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## Daily alternating deferasirox and deferiprone therapy for 'hard-to-chelate' $\beta$ -thalassemia major patients

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**Daily alternating deferasirox and deferiprone therapy for 'hard-to-chelate'  $\beta$ -thalassemia major patients**

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Keywords:	$\beta$ -thalassemia , iron overload, chelation therapy



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3 **Daily alternating deferasirox and deferiprone therapy for ‘hard-to-**  
4 **chelate’  $\beta$ -thalassemia major patients**  
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3 **To the editor:** Chelation therapy for treating iron overload has changed the prognosis for  
4 patients with thalassemia major [1]. At present, three drugs are available to reduce iron overload in  
5 these patients: deferoxamine (DFO), which is given subcutaneously; and the oral agents deferasirox  
6 (DFX), and deferiprone (DFP). The efficacy of combined chelation treatment with DFO and DFP  
7 has been shown to be additive and to increase the probability of success in patients who have  
8 previously failed on monotherapy [2].  
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15 Here, we report the successful use of a daily alternating regimen of DFP and DFX therapy  
16 used to provide lifesaving chelation therapy in two thalassemia major patients treated at the Centro  
17 della Microcitemia e Anemie Congenite in Genova, Italy who were considered to be untreatable  
18 with both mono- and dual DFO–DFP therapy.  
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22 Patient 1 is a 20-year-old female who was splenectomized at the age of 14. She started  
23 chelation therapy with DFO by subcutaneous infusion (given over 8–12 hours) at 50 mg/kg/day for  
24 5 days per week at the age of 3 years and was compliant until the age of 18 years, when she began  
25 to experience systemic skin reactions and fever each time she received a DFO infusion. Her therapy  
26 was switched to DFP (75 mg/kg in three doses per day), but after 1 month the patient showed  
27 difficulties in movement due to pain in her knees and hips, which resolved after DFP was  
28 discontinued. DFX was prescribed it at 30 mg/kg/day, but the patient showed significant proteinuria  
29 (1 g/l), which disappeared after discontinuation of therapy but reappeared from the second day of  
30 therapy on three subsequent rechallenges with DFX at 20mg/kg/day. DFP therapy was restarted, but  
31 after 2 weeks the patient again experienced symptoms of arthralgia. During this period the patient  
32 was receiving a mean of 0.56 mL red blood cells/kg/day, equivalent to 11.78 g of iron per annum.  
33 Her ferritin levels increased from 1250 ng/ml to 6100 ng/ml and a liver iron concentration (LIC) of  
34 16.1 mg/Fe/g liver/dw, although cardiac MRI indicated a myocardial T2\* of 31 milliseconds [3, 4].  
35 The patient refused intravenous DFO treatment via an implantable device.  
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47 After having obtained written informed consent, the patient was started on DFP 85 mg/kg in  
48 three doses/day and DFX 30 mg/kg/day administered on alternating days. The regimen was well  
49 tolerated and no kidney function alterations, arthralgia or other safety problems were noted. After 1  
50 year of therapy the patient had not experienced any side effects, her ferritin levels had decreased to  
51 2850 ng/ml, with a LIC of 6.6 mg/Fe/g liver/dw. Her cardiac T2\* remained stable (32.8 mms).  
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56 Patient 2 is a 33-year-old female who commenced chelation therapy with subcutaneous DFO  
57 when she was 4 years old. Following a successful pregnancy at age 29, she experienced systemic  
58 skin reactions, fever and pain to every subcutaneous DFO dose. DFX was initiated at doses of 30  
59 mg/kg/day, but had to be discontinued due to skin reaction affecting her trunk and arms. When the  
60 patient was subsequently twice rechallenged at a lower dose (as per the manufacturer's label),

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3 however, the skin reaction reappeared. DFP was prescribed at 75 mg/kg in three doses/day, but this  
4 caused a persistent neutropenia with an absolute neutrophil count (ANC) nadir of  $\approx 1000/\mu\text{L}$ . The  
5 patient, who was receiving a mean of 0.41 mL red blood cells/kg/day, equivalent to 9.96 gr of iron  
6 per annum, then underwent a period of intravenous DFO infusion therapy lasting 12 hours per day.  
7 Although we were able to maintain a ferritin level of 800 ng/ml, a LIC of 2.1 mg/Fe/g liver/dw and  
8 a myocardial T2\* of 28.24 mms, the impact on the patient's quality of life was severe.  
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14 We initiated a regimen consisting of DFP 75 mg/kg in three doses/day, alternating daily with  
15 DFX 30 mg/kg/day. After 1 year of therapy, the patient had not experienced any adverse reactions.  
16 Her ferritin levels and LIC decreased (ferritin 335 ng/ml; LIC 1.3 mg/Fe/g liver/dw) and her  
17 cardiac MRI T2\* remained stable (30.5 mms), prompting an adjustment of the DFX dose to 25  
18 mg/kg/day.  
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23 This is the first report describing alternating therapy with DFX and DFP. This regimen has  
24 proved safe and effective in maintaining a low iron burden and, in the case of Patient 1, in reducing  
25 iron overload (Figure 1). Neither patient experienced any of the safety problems previously  
26 experienced with daily monotherapy with either DFO, DFX or DFP alone.  
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30 Larger studies are needed to confirm the present findings in otherwise untreatable  
31 thalassemia major patients, and to determine if this approach might be an alternative option in other  
32 patients requiring iron chelation therapy.  
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14 **Legend**

15 Figure 1: Trends in patients' ferritin values during iron chelation therapy with daily alternating  
16 DFX-DFP  
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For Peer Review

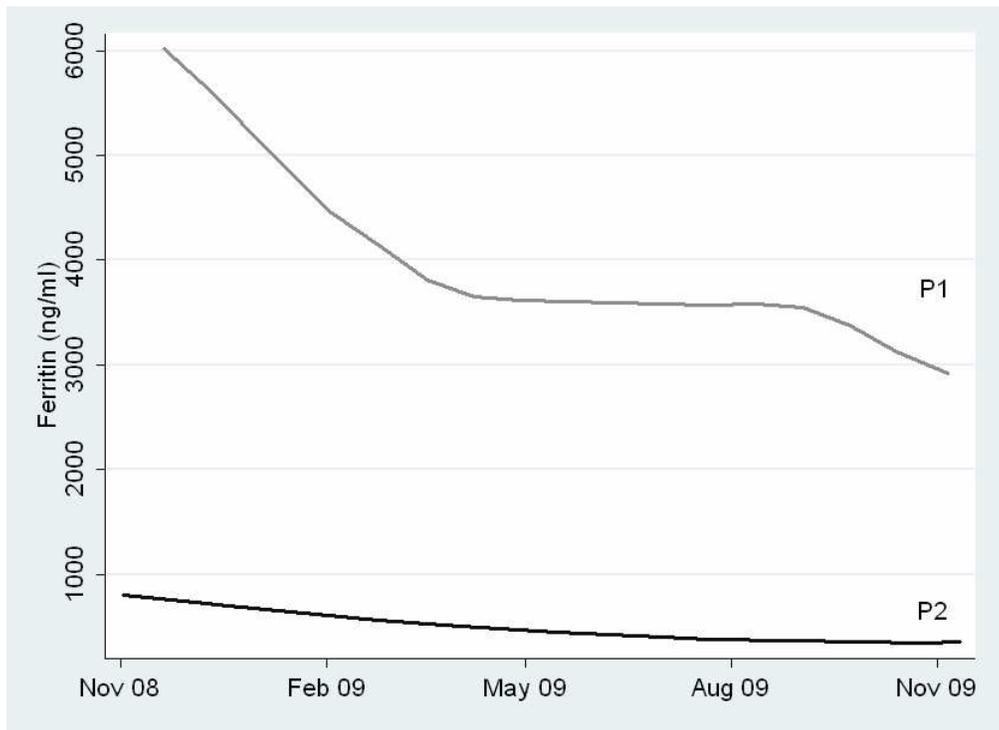
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**Figure legend**

Figure 1: Trends in patient ferritin values during iron chelation therapy with daily alternating DFX–DFP.

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