

A Phase 1b, Double-Blind, Placebo-Controlled Study of DISC-0974, an Anti-Hemojuvelin Antibody, in Patients with Non-Dialysis-Dependent Chronic Kidney Disease and Anemia

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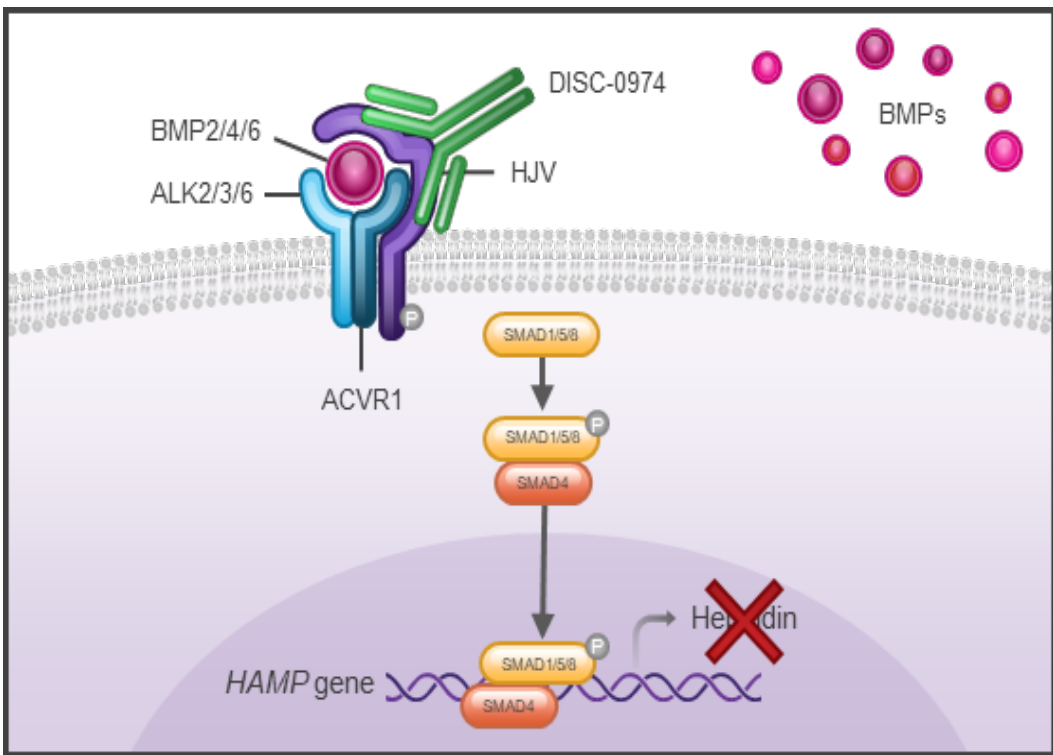


INTRODUCTION

Anemia affects 30 to 40% of the non-dialysis-dependent chronic kidney disease (NDD-CKD) population.^{1,2} Inflammation and impaired renal clearance in CKD increase plasma hepcidin, which regulates absorption of dietary iron and systemic iron distribution. DISC-0974 is an investigational, monoclonal antibody that suppresses hepcidin.

Reducing hepcidin and mobilizing iron is a novel approach to treatment of anemia in CKD.

A healthy-volunteer study demonstrated dose-dependent reductions in serum hepcidin, increases in serum iron, and increasing trends in hemoglobin with a favorable safety profile.³



AIM

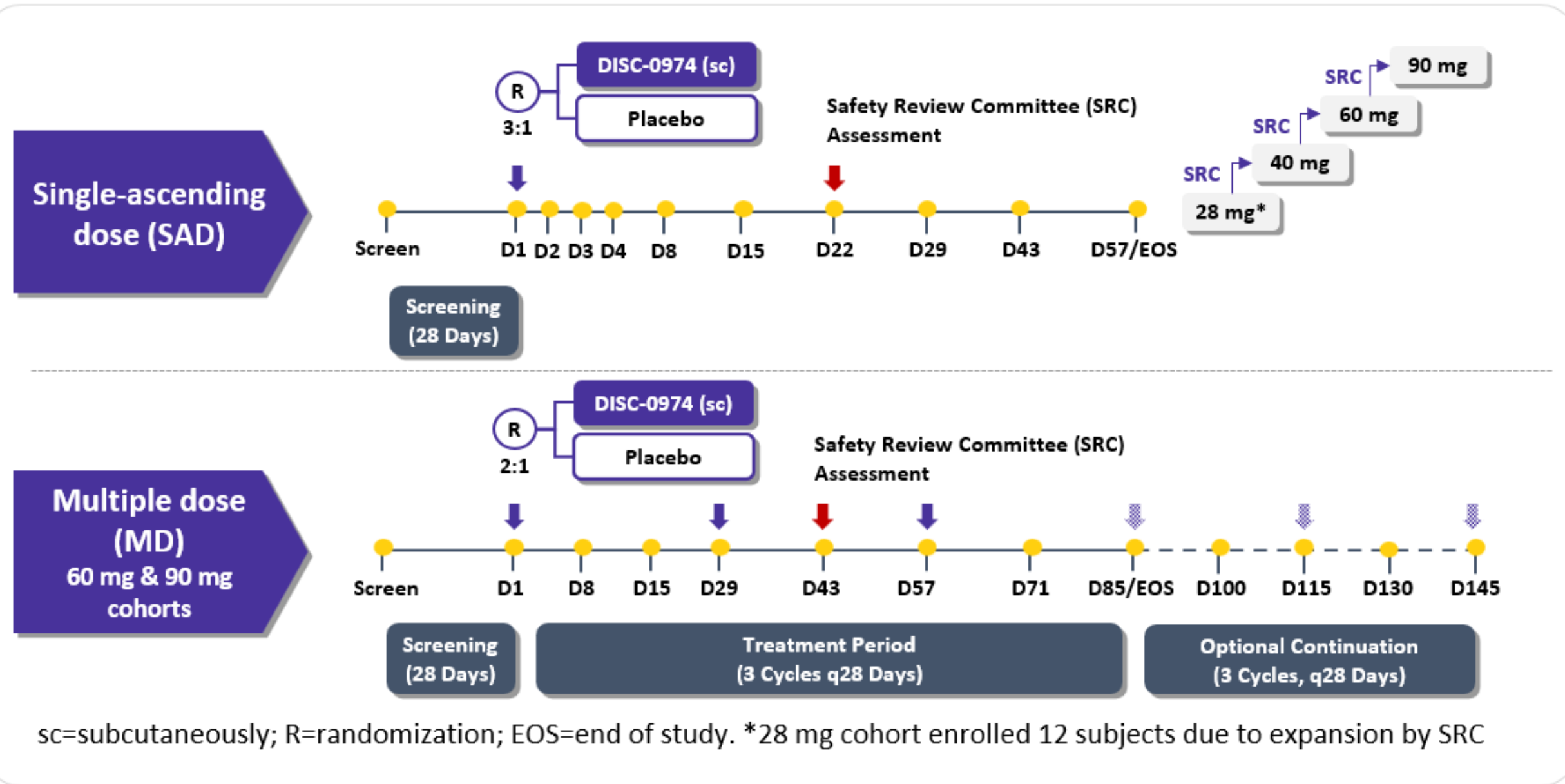
DISC-0974-103 is a Phase 1b, double-blind, placebo-controlled study (NCT05745883) to assess safety, tolerability, PK, PD, and efficacy of single (dose-escalation) and multiple doses of subcutaneous (SC) DISC-0974 in participants with NDD-CKD and anemia.

METHODS

Study Population

- ✓ Stage II-V CKD; adult
- ✓ Not receiving dialysis
- ✓ Hemoglobin (Hgb) <11 g/dL
- ✓ Transferrin saturation ≤35%
- ✓ Serum ferritin ≥50 µg/L
- ✓ Wash-out of anemia-directed therapies (eg, pRBCs, ESAs, or intravenous (IV)/oral iron required)
- ✓ All participants received 300-mg ferrous gluconate (~35 mg elemental iron) 3 times weekly

Study Schema



Study Key Endpoints

- **Primary:** Safety and tolerability of DISC-0974, assessed by TEAEs, vital signs, physical exam, electrocardiogram, and laboratory testing
- **Secondary:** PK/PD markers of iron regulation and hematologic parameters

RESULTS

Data as of October 10th, 2025

Table 1. Baseline and Demographics

Baseline Characteristics	SAD Cohort					MD Cohort		
	28 mg DISC-0974 (n=9)	40 mg DISC-0974 (n=6)	60 mg DISC-0974 (n=6)	90 mg DISC-0974 (n=6)	Pooled Placebo (n=9)	60 mg DISC-0974 (n=7)	90 mg DISC-0974 (n=6)	Pooled Placebo (n=6)
Age, median (range), years	69.0 (55, 78)	61.5 (37, 80)	69.5 (57, 82)	68.0 (50, 87)	73.0 (60, 83)	68 (43, 84)	70 (57, 88)	74 (41, 79)
Male, n (%)	3 (33.3)	3 (50.0)	1 (16.7)	3 (50.0)	3 (33.3)	4 (57.1)	1 (16.7)	3 (50.0)
CKD Stage, n (%)								
Stage 2	0	1 (16.7)	1 (16.7)	0	0	0	0	0
Stage 3	2 (22.2)	0	2 (33.3)	1 (16.7)	4 (44.4)	3 (42.9)	2 (33.3)	3 (50.0)
Stage 4	5 (55.6)	5 (83.3)	3 (50.0)	3 (50.0)	5 (55.6)	2 (28.6)	3 (50.0)	2 (33.3)
Stage 5	2 (22.2)	0	0	2 (33.3)	0	2 (28.6)	1 (16.7)	1 (16.7)
Baseline hepcidin ^a								
Median (range), ng/mL	61.7 (25.7, 172.5)	65.4 (52.6, 108.4)	59.1 (26.9, 156.9)	60.4 (30.3, 161.1)	57.2 (22.3, 122.3)	52.7 (24.9, 127.6)	53.4 (40.5, 185.2)	26.9 (16.6, 92.7)
Mean (SD), ng/mL	77.1 (42.0)	71.0 (19.5)	72.3 (47.0)	74.6 (46.6)	58.1 (29.7)	61.0 (33.5)	77.2 (56.3)	37.0 (28.6)
Baseline hemoglobin ^a , median (range), g/dL	9.8 (8.6, 10.6)	10.6 (10.0, 11.2)	10.8 (10.1, 11.0)	10.3 (9.8, 10.9)	9.7 (9.3, 11.1)	10.0 (9.1, 10.7)	10.6 (8.6, 11.1)	10.5 (8.2, 11.3)
Baseline TSAT, median (range), %	18.0 (12, 24)	22.5 (8, 35)	21.5 (12, 29)	26.5 (14, 34)	20.0 (9, 26)	21.3 (14, 29)	22.8 (14, 33)	17.5 (15, 26)
Baseline serum iron ^a , median (range), ng/mL	55.0 (34, 94)	69.5 (29, 87)	66.5 (35, 83)	74.0 (51, 87)	54.0 (32, 85)	75.0 (42, 79)	55.0 (43, 74)	43.0 (29, 68)
Baseline ferritin ^a , median (range), ng/mL	262 (157, 465)	302 (141, 620)	266 (75, 737)	272 (124, 837)	319 (95, 716)	184 (108.7, 384.5)	344.3 (112.5, 625)	129.8 (78, 191)
Baseline EPO ^a , median (range), mIU/mL	18.9 (7.8, 24.2)	13.6 (2.4, 21.9)	13.8 (6.2, 32.2)	10.3 (3.6, 40.3)	18.1 (10.4, 28.4)	10.8 (4.5, 36.1)	13.7 (4.9, 27.4)	13 (6.5, 34.9)
Baseline EPO ≥15 mIU/mL, n (%)	5 (55.6)	3 (50.0)	3 (50.0)	2 (33.3)	5 (55.6)	2 (28.6)	3 (50.0)	2 (33.3)

CKD=chronic kidney disease, EPO=erythropoietin. ^aBaseline is an average of screening and pre-dose measurements. Normal range: hepcidin: 6.7-85.6 ng/mL (M), 4.4-47.3 ng/mL (F); hemoglobin: 13.2-16.6 g/dL (M), 11.6-15 g/dL (F); TSAT: 15-50%; iron: 59-158 ng/mL (M), 37-145 ng/mL (F); ferritin 17.9-464 ng/mL (M), 11.1-264 (F) ng/mL; EPO 2.6-18.5 mIU/mL.

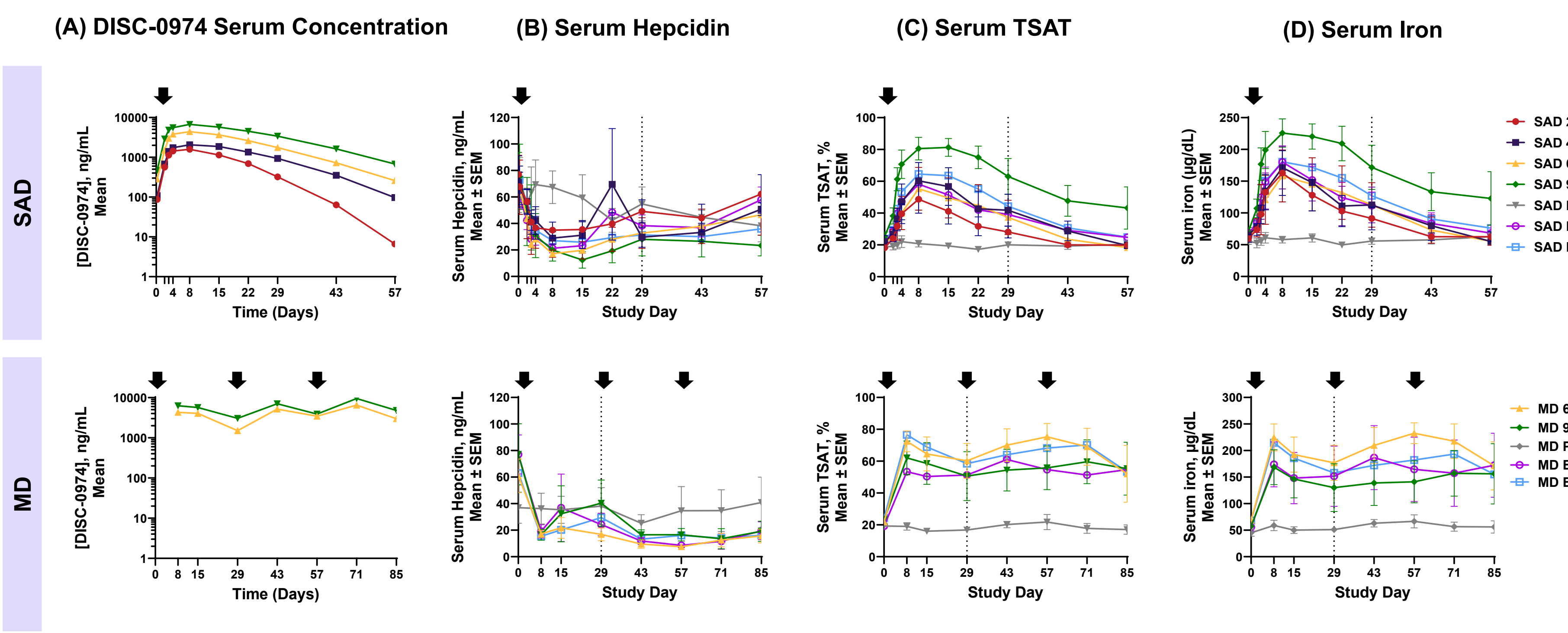
Table 2. Summary of Safety

Preferred Term	SAD Cohort					MD Cohort		
	28 mg DISC-0974 (n=9)	40 mg DISC-0974 (n=6)	60 mg DISC-0974 (n=6)	90 mg DISC-0974 (n=6)	Pooled Placebo (n=9)	60 mg DISC-0974 (n=7)	90 mg DISC-0974 (n=6)	Pooled Placebo (n=6)
Any TEAE, n (%)	3 (33.3)	4 (66.7)	5 (83.3)	3 (50.0)	6 (66.7)	4 (57.1)	6 (100.0)	4 (66.7)
Related TEAE, n (%)	0	0	3 (50.0)	0	0	0	0	0
Serious TEAE, n (%)	2 (22.2)	0	1 (16.7)	0	0	0	2 (33.3)	1 (16.7)
Grade ≥3 TEAE, n (%)	1 (11.1)	1 (16.7)	0	1 (16.7)	0	0	2 (33.3)	1 (16.7)

Related TEAEs: 1 participant with Grade 2 hyperkalemia; 1 participant with Grade 1 dizziness; 1 participant with Grade 1 eosinophilia and Grade 2 renal failure (Creatinine 1.3x baseline at D29 with resolution by D57), all SAD cohort treated at 60 mg. **Grade ≥3 and Serious TEAEs:** 1 participant treated at 28 mg with Grade 4 ESRD (dialysis eligible prior to enrollment); 1 MD participant treated at 90 mg with Grade 3 cardiac failure congestive, Grade 3 eosinophilic esophagitis, Grade 3 pneumonia, Grade 3 pleurisy, and Grade 5 (fatal) Non-Hodgkin's lymphoma; 1 MD participant treated at 90 mg with Grade 3 toxic encephalopathy; 1 MD placebo participant with Grade 3 ESRD. **Grade ≥3 and Non-serious TEAEs:** 1 participant treated at 28 mg with Grade 4 anemia and Grade 3 fluid retention; 1 participant treated at 40 mg with Grade 3 hypervolemia; 1 SAD participant treated at 90 mg with Grade 3 anemia and Grade 3 hyperkalemia; 1 MD participant treated at 90 mg with Grade 3 anemia. **Serious TEAEs and Grade <3:** 1 participant treated at 28 mg with Grade 2 atrial fibrillation (medical history of atrial fibrillation); 1 SAD participant treated at 60 mg with Grade 1 atrial fibrillation (medical history of atrial fibrillation). *Based on SRC review of the efficacy of the 90 mg MD cohort, participants were maintained on 60 mg for the OLE portion of the study.

DISC-0974 leads to reduction in hepcidin and iron mobilization that is generally dose dependent and sustained in MD cohort

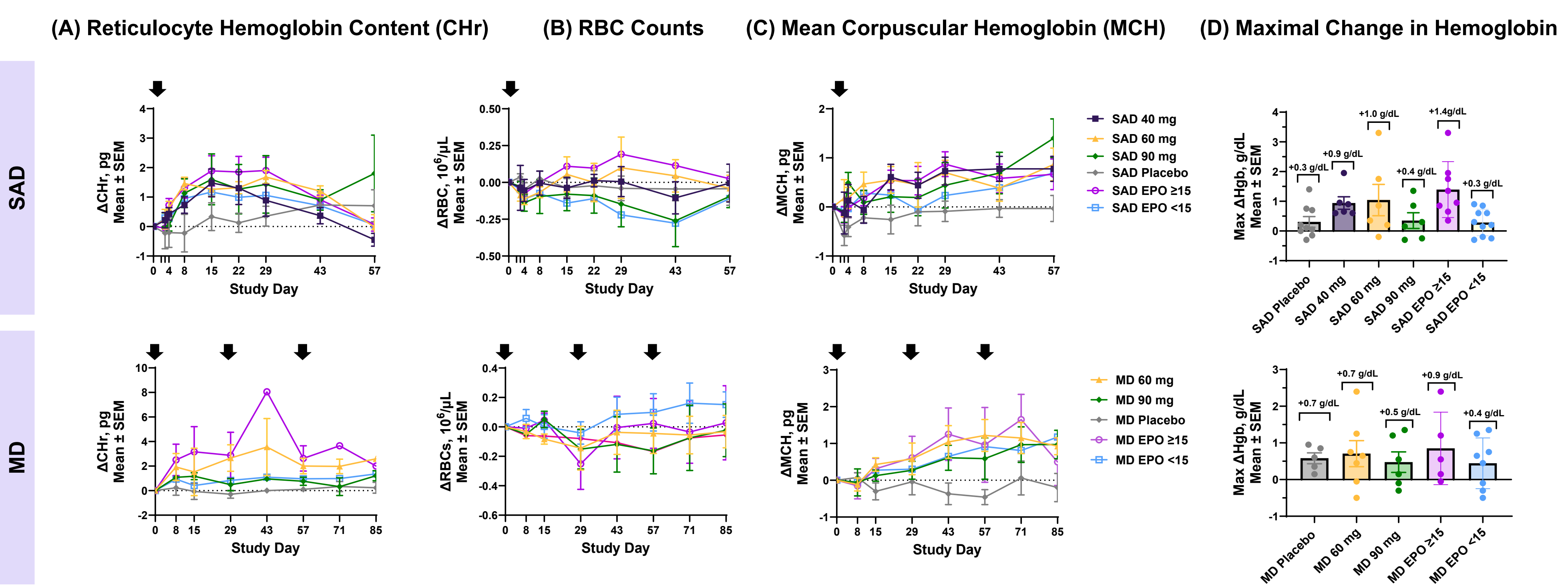
Figure 1. (A) Mean DISC-0974 concentration over time. Mean (SEM) serum hepcidin (B), serum TSAT (C), and serum iron (D) after administration of placebo (gray), and DISC-0974 at 28 mg (red), 40 mg (blue), 60 mg (yellow), 90 mg (green), and pooled DISC-0974-dosed participants with baseline erythropoietin (EPO) ≥15 (magenta) or <15 (light blue) mIU/mL.



For participants receiving rescue therapy (1 SAD placebo participant, 2 SAD participants dosed at 28 mg, 1 MD placebo participant, and 1 MD participant dosed at 90 mg), serum hepcidin, TSAT, iron data are excluded starting on the date of therapy initiation. MD=multiple dose. SAD=single-ascending dose. ▼ Indicates DISC-0974 dosing.

DISC-0974 increases hemoglobinization and increases hemoglobin in a subset of participants

Figure 2. Mean (SEM) change from baseline (CFB) for reticulocyte hemoglobin after administration (A), RBC counts (B), mean corpuscular hemoglobin (C) of placebo (gray), and DISC-0974 at 40 mg (blue), 60 mg (yellow), 90 mg (green), and pooled DISC-0974-dosed participants with baseline erythropoietin (EPO) ≥15 (magenta) or <15 (light blue) mIU/mL (D). Mean (SEM) maximal CFB in hemoglobin after treatment through end of study with dots representing individual values.



Hematologic responses are depicted for participants dosed 40-90 mg. For participants receiving rescue therapy (1 SAD placebo participant, 1 MD placebo participant, and 1 MD participant dosed at 90 mg), ChR, RBC count, MCH, and Hgb data are excluded starting on the date of therapy initiation. MD=multiple dose. SAD=single-ascending dose. ▼ Indicates DISC-0974 dosing.