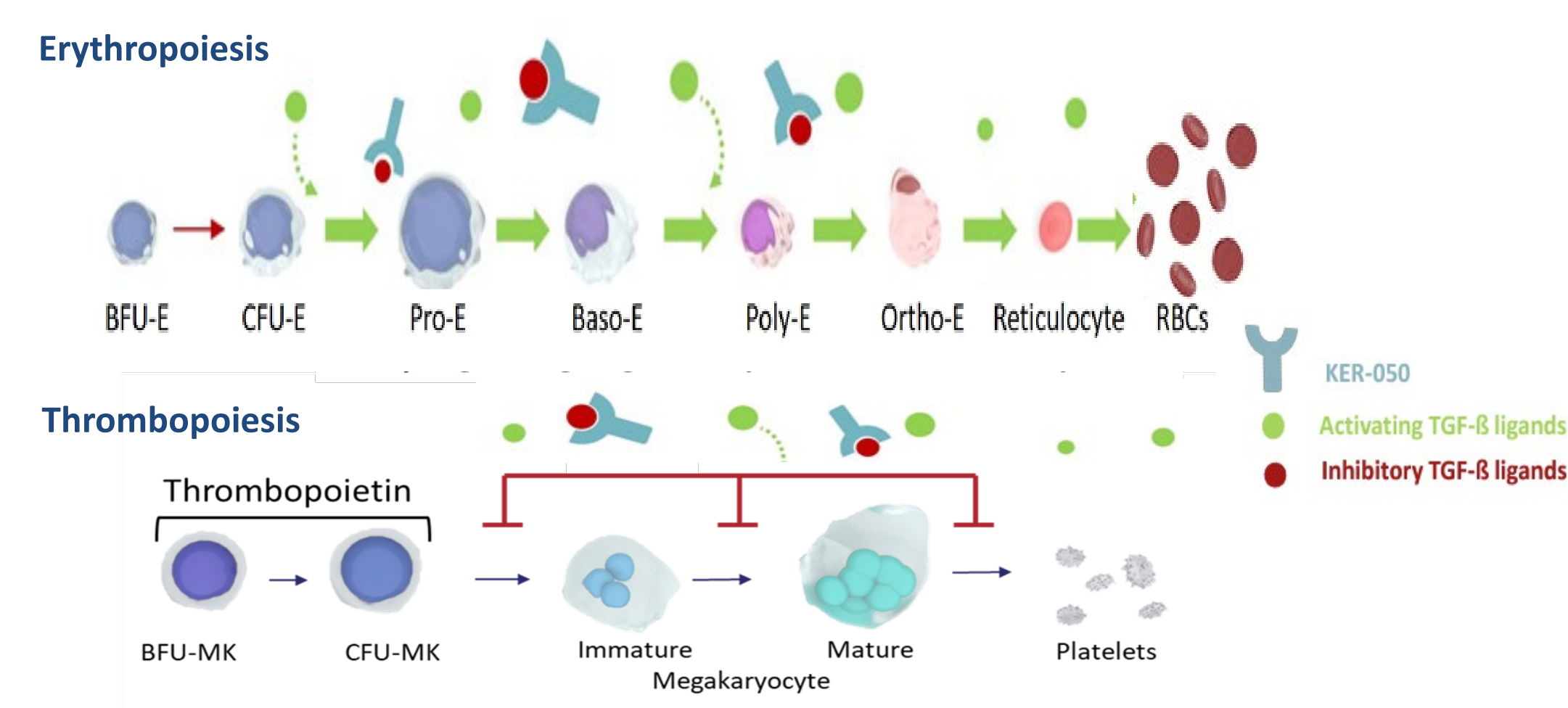


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INTRODUCTION

- Dysregulated TGF- β signaling contributes to ineffective hematopoiesis in myelodysplastic syndrome (MDS).¹
- Many patients develop high transfusion burden (HTB) defined as requiring ≥ 4 units of RBC transfusions over an 8-week period. This transfusion dependency contributes to inferior, progression-free survival in these patients who have a high unmet medical need.²
- KER-050 is a recombinant fusion protein that is designed to inhibit SMAD2/3 signaling by binding select TGF- β superfamily inhibitory ligands (activin A and B, GDF 8 and 11), to promote maturation and differentiation of early- and late-stage erythroid and megakaryocyte precursors.^{3,4}
- In a Phase 1 study⁵, KER-050 elicited a rapid and sustained increase in reticulocytes followed by increases in hemoglobin in healthy volunteers. Clinically relevant increases in platelet counts were also observed.



STUDY DESIGN

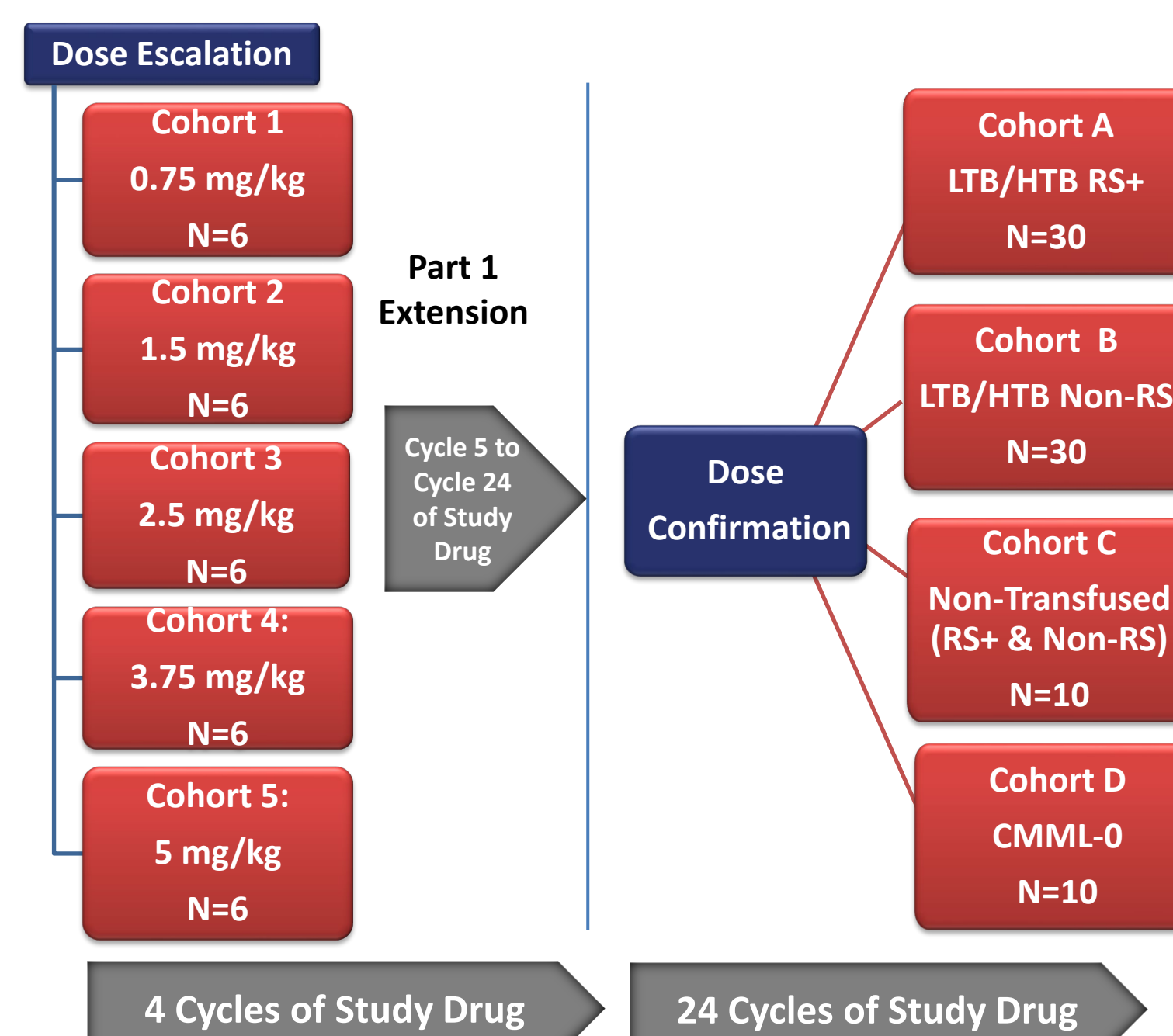
Primary objectives:

- To evaluate safety and tolerability

Key Eligibility criteria:

- IPSS-R very low to intermediate risk MDS
- Anemia, defined as Hgb < 10 g/dL or requiring RBC transfusions

Part 1: Dose Escalation



Select Endpoints:

- Primary: Safety and Tolerability
- Key Efficacy endpoints:
 - IWG 2006 Hematologic improvement (HI-E) for 8 weeks
 - RBC transfusion independence for 8 weeks

BASELINE CHARACTERISTICS

Table 1: Demographics and Baseline Characteristics, Part 1, Dose Escalation

	KER-050 Dose Level (mg/kg)					
	0.75 (N=6)	1.5 (N=6)	2.5 (N=6)	3.75 (N=6)	5 (N=7)	All (N=31)
Age, Mean (range)	75.5	68.3	72	73.3	76.7	73.3 (55-88)
Female, n (%)	5	1	4	2	0	12 (38.7%)
Years since MDS Diagnosis, Mean (range)	2.68	2.16	0.85	2.73	7.4	2.61 (0.2-8.6)
RS positive	3	3	3	4	4	17 (54.8%)
Transfusion Burden						
Non-Transfused (NT), 0 units	3	0	1	1	0	5 (16.1%)
Low Transfusion Burden (LTB), < 4 units	2	0	1	2	3	8 (25.8%)
High transfusion burden (HTB) ≥ 4 units	1	6	4	3	4	18 (58.1%)
WHO MDS Classification, n (%)						
MDS-MLD	3	3	3	1	3	13 (41.9%)
MDS-RS-MLD	2	2	3	4	3	14 (45.2%)
MDS-RS-SLD	0	1	0	0	0	1 (3.2%)
MDS with isolated del(5q)	1	0	0	0	0	1 (3.2%)
N/A	0	0	0	1	1	2 (6.5%)
Prior ESA Therapy, n (%)	0	0	2	1	0	3 (9.7%)
Iron chelator, n (%)	0	2	2	2	1	7 (22.6%)
Efficacy Evaluable Patients*, n (%)	6	4	6	6	5	27 (87.1%)
Efficacy Evaluable HTB Patients**, n (%)	1	4	4	3	4	16/18 (88.9%)

*Patients with at least 8 weeks of post-treatment HGB and transfusion assessments were defined as efficacy evaluable.

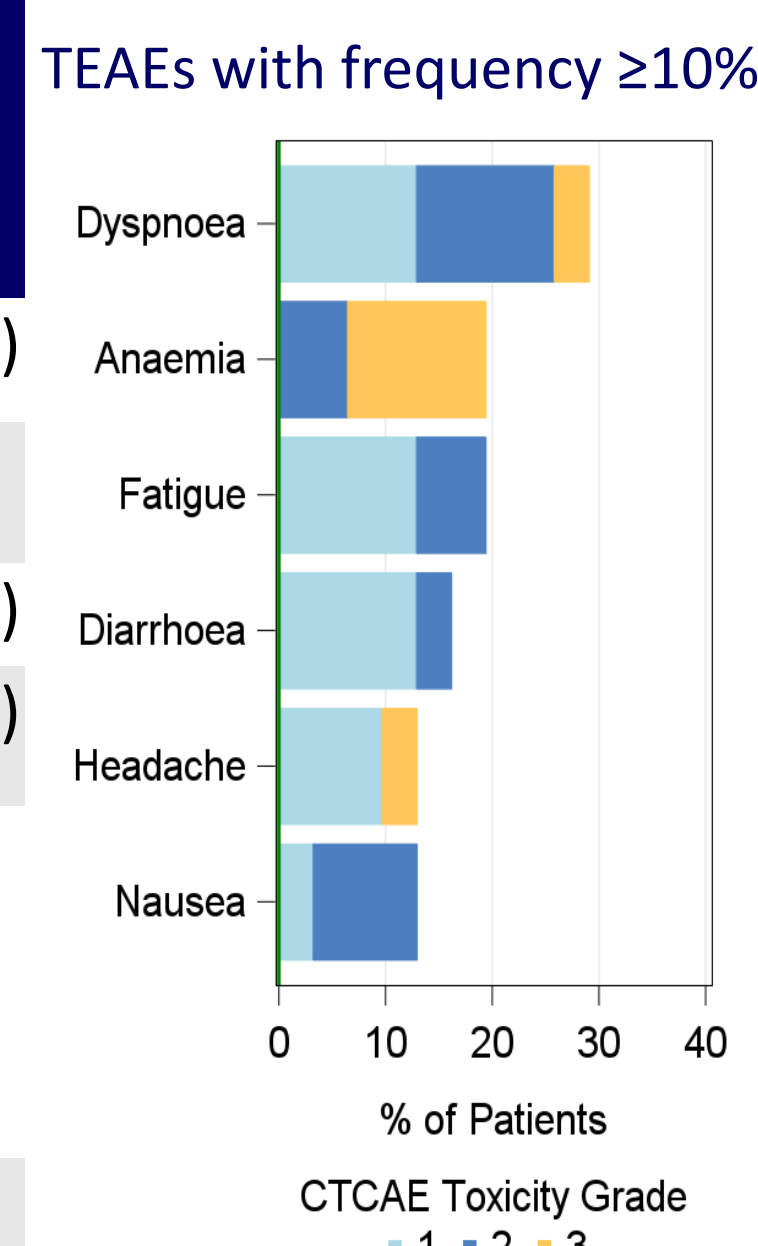
** Percentage was based on all HTB patients.

SAFETY AND TOLERABILITY

Table 2: KER-050 was generally well-tolerated in Part 1

n (%)	KER-050 Dose Level (mg/kg)					
	0.75 (N=6)	1.5 (N=6)	2.5 (N=6)	3.75 (N=6)	5 (N=7)	All (N=31)
TEAE	6 (100)	6 (100)	6 (100)	5 (83.3)	6 (85.7)	29 (93.5)
Related TEAE	1 (16.7)	0	1 (16.7)	1 (16.7)	2 (28.6)	5 (16.1)
Grade ≥ 3	1 (16.7)	1 (16.7)	3 (50.0)	2 (33.3)	5 (71.4)	12 (38.7)
SAE	1 (16.7)	2 (33.3)	1 (16.7)	2 (33.3)	4 (57.1)	10 (32.3)
TEAE requiring dose modification	0	0	0	1 (16.7)	1 (14.3)	2 (6.5)
Death	0	1 (16.7)	0	0	0	1 (3.2)

As of Apr 3, 2022 data cut off date



- No dose limiting toxicity was reported in the dose escalation cohorts and no patients progressed to AML.
- 4 patients discontinued study drug: 1 withdrew consent, 1 death (unrelated to study drug, per autopsy due to obesity-associated heart disease), 2 withdrew due to unrelated TEAE.

PRELIMINARY RESULTS

Table 3: Efficacy Summary of 8-week Endpoints Achieved in MDS patients

Response Summary	Response Rate, n/m (%)	
	All evaluable patients	HTB evaluable patients
Overall Erythroid Response (HI-E or TI)	14/27 (51.8%)	11/16 (68.8%)
IWG 2006 HI-E	12/26 (46.2%)	11/16 (68.8%)
Transfusion independence (TI*)	9/20 (45%)	7/16 (43.8%)
RS+	6/12 (50%)	4/9 (44.4%)
Non-RS	3/8 (37.5%)	3/7 (42.9%)

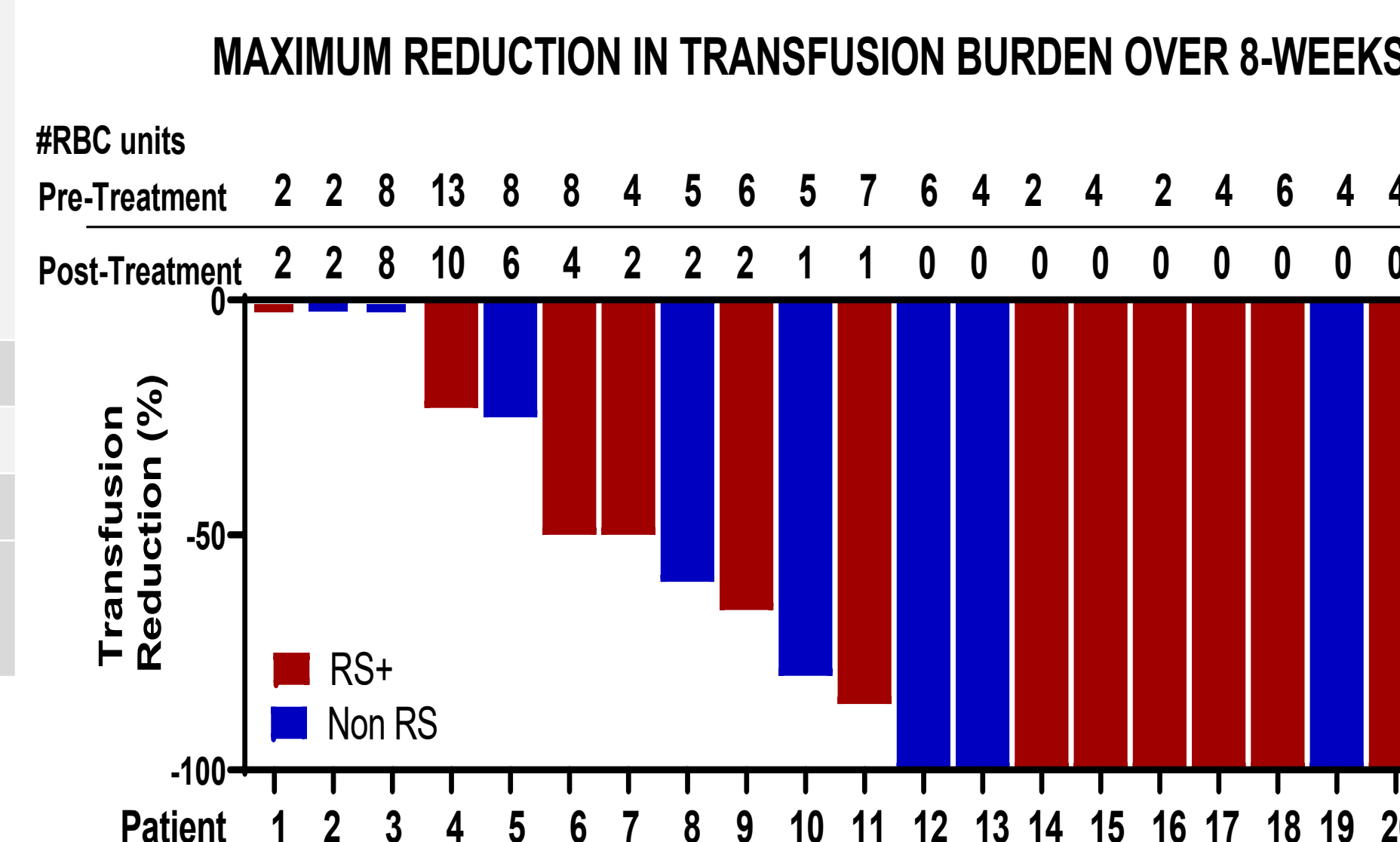
IWG 2006 HI-E: ≥ 1.5 g/dL Hgb x 8 weeks (NT and LTB); Transfusion reduction ≥ 4 RBC units over 8 weeks (HTB)

TI: Transfusion free period 8 weeks

*Baseline Transfusion Requirement ≥ 2 RBC units

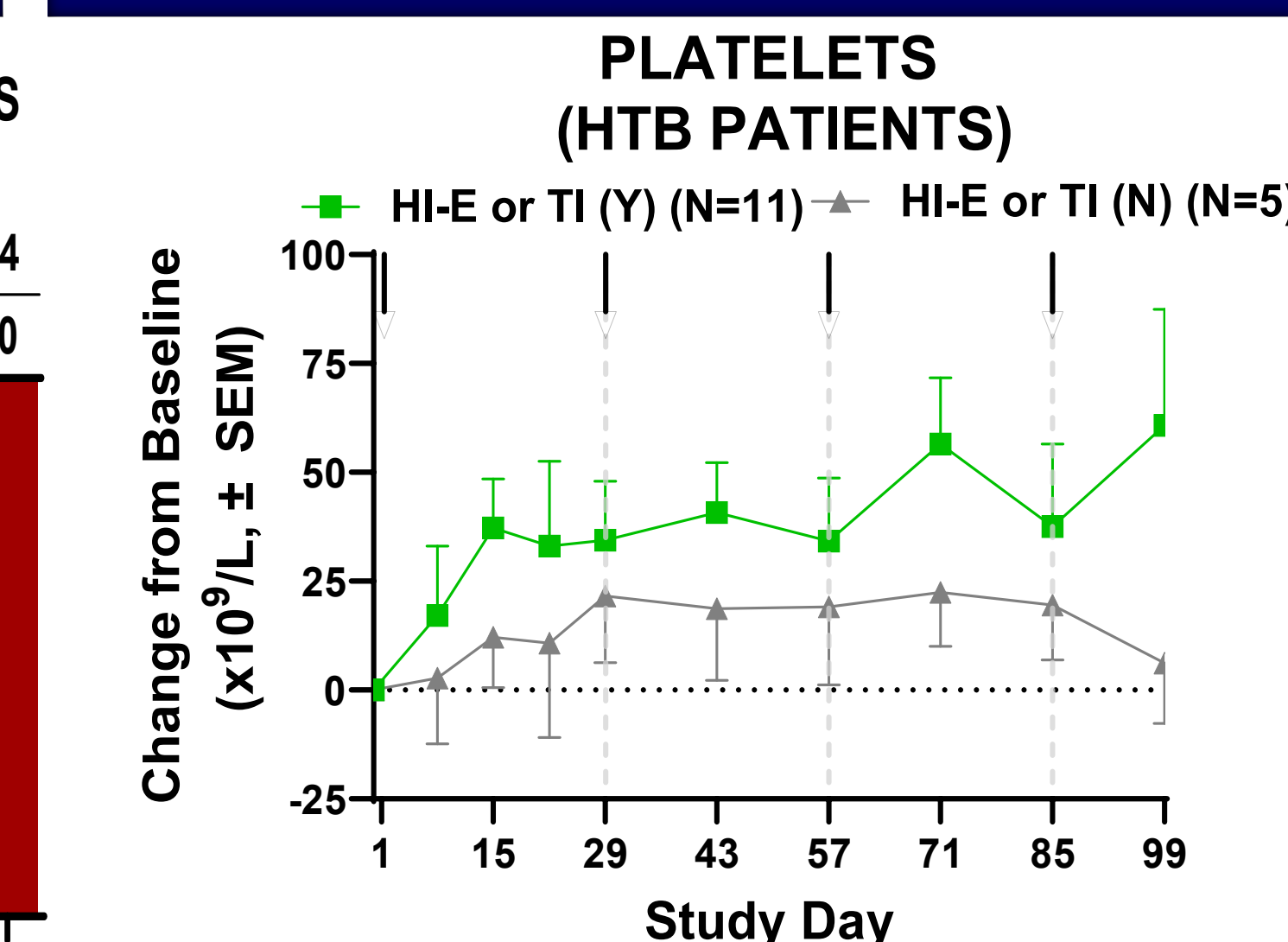
n = responders in each category; m = 8-week evaluable population as of Apr 3, 2022, data cutoff date

Figure 1. Treatment with KER-050 Resulted in HI-E and TI in Transfusion Dependent Non-RS and RS+ MDS patients



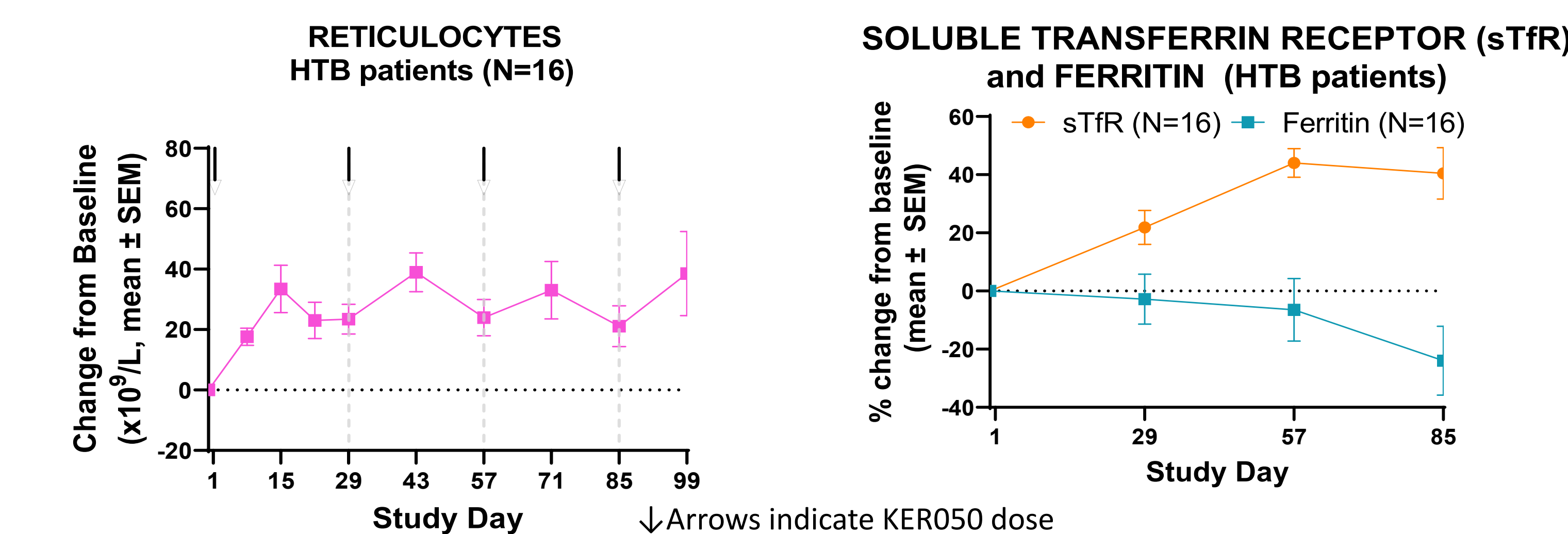
Improvements in transfusion burden were seen across LTB and HTB patients. Specifically, 7/16 HTB and 2/4 LTB patients achieved TI after KER-050 treatment.

Figure 2. Sustained Increase in Platelets Observed in HTB Patients Achieving HI-E or TI with KER-050 Treatment



Maximum increase in platelets from baseline in HTB patients achieving HI-E or TI was 96.6 $\times 10^9$ /L (mean), range 13.8-234.8 $\times 10^9$ /L.

Figure 3. Observed Changes in Hematologic and Ferrokinetic Biomarkers Support Induction of Erythropoiesis with KER-050 Treatment in all HTB Patients



- Reticulocytes (RETs) increased over the course of the study in HTB patients, and mean maximum increase from baseline was 62.9 $\times 10^9$ /L, range 15.7-145.8 $\times 10^9$ /L
- Mean absolute ferritin at baseline in HTB patients was 1359.2 ng/mL, range 230.5 to 5829.1 ng/mL; mean maximum reduction in ferritin was 29.1%, range 0 to 92% and mean maximum sTfR increase was 52.9%, range 9.9-116.4%.

SUMMARY

- Primarily transfusion-dependent MDS patients with MLD and elevated ferritin were enrolled in Part 1 of this study
- KER-050 was generally well-tolerated as of data cut-off date
- HI-E and TI ≥ 8 weeks have been observed in MDS patients treated with KER-050 across varying transfusion burdens, with 44% of HTB patients achieving TI
- Increases in platelets have been observed in HTB patients achieving HI-E or TI which supports the potential of KER-050 as a treatment for multilineage cytopenias in difficult-to-treat HTB patients
- Observed PD effects in RETs, sTfR and ferritin support the proposed mechanism of action of increasing erythropoiesis

Part 2 of the study has been initiated following endorsement by safety review committee at a starting dose of 3.75mg/kg with the option to up-titrate to 5 mg/kg

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DISCLOSURES

Arbelaez A: Travel subsidies from Amgen. **Chee L:** Honoraria and membership in board of directors/advisory committees for Novartis. **Fong CY:** Paid consultancy for AbbVie, Amgen, Astellas, BMS, Novartis, Pfizer; honoraria: Novotech and Specialized therapeutics. **Ross DM:** Honoraria and membership in board of directors/advisory committees for Novartis, paid consultancy, membership on board of directors/advisory committees and research funding BMS, consultancy and honoraria Keros **Wight J:** Honoraria and travel subsidies: AbbVie and Janssen **Cooper S, Feng W, Lachey J, McGinty A, Natarajan HD, Rovaldi C** are employees of and security holders in Keros Therapeutics, Inc. All other authors have reported no disclosures

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