

excess iron related damage seems to be dose dependent, this harmful process probably starts when small amounts become present – therefore iron chelation therapy might be indicated theoretically whenever the ferritin level turns abnormal.

Table 1. A: Indication for upfront ICT. B: ICT indicated if se ferritin is above the threshold level that is to be determined

	EPO	HFE C282Y/H63D	JAK2 V617F	Ring sideroblasts
A: MDS at immediate risk for IO	Low/Normal	mutant	wt	present
B: MDS not at immediate risk for IO	high	wt	mutant	non

Abbreviations: IO, iron overload; ICT, iron chelation therapy; EPO, erythropoietin; HFE, hemochromatosis gene; wt, wild type gene; JAK2, janus kinase 2 gene.

P101 Deferiprone as a second line treatment in myelodysplastic syndromes. Case report

M. Iastrebnier^{1*}, A. Flores², L. Quiroga³, L. Beligoy⁴, R. Colimodio⁵. ¹San Luis Medical Center, Buenos Aires, Argentina; ²Fundacion Sanatorio Guemes, Argentina; ³Hospital Churrucua, Argentina; ⁴Centro de Enfermedades Renales Resistencia Chaco, Argentina; ⁵CDTHO Mercedes Buenos Aires, Argentina
*E-mail: miastrebnier@gmail.com

Introduction: Low and intermediate-1 (INT-1) myelodysplastic syndrome (MDS) risk groups mainly suffer from cytopenia; 80–90% of MDS patients require transfusions at any time of their follow up; consequently, some of them develop iron overload and get a liver, cardiologic and/or endocrine condition. Iron chelators ameliorate these findings, offer a better quality of life and avoid an early death.

Objective: To report clinic-hematologic results by using deferiprone (L1) as a second line chelation treatment.

Methods: From March 2007 through December 2008, we analyzed six low and INT-1 risk MDS patients under L1 treatment. Dosage: 75 mg/kg/day (table 1).

Table 1. Patient characteristics

Pt#	Age/gender	Subtype	IPSS	Cytogenetics
1	63/M	RCMD	INT-1	47XY+8,del(20)(q11)
2	55/M	RCMD	INT-1	Normal
3	64/M	RA	INT-1	Normal
4	73/F	RA	Low	Normal
5	62/M	5q-Sd	Low	46XYdel(5)(q13q33)
6	66/M	RCMD	INT-1	Monosomy 7

Median number of units transfused by patient: 23 and average transfusion rate: 3 Units/month.

Results: Median time of treatment: 5 months.

Table 2. “Ferritin (ng/ml)”

Pt#	Start Treatment	5 months of treatment
1	1678	1220
2	3100	2490
3	1820	1300
4	1540	1590
5	3100	2230
6	1650	1254

Side Effects: pruritus 2/6, arthralgias 3/6, mialgias 2/6 and mild neutropenia 1/6. Neutropenia forced stopping a L1 treatment and showed an acceptable Filgastrim response, however, it did not occur again after re-treatment.

Discussion: Despite the short-term follow up, deferiprone was effective in reducing ferritin levels without serious side effects, further studies are necessary in this issue.

P102 A multi-center, open label study evaluating the efficacy of iron chelation therapy with deferasirox in transfusional iron overload patients with myelodysplastic syndromes or aplastic anemia using quantitative R2 MRI

Y. Min^{1*}, J. Cheong¹, H. Kim², K. Lee³, S. Yoon⁴, J. Lee⁵, H. Park⁶, H. Kim⁷, H. Shim³, C. Seung⁸, C. Kim⁹, J. Chung¹⁰, M. Hyun¹¹, D. Jo¹², C. Jung¹³. ¹Yonsei University, Seoul, Korea; ²Chonnam National University, Korea; ³Ulsan University, Korea; ⁴Seoul National University, Korea; ⁵Gachon University, Korea; ⁶Soonchunhyang University, Korea; ⁷Hallym University, Korea; ⁸Ewha Womans University, Korea; ⁹Inha University, Korea; ¹⁰Pusan National University, Korea; ¹¹Yeungnam University, Korea; ¹²Chungnam National University, Korea; ¹³Sungkyunkwan University, Korea
*E-mail: jwcheong70@yuhs.ac

Transfusion-related iron overload and its consequences are emerging challenges in chronically transfused patients with myelodysplastic syndromes (MDS) or aplastic anemia (AA). Measurement of liver iron concentration (LIC) is used as a surrogate for total iron burden to guide chelation therapy in transfusion-dependent patients. Although deferasirox (Exjade[®], ICL670) is an oral iron chelation agent that is now widely available for the treatment of transfusional hemosiderosis, the clinical data on its specific benefits of iron chelation, including reduction of LIC, in transfusion-related iron overload patients with MDS or AA has been limited. We have prospectively investigated the efficacy of deferasirox for iron chelation by serial measurement of serum ferritin level and LIC, which is measured in vivo using quantitative tissue proton transverse relaxation rates (R2) magnetic resonance imaging (MRI), in transfusional iron overload patients with MDS or AA. Here we report the interim analysis data. A total of 79 patients with de

novo MDS (n=29) or idiopathic AA (n=50) showing serum ferritin level over 1,000 ng/mL were enrolled from 23 institutes. All patients were regularly transfused and received a median of 30 red blood cells (RBC) units in the year prior to the start of the study. Among MDS cases, 3 (10.3%), 20 (69.0%), and 4 cases (13.8%) were categorized as IPSS low-risk, intermediate-1-risk, and intermediate-2-risk group, respectively. In AA cases, 34 (64%) were severe form. Mean value of serum ferritin level in enrolled patients was $4,788 \pm 3,996$ ng/mL in MDS and $4,188 \pm 2,992$ ng/mL in AA at the time of deferasirox initiation. LIC value was measured using quantitative R₂ MRI and FerriScan (Resonance Health, Australia) analysis. Mean value of LIC was 24.4 ± 16.0 mg Fe/g dry weight in MDS and 22.4 ± 13.8 mg Fe/g dry weight in AA mg Fe/g. Linear regression analysis indicated a close correlation between serum ferritin level and LIC ($r=0.55$, $p < 0.001$). Deferasirox was given orally at a dose of 20 mg/kg/day for at least 6 months to all patients. If the serum ferritin fell below 500 ng/mL, treatment was withheld. A consistent decrease in the serum ferritin level was demonstrated during the first 6 months in vast majority of patients despite of continued transfusion (209.7 ± 159.9 ng/mL and 324.0 ± 289.4 ng/mL per month in MDS and AA, respectively). Over the study period, patients with MDS and AA received a mean of 3.7 and 2.7 units RBC per month, respectively. At 12 months, s-ferritin significantly decreased by 1824.0 ng/mL from baseline values, a reduction of 38.1% for patients with MDS ($P < 0.0001$) and significantly decreased by 3559.1 ng/mL from baseline values, a reduction of 85.0% for patients with AA ($P < 0.0001$). One-year follow-up R₂ MRI could be evaluated in 23 cases. At 12 months, LIC decreased by 11.2 mg Fe/g DW from baseline values, a reduction of 35.7% for patients with MDS, and significantly decreased by 8.1 mg Fe/g DW from baseline values, a reduction of 27.6% for patients with AA ($P=0.0028$). During the study, the patients with lower transfusional requirements (<4 units/month) showed significantly more reduction of LIC level by deferasirox than those with higher transfusional requirements (≥ 4 units/month) (35.7% vs. 2.8%; $P < 0.0001$). The most common drug-related adverse events (AE) were gastrointestinal disturbances, non-progressive increase in serum creatinine, and skin rash. However, AE were transient and mild-to-moderate in severity. Deferasirox was discontinued in 28 (35.4%) cases because of death (7 in MDS and 6 in AA), patient refusal (11 cases), and decrease in the serum ferritin level below 500 ng/mL (4 cases). All death was ascribed to disease-related causes including cytopenia in nine (11.4%) and disease progression in one (1.3%). This study clearly shows that deferasirox is effective in reducing LIC and serum ferritin level in transfusional iron overload patients with MDS or AA, even with ongoing transfusion requirement, and is well tolerated. Careful assessment of patient's transfusion requirement will be important in making dose adjustment according to purpose of iron chelation. Data

from extension phase of this clinical trial may expand our knowledge about the beneficial effects of deferasirox on prolonging survival and improving quality of life in these patients.

P103 Iron chelation treatment in patients with myelodysplastic syndromes (MDS): the experience of the Hellenic MDS Study Group

A. Kouraklis, A. Symeonidis, A. Galanopoulos, G. Kaifa, I. Tavernarakis, G. Tsirakis, E. Michali, P. Tsafaridis, K. Loukidis, A. Aggelidis, N. Zoumbos. *Hellenic National Registry of Myelodysplastic and Bone Marrow Failure Syndromes' Study Group of the Hellenic Society of Hematology, Greece*

Background and Rationale: Iron chelation is an essential component of the supportive treatment for transfusion-dependent and/or iron overloaded patients with MDS. The last few years, the availability of the orally administered iron chelators has recharged the interest on this kind of treatment.

Patients and Methods: We retrospectively analyzed the efficacy, tolerability and adverse effects of this type of treatment in a cohort of 82 patients with MDS. Patients were 26 females and 56 males, with a median age of 72.5 years (range, 32–89 years), were followed in 10 Hellenic Hematological departments, and according to WHO classification were diagnosed as del-5q syndrome (n=4), RA (n=10), RARS (n=15), RCMD (n=17), RCMD-RS (n=10), RAEB-1 (n=16), RAEB-2 (n=7), CMML-dysplastic (n=1), fibrotic MDS (n=1) and hypoplastic MDS (n=1). IPSS was Low in 30, Int-1 in 33, Int-2 in 9 and High in 1 patient. Seventy-nine patients were completely transfusion-dependent and 3 were iron overloaded, without being regularly transfused. Treatment with desferrioxamine (DFO) was applied in 53 patients (39 males, 14 females), whereas DFX was administered in 39 patients (in 12 following previous DFO therapy) and deferiprone (DFP) in 6 (in 4 following DFO therapy). There were no findings of impaired renal function in any patient.

Results: Median pretreatment ferritin levels were 2750 ng/mL (range, 762–14960 ng/mL) and median number of transfused RBC units was 52 per patient (range, 16 to more than 500) for patients treated with DFO, and 29/53 patients exhibited elevated serum ALT levels. Estimation of tissue iron burden by MRI in 8 patients revealed severe liver hemosiderosis ($T2^*$ values < 5 ms) although cardiac iron was normal in all patients ($T2^* > 25$ ms). Patients were administered 1–67 iv or sc courses of DFO, but only 41 of them received at least 3 cycles and were considered evaluable for response. Among them, 19 achieved a favorable response and the median post-treatment ferritin dropped to 1195 ng/mL (range, 476–5000 ng/mL), whereas the remaining 22 patients did not respond. Two of the