A PHASE 2, OPEN-LABEL, ASCENDING DOSE STUDY OF KER-050 FOR THE TREATMENT OF ANEMIA IN PATIENTS WITH VERY LOW, LOW, OR INTERMEDIATE RISK MYELODYSPLASTIC SYNDROMES

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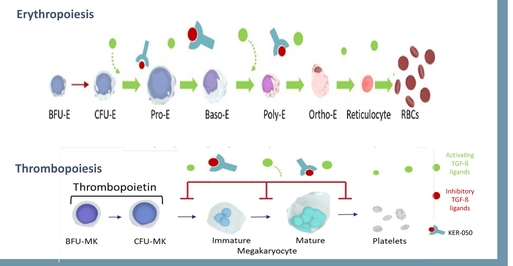
INTRODUCTION

- Dysregulated TGF-β signaling with overactive SMAD2/3 signaling contributes to ineffective hematopoiesis in MDS.[1]
- 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. [2]
- In a Phase 1 study, KER-050 elicited rapid and sustained increase in reticulocytes followed by increases in hemoglobin in healthy volunteers. Clinically relevant increases in platelet counts were also observed.[3]



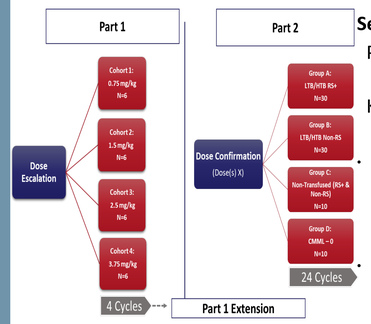
STUDY DESIGN

Primary objectives:

- To evaluate safety and tolerability

Key Eligibility criteria:

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



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 by Cohort and RS Status

	KER-050 Dose Level (mg/kg)				
	0.75 (N=6)	1.5 (N=6)	2.5 (N=6)	3.75 (N=6)	All (N=24)
Age, mean (range)	75.5	68.3	72.0	73.3	72.3 (55 - **88**)
Male, n (%)	1	5	2	4	12 (50%)
Years since MDS diagnosis, mean (range)	2.7	2.2	0.9	2.7	2.2 (0.2 – 8.6)
WHO Disease Category, n (%)					
MDS-MLD	3	3	3	1	10 (42%)
MDS-RS-MLD	2	2	3	3	10 (42%)
MDS-RS-SLD	0	1	0	0	1 (4%)
MDS with del(5q)	1	0	0	0	1 (4%)
N/A	0	0	0	2	2 (8%)
Transfusion Burden*,	3	0	1	1	5 (21%)
NT	2	0	1	2	5 (21%)
LTB	1	6	4	3	14 (58%)
HTB					
RS status (RS +)	3	3	3	4	13 (54%)
Prior ESA Treatment, n (%)	0	0	2	1	3 (13%)
Iron chelator, n (%)	0	2	2	2	6 (25%)
Efficacy Evaluable n (%) (8-week endpoints)**	6	4**	6	0	16 (67%)

Mean (SD)	RS Status	
	RS +	Non-RS
EPO (IU/L)	326.0 (826.2)	490.2 (855.7)
Reticulocytes (10^9/L)	39.1 (28.0)	29.8 (24.8)
Platelets (10^9/L)	228.4 (67.8)	134.6 (55.5)
TPO (pg/mL)	74.2 (69.3)	42.8 (60.1)
sTfR (mg/L)	1.9 (1.0)	1.2 (0.6)

*NT: Non-transfused anemia (no RBC transfusions x 8 weeks), LTB: low-transfusion burden (1-3units RBCs x 8 weeks), HTB: high transfusion burden (≥4units RBCs x 8 weeks)

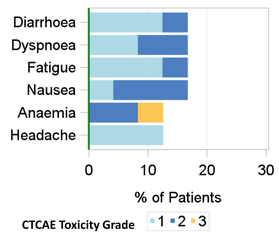
*2 participants in Cohort 2 (1.5mg/kg) were not efficacy-evaluable due to withdrawal of consent (n=1) and death (n=1) and 6 participants in Cohort 4 (3.75 mg/kg) were not efficacy evaluable as had not completed 8-weeks on study at the Oct 25, 2021, data cutoff date.

SAFETY AND TOLERABILITY

Table 2: Few treatment-related AEs and no dose-dependent AEs

n (%)	KER-050 Dose Level (mg/kg)				
	0.75 (N=6)	1.5 (N=6)	2.5 (N=6)	3.75 (N=6)	All (N=24)
Any TEAE	6 (100)	6 (100)	6 (100)	3 (50.0)	21 (87.5)
Treatment-related AE*	1 (16.7)	0	2 (33.3)	1 (16.7)	4 (16.7)
Grade ≥3 TEAE	1 (16.7)	1 (16.7)	2 (33.3)	1 (16.7)	5 (20.8)
Any serious TEAE**	1 (16.7)	2 (33.3)	0	2 (33.3)	5 (20.8)
Any TEAE requiring dose modification	0	0	0	1 (16.7)	1 (4.2)
Death	0	1 (16.7)	0	0	1 (4.2)

TEAEs with frequency ≥10%



*Treatment related AEs with maximum grade: Grade 2 (Rash, Diarrhea, Nausea, Peripheral edema), Grade 1 (Headache, Pain in extremity, Abdominal pain).
**Serious TEAEs with maximum grade: Grade 5 (Death), Grade 3 (Anaemia, Pneumonia, Pneumothorax), Grade 2 (Pyrexia, Cardiac failure congestive). None of the serious TEAEs were deemed related to study drug
No treatment-related SAEs observed.

PRELIMINARY RESULTS

Table 3: Efficacy summary of 8-week endpoints achieved

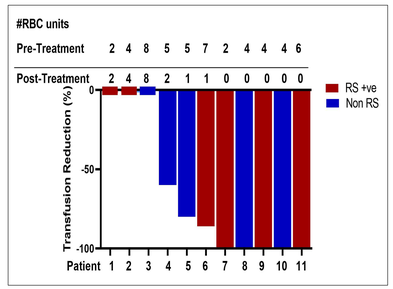
Response Summary	Response Rate n/m (%)
Overall Erythroid Response	8/16 (50%) 3 Non-RS, 5 RS+
IWG 2006 HI-E	7/16 (43.8%)
TI*	5/11 (45.5%)

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

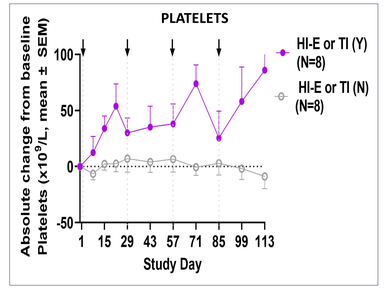
*Baseline Transfusion Requirement ≥2 RBC units
n = responders in each category; m = 8-week evaluable population as of Oct 25, 2021, data cutoff date

Figure 1: Achievement of HI-E and Transfusion Independence in Non-RS and RS+ MDS Patients with KER-050 Treatment



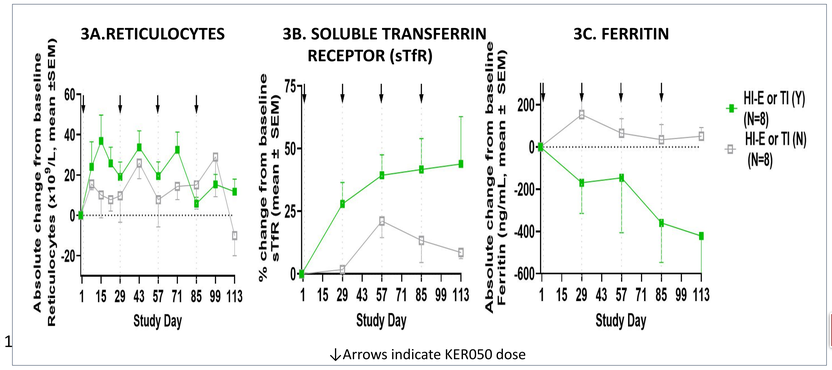
TI response rate: RS +ve 3/6; Non RS 2/5

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



No thrombocytosis or thrombotic events observed.

Figure 3: Observed Changes in Hematologic and Ferrokinetic Biomarkers Support Induction of Erythropoiesis With KER-050 Treatment.



Pharmacokinetics: Dose-proportional PK to date

SUMMARY

- KER-050 has been generally well-tolerated up to the 3.75mg/kg q4W regimen in this ongoing study
- HI-E (43.8%) and transfusion independence (45.5%) were achieved in both non-RS and RS+ participants
- These data suggest that KER-050 promotes erythropoiesis and thrombopoiesis in patients with MDS
  - Observed increases in reticulocytes, sTfR and decreases in Ferritin in patients achieving HI-E or TI
  - Observed increases in platelets observed in patients achieving HI-E or TI
- These data support the continued development of KER-050 as a treatment for ineffective hematopoiesis in MDS

REFERENCES

1. Zhou L et al. Blood- 2008; 112-3434
2. Ordonez C et al. poster presentation at the 25th European Hematology Association Congress 2020 Abstract# EP806
3. LaMora J et al poster #2068 ASH 2021

DISCLOSURES

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 **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. **Wight J**: Honoraria and travel subsidies: AbbVie and Jannsen
Cooper S, Furutani E, Jiang Y, Lachey J, Natarajan HD are employees of and security holders in Keros Therapeutics, Inc.
Rovaldi C and **Barger R** are paid consultants and security holders in Keros Therapeutics, Inc.
All other authors have reported no disclosures

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