2800 24-Month Analysis of the Impact of Chelation on Clinical Outcomes in a 600 Patient Registry of Lower-Risk MDS Patients

Program: Oral and Poster Abstracts
Session: 633. Myelodysplastic Syndromes: Poster II
Sunday, December 11, 2011, 6:00 PM-8:00 PM
Hall GH (San Diego Convention Center)

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Introduction: Many patients with MDS require regular transfusions. Several reviews have documented poorer clinical outcomes and overall survival (OS) in transfusion-dependent MDS patients. A US registry of 600 lower-risk MDS patients prospectively collected data on clinical outcomes in chelated and non-chelated transfused patients. This 24-month interim analysis reports on cardiac events, leukemic transformation and OS.

Methods: This is a 5-year, non-interventional registry in MDS patients (aged ≥18 years) with lower-risk MDS (based on WHO, FAB and/or IPSS criteria) from 107 US centers. Patients had to have transfusional iron overload (serum ferritin ≥1000 µg/L and/or ≥20 packed red blood cell units and/or ongoing transfusion requirement of ≥6 units every 12 weeks). Follow-up was every 6 months for up to 60 months or death. Use of chelation therapy was not required. Chelated patients were those who had ever used iron chelation; a sub-analysis was done on patients with ≥6 months chelation. Assessments included demographics, disease status, MDS therapy, comorbidities, and causes of death. Differences between non-chelated and chelated patients are reported.

Results: 600 patients enrolled; as of May 26, 2011, 249 continued in the registry. 351 patients discontinued due to: lost to follow-up (n=51, 8.5%); death (n=278, 46.3%); other (n=22, 3.7%). 263/600 patients received chelation therapy, of whom 191 received ≥6 months.

Table 1. Demographics, IPSS risk status and transfusion burden

	Non-chelated n(%)*	Chelated n(%)*	Chelated ≥6 months n(%)*
Age, yrs Median (range)	77 (47-99)	75 (21-94)	74 (21-94)
Male:Female ratio	1.42:1	1.31:1	1.20:1
IPSS risk status – low	56 (33.7)	56 (44.1)	38 (40.0)
IPSS risk status - INT-1	110 (66.3)	71 (55.9)	57 (60.0)
Baseline ferritin, ng/mL Median (range)	1353 (3-7379)	1512 (81-16422)	1500 (81-16422)
Median number of Lifetime units transfused	20.0	39.0	44.0
Units transfused/4 weeks while on registry	1.51	2.11	2.19

*n (%) unless otherwise indicated

Leukemic transformation and cardiac events were more common in non-chelated patients (Table 2). Time to leukemic transformation was significantly shorter in non-chelated versus chelated patients. A greater percentage of deaths occurred in non-chelated patients; time to death was significantly shorter in non-chelated versus chelated patients. The most frequent reasons for death were MDS/AML, cardiac, and infection.

Table 2. Summary of AML transformation, cardiac events and deaths

	Patient categories

	Non-chelated	Chelated	
	n (%)	All n (%)	≥6 months n (%)
AML transformation	30 (8.9)	12 (4.6)	10 (5.2)
Mean±SD time to transformation (mos)	27.3±20.3	40.6±25.3	40.8±27.0
Cardiac events	155 (46.0)	113 (43.0)	76 (39.8)
Deaths			
Number (%)	171 (50.7)	107 (40.7)	70 (36.6)
Median (25th, 75th percentiles) time to death (mos)*	52.2[†] (24.0, 136.2)	99.3[†‡] (54.1, NA)	104.4[‡] (63.4, NA)
Causes of Death			
MDS/AML	75 (22.3)	47 (17.9)	32 (16.8)
Cardiac	28 (8.3)	15 (5.7)	10 (5.2)
Infection	22 (6.5)	8 (3.0)	8 (4.2)
Unknown	16 (4.7)	10 (3.8)	6 (3.1)
Other	10 (3.0)	9 (3.4)	4 (2.1)
Malignancy	9 (2.7)	3 (1.1)	0
Respiratory	7 (2.1)	7 (2.7)	4 (2.1)
Multiorgan failure	2 (0.6)	2 (0.8)	2 (1.0)
CVA	1 (0.3)	4 (1.5)	3 (1.6)
GvHD/transplant	1 (0.3)	2 (0.8)	1 (0.5)

NA, not attained; CVA, cerebrovascular accident; GvHD, graft versus host disease.

*Time to death from diagnosis.

[†]$P<0.0001$, non-chelated vs chelated [‡]$P<0.0001$, non-chelated vs chelated≥6 months.

At baseline, non-chelated patients had a higher incidence of cardiac disorders than chelated patients (51.3% vs 35%). While on the registry, non-chelated patients had a higher incidence of comorbidities than did chelated patients, predominantly vascular, cardiac and endocrine. Lifetime use of MDS therapies (pre- and on-registry) was lower among non-chelated versus chelated patients (88.4% vs 94.3%).

Conclusions: At the 24-month analysis, use of chelation was associated with lower AML transformation, fewer cardiac events, and better OS. The two patients groups had similar age, gender, and risk status breakdown (IPSS); however the non-chelated group had a higher prevalence of cardiac comorbidities. Ongoing follow-up for the 5-year duration of this registry will provide further data on differences in outcomes between chelated and non-chelated patients.