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ORAL ABSTRACTS

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Utilization Patterns and Outcomes from Iron Chelation in Elderly Patients with Low-Risk Myelodysplastic Syndrome

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Introduction:
Iron overload from red blood cell (RBC) transfusions is a source of morbidity and mortality in patients with myelodysplastic syndromes (MDS). Evidence supporting iron chelation therapy (ICT) in Low-Risk MDS (LR-MDS) is controversial on account of studies conducted in highly selected patients and limited clinical trial data. We conducted a large population analysis aimed at defining real-world ICT utilization in LR-MDS and associated outcomes.
Methods:
We included patients diagnosed with MDS from 2007 to 2017 in SEER-Medicare using ICD-O-3 codes, aged 66 or older, with continuous Medicare parts A, B, and D. Exclusion criteria included patients with high-risk histology (MDS with excess blasts), less than 2-year survival, without complete follow-up, or enrolled in HMO. ICT eligibility was defined as ICD-9/10 codes for transfusion-related iron overload and/or cumulative ≥20 RBC units within ≤2 years of MDS diagnosis. ICT was identified from HCPCS codes for deferoxamine or prescription records for deferasirox or deferiprone. Explanatory variables included age, sex, race, rurality, socioeconomic quintile, marital status, geographic region, MDS histologic subtype, year of diagnosis, Charlson comorbidity index (CCI), and MDS therapies, including erythropoietin-stimulating agents (ESA), hypomethylating agents (HMA), and lenalidomide, identified from HCPCS codes and prescription records. Outcomes were identified through validated algorithms using ICD-9/10 codes and included overall survival (OS), progression to acute myeloid leukemia (AML), and complications related to iron overload, comprising heart failure, non-ischemic heart disease, atrial fibrillation/flutter, and liver disease/cirrhosis. To control for confounding, we implemented 3 approaches: multivariable Cox-proportional hazards regression, propensity score matching (PSM) by conditional probability of receiving ICT, and cause-specific regression with competing risk of death.
Results:
We analyzed 2,564 LR-MDS patients who were eligible for ICT. The mean ± SD age was 81 ± 6 years and 56.2% were male. Only 393 (15.3%) of these patients received ICT. The initial agent of choice was deferasirox in 203 (51.7%), deferoxamine in 188 (47.8%), and deferiprone in 2 (0.5%). Median ICT duration was 7 months (IQR 1-20). Chelated patients were younger (median age 79 vs 81, p<0.01), more likely to have histology with ringed sideroblasts [RS] (17.8% vs 7%, p<0.01), had less comorbid burden (median CCI 1 vs 2, p<0.01), and were more frequently treated with ESA (42.8% vs 33%, p<0.01), HMA (59% vs 49.8%), and lenalidomide (27% vs 11.1%, p<0.01), than those not treated with ICT. Their median monthly RBC transfusion density was 4 (IQR 2-6). Factors predicting ICT use were histology with RS (OR=1.9, 95%CI 1.4 - 3.8), RBC transfusion density (OR=1.1 per 4 units/month, 95%CI 1.1-1.2), and therapy with ESA (OR=1.5, 95%CI 1.2-1.9), HMA (OR=1.3, 95%CI 1.1-1.8), or lenalidomide (OR=2.6, 95%CI 1.9-3.5). Among patients who received ICT, 352 (89.6%) were considered transfusion dependent (≥2 RBC units within 8 weeks before starting ICT). Of them, 278 (78.9%) achieved hematologic response (≥50% decrease in RBC units following ICT). ICT was associated with decreased risk of death (HR=0.52, 95%CI 0.46-0.59) in the multivariable model adjusting for all listed covariates. The PSM matched 379 chelated (96.4% case rate) with 729 non-chelated patients and yielded similar results for OS benefit from ICT (HR=0.53, 95%CI 0.46-0.61). Table 1 shows results for other outcomes. Across models, ICT was associated with 43-49% decreased risk of AML transformation and 23-32% reduced risk of adverse cardiac outcomes. Cardiac benefit was predominantly driven by a lower risk of heart failure. No significant association was observed between ICT and hepatic outcomes.

Conclusions:
Our results suggest that ICT is associated with fewer transfusions, improved OS, lower risk of AML, and less adverse cardiac outcomes in LR-MDS. Our older, unselected cohort better reflects real-world LR-MDS patients and builds upon OS benefit reported in more restricting settings. Given the link between clonal hematopoiesis, cardiovascular disease and LR-MDS, defining ICT's effect on molecular and clonal dynamics could clarify the mechanism behind improved cardiac outcomes.

Disclosures No relevant conflicts of interest to declare.

Table 1. Outcomes associated with ICT in LR-MDS

Outcome	Multivariable Model*		Propensity Score Model*		Competing Risk Model*	
	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
Overall Survival	0.52 (0.46 - 0.59)	<0.01	0.53 (0.46 - 0.61)	<0.01	-	-
Time to AML	0.51 (0.39 - 0.66)	<0.01	0.57 (0.43 - 0.76)	<0.01	0.56 (0.42 - 0.74)	<0.01
Composite Cardiac Outcome	0.68 (0.56 - 0.83)	<0.01	0.71 (0.57 - 0.87)	<0.01	0.77 (0.61 - 0.98)	0.04
Heart Failure	0.70 (0.58 - 0.84)	<0.01	0.69 (0.56 - 0.85)	<0.01	0.82 (0.65 - 1.04)	0.10
Non-Ischemic Heart Disease	0.80 (0.64 - 0.99)	0.04	0.80 (0.63 - 1.03)	0.08	1.07 (0.79 - 1.45)	0.66
Arrhythmia	0.73 (0.58 - 0.91)	<0.01	0.70 (0.55 - 0.89)	<0.01	0.86 (0.66 - 1.13)	0.27
Liver Disease/ Cirrhosis	1.04 (0.79 - 1.36)	0.81	1.04 (0.76 - 1.42)	0.80	1.31 (0.94 - 1.84)	0.11

ICT: Iron Chelation Therapy, LR-MDS: Low-Risk Myelodysplastic Syndrome, HR: Hazard Ratio, 95% CI: Confidence Interval, AML: Acute Myeloid Leukemia
* Adjusted for age, sex, race/ethnicity, rurality, socioeconomic quintile, marital status, geographic region, MDS histology, year of MDS diagnosis, comorbidity index, and MDS therapies (ESA, HMA, and lenalidomide).

Figure 1

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