Early Real-World Use and Hematologic Outcomes With Imetelstat in Patients With Myelodysplastic Syndromes: Insights From a United States Community Oncology Chart Review

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MDS - 775

Background

- Imetelstat was approved for select adults with lower-risk (LR) myelodysplastic syndromes (MDS) and red blood cell (RBC) transfusion-dependent anemia after erythropoiesis-stimulating agent (ESA) failure, ineligibility, or relapse[1,2]
- In the Phase 3 IMerge trial (NCT02598661), imetelstat improved RBC transfusion independence (TI) and hemoglobin (Hb) levels versus placebo[3]
- Early real-world evidence following approval remains limited, particularly in community practice settings where clinicians are gaining experience with patient selection and cytopenia management

This study evaluated early real-world treatment patterns and hematologic outcomes among MDS patients receiving imetelstat in community oncology settings

Methods

- **Design:** retrospective, descriptive real-world study used Ontada's iKnowMed electronic health record (EHR) data from United States (US) community oncology practices, capturing longitudinal outpatient demographics, diagnosis, laboratory values, treatment exposure, and clinically relevant outcomes
- **Population:** adults with MDS who initiated imetelstat between June 6, 2024, and May 31, 2025, identified from structured EHR data and confirmed by medical record abstraction; the index date was the first imetelstat administration; patients were followed until death, last available EHR activity, or the end of the observation period
  - Exclusion criteria: interventional trial participation on/after the index date, or receipt of systemic therapy for another primary cancer during follow-up
- **Cohort:** of 51 identified patients, 34 were randomly selected for abstraction and 30 confirmed eligible; baseline characteristics, prior therapies, line of therapy, Hb outcomes, and RBC transfusion independence were summarized descriptively
- **Hb outcomes:** baseline Hb was the minimum value within 8 weeks pre-index (nadir; sensitivity analysis used the value closest to the index within that window); post-index Hb was assessed over the treatment observation window plus a post-treatment grace period (30 and 45 days); change in Hb was the difference between the average post-index Hb value and the minimum pre-index Hb value; post-index Hb was also summarized

  Hb sensitivity analyses: excluded Hb measurements recorded within 14 days after transfusion; analyzed in the overall evaluable population and repeated among patients who received ≥2 imetelstat administrations
- **RBC-TI:** ≥8-week RBC-TI was defined as the proportion without recorded RBC transfusion during any consecutive 8-week period after imetelstat initiation; incomplete transfusion documentation limited interpretation, so Hb change was emphasized as the pragmatic hematologic outcome
- **Cytopenias:** thrombocytopenia and neutropenia events were defined based on platelet count and absolute neutrophil count (ANC) laboratory values, respectively, and graded programmatically per the Common Terminology Criteria for Adverse Events (CTCAE), version 6.0
- **Statistics:** all analyses were descriptive; categorical variables were summarized as frequencies and percentages; continuous variables as means, medians, standard deviations, and ranges
  - No formal hypothesis testing was performed

Results

Baseline Characteristics (Table 1)

- Patients were older and heavily pretreated: 76.7% >75 years; 83.3% received ≥2 prior lines of therapy (100% ESA; 72.4% luspatercept)
- Disease biology was heterogeneous, including ring sideroblast (RS)-positive and RS-negative disease

Table 1. Baseline Demographic and Clinical Characteristics

	Imetelstat (N=30)
Age group at index, n (%), y	
≤75	7 (23.3)
>75	23 (76.7)
Sex, n (%)	
Female	7 (23.3)
Male	23 (76.7)
Cytogenetic abnormality at diagnosis, n (%)	
Del(5q)	4 (13.3)
Other	26 (86.7)
Not documented	4 (13.3)
RS status, n (%)	
RS positive	12 (40.0)
RS negative	13 (43.3)
Not documented	5 (16.7)
IPSS-R risk category at diagnosis (physician documentation), n (%)	
Intermediate (>3.0 - ≤4.5 points)	3 (10.0)
High (>4.5 - ≤6.0 points)	14 (46.7)
Not documented	13 (43.3)
Hb, g/dL, median	7.7
ANC count (×10⁹/L), n (%)	
ANC ≥1.5	18 (60.0)
ANC ≥1.0 - <1.5	6 (20.0)
ANC ≥0.5 - <1.0	<3
ANC <0.5	<3
Not documented	<3
Platelet count (×10⁹/L), n (%)	
>150	13 (43.3)
100-150	7 (23.3)
75 - <100	<3
50 - <75	3 (10.0)
25 - <50	0
<25	3 (10.0)
Serum EPO (mU/mL), n (%)	
<200	<3
200-500	7 (23.3)
>500	9 (30.0)
Not documented	12 (40.0)
Prior therapy, %	
ESA	100
Luspatercept	72.4
HMA	53.6
Lenalidomide	28.6
≥2 prior lines of therapy at initiation	83.3

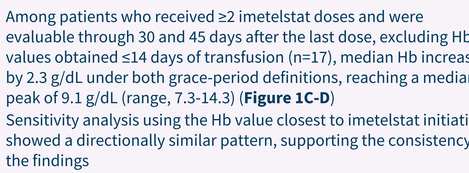
ANC, absolute neutrophil count; EPO, erythropoietin; ESA, erythropoiesis-stimulating agent; Hb, hemoglobin; HMA, hypomethylating agent; IPSS-R, Revised International Prognostic Scoring System; MDS, myelodysplastic syndromes; RS, ring sideroblast.

Treatment Patterns

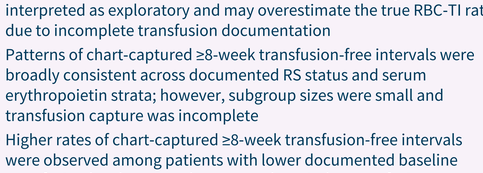
- Imetelstat was typically initiated after multiple prior therapies, consistent with early real-world adoption in heavily pretreated patients (median 42.6 months after MDS diagnosis)
- Median imetelstat treatment duration was 8.9 weeks (maximum, 57 weeks), with wide interpatient variability
- Dose holds and dose reductions were common, reflecting active cytopenia management (see Early Cytopenia Patterns)

Figure 1. Hb Change Over Time in Patients Treated With Imetelstat

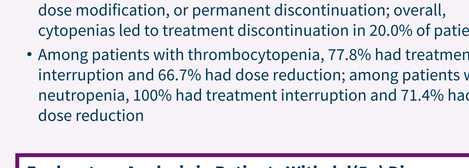
A. All Evaluable Patients With Pre- and Post-Index Hb Data (n=24). Grace Period of 30 Days (Excluding Values ≤14 Days of Transfusion)



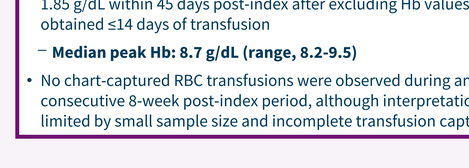
B. All Evaluable Patients With Pre- and Post-Index Hb Data (n=24). Grace Period of 45 Days (Excluding Values ≤14 Days of Transfusion)



C. Patients Who Received ≥2 Doses of Imetelstat With Pre- and Post-Index Hb Data (n=17). Grace Period of 30 Days (Excluding Values ≤14 Days of Transfusion)[a]



D. Patients Who Received ≥2 Doses of Imetelstat With Pre- and Post-Index Hb Data (n=17). Grace Period of 45 Days (Excluding Values ≤14 Days of Transfusion)[a]



Hb, hemoglobin
[a]Hb values at later post-index time points reflect the subset of patients with longer imetelstat exposure and available laboratory follow-up. The maximum observed imetelstat treatment duration was 57 weeks, with Hb follow-up extending beyond treatment during the pre-specified post-treatment grace period.

Hb Outcomes

- Hb change was evaluated as a pragmatic exploratory hematologic signal rather than a definitive effectiveness endpoint, with consistency assessed across multiple analytic approaches, including alternative baseline definitions, post-treatment laboratory grace periods, and analyses designed to minimize transfusion-related confounding
- Among all evaluable patients with pre- and post-index Hb data (N=24), median Hb increased by 2.3 to 2.7 g/dL depending on the grace-period definition, with peak Hb values of 9.0 to 9.3 g/dL
- The magnitude of Hb improvement was preserved after excluding Hb values obtained ≤14 days of transfusion (n=24), with a median increase of 2.5 g/dL and a median peak of 8.9 g/dL (range, 6.2-14.3) with a grace period of 30 days (**Figure 1A**), and a median increase of 2.5 g/dL with a median peak of 9.1 g/dL (range, 6.2-14.3) with a grace period of 45 days (**Figure 1B**). This sensitivity analysis reduces concern that the observed Hb gains were driven by recent transfusion effects
- Among patients who received ≥2 imetelstat doses and were evaluable through 30 and 45 days after the last dose, excluding Hb values obtained ≤14 days of transfusion (n=17), median Hb increased by 2.3 g/dL under both grace-period definitions, reaching a median peak of 9.1 g/dL (range, 7.3-14.3) (**Figure 1C-D**)
- Sensitivity analysis using the Hb value closest to imetelstat initiation showed a directionally similar pattern, supporting the consistency of the findings

Exploratory Chart-Captured RBC Transfusion Outcomes

- A chart-captured transfusion-free interval of ≥8 consecutive weeks was observed in 73.3% of patients; however, this finding should be interpreted as exploratory and may overestimate the true RBC-TI rate due to incomplete transfusion documentation
- Patterns of chart-captured ≥8-week transfusion-free intervals were broadly consistent across documented RS status and serum erythropoietin strata; however, subgroup sizes were small and transfusion capture was incomplete
- Higher rates of chart-captured ≥8-week transfusion-free intervals were observed among patients with lower documented baseline transfusion burden or no documented pre-index transfusions

Early Cytopenia Patterns

- Severe cytopenias were observed early after initiation, particularly around the 60-day assessment
- At approximately 60 days, laboratory-defined grade 3 or 4 cytopenias were more frequently observed among patients with impaired baseline counts; observed rates should be interpreted cautiously because denominators were small and varied with laboratory availability
- Grade 3 or 4 neutropenia at ~60 days was observed in 27.8% of patients with baseline ANC <1.5 × 10^9/L versus 5.6% of patients with baseline ANC ≥1.5 × 10^9/L
- Grade 3 or 4 thrombocytopenia at ~60 days was observed in 30.8% of patients with baseline platelet counts ≤150 × 10^9/L versus 7.7% of patients with baseline platelet counts >150 × 10^9/L
- Observed rates at ~90 days appeared lower or similar across subgroups
- Cytopenias were generally managed with treatment interruption, dose modification, or permanent discontinuation; overall, cytopenias led to treatment discontinuation in 20.0% of patients
- Among patients with thrombocytopenia, 77.8% had treatment interruption and 66.7% had dose reduction; among patients with neutropenia, 100% had treatment interruption and 71.4% had dose reduction

Exploratory Analysis in Patients With del(5q) Disease

- Among the 4 patients with del(5q) MDS, all previously exposed to lenalidomide, ESAs, and luspatercept, median Hb increased by 1.85 g/dL within 45 days post-index after excluding Hb values obtained ≤14 days of transfusion
  - **Median peak Hb: 8.7 g/dL (range, 8.2-9.5)**
- No chart-captured RBC transfusions were observed during any consecutive 8-week post-index period, although interpretation is limited by small sample size and incomplete transfusion capture

Conclusions

- In this early real-world community oncology experience, imetelstat was used primarily in older, heavily pretreated patients with MDS
- Hb trends were directionally favorable across multiple exploratory analytic approaches, including recent transfusion timing and alternative baseline Hb definitions
- Although chart-captured RBC-TI should be interpreted cautiously because of incomplete documentation, the preserved Hb signal is consistent with the clinical activity of imetelstat in routine practice
- Exploratory findings in a small subgroup of patients with del(5q) MDS suggest potential clinical activity despite extensive prior treatment exposure, although these observations require confirmation in larger cohorts
- Together, these findings provide early evidence of clinical benefit outside the trial setting and reinforce the importance of patient selection, early cytopenia monitoring, and timely dose modification to support continued treatment

Study Highlights

Evidence Gap

Early post-approval real-world evidence for imetelstat remains limited, particularly in community oncology settings where patient selection, treatment duration, transfusion documentation, and cytopenia management may differ from clinical trial settings

Main Finding

In an older, heavily pre-treated community-practice population, imetelstat was associated with consistent Hb improvement signal despite short treatment exposure and later-line use

Effectiveness Signal

Hb improvement was consistent across analytic definitions, including analyses that excluded Hb values obtained within 14 days of transfusion

Practice Implications

The preserved Hb signal supports continued evaluation of imetelstat benefit in routine practice while reinforcing the need for early cytopenia monitoring and timely dose modification to help appropriate patients remain on therapy

References

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2. RYTELO® imetelstat summary of product characteristics. Geron Corporation; 25.
3. Platzbecker U and Santini V, et al. *Lancet*. 24;403(10423):249-260.

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