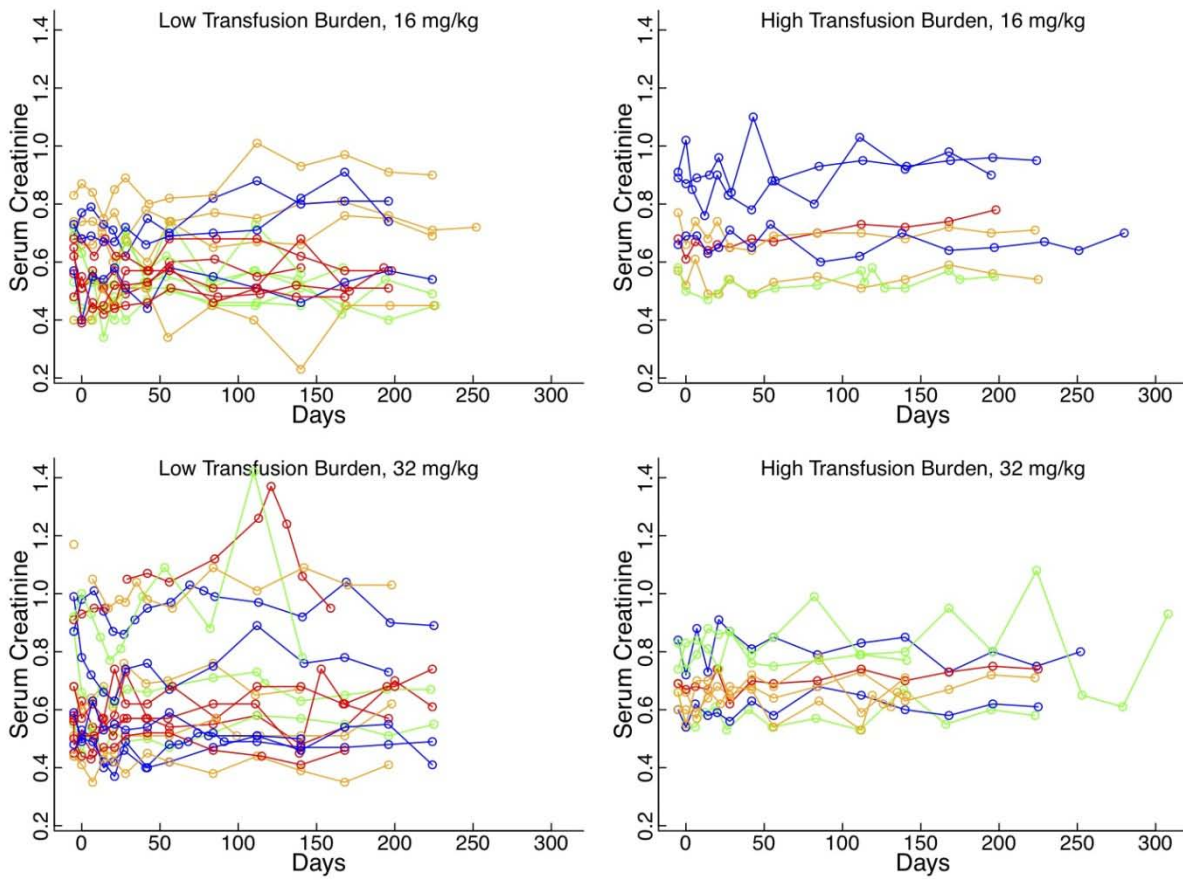


Supplemental Information

Supplement Figure 1: Elaboration on Data in Figure 1.

The doses represented are the FBS0701 salt form. i.e. 16 mg/kg/d fo salt form is equivalent to 14.5 mg/kg/d, and 32 mg/kg/day equivalent to 29 mg/kg/day dose of free drug.

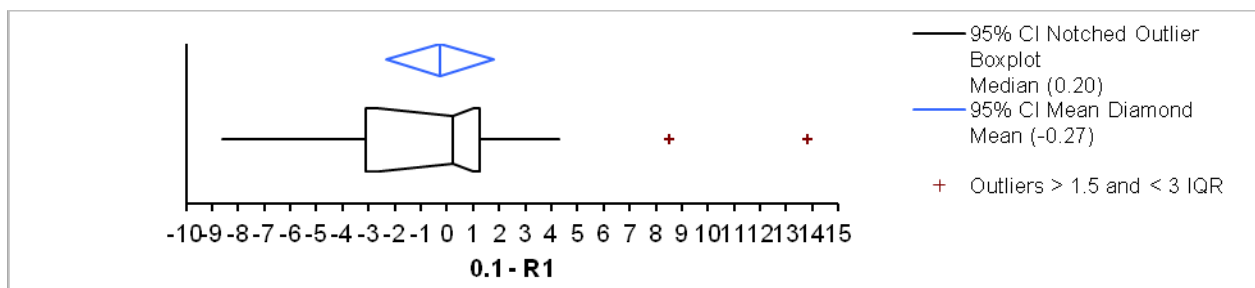
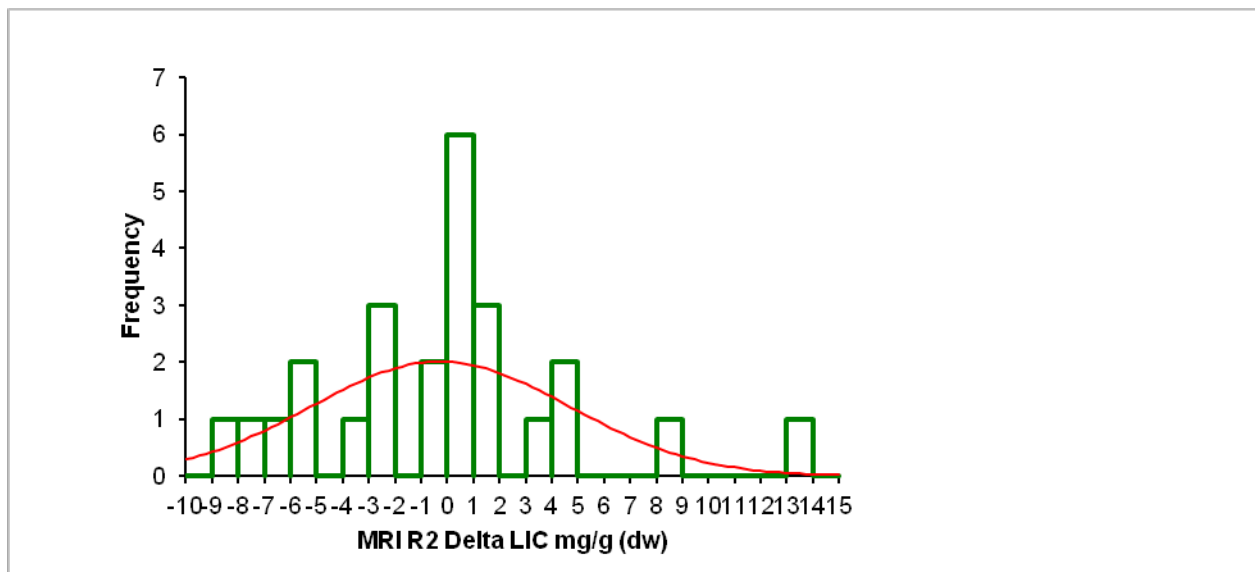


Screening Value Displayed at -5 Days

Mon Oct 3 08:31:46 2011

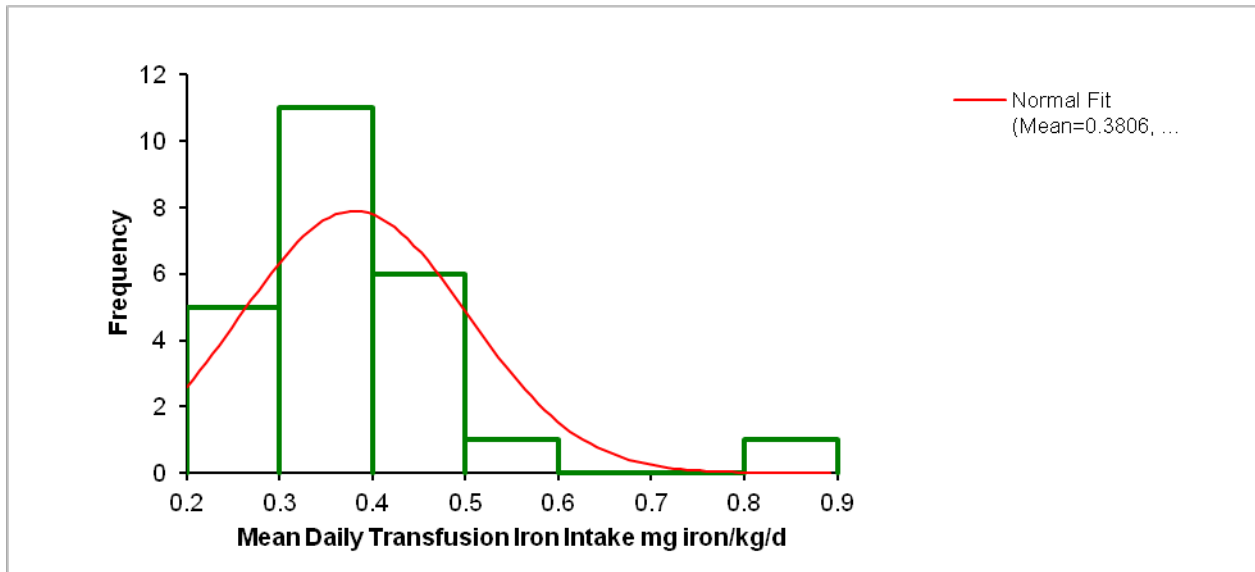
Supplemental figure 2. Statistical Analysis of the Data Represented in Figure 3.

The data regarding the change in LIC at 24 weeks in response to an FBS0701 dose of 29 mg/kg/d can be described by a normal distribution with a mean of -0.3 mg/g liver (dw) (95% CI -2.31 to 1.78), a standard deviation (SD) of 4.95 (95% CI 3.86 to 6.89) and a median of 0.2 (95% CI -2.6 to 1). The Interquartile Range (IQR) is 4.27, thus, two patients with the greatest increase in LIC would be regarded as outliers (outlier >1.5 IQR). If these two patients were not included in the analysis of the 29 mg/kg/d dose group, the mean change in LIC would be -1.26 mg/g liver (dw).

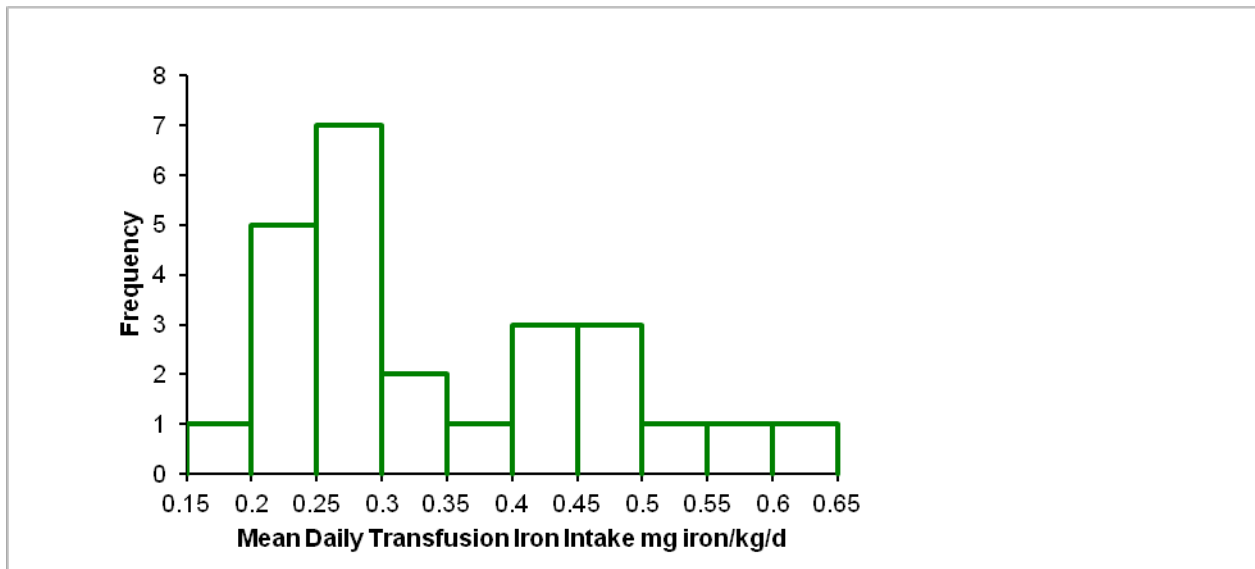


Supplemental figure 3. Distribution of Transfusion Iron Intake

Supplemental Figure 3a: Mean Daily Transfusion Iron Intake (TII) in the Low Dose Group



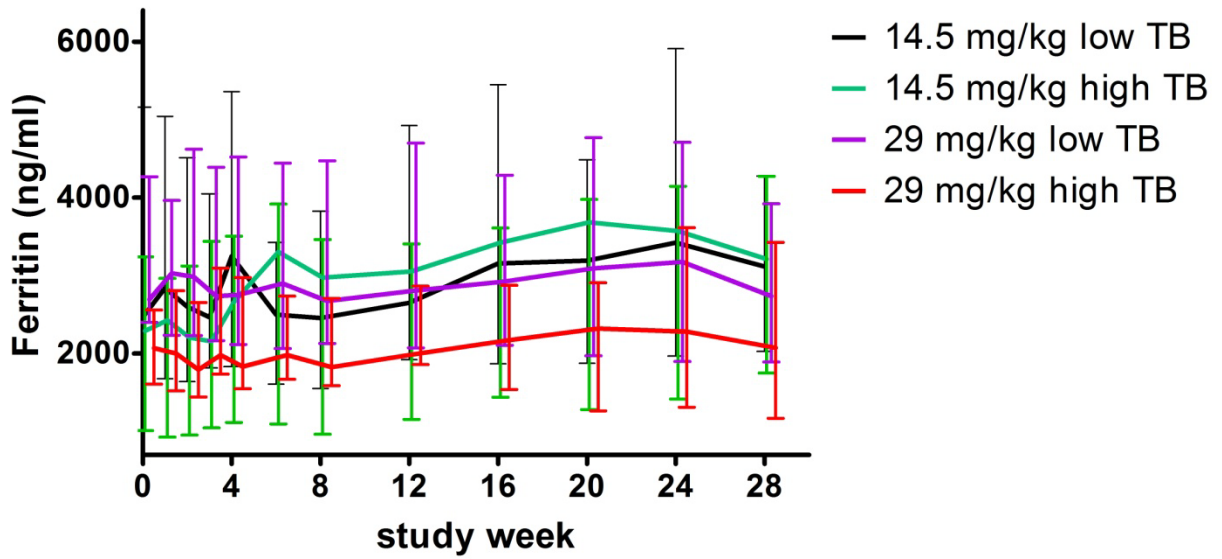
Supplemental figure 3b. Mean Daily Transfusion Iron Intake (TII) in High Dose Group



Supplemental Figure 4: Ferritin values during the study time frame, by dose and transfusional iron burden cohort.

Median ferritin values are show. Error bars represent the inter-quartile range.

Ferritin by dose/transfusion burden cohort



Supplemental Table 1. Treatment-related adverse events in the FBS0701 phase 2 trial

Pt ID	Adverse Event by System Organ Class and Preferred Term	Severity	Causality	Outcome	FBS0701 Treatment Arm (mg/kg/d)
Infections and infestations					
0713	Upper Respiratory Tract Infection	Moderate	Possibly Related	Resolved	32
Gastrointestinal disorders					
0204	Abdominal Distention	Mild	Possibly Related	Resolved	16
0304	Flatulence	Mild	Possibly Related	Not Resolved	16
0314	Flatulence	Mild	Possibly Related	Resolved	16
0401	Flatulence	Mild	Possibly Related	Resolved	16
0306	Flatulence	Mild	Possibly Related	Resolved	16
0101	Nausea	Mild	Possibly Related	Resolved	32
0301	Clinical Colitis	Mild	Possibly Related	Resolved	32
0402	Flatulence	Mild	Possibly Related	Resolved	32
0402	Constipation	Mild	Possibly Related	Resolved	32
0402	Abdominal Pain	Mild	Possibly Related	Resolved	32
0402	Abdominal Pain	Mild	Possibly Related	Resolved	32
0503	Dyspepsia	Mild	Probably Related	Not Resolved	32
0706	Diarrhea	Mild	Possibly Related	Resolved	32
1012	Abdominal Pain Upper	Mild	Probably Related	Resolved	32
1106	Abdominal Pain	Mild	Possibly Related	Resolved	32
1202	Flatulence	Mild	Possibly Related	Resolved	32
0102	Diarrhea	Mild	Probably Related	Resolved	32
0403	Constipation	Mild	Possibly Related	Resolved	32
Nervous system disorders					
0401	Headache	Mild	Possibly Related	Resolved	16
0405	Headache	Mild	Possibly Related	Resolved	32
1202	Headache	Moderate	Possibly Related	Resolved	32
Investigations					
0304	Transaminases Increased	Moderate	Probably Related	Resolved	16
0305	Transaminases Increased	Moderate	Probably Related	Resolved	16
0404	Transaminases Increased	Mild	Possibly Related	Resolved	16
0101	Urine Color Abnormal	Mild	Probably Related	Not Resolved	32

0402	Transaminases Increased	Mild	Possibly Related	Resolved	32
0405	Transaminases Increased	Mild	Possibly Related	Resolved	32
0506	Creatinine Increased	Moderate	Possibly Related	Resolved	32
0406	Transaminases Increased	Mild	Possibly Related	Resolved	32
0309	Transaminases Increased	Mild	Possibly Related	Resolved	32
0309	Gamma-glutamyltransferase Increased	Mild	Possibly Related	Resolved	32
0315	Gamma-glutamyltransferase Increased	Mild	Possibly Related	Resolving	32
0315	Alanine Aminotransferase Increased	Mild	Possibly Related	Resolving	32
0403	Transaminases Increased	Moderate	Possibly Related	Resolved	32
Eye disorders					
1202	Photophobia	Moderate	Possibly Related	Not Resolved	32
Musculoskeletal and connective tissue disorders					
0401	Arthralgia	Mild	Possibly Related	Resolved	16
0402	Arthralgia	Mild	Possibly Related	Resolved	32
Metabolism and nutrition disorders					
0708	Decreased Appetite	Mild	Possibly Related	Resolved	16
Cardiac disorders					
0101	Palpitations	Mild	Possibly Related	Resolved	32
Skin and subcutaneous tissue disorders					
0309	Sweat Discoloration	Mild	Possibly Related	Resolved	32
Blood and lymphatic system disorders					
0701	Thrombocytopenia	Mild	Possibly Related	Resolved	16
Renal and urinary					
0708	Chromaturia	Mild	Possibly Related	Not Resolved	16
0102	Chromaturia	Mild	Probably Related	Not Resolved	32
0313	Chromaturia	Mild	Probably Related	Resolved	32

(Supplemental Table 1, continued from prior page)

Supplemental Table 2: Pharmacodynamics**Safety Population**

Parameter	Time Point	14.5 mg/kg/d (N=24)	29 mg/kg/d (N=27)	p-value ^[3]
R2 Liver Iron Concentration (mg/g dry tissue) ^[1]	Baseline ^[2]			
	N	24	27	
	Mean (SD)	13.2 (6.64)	13.9 (7.82)	
	Median	11.9	11.4	
	Min, Max	4.3, 24.5	3.9, 30.2	
	Week 12			
	N	24	25	
	Mean (SD)	15.9 (9.45)	13.6 (8.68)	
	Median	11.7	10.7	
	Min, Max	4.8, 34.6	4.6, 34.2	
	Change from Baseline to Week 12			0.0025
	N	24	25	
	Mean (SD)	2.7 (4.05)	-0.2 (2.83)	
	Median	0.9	0.1	
	Min, Max	-4.5, 10.8	-6.9, 4.4	
	Week 24			
	N	24	25	
	Mean (SD)	16.3 (10.57)	13.2 (8.51)	
	Median	11.5	9.3	
	Min, Max	4.6, 37.4	3.4, 30.8	
	Change from Baseline to Week 24			0.0287
	N	24	25	
	Mean (SD)	3.1 (5.55)	-0.3 (4.95)	
	Median	1.1	0.2	
	Min, Max	-4.9, 19.0	-8.6, 13.8	

Parameter	Time Point	14.5 mg/kg/d (N=24)	29 mg/kg/d (N=27)	p-value ^[3]
LIC normalized for initial LIC (%) ^[4]	Week 12			0.0162
	N	24	25	
	Mean (SD)	18.1 (27.30)	-0.6 (24.80)	
	Median	13.0	1.4	
	Min, Max	-22.6, 101.8	-46.0, 67.2	
	Week 24			0.0336
	N	24	25	
	Mean (SD)	20.1 (33.86)	-0.7 (34.31)	
	Median	11.3	2.6	
	Min, Max	-41.9, 103.3	-50.7, 95.8	

^[1] Per FerriScan® MRI.

^[2] Baseline MRI was to be performed from Days -14 to -7; the Relative Day column in the listings captures the actual number of days prior to dosing that the MRI was conducted.

^[3] P-value is from Analysis of Covariance model with effects for treatment group, baseline value and historical transfusion burden

for R2 Liver Iron Concentration. P-value is from Analysis of Covariance model with effect for treatment group and historical transfusion burden for LIC normalized for initial LIC and LIC normalized for iron intake by blood transfusion

^[4] LIC normalized for initial LIC is the percentage change from baseline in LIC.