Efficacy and Safety of Deferasirox

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Abstract

Deferasirox represents a new class of once-daily iron chelators. It was first licensed in 2005 for the treatment of adult and pediatric patients with chronic iron overload due to blood transfusions. These approvals were based on data from the core program of one-year clinical trials, which involved more than 1,000 patients in what is the largest and most rigorous prospective clinical evaluation of any iron-chelating agent to date. Deferasirox has been studied in adults and children with a wide range of conditions, including β-thalassemia, myelodysplastic syndromes, and sickle cell disease. Recent data have highlighted the importance of timely deferasirox dose adjustments and described the efficacy and safety of deferasirox at doses >30mg/kg/day. The pharmacokinetic profile of deferasirox across all age groups shows it to be well absorbed, with a mean elimination half-life of eight to 16 hours that supports once-daily dosing. In clinical trials, deferasirox has demonstrated consistent dose-dependent efficacy, producing sustained reductions in serum ferritin, labile plasma iron, and cardiac iron load. The safety profile of deferasirox presents mostly as mild adverse events (primarily gastrointestinal symptoms, skin rash, and increases in serum creatinine) that resolve rapidly with no reports of progressive renal, hepatic, or bone marrow effects. This adverse event profile is seen to be manageable with appropriate clinical monitoring. Data from the extension phases of these studies are beginning to accumulate, with experience of up to seven years of deferasirox therapy now available. Deferasirox represents a significant development in the treatment of iron overload and has further potential applications.

Keywords

Deferasirox, iron chelation, anemia, serum ferritin, labile plasma iron, myelodysplastic syndromes, safety, efficacy

Disclosure: Maria Domenica Cappellini, MD, is a member of the speaker's bureau and board for protocol 2209 (Exjade in Thalassemia Intermedia) for Novartis and a member of the European Gaucher Registry sponsored by Genzyme. Laura Zanaboni, MD, has no conflicts of interest to declare.

Received: June 2, 2009 **Accepted:** October 29, 2009 *DOI: 10.17925/OHR.2009.02.0.68*

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Support: Supported by Novartis Pharmaceuticals Corporation.

Blood transfusion therapy and accompanying iron chelation have dramatically improved the quality of life for many patients with severe anemias. Diseases such as β-thalassemia, once fatal in early childhood, can now be managed as chronic conditions compatible with prolonged life. Today, life expectancy varies between 25 and 55 years, depending on patient compliance with medical treatment, particularly iron chelation therapy. Deferoxamine (Desferal®, DFO; Novartis Pharma AG, Basel, Switzerland) is the current reference standard of care; however, it requires subcutaneous infusion lasting eight to 12 hours per day, five to seven days a week for as long as the patient continues to receive blood transfusions. This regimen is problematic for many patients, interfering significantly with their daily life and, therefore, often resulting in poor patient compliance.[1] A three-times-daily agent, deferiprone (Ferriprox®; Apopharma, Toronto, Canada), became available in Europe in 1999 and is available outside the US and Canada for the second-line treatment of iron overload in adult patients with thalassemia major for whom DFO therapy is contraindicated, inadequate, or intolerable.[2]

Deferasirox (Exjade®; Novartis Pharma AG, Basel, Switzerland) was developed in response to the significant clinical need for a convenient, effective, and well-tolerated oral iron-chelating agent. Deferasirox was designed through a rational drug development program to require only once-daily dosing. In pre-clinical studies, deferasirox was seen to be more effective than DFO in mobilizing iron from the hepatocellular pool.[3] It is predominantly metabolized by glucoronidation, with subsequent biliary excretion.[4] Deferasirox and its metabolites are mainly excreted in the feces (84% of the dose); renal excretion is minimal (8% of the dose, 6% as hydroxylated deferasirox). Deferasirox is approved in over 90 countries worldwide for the treatment of chronic iron overload due to blood transfusions in patients from two years of age upwards.

Clinical Experience with Deferasirox

Efficacy

The deferasirox clinical development program is the largest ever conducted for any iron-chelating agent. Five pivotal clinical studies have

assessed the efficacy, safety, and tolerability of deferasirox across a number of transfusion-dependent anemias.[5–9] The trial program is also notable for its inclusion of patients with a wide range of ages. Pediatric patients were well represented, with approximately 40% of patients being two to 16 years of age. Older adults have also been represented in studies of patients with myelodysplastic syndromes (MDS). To date, up to 1,000 patients with a variety of different anemias have been involved in the core program of one-year studies, more than 900 of whom have continued to receive deferasirox in the extension phases that will gather data for up to an additional four years. An overview of key deferasirox clinical efficacy data is given in *Table 1*.

A randomized, double-blind, placebo-controlled, phase I dose-escalation study in 24 iron-overloaded patients with β-thalassemia was the first to demonstrate that deferasirox could reduce iron burden in humans.[10] Pharmacokinetic evaluations in this study were consistent with pre-clinical evidence that deferasirox is absorbed promptly and is detectable in the blood for 24 hours. The plasma concentration of deferasirox was also found to be proportional to dose. Although three dose groups (10, 20, or 40mg/kg/day) were evaluated and all three doses resulted in a positive net iron excretion, the investigators concluded that deferasirox 20–30mg/kg/day offered the most effective chelation combined with reasonable tolerability. Based on these findings, the recommended starting dose of deferasirox for most patients is 20mg/kg/day, with dose titration in increments of 5–10mg/kg/day based on trends in serum ferritin.

The effect of deferasirox and DFO on liver iron concentration (LIC) was compared in a 48-week study on 71 iron-overloaded adults with β-thalassemia at four centers in Italy. Over the study period, deferasirox 20–30mg/kg/day showed similar efficacy to DFO 40mg/kg/day based on reductions in LIC.[7] Analysis of data from another study in patients with β-thalassemia (n=586) showed that transfusional iron load markedly affects the efficacy of deferasirox and serum levels of ferritin.[11] It is therefore essential that both iron intake and serum ferritin levels are monitored in order to determine the most appropriate dose of deferasirox to reduce iron load. This monitoring strategy was supported by the results of the Evaluation of Patients' Iron Chelation (EPIC) study, which was a phase IV prospective multicenter trial involving 1,744 patients over two years of age with transfusion-dependent anemia. EPIC aimed to evaluate the effect of fixed starting doses of deferasirox based on transfusion history, with dose titration every three months according to trends in serum ferritin and safety markers. Overall, median serum ferritin significantly decreased by 264ng/ml during the one-year study period ($p<0.0001$).[12] The changes in serum ferritin were reflective of dosage adjustments and mean iron intake during the study. A retrospective analysis of data from 228 patients participating in four studies of patients with various transfusion-dependent anemias showed that deferasirox doses of >30mg/kg/day effectively reduce iron burden without compromising tolerability.[13] Therefore, patients who are heavily transfused and may require higher doses to compensate for ongoing iron loading can receive appropriate therapy without affecting tolerability.

As well as affecting serum ferritin levels and LIC, deferasirox can reduce levels of labile plasma iron (LPI) in patients with β-thalassemia major and other transfusion-dependent anemias.[14,15] LPI is a directly chelatable form of non-transferrin-bound iron that is readily taken up by cells and is able to participate in redox cycling reactions, resulting in the formation of harmful reactive oxygen species (ROS).[16,17] Deferasirox doses of ≥20mg/kg/day provided a sustained reduction in LPI levels and may therefore contribute to a reduction in unregulated tissue iron loading.[14,15]

The efficacy of deferasirox has also been evaluated in pediatric patients with β-thalassemia as young as two years of age. The pharmacokinetic profile of deferasirox in pediatric patients (two to seven years of age) also supports a once-daily dosing regimen; however, the steady-state exposure to deferasirox in children and adolescents is ~20–30% lower than in adults.[7] Longer-term data in pediatric patients treated with deferasirox for up to five years have now demonstrated a dose-dependent reduction in iron burden and no negative impact on growth and sexual development.[18,19]

Recent clinical data support the efficacy of deferasirox in the removal of cardiac iron and prevention of myocardial siderosis in patients with β-thalassemia major.[20–23] A cardiac substudy of the EPIC trial analyzed changes in myocardial T2* (mT2*) during one year of deferasirox treatment in 114 patients with baseline mT2* of <20ms (indicative of cardiac iron accumulation).[21] These patients were treated with deferasirox starting at 30mg/kg/day, which could be adjusted by 5–10mg/kg/day according to serum ferritin level, six-month mT2*, and safety parameters. Deferasirox treatment at a mean dose of 32.6mg/kg/day significantly improved mT2* from a geometric mean of 11.2ms at baseline to 12.9ms after one year; left ventricular ejection fraction (LVEF) was maintained at ~67%.[21] This cardiac substudy also identified a group of 78 patients with normal baseline cardiac iron levels (mT2* ≥20ms).[23] At baseline, geometric mean T2* was 32.0ms; after one year of deferasirox treatment at a mean dose of 27.6mg/kg/day mT2* was 32.5ms, indicating good control of cardiac iron levels. During treatment, LVEF showed a significant increase from 67.7 to 69.6% ($p<0.0001$), and body iron burden (assessed by serum ferritin and LIC) showed significant decreases.[23]

While the majority of deferasirox studies have involved patients with β-thalassemia major, a wide range of other patient types have been investigated, for whom data continue to accumulate. While there is a general paucity of clinical experience in patients with thalassemia intermedia, initial evaluation of deferasirox use in this patient population has shown effective management of iron burden, with good tolerability.[24,25] An ongoing one-year trial of deferasirox treatment in more than 150 patients is the first large-scale study of such an agent in this patient population; results from this trial have not yet been reported. A large population of patients with sickle cell disease (SCD) has also been investigated. In an open-label trial, 195 adult and pediatric patients with SCD (three to 54 years of age) were treated with deferasirox or DFO.[9] Treatment with deferasirox (10–30mg/kg/day) for one year resulted in significant reductions in LIC ($p<0.05$) compared with baseline; decreases in serum ferritin were also observed, although with moderate variability between patients. Deferasirox demonstrated similar efficacy and safety profiles in transfused adult and pediatric patients with SCD compared with DFO. Three-and-a-half-year data from the extension phase of this study are also available, demonstrating that deferasirox provided a continued reduction in serum ferritin over the course of the study and that the incidence of drug-related adverse events (AEs) decreased after the first year.[26] A smaller one-year study of 31 SCD patients has also shown effective reduction in iron levels and manageable tolerability with

Table 1: Overview of Deferasirox Clinical Efficacy Data

Study Name/Number	Patients Recruited	Treatments	Duration	Efficacy Outcome
Phase I, multiple-dose, iron balance study (No. 104)[10]	24 adult patients with β-thalassemia	Deferasirox 10–40mg/kg/day	12 days	Deferasirox was absorbed promptly and was detectable in the blood for 24 hours. At a steady state, deferasirox levels were proportional to dose. All doses resulted in positive net iron excretion.
Phase I, single-dose, safety, efficacy and pharmacokinetic study (No. 103)[41]	24 patients with β-thalassemia	Deferasirox 2.5–80mg/kg/day	Single dose	The plasma half-life of 11–19 hours supports once-daily dosing.
Phase II, randomized deferasirox versus DFO safety and LIC study (No. 105)[7]	71 patients with β-thalassemia	Deferasirox 10 or 20mg/kg/day or DFO	48 weeks (+ extension phase)	Deferasirox 20mg/kg/day showed similar efficacy to DFO in terms of reduction in LIC.
Phase II, single-arm, safety and LIC study (No. 106)[6]	40 pediatric patients with β-thalassemia (children 2–12 years of age and adolescents 12–17 years of age)	Deferasirox 10mg/kg/day	48 weeks (+ extension phase)	LIC increased from week 12 as mean daily iron intake was higher than excretion. Steady-state plasma levels of deferasirox and its iron complex, Fe-[deferasirox]2, comparable between children and adolescents.
Phase II, single-arm, LIC and tolerability study (No. 108)[8]	184 pediatric/adult patients with β-thalassemia, MDS, rare anemias	Deferasirox 5–30mg/kg/day	1 year (+ extension phase)	In patients with baseline LIC ≥7mg Fe/g dry weight (dw), deferasirox initiated at 20 or 30mg/kg/day produced statistically significant decreases in LIC ($p<0.001$); decreases greatest in MDS and least in DBA. LIC changes dependent on dose ($p<0.001$) and transfusional iron intake ($p<0.01$), but not statistically different between disease groups.
Phase II, randomized deferasirox versus DFO open-label safety and LIC study (No. 109)[9]	195 adult and pediatric patients 3–54 years of age with SCD	Deferasirox 5–30mg/kg/day or DFO	1 year (+ extension phase)	Dose-dependent changes in iron burden were observed; iron balance was achieved at 10–20mg/kg/day, iron reduction achieved at 30mg/kg/day. 3.5-year follow-up data show continued reduction in iron burden.[26]
Phase III, randomized LIC and tolerability (No. 107)[5]	586 pediatric/adult patients with β-thalassemia or DFO	Deferasirox 5–30mg/kg/day	1 year (+ extension phase)	Deferasirox doses of 20 or 30mg/kg/day provided dose-dependent changes in LIC. Deferasirox doses of 5 and 10mg/kg/day were insufficient to balance iron uptake in this heavily transfused population.
Pooled analysis of core extension study data (No. 105-108)[u]	472 adult and pediatric patients with β-thalassemia	Deferasirox overall mean daily dose of 22.1mg/kg/day	4.5 year	4.5-year extension study data showed ongoing dose-dependent reductions in serum ferritin with deferasirox treatment.
EPIC, open label, single-arm study (No. 2409)[12]	1,744 patients with transfusion-dependent anemias	Deferasirox up to 40mg/kg/day	1 year (+ extension phase)	A significant reduction in median serum ferritin levels was seen ($p<0.0001$). Subgroup analyses demonstrated the importance of individualizing dosing according to the rate of iron intake from ongoing blood transfusions, as well as current iron burden and target serum ferritin levels. In a subgroup of 937 patients with β-thalassemia, ≥30mg/kg/day deferasirox produced the largest reduction in serum ferritin.[42] In a subgroup of 341 MDS patients, median serum ferritin levels were significantly reduced compared with baseline.[29]
ESCALATOR, open-label, single arm-study (No. 2402)[43]	237 pediatric/adult patients with β-thalassemia (previously unsuccessfully treated with DFO or deferiprone)	Deferasirox up to 30mg/kg/day	1 year (+ extension phase)	In patients with a baseline LIC of ≥7mg Fe/g dw (therapeutic goal of LIC reduction), mean LIC significantly decreased during treatment ($p<0.001$). In patients with a baseline LIC of <7mg Fe/g dw (therapeutic goal of LIC maintenance), levels were maintained at approximately baseline levels. Dose adjustments during the extension phase resulted in a significant reduction in iron burden, and more patients were able to achieve LIC <7mg Fe/g dw with a longer course of deferasirox treatment (2.7 years).[44]

DBA = Diamond–Blackfan anemia; DFO = deferoxamine; LIC = liver iron concentration; MDS = myelodysplastic syndromes; SCD = sickle cell disease.

deferasirox therapy.[27] Deferasirox has also been shown to maintain or reduce body iron in patients with MDS in several clinical trials.[8,28–30] The EPIC study has recruited the largest population of MDS patients in any trial to date (n=341).[29] This group of patients had a high transfusion requirement and iron burden but nearly 50% had received no chelation therapy before entering the study. During the one-year treatment period, deferasirox

Table 2: Overview of Clinical Study Safety Data Supporting Deferasirox

Study Name/Number	Patients Recruited	Treatments	Duration	Safety Outcome
Phase II, single-arm, safety and LIC study (No. 106)[6]	40 pediatric patients with β-thalassemia (children 2–12 years of age and adolescents 12–17 years of age)	Deferasirox 10mg/kg/day (adjusted dose in extension)	48 weeks (+ extension phase)	Deferasirox was generally well tolerated and no patient discontinued therapy due to AEs. Five-year extension data showed no evidence of progressive renal, hepatic, or bone marrow dysfunction, and growth and sexual development progressed normally.[18]
Phase II, single-arm, LIC and tolerability study (No. 108)[8]	184 pediatric/adult patients with β-thalassemia, MDS, and rare anemias	Deferasirox 5–30mg/kg/day	1 year (+ extension phase)	Deferasirox had a safety profile compatible with long-term use. No disease-specific safety/tolerability effects. Most common AEs: gastrointestinal disturbances, skin rash, and non-progressive serum creatinine increases.
Phase II, open-label, randomized, safety and LIC study (No. 109)[9]	195 adult and pediatric patients 3–54 years of age with SCD	Deferasirox 5–30mg/kg/day or DFO	1 year (+ extension phase)	Deferasirox had acceptable tolerability. AEs mostly mild, transient nausea, vomiting, diarrhea, abdominal pain, and skin rash. Abnormal laboratory results: mild non-progressive increases in serum creatinine and reversible elevations in liver function. Extension study data (3.5-year data) showed a decrease in the incidence of drug-related AEs after the first year, with no evidence of progressive increases in serum creatinine.[26]
Phase III, randomized LIC and tolerability study (No. 107)[5]	586 pediatric/adult patients with β-thalassemia	Deferasirox 5–30mg/kg/day or DFO	1 year (+ extension phase)	Most common AEs: rash, gastrointestinal disturbances, and mild non-progressive increases in serum creatinine. No agranulocytosis, arthropathy, or growth failure was associated with deferasirox.
Pooled analysis of core extension study data (No. 105–108)[34]	472 adult and pediatric patients with β-thalassemia	Deferasirox overall mean daily dose of 22.1mg/kg/day	4.5 year	Deferasirox was generally well tolerated, with the frequency of investigator-reported AEs decreasing over long-term treatment. There were no changes in liver or renal function that differed significantly from the one-year core trials, and there was no evidence of progressive liver/renal dysfunction.
Phase II, open-label, efficacy and safety study (No. US03)[28]	176 patients with lower-risk MDS	20–40mg/kg/day	1 year (+ extension phase)	The most common AEs were diarrhea, rash, and nausea. Of 147 patients with normal baseline serum creatinine, 18% increased >ULN on at least two occasions. 5 and 13% of patients experienced new-onset cases of thrombocytopenia and neutropenia, respectively, none suspected to be related to deferasirox.
EPIC, open label, single-arm study (No. 2409)[12]	1,744 transfusion-dependent anemias	Deferasirox up to 40mg/kg/day	1 year (+ extension phase)	Deferasirox was generally well tolerated, with a safety profile consistent with data from previous clinical trials.
ESCALATOR, open-label, single-arm study (No. 2402)[43]	237 pediatric/adult patients with β-thalassemia (previously unsuccessfully treated with DFO or deferiprone)	Deferasirox up to 30mg/kg/day	1 year (+ extension phase)	Drug-related AEs were mostly mild to moderate and resolved without discontinuing treatment. The overall safety profile was maintained with a low discontinuation rate in the extension phase.[44]

AE = adverse event; DFO = deferoxamine; LIC = liver iron concentration; MDS = myelodysplastic syndromes; SCD = sickle cell disease.

produced significant reductions in serum ferritin.[29] A further clinical study (US03) evaluated the efficacy and safety of deferasirox 20mg/kg/day in a single group of 176 heavily transfused patients with lower-risk MDS (median age 71 years; range 21–90). After one year of treatment, deferasirox significantly reduced serum ferritin by 859±1,548ng/ml and trough LPI normalized in all patients.[31] Smaller patient populations evaluated with deferasirox include aplastic anemia and Diamond–Blackfan anemia (DBA), and effective reductions in iron load have been demonstrated in these rare anemias.[8,32,33]

As most patients receiving regular transfusions require lifelong iron chelation therapy, the long-term efficacy and safety of deferasirox is continuing to be assessed in extension phases to the one-year core trials. These extension phases have now reported follow-up of patients receiving deferasirox for up to a median of 4.5 years. The results of these studies confirm that deferasirox efficacy is both dose- and transfusion-dependent,[33] even in patients who could not be chelated with DFO and/or deferiprone due to toxicity, lack of response or failure to comply with treatment regimens.[34,35]

Safety

Evaluation of the safety and tolerability of deferasirox has been a key objective of all pivotal clinical trials. AEs and serious AEs have been extensively monitored throughout the program and continue to be assessed in the extension phases. Deferasirox has a defined safety profile that is clinically manageable with regular monitoring in adult and pediatric patients; an overview of key clinical safety data is given in *Table 2*. The most frequent AEs reported during the extension phases to the deferasirox registration studies include transient, mild to moderate gastrointestinal disturbances and skin rash; drug-related AEs were generally transient and

Table 3: Proposed Patient Management Approaches/Algorithms for Responding to Adverse Events in Patients Receiving Deferasirox

Adverse Event	Incidence in Core Trials (%)	Management Approach
Gastrointestinal		
Diarrhea	8.8	Patients should take an antidiarrheal for up to two days, and keep hydrated. Deferasirox could be taken in the evening rather than the morning. Products such as Lactaid (if the patient is lactose-intolerant) or probiotics (acidophilus or lactobacillus) could be added to the diet.
Abdominal pain	5.0	Patients should sip water or other clear fluids and avoid solid food for the first few hours. Avoid narcotic pain medications and non-steroidal anti-inflammatory drugs. Deferasirox could be taken in the evening rather than the morning.
Nausea/vomiting	14.3	Patients should drink small, steady amounts of clear liquids, such as electrolyte solutions, and keep hydrated.
Skin Rash		
Mild to moderate	4.3	Likely to resolve spontaneously. Deferasirox should be continued without dose adjustment.
Severe	0.4	Deferasirox should be interrupted and reintroduced at a lower dose. Patients should take low-dose oral steroids for a short period of time.
Renal Changes		
All renal change	36	Serum creatinine levels should be assessed in duplicate before therapy, then monthly. If patients have additional renal risk factors, serum creatinine levels should be monitored weekly for the first month or after modification of deferasirox therapy, then monthly.
>33% above pre-treatment values at two consecutive visits (not attributed to other causes)	11	Deferasirox dose should be reduced by 10mg/kg/day.
Progressive increases beyond the ULN	0	Deferasirox should be interrupted, then re-initiated at a lower dose followed by gradual dose escalation if the clinical benefit outweighs the potential risks
Pediatrics, >33% above pre-treatment values and above the age-appropriate ULN at two consecutive visits	11	Deferasirox dose should be reduced by 10mg/kg/day.
Changes in Liver Function		
All liver function change	2[a]	Liver function should be monitored monthly. Following any severe or persistent elevations in serum transaminase levels, dose modifications should be considered. Deferasirox therapy can be cautiously re-introduced once transaminase levels return to baseline
Other Effects		
Auditory and ocular	<1	Auditory and ophthalmic function should be tested before initiating therapy and annually thereafter.

a. Elevations in serum liver transaminases reported as adverse events. ULN = upper limit of normal.
Source: Vichinsky E, Clinical application of deferasirox: Practical patient management, American Journal of Haematology, *Volume 83, Issue 5, 2007, 398–402 (table 1, page 399).*

of mild to moderate severity.[19,34] Mild, non-progressive increases in serum creatinine (generally within the upper limit of normal [ULN]) were observed in approximately one-third of patients in the pivotal one-year clinical trials of deferasirox. Creatinine levels returned spontaneously to normal in more than two-thirds of patients who experienced these mild increases.[36] There were no cases of moderate to severe renal insufficiency or renal failure, and no patients permanently discontinued therapy due to creatinine rises. Data over a median period of 4.5 years of treatment have confirmed that these increases are non-progressive.[34] Most AEs experienced by patients during treatment with deferasirox resolve spontaneously and do not require discontinuation or interruption of treatment. Algorithms for skin rash and diarrhea, two of the most common AEs experienced by patients during treatment with deferasirox, have been developed to help guide clinicians in resolving these AEs. A summary of the management approaches to a range of potential events has been previously published (see *Table 3*).[37] The safety profile of deferasirox in pediatric patients is similar to that of adult patients during up to five years of follow-up.[18,19] The recommended starting dose and dosing modifications are the same for pediatric and adult patients. To date, there have been no reports of progressive renal, hepatic, or bone marrow dysfunction and no reports of deferasirox treatment having a negative impact on growth and sexual development.[18,19,38] In adult or elderly MDS patients, the incidence of gastrointestinal events was seen to be higher than that previously observed in the thalassemia population.[29] The discontinuation rate in these patients was also higher and investigations are ongoing to determine possible contributing factors such as existing comorbidities and the advanced age of this patient subgroup.[29] Product information for deferasirox includes monthly monitoring of serum creatinine levels and creatinine clearance in patients who have pre-existing renal conditions, are elderly, have comorbid conditions that may affect renal function, or are receiving medicinal products that depress renal function. Blood counts and liver function should also be monitored monthly.

Patient Preferences

As deferasirox is an oral iron chelator, it might be expected that patient compliance would be superior to that seen with DFO infusions. Assessment of patient preferences among patients with β-thalassemia has demonstrated greater satisfaction with, and convenience of, deferasirox

therapy compared with DFO, with 97% of patients with β-thalassemia who switched to deferasirox from DFO preferring deferasirox. Patients preferred deferasirox due to greater convenience (37%), no injection-site soreness (25%), and less disruption to their day (23%).[39] Similar results have been seen among SCD patients.[40] Greater satisfaction and convenience with deferasirox may translate into improvements in patient compliance and increased effectiveness of chelation therapy.

Conclusions

The clinical development program for deferasirox has included a wide range of patients with different anemias across all age groups. In these clinical studies, deferasirox has shown consistent efficacy and a manageable safety profile. The results from long-term follow-up and the large-scale EPIC trial have provided strong evidence that further supports these observations across populations with transfusional iron overload. Clinical management experience supports monthly monitoring and regular dose adjustments for patients, which should be guided by trends in serum ferritin and customized to meet individual patient needs and treatment goals. Recent findings on deferasirox cardiac efficacy in terms of prevention and treatment of cardiac iron accumulation demonstrate the potential for deferasirox therapy to address this important aspect of patient management. Deferasirox can be regarded as a much-needed development in the treatment of chronic iron overload, particularly in patients with anemia who have received repeated blood transfusions. ■

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