Durable Transfusion Independence in Lower-Risk Myelodysplastic Syndromes Is Associated With Better Survival: A Population Level Analysis Based on a Large US Health Insurance Claims Database

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Introduction

- RBC transfusions are needed in 50% to 90% of patients with MDS, and nearly half those will require ≥1 platelet transfusion[1]
- In patients with MDS and anemia, patients' QOL is impaired by an increasing need for RBC transfusions, which leads to increased medical resource utilization and represents an economic burden[2]
- The few approved therapeutic options available for the treatment of LR-MDS have limited efficacy and durability, and patients' disease subsequently becomes resistant and requires long-term treatment with RBC transfusions[3-5]
- Patients with RBC-TD MDS that is relapsed or refractory to/ineligible for ESAs have a higher risk of progression to AML and worsened survival than patients with continued response to ESAs[4]
- The key treatment goals for LR-MDS are to manage anemia with fewer transfusions, increase QOL, limit disease progression, and improve survival

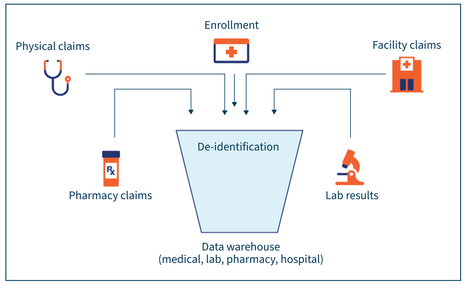
Aim

- To assess baseline RBC-TD before 1L and 2L of therapy, durability of TI, and associated survival among patients with LR-MDS treated with current standard-of-care therapies in a large US health insurance claims database between October 2015 and June 2022

Methods

- Optum Clinformatics Data Mart is a HIPAA-compliant, administrative claims database of approximately 17- to 19-million annual lives, for a total of >76-million unique lives over a 9-year period
- The database is estimated to contain 70% to 90% of death records of health plan members
- Eligibility-controlled data include integrated patient-level enrollment information derived from claims submitted for all medical and pharmacy health care services, related health care costs, and resource utilization (**Fig. 1**)

Figure 1: Optum's De-identified Clinformatics® Data Mart Database



Patients and outcomes

- Patients with LR-MDS were identified through 5 relevant ICD-10 diagnosis codes and patient index date identification between October 2015 and June 2022 (**Table 1**)
- Eligible patients had no MDS/AML diagnosis and no use of HR-MDS or AML medication before their respective index diagnosis dates (**Fig. 2**)
  - Lines of treatment were determined based on claims for MDS treatments contained in the database
- IPSS-R or other risk score classification information was not available in the database, and ICD-10 diagnosis codes were used as a proxy for the identification of LR-MDS; these codes have been used previously in published studies[6]
- Outcomes of interest included transfusion burden (RBC U/8 wk), the proportion of patients who were TI before and after different lines of treatment, and time to 8- and 16-week continuous TI

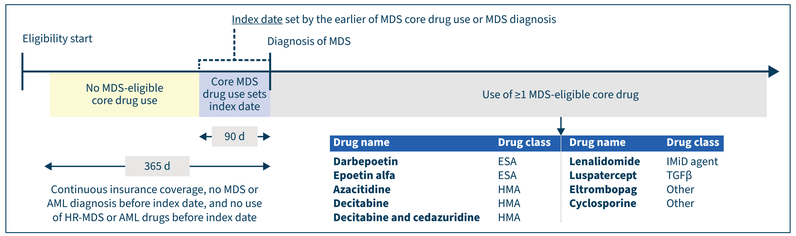
Analysis

- rwPFS, defined as time to next treatment (as a proxy for progression) or progression to HR-MDS, AML, or death, whichever came first, was evaluated
- Kaplan-Meier analysis of rwPFS and OS was performed

Table 1. Diagnosis Codes for Low/Intermediate-Risk MDS

Description	ICD-10 code	WHO 2008 classification[7]
Refractory anemia RS−	D46.0	RA
Refractory anemia RS+	D46.1	RARS
Refractory cytopenia with multilineage dysplasia	D46.A	RCMD
Refractory cytopenia with multilineage dysplasia and RS+	D46.B	RCMD-RS
MDS unspecified	D46.9	MDS-U

Figure 2. LR-MDS Based on Patient ICD-10 Code and Index Date Identification



Results

Demographics and characteristics

- This analysis comprised 5662 patients diagnosed with LR-MDS according to 5 clinical diagnostics codes who received ≥1 line of treatment (**Table 2**)
- Of the patients enrolled from the database, 87% had MDS unspecified and were diagnosed under ICD-10 code D46.9
- Most patients were men of non-Hispanic, White ethnicity and were members of Medicare Advantage health care insurance
- Overall, 3796 (67%) and 958 (17%) patients received frontline monotherapy with ESAs and HMAs, respectively
- 79% of patients with sEPO records (n = 496) had levels of <200 mIU/mL before treatment; mean (SD) sEPO at index treatment was 183.2 (357.8) mIU/mL

Table 2. Baseline Demographics and Characteristics

Characteristic*	Overall (n = 5662)	ICD-10 classification			
		D46.1 (n = 233)	D46.0 (n = 229)	D46.A, D46.B (n = 298)	D46.9 (n = 4902)
Age, median (range), y	79 (73-84)	77 (73-83)	80 (71-85)	78 (72-83)	79 (73-84)
Sex, n (%)					
Female	2432 (43)	103 (44)	108 (47)	109 (37)	2112 (43)
Male	3228 (57)	130 (56)	121 (53)	188 (63)	2789 (57)
Race, n (%)					
Non-Hispanic White	4132 (76)	179 (81)	139 (65)	234 (82)	3580 (76)
Non-Hispanic Black	597 (11)	22 (10)	36 (17)	20 (7)	519 (11)
Hispanic	526 (10)	15 (7)	22 (10)	24 (8)	465 (10)
Other	407 (7)	17 (7)	32 (14)	20 (7)	338 (7)
Insurance type closest to index treatment, n (%)					
Commercial	483 (9)	20 (9)	18 (8)	29 (10)	416 (8)
Medicare	5179 (91)	213 (91)	211 (92)	269 (90)	4486 (92)

*Reported in ≥5% of patients in either group to maintain de-identification.

Treatment use in 2L

- Monotherapies were the primary treatment choice in 2L, which consisted of ESA (40%), HMA (21%), luspatercept (9%), or a combination thereof (19%; **Fig. 3**)

RBC transfusions before and during lines of treatment

- In the 16 weeks before 1L initiation, 35% of patients received ≥1 RBC transfusion (**Table 3**)
- During 1L, 45% of patients received ≥1 RBC transfusion; of those, 49% received >3 U, and 24% received >6 U during any 8-week period
- More patients received ≥1 RBC transfusion during 2L than in the 16 weeks before 2L initiation
- Among patients receiving ≥1 transfusion during 2L, 61% and 31% had >3 and >6 U/8 wk, respectively
- TB increased with subsequent lines of treatment across all patient subtypes and was greater for patients with RS+ disease during 2L treatment (**Figs. 4** and **5**)

Figure 3. Treatment Use in 2L (n = 1245)

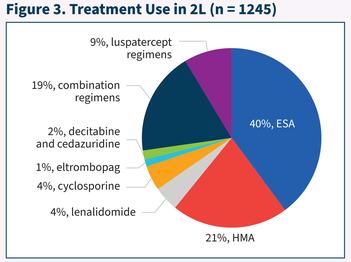


Table 3. RBC Transfusions 16 Weeks Before and During 1L and 2L

	16 wk before treatment (n = 5662)	1L (n = 5662)	16 Wk before 2L (n = 1245)	2L (n = 1245)
Duration, d				
Mean (SD)		239 (304)		234 (272)
Median (IQR)		123 (51-298)		134 (59-295)
≥1 RBC transfusion, n (%)				
Yes	2000 (35.3)	2563 (45.3)	612 (49.2)	682 (54.8)
No	3662 (64.7)	3099 (54.7)	633 (50.8)	563 (45.2)
RBC transfusions, n (%)[a]				
1-3 U/8 wk	1286 (64.3)	1303 (50.8)	273 (44.6)	265 (38.9)
4-6 U/8 wk	500 (25.0)	656 (25.6)	195 (31.9)	203 (29.8)
>6 U/8 wk	214 (10.7)	604 (23.6)	144 (23.5)	214 (31.4)

[a]Units were the maximum units of any rolling 8-week period in the evaluation period. If a patient was followed for <8 weeks, their total number of units was used.

Figure 4. RBC Transfusion by RS Status Received 16 Weeks Before and During 1L and 2L

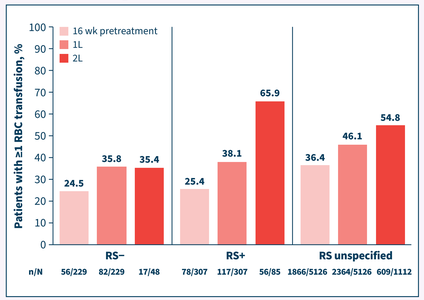
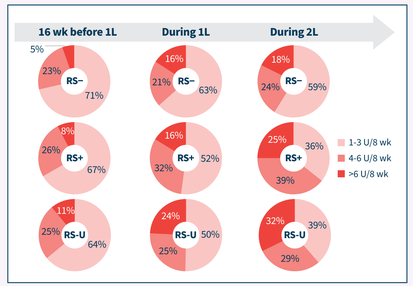


Figure 5. RBC Transfusion Units by RS Status Received 16 Weeks Before and During 1L and 2L



Percentages do not add to 100% due to value rounding.

RBC transfusions in patients treated with luspatercept

- Mean duration of 2L luspatercept treatment was 238 days
- Of 107 patients, 77% and 64% received ≥1 RBC transfusion before and during 2L, respectively
- In total, 59% of patients still required ≥4 U during 2L with luspatercept, albeit the sample size was small

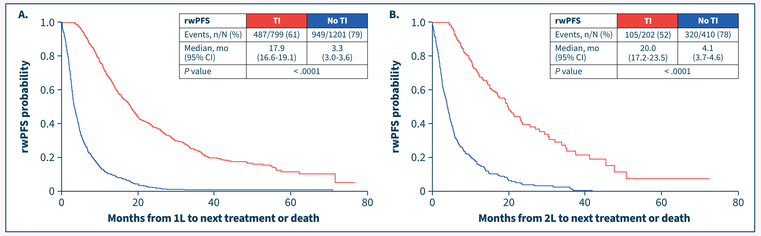
Time to continuous TI

- Median time to 8-week TI was 2.8 and 3.7 months from start of 1L and 2L, respectively
- Median time to 16-week TI was 5.3 and 6.7 months from start of 1L and 2L, respectively
- Among 612 patients who received ≥1 transfusion in the 16-week period before 2L, 33% achieved 16-week TI with subsequent therapies

Patient outcomes analysis

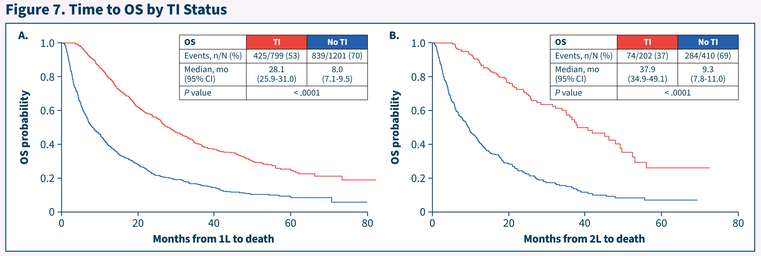
- Median rwPFS from the start of 1L and 2L, respectively, was significantly longer in patients who achieved 16-week TI after treatments than in patients who did not ($P < .0001$; **Fig. 6**)
- TI responders also had significantly greater improvement in median OS from 1L and 2L than nonresponders ($P < .0001$ for both; **Fig. 7**)

Figure 6. rwPFS by TI Status



Analysis limited to patients who received ≥1 transfusion in the 16-week period before start of (A) 1L and (B) 2L.

Figure 7. Time to OS by TI Status



Analysis limited to patients who received ≥1 transfusion in the 16-week period before start of (A) 1L and (B) 2L.

Conclusions

- **Claims data from >5600 patients indicate that achievement of TI was associated with improved survival, suggesting that RBC-TD is a modifiable predictor of clinical outcomes in LR-MDS**
- **However, despite currently available standard-of-care therapies, RBC-TD after any line of treatment is associated with poorer outcomes**
- **Our study results suggest that novel therapies that provide durable TI may delay progression, improve QOL, and prolong survival of patients with LR-MDS**
- **Limitations of our analysis include:**
  - **LR-MDS was defined based on ICD-10 codes and not the IPSS-R or other risk score classifications**
  - **Transfusion data were captured using claims without access to hemoglobin levels**
  - **Small sample size for some subgroups**

ABBREVIATIONS

1L, first line; 2L, second line; AML, acute myeloid leukemia; ESA, erythropoiesis-stimulating agent; HMA, hypomethylating agent; HR-MDS, higher-risk myelodysplastic syndromes; HIPAA, Health Insurance Portability and Accountability Act; ICD-10, International Classification of Diseases, Tenth Revision; IPSS-R, revised International Prognostic Scoring System; IQR, interquartile range; lab, laboratory; LR-MDS, lower-risk myelodysplastic syndromes; MDS, myelodysplastic syndromes; OS, overall survival; QOL, quality of life; RBC, red blood cell; RS, ring sideroblast; rwPFS, real-world progression-free survival; sEPO, serum erythropoietin; TD, transfusion dependence; TGFβ, transforming growth factor beta; TI, transfusion independence; WHO, World Health Organization.

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