

Deferasirox desensitization



Karen E. Bruner, MD, and Kevin M. White, MD

Clinical Implications

- Deferasirox is the only oral iron chelator approved for pediatric use in the United States; however, it is known to cause a maculopapular rash in up to 10% of the patients. Desensitization to deferasirox is possible using a conservative outpatient desensitization protocol.

TO THE EDITOR:

Iron overload is a common complication of frequent blood transfusions, often requiring years of treatment with iron chelators. Deferasirox is an oral iron chelator taken daily.¹ It is the only oral iron chelator currently approved for pediatric use by the Food and Drug Administration. It is available as a tablet that is dissolved in water or juice. It is often preferred to the alternative iron chelator, deferoxamine, which must be given subcutaneously and requires daily infusions over 10 to 12 hours.¹

Deferasirox has been reported to cause a maculopapular eruption in up to 10% of the patients.¹ Some rashes have been associated with systemic symptoms, as was reported in a 75-year-old woman with a history of acute myeloid leukemia.² That patient had initial onset of maculopapular rash 15 days after starting the medication. The rash improved with intravenous and topical steroids as well as antihistamines. The rash recurred within 4 hours of restarting the medication 3 weeks later and was associated with fever and hypotension. A patch test to deferasirox was subsequently negative.

Our patient is a 17-year-old male with relapsed acute lymphocytic leukemia and iron overload due to repeat blood transfusions. He experienced a pruritic maculopapular rash after increasing his dose of deferasirox. He had previously been on deferasirox at a dose of 500 mg daily for 1 month, but had also been on dexamethasone during that time as part of his chemotherapy regimen, which also included 6-mercaptopurine and methotrexate. The day his dexamethasone was stopped, his dose of deferasirox was increased to 1000 mg. He also received a replacement dose of intravenous immunoglobulin for hypogammaglobulinemia. He developed a pruritic, blotchy rash limited to his palms only several hours later at home. His parents held his deferasirox for 2 days, during which time the rash spontaneously cleared without treatment. At the follow-up appointment with his oncologist, the rash was believed to be due to intravenous immunoglobulin and the patient was told to restart deferasirox at 1000 mg. He then developed a pruritic maculopapular rash 8 to 12 hours later and fever to 102°F. His rash initially started on his face and then spread to his trunk and genitalia, finally progressing outward to the extremities over 7 to 10 days (see Figure 1). He was treated with oral steroids and H₁- and H₂-blockers initially as an inpatient until his fever



FIGURE 1. Initial maculopapular rash associated with fever.

TABLE I. Deferasirox desensitization protocol

Dose (mg)	Interval (d)
0.05	3
0.1	4
0.2	3
0.5	4
1	3
2	4
4	3
8	4
16	3
32	4
64	3
125	4
250	3
500	7
750	7
1000	7
1500	7
2000	7

defervesced and then as an outpatient with gradual resolution of rash over 2 to 3 weeks. A T-cell-mediated, non-IgE mechanism was suspected given the delayed onset of rash and fever. No skin tests were performed given low suspicion for an IgE-mediated reaction.

The patient's initial ferritin level was 3771 ng/mL (normal range, 24-336 ng/mL). He was expected to require daily iron chelation therapy for up to 2 to 3 years. The daily 10- to 12-hour subcutaneous infusions required for deferoxamine treatment combined with the patient's fear of needles made deferoxamine an unwieldy option for the patient and family. They and their oncologist requested desensitization to deferasirox as an alternative.

Initially, we attempted desensitization as an inpatient, starting at 1/1000 of the goal dose, modeling our protocol after TMP-SMX outpatient desensitization protocols.³ The patient was premedicated with cetirizine 10 mg. Unfortunately, he developed itchy palms followed by pruritic rash and flushing 3 hours after the second dose and the procedure had to be terminated. The rash and pruritus were similar to his first reaction but less severe. He was treated with oral steroids and hydroxyzine with gradual resolution of rash over 3 days.

We then decreased the starting dose to 1/100,000 of the goal dose and doubled the dose every 3 to 4 days. This was done as an outpatient and was successful until the 500-mg dose, when the patient was unable to tolerate a full doubling of the dose because of itching. We then increased the dose at a slower rate, as described in Table I, until reaching the goal 2000-mg dose.

It took 3 months to achieve the goal dose using this regimen. The patient's ferritin level decreased more than 1000 ng/mL during the desensitization period. He was then able to continue on his goal dose for at least 9 months without problems. He then developed nausea and vomiting from the medication, which is a known adverse effect reported in 10% of the patients. He discontinued deferasirox because of gastrointestinal intolerance. His ferritin level had decreased to 1048 ng/mL when he stopped the medication.

To our knowledge, this is the first report of a successful desensitization to deferasirox. Given that deferasirox is the only oral iron chelator approved for pediatric use in the United States and that maculopapular rash is a known adverse reaction of the medication, it leaves pediatric patients with deferoxamine as

their only other option for iron chelation therapy. Compliance with deferoxamine is often suboptimal given the need for time-intensive daily subcutaneous infusions.⁴ For this reason, it is important for allergists to know that a slow, conservative desensitization protocol can be successful in an outpatient setting. Deferasirox desensitization may allow patients an improved quality of life and increase medication compliance for the treatment of iron overload.

Acknowledgments

This activity has not received external commercial support. No unapproved/investigative use of a product/device is discussed. The opinions or assertions herein are the private views of the authors and are not to be construed as reflecting the views of the Department of the Air Force or the Department of Defense.

Department of Allergy/Immunology, Wilford Hall Ambulatory Surgical Center, San Antonio, Texas

Conflicts of interest: The authors declare that they have no relevant conflicts of interest.

Received for publication June 23, 2015; revised August 14, 2015; accepted for publication September 4, 2015.

Available online October 21, 2015.

Corresponding author: Karen E. Bruner, MD, Allergy/Immunology, 2200 Bergquist Dr, Ste 1, Lackland AFB, TX 78236. E-mail: kbrunerva@gmail.com.

2213-2198

Published by Elsevier Inc. on behalf of the American Academy of Allergy, Asthma & Immunology

<http://dx.doi.org/10.1016/j.jaip.2015.09.007>

REFERENCES

1. Kwiatkowski JL. Oral iron chelators. *Hematol/Oncol Clin North Am* 2010;24:229-48.
2. Ohshita A, Nakai N, Katoh N, Konishi K. A maculopapular-type eruption associated with deferasirox administration. *J Am Acad Dermatol* 2013;69:e265-7.
3. Drug allergy: an updated practice parameter. *Ann Allergy Asthma Immunol* 2010;105:259-73. Table 10.
4. Sharma A, Arora E, Singh H. Hypersensitivity reaction with deferasirox. *J Pharmacol Pharmacotherapeut* 2015;6:105-6.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.