

**Deferasirox (ICL670; Exjade) reduces serum ferritin and labile plasma iron in patients with myelodysplastic syndromes.**

*A List (abstract 1470)*

A mainstay of therapy for patients with MDS is RBC transfusions to manage symptomatic anemia. Iron accumulation as a result of transfusion therapy is associated with significant morbidity and mortality. In a retrospective study in iron-overloaded patients with low-risk MDS, iron accumulation was associated with an incremental decline in OS, with a HR of 1.36 for every 500 ng/mL increase in serum ferritin levels above 1000 ng/mL. The ongoing US03 trial is evaluating long-term efficacy (assessed by changes in serum ferritin and LPI) and safety (incidence and type of AEs) of deferasirox (starting dose 20 mg/kg/day) in patients with low- to intermediate-risk MDS.

Data on 173 patients (median age 71 years) are available. Patients had been transfused for a mean of 3.5 years and mean baseline serum ferritin was 3398 ng/mL. After 12 months of deferasirox therapy, mean serum ferritin decreased by  $859 \pm 1548$  ng/mL. Mean deferasirox dose was 21 mg/kg/day and mean transfusion rate was 4.1 RBC units/month. Trough LPI levels normalized in all patients over the treatment period.

Of 165 patients who were eligible for safety evaluation, 10 (6%) discontinued deferasirox treatment secondary to suspected AEs, and six (4%) discontinued treatment secondary to serious AEs (two cases of rash, one thrombocytopenia, two pneumonia and one gastric carcinoma). There were 52 new cases of neutropenia (32% of patients) and 22 of thrombocytopenia (13%) during the 12 months of deferasirox therapy. There were 11 deaths (7%) during the 12 months of the study; none were judged to be related to deferasirox treatment.

Of 140 patients with serum creatinine level measurements at baseline, 119 had normal levels and 21 had abnormal levels. Of the 119 patients with normal serum creatinine levels at baseline, 35 (25%) demonstrated increases >ULN (maximum of

2.2 mg/dL) over 12 months. Of the 21 patients with abnormal serum creatinine levels at baseline, 11 (52%) increased >33% above baseline over 12 months.

This study shows that deferasirox therapy can effectively decrease serum ferritin levels over 1 year in patients with low- to intermediate-risk MDS, with no unexpected safety concerns. These are the first data to show that deferasirox decreases LPI in MDS patients. The findings demonstrate that deferasirox reduces iron burden in patients with MDS, confirming the recently published data from study 108 but in a larger cohort of patients. Ongoing assessments evaluating cardiac, hepatic and endocrine function will evaluate the impact of iron reduction on morbidity and mortality in MDS.