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Clinical Parameters in 391 Iron-Overloaded Patients with Lower-Risk MDS Enrolled in a Prospective, Non-Interventional Multicenter Registry.

Guillermo Garcia-Manero[*,1], Billie J. Marek[*,2], Roger M. Lyons[3], Noelia Martinez-Lopez[*,4], Carole Paley[4] and Peter L. Greenberg[5]

[1] University of Texas MD Anderson Cancer Center, Houston, TX, USA,
[2] Texas Oncology-South Texas Cancer Center, McAllen, TX, USA,
[3] Cancer Care Centers South Texas/US Oncology, San Antonio, TX, USA,
[4] Novartis Pharmaceuticals, East Hanover, NJ, USA,
[5] Division of Hematology, Stanford University Medical Center, Stanford, CA, USA

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Introduction: Despite recent improvements in therapies for patients with myelodysplastic syndromes (MDS), 60–80% will require continuing packed red cell blood (pRBC) transfusions for prolonged periods. Complications resulting from the iron burden may, therefore, become clinically significant for many patients during the course of their disease. Patients with lower-risk MDS have a greater chance of developing the long-term toxicity of iron overload because of their prolonged survival, and are more likely to benefit from effective iron chelation therapy. This report describes data from a registry designed to study the impact of iron overload and iron chelation therapy on organ function and survival in patients with lower-risk MDS.

Methods: This is an ongoing, prospective, non-interventional, multicenter 5-year registry in 107 US centers, enrolling 600 patients (aged ≥18 years) with lower-risk MDS (by WHO, FAB and/or IPSS criteria) and transfusional iron overload (defined as serum ferritin ≥1000 µg/L and/or having received ≤20 cumulative pRBC units and/or an ongoing transfusion requirement ≥6 units every 12 weeks). Follow-up will be performed at least every 6 months for a maximum of 60 months or until death. Recommended assessments include serum ferritin, creatinine, calculated creatinine clearance, echocardiograms, and endocrine and hematological status.

Results: As of May 31 2009, 391 patients have enrolled in the registry. Demographic data are available from 389 patients. Median age: 74.4 years (range 21–99); male: 218, female: 171; ethnicity: 331 Caucasian (85%), 25 African-American (6%), 24 Hispanic (6%), five Asian (1%), two Native American (0.5%), and two other (0.5%). The median time since diagnosis (n=385) was <3 years in 217 patients (56%); ≥3–<5 years in 72 (19%); ≥5–<7 years in 48 (12%); and ≥7 years in 48 (12%). The MDS classification of the patients by WHO, FAB and IPSS, as well as patients' serum ferritin and transfusion burden, are summarized in the table.

Classification	N	%
WHO	141	36%
Refractory anemia (RA)	41	29%
RA with ringed sideroblasts (RARS)	55	39%
Refractory cytopenia with multilineage dysplasia (RCMD)	19	13%

RCMD with ringed sideroblasts	10	7%
MDS associated with isolated del 5q	14	10%
Unclassified MDS	2	1%
FAB	68	17%
RA	25	37%
RARS	25	37%
RA with excess blasts <11%	18	26%
IPSS	176	45%
Low	75	43%
Int-1	101	57%

Parameter	N	Mean ± SD	Median
Serum ferritin, µg/L	312	1806 ± 1316	1460 (normal range 12–370)
Total transfusions, n	376	26.6 ± 35.1	16
Years of transfusion	307	3 ± 5	2

The most frequent concomitant conditions classified by organ (n=384 patients) were: 205 (53%) patients with vascular, 160 (42%) endocrine, and 171 (45%) cardiac dysfunction. At registry entry, 249 patients were receiving erythropoietin; 61 granulocyte colony stimulating factor; seven hydroxyurea; 25 thalidomide (Thalomid); 147 5-azacytidine (Vidaza); 95 lenalidomide (Revlimid) and 90 decitabine (Dacogen). 137 of 391 (35%) patients were on iron chelation therapy at study entry: 34 (9%) received deferoxamine for mean and median treatment durations of 803 and 383 (range 1–4386) days, respectively, while 117 (30%) received deferasirox for mean and median durations of 488 and 396 (9–1269) days, respectively. Calculated creatinine clearance was normal (>80 mL/min) in 37 (9%) patients; mildly abnormal (51–80 mL/min) in 30 (8%); and moderately abnormal (30–50 mL/min) in nine (2%) patients.

Conclusions: These baseline data indicate the demographic distribution as well as the co-morbidities associated with lower-risk MDS patients. In spite of recent guidelines, fewer than 50% of iron-overloaded patients are receiving any iron chelation treatment, despite the presence of cardiac, vascular and endocrine concomitant conditions in 40-54% of patients. Recent retrospective data highlights the impact of chelation on mortality in lower-risk MDS patients. This ongoing registry will prospectively assess the impact of iron chelation on survival and organ function in iron-overloaded patients with lower-risk MDS.

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Footnotes

* Asterisk with author names denotes non-ASH members.

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