BACKGROUND

- The myelodysplastic syndromes (MDS) typically affect older individuals.
- High-risk MDS patients are usually treated first with hypomethylating agents (HMAs; azacitidine [AZA] or decitabine [DEC]).
- Presently, there are no approved therapeutic treatment options for those who have failed initial treatment with an HMA; 2nd-line therapeutic approaches are unproven and may include lenalidomide (LEN), switching to a different HMA, or supportive care.
- There is little published information on the treatment patterns of MDS patients after failed HMA therapy who become eligible for 2nd-line therapy.

OBJECTIVE

To describe treatment patterns of MDS patients who have failed or become intolerant to HMA therapy.

METHODS

Study Design and Data Source

- Retrospective cohort study of a large US, HIPAA-compliant, commercial health insurance claims database.
- Timeframe: 1/1/2008 to ≥ 6 months after patients became candidates for 2nd-line MDS treatment, until the end of enrollment, or study end (12/31/2012).

Study Population

- We identified patients with an MDS-associated medical claim (ICD-9-CM diagnosis codes 283.7x) being treated with an HMA in the identification (ID) period (1/1/2009–12/31/2011) who were considered to have failed initial HMA treatment (AZA or DEC).
- The index date was the date on which patients were defined as eligible for 2nd-line therapy (i.e., initiated HMA treatment but then stopped for ≥ 2 months, switched to another HMA, or had been on the same HMA for > 7 months).

RESULTS

Baseline Patient and Disease Characteristics

- Of 38,702 patients diagnosed with MDS in the ID period, 3,356 used an HMA (Figure 1).
- Among 402 patients eligible for 2nd-line MDS therapy (Figure 1), mean age was 72.9 years and 40% were female (Table 1).
- 386 (96.0%) patients had a cytopenia, including anemia (92.8%), neutropenia (53.0%), or thrombocytopenia (52.7%); Table 1).
- The mean Charlson comorbidity score was 3.6 (Table 1).
- AML/MDS dual diagnosis was present in 24.1% of patients at baseline (Table 1).

1st Line Treatment Patterns

- 283 (70.4%) and 123 (30.6%) of patients had used AZA and DEC, respectively.
- Patients averaged 6.1 (SD=5.1) HMA treatment cycles (6.4 for AZA or 5.4 (0) for DEC) prior to being considered potential candidates for 2nd-line therapy.
- 193 (48.0%) patients had “early” discontinuation (47.1% for AZA, 50.0% for DEC), defined as less than ≤ 5 treatment cycles before stopping or switching among HMAs.
- Among all 402 patients eligible for 2nd-line treatment, 320 (79.6%) received hematologic supportive care interventions: 208 (51.7%) received transfusions, 206 (51.2%) ESA, and 170 (42.3%) growth factors, at least one or more times.

OUTCOMES

1st- and 2nd-line treatment patterns:

- MDS-specific therapy: AZA, DEC, or LEN.
- Utilization of hematologic supportive care agents, including erythropoiesis-stimulating agents (ESA), growth factors (i.e., granulocyte and granulocyte-macrophage colony-stimulating factors), and blood transfusions.

1st-line treatment only: Number of AZA or DEC cycles, defined as continuous treatment periods without a gap of >7 days, and the gap between observed cycles could not be ≥ 60 days.

2nd Line Treatment Interventions

- Among 402 patients eligible for 2nd-line therapy, 32 (8.0%) switched to another HMA.
- The following treatments were received during 6 months’ followup among these 402 patients: AZA: 121 (30.1%) DEC: 74 (18.4%) Lenalidomide: 18 (4.5%)
- Supportive care: 247 (61.4%)

CONCLUSION

- These data suggest that a significant proportion of MDS patients are candidates for 2nd-line treatment after AZA and DEC.
- Discontinuation of 1st-line MDS treatment with less than ≤ 5 HMA treatment cycles is frequent in high-risk patients.
- AZA was used more often than DEC or LEN as 1st-line MDS therapy.
- The clinical reasons for early HMA discontinuation warrant further investigation, as does the frequency of need for co-administered hematologic supportive care interventions.
- Switching HMA occurs in a minority of patients after failing 1st-line HMA therapy.
- Safe and effective 2nd-line therapies that reduce cytopenias are needed for these patients.

REFERENCES


Decision tree: 2nd-line HMA therapy in MDS patients.