



EUROPEAN
HEMATOLOGY
ASSOCIATION

Administration of KER-050, A Novel ACTRIIA Ligand Trap, To Healthy Participants Elicited Robust and Sustained Increases in Hemoglobin and Platelets

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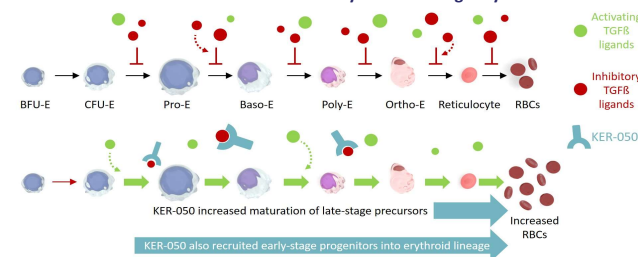
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INTRODUCTION

- Members of the TGF- β family of proteins have been shown to regulate multiple blood cell lineages.
- KER-050, a novel activin type 2A receptor (ActRIIA) ligand trap comprised of a modified ActRIIA extracellular domain fused to the Fc of a human IgG, is designed to inhibit GDF8, GDF11, activin A, and activin B thereby reducing SMAD 2/3 activation and resulting in increased red blood cell (RBC) production.
- In mice, a research form of KER-050 has been shown to affect both early and late stage maturation, resulting in increases in RBCs, hematocrit (Hct), hemoglobin (Hgb), and reticulocytes. **Visit poster EP786 for more information.**
- The objective of this Phase 1 study was to evaluate the safety, tolerability, pharmacokinetics (PK), and pharmacodynamic (PD) effects of ascending dose levels of KER-050 in healthy post-menopausal women.

KER-050 Has Been Shown to Affect Both Early and Late Stage Erythroid Maturation



OBJECTIVE & METHODS

Primary objectives: safety, tolerability, PK

Secondary objectives: PD hematology and bone biomarkers

Total of 48 healthy post-menopausal women enrolled

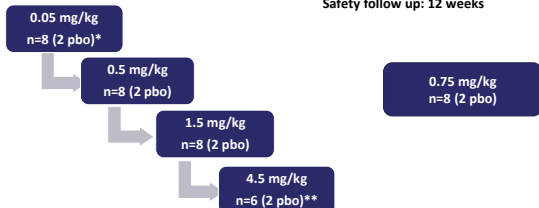
- 38 in Part 1 – 30 KER-050 and 8 placebo, single dose

- 10 in Part 2 – 8 KER-050 and 2 placebo, two doses 28 days apart

Part 1: Single Ascending Dose

Treatment: Single subcutaneous dose

Safety follow up: 12 weeks



* 1 subject in placebo group discontinued prematurely (withdrew consent)

** 10 subjects planned; enrollment stopped at 8 after seeing robust effects in Hgb

Part 2: Multiple Ascending Dose

Treatment: Two subcutaneous doses

(28 days apart)

Safety follow up: 12 weeks

RESULTS: SAFETY

- KER-050 was well tolerated at dose levels up to 4.5 mg/kg
- While one subject in placebo group withdrew consent, there were no discontinuations due to treatment-related adverse events
- No treatment-related serious adverse events were reported
- Adverse events (AE) in all KER-050 treatment groups were mild to moderate in severity
- Of the most common AE observed increased hemoglobin and hypertension are consistent with the mechanism of action of KER-050
- Reversible, mild hypertension events observed in subjects with approximately 3 g/dL increase in Hgb

AEs Occurring in ≥ 2 Subjects in SAD n(%)

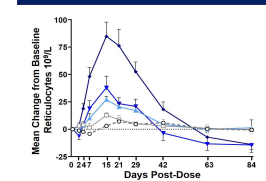
	Pbo	0.05 mg/kg	0.5 mg/kg	1.5 mg/kg	4.5 mg/kg	Overall
Hgb increased				4 (50.0)	4 (66.7)	8 (21.1)
Headache	2 (25.0)	1 (12.5)	1 (12.5)	1 (12.5)	2 (33.3)	7 (18.4)
URT infection	2 (25.0)	1 (12.5)		2 (25.0)	1 (16.7)	6 (15.8)
Hypertension					4 (66.7)	4 (10.5)
Nausea		1 (12.5)	3 (37.5)			4 (10.5)
Influenza like illness		1 (12.5)	1 (12.5)	1 (12.5)		3 (7.9)
Vomiting		1 (12.5)	2 (25.0)			3 (7.9)
Cough	1 (12.5)		1 (12.5)			2 (5.3)
Influenza	1 (12.5)	1 (12.5)				2 (5.3)
Toothache				2 (25.0)		2 (5.3)
Viral URTI				1 (12.5)	1 (16.7)	2 (5.3)

AEs Occurring in ≥ 2 Subjects in MAD n(%)

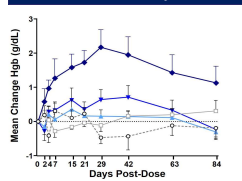
	Placebo	0.75 mg/kg	Overall
Headache	2 (100)	7 (87.5)	9 (90)
Increased Hgb		4 (50)	4 (40)
Gastroenteritis		3 (37.5)	3 (30)
Injection site erythema		3 (37.5)	3 (30)
Catheter site pain	1 (50)	1 (12.5)	2 (20)
Dizziness	1 (50)	1 (12.5)	2 (20)

RESULTS: PHARMACOKINETICS AND PHARMACODYNAMICS

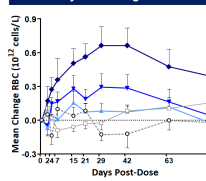
Rapid Increase in Reticulocytes Potentially Indicative of Effect on Terminal Differentiation



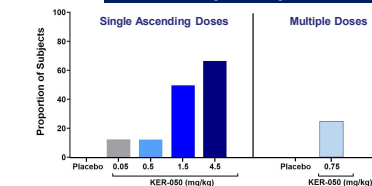
Increases in Hgb Beyond Day 15 Potentially Indicative of Effect on Early Precursors



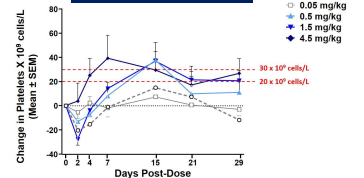
Change in RBC Durable for up to 84 Days After Single Dose*



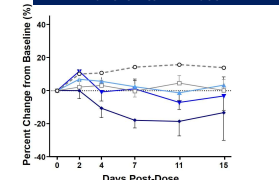
Proportion of Subjects with Change in Hemoglobin ≥ 1.5 g/dL



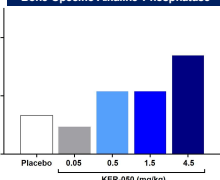
Clinically Meaningful Increases from Baseline in Platelets



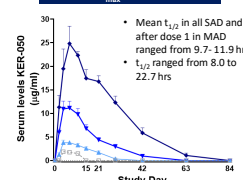
Decreased FSH Levels: A Pharmacodynamic Marker of Activin Inhibition



Maximum % Change from Baseline in Bone Specific Alkaline Phosphatase



Dose Proportional Increases in C_{max} and AUC**



CONCLUSIONS

- KER-050, a novel activin type 2A receptor (ActRIIA) ligand trap, has been shown in mice to affect both early and late stage maturation.
- Administration of KER-050 to healthy participants was well-tolerated and had a favorable safety profile.
- KER-050's differentiated pharmacologic effects on RBCs and platelets have the potential to treat multiple cytopenias.
- Robust and sustained increases observed in RBCs, Hgb and reticulocytes that potentially support the dual mechanism of promoting early and late stages erythropoiesis.
- Clinically meaningful increase observed in platelets after a single dose, which we believe differentiates KER-050 from other agents that only affect RBCs.
- KER-050's effect on follicle-stimulating hormone are indicative of activin inhibition.
- KER-050's effect on bone-specific alkaline phosphatase indicates potential effect to increase bone mass.
- The half-life coupled with the PD effect observed in the hematologic parameters support the potential for administration of monthly or less frequent dosing, which we believe will decrease the burden on patients and improve compliance.
- Planning Phase 2 trials in diseases that arise from ineffective hematopoiesis:
 - Myelodysplastic syndromes (expect to initiate Phase 2 trial in 2H2020)
 - Myelofibrosis (expect to initiate Phase 2 trial in 2021)

ACKNOWLEDGEMENTS

We would like to thank the research participants, Dr. Ben Snyder (Principal Investigator, Nucleus Network, Melbourne Australia) and Dr. Jana Baskar (Medical Director, Australia and New Zealand, IQVIA).

REFERENCES

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CONTACT INFORMATION

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*This graph has been updated as of April 2021 to appropriately label the y-axis.

**This graph has been updated as of February 2021 to appropriately identify the dose levels.