Background

• Hypomethylating agents (HMAs) are the standard of care for the treatment of patients with higher-risk myelodysplastic syndromes (MDS).

• Real-world studies have shown that persistence with intravenous (IV) and subcutaneous (SC) HMAs among patients with higher-risk MDS is poor, with over one-third of treated patients receiving <4 cycles or having a ≥40-day gap in therapy despite recommendations for at least 4–6 cycles to elicit response in the absence of progression or unacceptable toxicities.

• Our prior analyses using the Surveillance, Epidemiology, and End Results (SEER)-Medicare linked database found that 44% of higher-risk MDS patients initiating HMAs were non-persistent to HMAs.

• Further, patients who were HMA non-persistent had worse health outcomes and incurred higher direct healthcare costs than those who were HMA persistent.

• Patients who were HMA persistent had a higher overall survival (13.8 months) than patients who were HMA non-persistent (9.5 months) and those with no HMA use (3.8 months).

• Patients who were HMA non-persistent incurred significantly higher total per-patient-month healthcare costs compared with patients who were HMA persistent ($18,013 vs $13,893, p<0.001).

• The Medicare component provides information recorded on Medicare claims for covered healthcare services from the time of Medicare eligibility until death.

• HMAs are generally covered healthcare services from the time of Medicare eligibility until death.

• Clinical and demographic information, and cause of death for people with cancer.

• Incurred higher direct healthcare costs than those who were HMA persistent.

Objective

• This study explored the factors associated with early discontinuation of HMA therapy in patients with higher-risk MDS.

Methods

• This was an observational, retrospective cohort study using the 2010–2016 SEER-Medicare linked database.

• – The SEER program covers patients from 18 cancer registries and includes data on clinical and demographic information, and cause of death for people with cancer.

• – The Medicare component provides information recorded on Medicare claims for covered healthcare services from the time of Medicare eligibility until death.

• Patients were included who had a new diagnosis of MDS and an International Classification of Diseases for Oncology (3rd edition) code for refractory anemia with excess blasts (RAEB) or refractory anemia with excess blasts in transformation (RAEB-T).

• Other cancer diagnosis in the 12 months after MDS diagnosis.

• Not continuously enrolled in Medicare.

• Enrolled in an HMO within 12 months of MDS diagnosis.

• Diagnosis date is after death date.

• Other cancer diagnosis in the 12 months before MDS diagnosis.

• Enrolled in Medicare within 12 months of enrollees who were a claims-based identifier for HMA discontinuation were observed for granulocyte colony stimulating factor use after only 1 cycle vs ≥4 cycles (p=0.004). These trends were most pronounced among patients who discontinued HMA therapy in the first 45 days of treatment. (Figure 2).

• Among treatment-related factors, the most statistically significant association with HMA discontinuation was observed for granulocyte colony stimulating factor use (OR 1.26, 95% CI 1.13–1.40, p<0.001). Number of pills per day was not a predictor of HMA discontinuation (OR 1.009, p=NS).

Results

• In total, 654 patients with MDS were treated with HMAs and included in the current analysis, with a median follow-up time from HMA initiation to last claims of 12 months (interquartile range, 6–17 months).

• Among all patients, the mean (SD) age at diagnosis was 77.9 (5.3) years, 62% were male, and 25% of patients were non-Hispanic White.

• Overall, 193 (29.1%) patients discontinued before 4 cycles; of these, 91 (47.2%) were male, and 85.5% of patients were non-Hispanic White.

• Age at diagnosis, median (IQR) 79 (73–84) vs 76 (70–80).

• HMA discontinuation was observed for granulocyte colony stimulating factor use after only 1 cycle vs ≥4 cycles (p=0.004).

• Significant predictors for early HMA discontinuation included older age and poor performance status.

Conclusions

• Generalizability of the study findings is limited to patients with MDS aged >65 years and those with higher-risk MDS.

• The SEER-Medicare linked database has some limitations, including lack of clinical data such as specific blood cell counts and cytogenetics needed to calculate risk score, and treatment persistence was not captured in the SEER-Medicare database.

• Further research is warranted to fully elucidate the reasons for early discontinuation in this population.

• This real-world study, almost one-third of HMA patients treated with HMA discontinued treatment before 4 cycles, with almost half of these patients discontinuing after only 1 cycle.

• Predictors of HMA discontinuation included older age and poor PS. Novel approaches are needed to improve persistence with HMA therapy and associated outcomes, particularly among these highest-risk groups.

Figure 1. Cohort Selection of Patients With Higher-Risk MDS

Figure 2. Multivariable Logistic Regression Analysis of Predictors of Early HMA Discontinuation

Table 1. Characteristics of Patients With Higher-Risk MDS Stratified by Number of HMA Cycles Completed Before Discontinuation

References

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