or visit: https://tiny.one/Ac72735ADy

Presented at Society of Hematologic Oncology (SOHO) Annual Meeting, Houston, TX, USA, September 9–12, 2026. For questions or comments, please contact Dr Rami Komrokji: Rami.Komrokji@moffitt.org