

ORAL PRESENTATION

Positive impact of iron chelation therapy (CT) on survival in regularly transfused MDS patients. A prospective analysis by the GFM.

C Rose (abstract 249)

<TOP line summary>

This study reported the positive impact on survival by iron chelation therapy in 165 patients with MDS referred to 18 French centers. Median OS from diagnosis was significantly improved in chelated patients (n=76) compared with non-chelated patients (n=89) (115 vs 51 months respectively; $P < 0.0001$). After adjustment for other prognostic parameters (sex, age, IPSS, transfusion requirement), this survival difference remained significant.

Supportive therapy with red blood cell (RBC) transfusions is the mainstay of treatment for most patients with MDS. In 2005, Malcovati et al reported that iron overload resulting from transfusion therapy in patients with MDS contributes to shortened survival. The authors prospectively surveyed 170 patients with MDS referred to 18 French centers for RBC transfusions during a 1-month period in 2005 about hematological characteristics, RBC transfusion requirement and iron chelation therapy. For the current study, the OS of this prospective cohort was re-analyzed with a reference date of May 15, 2007.

A total of 165 patients with a median age of 77 years (range: 14–95) have been analyzed (five patients were lost to follow-up).

< WHO classification>

category	No. of patients (%)
RA	13 (10%)
RARS	30 (23%)
RCMD	6 (5%)
RCMD-RA	5 (4%)
RAEB- I	28 (21%)
RAEB-II	10 (8%)
5q- Sd	11 (7%)
CMML	8 (6%)
Unclassified	21 (16%)

WHO classification was not available for 33 patients. Most patients had low (27%) or Int-1 (32%) IPSS risk scores; 10% and 2% had Int-2- and high IPSS risk scores, respectively. IPSS risk was not available for 29% of patients. The median interval from diagnosis to onset of chelation therapy was 30 months.

A total of 76 (46%) patients received chelation therapy for at least 6 months. Median duration of chelation therapy was 35 months (range:0–192). For the purposes of this analysis, patients were classified as having received ‘standard’ chelation therapy or ‘low’ chelation therapy.

Treatment	Standard chelation therapy (n=57)	Low chelation therapy (n=19)
DFO	continuous subcutaneous (8 hours, 40 mg/kg/day, 3–5 days per week)	subcutaneous bolus injection or intravenous (50–100 mg/kg/day once after each RBC transfusion)
Deferiprone	30–75 mg/kg/day	
Combination	deferiprone plus DFO	
Deferasirox	20–30 mg/kg/day	

<Change in serum ferritin level>

	SF ng/ml, (range)
At diagnosis	569 (9–2500)
Onset of chelation therapy	1436 (436–6572)
Last evaluation	1498 (272–7502)

Compared with non-chelated patients, patients who received chelation therapy had a significantly higher number of RBC units transfused, were lower in age, and had slight differences in IPSS classification (low; int-1,int-2/high in 27%, 53%, 20% of non chelated versus 49%,36%,15% of chelated pts). Median OS from diagnosis was significantly improved in chelated patients compared with non-chelated patients (115 vs 51 months respectively; $P<0.0001$). After adjustment for other prognostic parameters (sex, age, IPSS, transfusion requirement), this survival difference remained significant. A longer interval from diagnosis to onset of chelation therapy did not influence OS; however, median OS was significantly longer with standard chelation therapy compared with low chelation therapy (120 months vs 69 months; $P<0.001$). In multivariate analysis, good chelation therapy had positive effect (Hazard ratio 0.215, $P<0.0002$), IPSS>1(Hazard ratio 3.888, $P<0.0030$) and RBC>3 units/month (Hazard ratio 2.122, $P<0.0757$) had negative effect on survival.

This prospective analysis strongly suggests that chelation therapy provides a survival benefit in heavily transfused, low- to intermediate-risk (IPSS) patients with MDS. In the context of other studies presented at ASH, this analysis by Rose et al adds to the evidence that iron overload in patients with MDS is a negative prognostic marker for survival and that these patients require iron chelation therapy.