

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

Highlights Report

**Safety of Deferasirox (Exjade[®]) in Myelodysplastic
Syndromes (MDS) and Non-MDS Patients with
Transfusional Iron Overload: A Pooled Analysis
Focusing On Renal Function**

***M Schmid, MD Cappellini, JB Porter, P Greenberg, T
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Abstract 1768

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Safety of Deferasirox (Exjade®) in Myelodysplastic Syndromes (MDS) and Non-MDS Patients with Transfusional Iron Overload: A Pooled Analysis Focusing On Renal Function (Abstract # 1768)

M Schmid, MD Cappellini, JB Porter, P Greenberg, T Lawniczek, S Glaser, V Dong and N Gattermann

A number of clinical studies have demonstrated the efficacy and safety profile of deferasirox in patients with various chronic anemias.¹⁻⁴ Understanding the safety profile, especially in regard to renal function, is particularly relevant in patients with MDS due to their advanced age and associated decline in renal function which may result in a reduced ability to compensate for additional renal stress. This pooled, retrospective, 1-year analysis from five deferasirox studies (US02, US03, 2409, 107 and 108) is the first to characterize the safety profile of deferasirox, with an emphasis on renal function, in such a large population of patients.

Overall, 1798 patients with β -thalassemia (n=951), MDS (n=584) and other anemias (n=263) were included in the analysis.

Mean deferasirox dose, iron intake and discontinuation rates are shown in Table 1. The discontinuation rate was highest in the MDS population (n=272, 46.6%) and other anemias (n=82, 31.2%) and lowest in β -thalassemia (n=110, 11.6%). The most common reasons for discontinuation were AEs and consent withdrawal.

Table 1. Deferasirox therapy by underlying anemia

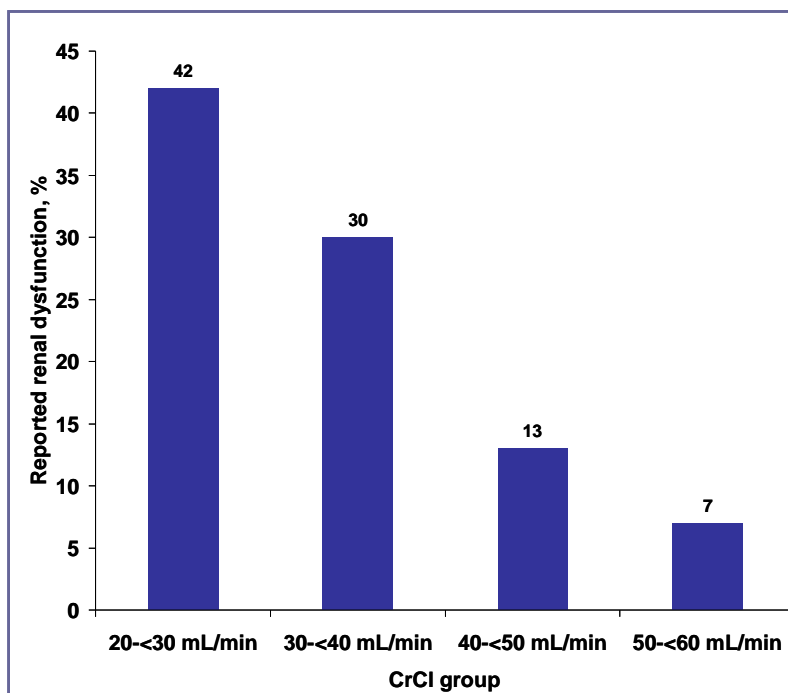
	β-thalassemia n=951	MDS n=584	Other anemias n=263
Mean deferasirox dose, ng/mL	23.5	20.3	19.9
Mean transfusional iron intake, mg/kg/day	0.34	0.32	0.23
% of patients remaining in the study at 1 year	88%	53%	69%

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Most patients with β -thalassemia (99.6%) and other anemias (76.7%) had baseline creatinine clearance (CrCl) ≥ 60 mL/min. More patients from the older (mean age: 68.9) MDS patient group had CrCl < 60 mL/min and also reported renal dysfunction AEs over the course of therapy than patients with β -thalassemia or other anemias. However patients with MDS with a baseline CrCl < 60 mL/min and ≥ 60 mL/min had similar declines in renal function over the course of therapy. The proportion of deaths in patients with MDS with a baseline CrCl < 60 mL/min (10.1%) was similar to those with a baseline CrCl ≥ 60 mL/min (7.4%).

In the MDS group decreasing CrCl rate was associated with an increasing incidence of renal dysfunction AEs which occurred in a total of 42% of patients with CrCl 20– < 30 mL/min; 30% in the 30– < 40 mL/min category; 13% in the 40– < 50 mL/min category; and 7% in the 50– < 60 mL/min category (Figure 1). The odds of reporting a renal dysfunction AE were 4- and 22-fold greater for patients with CrCl 40– < 60 and < 40 mL/min, respectively, than for patients with CrCl ≥ 60 mL/min.

Figure 1. Reported renal dysfunction by CrCl group



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This analysis confirms previously reported findings that patients with MDS treated with deferasirox had more discontinuations and reported a higher number of AEs and deaths than patients with β -thalassemia.⁵ The advanced age and disease-related complications of this patient group are likely to be important factors affecting the safety profile of deferasirox in this group: MDS patients with CrCl <40 mL/min were >70 years with preexisting co-morbidities such as chronic renal insufficiency, diabetes, hypertension and congestive heart failure. The outcomes of this study indicate that while deferasirox may be used in patients with CrCl \geq 60 mL/min, it should be used with close monitoring in patients with impaired renal function (CrCl 40–<60 mL/min). Patients with baseline CrCl <40 mL/min should not receive deferasirox.

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

For patient groups that start with creatinine clearance (CC) values close to the lower limit of normal (LLN), such as elderly patients with MDS, it is not surprising that a higher proportion of patients have values in the abnormal range and that these are then reported as AEs.

In this study, the relationship between baseline and end of study CC was linear, with no paradigm shift for any given pre-treatment CC value. Despite this, the cautious recommendation of the authors that deferasirox may be used in pts with baseline CrCl 40–<60 mL/min with close monitoring, but should not be used in patients with baseline CrCl <40 mL/min seems sensible.

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