

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

**Highlights Report**

**Deferasirox (Exjade®) ≥30 mg/kg/day is Effective in  
Reducing Iron Burden in Thalassemia Major Patients  
Previously Chelated with Monotherapy or  
Combination Therapy**

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Habr, G Domokos, B Roubert and MD Cappellini***

***Abstract 4058***

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Thalassemia Major Patients Previously Chelated with Monotherapy or  
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In patients with  $\beta$ -thalassemia major, iron overload indicated by serum ferritin levels >2500 ng/mL is associated with significant negative outcomes including cardiac disease and organ failure.<sup>1,2</sup> Despite the availability of iron chelation therapy, on enrollment to the prospective EPIC trial, 834 patients with  $\beta$ -thalassemia major who had received prior chelation therapy with deferoxamine (DFO) and/or deferiprone for an average of 10.8 years had a median baseline serum ferritin level of 3139 ng/mL. This indicates that prior iron chelation had been less than optimal in these patients. Previous studies have shown that in some iron overloaded patients with  $\beta$ -thalassemia deferasirox doses  $\geq 30$  mg/kg/day may be required to reduce serum ferritin levels.<sup>3-5</sup> It is interesting to assess whether these deferasirox doses may be an effective option in patients for whom alternative regimens were sub-optimal.

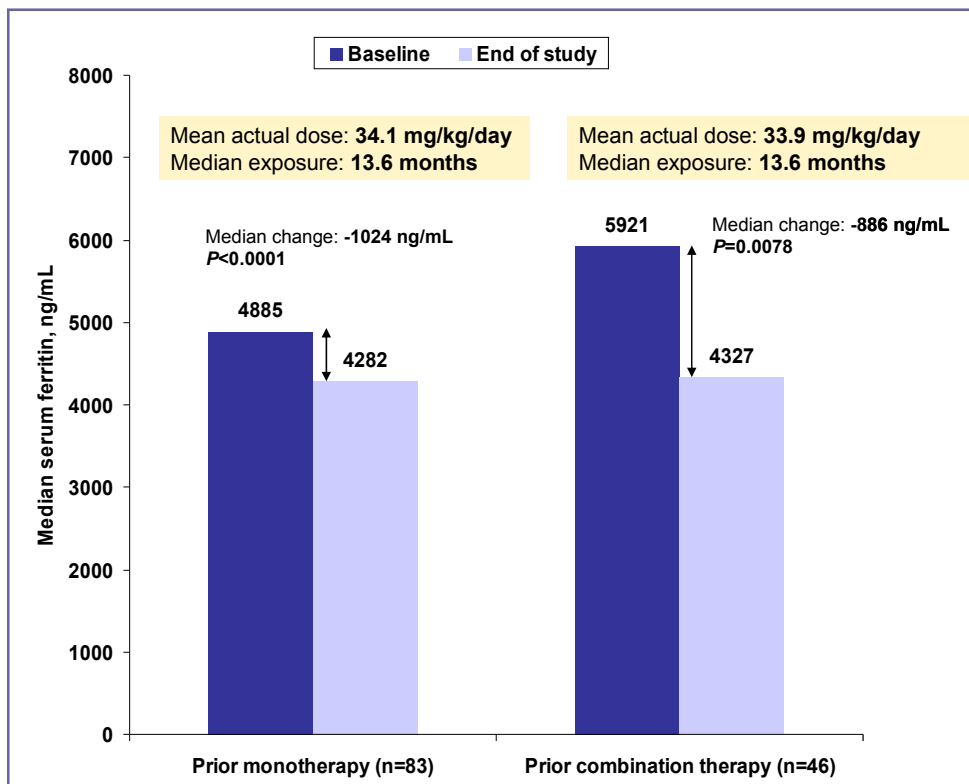
This post-hoc subgroup analysis shows that over the 1-year treatment period of the EPIC trial, 129 patients with  $\beta$ -thalassemia who had been previously chelated received a mean actual deferasirox dose of  $\geq 30$  mg/kg/day. The baseline patient characteristics are shown in Table 1 and one-year treatment outcomes are shown in Figure 1.

**Table 1. Patient characteristics at baseline**

|  | <b>Prior monotherapy<br/>(n=83)</b> | <b>Prior combination<br/>therapy (n=46)</b> |
|--|-------------------------------------|---|
| Mean age $\pm$ SD, years (range)                               | 19.5 $\pm$ 8.2 (2–39)               | 23.0 $\pm$ 7.2 (10–40)                      |
| Mean duration of previous chelation<br>therapy $\pm$ SD, years | 11.7 $\pm$ 7.7 (n=81)               | 14.5 $\pm$ 7.9 (n=45)                       |

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**Figure 1. Median serum ferritin at baseline and following deferasirox  $\geq 30$  mg/kg/day in prior monotherapy and combination therapy patients**



Labile plasma iron (LPI) is a directly chelatable component of non-transferrin-bound iron (NTBI) and is highly toxic as it can catalyze the formation of harmful free hydroxyl radicals.<sup>6</sup> Suppression of this species is an important goal of iron chelation therapy. LPI levels were assessed at baseline and end-of-study. In prior monotherapy and combination therapy patients, respectively, mean LPI levels decreased by 0.19 and 0.26  $\mu\text{mol/L}$  after 1 year (Table 2).

**Table 2. Mean ( $\pm$  SD) LPI at baseline and end-of-study**

|              | Prior monotherapy<br>(n=56) | Prior combination therapy<br>(n=34) |
|--------------|-----------------------------|-------------------------------------|
| Baseline     | 1.3 $\pm$ 2.1               | 1.7 $\pm$ 3.1                       |
| End-of-study | 1.1 $\pm$ 2.6               | 1.4 $\pm$ 2.7                       |

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In total, 54 patients (41.9%) had an AE that was assessed as related to study drug; these were mild-to-moderate in most (n=47) patients. The most common AEs were rash and diarrhea.

In these heavily iron overloaded, previously chelated patients, deferasirox monotherapy at doses  $\geq 30$  mg/kg/day led to significant and clinically relevant reductions in serum ferritin. The safety profile was consistent with previously published data in patients with  $\beta$ -thalassemia major,<sup>3,4</sup> and confirms pooled data from other studies showing that doses  $\geq 30$  mg/kg/day are not associated with an increase in the incidence of AEs or a worsening of renal or liver function. Switching from other chelation regimens to oral deferasirox monotherapy  $\geq 30$  mg/kg/day can provide clinically relevant reductions in serum ferritin in iron overload patients with  $\beta$ -thalassemia whose therapeutic goal is to reduce iron burden. Longer-term studies would assess whether deferasirox therapy could continue to reduce serum ferritin to  $< 2500$  ng/mL to minimize serious complications of iron overload.

***Expert commentary: Dr John Porter, University College London, UK***

*The use of LPI is very much, 'proof of concept' at this stage. This is to say that it is theoretically desirable to remove this form of iron which is thought to be taken into cardiac and other tissues rapidly. However, it is not known how it should be used for patient monitoring and its prognostic significance has yet to be demonstrated.*

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