

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

Highlights Report

**Deferasirox (Exjade®) Treatment of Chelation-Naive
and Pre-Chelated MDS Patients with Transfusional
Iron-Overload in the Medical Practice: Results From
the Observational Studies Extend and Exjange**

***Gattermann N, Leismann O, Schlag R,
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Abstract 3805

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Deferasirox (Exjade®) Treatment of Chelation-Naive and Pre-Chelated MDS Patients with Transfusional Iron-Overload in the Medical Practice: Results From the Observational Studies Extend and Exjange (Abstract # 3805)

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Many patients with MDS undergo regular red blood cell transfusions as supportive care which can result in iron overload.¹ This effect may be exacerbated in MDS by increased gastrointestinal iron absorption due to ineffective erythropoiesis.^{1,2} Clinical sequelae stemming from secondary hemochromatosis in MDS include organ damage, heart failure and diabetes³⁻⁶ and for this reason a number of international guidelines recommend initiation of iron chelation therapy in regularly transfused patients with lower-risk MDS.⁷ Chelation therapy has also been shown to reverse iron overload and may prolong survival.⁸

The once-daily oral iron chelator deferasirox has been evaluated in the clinical trial setting where it has been shown to reduce or maintain body iron in patients with MDS⁹ and β -thalassemia.¹⁰ To evaluate the efficacy, safety and tolerability of deferasirox over 1 year in the daily routine situation of office-based physicians, the post-marketing, observational studies eXtend and eXjange were undertaken in chelation naïve and pre-chelated patient populations, respectively.

Deferasirox was prescribed according to the Summary of Product Characteristics with an initial dose of 20 mg/kg/day.

Table 1. MDS patient characteristics at baseline and EOS

	MDS eXtend patients n = 123	MDS eXjange patients n = 44
Mean age	70.4	69.9
Female: male, n	58:65	20:24
Median BL serum ferritin (range), ng/mL	2679 (184 – 16500)	2442 (521 – 8565)
Median EOS serum ferritin, ng/mL	2000	2077

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eXtend (chelation naïve) population

- Overall, median serum ferritin decreased from 2846 to 2000 ng/mL over 1 year (-723 ng/mL; $P < 0.0001$)
- Deferasirox dose was increased in 8 and decreased in 5 MDS patients
- In the MDS sub-population, serum ferritin decreased from 2679 ng/mL to 2000 ng/mL (-662 ng/mL; $P = 0.0002$).

eXjange (pre-chelated) population

- In the overall population, decreases in serum ferritin from 2378 to 2063 ng/mL (-276 mg/mL; $P < 0.03$) were observed
- Dose was increased in 1 and decreased in 5 MDS patients
- In the MDS sub-group, serum ferritin decreased from 2442 to 2077 ng/mL (-716 ng/mL; $P = 0.06$).

Serum ferritin decreases in both groups were deferasirox dose-dependent.

The majority of adverse events (AEs) were mild-to-moderate in both trials (Table 2). Drug-related serious AEs were documented in 5 chelation naïve and 2 pre-chelated MDS patients; 39 deaths occurred - none assessed as drug related.

Table 2. Most common drug-related adverse events in the MDS population (≥5% overall)

AE, n(%)	MDS eXtend (n = 123)	MDS eXjange (n = 44)
Diarrhea	13 (11)	4 (9)
Nausea	11 (9)	3 (7)
Rash	8 (7)	1 (2)
Serum creatinine increase	6 (5)	4 (9)

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The median serum creatinine increase in chelation naïve and pre-chelated patients, respectively, was 0.1 mg/dL, and 0.2 mg/dL (all values within the normal age-specific ranges).

This large observational study demonstrated that deferasirox can achieve substantial reductions in iron burden when prescribed in the routine clinical environment of office-based physicians. Observed decreases in serum ferritin were dose-dependent highlighting the importance of dose adjustment in line with clinical efficacy and safety parameters. Using such a strategy, deferasirox was well tolerated with a safety profile comparable with other reports in this elderly patient group.^{9,11}

High baseline median serum ferritin levels in pre-chelated individuals (2442 ng/mL) indicate that previous chelation regimens were largely sub-optimal and high median levels in chelation naïve patients (2679 ng/mL) emphasize the importance of monitoring and prompt initiation of chelation to avoid adverse sequelae. These studies indicate that deferasirox provides a safe and effective treatment option for transfusion-dependent MDS at risk of the clinical sequelae of iron overload.

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

We now have data up to 5 years with deferasirox. It is important to note that no new tolerability issues are yet to emerge. Furthermore levels of ferritin are being achieved in thalassemia major without new tolerability issues and other patients where DFO therapy would have been reduced. Clear 'stopping rules' based on evidence are yet to emerge. However the general principle of a 'soft landing' should be adopted - that is to say that as ferritin falls towards 500µg/L the dose should be gradually reduced but in my opinion therapy should not be stopped or interrupted while blood transfusion continues.

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