ELSEVIER

Blood 142 (2023) 6994–6996

The 65th ASH Annual Meeting Abstracts

ONLINE PUBLICATION ONLY

722.ALLOGENEIC TRANSPLANTATION: ACUTE AND CHRONIC GVHD, IMMUNE RECONSTITUTION

Preliminary Safety Results of the Open-Label Phase of a 2-Part Phase 1b Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Efficacy of an Investigational Microbiome Therapeutic, SER-155, in Adults Undergoing Hematopoietic Cell Transplantation

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Background: In patients undergoing allogeneic hematopoietic cell transplantation (allo-HCT), low gastrointestinal (GI) microbial diversity is associated with risk of bloodstream infections (BSIs), acute graft-versus-host disease (aGvHD), and death. SER-155 is an investigational cultivated microbiome therapeutic rationally designed to improve clinical outcomes in allo-HCT patients by preventing pathogen domination, promoting epithelial barrier integrity, and reducing colonic inflammation. SER-155-001 is a 2-part, Phase 1b study evaluating the safety, tolerability, pharmacokinetics, and efficacy of SER-155 in adults undergoing allo-HCT. Here, we present preliminary safety and tolerability data from the open-label Cohort 1 through Day 100 post HCT.

Study Design and Methods: Adult recipients of allo-HCT were eligible for screening. Patients were excluded if they: a) were planned for umbilical cord blood or ex vivo T-cell depletion, b) had received a fecal microbiota transplant or any live biotherapeutic product within 3 months prior to screening, and/or c) had evidence of relapse or progression of hematologic malignancy (minimal residual disease was allowed). HCT conditioning and aGvHD prophylaxis were per investigator discretion.

Following screening, patients received two treatment courses (before conditioning and after neutrophil engraftment) comprised of microbiome conditioning with 4 days of oral vancomycin (to facilitate engraftment of SER-155 strains) followed by 10 days of oral SER-155 (see study design schematic, **Figure 1**). The primary endpoint was the incidence and severity of adverse events (AEs), serious adverse events (SAEs), and adverse events of special interest (AESIs), designated as invasive infection, BSI, and GI infection.

Results:

Fifteen adult patients were enrolled and 13 received study drug (safety population). Of these 13 patients, the median age was 67.0, all were White, and 54% were male. Underlying diseases included acute myeloid leukemia (6 patients [46.2%]); myelodysplastic syndromes and myeloproliferative neoplasms (2 patients each [15.4%]; and acute lymphoblastic leukemia, chronic myeloid leukemia, and classic Hodgkin's lymphoma (1 patient each [7.7%]). Ten patients (76.9%) received peripheral blood stem cells; 9 (69.2%) had an unrelated donor, 8 (61.5%) underwent a reduced-intensity conditioning regimen, and 3 (23.1%) received myeloablative conditioning. Eleven patients received allo-HCT, all patients had neutrophil engraftment within the expected timeframe and 10 had 100-day follow-up data available. Nine of these patients (81.8%) received tacrolimus/methotrexate-based GvHD prophylaxis.

SER-155 was generally well-tolerated (**Table 1**). Treatment-emergent AEs (TEAEs) were observed in all patients as is expected in this patient population. One TEAE considered unrelated to study drug, resulted in study discontinuation. Most AEs were gastrointestinal in nature with diarrhea being the most common AE. No SAEs were considered related to SER 155, and most SAEs and AESIs occurred after HCT and before starting the second course of SER-155. No deaths occurred prior to Day 100. Three deaths occurred after Day 100, all deemed to be unrelated to study drug by the investigators. No BSIs attributable to organisms in SER-155 occurred.

Commencement of the double-blind, randomized, placebo-controlled Cohort 2 (n=60) was initiated following approval of the Data Safety Monitoring Committee.

Conclusions: In patients enrolled in this open-label Cohort 1 of this Phase 1b study, SER-155 was well-tolerated through Day 100. Although sample size is limited, the observed safety and tolerability profile of SER-155 in this patient population is consistent with multiple preclinical assessments supporting the safety of SER-155 for therapeutic use. Enrollment in the double-blind, randomized, placebo-controlled second cohort to assess safety, efficacy, and changes in microbiome composition and function is ongoing.

Disclosures Ponce: *Ceramedix:* Membership on an entity's Board of Directors or advisory committees; *Incyte Corporation:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *Kadmon/Sanofi Pharmaceuticals:* Membership on an entity's Board of Directors or advisory committees; *Evive Biotechnology:* Membership on an entity's Board of Directors or advisory committees. **Khera:** *Incyte:* Honoraria. **Defilipp:** *Incyte:* Consultancy, Research Funding; *Regimmune:* Research Funding; *Taiho Oncology:* Research Funding; *Sanofi:* Consultancy; *MorphoSys:* Consultancy; *Inhibrx:* Consultancy; *PharmaBiome AG:* Consultancy; *Ono Pharmaceutical:* Consultancy. **Lichter:** *Seres Therapeutics:* Current Employment, Current equity holder in publicly-traded company. **Peled:** *Seres Therapeutics:* Other: travel fees, Patents & Royalties: Intellectual property fees, Research Funding; *DaVolterra:* Consultancy; *CSL Behring:* Consultancy; *MaaT Pharma:* Consultancy; *Probiotics Plus Research:* Current equity holder in publicly-traded company, Membership on an entity's Board of Directors or advisory committees. **van den Brink:** *Lygenesis:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees; *Rheos Medicines:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees; *Seres Therapeutics:* Consultancy, Current holder of *stock options* in a privately-held company, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: IP licensing , Research Funding; *Thymofox:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees; *Vor Biopharma:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees; *Juno Therapeutics:* Other: IP licensing; *Wolters Kluwer:* Patents & Royalties; *Notch Therapeutics:* Consultancy, Current holder of *stock options* in a privately-held company, Honoraria, Membership on an entity's Board of Directors or advisory committees; *Nektar Therapeutics:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees; *Frazier Healthcare Partners:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees; *Pluto Immunotherapeutics:* Consultancy, Current holder of *stock options* in a privately-held company, Honoraria, Membership on an entity's Board of Directors or advisory committees; *DKMS (a non-profit organization):* Membership on an entity's Board of Directors or advisory committees; *Ceramedix:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees; *GlaxoSmithKline:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees; *Da Volterra:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees. **Brady:** *Seres Therapeutics:* Current Employment, Current equity holder in publicly-traded company. **Puhl:** *Seres Therapeutics:* Current Employment, Current equity holder in publicly-traded company. **Glick:** *Seres Therapeutics:* Current Employment, Current equity holder in publicly-traded company. **Hasson:** *Seres Therapeutics:* Current Employment, Current equity holder in publicly-traded company; *Sage Therapeutics:* Current equity holder in publicly-traded company. **McGovern:** *Seres Therapeutics:* Current Employment, Current equity holder in publicly-traded company. **von Moltke:** *Cara Therapeutics:* Current equity holder in private company, Membership on an entity's Board of Directors or advisory committees; *Seres Therapeutics:* Current Employment, Current equity holder in publicly-traded company. **Tejura:** *Seres Therapeutics:* Current Employment, Current equity holder in publicly-traded company.

https://doi.org/10.1182/blood-2023-180119

Figure 1. Per Protocol Study Design of the Open-Label Phase (Cohort 1) of SER-155-001

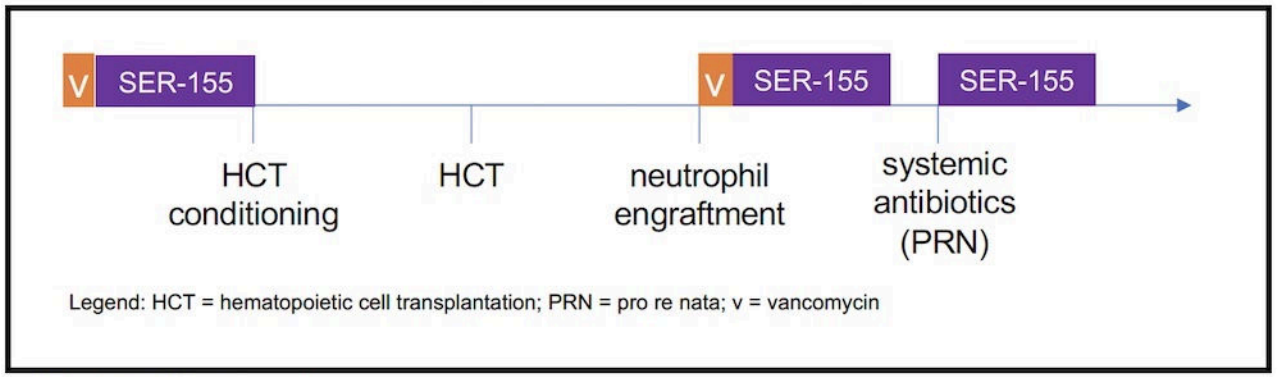

Table 1. Safety Overview

Patients with ≥1 Event	Analysis Period				
	Short-Term Safety Follow-Up Period (through Day 100 post HCT)				
	Initiation of Study Drug Course 1 to Initiation of Study Drug Course 2				
	Prior to Conditioning HCT	During Conditioning HCT*	HCT to Study Drug Course 2*	Total	
	SER-155 N=13 n (%)	SER-155 N=11 n (%)	SER-155 N=11 n (%)	SER-155 N=13 n (%)	SER-155 N=13 n (%)
TEAEs	8 (61.5)	9 (81.8)	11 (100)	13 (100)	13 (100)
Vancomycin Related TEAEs	2 (15.4)	0	0	2 (15.4)	3 (23.1)
SER-155 Related TEAEs	3 (23.1)	0	0	3 (23.1)	4 (30.8)
Treatment Related TEAEs	3 (23.1)	0	0	3 (23.1)	4 (30.8)
Serious TEAEs	0	0	4 (36.4)	4 (30.8)	6 (46.2)
Treatment-emergent AESIs	0	0	6 (54.5)	6 (46.2)	6 (46.2)
Grade 3 or higher TEAEs	1 (7.7)	3 (27.3)	8 (72.7)	9 (69.2)	10 (76.9)
TEAEs Leading to Study Discontinuation	1 (7.7)	0	0	1 (7.7)	1 (7.7)
TEAEs Leading to Death	0	0	0	0	0

Abbreviations: AE=adverse event; AESI=adverse event of special interest; HCT=hematopoietic stem cell transplantation; N=number of subjects who received a specific treatment for the specific period; n=number of subjects with adverse events; TEAE=treatment-emergent adverse event
* Patients who received study drug and underwent HCT.

Figure 1