Time toxicity for patients receiving oral versus parenteral hypomethylating agents for myelodysplastic syndromes/neoplasms

Robert S. Epstein,[1] Amer M. Zeidan,[2] Abisola Olopoenia,[3] Halley Costantino,[3] Kushal Modi,[3] Tehseen Salimi,[4] Terri Washington,[4] JoAnn Krenitsky[1]

[1]Epstein Health LLC, Woodcliff Lake, NJ, USA; [2]Yale University and Yale Cancer Center, New Haven, CT, USA; [3]Oracle Life Sciences, Austin, TX, USA; [4]Taiho Oncology, Inc, Princeton, NJ, USA

Background

- Patients with cancer spend substantial time at healthcare facilities receiving care.[1,2]
  - A recent study of patients with advanced cancer reported that patients spent 10% of their remaining days at healthcare encounters.[3]
  - The time spent coordinating, traveling to, waiting for, and receiving cancer treatment has been defined as "time toxicity."[4]
- Patients with higher-risk myelodysplastic syndromes/neoplasms (MDS) treated with hypomethylating agents (HMAs) are generally older (median age of 73 years at diagnosis).[5]
- Median overall survival (mOS) for patients with MDS treated with HMAs ranges between 12.0-31.8 months in clinical trials[6-10] and 11-17 months in real-world studies.[11,12]
  - Early clinical trials reported mOS of 12.0-24.5 months.[6-9]
  - The recent ASCERTAIN trial reported mOS of 31.8 months.[10]
  - Parenteral HMAs require patients to spend 5-7 consecutive days in clinics,[13,14] which imposes a substantial time burden relative to life expectancy.
- In prior surveys, patients receiving intravenous or subcutaneous (IV/SC) HMAs have reported logistical challenges and interference with activities of daily living associated with IV/SC HMA administration.[5,15]
- Oral decitabine and cedazuridine (DEC-C), approved (July 2020) by the US Food and Drug Administration for the treatment of MDS and chronic myelomonocytic leukemia, offers an alternative to parenteral HMAs.[10,16]
- In a recent survey examining MDS-treatment experience of receiving oral DEC-C, patients reported minimal interference with activities of daily living and improved quality of life (QOL) with oral DEC-C, compared with IV/SC HMAs.[17]
  - Most patients (91%) also reported that oral DEC-C reduced the number of times needed to travel to healthcare facilities.[17]
  - Oral DEC-C may be a treatment option to mitigate the time toxicity associated with MDS treatment by increasing the number of "home days" for patients.

Objective

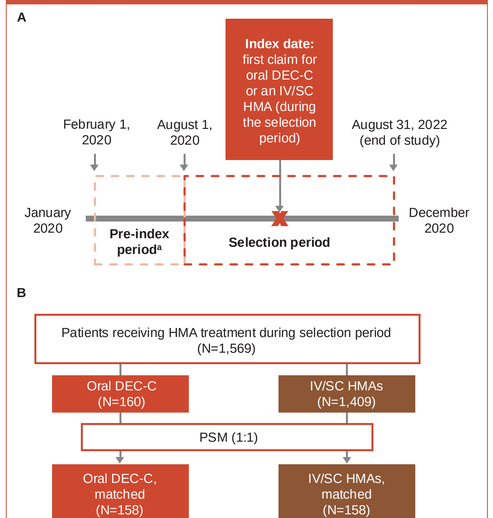
- This study evaluates the overall time burden of patients with MDS receiving oral HMA therapy compared with IV/SC HMAs.

Methods

Study design and patient cohorts

- This was a retrospective analysis of adult patients with MDS, using the US Cerner Enviza claims database.
  - This database contains prescription and/or medical claims of over 170 million individuals in the past 5 years and over 91 million individuals in the past 12 months, collected from 150+ private insurers in the US, including Medicaid managed care and Medicare Advantage plans.
- Adults diagnosed with MDS (based on *International Classification of Disease, Tenth Revision, Clinical Modification [ICD-10-CM]* code D46.x [all risk levels]) who had ≥1 claim for an HMA (oral HMA [oral DEC-C] or IV/SC HMA) between August 1, 2020 and August 31, 2022, were included (**Figure 1A**).
- Index date was defined as either the first pharmacy claim for oral DEC-C or the first medical claim for an IV/SC HMA.

Figure 1: Timeline for the retrospective database analysis (A) and patient cohort selection (B)



[a]The 6-month pre-index period was determined relative to index date.
DEC-C, decitabine and cedazuridine; HMA, hypomethylating agent; IV/SC, intravenous or subcutaneous; PSM, propensity score matching

Data analyses and outcomes

- Demographics and clinical characteristics were obtained during the 6-month pre-index period.
- Propensity score matching (PSM; 1:1) was performed on the treatment groups to balance confounding factors (age, sex, acute myeloid leukemia [AML] diagnosis, Charlson Comorbidity Index [CCI] score, and red blood cell [RBC] transfusion).
  - After matching, all covariates in the PSM were balanced (standardized mean differences <0.2[18]; **Figure 1B**); however, there were more patients in the oral HMA cohort receiving RBC transfusion than in the IV/SC HMA cohort.
- Healthcare resource utilization (HCRU) was assessed during the 6-month follow-up period after the index date for the oral and IV/SC HMA–administered patients (matched cohorts).
- To include only distinct encounter days, healthcare encounters were de-duplicated by date using a tiered approach (inpatient visits and hospitalization > emergency room [ER] visits > parenteral HMA administration > transfusion events > outpatient visits).
- Each visit was counted as 1 healthcare encounter day, except for hospitalizations, where the number of hospitalized days per visit were also counted; mean (SD) healthcare encounter days were calculated for each category.
- The combined mean (SD) healthcare encounter days for oral and IV/SC HMA groups were evaluated by summing the mean days for all healthcare encounters.

Results

Demographics and clinical characteristics of patients receiving oral or IV/SC HMA therapy (matched cohorts)

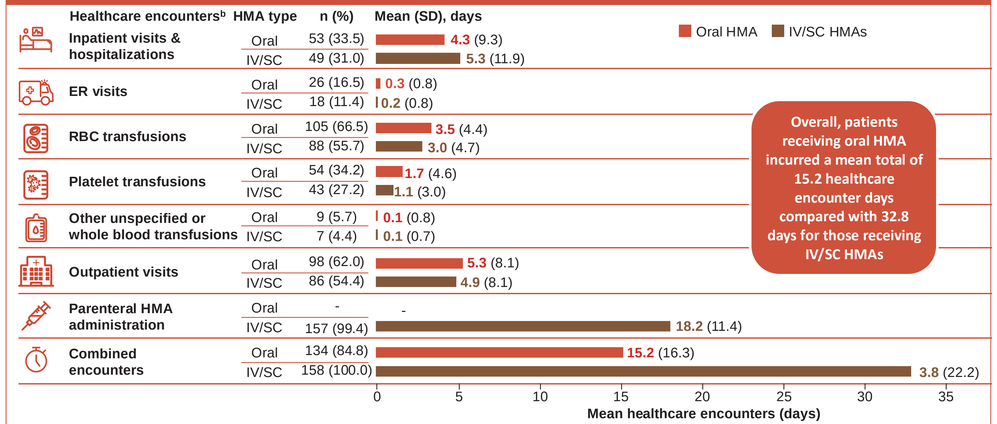
- Among the matched cohorts (N=158 each), median age was 72.0 years and 74.0 years for the oral DEC-C and IV/SC HMAs groups, respectively; 66.5% and 69.6%, respectively, were male (**Table 1**).
- Mean CCI scores were 3.5 for the oral DEC-C and 3.2 for IV/SC HMA groups; 14.6% and 15.8%, respectively, had an AML diagnosis pre-index.
- At pre-index, 58.9% of patients in the oral DEC-C cohort and 48.1% in the IV/SC HMA cohort received RBC transfusions; 24.1% and 20.9%, respectively, received platelet transfusions.

Table 1: Demographics and clinical characteristics among patients receiving oral or IV/SC HMA therapy (matched cohorts)

Patient characteristics	Oral HMA (N=158)	IV/SC HMAs (N=158)
Age, years		
Mean (SD)	70.8 (12.6)	72.0 (12.8)
Median (range)	72.0 (29-90)	74.0 (27-90)
Male, n (%)	105 (66.5)	110 (69.6)
Race/ethnicity, n (%)		
Asian or Pacific Islander	3 (1.9)	8 (5.1)
Black or African American	12 (7.6)	11 (7.0)
Hispanic	4 (2.5)	13 (8.2)
White	55 (34.8)	57 (36.1)
Other	4 (2.5)	6 (3.8)
Unknown	80 (50.6)	63 (39.9)
Insurance type, n (%)		
Commercial	59 (37.3)	44 (27.9)
Medicaid	23 (14.6)	40 (25.3)
Medicare Advantage	72 (45.6)	73 (46.2)
Unknown/other	4 (2.5)	1 (0.6)
Index HMA treatment, n (%)		
Azacitidine	0	119 (75.3)
Decitabine	0	39 (24.7)
Oral DEC-C	158 (100.0)	0
CCI score		
Mean (SD)	3.5 (3.0)	3.2 (2.8)
≥3, n (%)	88 (55.7)	83 (52.5)
Cancer diagnosis, n (%)		
Any cancer	81 (51.3)	74 (46.8)
AML	23 (14.6)	25 (15.8)
CMML	8 (5.1)	7 (4.4)
Cancer other than AML or CMML	72 (45.6)	65 (41.1)
Transfusions, n (%)		
RBC	93 (58.9)	76 (48.1)
Platelet	38 (24.1)	33 (20.9)
Stem cell transplant	4 (2.5)	1 (0.6)
ESA or G-CSF	3 (1.9)	1 (0.6)

AML, acute myeloid leukemia; CCI, Charlson Comorbidity Index; CMML, chronic myelomonocytic leukemia; DEC-C, decitabine and cedazuridine; ESA, erythropoiesis-stimulating agent; G-CSF, granulocyte colony–stimulating factor; HMA, hypomethylating agent; IV/SC, intravenous and subcutaneous; RBC, red blood cell.

Figure 2: MDS-specific[a] healthcare encounters among patients receiving oral or IV/SC HMAs (matched cohorts)



[a]Defined as HCRU claims with MDS highlighted in the primary or secondary position. [b]Based on de-duplicated data as described in the Data analysis and outcomes section.
ER, emergency room; HCRU, healthcare resource utilization; HMA, hypomethylating agent; IV/SC, intravenous and subcutaneous; MDS, myelodysplastic syndromes; RBC, red blood cell.

Healthcare encounter days among patients receiving oral or IV/SC HMAs

- During the 6-month follow-up period, patients receiving oral HMA had fewer mean inpatient and hospitalization days compared with patients receiving IV/SC HMAs (4.3 vs 5.3 days, respectively; **Figure 2**).
- Mean ER and outpatient visits were slightly higher among patients receiving oral HMA compared with patients receiving IV/SC HMAs (ER visits: 0.3 vs 0.2 days; outpatient visits: 5.3 vs 4.9 days).
- Most healthcare encounters for the oral HMA cohort were in the outpatient setting (34.9%), while most healthcare encounters for the IV/SC HMA cohort were attributed to parenteral HMA administration (55.5%), followed by inpatient (16.2%) and outpatient visits (14.9%).
- Overall, patients receiving oral HMA incurred a mean total of 15.2 healthcare encounter days compared with 32.8 days for patients receiving IV/SC HMAs.

CONCLUSIONS

- **This study, which, to date, is the first report of time toxicity among patients with MDS treated with HMA therapy, demonstrated that patients receiving oral HMA experienced less than half the time burden of patients receiving IV/SC HMAs.**
- **Parenteral HMA administration accounted for 56% of the time burden incurred by patients receiving IV/SC HMAs.**
- **These data, in conjunction with patient survey data reporting high treatment convenience and improvements in QOL with oral DEC-C,[17] support the consideration of oral HMAs as an alternative to chronic parenteral HMA therapy.**
- **Oral DEC-C has the potential to reduce the time toxicity and treatment burden associated with administration of IV/SC HMAs.**
- **Increased understanding of time toxicity and home days for cancer care may help clinicians better guide patients on treatment strategies to best align with patients' preferences and goals.**

References

1. DOI: 10.1200/JCO.2023.41.16_suppl.1537. **2.** DOI: 10.1200/JCO.2023.41.16_suppl.e13660. **3.** DOI: 10.1200/OP.19.00328. **4.** DOI: 10.1200/JCO.21.02810. **5.** DOI: 10.1016/j.clml.2021.09.009. **6.** DOI: 10.1002/cncr.21792. **7.** DOI: 10.1200/JCO.2008.19.6550. **8.** DOI: 10.1016/S1470-2045(09)70003-8. **9.** DOI:10.1200/JCO.2002.04.117. **10.** DOI: 10.1016/S2352-3026(23)00338-1. **11.** DOI: 10.1182/blood-2017-10-811729. **12.** DOI: 10.1080/10428194.2019.1703970. **13.** Vidaza (azacitidine). Prescribing Information. Celgene Corporation; September 2022. **14.** Dacogen (decitabine). Prescribing Information. Otsuka America Pharmaceutical, Inc; June 2020. **15.** DOI: 10.1016/j.clml.2022.04.023. **16.** INQOVI (decitabine and cedazuridine). Prescribing information. Taiho Oncology, Inc; March 2022. **17.** Zeidan AM, et al. Abstract presented at: 17th International Congress on Myelodysplastic Syndromes; May 3-6, 2023; Marseille, France. **18.** DOI: 10.1023/A:1020363010465.

Limitations
Results from this retrospective study should be interpreted with caution, because they can establish only associations, not causal relationships, and may not be generalizable.

Acknowledgements
This study was funded by Taiho Oncology, Inc. Medical writing support was provided by Envision Value & Access (a division of Envision Pharma Group) and funded by Taiho Oncology, Inc.

Corresponding author
Tehseen Salimi (TSalimi@taihooncology.com

Please scan this Quick Response (QR) code with your smartphone app to view an electronic version of this poster. Copies of this poster obtained through QR code are for personal use only and may not be reproduced without permission from the authors of this poster.

Presented at SOHO Annual Meeting; September 4-7, 2024; Houston, TX