Preliminary efficacy and safety analysis of the MAXILUS study of luspatercept initiated at the maximum approved dose in transfusion-dependent lower-risk myelodysplastic syndromes

PF634

Matteo Giovanni Della Porta,[1,2] Maria Diez Campelo,[3] Valeria Santini,[4] Rena Buckstein,[5] Lionel Adès,[6] Lea Sahagun,[7] Gitanjali Das,[7] Tanisha Bryant,[7] Tatiana Zelinsky,[7] Yinzhi Lai,[7] Dimana Miteva,[8] Ali McBride,[7] Krzysztof Madry,[9] David Valcarcel,[10] Jose Miguel Torregrosa-Diaz,[11] Dries Deeren,[12] Sebastian Grosicki,[13] Sangeetha Venugopal,[14] Uwe Platzbecker,[15] Amer M. Zeidan[16]

[1]Cancer Center IRCCS Humanitas Research Hospital, Milan, Italy; [2]Humanitas University, Milan, Italy; [3]University Hospital of Salamanca, Institute of Biomedical Research of Salamanca, Salamanca, Spain; [4]MDS Unit, Hematology, University of Florence, Florence, Italy; [5]Sunnybrook Health Sciences Centre, Toronto, ON, Canada; [6]Service Hématologie Séniors, Hôpital Saint-Louis (AP-HP), Paris Cité University and INSERM U944, Paris, France; [7]Bristol Myers Squibb, Princeton, NJ, USA; [8]Bristol Myers Squibb, Boudry, Switzerland; [9]Department of Hematology, Transplantation and Internal Medicine, Medical University of Warsaw, Warsaw, Poland; [10]Hospital Universitari Vall d'Hebron, Barcelona, Spain; [11]Service d'hématologie, CHU de Poitiers, Poitiers, France; [12]AZ Delta Roeselare, Roeselare, Belgium; [13]Silesian Medical University, Katowice, Poland; [14]University of Miami, Miami, FL, USA; [15]University Hospital Leipzig, Leipzig, Germany; [16]Yale University School of Medicine, New Haven, CT, USA

Introduction

- Myelodysplastic syndromes (MDS) are characterized by ineffective erythropoiesis, which leads to cytopenias (predominantly anemia) and often require red blood cell (RBC) transfusions[1]
- Luspatercept is an erythroid maturation agent shown to improve RBC morphology and hemoglobin (Hb) levels
- Luspatercept is approved to treat anemia in patients with transfusion-dependent (TD) lower-risk (LR)-MDS who are naive or exposed to erythropoiesis-stimulating agent (ESA) treatment[2]
- The COMMANDS and MEDALIST phase 3 trials showed that luspatercept improved RBC-transfusion independence (RBC-TI) in patients with TD LR-MDS[3-5]
  - In these studies, the starting luspatercept dose was 1.0 mg/kg; patients may have had their dose titrated to 1.33 mg/kg and then 1.75 mg/kg
  - Two-thirds of patients were titrated to the maximum approved luspatercept dose (1.75 mg/kg), which helped them achieve or maintain their clinical response
  - With 77% to 80% of patients receiving ≥ 1 dose escalation, no new safety signals were observed

Objective

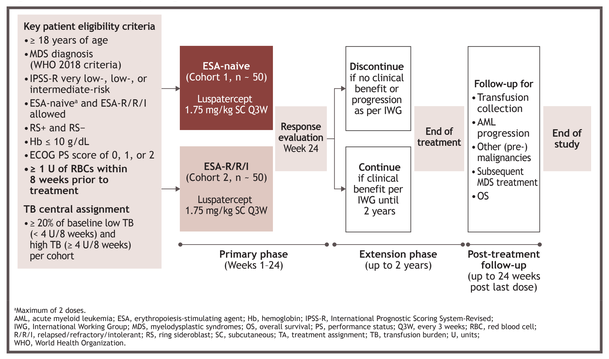
- To report preliminary efficacy and safety of luspatercept from the phase 3b MAXILUS study, in which patients with TD LR-MDS were treated at the maximum approved dose (1.75 mg/kg)

Methods

Study design

- MAXILUS (NCT06045689) is a phase 3b, open-label trial (**Figure 1**)
- Eligible patients were ≥ 18 years of age with International Prognostic Scoring System-Revised (IPSS-R)–defined very low-, low-, or intermediate-risk MDS and an ECOG performance status score of ≤ 2
- Patients were assigned to 1 of 2 cohorts to receive treatment with luspatercept 1.75 mg/kg subcutaneously every 3 weeks
  - Cohort 1: ESA-naive
  - Cohort 2: ESA-relapsed/refractory/intolerant (R/R/I)
- The primary endpoint was RBC-TI for ≥ 8 weeks with a concurrent mean Hb increase of ≥ 1.0 g/dL from Weeks 1 to 24
- Secondary endpoints were RBC-TI for ≥ 8 weeks from Weeks 1 to 24, RBC-TI for ≥ 12 weeks from Weeks 1 to 24, disease progression to acute myeloid leukemia (AML), and safety

Figure 1. MAXILUS study design



[a]Maximum of 2 doses.
AML, acute myeloid leukemia; ESA, erythropoiesis-stimulating agent; Hb, hemoglobin; IPSS-R, International Prognostic Scoring System-Revised; IWG, International Working Group; MDS, myelodysplastic syndromes; OS, overall survival; PS, performance status; Q3W, every 3 weeks; RBC, red blood cell; R/R/I, relapsed/refractory/intolerant; RS, ring sideroblast; SC, subcutaneous; TA, treatment assignment; TB, transfusion burden; U, units; WHO, World Health Organization.

Results

Patients

- The data cutoff date was January 15, 2025
- A total of 90 patients received ≥ 1 dose of luspatercept (ESA-naive, n = 40; ESA-R/R/I, n = 50; **Table 1**)
- The median age was 77.0 years in the ESA-naive cohort and 76.0 years in the ESA-R/R/I cohort; median time since original MDS diagnosis was 2.5 months and 23.4 months, baseline transfusion burden of < 4 U/8 weeks was 77.5% and 50.0%, and ring sideroblast–positive status was 57.5% and 62.0%, respectively

Table 1. Patient demographic and disease characteristics[a]

	ESA-naive (n = 40)	ESA-R/R/I (n = 50)
Age, median (IQR), years	77.0 (73.0-82.0)	76.0 (70.0-81.0)
Sex, female, n (%)	10 (25.0)	17 (34.0)
Region, n (%)		
Europe	32 (80.0)	46 (92.0)
North America	8 (20.0)	4 (8.0)
Time since original MDS diagnosis,[b] median (IQR), months	2.5 (0.2-10.0)	23.4 (7.8-64.5)
Baseline TB, median (IQR), RBC U/8 weeks	2.0 (1.0-3.0)	3.5 (2.0-6.0)
Baseline TB category, n (%)		
< 4 U/8 weeks	31 (77.5)	25 (50.0)
4 to < 6 U/8 weeks	6 (15.0)	6 (12.0)
≥ 6 U/8 weeks	3 (7.5)	19 (38.0)
Baseline Hb, median (IQR), g/dL	8.1 (7.3-8.6)	7.4 (6.9-7.7)
IPSS-R risk classification,[c] n (%)		
Very low	1 (2.5)	5 (10.0)
Low	29 (72.5)	34 (68.0)
Intermediate	10 (25.0)	11 (22.0)
RS status, n (%)		
RS+	23 (57.5)	31 (62.0)
RS−	17 (42.5)	19 (38.0)
***SF3B1* mutation status, n (%)**		
Mutated	20 (50.0)	29 (58.0)
Non-mutated	18 (45.0)	21 (42.0)
Not reported	2 (5.0)	0

Data cutoff date: January 15, 2025.
[a]Data are among the all-treated population, defined as all patients who received ≥ 1 dose of study intervention.
[b]Data cleaning issues may exist for some data that report time since diagnosis as the ranges for the ESA-naive cohort (−0.3 to 12.6) and the ESA-R/R/I cohort (−12.5 to 99.5) include negative values.
[c]IPSS-R risk classification was by institutional analysis.
ESA, erythropoiesis-stimulating agent; Hb, hemoglobin; IPSS-R, International Prognostic Scoring System-Revised; MDS, myelodysplastic syndromes; RBC, red blood cell; R/R/I, relapsed/refractory/intolerant; RS, ring sideroblast; TB, transfusion burden; U, units.

Treatment exposure

- The median (range) duration of treatment exposure was 20.6 (1-37) weeks for the ESA-naive cohort and 23.9 (3-60) weeks for the ESA-R/R/I cohort
- Treatment discontinuation occurred in 5.0% of patients in the ESA-naive cohort and in 26.0% of patients in the ESA-R/R/I cohort (**Table 2**)
- One or more dose reductions occurred in 5.0% of patients in the ESA-naive cohort and in 10.0% of patients in the ESA-R/R/I cohort (**Table 2**)

Table 2. Treatment exposure[a]

Patients, n (%)	ESA-naive (n = 40)	ESA-R/R/I (n = 50)
Patients on treatment	38 (95.0)	37 (74.0)
Patients who discontinued	2 (5.0)	13 (26.0)
Primary reason for discontinuation		
Lack of efficacy	1 (2.5)	5 (10.0)
Withdrawal by patient	1 (2.5)	3 (6.0)
Death	0	1 (2.0)
Progressive disease	0	2 (4.0)
Other	0	2 (4.0)
Patients with ≥ 1 dose delay	7 (17.5)	13 (26.0)
Patients with ≥ 1 dose reduction	2 (5.0)	5 (10.0)
Primary reason for dose adjustment		
AE	1 (2.5)	1 (2.0)
Hb increase > 2.0 g/dL compared with previous dose	0	2 (4.0)

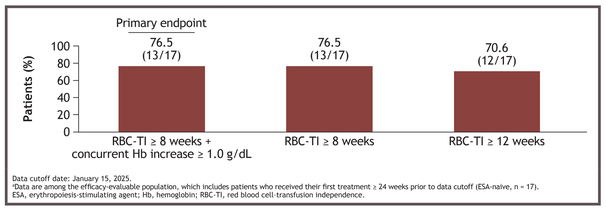
Data cutoff date: January 15, 2025.
[a]Data are among the all-treated population, defined as all patients who received ≥ 1 dose of study intervention.
AE, adverse event; ESA, erythropoiesis-stimulating agent; Hb, hemoglobin; R/R/I, relapsed/refractory/intolerant.

Efficacy

ESA-naive cohort

- 76.5% of patients in the ESA-naive cohort (evaluable patients, n = 17) achieved RBC-TI ≥ 8 weeks (Weeks 1-24) with concurrent Hb increase ≥ 1.0 g/dL (**Figure 2**)
  - 70.6% of ESA-naive patients achieved RBC-TI ≥ 12 weeks (Weeks 1-24)

Figure 2. ESA-naive cohort preliminary efficacy: RBC-TI (Weeks 1-24; n = 17[a])



Data cutoff date: January 15, 2025.
[a]Data are among the efficacy-evaluable population, which includes patients who received their first treatment ≥ 24 weeks prior to data cutoff (ESA-naive, n = 17).
ESA, erythropoiesis-stimulating agent; Hb, hemoglobin; RBC-TI, red blood cell-transfusion independence.

- An increase in Hb was observed for the ESA-naive cohort (evaluable patients, n = 15) with a median (IQR) change from baseline to maximum Hb value (Weeks 1-24) of 2.8 (2.3-3.8) g/dL (**Table 3**)

Table 3. ESA-naive cohort summary of Hb levels

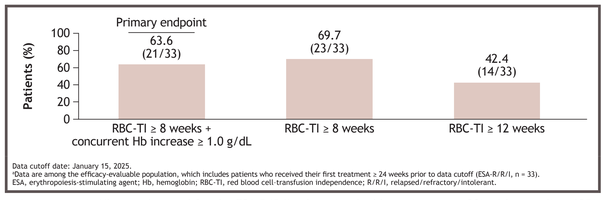
	Median (IQR) g/dL
Baseline Hb (n = 40)[a]	8.1 (7.3-8.6)
Change from baseline to maximum Hb value (n = 15)[b]	2.8 (2.3-3.8)
Primary endpoint responders' (n = 13)[c] change from baseline to maximum Hb value	3.2 (2.3-4.1)

Data cutoff date: January 15, 2025.
[a]Data are among the all-treated population, defined as all patients who received ≥ 1 dose of study intervention (ESA-naive, n = 40).
[b]Data are among patients in the efficacy-evaluable population who had both baseline and post-baseline values (ESA-naive, n = 15).
[c]Data are among patients in the ESA-naive cohort who achieved RBC-TI ≥ 8 weeks (Weeks 1-24) with a concurrent mean Hb increase of ≥ 1.0 g/dL (n = 13).
ESA, erythropoiesis-stimulating agent; Hb, hemoglobin; RBC-TI, red blood cell-transfusion independence.

ESA-R/R/I cohort

- 63.6% of patients in the ESA-R/R/I cohort (evaluable patients, n = 33) achieved RBC-TI ≥ 8 weeks (Weeks 1-24) with concurrent Hb increase ≥ 1.0 g/dL (**Figure 3**)
  - 42.4% of ESA-R/R/I patients achieved RBC-TI ≥ 12 weeks (Weeks 1-24)

Figure 3. ESA-R/R/I cohort preliminary efficacy: RBC-TI (Weeks 1-24; n = 33[a])



Data cutoff date: January 15, 2025.
[a]Data are among the efficacy-evaluable population, which includes patients who received their first treatment ≥ 24 weeks prior to data cutoff (ESA-R/R/I, n = 33).
ESA, erythropoiesis-stimulating agent; Hb, hemoglobin; RBC-TI, red blood cell-transfusion independence; R/R/I, relapsed/refractory/intolerant.

- An increase in Hb was observed for the ESA-R/R/I cohort (evaluable patients, n = 29) with a median (IQR) change from baseline to maximum Hb value (Weeks 1-24) of 2.4 (1.9-2.9) g/dL (**Table 4**)

Table 4. ESA-R/R/I cohort summary of Hb levels

	Median (IQR) g/dL
Baseline Hb (n = 50)[a]	7.4 (6.9-7.7)
Change from baseline to maximum Hb value (n = 29)[b]	2.4 (1.9-2.9)
Primary endpoint responders' (n = 23)[c] change from baseline to maximum Hb value	2.2 (1.9-3.3)

Data cutoff date: January 15, 2025.
[a]Data are among the all-treated population, defined as all patients who received ≥ 1 dose of study intervention (ESA-R/R/I, n = 50).
[b]Data are among patients in the efficacy-evaluable population who had both baseline and post-baseline values (ESA-R/R/I, n = 29).
[c]Data are among patients in the ESA-R/R/I cohort who achieved RBC-TI ≥ 8 weeks (Weeks 1-24) with a concurrent mean Hb increase of ≥ 1.0 g/dL (n = 23).
ESA, erythropoiesis-stimulating agent; Hb, hemoglobin; RBC-TI, red blood cell-transfusion independence; R/R/I, relapsed/refractory/intolerant.

Safety

ESA-naive cohort

- Treatment-emergent adverse events (TEAEs) were reported in 72.5% of patients in the ESA-naive cohort (**Table 5**)
- Grade 3 or 4 TEAEs occurred in 37.5% of patients in the ESA-naive cohort; 2.5% were related to treatment
- TEAEs leading to drug interruption occurred in 5.0% of patients in the ESA-naive cohort
- Treatment-emergent events of interest were reported in 22.5% of patients in the ESA-naive cohort
  - No thromboembolic events were observed thus far
  - The rate of asthenia (including fatigue) was 7.5% for patients in the ESA-naive cohort
- At the time of this analysis, no patients progressed to AML

Table 5. Summary of safety, including TEAEs,[a] in the ESA-naive cohort

Patients, n (%)	ESA-naive (n = 40)
Any grade TEAE	29 (72.5)
Any grade treatment-related TEAE	5 (12.5)
Grade 3/4 TEAE	15 (37.5)
Grade 3/4 treatment-related TEAE	1 (2.5)
Serious TEAEs[b]	9 (22.5)
TEAEs leading to drug interruption	2 (5.0)
TEAEs leading to dose reduction	1 (2.5)
TEAEs leading to permanent discontinuation of study intervention	0
Progression to AML	0
Patients with ≥ 1 treatment-emergent EOI[c]	9 (22.5)
Asthenia (including fatigue)	3 (7.5)
Hypertension	3 (7.5)
Fractures	2 (5.0)
Kidney toxicity	2 (5.0)
Malignancies	0

Data cutoff date: January 15, 2025.
[a]Data are among the all-treated population, defined as all patients who received ≥ 1 dose of study intervention.
[b]No patients reported that a serious TEAE was treatment related.
[c]No patients experienced EOIs of extramedullary hemopoiesis masses, immunogenicity hypersensitivity type reactions, immunogenicity injection local type reactions, liver toxicity, premalignant disorders, or thromboembolic events.
AML, acute myeloid leukemia; EOI, event of interest; ESA, erythropoiesis-stimulating agent; TEAE, treatment-emergent adverse event.

ESA-R/R/I cohort

- TEAEs were reported in 84.0% of patients in the ESA-R/R/I cohort (**Table 6**)
- Grade 3 or 4 TEAEs occurred in 42.0% of patients in the ESA-R/R/I cohort; 6.0% were related to treatment
- TEAEs leading to drug interruption occurred in 16.0% of patients in the ESA-R/R/I cohort
- Treatment-emergent events of interest were reported in 44.0% of patients in the ESA-R/R/I cohort
  - No thromboembolic events were observed thus far
  - The rate of asthenia (including fatigue) was 26.0% for patients in the ESA-R/R/I cohort
- At the time of this analysis, no patients progressed to AML

Table 6. Summary of safety, including TEAEs,[a] in the ESA-R/R/I cohort

Patients, n (%)	ESA-R/R/I (n = 50)
Any grade TEAE	42 (84.0)
Any grade treatment-related TEAE	17 (34.0)
Grade 3/4 TEAE	21 (42.0)
Grade 3/4 treatment-related TEAE	3 (6.0)
Serious TEAEs[b]	15 (30.0)
TEAEs leading to drug interruption	8 (16.0)
TEAEs leading to dose reduction	1 (2.0)
TEAEs leading to permanent discontinuation of study intervention	1 (2.0)
Progression to AML	0
Patients with ≥ 1 treatment-emergent EOI[c]	22 (44.0)
Asthenia (including fatigue)	13 (26.0)
Hypertension	3 (6.0)
Fractures	5 (10.0)
Kidney toxicity	3 (6.0)
Malignancies	2 (4.0)

Data cutoff date: January 15, 2025.
[a]Data are among the all-treated population, defined as all patients who received ≥ 1 dose of study intervention.
[b]No patients reported that a serious TEAE was treatment related.
[c]No patients experienced EOIs of extramedullary hemopoiesis masses, immunogenicity hypersensitivity type reactions, immunogenicity injection local type reactions, liver toxicity, premalignant disorders, or thromboembolic events.
AML, acute myeloid leukemia; EOI, event of interest; ESA, erythropoiesis-stimulating agent; R/R/I, relapsed/refractory/intolerant; TEAE, treatment-emergent adverse event.

Conclusions

- In this preliminary analysis, luspatercept initiated at the maximum approved dose (1.75 mg/kg) was well tolerated among patients in the ESA-naive and ESA-R/R/I cohorts
  - Low rates of discontinuation and dose modifications were reported
  - No new safety signals occurred, and no thromboembolic events were observed
  - No patients progressed to AML at the time of this analysis
- The ESA-naive cohort showed high response rates, with > 70% of patients achieving sustained RBC-TI responses of ≥ 12 weeks and a low rate of adverse events, including fatigue
- The preliminary results of the MAXILUS study indicate that starting luspatercept at the maximum approved dose was well tolerated, with no new safety signals observed
- Efficacy data in this small number of patients remain preliminary, and forthcoming data disclosures will provide additional insight on the benefit-risk profile of luspatercept initiated at the maximum approved dose

References

1. Platzbecker U et al. *Leukemia*. 2021;35:2182-2198.
2. Reblozyl® (luspatercept-aamt). Package insert. Bristol Myers Squibb; May 2024.
3. Della Porta MG et al. *Lancet Haematol*. 2024;11:E646-E658.
4. Garcia-Manero G et al. *Blood*. 2024;144(Supplement 1):350.
5. Fenaux P et al. *N Engl J Med*. 2020;382:140-151.

Acknowledgments

- The patients and families who made the study possible
- The clinical study teams who participated
- Study drugs were provided by Bristol Myers Squibb (Princeton, NJ, USA)
- The study was supported by Celgene, a Bristol Myers Squibb Company, in collaboration with Acceleron Pharma Inc., a wholly owned subsidiary of Merck & Co., Inc., Rahway, NJ, USA
- All authors contributed to and approved the poster
- Writing and editorial assistance were provided by Annabel Black, PhD, of Lumanity Communications Inc., and were funded by Bristol Myers Squibb

Disclosures

MGDP served as a consultant or in an advisory role for Bristol Myers Squibb, GSK, and AbbVie. MDC consulted or participated in an advisory role for Bristol Myers Squibb/Celgene, Novartis, GSK, and Blueprint Medicines; received travel and accommodation expenses from Gilead Sciences; and received honoraria from Bristol Myers Squibb/Celgene and Novartis. VS served as a consultant or in an advisory role for Bristol Myers Squibb/Celgene, Novartis, Gilead Sciences, AbbVie, Syros, Servier, Geron, CTI, Otsuka, Curis, and Ascentage Pharma; had travel, accommodations, or other expenses paid or reimbursed by Janssen-Cilag; received honoraria from Bristol Myers Squibb/Celgene and Novartis; and received institutional research funds from Celgene. RB received funding for her myelodysplastic syndromes/neoplasm registry and honoraria from Bristol Myers Squibb. LA received honoraria from Celgene, AbbVie, Jazz Pharmaceuticals, and Novartis; and received research funding from Celgene (inst). TB, TZ, YL, and AM are employees of and may own stock in Bristol Myers Squibb. DM is an employee of and may own stock in Bristol Myers Squibb; had travel, accommodations, or other expenses paid or reimbursed by Bristol Myers Squibb; and received compensation for a leadership role from Bristol Myers Squibb. KM served on an advisory board for AbbVie and Bristol Myers Squibb; and received lecture fees from AbbVie, Bristol Myers Squibb, and Teva. DV received consulting fees from Amgen, Astellas Pharma, Bristol Myers Squibb, Jazz Pharmaceuticals, Kite Pharma, Merck Sharp & Dohme, Novartis, Sanofi, and Sobi; received honoraria from Aglos, Amgen, Astellas Pharma, Bristol Myers Squibb, Gebro, Grifols, Janssen, Jazz Pharmaceuticals, Kite Pharma, Merck Sharp & Dohme, Novartis, Pfizer, Sanofi, and Sobi; received travel support from Bristol Myers Squibb, Jazz Pharmaceuticals, Novartis, Sanofi, and Sobi; and received advisory or data safety monitoring board fees from Amgen, Bristol Myers Squibb, Grifols, Jazz Pharmaceuticals, Novartis, Servier, and Sobi. AMZ received grant support from AbbVie, Amgen, Astex, Bristol Myers Squibb, Celgene, Geron, Kura, Novartis, Otsuka, Shattuck Labs, and Syros; and received consulting fees and honoraria from AbbVie, Aglos, Akeso Pharma, ALX Oncology, Amgen, Astellas Pharma, BeiGene, BioCryst, Bristol Myers Squibb, Boehringer Ingelheim, Celgene, Chiesi, Daiichi Sankyo, Epizyme, Faron, Genentech, Geron, Gilead Sciences, Gycommimetics, Hikma, Janssen, Karyopharm, Keros, Kura, Kyowa Kirin, Lava Therapeutics, Mendus, Notable, Novartis, Orum, Otsuka, Pfizer, Regeneron, Rigel Pharmaceuticals, Schrödinger, Servier, Sumitomo Pharma, Syndax, Syros, Taiho, Takeda, Treadwell, Vincerx, and Zentalis. LS, GD, JMT-D, DD, SG, SV, and UP have no disclosures to report.

Scientific Content on Demand

To request a copy of this poster:

Scan QR code
via a barcode reader application

QR codes are valid for 90 days after the congress presentation date.

Presented at the European Hematology Association (EHA) Congress; June 12-15, 2025; Milan, Italy