RALLY-MF: Initial efficacy of a Phase 2 study of selcodebart (DISC-0974), an anti-hemojuvelin antibody, to treat anemia in myelofibrosis

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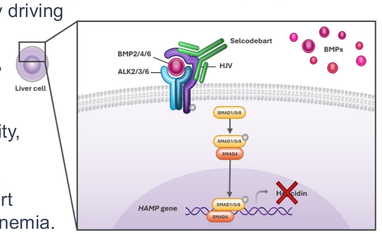
INTRODUCTION

Hepcidin, a central regulator of iron homeostasis, is pathologically elevated in patients with myelofibrosis (MF) and anemia.[1] Selcodebart is an investigational, first-in-class, monoclonal antibody that blocks hemojuvelin, a co-receptor in the bone morphogenetic protein-signaling pathway driving hepcidin expression.[2]

This Phase 2, open-label, multiple ascending-dose study (NCT05320198) assesses safety, tolerability, pharmacokinetics, pharmacodynamics (PD), and efficacy of selcodebart in patients with MF and anemia.



METHODS

Study population

- N = ~90 participants (~30 per transfusion cohort), inclusive of 12 Phase 1b participants dosed at 50 mg
- Adult participants with MF and anemia:
  - Hemoglobin (Hgb) <10 g/dL on ≥3 assessments over 84 days, *Or*
  - 1-12 packed red blood cell units transfused in 84 days
- Severity: Dynamic International Prognostic Scoring System Intermediate-1 (DIPSS INT-1) to High
- +/- Janus kinase inhibitor (JAKi) permitted

Study is ongoing. N=61 per data cut of 27 Apr 2026 including data through 20 Mar 2026 visit.

Study design

Screening (28 Days) → **Treatment Period** (6 Cycles q28 Days) → **Follow-Up** (28 Days) → **Continuation Treatment** (Optional, q28 Days)

Dosing: SC at 50 mg (w/dose escalation to 75 mg on Day 57 if insufficient response[a])
Key endpoints: hematologic response, PD markers of mechanism engagement, safety and tolerability

Baseline Transfusion	Major Hematologic Response	Minor Hematologic Response	Overall Response
nTD (Hgb <10 and 0 units transfused)[b]	Mean Hgb ↑1.5 g/dL ≥12 weeks (rolling window)	Mean Hgb ↑1 g/dL ≥12 weeks	Major + minor hematologic responses
TD Low (1-2 units transfused)[b]	Transfusion independence ≥16-week (rolling window) and Hgb ≥7 g/dL	≥50% reduction in transfusions from baseline over rolling 12-week window	
TD High (3-12 units transfused)[b]	Transfusion independence ≥12 weeks (rolling window) and Hgb ≥7 g/dL	≥50% reduction in transfusions from baseline over rolling 12-week window	

Criteria adapted from Tefferi et al, Blood, 2024.[3]
[a] Insufficient response: nTD/TD Low = no Hgb values ≥1 g/dL from baseline by Day 57 (excluding values within 14 days of transfusion); TD High = continued average monthly transfusion rate at Day 57 equal or greater than in the 84 days prior to Screening. [b] During the 84 days prior to Screening. nTD = non-transfusion dependent; SC = subcutaneous; TD = transfusion dependent.

Selcodebart is an investigational agent and is not approved for use as therapy in any jurisdiction worldwide.

RESULTS

Table 1. Baseline characteristics and demographics

Characteristic	nTD (n=35)	TD Low (n=13)	TD High (n=13)	Overall (n=61)
Age, median (range), years	70.0 (31, 83)	75.0 (60, 87)	73.0 (60, 87)	71.0 (31, 87)
Male, n (%)	18 (51.4)	7 (53.8)	8 (61.5)	33 (54.1)
Race, n (%)				
White	31 (88.6)	12 (92.3)	11 (84.6)	54 (88.5)
Black or African American	1 (2.9)	0	0	1 (1.6)
Asian	1 (2.9)	1 (7.7)	1 (7.7)	3 (4.9)
Other	2 (5.7)	0	1 (7.7)	3 (4.9)
Concomitant JAKi medication, n (%)	17 (48.6)	6 (46.2)	9 (69.2)	32 (52.5)
Ruxolitinib	8 (22.9)	3 (23.1)	4 (30.8)	15 (24.6)
Momelotinib	8 (22.9)	3 (23.1)	4 (30.8)	15 (24.6)
Pacritinib	1 (2.9)	0	1 (7.7)	2 (3.3)
DIPSS, n (%)				
Intermediate-1	1 (2.9)	1 (7.7)	0	2 (3.3)
Intermediate-2	33 (94.3)	9 (69.2)	9 (69.2)	51 (83.6)
High	1 (2.9)	3 (23.1)	4 (30.8)	8 (13.1)
JAK2 mutation present, n (%)	13 (37.1)	7 (53.8)	7 (53.8)	27 (44.3)
Baseline hepcidin				
Median (range), ng/mL	39.1 (9.8, 174.1)	109.9 (37.4, 209.8)	108.0 (21.3, 227.3)	66.0 (9.8, 227.3)
Mean (SD), ng/mL	60.3 (49.0)	97.0 (49.9)	120.1 (66.3)	81.6 (58.2)
Baseline hemoglobin, median, g/dL	8.9	7.7	7.6	8.4

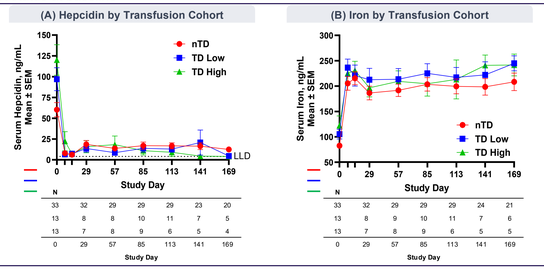
Table 2. Summary of safety

Preferred Term	nTD (n=35)	TD Low (n=13)	TD High (n=13)	Overall (n=61)
Any TEAE, n (%)	33 (94.3)	12 (92.3)	11 (84.6)	56 (91.8)
Related TEAE, n (%)	6 (17.1)	4 (30.8)	5 (38.5)	15 (24.6)
SAE, n (%)	8 (22.9)	1 (7.7)	3 (23.1)	12 (19.7)
AESI, n (%)	2 (5.7)	0	0	2 (3.3)
Grade ≥3 TEAE, n (%)	13 (37.1)	6 (46.2)	6 (46.2)	25 (41.0)

Related TEAEs occurring in ≥2 participants overall: diarrhea (n=5); none were SAEs.
SAEs and Grade ≥3 AEs occurring in >1 participant: hypotension (n=2), cellulitis (n=2).
SAEs and Grade <3 AEs: atrial fibrillation (n=1), upper gastrointestinal hemorrhage (n=1).
Grade ≥3 AEs and non-serious AEs occurring in >1 participant: anemia (n=7), lymphocyte count decreased (n=3), platelet count decreased (n=2).
AESI: AEs related to decrease in renal function (creatinine increase Grade 2 or higher from baseline, per CTCAE criteria and acute kidney injury).
AESIs: Blood creatinine increased (n=2), Chronic kidney disease (n=1); none related to study drug. One participant withdrew due to unrelated AEs of Nephrolithiasis (SAE), Chronic kidney disease (SAE/AESI, worsening of existing pre-existing condition), and *Clostridium* colitis.
AESI = adverse event of special interest; CTCAE = Common Terminology Criteria for Adverse Events; SAE = serious adverse event; TEAE = treatment-emergent adverse event.

Selcodebart dosing leads to sustained hepcidin reduction and iron mobilization

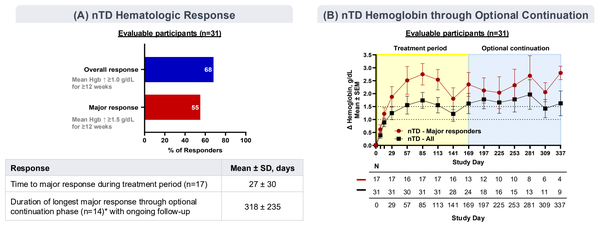
Figure 1. Mean (SEM) change over time in serum hepcidin **(A)** and serum iron **(B)** by transfusion cohort status at baseline



Analysis excludes values within 7 days of transfusion receipt. LLD = lower limit of detection.

55% nTD participants achieved mean Hgb ↑ of 1.5 g/dL for ≥12 weeks; Hgb increase is maintained through continuation phase

Figure 2. (A) Percentage of study nTD participants with follow-up through visit Day 113 that achieved a hematologic response. **(B)** Mean (SEM) change in Hgb from baseline

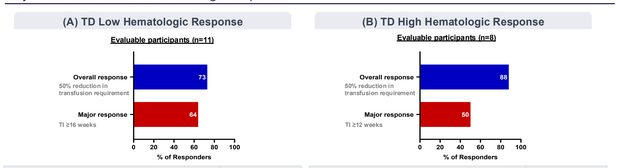


Response	Mean ± SD, days
Time to major response during treatment period (n=17)	27 ± 30
Duration of longest major response through optional continuation phase (n=14)* with ongoing follow-up	318 ± 235

Analysis excludes values within 7 days of transfusion receipt. 4 nTD participants were considered non-evaluable due to follow-up < Day 113 at the time of data cut. 9 nTD participants with evaluable hematologic response had a per protocol dose escalation at visit Day 57 due to insufficient response. 8 nTD participants had a per protocol dose hold due to Hgb ≥12 g/dL.
* 14 of 17 major responders had follow-up through EOS and were eligible to enter optional continuation phase at the time of data cut. EOS = end of study.

64% TD Low participants achieved ≥TI-16*, and 50% of TD High participants achieved ≥TI-12*

Figure 3. Percentage of study TD Low **(A)** and TD High **(B)** participants with follow-up through visit Day 113 that achieved a hematologic response



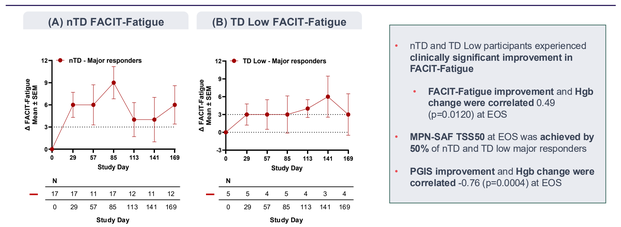
Response	Mean ± SD, days
Time to major response (n=7)	4 ± 8
Duration of longest major response through optional continuation phase (n=6)** with ongoing follow-up	345 ± 243

Response	Mean ± SD, days
Time to major response (n=4)	2 ± 1
Duration of longest major response through optional continuation phase (n=2)** with ongoing follow-up	239 ± 18

Analysis excludes values within 7 days of transfusion receipt. 2 TD Low, 5 TD High participants were considered non-evaluable due to follow-up < Day 113 at the time of data cut. 5 TD Low, 4 TD High participants with evaluable hematologic response had a per protocol dose escalation at visit Day 57 due to insufficient response. 1 TD Low participant had a per protocol dose hold due to Hgb ≥12 g/dL.
* Minimum Hgb of 7 g/dL required. ** 6/7 TD Low, 3/4 TD High major responders had follow-up through EOS and were eligible to enter optional continuation phase at the time of data cut, 1 TD High participant did not proceed to continuation phase.
TI = transfusion independent.

Hgb increase in nTD and TD Low participants is associated with improvement in patient-reported outcomes

Figure 4. Mean change from baseline in FACIT-Fatigue for nTD **(A)** and TD Low **(B)** participants

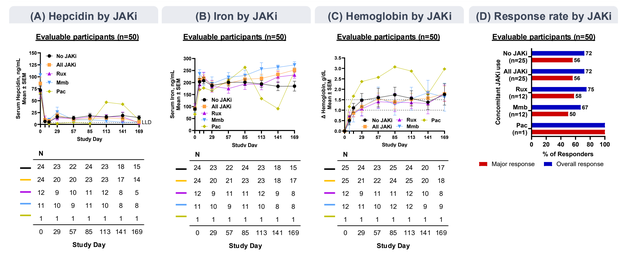


- nTD and TD Low participants experienced **clinically significant improvement in FACIT-Fatigue**
  - **FACIT-Fatigue improvement** and **Hgb change were correlated** 0.49 (p=0.0120) at EOS
- **MPN-SAF TSS50** at EOS was **achieved by 50%** of nTD and TD low major responders
- **PGIS improvement** and **Hgb change were correlated** -0.76 (p=0.0004) at EOS

A 3-point change in the FACIT-Fatigue score is considered the threshold for clinical significance.[4]
MPN-SAF TSS50 = Myeloproliferative Neoplasm Assessment Total Symptom Score 50% reduction; PGIS = Patient Global Impression of Severity.

Selcodebart leads to hepcidin reduction, iron mobilization, and hematologic response regardless of concomitant JAKi use

Figure 5. Mean absolute serum hepcidin **(A)**, serum iron **(B)**, mean CFB in Hgb **(C)** and hematologic response **(D)** by concomitant JAKi use in participants with follow-up through visit Day 113 (evaluable)



Analyses exclude values within 7 days of transfusion receipt. Participant on concomitant pacritinib had study drug dose held on Days 85 and 113 due to Hgb ≥12 g/dL. CFB = change from baseline; Mmb = momelotinib; Pac = pacritinib; Rux = ruxolitinib.

CONCLUSIONS

- Selcodebart was safe and generally well tolerated
- Selcodebart resulted in **sustained decrease in hepcidin** and **increase in serum iron** in participants regardless of concomitant JAKi therapy or baseline transfusion requirement
- Selcodebart resulted in meaningful hematologic responses across cohorts:
  - **55% of nTD participants achieved mean hemoglobin increase of ≥1.5 g/dL for ≥12 weeks**
  - **64% of TD Low participants achieved ≥TI-16 weeks**
  - **50% of TD High participants achieved ≥TI-12 weeks**
- **Major responses were achieved regardless of baseline JAKi therapy**
  - 56% of participants on concomitant JAKi (n=25) achieved a major response
  - 56% of participants not on concomitant JAKi (n=25) achieved a major response
- **Increase in hemoglobin** after selcodebart dosing was **correlated with improvement in patient-reported outcomes**

References

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