

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

Highlights Report

**Efficacy and Safety of Deferasirox (Exjade®) in
Patients with β -Thalassemia Major Treated for up to
5 Years**

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Abstract 4063

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Efficacy and Safety of Deferasirox (Exjade®) in Patients with β -Thalassemia Major Treated for up to 5 Years (Abstract # 4063)

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Transfused patients with β -thalassemia require life-long iron chelation therapy to avoid the clinical consequences of iron overload including cardiac failure and death.¹ The long-term efficacy, safety and tolerability of an iron chelator are therefore essential to achieve good clinical outcomes. Deferasirox is an oral iron chelator with a plasma half-life suitable for daily dosing. Studies have indicated that β -thalassemia patients have high satisfaction with and adherence to deferasirox that may encourage compliance with treatment, and improved outcomes.²

Following a large, phase III clinical trial in which patients received either deferasirox or deferoxamine for 1 year, patients were invited to enroll in an extension phase during which they would receive deferasirox for an additional 4 years. Thus 555 patients have received deferasirox for either 5 years (original 'deferasirox' cohort, n=296) or 4 years ('crossover' from deferoxamine cohort, n=259). Serum ferritin, liver iron concentration (LIC), and safety and tolerability data were compared over these periods.

Following the core year, deferasirox dose adjustments were permitted to allow optimal dosing (Table 1). Overall, 115 (38.9%) and 69 (26.6%) patients discontinued therapy from the deferasirox and crossover cohorts, respectively, most commonly because of AEs or withdrawal of consent.

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Table 1. Deferasirox dosing and exposure

Characteristic	Deferasirox cohort (n=296)	Crossover cohort (n=259)	All patients (n=555)
Mean actual deferasirox dose \pm SD, mg/kg/day	21.6 \pm 6.4	23.2 \pm 5.9	22.4 \pm 6.2
Mean final actual dose \pm SD, mg/kg/day	24.4 \pm 8.7	27.0 \pm 8.0	25.6 \pm 8.5

At these doses, deferasirox was effective at significantly reducing LIC from baseline after one year of exposure until the end of study in both cohorts. Likewise, median serum ferritin levels significantly decreased by a median of 775 ng/mL in patients in the deferasirox cohort who had received at least 5 years' deferasirox (n=182), and by 371 ng/mL in patients in the crossover cohort who had received at least 4 years' deferasirox (n=151). The proportion of patients who had a serum ferritin level of \leq 1000 ng/mL increased from 12% (n=69) at the start of treatment to 33% (n=181) at the end of study; the proportion who had a serum ferritin level of <1000 ng/mL at two consecutive assessments was much higher at 45% (n=249).

The most common investigator-assessed drug-related AEs were generally transient and of mild-to-moderate severity and their frequency decreased from year to year. Adverse events were similar to those described in the one-year core trials.³ Deferasirox did not appear to have any adverse effects on growth or development in pediatric patients.

Long-term deferasirox treatment for up to 5 years significantly decreased iron burden in patients with β -thalassemia and an increasing percentage of patients achieved their therapeutic goals with appropriate dosing. Significant improvements in LIC and serum ferritin were also observed after switching from DFO to deferasirox suggesting that patients can be effectively switched to once-daily deferasirox from other, possibly less convenient, chelation regimens.

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

Gastrointestinal AEs gradually decrease in frequency with time. While this may in part be due to patient dropouts, this cannot explain the decrease by itself, as dropouts have been relatively rare. For patients experiencing GI side effects such as diarrhea, nausea, abdominal pain or constipation, I usually advise trying to administer deferasirox after food or in the evening. If this does not improve symptoms, sometimes splitting the dose is helpful.

A study that we presented at ASH 2008 showed that after about 3 years of therapy, some patients became less adherent and that this led to adverse trends in body iron stores and distribution in some patients. As with any chelation therapy, and with any chronic therapy, the availability of time in the clinic to discuss adherence and motivational issues is vital. We work with a clinical psychologist in the clinic to maximize adherence.

References

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3. Cappellini MD, Cohen A, Piga A *et al.* A phase 3 study of deferasirox (ICL670), a once-daily oral iron chelator, in patients with b-thalassemia. *Blood* 2006;107:3455-3462.