

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

Highlights Report

Expert overview

***Dr Stuart Goldberg
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Dr Goldberg discussed the data on the use of oral iron chelation presented at the 2009 Annual Meeting of the American Society of Hematology, with a particular emphasis on the implications for treatment of transfused patients with Myelodysplastic Syndromes (MDS).

It is well established that iron chelation therapy with DFO is effective in preventing cardiac damage and prolonging survival among pediatric patients with β -thalassemia.¹ At ASH 2009, encouraging data from the 2 year follow-up of the EPIC cardiac sub-study demonstrated the ability of the oral iron chelator deferasirox to remove iron from the heart, with improvements in myocardial T2*, and maintenance of normal cardiac function during prolonged transfusional support in β -thalassemia patients.² Since cardiac disease is also a leading cause of non-leukemic death among patients with MDS, reduction in cardiac-related iron toxicity could have important implications in this elderly population that is already experiencing cardiac strain from chronic anemia.^{3,4} To date it has been difficult to demonstrate iron deposition in MDS patients. It has been hypothesized however that the presence of labile iron may result in damage to the heart and other organs even before the deposition of iron commences.

Cardiac complications are not the only possible detrimental consequence of iron overload in MDS. In a 2009 study of over 500 newly diagnosed MDS patients from the US Medicare database followed for 3 years, cardiac disease, diabetes, infections, and leukemic transformation all had greater prevalence in transfused compared with non-transfused patients.⁵ Whilst this and other associations between transfusions and poor outcomes have been known for some time, the evidence that iron chelation therapy can improve outcomes in MDS has been limited. For this reason, the demonstration by Gattermann *et al.* of an improvement in liver function in MDS patients receiving deferasirox is of particular interest. In the MDS sub-population of the EPIC study, liver transaminase decreases correlated with reductions in serum

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ferritin, showing that a clinically-relevant organ improvement could be achieved in MDS patients receiving iron chelation therapy with deferasirox.⁶

During the deferasirox registration studies, most attention was paid to the urgent needs of transfusion-dependent younger thalassemia and SCD patients. However, the number of studies in elderly patients with MDS is now increasing. Results of two large trials (EPIC⁷ and US03⁸), which have recruited a total of over 500 elderly MDS patients, were updated at ASH 2009. These studies demonstrate that deferasirox can be used safely, and is effective at reducing iron overload in these older individuals. The adverse event profiles were also very similar to those seen in registration studies, with slight increases in the frequencies of gastro-intestinal effects including diarrhea and nausea.⁹ Strategies to mitigate toxicities, including night-time administration, adequate hydration, and use of anti-diarrheal/anti-emetic medications, are advised. Elevations of serum creatinine were common in both trials, and patients who report with elevated baseline serum creatinine levels should be monitored carefully while receiving deferasirox. Additionally, appropriate dose escalations in response to parameters of iron overload and/or increased transfusion burden to obtain the desired iron reductions are an important, and sometimes overlooked, aspect of deferasirox therapy. In the MDS population, changes in hematopoietic function and transfusion burden following disease-modifying therapy, disease progression and presence of adverse events may all require dose adjustments to ensure chelation goals are met and therapy is tolerable.

Looking to the future, a prospective, randomized, placebo-controlled study will be starting in early 2010 specifically to address the question of improved clinical outcomes in the MDS population following deferasirox therapy. The results of this and other studies will hopefully provide evidence to support current clinical guidelines that advise initiation of iron chelation therapy at serum ferritin levels of ≥ 1000 ng/mL¹⁰ and address other outstanding queries regarding the effects of iron overload and iron chelation therapy in MDS. These include the association between iron chelation therapy and improvements in hematopoiesis, whether rates of leukemic progression are affected following suppression of toxic iron,¹¹ and the benefits of iron chelation in the HSCT setting.

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