Supplementary Materials: Evaluation of Pharmacokinetics and Pharmacodynamics of Deferasirox in Pediatric Patients

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Table S1. Predicted and measured C_{trough} for in the present patient population and statistical analysis showing significant differences among groups with and without hepatic/renal adverse events

Group	A	B	C	D	Pooled Total
observations (N)	18	18	36	36	108
sum (Σx_i)	626.51	539.89	149.94	135.31	1,451.65
mean (x)	34.81	29.99	4.17	3.76	13.44
sum of squares (Σx^2_i)	32,252.15	24,563.57	1,293.46	907.17	59,016.35
sample variance (S^2)	614.46	492.36	19.11	11.39	369.20
sample standard deviation (S)	24.79	22.19	4.37	3.38	19.22
standard deviation of mean (SEx)	5.84	5.23	0.73	0.56	1.85

Table S2. Final statistical analysis of predicted and measured C_{trough} in the present patient population in relation to hepatic/renal adverse events

Source	sum of squares SS	degrees of freedom (vv)	mean square (MS)	F statistic	p-value
Group	19,620.99	3	6,540.33	34.21	1.78e-15
Error	19,883.54	104	191.19		
Total	39,504.53	107			

Table S3. Results of comparisons between groups in relation to hepatic/renal adverse events. The analyses have been performed by Bonferroni and Holm tests. Results are expressed as follows: [a], Bonferroni and Holm T-statistic; [b], Bonferroni p-value; [c], Holm p-value; [d]; Bonferroni and Holm interference

Groups	B	C	D
A	1.04[a] / 1.79[b] 0.60[c] Not significant[d]	7.68 / 5.57e-11 4.65e-11 p<0.01	7.78 / 3.36e-11 3.36e-11 p<0.01
B		6.47 / 1.95e-08 9.77e-09 p<0.01	6.58 / 1.21e-08 8.05e-09 p<0.01
C			0.13 / 5.41 0.90 Not significant

Table S4. Post-hoc Tukey test in relation to hepatic/renal adverse events.

Groups pair	Tukey HSD		
	Q statistic	p-value	Inferfence
A vs B	1.48	0.70	Not significant
A vs C	10.86	0.001	** p<0.01
A vs D	11.00	0.001	** p<0.01
B vs C	9.15	0.001	** p<0.01
B vs D	9.30	0.001	** p<0.01
C vs D	0.18	0.90	Not significant

Note: **, statistically significant results

Table S5. Post-hoc Scheffé test in relation to hepatic/renal adverse events.

Groups pair	Scheffé		
	T-statistic	p-value	Inferfence
A vs B	1.04	0.78	Not significant
A vs C	7.68	3.63e-10	** p<0.01
A vs D	7.78	2.23e-10	** p<0.01
B vs C	6.47	1.03e-07	** p<0.01
B vs D	6.57	6.48e-08	** p<0.01
C vs D	0.13	1.00	Not significant

Note: **, statistically significant results

Table S6. Post-hoc Bonferroni and Holm tests in relation to hepatic/renal adverse events.

	Bonferroni and Holm	Bonferroni		Holm	
Groups pair	T-statistic	*p*-value	Inferfence	*p*-value	Inferfence
A vs B	1.04	1.79	insignificant	0.6294870	insignificant
A vs C	7.68	5.57e-11	** p<0.01	4.65e-11	** p<0.01
A vs D	7.78	3.36e-11	** p<0.01	3.36e-11	** p<0.01
B vs C	6.47	1.95e-08	** p<0.01	9.77e-09	** p<0.01
B vs D	6.57	1.21e-08	** p<0.01	8.05e-09	** p<0.01
C vs D	0.13	5.41	Not significant	0.90	Not significant

Note: **, statistically significant results

Table S7. Predicted and measured C_{trough} in the present patient population and statistical analysis showing significant differences among groups with and without hematological adverse events

Group	A	B	C	D	Pooled Total
observations (N)	16	16	38	38	108
sum (Σx_i)	559.36	487.13	217.10	188.07	1,451.66
mean (x)	34.96	30.45	5.71	4.95	13.44
sum of squares (Σx^2_i)	30,873.09	23,517.33	2,672.67	1,953.39	59,016.48
sample variance (S^2)	754.52	579.09	38.71	27.64	369.20
sample standard deviation (S)	27.47	24.06	6.22	5.26	19.22
standard deviation of mean (SEx)	6.87	6.02	1.01	0.85	1.85

Table S8. Final statistical analysis of predicted and measured C_{trough} in the present patient population in relation to hematological adverse events

Source	sum of squares SS	degrees of freedom (νν)	mean square (MS)	F statistic	*p*-value
Group	17,045.14	3	5,681.72	26.31	9.62e-13
Error	22,459.16	104	215.95		
Total	39,504.29	107			

Table S9. Results of comparisons between groups in relation to hematological adverse events
. The analyses have been performed by Bonferroni and Holm tests. Results are expressed as follows: [a], Bonferroni and Holm T-statistic; [b], Bonferroni p-value; [c], Holm p-value; [d]; Bonferroni and Holm interference

Groups	B	C	D
A	0.87[a] / 2.32[b] 0.77[c] Not significant[d]	6.68 / 7.31e-09 6.09e-09 p<0.01	6.85 / 3.17e-09 3.17e-09 p<0.01
B		5.65 / 8.56e-07 4.28e-07 p<0.01	5.82 / 3.92e-07 2.61e-07 p<0.01
C			0.23/ 4.93 0.82 Not significant

Table S10. Post-hoc Tukey test in relation to hematological adverse events.

Groups pair	Tukey HSD		
	Q statistic	p-value	Inferfence
A vs B	1.23	0.80	Not significant
A vs C	9.44	0.001	** p<0.01
A vs D	9.69	0.001	** p<0.01
B vs C	7.99	0.001	** p<0.01
B vs D	8.23	0.001	** p<0.01
C vs D	0.32	0.90	Not significant

Note: **, statistically significant results

Table S11. Post-hoc Scheffé test in relation to hematological adverse events.

	Scheffé		
Groups pair	T-statistic	p-value	Inferfence
A vs B	0.87	0.86	Not significant
A vs C	6.68	4.01e-08	** p<0.01
A vs D	6.85	1.80e-08	** p<0.01
B vs C	5.65	3.73e-06	** p<0.01
B vs D	5.82	1.78e-06	** p<0.01
C vs D	0.23	1.00	Not significant

Note: **, statistically significant results

Table S12. Post-hoc Bonferroni and Holm tests in relation to hematological adverse events.

Groups pair	Bonferroni and Holm T-statistic	Bonferroni		Holm	
		p-value	Inferfence	*p*-value	Inferfence
A vs B	0.87	2.32	insignificant	0.77	insignificant
A vs C	6.68	7.31e-09	** p<0.01	6.09e-09	** p<0.01
A vs D	6.83	3.17e-09	** p<0.01	3.17e-09	** p<0.01
B vs C	5.65	8.56e-07	** p<0.01	4.28e-07	** p<0.01
B vs D	5.82	3.92e-07	** p<0.01	2.61e-07	** p<0.01
C vs D	0.23	5.41	Not significant	0.82	Not significant

Note: **, statistically significant results
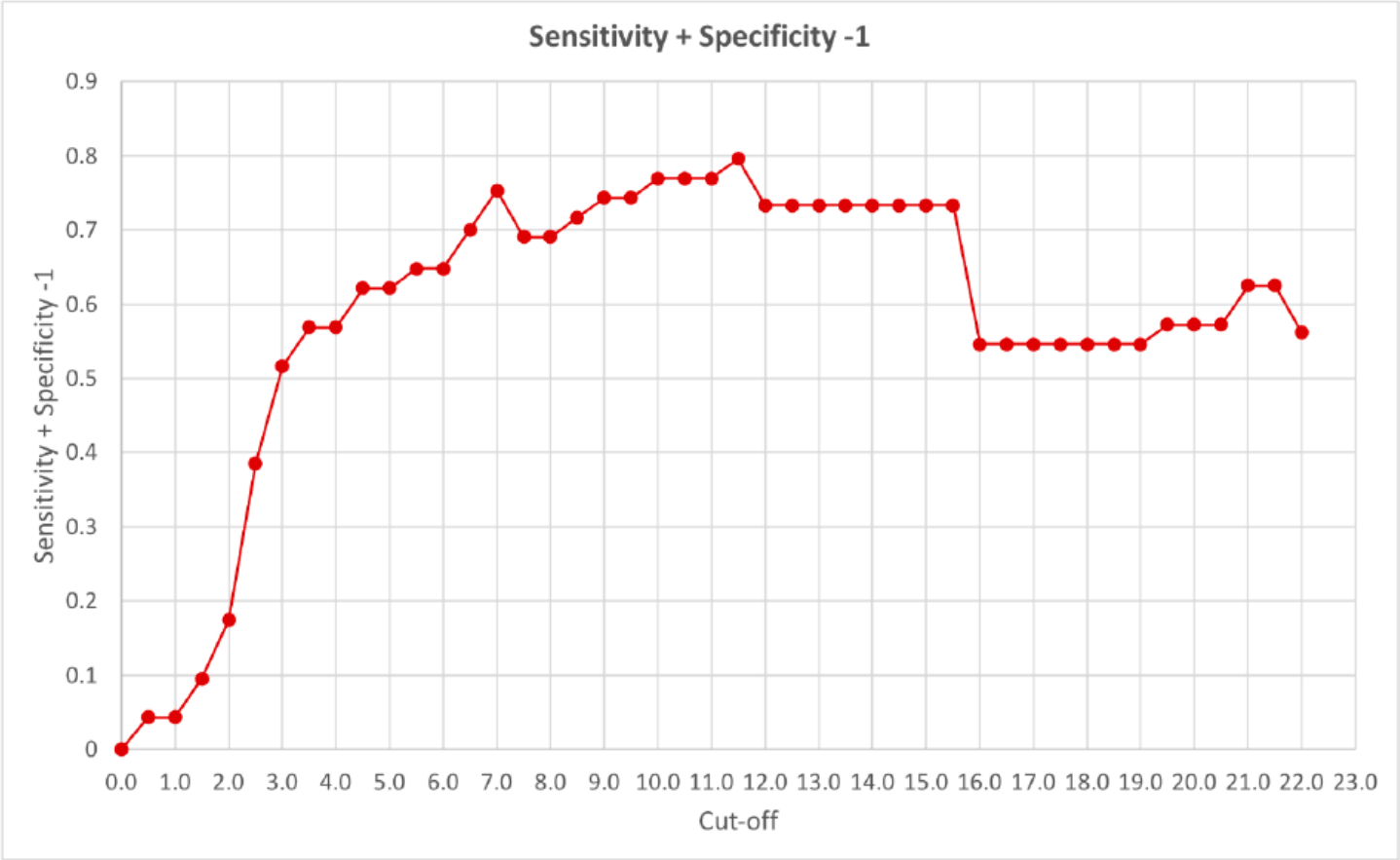
Figure S1

Figure S1. Graph plotting the Youden test results of Ctrough threshold for hematological toxicities.
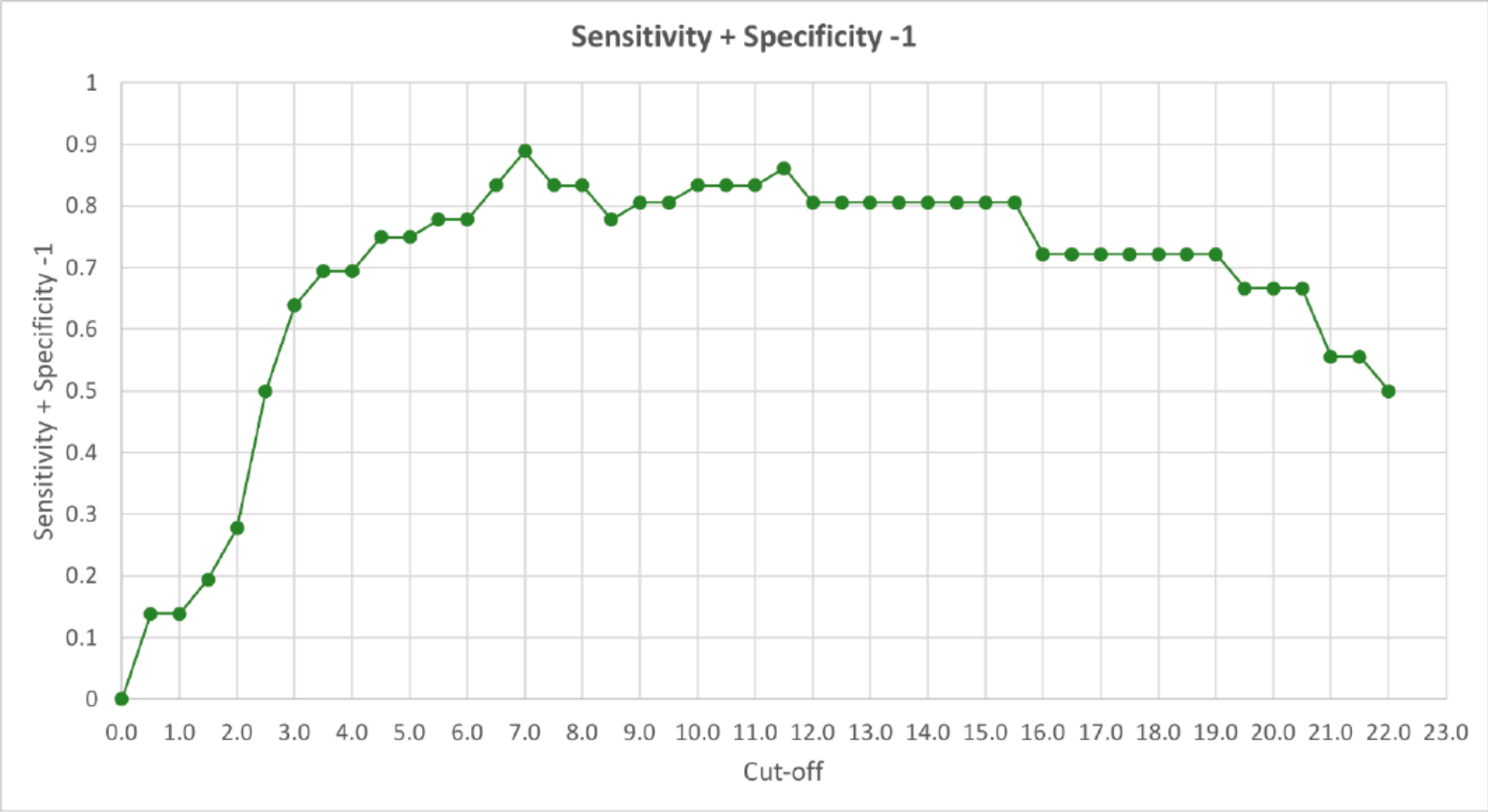
Figure S2

Figure S2. Graph plotting the Youden test results of C_{trough} threshold for hepatic/renal toxicities.