

**The 49th American Society of Hematology (ASH) Meeting and Exposition
Atlanta, Georgia, USA, 8–11 December 2007**

Summary of key presentations

The 49th Annual American Society of Hematology (ASH) congress was one of the largest ever (~30000 attendees from around the world), reflecting recent developments in basic science and the substantial progress being made in the hematologic diseases. In total, 3700 abstracts were accepted for poster or oral presentation and a further 1400 accepted for publication only. The abstracts can be viewed online at <http://www.abstracts2view.com/hem07> or in *Blood* 2007;10(11). Here we provide an overview of the latest data that were presented at the congress related to the myelodysplastic syndromes (MDS) and stem cell transplantation (SCT).

POSTER PRESENTATION

Long-term treatment with deferasirox (Exjade, ICL670), a once-daily oral Iron chelator, is effective in patients with transfusion-dependent anemias. MD Cappellini (abstract 2777)

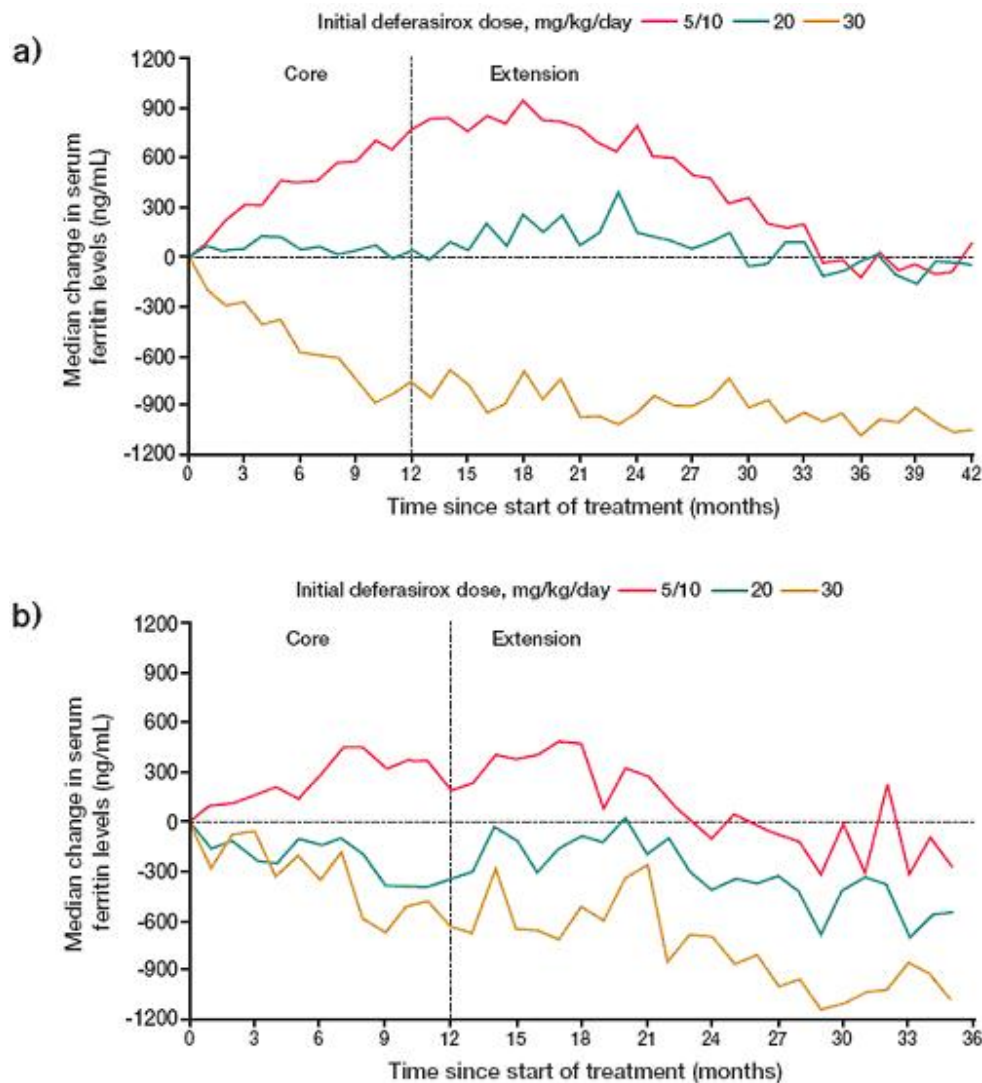
The efficacy and safety of deferasirox was established during five 1-year core registration trials involving more than 1000 patients. In these core phases deferasirox 5 and 10 mg/kg/day doses were generally insufficient to balance iron intake from ongoing transfusions, while 20 and 30 mg/kg/day maintained or reduced iron balance, respectively. As regularly transfused patients will require lifelong iron chelation therapy, it is essential to assess the long-term efficacy and safety of deferasirox. This analysis evaluated serum ferritin levels and safety data accumulated during long-term treatment with deferasirox in patients with various transfusion-dependent anemias who entered the 4-year extension phases to four deferasirox registration studies (106–109).

Overall, 964 patients have received treatment with deferasirox. A total of 652 received deferasirox in the core trials and have been on treatment for a median of 3.4 years, while 312 crossed over to deferasirox on the extension phases and have been on treatment for a median of 2.2 years. Overall, 172 patients (17.8%) from the deferasirox and crossover cohorts have discontinued treatment due to: AEs (n=63; 6.5%), consent withdrawal (n=53; 5.5%), unsatisfactory therapeutic effect (n=15; 1.6%) and other reasons, including abnormal laboratory results and death (n=41; 4.3%). Only 17 (1.8%) patients have discontinued in the past 12 months.

In patients in the deferasirox cohort with β -thalassemia (n=421), initial doses of 5/10 mg/kg/day were insufficient to offset ongoing transfusional iron intake, leading to a steady increase in iron burden during the core phases. Subsequent dose increases in the extension phases resulted in a median serum ferritin reduction to around baseline levels (Figure 1a). Patients with β -thalassemia who received 20 mg/kg/day generally maintained their iron burden over the core and extension phases, while those who received 30 mg/kg/day had a statistically significant reduction from baseline in serum ferritin levels ($P=0.0020$; Figure 1a). Patients in the deferasirox

cohort with other anemias (n=231) exhibited similar trends, although those who received 20 mg/kg/day appeared to exhibit more marked reductions in serum ferritin (Figure 1b).

Figure 1. Median change from baseline in serum ferritin levels by initial dose group in patients with a) β -thalassemia in the deferasirox cohort and; b) other anemias in the deferasirox cohort



Drug-related AEs were generally transient and of mild-to-moderate severity. The most common AEs included nausea (n=99, 10.3%), diarrhea (n=86, 8.9%), vomiting (n=60, 6.2%), abdominal pain (n=50, 5.2%) and rash (n=50, 5.2%). No patients have

developed progressive increases in serum creatinine levels $>2 \times$ ULN. Two patients discontinued due to stable creatinine increases of $1.5 \times$ ULN and confounding circumstances (concomitant cyclosporine and multiple infections, respectively).

This analysis therefore demonstrates that deferasirox has dose-dependent efficacy over 3.5 years of treatment. The reduction in serum ferritin in the 5 and 10 mg/kg/day dose cohorts following dose escalation confirms that the lack of efficacy in the 1-year core studies was due to insufficient exposure to chelation. Deferasirox dose must be titrated for each patient according to the rate of iron intake from ongoing blood transfusions, current iron burden, safety markers and target serum ferritin levels for individual patients. Deferasirox was generally well tolerated with a clinically manageable safety profile over the median 3.5-year treatment period.