

responders exhibited an improved transfusion rate following DFO treatment. Four patients manifested local reactions, and in another one deterioration of auditory function was noted. Regarding the group of patients treated with DFX (dose administered 10–20 mg/kg/d), median pretreatment ferritin was 2028 ng/mL (range, 713–6580 ng/mL) and median number of transfused RBC units was 45 per patient (range, 16–123). A pretreatment MRI examination was performed in 11 patients and liver values were abnormal in 10 ( $T2^* < 5$  ms), whereas one patient demonstrated also a moderate degree of cardiac siderosis ( $T2^*$  value 13.4 msec). After a median treatment duration of 11 months, 24 of 31 evaluable patients (77.4%) have demonstrated a favorable response, with a drop of their median post-treatment ferritin to 880 ng/mL (range, 399–2803 ng/mL). A re-evaluation with MRI has been scheduled after 12 months of treatment. One patient manifested severe gastrointestinal disturbances with DFX, which persisted despite dose de-escalation, and she denied further treatment with the drug. Finally, 5 of the 6 patients treated with DFP at a dose of 75 mg/kg/dm have tolerated treatment well, and only in one patient DFP was withdrawn due to a generalized, grade III skin reaction. No patient exhibited neutropenia. Treatment was effective in 3/5 patients and after a median treatment duration of 13 months ferritin levels have been dropped from a baseline of 2350 ng/mL (range, 970–3325 ng/mL) to 1075 ng/mL (range, 361–2165 ng/mL).

**Discussion and Conclusive remarks:** In our cohort of 82 patients with MDS, iron chelation treatment was effective with all the three available chelators. DFO treatment is less well tolerated due to the discomfort of parenteral administration. This was the reason for the administration of DFP in a small group of 6 patients before the commercial availability of DFX. DFP however was not associated with neutropenia. DFX is currently considered the chelator agent of choice and in our group was effective in 77, 4% of the patients.

**P104 Change in liver iron concentration (LIC), serum ferritin (SF) and labile plasma iron (LPI) over 1 year of deferasirox (Exjade®) therapy in a cohort of patients with MDS**

P.L. Greenberg<sup>1</sup>, C.A. Koller<sup>2</sup>, T. Glynos<sup>3</sup>, C. Paley<sup>3</sup>, C. Schiffer<sup>4</sup>. <sup>1</sup>Division of Hematology, Stanford University Medical Center, Stanford, CA, USA; <sup>2</sup>MD Anderson Cancer Center, Houston, TX, USA; <sup>3</sup>Novartis Pharmaceuticals, East Hanover, NJ, USA; <sup>4</sup>Wayne State University, Detroit, MI, USA

**Background:** US02 is the first prospective study evaluating the effects of deferasirox on LIC, SF and LPI in patients with IPSS Low- and Int-1-risk MDS.

**Methods:** Twenty-four patients were enrolled. Initial deferasirox dose was 20 mg/kg/day with adjustments to 10 or 30 mg/kg/day based on safety and efficacy assessments. LIC was evaluated at baseline (BL), 6 and 12 months by R2 MRI. SF, safety analyses and trough LPI levels were also evaluated.

**Results:** For the nine patients who completed 12 months, mean dose of deferasirox was 20.1 mg/kg/day. Mean SF±SEM: 4416±1269 µg/L at BL, 2685±316 µg/L at 12 months (−14.8%,  $p=0.3$ ). Mean LIC±SEM: 23.72±3.82 mg Fe/g dry weight (dw) at BL, 16.79±3.80 mg Fe/g dw at 12 months (−7.8%,  $p=0.2$ ). Of the nine completers, seven (78%) achieved decreases in SF of ≥500 µg/L and >20% from BL. Mean LPI±SEM (n=8): 0.8±0.2 µmol/L at BL, 0.1±0.1 µmol/L at 12 months (−78.2%,  $p=0.02$ ). Safety: 7/24 patients (29%) had creatinine increases >33% above BL on ≥2 occasions. 14 serious AEs were reported in 11 patients. 1/14 was considered drug related (severe diarrhea/lower abdominal cramping); the patient completely recovered within 1 day following treatment. Fifteen patients (63%) discontinued treatment: non-treatment-related death (n=3); withdrew consent (n=4); MDS progression (n=2); AEs [(n=5); four of which were related to study drug]; unsatisfactory therapeutic effect (n=1).

**Conclusions:** Deferasirox therapy significantly reduced LPI in the nine patients who completed one year of therapy. LPI normalized (<0.5 LPI units) in 80% of the patients. Larger studies are ongoing to evaluate the clinical benefit of deferasirox in this patient population.

**P105 Decrease in intra- and extra-cellular free iron species and oxidative stress parameters and increase in serum and urinary hepcidin during treatment with deferasirox in iron-loaded patients with MDS**

H. Ghoti<sup>1</sup>, E. Fibach<sup>2</sup>, D. Merkel<sup>3</sup>, J. Amer<sup>2</sup>, A. Nagler<sup>3</sup>, G. Perez-Avraham<sup>4</sup>, S. Grisariu<sup>2</sup>, E. Naparstek<sup>5</sup>, A. Ackerstein<sup>6</sup>, G. Olbina<sup>7</sup>, M. Westerman<sup>7</sup>, T. Ganz<sup>8</sup>, E.A. Rachmilewitz<sup>1</sup>. <sup>1</sup>The E. Wolfson Medical Center, Holon, Israel; <sup>2</sup>Hadassah – Hebrew University Medical School, Jerusalem, Israel; <sup>3</sup>Chaim Sheba Medical Center, Tel-Hashomer, Israel; <sup>4</sup>Soroka University Medical Center, Beer-Sheva, Israel; <sup>5</sup>Tel Aviv Sourasky Medical Center, Tel Aviv, Israel; <sup>6</sup>Novartis, Petah Tikva, Israel; <sup>7</sup>Intrinsic LifeSciences LLC, La Jolla, CA, USA; <sup>8</sup>David Geffen School of Medicine at UCLA, Los Angeles, CA, USA

**Purpose:** This study measured free iron species – labile plasma iron (LPI) and intracellular free labile iron pool (LIP) – as well as serum ferritin, and serum and urinary hepcidin, in iron-overloaded patients with low-risk myelodysplastic syndromes (MDS) following treatment with the once-daily iron chelator, deferasirox. Changes in