Treatment Patterns and Clinical Outcomes in Patients With Lower-Risk Myelodysplastic Syndromes Treated With First-Line Luspatercept

6412

Findings From a Medical Record Review in France and Germany

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Introduction

- In patients with lower-risk myelodysplastic syndrome (LR-MDS), luspatercept has demonstrated significant clinical benefit in treating transfusion-dependent (TD) anemia in randomized clinical trials[1-3]
- Based on the findings of the pivotal phase 3 COMMANDS trial,[3,4] luspatercept received expanded approval for first-line (1L) use in patients aged ≥18 years with TD LR-MDS by the European Commission in March 2024
- Luspatercept's use patterns and associated clinical outcomes in treatment-naive patients with LR-MDS in real-world settings are not well documented

Objective

- This study aimed to describe baseline characteristics, treatment patterns, and clinical outcomes in patients with LR-MDS treated with 1L luspatercept in France and Germany

Methods

Study design

- A retrospective review of medical records of patients with LR-MDS initiating 1L treatment with luspatercept in France and Germany was performed
- Medical record screening, review, and data abstraction were led by practicing physicians (hematologists, oncologists, or hematologist-oncologists) who had ≥3 years of experience treating patients with MDS (having treated ≥1 patient with luspatercept in the past 1 year) and were the primary decision-makers in the treatment of their patients
- Data were entered directly into a web-based, electronic data collection form (data abstraction period, December 2024 to January 2025)

Patient inclusion criteria

- Confirmed diagnosis of primary LR-MDS according to International Prognostic Scoring System (IPSS) or the Revised IPSS (IPSS-R) risk scoring
- Initiated treatment with luspatercept after June 2020 in France and after May 2023 in Germany (date of luspatercept initiation defined the study index date)
- At least 12 months of complete medical record or history before initiation of luspatercept treatment
- Known ring sideroblast (RS) status at the index date
- Aged ≥18 years at the index date
- At least 6 months of follow-up after index date (unless the patient died earlier)

Patient exclusion criteria

- Received luspatercept or another MDS-specific treatment as part of a clinical trial
- Evidence of other malignant neoplasms prior to MDS diagnosis
- History of acute myeloid leukemia prior to MDS diagnosis

Study measures and analysis

- Baseline characteristics (eg, demographics, genetic risk factors at MDS diagnosis) and use of treatments after LR-MDS diagnosis were analyzed
- Baseline transfusion status was assessed during the 16-week preindex period and classified as nontransfusion-dependent (NTD) for 0 red blood cell (RBC) units and TD for >0 RBC units (low transfusion burden, 1-7 units; high transfusion burden, ≥8 units)
- For patients with TD, achieving transfusion independence (TI) (ie, 0 RBC units) was the main outcome parameter and was assessed over any 12-week period during the first 6 months postindex period (12-week TI)
- Hemoglobin (Hb) response (ie, increase of ≥1.5 g/dL compared with the baseline Hb level) within 6 months of treatment initiation also was assessed
- Time to discontinuation (TTD) and time to 12-week TI were analyzed using the Kaplan-Meier method

Results

- 39 physicians (18 in France and 21 in Germany) from both academic (56.4%) and community (43.6%) settings participated in the study
- 110 patients (53 in France and 57 in Germany) meeting study eligibility criteria were included in the analysis (median age, 74 years; 54.5% male)
- Median follow-up was 13.1 months (first quartile [Q1], 10.1; third quartile [Q3], 22.4) from MDS diagnosis and 9.8 months (Q1, 7.4; Q3, 13.3) from luspatercept initiation
- Median time from LR-MDS diagnosis to 1L luspatercept initiation was 1.6 months (Q1, 0.6; Q3, 5.6)
- Baseline clinical characteristics are shown in **Table 1**

Table 1. Baseline clinical characteristics

Total patients (N=110)	n	%
IPSS-R risk status at initial LR-MDS diagnosis		
Patients with known data	105	95.5
Very low	7	6.7
Low	58	55.2
Intermediate	40	38.1
RBC TD status at baseline		
Patients with known data	106	96.4
NTD at luspatercept initiation	21	19.8
TD at luspatercept initiation	85	80.2
Low transfusion burden (1-7 units in the past 16 weeks)	46	54.1
High transfusion burden (≥8 units in the past 16 weeks)	39	45.9
RS status at baseline		
Patients with known status	110	100
RS+	67	60.9
RS-	43	39.1
Key genetic factors at or before luspatercept initiation		
Del(5q) abnormality		
Patients with known status	110	100
Yes	11	10
No	99	90
***SF3B1* mutation**		
Patients with known status	93	84.5
Positive (mutant)	38	40.9
Negative (wild-type)	55	59.1
Hemoglobin (g/dL) level at baseline (most recent measurement within 16-week before luspatercept initiation)		
Median (Q1, Q3)	8.0 (7.0, 8.7)	
Total duration of follow-up (in months) from luspatercept initiation		
Median (Q1, Q3)	9.2 (7.8, 13.9)	

Luspatercept usage patterns

- Average dose at luspatercept initiation was 1.0 mg/kg (standard deviation [SD], 0.1) among those with known dosing data (n=108), with a majority (96.4%) receiving a 3-weekly cycle
- One-third of patients (33.6% [n=37]) received a dose increase (**Table 2**)

Table 2. Luspatercept dose before and after modification, among patients with an increase

Total patients (N=37)	n	%
1 mg/kg to 1.2 mg/kg	1	2.7
1 mg/kg to 1.3 mg/kg	4	10.8
1 mg/kg to 1.33 mg/kg	15	40.5
1 mg/kg to 1.75 mg/kg	12	32.4
1.33 mg/kg to 1.75 mg/kg	4	10.8
Missing data	1	2.7

[a] Approved dose levels for dose escalation as per luspatercept label are 1.33 mg/kg and 1.75 mg/kg.

- In Kaplan-Meier analysis, the estimated median TTD of luspatercept therapy was 25.3 months (95% confidence interval [CI], 19.4-not estimable [NE])
  - The estimated proportion of patients who remained on therapy at 12 and 24 months was 68.4% and 57.9%, respectively
- Overall, 30% (n=33) discontinued luspatercept therapy
  - Average dose at discontinuation (irrespective of whether patients had a dose increase) in patients with known data (n=33) was 1.4 mg/kg (SD, 0.4); median was 1.3 mg/kg (range, 1.0-1.8)
- Among those who discontinued (n=33), the majority (54.5% [n=18]) had their dose at discontinuation at or below 1.33 mg/dL
- The most common reason for discontinuation among patients who remained alive as of the last follow-up was "lack of efficacy" (67.9% among all patients who discontinued [n=19/28] and 38.5% among patients who discontinued with dose at or below 1.33 mg/dL [n=5/13])

Table 3. TI outcomes within 6 months in patients who were TD at baseline, overall and by RS status

	All patients		RS negative at baseline		RS positive at baseline	
Total patients, N	110		43		67	
TD at baseline AND received index treatment for at least 12 weeks to assess outcome, n (%)	81	73.6%	33	76.7%	48	71.6%
Achieved 12-week TI (i.e., required 0 units of RBCs over a 12-week period within 6 months of treatment)						
Yes	52	64.2%	19	57.6%	33	68.8%
No	29	35.8%	14	42.4%	15	31.3%
Time to 12-week TI from index date (in months)						
Observed (among patients who achieved TI)						
Mean (SD)	1.3	1.2	0.9	1.1	1.5	1.2
Median	1.1		0.3		1.4	
Minimum, maximum	0	3.2	0	3.2	0	3.2
Estimated (from Kaplan-Meier analysis, among all patients)						
Mean (standard error)	2	0.1	1.9	0.3	2	0.2
Median	2.4		2.6		2.3	
95% CI	1.6	3.1	0.7	NE	1.4	3.1

Clinical outcomes

- Results for clinical outcomes (12-week TI achievement and Hb response) are presented in **Tables 3 and 4** for all patients and by RS status

Table 4. Hemoglobin response within 6 months in all patients, patients with TD, and patients with NTD, overall and by RS status

Hemoglobin level increased by ≥1.5 g/dL	All patients	RS negative at baseline	RS positive at baseline
Total patients (TD or NTD), N	110	43	67
Patients with known data, n (%)	98 (89.1)	38 (88.4)	60 (89.6)
Yes	52 (53.1)	21 (55.3)	31 (51.7)
No	46 (46.9)	17 (44.7)	29 (48.3)
TD patients, N	85	37	48
Patients with known data, n (%)	78 (91.8)	34 (91.9)	44 (91.7)
Yes	40 (51.3)	18 (52.9)	22 (50.0)
No	38 (48.7)	16 (47.1)	22 (50.0)
NTD patients, N	21	5	16
Patients with known data, n (%)	17 (81.0)	4 (80.0)	13 (81.3)
Yes	11 (64.7)	3 (75.0)	8 (61.5)
No	6 (35.3)	1 (25.0)	5 (38.5)

Limitations and strengths

- Patients selected for study inclusion represent a "convenience" sample in that the records were obtained from physicians who are willing to participate in the study; therefore, findings may not be generalizable
- Study represents clinical practice in Germany and France and may not be generalizable to other countries
- Data were entered directly by the treating physicians and therefore may be subject to entry errors and resulting inaccuracies in reporting
- A customized electronic data collection form allowed for uniform collection of important study measures that involved clinician interpretation and study measures that are typically not available in pre-existing coded data sources
- Some analysis subgroups represent small sample sizes (e.g., patients with NTD RS), which is a reflection of clinical practice

CONCLUSIONS

- In this retrospective study, patients with LR-MDS treated with 1L luspatercept showed substantial clinical response with high rates of TI achievement and Hb response during the first 6 months after treatment initiation, regardless of RS status
- Most patients continued with the luspatercept therapy for over a year, and among those who discontinued, a considerable proportion discontinued before reaching the optimal recommended target dose of 1.75 mg/kg despite citing lack of efficacy as one of the top reasons for discontinuation
- Overall, these findings complement efficacy data from clinical trials and highlight the real-world effectiveness of 1L treatment with luspatercept in LR-MDS

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