POSTER PRESENTATION

Improved leukemia-free and overall survival in patients with myelodysplastic syndrome receiving iron chelation therapy: A subgroup analysis.

H Leitch (abstract 1469)

<TOP line summary>

At ASH2006, the authors demonstrated improved OS in 18 patients with low and Int-1 IPSS risk MDS and iron overload who received iron chelation therapy in multivariate analysis of 178 patients. In the current study, they showed IPSS score (P=0.0001) and iron chelation therapy (P=0.03) were also significant factors for LFS. LFS and OS in MDS pts with iron overload receiving iron chelation therapy were improved compared to non- iron chelation therapy control pts matched for baseline features.

MDS is characterized by ineffective hematopoiesis and the risk of progression to acute myeloid leukemia. Many MDS patients require RBC transfusions, risking iron overload-related organ dysfunction. The authors previously reported the retrospective review for 178 MDS to evaluate the survival impact by iron chelation therapy (#249, ASH2006). 18 patients received standard iron chelation therapy (DFO 0.5-3g by subcutaneous infusion over 12 hours, 5 days per week) and all of them were low and Int-1 IPSS risk. In a multivariate analysis demonstrated improved OS in the patients who received iron chelation therapy.

In the current study, the authors examined the effect of iron chelation therapy on leukemia-free survival (LFS), cytopenias and RBC transfusion requirements. To

control for possible bias between iron-chelated patients and non- chelated patient groups, a subgroup analysis was also performed in which each of the 18 iron-chelated patients was matched to a non-chelated control patient on the basis of gender, neutrophil count, platelet count and hemoglobin (Hb) at diagnosis, MDS subtype, number of cytopenias, karyotype, IPSS score, ECOG Performance Status, number of serious infections, initial serum ferritin level, total RBC units received, primary MDS treatment, and duration of follow-up.

In a univariate analysis using all patients (n=178), significant factors for LFS included: MDS subtype; IPSS risk; increased serum ferritin level; total RBC units transfused; ≥1 serious infection; and having received iron chelation therapy (all $P<0.05$). In a multivariate analysis (n=178), significant factors for LFS were: IPSS score ($P=0.0001$) and iron chelation therapy ($P=0.03$).

In the subgroup analysis comparing iron-chelated patients to 18 control patients, most clinical characteristics were not significant but iron-chelated patients were older and higher in serum ferritin. Median follow-up was 51.4 (range: 7.1–225.8) months in iron-chelated patients and 44.8 (range: 10.1–224) months in control patients.

	Iron-chelated patients (n=18)	Matched control patients (n=18)
Median LFS	Not reached at 226 months	38 months
Four-year LFS	64%	49%
	$P=0.009$	

Median OS	Not reached at 226 months	40.5 months
Four-year OS	64%	49%
	P=0.01	

There were 5 deaths (28%) in Iron-chelated patients and 15 (83%) in control patients.

Cause of death / No.of patients	Iron-chelated patients (total n=18, death n=5)	Matched control patients (total n=18, n=15))
cardiac/IOL	2	
infection	1	2
bleeding	0	2
Other MDS-related	1	6
AML	1	4
MDS-unrelated	0	1

Although non-ICT pts were older, only 1 death was age-related and all others were from MDS. One ICT pt developed AML at 15 mo from MDS Dx as did 4 non-ICT pts (p=0.06) at a median of 35 (19-71) mo; 2 pts received chemotherapy and both died of progressive AML.

In iron-chelated patients, mean ± SE initial/pre-iron-chelated serum ferritin levels were higher than in control patients (4038 ± 627 vs 1759 ± 1108 ng/mL respectively, *P*=0.09), and follow-up levels decreased for iron-chelated patients (3070 ± 411, *P*=0.09), but not for control patients (2185 ± 96 ng/mL, *P*=NS). There was no difference between iron-chelated patients and control patients in initial and follow-up neutrophil count, platelet count, or RBC transfusion requirements.

In conclusion, LFS and OS in patients with MDS receiving iron chelation therapy were improved compared to non-iron-chelated control patients matched for baseline features. These results support findings in the larger cohort of MDS patients and suggest there may be a beneficial effect of iron chelation therapy on AML transformation and OS.