A retrospective study to assess real-world treatment patterns and outcomes in luspatercept-treated patients with myelofibrosis-associated anemia who required red blood cell transfusion in the United States

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Introduction

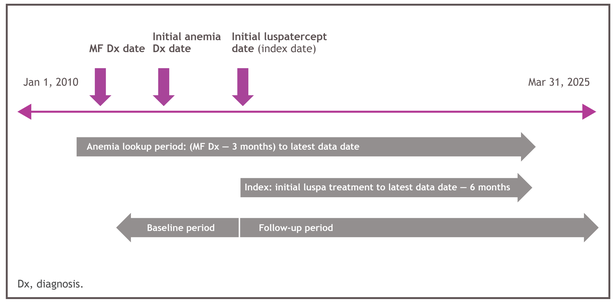
- Anemia is a common and serious clinical manifestation in patients with myelofibrosis (MF), contributing to poor quality of life and reduced survival[1]
- Existing treatments for MF-associated anemia are limited by suboptimal efficacy and significant side effects, prompting the development of effective and durable novel treatments to address anemia while optimizing the benefits of JAK inhibitor (JAKi) therapy[2]
- Luspatercept, a first-in-class erythroid maturation agent, is recommended in the NCCN Clinical Practice Guidelines in Oncology for Myeloproliferative Neoplasms as a category 2A recommendation for the management of MF-associated anemia[3]
  - In the phase 2 ACE-536-MF-001 study (NCT03194542), luspatercept showed an increase in hemoglobin levels and red blood cell transfusion (RBCT) independence (RBCT-TI), and reduced transfusion burden in patients with MF[4]
  - The phase 3 INDEPENDENCE study (NCT04717414) is evaluating luspatercept versus placebo in transfusion-dependent (TD) patients with MF-associated anemia receiving concomitant JAKi. In line with previous results from the phase 2 trial, luspatercept with concomitant JAKi demonstrated clinically meaningful improvements in RBC-TI, reduction in RBCT burden, hemoglobin improvement, and a tolerable safety profile[5]
- Real-world (RW) evidence on the effectiveness and utilization of luspatercept in patients with MF-associated anemia requiring RBCTs is limited
- The aim of this study was to describe baseline characteristics, treatment patterns, and outcomes of patients with MF-associated anemia who required RBCT and were treated with luspatercept in the RW setting

Methods

Study design

- Myelofibrosis Anemia patients Real-World trEatment pattern of Luspatercept treatment: the MARWEL study, a claims database study, is a retrospective RW analysis of patients with MF-associated anemia who required RBCT (transfusion requiring; TR) or were RBCT dependent (TD), who were treated with luspatercept in the US (**Figure 1**)
  - TR was defined as patients with 1 RBCT event within 12 weeks prior to luspatercept start; TD was defined as patients with ≥ 2 RBCT events in the same baseline period
  - Index date was defined as luspatercept initiation date
  - Each RBCT event was assumed to be equal to 2 RBCT units

Figure 1. MARWEL study design



Dx, diagnosis.

Patient inclusion and exclusion criteria

- Adult patients (≥ 18 years) in the US were identified from the Optum Clinformatics® Data Mart Database if they had an MF diagnosis (from January 1, 2010), an anemia diagnosis within 3 months before or after MF diagnosis, and initiated ≥ 1 luspatercept treatment (index date) after January 1, 2020
- Eligible patients had ≥ 1 RBCT within 12 weeks prior to the index date
- Patients had continuous medical and pharmacy enrollment for ≥ 6 months before and after luspatercept initiation unless the patients were deceased
- Patients were excluded if they were diagnosed with other primary cancers within 6 months prior to index date, defined as ≥ 1 inpatient or ≥ 2 outpatient diagnosis claims on 2 different dates

Key outcomes

- RBC-TI was defined as the proportion of subjects who become RBCT free over any consecutive 12-week (RBC-TI 12) or 16-week (RBC-TI 16) period, starting from index date up to week 24
- Duration of response was defined as the maximum duration of a response calculated from the start of TI response to the first subsequent RBCT; otherwise, the duration is censored at the the end of the follow-up
- RBCT reduction was defined as the proportion of patients who reduce their transfusion burden by ≥ 50% from baseline over any consecutive 12-week period starting from index date up to week 24
- RW time to treatment discontinuation (rwTTD) was defined as the length of time observed in RW data from initiation of luspatercept to last dose by Kaplan-Meier estimation. Discontinuation was defined as death, switch to other anemia treatments, or a gap of ≥ 120 days between the last dose and end of follow up. Otherwise, the patient was censored

In this RW study, patients with MF who required RBCT and were treated with luspatercept achieved clinically meaningful benefits, including 12- and 16-week RBC-TI and ≥ 50% RBCT reduction

Figure 4a. Rate of RBC-TI and proportion of patients achieving ≥ 50% reduction in transfusion burden by week 24

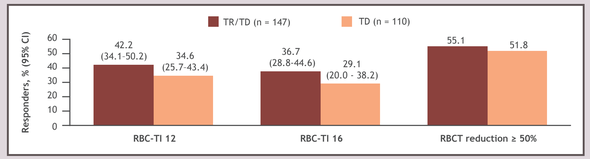


Figure 4b. Longest duration of RBC-TI response

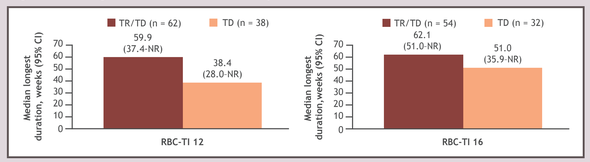
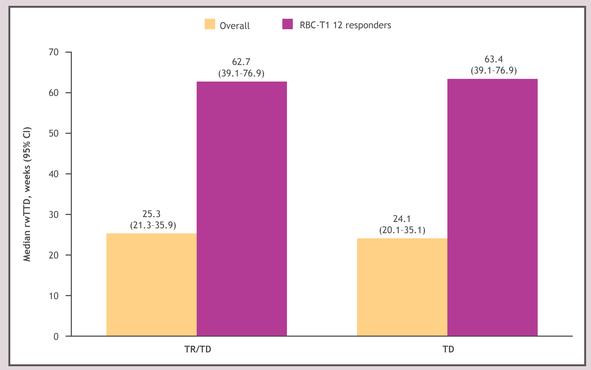


Figure 5. Time to treatment discontinuation



Results

Baseline characteristics

- At the end of data availability (March 31, 2025), the final study population who met the inclusion criteria and had received luspatercept consisted of 147 and 110 patients who were classified as TR/TD and TD, respectively
- The median (IQR) age was 78 (72–82) for the TR/TD cohort and 77 (72–82) for the TD cohort (**Table 1**)
- In TR/TD and TD patients, the median (IQR) times between MF diagnosis and index date were 1.1 and 0.90 years; 47.6% and 52.7% of the populations started luspatercept < 1 year after initial MF diagnosis
- In the 12 weeks prior to index date, the median number of RBCT events was 3 and 4 for the TR/TD and TD cohorts, respectively, and 58.5% and 78.2% of patients had ≥ 3 RBCT events, respectively

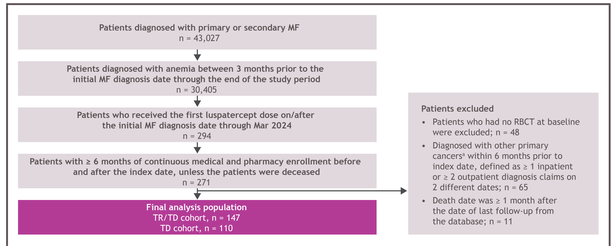
Treatment patterns

- In the TR/TD cohort, 48 patients were treated with JAKi any time post MF diagnosis
- In the TD cohort, 39 patients were treated with JAKi any time post MF diagnosis
- Ruxolitinib was the most frequently used JAKi in both cohorts (**Figure 3**)

Anemia-related outcomes in the TR/TD population

- The proportion (95% CI) of TR/TD patients who achieved RBC-TI 12 and RBC-TI 16 within 24 weeks after luspatercept initiation were 42.2% (34.1-50.2) and 36.7% (28.8-44.6)
- Of the TR/TD population, 55.1% patients achieved ≥ 50% RBCT reduction by 24 weeks (**Figure 4a**)
- The median (95% CI) longest duration of RBC-TI 12 and RBC-TI 16 was 59.9 (37.4-NR) weeks and 62.1 (51.0-NR) weeks, respectively (**Figure 4b**)

Figure 2. Patient attrition



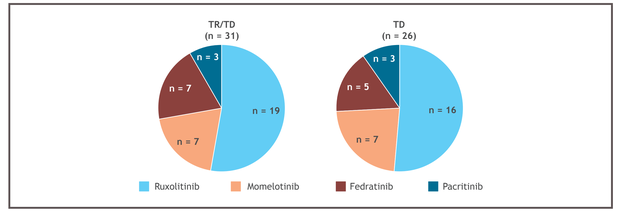
[a]Other primary cancers exclude MDS, basal or squamous cell carcinoma of skin, carcinoma in situ of the cervix, and carcinoma in situ of the breast.

Table 1. Baseline characteristics

	TR/TD (n = 147)	TD (n = 110)
Age at index luspatercept start, median (Q1, Q3)	78 (72, 82)	77 (72, 82)
Gender, male, n (%)	79 (53.7)	63 (57.3)
Race, n (%)		
White	109 (74.2)	85 (77.3)
Black	24 (16.3)	16 (14.6)
Asian	4 (2.7)	3 (2.7)
Missing	7 (4.8)	5 (4.6)
Unknown	3 (2.0)	1 (0.9)
MF subtype, primary, n (%)	58 (39.5)	39 (35.5)
Year of luspatercept index start, n (%)		
2020	25 (17.0)	18 (16.4)
2021	21 (14.3)	19 (17.3)
2022	23 (15.7)	16 (14.6)
2023	37 (25.2)	29 (26.4)
2024	41 (27.9)	28 (25.5)
Time between initial MF diagnosis and index date, median (IQR)	1.1 (0.5-3.4)	0.9 (0.4-2.5)
Time between initial MF diagnosis and index date, n (%)		
< 1 year	70 (47.6)	58 (52.7)
1-2 years	29 (19.7)	21 (19.1)
2-5 years	31 (21.1)	22 (20)
≥ 5 years	17 (11.6)	9 (8.2)
Treated with JAKi at any time after initial MF diagnosis, n (%)	48 (32.7)	39 (35.4)
Median follow-up time after index date, months (IQR)	12.5 (7.0-19.8)	12.1 (6.7-18.4)
Deceased, n (%)	91 (61.9)	73 (66.4)
Median number of RBCT events in the 12 weeks prior to index, median (IQR)[a]	3 (1.5-5)	4 (3-6)
Number of RBCT events in the 12 weeks prior to index, n (%)		
1	37 (25.2)	0 (0)
2	24 (16.3)	24 (21.8)
≥ 3	86 (58.5)	86 (78.2)

[a]1 event – 1 or 2 units RBCT.

Figure 3. Patients with concomitant JAKi treatment



Time to treatment discontinuation

- The median rwTTD, per Kaplan-Meier estimate, was 25.3 weeks in the TR/TD cohort and 24.1 weeks in the TD cohort (**Figure 5**)
  - The probability of remaining on treatment was 49.0% for the TR/TD cohort and 47.3% for the TD cohort at 6 months, and 30.5% and 27.1%, respectively, at 12 months (**Table 2**)
- Among RBC-TI 12 responders, the median rwTTD was 62.7 weeks in the TR/TD cohort and 63.4 weeks in the TD cohort
  - The probability of remaining on treatment was 71.0% for the TR/TD cohort and 78.9% for the TD cohort at 6 months, and 54.5% and 59.9%, respectively, at 12 months

Table 2. Probability of remaining on luspatercept treatment[a]

	TR/TD		TD	
Luspatercept time to rwTTD[b]	Overall (n = 147)	RBC-TI 12 responder (n = 62)	Overall (n = 110)	RBC-TI 12 responder (n = 38)
Patients who discontinued treatment, n (%)	119 (81.0)	43 (69.4)	96 (87.3)	30 (80.0)
Probability of remaining on treatment, %				
At 6 months	49.0	71.0	47.3	78.9
At 12 months	30.5	54.5	27.1	59.9

[a]Discontinuation defined as: 1) luspatercept was followed by another anemia treatment (ESA/danazol) regardless of gap, or 2) there was a gap ≥ 120 days between the last luspatercept until the end of follow up or death, or 3) patients initiated next line of luspatercept (gap > 120 days), or 4) patient died during treatment and last luspatercept use was within 120 days until death date.
[b]rwTTD defined as the length of time from initiation to discontinuation of a medication ([date of last recorded dose – date of first recorded dose] + 1 d).
d, day; ESA, erythroid-stimulation agent.

Limitations

- RBCT events may not be consistently recorded in RW clinical practice due to potential missing data from out-of-network providers; patients may not have received RBCT despite clinical presentation
- Claims data often lacks key clinical variables, such as hemoglobin levels and patient risk categories

Conclusions

- In this RW study, patients with MF who required RBCT and were treated with luspatercept showed clinically meaningful benefits
  - 42% and 35% of patients achieved 12-week RBC-TI in TR/TD and TD populations, respectively, with rates remaining stable over rolling 16-week periods
  - More than half of patients experienced a ≥ 50% RBCT reduction within 24 weeks of luspatercept initiation, even among those with very high baseline transfusion burden
  - Among responders, over half remained on luspatercept for ≥ 1 year, indicating durable benefit
- Luspatercept showed effectiveness in both TR/TD and TD populations, with greater benefit observed in patients with lower transfusion burden
- These RW findings generally corroborate and extend previous clinical trial results, supporting that luspatercept can be an effective option to increase transfusion independence and reduce transfusion burden in this population

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