

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

**Highlights Report**

**Initial Liver Iron Predicts Cardiac Chelation Efficacy  
of Deferasirox (Exjade®) Monotherapy in Chronically  
Transfused  $\beta$ -Thalassemia ( $\beta$ -Thal) Patients: 18- and  
24-Month Data**

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***Abstract 4069***

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Approximately 71% of transfused patients with  $\beta$ -thalassemia major will suffer cardiomyopathy, congestive heart failure and death as a consequence of cardiac iron overload, and effective iron chelation therapy is therefore a mainstay of their care.<sup>1</sup> Removing iron from the heart in severely iron overloaded patients is a treatment priority, but patterns of iron loading between different organs are complex.<sup>2</sup> The properties of an iron chelator must take these patterns into consideration.

This report confirms the results of the EPIC cardiac substudy<sup>3</sup> that deferasirox is effective at removing cardiac and liver iron in transfusion-dependent patients with  $\beta$ -thalassemia major. In total 28 patients enrolled in the study and 22 were evaluated at 18 months. At this point, 10/22 (45.5%) were receiving 40 mg/kg/day deferasirox.

13/27 patients had improvements in T2\* and 14/27 failed to improve, including five patients who discontinued therapy. The mean improvement in cardiac T2\* from baseline in all patients was 2.2 ms (22%;  $P=0.016$ ) and improvements in cardiac iron were correlated with changes in LIC ( $r^2 = 0.27$ ,  $P=0.013$ ). Overall, 13 patients' cardiac T2\* status improved, four remained stable (T2\* change <10%) and five worsened. Responding patients had progressively improved cardiac and liver iron levels throughout the study (2.4% and 3% per month respectively), whereas non-responsive patients experienced no improvement in LIC at any time-point, and cardiac T2\* steadily worsened (decreasing 0.84% per month).

Baseline LIC was a powerful predictor of response. Cardiac T2\* in 14 patients with baseline LIC <18.5 mg Fe/g dw improved 2.2% per month, with 13/14 patients showing large improvements and one patient remaining stable. In contrast, in eight patients with LIC >18.5 mg Fe/g dw, mean T2\* worsened 1.4% per month

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( $P < 0.0001$ ); three patients remained stable and five worsened significantly. The most common AEs during therapy were nausea ( $n=7$ ), diarrhea and rash ( $n=5$ ).

In this heavily iron overloaded population, deferasirox improved cardiac  $T2^*$  and this change increased once LIC fell to  $<5$  mg/g. For this reason, different measures of body iron are likely to be important when using deferasirox in patients with cardiac iron. LIC  $<18.5$  mg Fe/g dw was a strong predictor of favorable response and these findings indicate that deferasirox at 30–40 mg/kg/day provides good cardiac chelation in patients with mild to moderate cardiac and liver iron burdens. Further extension phase data from this study are awaited.

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

*There are previous studies linking LIC of  $>15-20$  mg/g dw to: progression of liver fibrosis, increased liver enzymes and increased risk of cardiac disease. Previously, it became fashionable to deny a relationship between LIC and cardiac risk, because cross sectional studies had failed to show correlations between these two variables. The study of Wood, as well as previous studies by the same group and others, clearly show that sustained high levels of liver iron increase the risk of cardiac disease but that there is a lag between these two so that cross sectional analysis misses this relationship.*

*These and other data clearly demonstrate the importance of controlling body iron over prolonged periods of time. In patients with high LIC values and where there is not a downward trend in LIC at conventional doses of chelation, intensification is therefore indicated.*

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**References**

1. Olivieri NF, Nathan DG, MacMillan JH *et al.* Survival in medically treated patients with homozygous  $\beta$ -thalassemia. *N Engl J Med* 1994;331:574-578.
2. Noetzli LJ, Carson SM, Nord AS *et al.* Longitudinal analysis of heart and liver iron in thalassemia major. *Blood* 2008;112:2973-2978.
3. Pennell DJ, Porter JB, Cappellini MD *et al.* Efficacy of deferasirox in reducing and preventing cardiac iron overload in  $\beta$ -thalassemia. *Blood* 2009.