KEROS THERAPEUTICS

Hematology Franchise: Program Updates and Summary of Data Presented at 28th Annual Congress of the European Hematology Association

June 9, 2023

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Keros Hematology Franchise

- Keros is harnessing the powerful biology of the TGF-β superfamily to develop product candidates with the potential to address the multiple mechanisms leading to ineffective erythropoiesis
  - KER-050: Designed to inhibit signaling by activin A, activin B, GDF8 and GDF11 to promote growth and differentiation of erythroid precursors and increase platelets
  - KER-047: Designed to inhibit activin receptor-like kinase-2 (ALK2) to inhibit hepcidin and mobilize iron for incorporation into hemoglobin

KER-050 clinical data are presented as of a data cutoff date of April 3, 2023.

28th Annual Congress of the European Hematology Association

Clinical Presentation

“KER-050 treatment improved markers of erythropoietic activity and hematopoiesis over six months which resulted in hematological responses across a broad, lower-risk MDS population”

- Abstract Code: S166

Preclinical Presentations

“A modified activin receptor type II ligand trap RKER-050 restored erythropoiesis in a mouse model of myelofibrosis”

- Abstract Code: P992

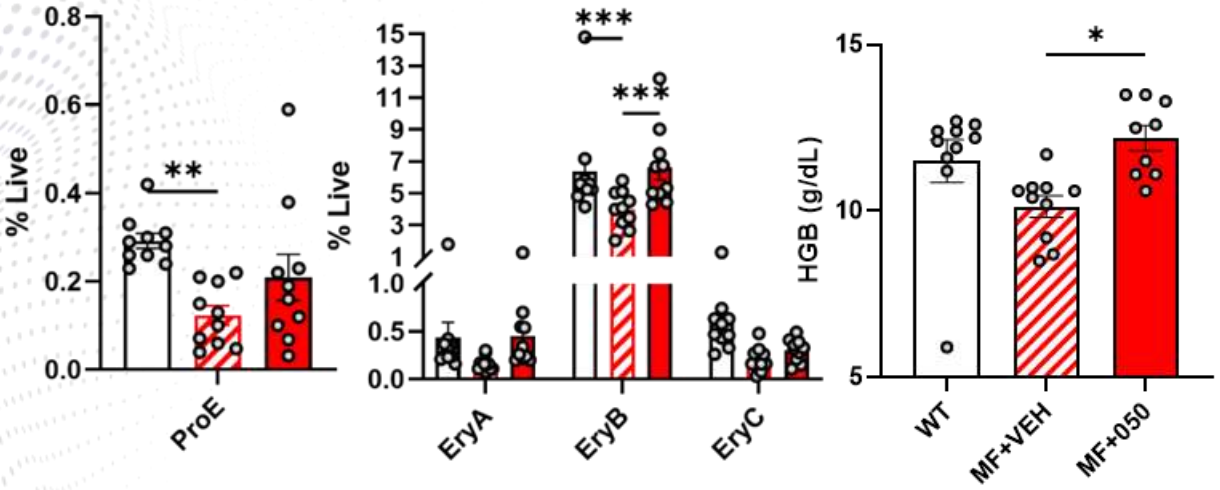
“Combining ALK2 inhibition with a modified activin receptor IIA ligand trap provided additive benefits in resolving anemia in a mouse model of anemia of inflammation”

- Abstract Code: P1488

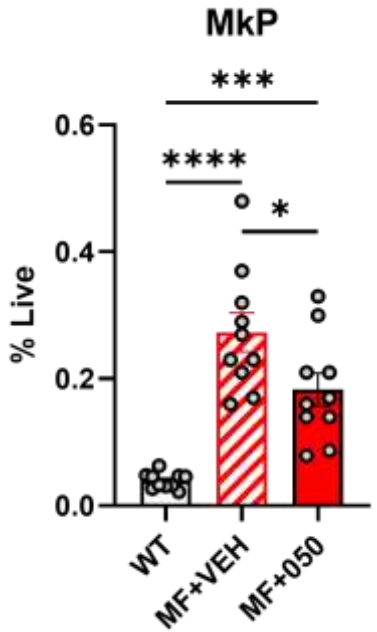
Myelofibrosis is Characterized by Ineffective Hematopoiesis

- Myelofibrosis (MF) is a group of rare cancers of the bone marrow in which the marrow is replaced by scar tissue and is not able to produce healthy blood cells
- MF is characterized by ineffective hematopoiesis, an enlarged spleen, bone marrow fibrosis and shortened survival. Patients often experience multiple disease-associated and treatment-emergent cytopenias, including anemia and thrombocytopenia
- The ineffective hematopoiesis in MF is driven by molecular abnormalities in the JAK-STAT signaling pathway, which leads to proliferation of red blood cell progenitors and platelet progenitors, or megakaryocytes
  - Megakaryocyte accumulation and breakdown is implicated in the inducement of bone marrow fibrosis
- KER-050 was evaluated for its ability to promote hematopoiesis in the Gata1low mouse model of myelofibrosis
  - Gata1 is an essential driver of megakaryocyte and erythroid differentiation
  - In both mice and humans, insufficient levels of Gata1 result in accumulation of megakaryocyte-erythroid precursors, bone marrow disruption and ineffective hematopoiesis

RKER-050 Treatment Restored Hematopoiesis in the Bone Marrow, Reversing Anemia and Normalizing Megakaryocyte Precursor Number in the Mouse Model of MF



Treatment of GATA1low mice with RKER-050 restored erythropoiesis to the bone marrow and reversed anemia



RKER-050 also reduced the MK hyperproliferation in BM, supporting a less congested BM

These data support the potential of KER-050 to treat the cytopenias, restore hematopoiesis in the bone marrow and reduce spleen size in patients with MF

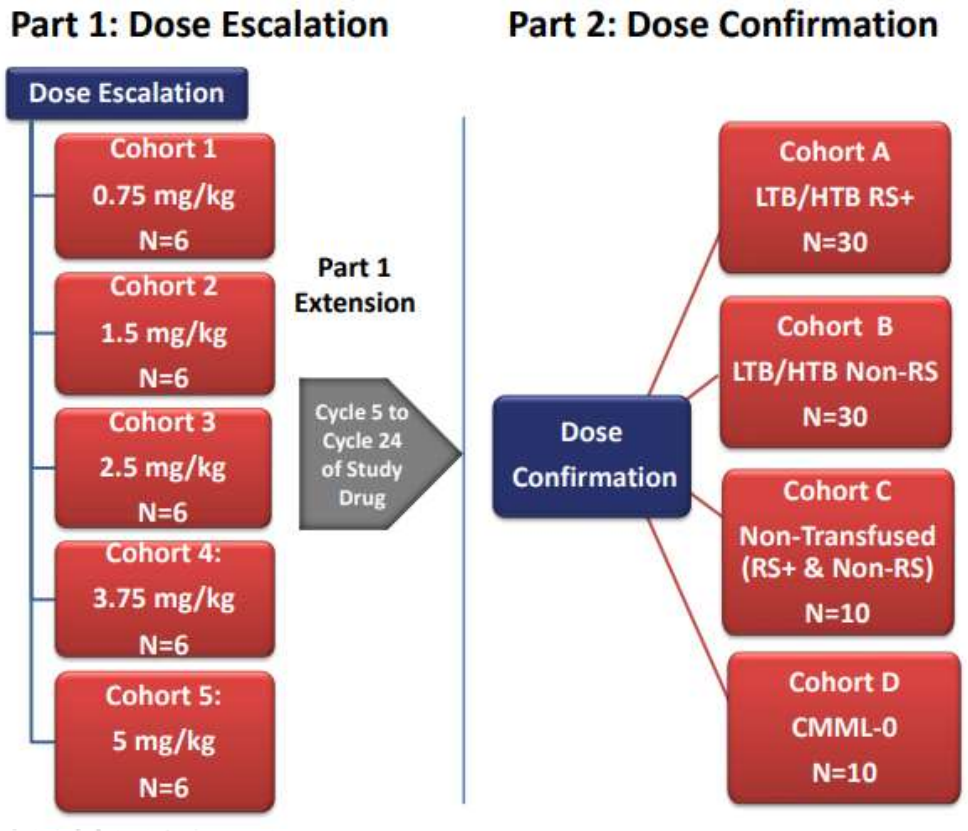
*p≤0.05,**p≤0.01,***p≤0.001,****p≤0.0001; WT = wild type; MF+VEH = MF mice with established anemia administered vehicle twice weekly for 12 weeks; MF+050 = MF mice with established anemia administered 10 mg/kg of RKER-050 twice weekly for 12 weeks; MkP = megakaryocyte progenitors

KER050-MD-201

A Phase 2 Clinical Trial Of KER-050 For The Treatment Of Anemia In Patients With Very Low, Low Or Intermediate Risk Myelodysplastic Syndromes (MDS)

MD-201: A Phase 2 Clinical Trial to Assess KER-050 in Low- to Intermediate-Risk MDS

Design and Dose Levels



- Primary Objective:
  - Assess safety and tolerability of KER-050
- Secondary Endpoints include:
  - Hematological Improvement- Erythroid (HI-E)
  - Transfusion Independence (TI) ≥8 weeks
- Ongoing Trial: Status as of April 3, 2023:
  - Part 1 Dose Escalation (N=31; completed)
  - RP2D: 3.75 mg/kg w/titration to 5 mg/kg/4 weeks
  - RP2D Experienced Patients: N=59
    - 25 patients from Part 1
    - 34 patients from Part 2

RP2D = Recommended Part 2 Dose

Data are presented as of a data cutoff date of April 3, 2023.

Enrolled Patient Population Included Difficult-to-Treat Patients With High Disease Burden

Parameter	RP2D (N=59)
Median Age, years (range)	74.0 (53-89)
Sex, n (%) Male	34 (57.6)
RBC Transfusion Status, units per 8 weeks, n (%)	
Non-transfused (NT), 0 units	12 (20.3)
Low Transfusion Burden (LTB), <4 units	16 (27.1)
High Transfusion Burden (HTB), ≥4 units	31 (52.5)
≥8 units	12 (20.3)
Ring Sideroblast Status, n (%)	
RS Positive	42 (71.2)
Non-RS	17 (28.8)
IPSS-R Risk Category, n (%)	
Very Low	8 (13.6)
Low	39 (66.1)
Intermediate	11 (18.6)
Missing	1 (1.7)
MDS WHO 2016 Classification, n (%)	
MDS	2 (3.4)
MDS-MLD	12 (20.3)
MDS-RS-MLD	29 (49.2)
MDS-RS-SLD	5 (8.5)
Missing	11 (18.6)
Prior ESA	13 (22.0)
Concurrent Iron Chelator	17 (28.8)

Data are presented as of a data cutoff date of April 3, 2023.

- Most required transfusions at baseline
  - Over half were high transfusion burden (HTB; ≥4 RBC units/8 wks)
  - Among HTB patients, 12/31 (38.7%) received ≥8 RBC units/8 wks
- Majority were ring sideroblast positive (RS+)
- Majority had multi-lineage dysplasia (MLD)

Opportunity to Evaluate Longer-Term Exposure to KER-050

Exposure of overall MDS RP2D Population as of the data cutoff date:

- 59 patients received ≥1 dose of KER-050 (included in safety population)
- Median duration of treatment = 225 days (≈32 weeks)
  - Range 6 to 649 days (≈1 to 93 weeks)
- Median doses received = 6
  - Range 1 to 22
    - 14 (23.7%) patients received ≥12 doses
    - 15 (25.4%) patients received <3 doses

Hematological response and markers of hematopoiesis are presented from exploratory analyses of RP2D patients with at least 6 months of KER-050 treatment or who have discontinued (n=37)

Data are presented as of a data cutoff date of April 3, 2023.

KER-050 Was Generally Well-Tolerated

- Most TEAEs were Grades 1 or 2 (51%)
- Most frequent TEAEs (in ≥15% of patients) regardless of causality were:
  - Fatigue, n=13 (22%)
  - Nausea, n=11 (18.6%)
  - Diarrhea, n=11 (18.6%)
  - Epistaxis, n=10 (16.9%)
  - COVID-19, n=9 (15.3%)
  - Dyspnea, n=9 (15.3%)
- Of the most frequent TEAEs, all were grade 1 or 2 except:
  - 1 Grade 3 (COVID-19)
  - 4 Grade 3 (Dyspnea)
- 1 treatment-related TESAE (Grade 2 Injection site reaction)
- 2 fatal TEAEs (cardiac failure and myocardial infarction); both determined to be unrelated to study treatment by the investigator
- No patients progressed to AML

Category	RP2D (N=59) n (%)
Any TEAE	53 (89.8)
Any treatment-related TEAE	19 (32.2)
Any TE serious AE (TESAE)	20 (33.9)
Any treatment-related TESAE	1 (1.7)
Any TEAE leading to death	2 (3.4)
Any TEAE leading to IMP Discontinuation[1]	6 (10.2)

[1] Related TEAEs leading to IMP discontinuation = injection site reaction; unrelated TEAEs = nodular melanoma, COPD and cardiac failure congestive (both in 1 patient), dyspnea, cardiac failure, and myocardial infarction

TEAE = Treatment Emergent Adverse Event
TESAE = Treatment Emergent Serious Adverse Event
IMP = Investigational Medicinal Product
AML = Acute Myeloid Leukemia

Data are presented as of a data cutoff date of April 3, 2023.

KER-050 Treatment Resulted in Hematological Response Across a Broad Population of Patients with Lower-Risk MDS

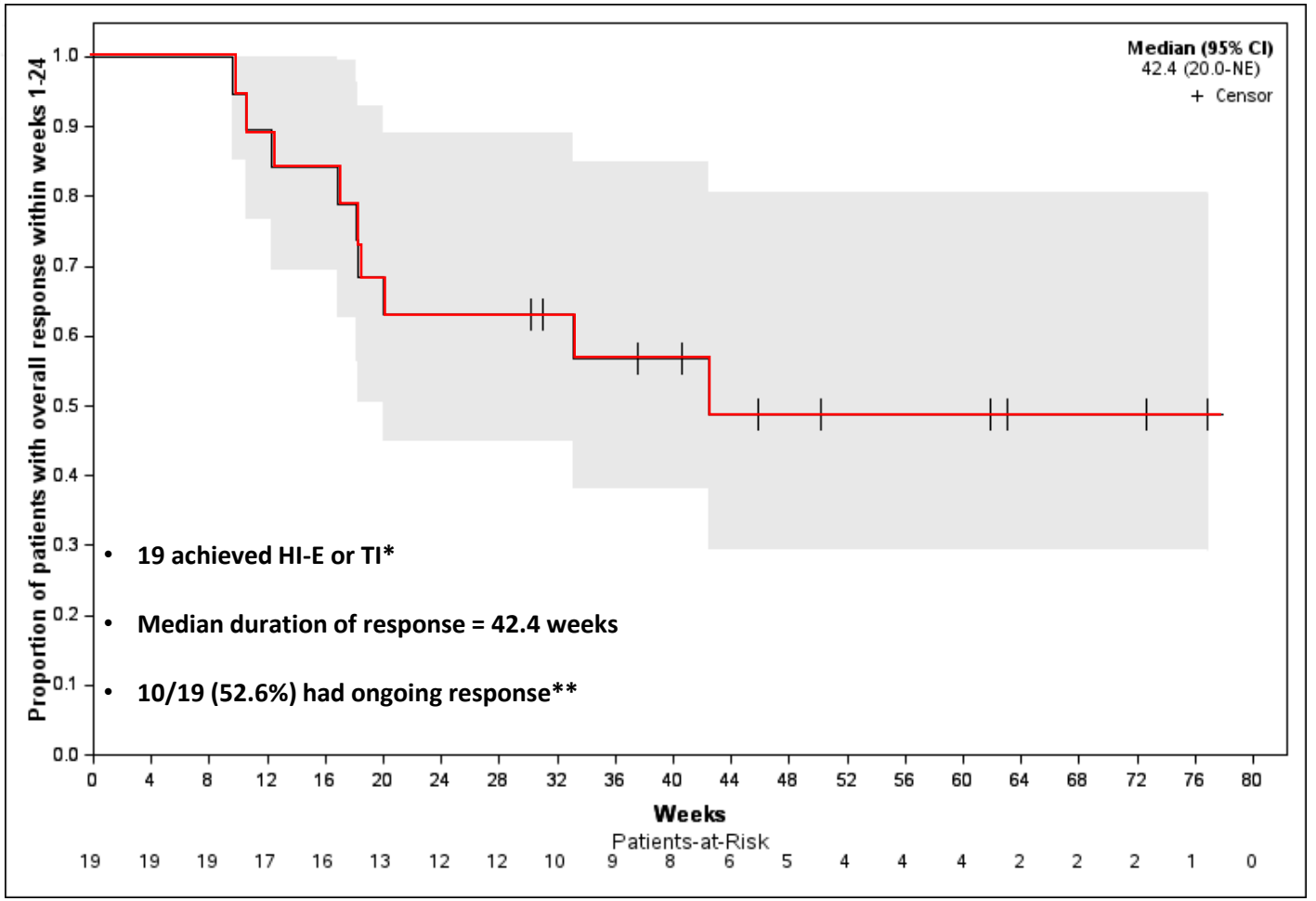
Response Endpoint	RP2D Patients[1]	
	All Evaluable	HTB Evaluable
Overall Erythroid Response (HI-E or TI)	19/37 (51.4)	11/22 (50)
IWG 2006 HI-E	19/37 (51.4)	11/22 (50)
TI ≥ 8 weeks[2] RS+ Non-RS	11/26 (42.3) 8/19 (42.1) 3/7 (42.9)	9/22 (40.9) 6/17 (35.3) 3/5 (60)

[1] Includes data for weeks 0-24 in RP2D patients with ≥24 weeks of treatment or who discontinued
[2] TI-evaluable patients received at least 2 RBC units in the 8 weeks prior to treatment initiation

- **Similar rates of HI-E and TI observed regardless of transfusion burden or RS status**
- **44.1%* of patients show a ≥30 x 10^9/L increase from baseline in platelet count sustained over at least 8 weeks**

*Percentage based on 34 patients who had at least 24 weeks of treatment or discontinued AND had both baseline and 8 weeks of post-baseline platelet data
Data are presented as of a data cutoff date of April 3, 2023.

Data Suggest KER-050 Elicited a Durable Response

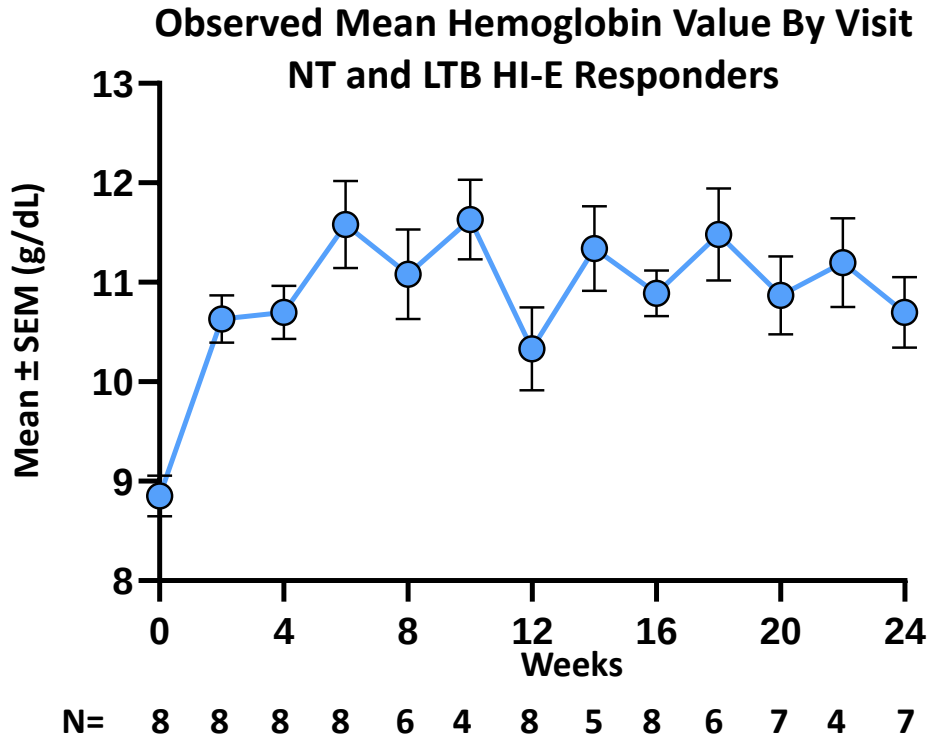


* During weeks 0-24 in RP2D patients with ≥24wk of treatment or who discontinued

**Patients with ongoing response censored at time of data cutoff, denoted by vertical lines

Data presented as of a data cutoff date April 3, 2023.

Sustained Increases in Hemoglobin Observed Over 6 Months of KER-050 Treatment

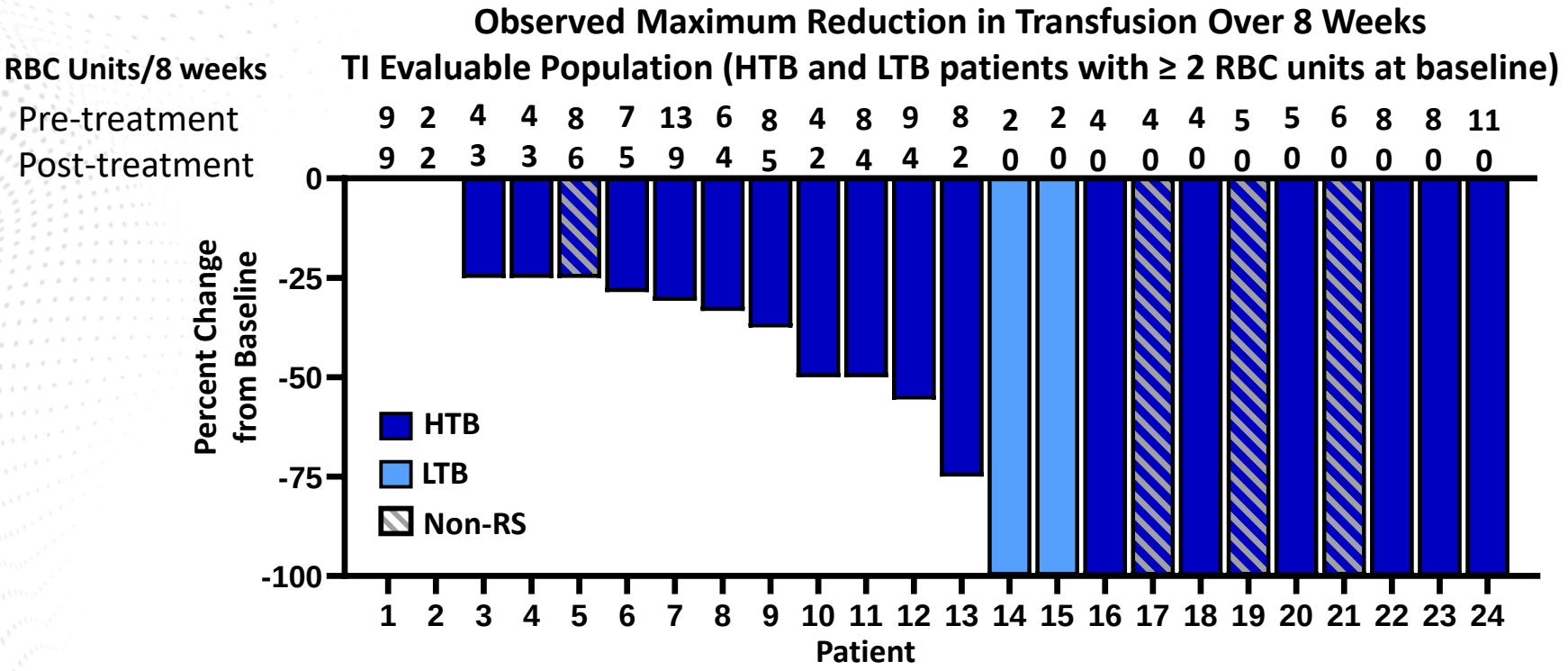


8/15 (53.3%) NT and LTB patients with ≥6 months of treatment (or discontinued) achieved HI-E response in first 24 weeks of treatment

Observed sustained increases in hemoglobin support durable response with KER-050

Data are presented as of a data cutoff date of April 3, 2023. Baseline hemoglobin calculated as average over 8-week pre-treatment period. Hemoglobin values within 14 days following a transfusion censored except for pre-transfusion values. Per protocol, KER-050 dose must be held at hemoglobin levels ≥12 g/dL.

Reductions in Transfusion Burden Observed with KER-050 Treatment



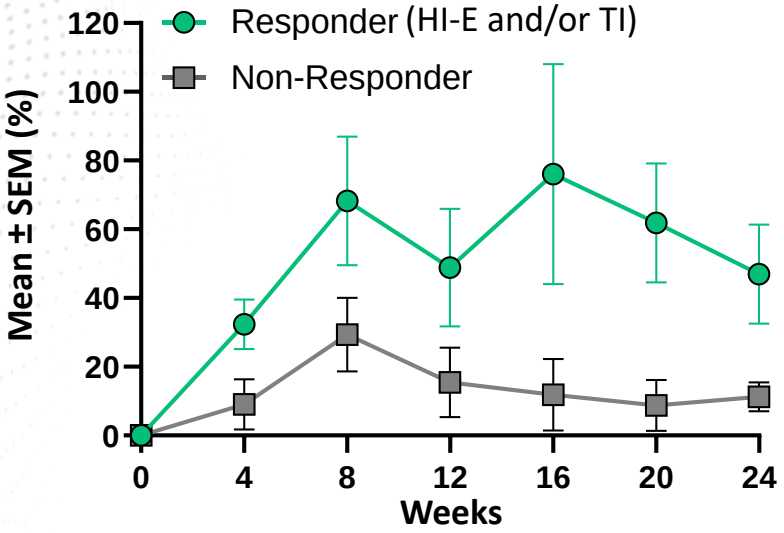
- Reduced transfusion burden observed in majority of LTB and HTB patients
- TI observed in both RS+ and non-RS patients
- TI achieved in patients with baseline transfusion burden ranging from 2 to 11 units/8 weeks

Data are presented as of a data cutoff date of April 3, 2023.

Note: 2 patients discontinued with insufficient data to determine 8-week transfusion reduction, and are not included in this plot

Data Suggest Enhanced Erythropoiesis and Potential to Reduce Iron Overload

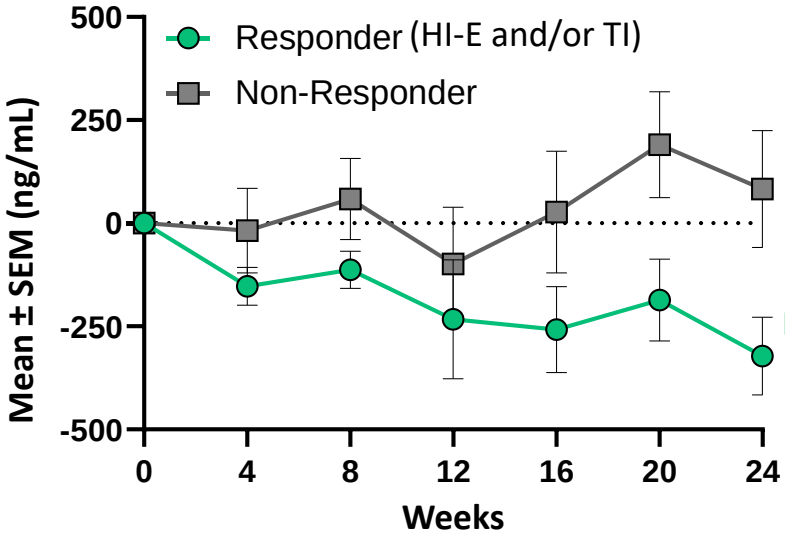
Observed Percent Change from Baseline In Soluble Transferrin Receptor (sTfR)



N=							
Responder (HI-E and/or TI)	19	16	10	16	11	17	15
Non-Responder	17*	15	7	11	7	9	7

*One patient was missing a baseline sTfR assessment.

Observed Change from Baseline In Ferritin



Mean Δ at week 24
-322 ng/mL

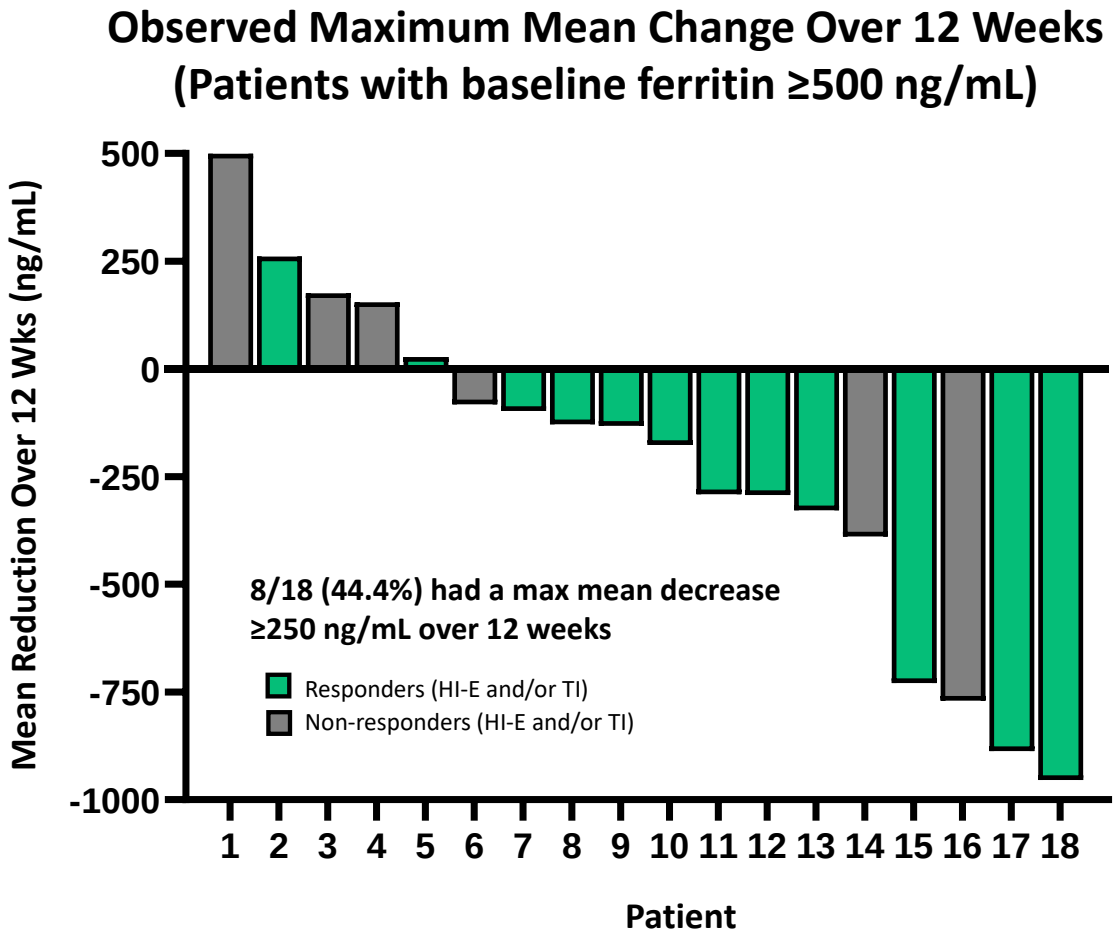
N=							
Responder (HI-E and/or TI)	19	17	17	17	18	17	16
Non-Responder	18	17	14	13	13	11	9

Data are presented as of a data cutoff date of April 3, 2023.

Observed Reductions in Serum Ferritin with KER-050 Treatment

Iron overload is a serious clinical complication in MDS

- A serum ferritin >1000 ng/mL is associated with 3x greater risk of death in MDS patients[1]
- Baseline ferritin in this analysis population (n=37):
  - Mean = 1026 ng/mL
  - Range = 86.3 to 5,829 ng/mL
  - 18 patients ≥500 ng/mL



[1]*A. Waszczuk-Gajda et al. 2016 Adv Clin Exp Med 25(4): 633-641*

Data are presented as of a data cutoff date of April 3, 2023.

Summary of KER-050 MDS Data

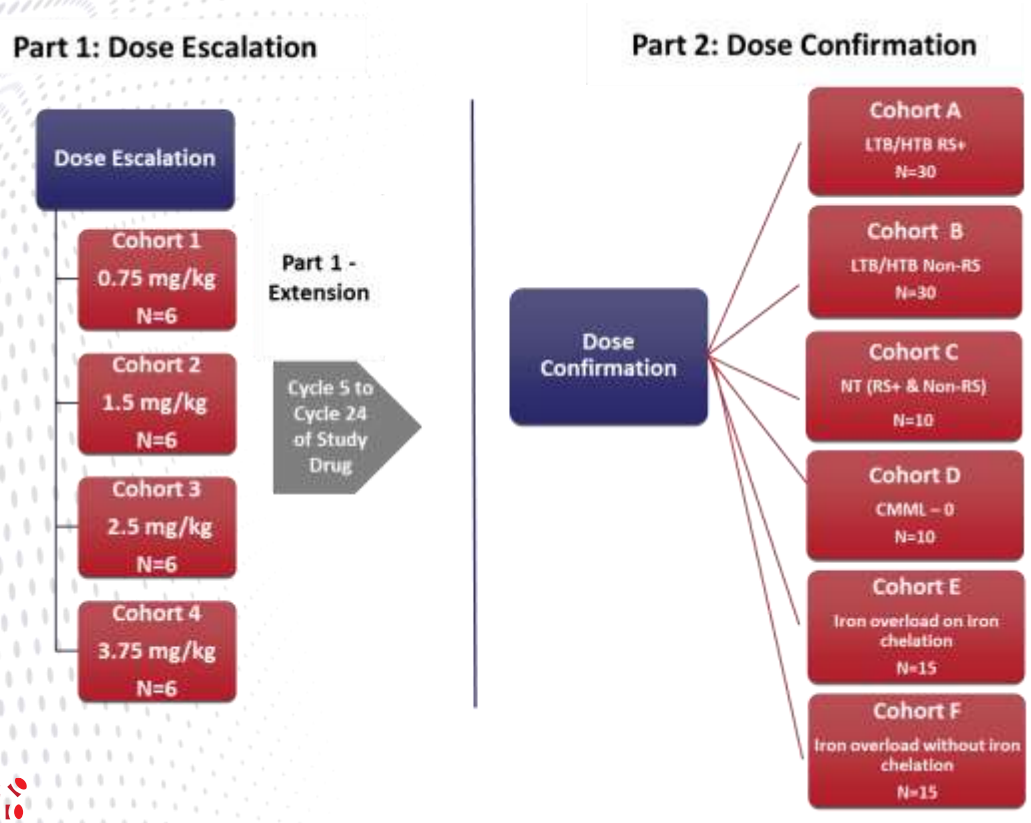
- KER-050 was generally well-tolerated; safety profile consistent to that previously reported for this trial
- Durable hematological responses were observed in a broad, lower-risk MDS population, including those with HTB and/or non-RS disease
- Observed decreases in serum ferritin, a marker of iron overload, may reflect:
  - Reduced iron overload due to reduced transfusion burden
  - Improved iron utilization with increased erythropoiesis

Data are presented as of a data cutoff date of April 3, 2023.

Phase 2 MDS Trial Amended to Evaluate KER-050 in Patients with Iron Overload

This trial has been expanded to include two cohorts of MDS patients with iron overload to further investigate the serum ferritin reductions observed as of the April 3, 2023 data cutoff date

Amended Phase 2 Clinical Trial Design and Dose Levels



- In lower-risk MDS patients, severe anemia and lack of effective treatment options leads to blood transfusions, often resulting in iron overload
  - This transfusional iron overload has negative consequences on hematopoiesis and cardiovascular health, and impacts progression to AML
- In MDS, patients that require 4 units of blood every 8 weeks will accumulate nearly 5 grams of iron in a year[1]
  - Typically, healthy adults have 3-4 grams of total body iron[2]
- Iron chelation therapy can reduce the degree of iron overload in patients, but its tolerability and safety profile limits its use in lower-risk MDS[3]

(1) 1 unit of RBC contains ~200 mg of iron; (2) Kohgo, 2008. International Journal of Hematology; and (3) Shah, 2016. J. Adv. Pract. Oncol.

Additional Hematology Program Updates

- **KER-050: Myelofibrosis**
  - This open label, two-part, multiple ascending dose Phase 2 clinical trial to evaluate KER-050 as a monotherapy and in combination with ruxolitinib in patients with myelofibrosis-associated cytopenias is ongoing
    - Following Safety Review Committee recommendation, dosing for Cohort 3 was initiated at 3.0 mg/kg in both combination and monotherapy arms
- **KER-047: Iron-refractory iron deficiency anemia (IRIDA)**
  - Our open label, two-part, dose-escalation and dose-expansion Phase 2 clinical trial to evaluate KER-047 in patients with IRIDA was originally planned to enroll 12 patients in a single center
    - In December 2022, we announced data from the one enrolled patient, which demonstrated the impact of KER-047 in reducing serum hepcidin and serum ferritin with observed increases in serum iron. This supports our hypothesized mechanism of action for KER-047 and will guide further development in this pathway
    - Difficulties with enrollment of this trial, given the small size of the patient population for this rare disease
    - We have decided to terminate this trial early, having observed data in the one patient enrolled that we believe is suggestive of proof of mechanism. The planned early termination is not on the basis of any safety concerns

Keros Anticipated Key Milestones

KER-050

• Complete enrollment in transfusion-dependent cohorts in Phase 2 MDS trial	H2 2023
• Announce additional data from Part 2 of Phase 2 MDS trial	H2 2023
• Announce dose escalation data from Phase 2 MF trial	H2 2023
• Initiate Part 2 of Phase 2 MF trial	H2 2023

KER-047

• Announce initial data from Phase 2 FID (MDS and MF) trial	H2 2023

KER-012

• Initiate Phase 2 PAH trial	H1 2023
• Initiate Phase 2 open-label biomarker trial	H2 2023

Q&A