Relationship Between Durable Transfusion Independence and Survival Outcomes in Patients With Lower-Risk Myelodysplastic Syndrome: An Analysis From US Health Insurance Claims Data

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Introduction

- RBC transfusion dependency is common in patients with MDS, for whom 50% to 90% are in need of RBC transfusions, and nearly half of these patients require ≥1 platelet transfusion[1]
- The increased need for RBC transfusions in patients with MDS and anemia impairs QOL[2]
- Limited efficacy and durability of available approved therapeutic options for the treatment of LR-MDS result in disease subsequently becoming resistant and dependent on long-term RBC transfusions[3-5]
- Patients with RBC-TD MDS relapsed or refractory to ESAs or ineligible for ESAs have a higher risk of progression to AML and worsened OS than patients continuously responsive to ESA treatments[4,5]
- Key treatment aims for LR-MDS are the management of anemia with fewer transfusions, maintaining or improving QOL, limiting disease progression, and prolonging survival[6]

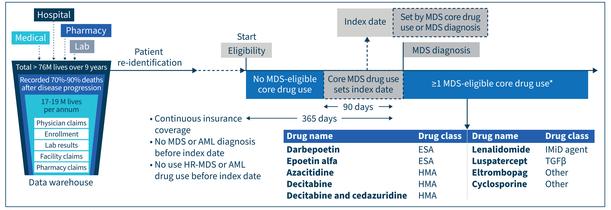
Aim

- 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 March 2023

Methods

- Eligibility-controlled data included 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



*Treatment lines based on MDS treatment claims in database.

Patients and outcomes

- IPSS-R or other risk score classification information was not found in the database
- ICD-10 diagnosis codes were used as an alternative for the identification of LR-MDS (**Table 1**); these codes have been used previously in published studies[7]
- Outcomes of interest included transfusion burden (RBC U/8 wk), percentages of patients who were TI before and after lines of treatment, and time to 8- and 16-week continuous TI

Table 1. Diagnosis Codes for Low/Intermediate-Risk MDS (Oct 2015 – Mar 2023)

Description	ICD-10 code	WHO 2016 classification[a]
Myelodysplastic syndrome RS−	D46.0	MDS
Myelodysplastic syndrome RS+	D46.1	MDS-RS
Myelodysplastic syndrome with multilineage dysplasia	D46.A	MDS-MLD
Myelodysplastic syndrome with multilineage dysplasia and RS+	D46.B	MDS-RS-MLD
MDS unclassifiable	D46.9	MDS-U

Analysis

- rwPFS – defined as the time to next treatment (as a proxy for progression) or progression to HR-MDS, AML, or death (whichever event occurred first)
- rwPFS and OS – by Kaplan-Meier analysis

Results

Baseline Demographics and Characteristics

- 6531 participants diagnosed with LR-MDS who received ≥1 line of treatment were included in the analysis (**Table 2**)
- 79% of patients with sEPO records (n = 564) had levels of <200 mIU/mL before treatment; mean (SD) sEPO at index treatment was 177.9 (347.8) mIU/mL

Table 2. Baseline Characteristics

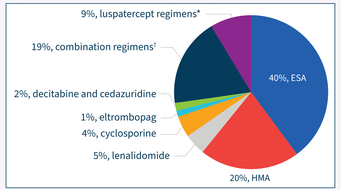
Characteristic*	Overall (n = 6531)	ICD-10 classification			
		D46.1 (n = 282)	D46.0 (n = 256)	D46.A, D46.B (n = 340)	D46.9 (n = 5653)
Age, median (range), y	79 (73-84)	77 (73-83)	80 (72-85)	78 (72-83)	79 (73-84)
Sex, n (%)					
Male	3721 (57)	157 (56)	134 (52)	214 (63)	3216 (57)
Female	2808 (43)	125 (44)	122 (48)	125 (37)	2436 (43)
Race, n (%)					
Non-Hispanic white	4796 (73)	216 (77)	158 (62)	266 (78)	4156 (74)
Non-Hispanic black	661 (10)	31 (11)	36 (14)	26 (8)	568 (10)
Hispanic	608 (9)	18 (6)	26 (10)	26 (8)	538 (10)
Other	466 (7)	17 (6)	36 (14)	22 (6)	391 (7)
Insurance type closest to index treatment, n (%)					
Medicare	5997 (92)	259 (92)	238 (93)	308 (91)	5192 (92)
Commercial	534 (8)	23 (8)	18 (7)	32 (9)	461 (8)

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

Treatment

- Treatment of choice in 2L was primarily monotherapies with ESA (40%) and HMA (20%), followed by combination regimens (19%) and luspatercept regimens (9%) (**Fig. 2**)

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



*Luspatercept alone or in combination with core drugs listed in **Fig. 1**. †Combinations of core drugs listed in **Fig. 1**.

Drug name	Drug class	Drug name	Drug class
Darbepoetin	ESA	**Lenalidomide**	IMiD agent
Epoetin alfa	ESA	**Luspatercept**	TGFβ
Azacitidine	HMA	**Eltrombopag**	Other
Decitabine	HMA	**Cyclosporine**	Other
Decitabine and cedazuridine	HMA		

RBC transfusions before and during lines of treatment

- Median duration of treatment was similar between patients during 1L and 2L (126 vs 133 days)
- More patients received ≥1 RBC transfusion during 2L than in the 16 weeks before 2L initiation (**Table 3**)
- Among patients receiving ≥1 transfusion during 2L, 70% had >2 U during any 8-week period
- TB increased with subsequent lines of treatment and was greater for patients with RS+ and RS− disease during 2L treatment (**Figs. 3** and **4**)

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

	16 wk before 1L (n = 6531)	1L (n = 6531)	16 wk before 2L (n = 1488)	2L (n = 1488)
Duration, d				
Mean (SD)		247 (320)		241 (290)
Median (IQR)		126 (53-306)		133 (60-301)
≥1 RBC transfusion, n (%)				
Yes	2301 (35)	2977 (46)	745 (50)	818 (55)
No	4230 (65)	3554 (54)	743 (50)	670 (45)
RBC transfusions, n (%)*				
1-2 U/8 wk	1199 (52)	1211 (41)	271 (36)	244 (30)
3-7 U/8 wk	922 (40)	1202 (40)	332 (45)	363 (44)
>8 U/8 wk	180 (8)	564 (19)	142 (19)	211 (26)

*Units were the maximum units during 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 3. RBC Transfusion by RS Status Received 16 Weeks Before and During 1L and 2L

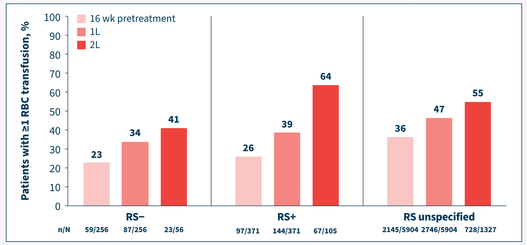
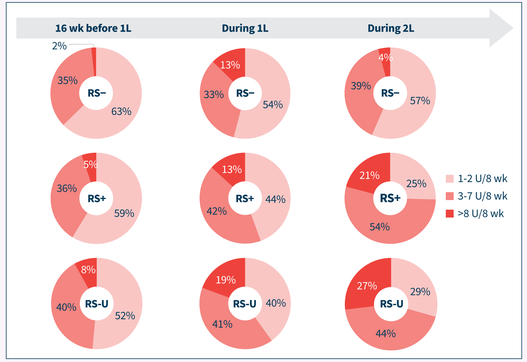


Figure 4. RBC Transfusion Units by RS Status Received 16 Weeks Before and During 1L and 2L



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

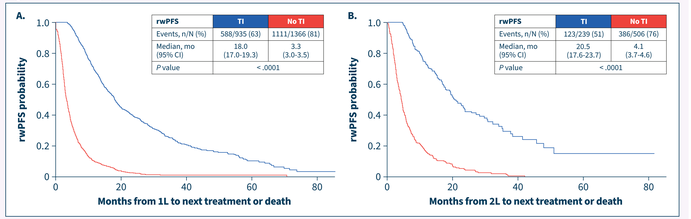
Time to continuous TI

- 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 5.1 and 6.7 months from start of 1L and 2L, respectively
- Among 745 patients who received ≥1 transfusion in the 16-week period before 2L, 32% achieved 16-week TI with subsequent therapies

Patient outcomes analysis

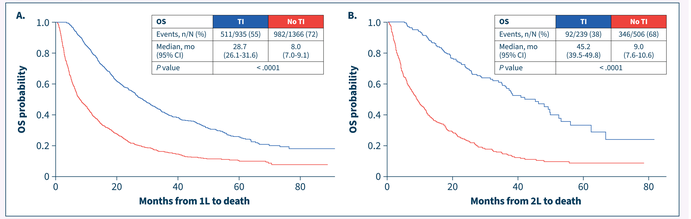
- Median rwPFS from the start of 1L and 2L was significantly longer in patients who achieved 16-week TI after treatments than in patients who did not ($P < .0001$; **Fig. 5**)
- Participants who achieved TI also had significantly greater improvement in OS from 1L and 2L than did those with no TI ($P < .0001$ for both; **Fig. 6**)

Figure 5. 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 6. 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 >6500 patients with LR-MDS suggest that RBC-TD may be a modifiable predictor of clinical outcomes and is associated with improved survival and the achievement of TI**
- **However, RBC-TD after any lines of treatment is associated with poorer outcomes, despite currently available standard-of-care therapies**
- **Results of this analysis indicate that achieving TI may delay progression to AML, preserve or improve overall QOL, and prolong survival of patients with LR-MDS**
- **Limitations of our analysis include the following:**
  - **LR-MDS was defined on the basis of ICD-10 codes and not IPSS-R or other risk score classifications**
  - **RBC transfusion data were captured using claims without access to patient hemoglobin levels**
  - **There was a small sample size for some population 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; ICD-10, International Classification of Diseases, Tenth Revision; IPSS-R, revised International Prognostic Scoring System; IQR, interquartile range; 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; TB, transfusion burden; TD, transfusion dependence; TGFβ, transforming growth factor beta; TI, transfusion independence; WHO, World Health Organization.

ACKNOWLEDGMENTS

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DISCLOSURES

The presenter, Shyamala Navada, reports current employment and equity holder in publicly traded company: Geron Corporation.

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