Deferiprone or deferasirox for cardiac siderosis in β thalassemia major (reply)

We thank KM Musallam and Ali T Taher[1] to have given us the opportunity to comment on our study more extensively. Firstly, to date, the goal of the physician responsible for the management of thalassemia is to tailor the chelation therapy for each patient according to the iron status in crucial organs like the heart and the specific efficacy of the different chelators. Thus, formal comparison in this phase are recommended. Our study is retrospective and this issue is clearly stressed in the paper.

Considering all three treatment groups together (desferrioxamine, deferiprone and deferasirox) we found a significant difference in the active treatment duration (P=0.001). At multiple comparisons, only desferrioxamine had been started significantly earlier than deferiprone and deferasirox but the time of active treatment was more comparable between deferiprone and deferasirox (P=0.100). Moreover, the group with longer active treatment was not the most effective. This supports data suggesting that not only the time of treatment but also intrinsic proprieties of the drugs explain their efficacy. We categorized patients who received the drugs for similar intervals of time and compared them in a secondary analysis. Because the duration of deferasirox therapy ranged from one to five years, we restricted the analysis to this duration of active chelation therapy. There were 30 patients in the deferiprone group, 24 patients in the deferasirox group and only 9 patients in the desferrioxamine group. The duration of the treatment was more homogeneous (P=0.442) in these treatment subgroups than when the overall groups were compared. Results of the comparison between the deferiprone and the deferasirox subgroups are shown in Table 1 and confirmed results observed when the overall groups were considered. Confidence intervals are also reported.

We tried to reduce the bias due to the retrospective analysis by reporting data to support the homogeneity of the three groups analyzed. The deferiprone and deferasirox groups showed comparable basal mean serum ferritin levels; therefore, we cannot attribute the results concerning the deferiprone group to a lower baseline iron burden. We agree with Musallam and Taher[1] regarding the complex relationship between cardiac iron and total body iron balance. In a cross sectional analysis in patients with a long history of chelation treatments, cardiac T2* does not correlate with serum ferritin concentration. Serum ferritin levels cannot be used, therefore, to predict cardiac iron.[2] Due to the comparable baseline ferritin levels, the lower heart T2* values found in the deferasirox group seem not to be related to a higher initial total iron load. Moreover, in all three groups at comparable levels of excellent/good compliance there were no significant differences in the basal mean serum ferritin levels in the 12 months before starting the active treatment and the mean serum ferritin levels in the last year of the active treatment. There was no significant increase in the mean serum ferritin levels in the deferasirox group as stated by the authors. However, we do not intend to draw attention to this. In fact, basal mean serum ferritin levels in the 12 months before starting the active treatment could also refer to many years before (see the active treatment duration) and the mean serum ferritin levels in the last year of the active treatment do not reflect the entire follow-up time between the two magnetic resonance imaging (MRI) scans (15-21 months).

Knowledge of the iron intake in our study population would have improved the interpretation of the data but unfortunately we did not have the information available in the data base. Comparable pre-transfusion hemoglobin level, percentages of splenectomized patients, and standardized and homogeneous transfusion regimens in our study population do not mean comparable iron intakes, although an imbalance in one group is unlikely. Moreover, multicenter randomized clinical trials, in which a significant number of the patients in this observational study had been previously enrolled, suggested blood transfusion requirement was comparable among the different chelation treated groups.[3-5]

However, we perfectly agree with Musallam and Taher that large prospective studies comparing the efficacy of deferiprone and deferasirox in removing and preventing cardiac siderosis are needed. All retrospective data should be developed first and only after that should prospective data be collected. We have recently presented our prospective data to the 2010 ASH Annual Meeting in

Table 1. Comparison between the deferiprone and the deferasirox subgroups.

	Deferiprone group (N=30)		Deferasirox group (N=24)		P	Difference	
	mean±SD	95% CI	mean±SD	95% CI		mean	95% CI
Age (years)	31±8		26±7		0.001		
Age at start of chelation (years)	8±10		5±5		ns		
Active treatment duration	2.7±1.2	2.3-3.2	2.2±1.4	1.7-2.8	ns	0.5	-0.2-1.2
Baseline mean serum ferritin (ng/mL)	1755±2277	872-2638	2491±2072	1460-3521	ns	-736	-2075-604
Global heart T2* (ms)	34.1±12.3	29.5-38.8	21.2±12.1	16.1-26.3	0.001	12.9	6.2-19.7
Liver T2* (ms)	6.8±6.9	4.2-9.4	5.2±5.0	3.1-7.3	ns	1.6	-1.7-5.0
Left ventricular EF (%)	64.0±6.3	61.6-66.4	59.1±7.1	55.9-62.2	0.012	4.9	1.1-8.7
Mean serum ferritin (ng/mL)	1669±1849	952-2386	2361±2010	1446-3276	ns	-692	-1806-423
Pts with global heart T2*<20 ms (%)	16.7		62.5		0.001		

ns: not significant; EF: ejection fraction.

which the changes in cardiac T2* expressed as mean difference were measured in a large cohort of thalassemia patients who had received one chelator alone between the baseline magnetic resonance imaging and MRI follow-up study at 18 ± 3 months.[6] These preliminary data confirm deferiprone monotherapy to be more effective than deferasirox in improving myocardial siderosis and a comparable efficacy between deferasirox and desferrioxamine.

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References

1. Musallam M, Taher AL. Deferiprone or deferasirox for cardiac siderosis in beta-thalassemia major. Haematologica. 2010;96(2):e5-e6.
2. Aessopos A, Fragodimitri C, Karabatsos F, Hatziliami A, Yousef J, Giakoumis A, et al. Cardiac magnetic resonance imaging R2* assessments and analysis of historical parameters in patients with transfusion-dependent thalassemia. Haematologica. 2007;92(1):131-2.
3. Maggio A, D'Amico G, Morabito A, Capra M, Ciaccio C, Cianciulli P, et al. Deferiprone versus deferoxamine in patients with thalassemia major: a randomised clinical trial. Blood Cells Molecul and Diseas. 2002;28(2):196-208.
4. Galia M, Midiri M, Bartolotta V, Morabito A, Rizzo M, Mangiagli A, et al. Potential myocardial iron content evaluation by magnetic resonance imaging in thalassemia major patients treated with Deferoxamine or Deferiprone during a randomized multicenter prospective clinical study. Hemoglobin. 2003;27(2):63-76.
5. Maggio A, Vitrano A, Capra M, Cuccia L, Gagliardotto F, Filosa A, et al Long-term sequential deferiprone-deferoxamine versus deferiprone alone for thalassaemia major patients: a randomised clinical trial. Brit J Haematol. 2009;145(2):245-54.
6. Pepe A, Rossi G, Meloni A, Dell'Amico C, Spasiano A, Capra M, et al. A T2* MRI Prospective Survey on Heart and Liver Iron in Thalassemia Major patients treated with Deferasirox versus Deferiprone and Desferrioxamine in monotheraphy. ASH Annual Meeting Abstracts. 2010, 2010;116(21):4267.