Supplementary Table 1 List of Independent Ethics Committees

Country/Site	**Name of Ethics Committee**	**Ethics Committees Approval Dates**				
		Protocol Version 1.0, 18 Jun 2009	**Protocol Amendment 1, 18 Sep 2009**	**Protocol Amendment 2, 12 Dec 2009**	**Protocol Amendment 3, 7 Jul 2010**	**Protocol Amendment 4, 07 Sep 2010**
Austria						
4301, 4302, 4303, 4304	Ethi-Kommission der Medizinischen Universitat Wien Norschkegasse 8b/6 - A- 1090 Vienna	Not applicable	Not applicable	Not applicable	Not applicable	28 Feb 2011
United Kingdom						
4401	NRES Committee East Midlands Northampton The Old Chapel Royal Standard Place Nottingham NG1 6FS	Not applicable	Not applicable	31 Dec 2009	Not applicable	22 Feb 2011
Denmark						
4501, 4502,	De	17 Aug 2009	17 Oct 2009	9 Feb 2010	23 Jul 2010	26 Oct 2010

Country/Site	Name of Ethics Committee	Ethics Committees Approval Dates				
		Protocol Version 1.0, 18 Jun 2009	**Protocol Amendment 1, 18 Sep 2009**	**Protocol Amendment 2, 12 Dec 2009**	**Protocol Amendment 3, 7 Jul 2010**	**Protocol Amendment 4, 07 Sep 2010**
4503, 4504, 4505	Videnskabsetiske Komitéer for Region Hovedstaden Kongens Vænge 2 DK-3400 Hillerød					
Hungary						
3601, 3602, 3603, 3604, 3605	Egészségügyi Tudományos Tanács Klinikai Farmakológiai Etikai Bizottsága (ETT-KFEB) Medical Research Council Ethics Committee for Clinical Pharmacology Arany János street 6-8 H-1051 Budapest	Not applicable	Not applicable	Not applicable	Not applicable	11 Oct 2011

Country/Site	Name of Ethics Committee	Ethics Committees Approval Dates				
		Protocol Version 1.0, 18 Jun 2009	**Protocol Amendment 1, 18 Sep 2009**	**Protocol Amendment 2, 12 Dec 2009**	**Protocol Amendment 3, 7 Jul 2010**	**Protocol Amendment 4, 07 Sep 2010**
India						
9101	Institutional Ethics Committee All India Institute of Medical Sciences New Delhi-110029 Delhi	07 Aug 2009	25 Feb 2010	24 Jan 2011	Not applicable	Not applicable
9102	Ethics Committee Asian Institute of Gastroenterology Somajiguda Hyderabad-500082 Andhra Pradesh		06 Mar 2010	06 Mar 2010	Not applicable	Not applicable
9103	Institutional Ethics Committee Bombay Hospital and Medical Research Centre 12 Marine Lines Mumbai-400020 Maharashtra	06 Jan 2010	06 Jan 2010	04 Nov 2010	Not applicable	Not applicable

Country/Site	Name of Ethics Committee	Ethics Committees Approval Dates				
		Protocol Version 1.0, 18 Jun 2009	**Protocol Amendment 1, 18 Sep 2009**	**Protocol Amendment 2, 12 Dec 2009**	**Protocol Amendment 3, 7 Jul 2010**	**Protocol Amendment 4, 07 Sep 2010**
9104	Institutional Ethics Committee Institute of Liver and Biliary Sciences (ILBS) Vasant Kunj New Delhi-110070 Delhi	19 Jan 2010	19 Jan 2010		Not applicable	Not applicable
9105	Institutional Ethics Committee Maulana Azad Medical College New Delhi-110002 Delhi		05 Dec 2009	02 Jun 2010	Not applicable	Not applicable
9106	Osmania Medical Ethics Committee Afzalgunj, Hyderabad-500012 Andhra Pradesh		18 Nov 2009	03 Jul 2010		
9107	Institutional Review Board Pushpawati Singhania	15 Oct 2009			Not applicable	Not applicable

Country/Site	Name of Ethics Committee	Ethics Committees Approval Dates				
		Protocol Version 1.0, 18 Jun 2009	**Protocol Amendment 1, 18 Sep 2009**	**Protocol Amendment 2, 12 Dec 2009**	**Protocol Amendment 3, 7 Jul 2010**	**Protocol Amendment 4, 07 Sep 2010**
	Research Institute Sheikh Sarai New Delhi-110017 Delhi					
9108	Institutional Ethics Committee Poona Medical Research Foundation Ruby Hall Clinic, 40 Sasoon Road Pune- 411001 Maharashtra	16 Sep 2009	14 Nov 2009	26 Apr 2010	Not applicable	Not applicable
9109	Ethics Committee-SMS Medical College Hospital Jawahar Lal Nehru Marg, Jaipur-302004 Rajasthan		15 Dec 2009	10 May 2010	Not applicable	Not applicable
9110	Shatabdi Super Speciality Hospital Ethics Committee		04 Dec 2009	24 May 2010	Not applicable	Not applicable

Country/Site	Name of Ethics Committee	Ethics Committees Approval Dates				
		Protocol Version 1.0, 18 Jun 2009	**Protocol Amendment 1, 18 Sep 2009**	**Protocol Amendment 2, 12 Dec 2009**	**Protocol Amendment 3, 7 Jul 2010**	**Protocol Amendment 4, 07 Sep 2010**
	Shatabdi Hospital, Suyojit City Center, Mumbai Naka, Nasik-422005 Maharashtra					
9111	Sanjeevni Ethics Committee Show Room No. B-2, Tonk Road, Jaipur-302015 Rajasthan			27 Apr 2010	Not applicable	Not applicable
9112	Institutional Ethics Committee M V Hospital and Research Centre Mirza Mandi Chowk Lucknow-226003 Uttar Pradesh			10 May 2010	Not applicable	Not applicable
9113	Independent Ethics Committee Mehta Hospital			26 Apr 2010	Not applicable	Not applicable

Country/Site	Name of Ethics Committee	Ethics Committees Approval Dates				
		Protocol Version 1.0, 18 Jun 2009	**Protocol Amendment 1, 18 Sep 2009**	**Protocol Amendment 2, 12 Dec 2009**	**Protocol Amendment 3, 7 Jul 2010**	**Protocol Amendment 4, 07 Sep 2010**
	Brahmin Mitra Mandal Society, Paldi Ahmedabad-380006 Gujarat					
9114	Institutional Ethics Committee Institute of Digestive and Liver Disease Dispur Hospital Ltd Ganeshguri Guwahati-781006 Assam			30 Apr 2010	Not applicable	Not applicable
9115	Central India Medical Research Ethics Committee Midas Institute of Gastroenterology, Midas Height 07- Central Bazar Road, Ramdaspeth Nagpur-440010 Maharashtra			21 May 2010	Not applicable	Not applicable

Country/Site	Name of Ethics Committee	Ethics Committees Approval Dates				
		Protocol Version 1.0, 18 Jun 2009	**Protocol Amendment 1, 18 Sep 2009**	**Protocol Amendment 2, 12 Dec 2009**	**Protocol Amendment 3, 7 Jul 2010**	**Protocol Amendment 4, 07 Sep 2010**
9116	Institutional Review Board Choithram Hospital and Research Centre Manik Bagh Road Indore-452014 Madhya Pradesh			20 May 2010	Not applicable	Not applicable
9117	Institutional Ethics Committee G B Pant Hospital Jawahar Lal Nehru Marg New Delhi-110002 Delhi			20 May 2010		
9118	CLINICOM (Committee for Evaluation of Protocol for Medical Research) “Bhooma”, No. 17, 17 A Cross Malleshwaram			05 Jun 2010		

Country/Site	Name of Ethics Committee	Ethics Committees Approval Dates				
		Protocol Version 1.0, 18 Jun 2009	**Protocol Amendment 1, 18 Sep 2009**	**Protocol Amendment 2, 12 Dec 2009**	**Protocol Amendment 3, 7 Jul 2010**	**Protocol Amendment 4, 07 Sep 2010**
	West Bangalore-560003 Karnataka					
9119	Institutional Ethics Review Board St. John's Medical College and Hospital Sarjapur Road Bangalore-560034 Karnataka			12 Jul 2010		
9120	Ethics Committee Nagarjuna Hospital Kanuru Vijaywada-520007 Andhra Pradesh			21 Jun 2010		
9121	Medanta-Independent Ethics Committee Sector-38 Gurgaon-122001 Haryana			09 Jul 2010		

Supplementary Table 2 Association of baseline parameters with treatment response (change in Hb ≥2 g/dL) in the IV sub-population (group A), FAS

					Logistic regression (OR (95% CI), p-value)
Parameter	**Level**	**N**	**n**	**(%)**	**Multiple predictor model**
Total dose (mg) (cont.)	<1000 mg	125	64	(51%)	1.25 (0.96;1.62), *p*=0.097
	1000 mg	52	45	(87%)	
	>1000 mg	40	37	(93%)	
Disease duration (cont.)	≤1 year	74	49	(66%)	1.01 (0.94;1.08), *p*=0.859
	1-5 years	65	43	(66%)	
	>5 years	80	55	(69%)	
Weight (cont.)	≤50 kg	71	45	(63%)	0.96 (0.67;1.40), *p*=0.846
	50-60 kg	73	49	(67%)	
	>60 kg	75	53	(71%)	
CRP	Negative	160	109	(68%)	
	Positive	59	38	(64%)	0.36 (0.15;0.85), *p*=0.020
Disease	Crohn's disease	66	42	(64%)	
	Ulcerative colitis	153	105	(69%)	2.29 (0.70;7.45), *p*=0.168

					Logistic regression (OR (95% CI), p-value)
Parameter	**Level**	**N**	**n**	**(%)**	**Multiple predictor model**
Ferritin (cont.)	≤5.5 µg/L	76	69	(91%)	1.00 (0.99;1.00), *p*=0.091
	5.5-13 µg/L	65	42	(65%)	
	>13 µg/L	78	36	(46%)	
Sex	F	139	85	(61%)	
	M	80	62	(78%)	2.10 (0.93;4.71), *p*=0.073
Hemoglobin (cont.)	≤9 g/dL	67	60	(90%)	0.43 (0.28;0.65), *p*<0.001
	9-10.5 g/dL	79	58	(73%)	
	>10.5 g/dL	73	29	(40%)	
Previous IV iron	No	184	120	(65%)	
	Yes	35	27	(77%)	2.47 (0.77;7.89), *p*=0.126
Platelets (cont.)	<300 10E3/µL	78	41	(53%)	1.00 (1.00;1.01), *p*=0.057
	300-400 10E3/µL	59	40	(68%)	
	>400 10E3/µL	82	66	(80%)	
Region	India	132	87	(66%)	

					Logistic regression (OR (95% CI), p-value)
Parameter	**Level**	**N**	**n**	**(%)**	**Multiple predictor model**
	Europe	87	60	(69%)	2.84 (0.74;10.91), *p*=0.128
TSAT	≤4%	80	70	(88%)	0.98 (0.94;1.02), *p*=0.251
	4-7%	59	43	(73%)	
	>7%	80	34	(43%)	

ORs for continuous baseline variables are for an increase of 1 unit unless for weight (10 kg), and total dose (100 mg)
ORs for categorical baseline variables are shown next to the non-reference level
ORs for categorical baseline variables are shown next to the non-reference level
Multiple: All predictors included in model.
CRP: In European, CRP was recorded as a continuous variable. If value ≤ 0.5 mg/dL (ULN), this was regarded as negative

Supplementary Table 3 Association of baseline parameters with treatment response (change in Hb ≥2 g/dL) in the oral sub-population (group B), FAS

					Logistic regression (OR (95% CI), p-value)
Parameter	**Level**	**N**	**n**	**(%)**	**Multiple predictor model**
Disease duration (cont.)	≤1 year	31	21	(68%)	0.93 (0.82;1.06), *p*=0.272
	1-5 years	39	28	(72%)	
	>5 years	38	17	(45%)	
Weight (cont.)	≤50 kg	35	22	(63%)	1.42 (0.83;2.41), *p*=0.200
	50-60 kg	34	22	(65%)	
	>60 kg	39	22	(56%)	
CRP	Negative	77	54	(70%)	
	Positive	31	12	(39%)	0.31 (0.09;1.06), *p*=0.062
Disease	Crohn's disease	37	13	(35%)	
	Ulcerative colitis	71	53	(75%)	6.53 (1.26;33.89), *p*=0.026
Ferritin (cont.)	≤5.5 µg/L	37	28	(76%)	1.01 (0.99;1.03), *p*=0.524
	5.5-13 µg/L	40	28	(70%)	
	>13 µg/L	31	10	(32%)	

					Logistic regression (OR (95% CI), p-value)
Parameter	**Level**	**N**	**n**	**(%)**	**Multiple predictor model**
Sex	F	67	36	(54%)	
	M	41	30	(73%)	1.39 (0.35;5.47), *p*=0.640
Hemoglobin (cont.)	≤9 g/dL	35	30	(86%)	0.55 (0.36;0.84), *p*=0.006
	9-10.5 g/dL	37	23	(62%)	
	>10.5 g/dL	36	13	(36%)	
Previous IV iron	No	89	58	(65%)	
	Yes	19	8	(42%)	0.45 (0.09;2.25), *p*=0.333
Platelets (cont.)	<300 10E3/µL	36	23	(64%)	1.00 (0.99;1.00), *p*=0.077
	300-400 10E3/µL	36	24	(67%)	
	>400 10E3/µL	36	19	(53%)	
Region	India	65	48	(74%)	
	Europe	43	18	(42%)	1.99 (0.26;15.11), *p*=0.507
TSAT	≤4%	48	37	(77%)	0.72 (0.58;0.89), *p*=0.002
	4-7%	31	17	(55%)	

					Logistic regression (OR (95% CI), p-value)
Parameter	**Level**	**N**	**n**	**(%)**	**Multiple predictor model**
	>7%	29	12	(41%)	

ORs for continuous baseline variables are for an increase of 1 unit unless for weight (10 kg), and total dose (100 mg)
ORs for categorical baseline variables are shown next to the non-reference level
ORs for categorical baseline variables are shown next to the non-reference level
Multiple: All predictors included in model. CRP: In European, CRP was recorded as a continuous variable. If value ≤ 0.5 mg/dL (UL N), this was regarded as negative

Supplementary Table 4 Summary of total score of Crohn's disease and ulcerative colitis disease activity assessment

Statistics	**Treatment Group**	
	Group A **(n = 219)**	**Group B** **(n = 108)**
Crohn's disease		
Total Harvey-Bradshaw Index score at screening		
n	66	37
Mean ± SD	2.47 ± 1.66	2.57 ± 1.71
Median (Min.; Max.)	2.00 (0 ; 5)	3.00 (0 ; 5)
Total score at week 8		
N	64	36
Mean ± SD	2.23 ± 2.59	2.58 ± 2.49
Median (Min.; Max.)	1.00 (0 ; 12)	2.00 (0 ; 8)
p^1		0.599
Ulcerative colitis		
Total Mayo score at screening		

Statistics	**Treatment Group**	
	Group A **(n = 219)**	**Group B** **(n = 108)**
N	153	71
Mean ± SD	3.39 ± 1.61	3.41± 1.51
Median (Min.; Max.)	4.00 (0 ; 6)	3.00 (0 ; 6)
Total score at week 8		
N	142	66
Mean ± SD	2.31± 1.57	2.06 ± 1.33
Median (Min.; Max.)	2.00 (0 ; 8)	2.00 (0 ; 6)
p[1]		0.158

[1]Test comparing change in disease activity from screening to week 8 (iron isomaltoside 1000 versus oral iron) in subjects with Crohn's disease/ulcerative colitis (ANCOVA with treatment, strata and country as factors, and screening value as covariate).

Supplementary Table 5 Number of patients with adverse drug reactions by preferred term

	Iron isomaltoside 1000							
	Total		**Infusion (group A1)**		**Bolus (group A2)**		**Oral iron sulphate (group B)**	
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Diarrhoea	3	1	2	2	1	<1	4	4
Flushing	6	3	3	3	3	3		
Hepatic enzyme increased	4	2	3	3	1	<1		
Hypersensitivity/drug hypersensitivity	4	2	1	<1	3	3		
Constipation							2	2
Hypertension	2	<1	2	2				
Hypotension	2	<1	2	2				
Abdominal pain	2	<1			2	2	1	<1
Nausea	2	<1			2	2	1	<1

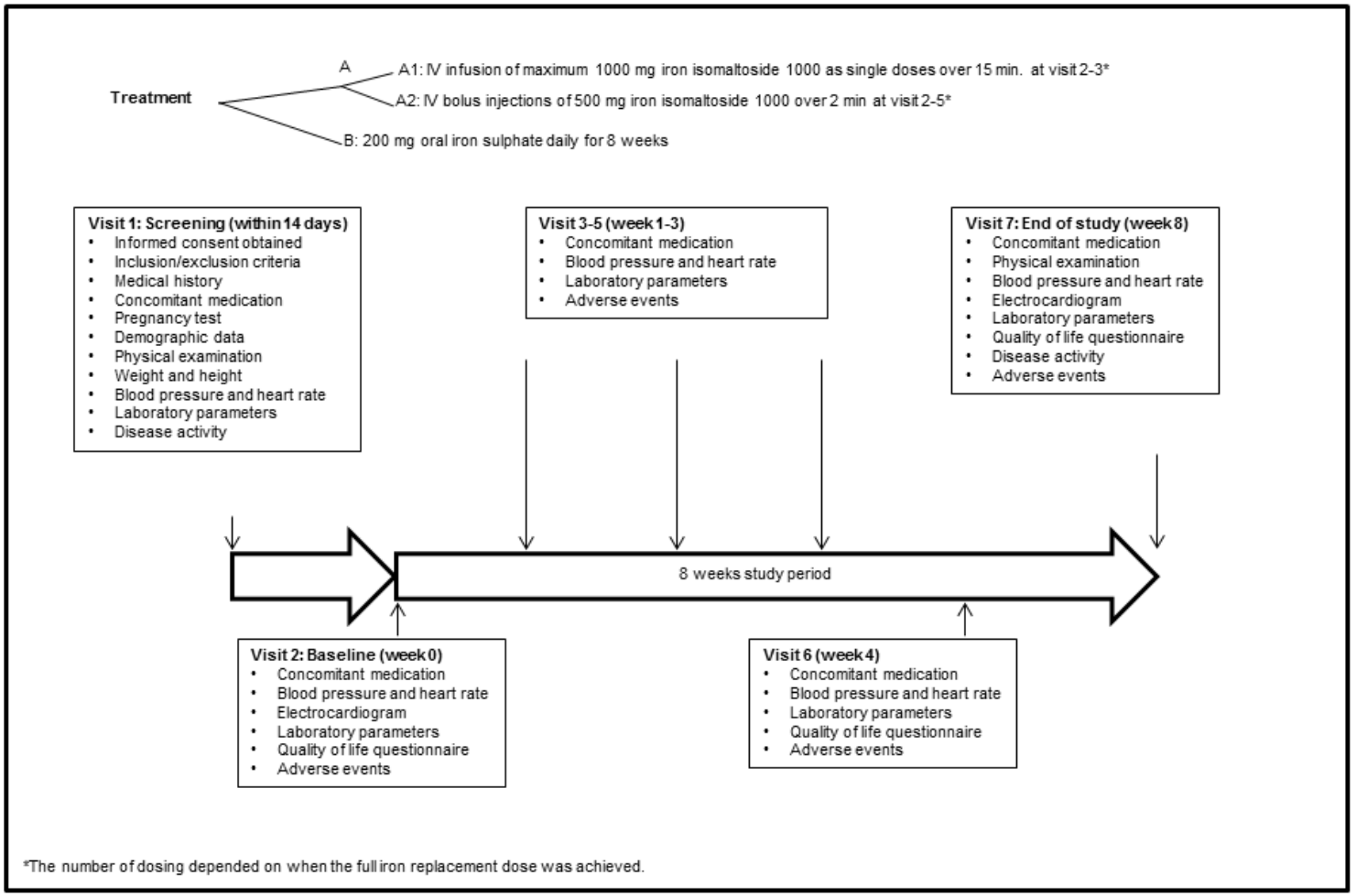
	Iron isomaltoside 1000							
	Total		**Infusion (group A1)**		**Bolus (group A2)**		**Oral iron sulphate (group B)**	
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Abdominal discomfort							1	<1
Acne							1	<1
Crohn's disease							1	<1
Drug intolerance	1	<1	1	<1			1	<1
Dysgeusia	1	<1	1	<1				
Dyspepsia	1	<1	1	<1				
Grand mal convulsion	1	<1	1	<1				
Headache	2	<1	1	<1	1	<1		
Pigmentation disorder	1	<1	1	<1				
Proctalgia	1	<1	1	<1				
Pyrexia	1	<1	1	<1				

	Iron isomaltoside 1000							
	Total		**Infusion (group A1)**		**Bolus (group A2)**		**Oral iron sulphate (group B)**	
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Urticaria	2	<1	1	<1	1	<1		
Abdominal pain upper	1	<1			1	<1		
Alopecia	1	<1			1	<1		
Ankylosing spondylitis	1	<1			1	<1		
Head discomfort	1	<1			1	<1		
Hyperhidrosis	1	<1			1	<1		
Rash	1	<1			1	<1		

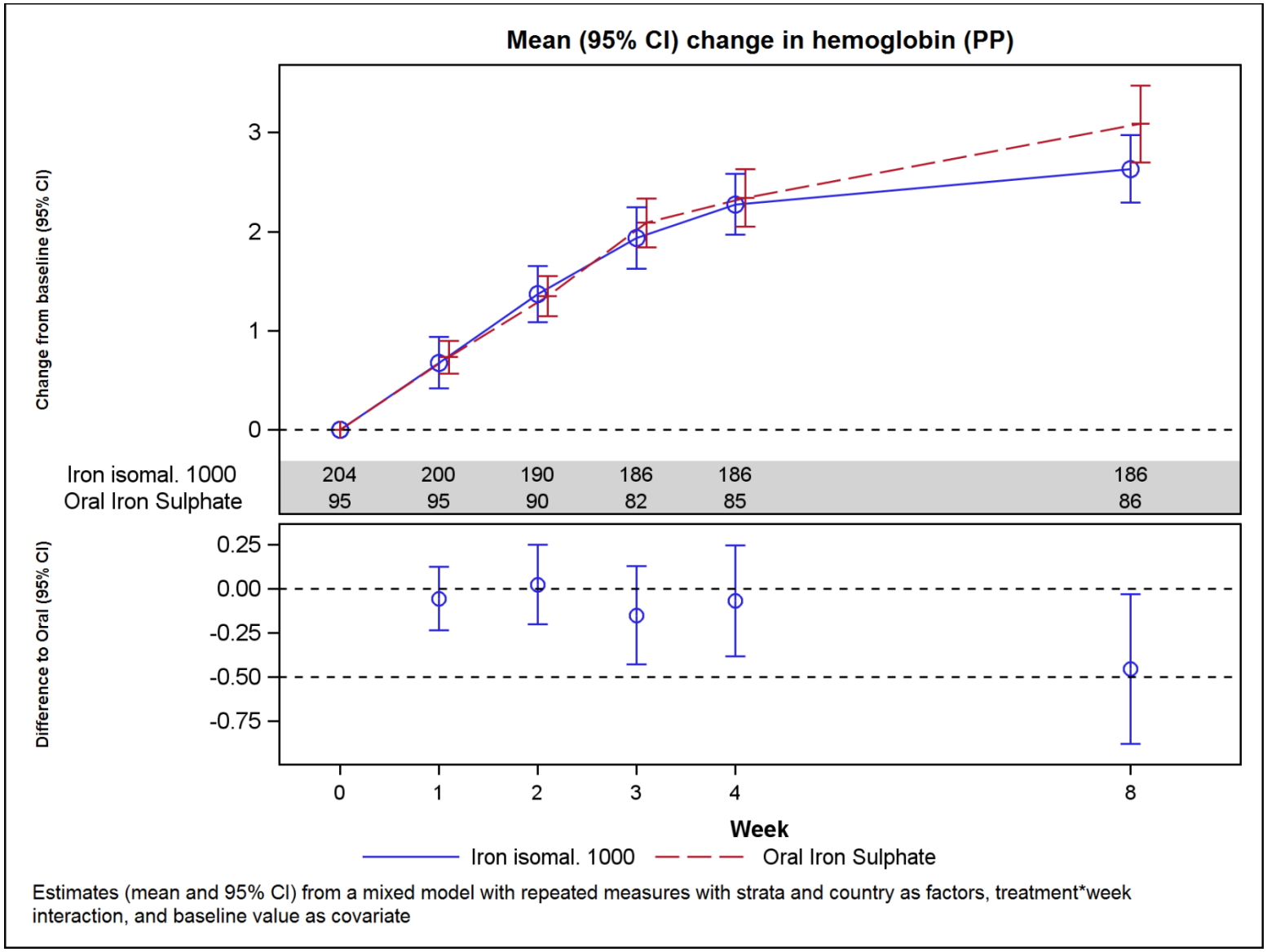
ADR (drug related events): Causality as recorded by investigator to study drug: possible or probable

Note: One patient could have more than one adverse event.

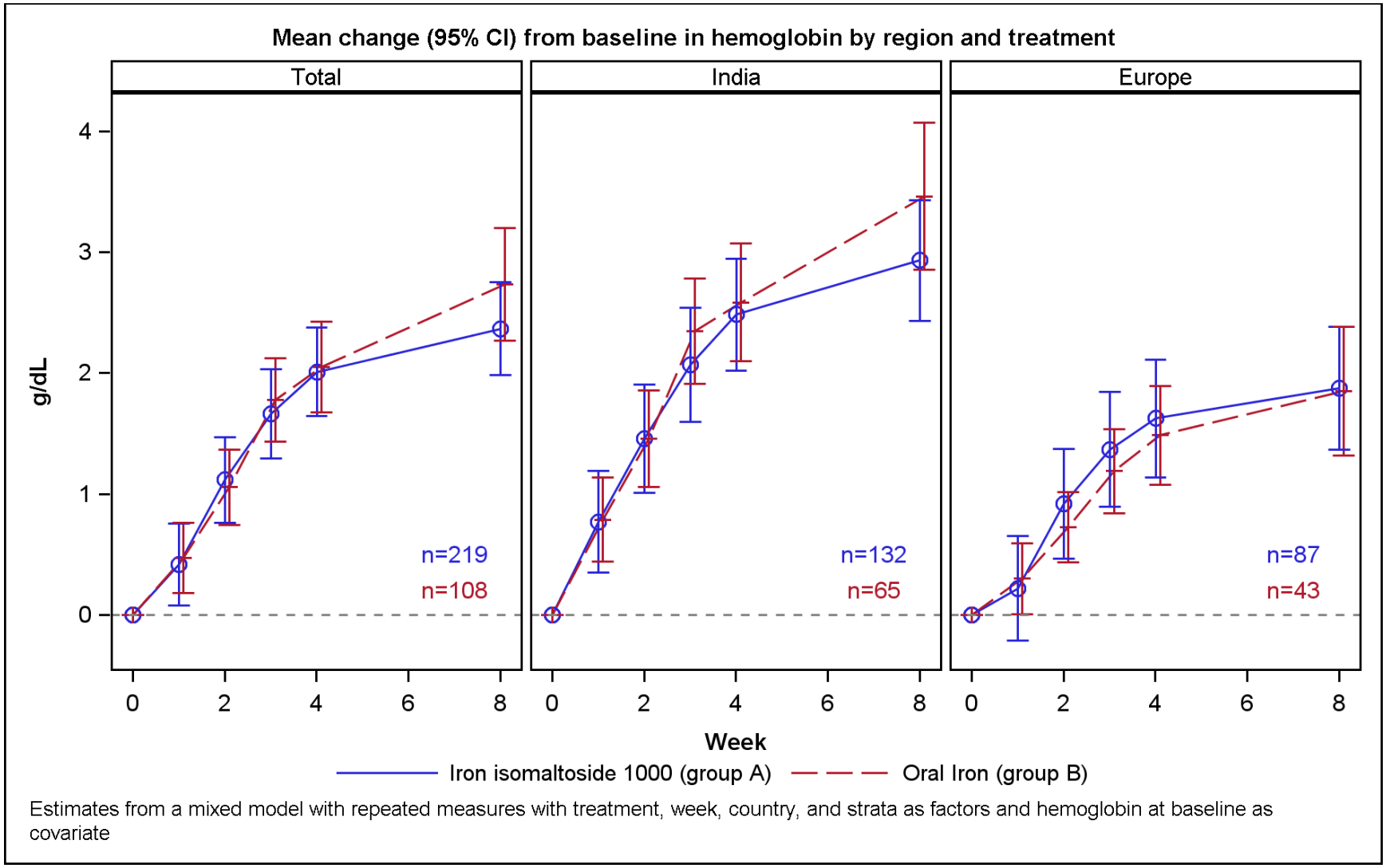
Supplementary Figure 1 Treatment and study assessments



Supplementary Figure 2 Mean (95% CI) change from baseline in hemoglobin by treatment, PP



Supplementary Figure 3 Mean (95% CI) change from baseline in hemoglobin by region and treatment



Supplementary Figure 4 Kaplan-Meier plot of responders (change in Hb ≥2 g/dL) by dose