

**2009 Annual Meeting of the  
American Society of Hematology**

**Highlights Report**

**Deferasirox (Exjade®) Is Effective and Well Tolerated  
in Chelation-Naive and Previously Chelated Patients  
with Transfusion-Dependent  
Myelodysplastic Syndromes (MDS)**

***Mathias Schmid, Agnès Guerci-Bresler, Matteo Della  
Porta, Kerry Taylor, Dany Habr, Gabor Domokos,  
Bernard Roubert, Christian Rose and Norbert  
Gattermann***

***Abstract 3806***

**Deferasirox (Exjade®) Is Effective and Well Tolerated in Chelation-Naïve and Previously Chelated Patients with Transfusion-Dependent Myelodysplastic Syndromes (MDS) (Abstract# 3806)**

***Mathias Schmid, Agnès Guerci-Bresler, Matteo Della Porta, Kerry Taylor, Dany Habr, Gabor Domokos, Bernard Roubert, Christian Rose and Norbert Gattermann***

Transfusion dependency and iron overload have been identified as negative prognostic factors for survival and progression to acute myeloid leukemia in patients with MDS.<sup>1,2</sup> Data suggest that iron chelation therapy may improve outcomes in lower-risk MDS sub-groups and many treatment guidelines for chelation therapy in MDS recommend initiation of chelation therapy when serum ferritin levels exceed 1000 ng/mL.<sup>3-6</sup>

Previous studies, including EPIC which recruited the largest cohort of MDS patients evaluated for any chelation therapy to date, have demonstrated that deferasirox maintains or reduces iron levels in patients with MDS.<sup>7-10</sup>

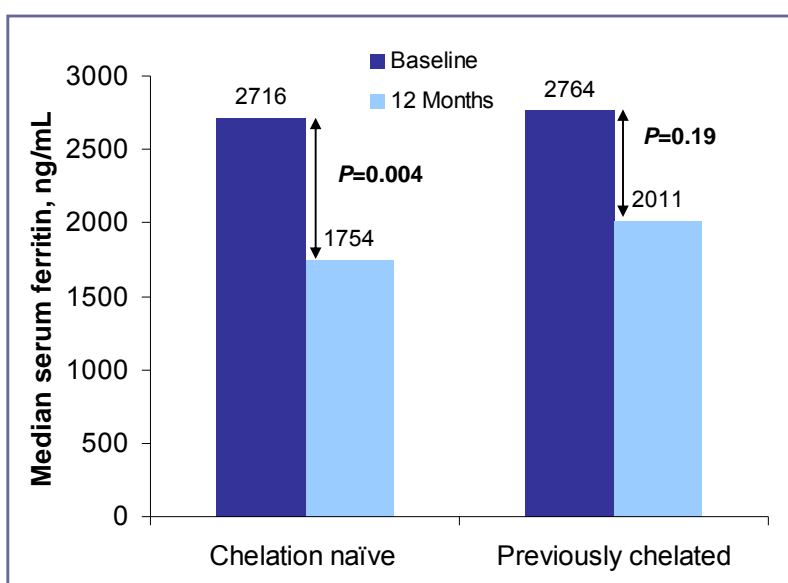
A total of 341 MDS patients were included in the study; 165 were chelation naïve and 176 had been previously chelated with deferoxamine (DFO; n=137, 77.8%), deferiprone (n=14, 8.0%), DFO + deferiprone combination (n=24, 13.6%) or deferasirox (n=1, 0.6%). Baseline serum ferritin and iron intake were comparable between chelation naïve and previously chelated groups.

Deferasirox was initiated in both groups at a dose of 10–30 mg/kg/day depending on transfusion requirement. Following dose adjustments based on 3-month serum ferritin trends the mean actual deferasirox dose over the 1-year treatment period was 18.7 mg/kg/day in the chelation naïve group and 19.7 mg/kg/day in the previously chelated group.

**2009 Annual Meeting of the American Society of Hematology  
Highlights Report**

There was an overall median serum ferritin decrease from 2730 ng/mL at baseline to 1904 ng/mL after 12 months. Median serum ferritin decreased from 2716 to 1754 ng/mL in chelation-naïve patients ( $P=0.004$ ) and from 2764 to 2011 ng/mL ( $P=0.19$ ) in previously chelated individuals (Figure 1). The median change between groups was not statistically significant.

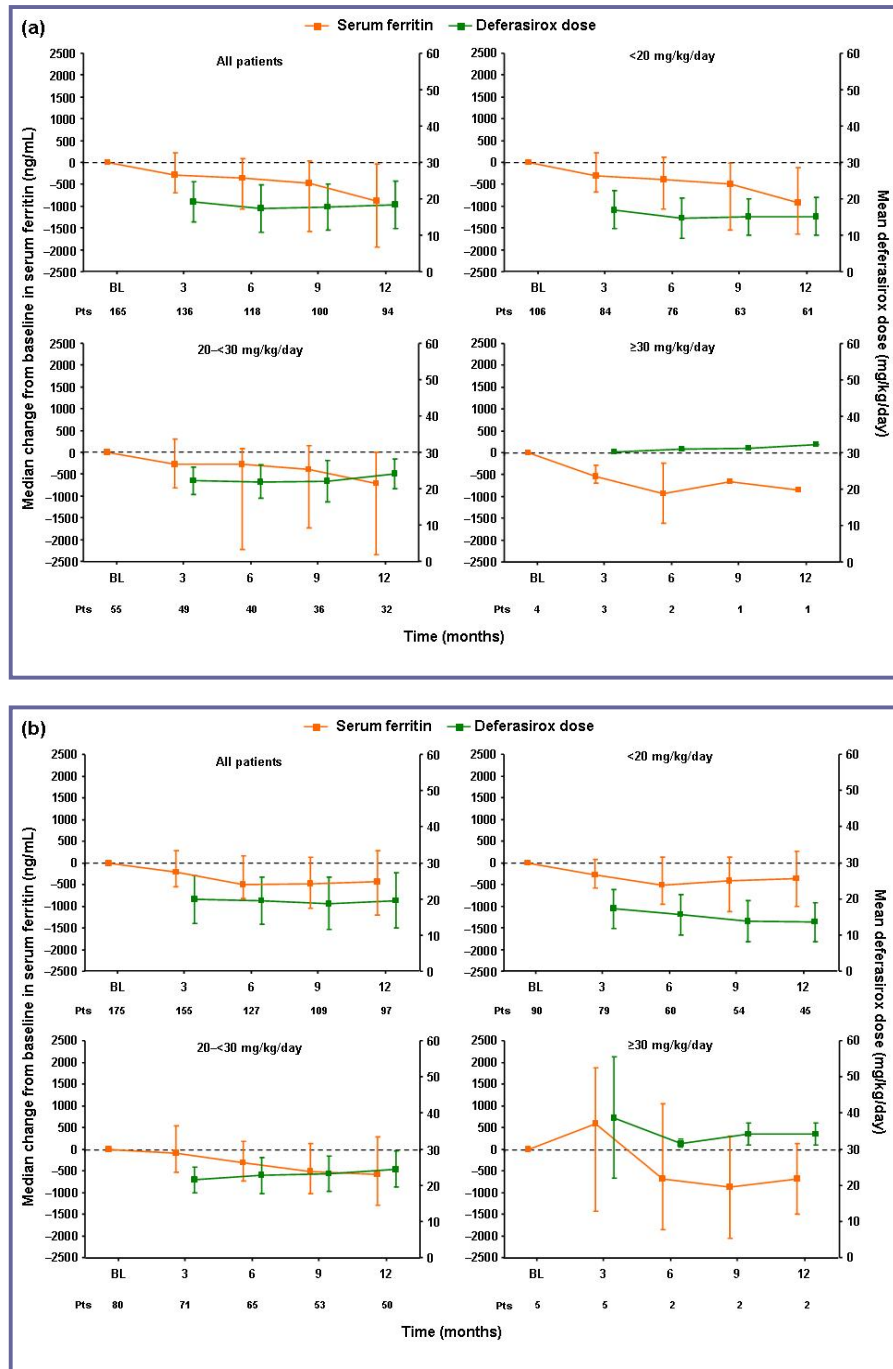
**Figure 1. Median serum ferritin at baseline and after 12 months' treatment, by chelation history**



In both groups, patients who had a relatively low mean iron intake and baseline iron burden were able to achieve median reduction in serum ferritin with an average actual dose of <20 mg/kg/day. Patients receiving a mean actual dose of  $\geq 20$ –<30 mg/kg/day had higher baseline serum ferritin and iron intake and therefore required these higher doses to achieve a similar decrease in serum ferritin. Patients who had the highest baseline serum ferritin and iron intake achieved a substantial serum ferritin reduction with an average actual dose of  $\geq 30$  mg/kg/day (Figures 2a and 2b)

2009 Annual Meeting of the American Society of Hematology  
Highlights Report

Figure 2. Change in serum ferritin by mean actual dose categories in (a) chelation-naïve and (b) previously chelated patients.



## **2009 Annual Meeting of the American Society of Hematology Highlights Report**

In total, 166 patients discontinued in similar proportions (47.3% vs 50.0%) in both groups. No deaths were considered related treatment, and the primary reasons for discontinuation were adverse events (the majority of which were gastrointestinal) and consent withdrawal. There were 19 drug-related serious AEs reported in 14 patients and there was no substantial difference in AE profile between groups. There was no progressive increase in mean serum creatinine.

Despite evidence associating lower serum ferritin levels with improved survival in patients with MDS, baseline serum ferritin in this cohort was >2500 ng/mL in both chelation naïve and previously-chelated patient groups indicating sub-optimal management of iron overload and a risk of associated sequelae. Approximately 50% had received no prior chelation therapy. Deferasirox therapy with adequate dose adjustment was effective in reducing serum ferritin over one year irrespective of prior chelation history. The safety profile was well defined, manageable and comparable with previously reported deferasirox data in MDS patients. These data indicate the need to monitor iron overload and that early initiation of appropriate deferasirox therapy could improve clinical outcomes for MDS patients.

### **References**

1. Malcovati L, Della Porta MG, Pascutto C *et al.* Prognostic factors and life expectancy in myelodysplastic syndromes classified according to WHO criteria: a basis for clinical decision making. *J Clin Oncol* 2005;23:7594-7603.
2. Sanz G, Nomdedeu B, Such E *et al.* Independent impact of iron overload and transfusion dependency on survival and leukemic evolution in patients with myelodysplastic syndrome. *Blood* 2008;112(11):abst 640.
3. Bennett JM. Consensus statement on iron overload in myelodysplastic syndromes. *Am J Hematol* 2008;83:858-861.
4. Gattermann N, Porter J, Lopes LF *et al.* Consensus statement on iron overload in myelodysplastic syndromes. *Hematol Oncol Clin North Am* 2005;19(Suppl 1):18-25.
5. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology v.1: Myelodysplastic Syndromes. 2009. Available at: [http://www.nccn.org/professionals/physician\\_gls/pdf/mds.pdf](http://www.nccn.org/professionals/physician_gls/pdf/mds.pdf).

**2009 Annual Meeting of the American Society of Hematology  
Highlights Report**

6. Rose C, Brechignac S, Vassilief D *et al.* Positive impact of iron chelation therapy (CT) on survival in regularly transfused MDS patients. A prospective analysis by the GFM. *Blood* 2007;110(11):abst 249.
7. Gattermann N, Schmid M, Della Porta M *et al.* Efficacy and safety of deferasirox (Exjade<sup>®</sup>) during 1 year of treatment in transfusion-dependent patients with myelodysplastic syndromes: results from EPIC trial. *Blood* 2008;112(11):abst 633.
8. Greenberg PL, Schiffer C, Koller CA *et al.* Change in liver iron concentration (LIC), serum ferritin (SF) and labile plasma iron (LPI) over 1 year of deferasirox (DFX/Exjade<sup>®</sup>) therapy in a cohort of myelodysplastic patients. *Blood* 2008;112(11):abst 5083 [USE LATER 2009 VERSION ID3516].
9. List AF, Baer MR, Steensma D *et al.* Iron chelation with deferasirox (Exjade<sup>®</sup>) improves iron burden in patients with myelodysplastic syndromes (MDS). *Blood* 2008;112(11):abst 634.
10. Porter J, Galanello R, Saglio G *et al.* Relative response of patients with myelodysplastic syndromes and other transfusion-dependent anaemias to deferasirox (ICL670): a 1-yr prospective study. *Eur J Haematol* 2008;80:168-176.