Safety and Efficacy Results from a Randomized, Double-blind, Placebo-controlled Cohort 2 of a Phase 1b Study of an Investigational Live Biotherapeutic, SER-155, in Adults Undergoing allo-HCT

Ponce MD, MS[1], S. Kosuri MD[2], N. Khera MD, MPH[3], H.S. Murthy MD[4], D. Fredricks MD, FACP, FIDSA[5], K. S. Sandhu MD[6], R. Nath MD[7], N. Farhadfar MD[8], W.J. Hogan MB, BCh[9], S. Tsai MD, PhD[10], T. Andermann MD, MPH[11], D. M. Walling MD, MMCI[12], D. I. Lichter ALM[12], K. Brady MS[12], J. Colabella MS[12], C. Patel[12], B. Hasson PhD[12], K. Ford MS[12], N. Hicks PhD[12], M. Chafee PhD[12], S. Sykes ALM[12], E. Walsh PhD[12], M-J Lombardo PhD[12], C. Ford PhD[12], B. Tejura MD[12], M. Henn PhD[12], L. von Moltke MD[12], M.R.M. van den Brink MD, PhD[1], J.U. Peled MD, PhD[1] and Z. DeFilipp MD[13]

[1] Adult Bone Marrow Transplantation Service, Memorial Sloan Kettering Cancer Center, New York, NY and Weill Cornell Medical College, New York, NY; [2] University of Chicago Medicine, Chicago, IL; [3] Mayo Clinic, Scottsdale, AZ; [4] Mayo Clinic Florida, Division of Hematology-Oncology, Jacksonville, FL; [5] Fred Hutchinson Cancer Center, Seattle, WA; [6] City of Hope National Medical Center, Duarte, CA; [7] Banner Health – MD Anderson Cancer Center, Gilbert, AZ; [8] University of Florida, Division of Hematology & Oncology, Gainesville, FL; [9] Mayo Clinic, Rochester, MN; [10] University of California Los Angeles (UCLA), Division of Hematology-Oncology, Los Angeles, CA; [11] University of North Carolina at Chapel Hill, Division of Infectious Diseases, Chapel Hill, NC; [12] Seres Therapeutics, Cambridge, MA; [13] Hematopoietic Cell Transplant and Cellular Therapy Program, Massachusetts General Hospital, Boston, MA

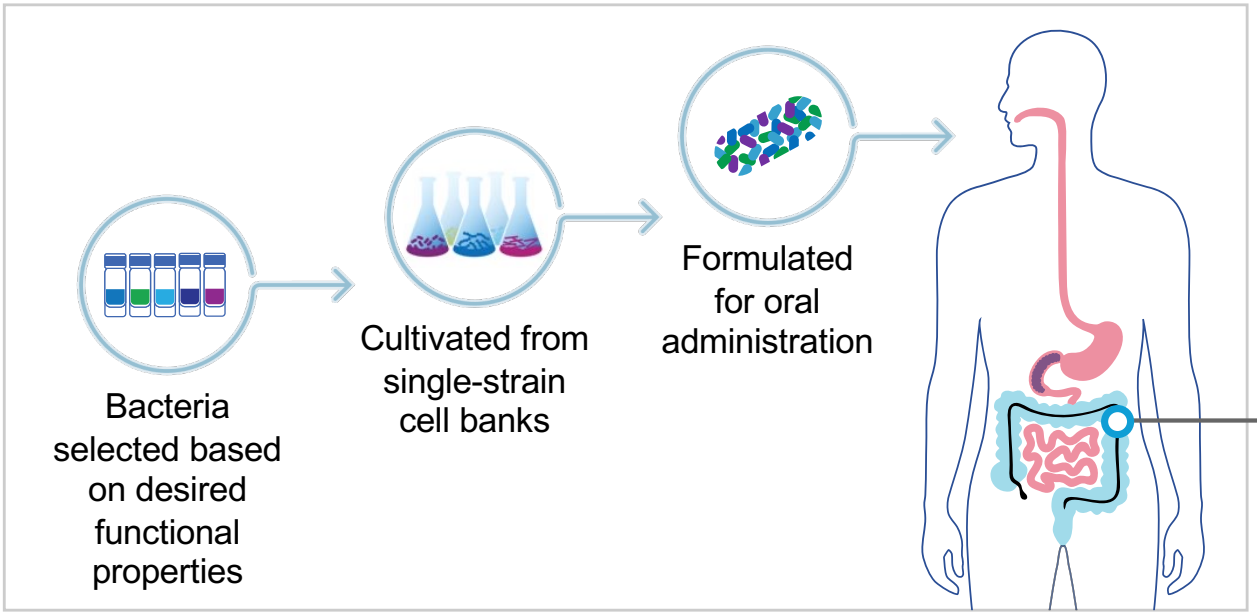
Disclosure statement

Doris M. Ponce, MD, MS

Consultant: Seres Therapeutics, Incyte, Sanofi, Evive, OncLive
Advisory Committee Member: Seres Therapeutics, Incyte, Sanofi
Research funding: Seres Therapeutics, Incyte, Sanofi

This Study was Sponsored by Seres Therapeutics

SER-155 is an Investigational, Cultivated Multi-Strain Bacterial Live Biotherapeutic Comprised of 16 Unique Human-Commensal Strains Encapsulated for Oral Use

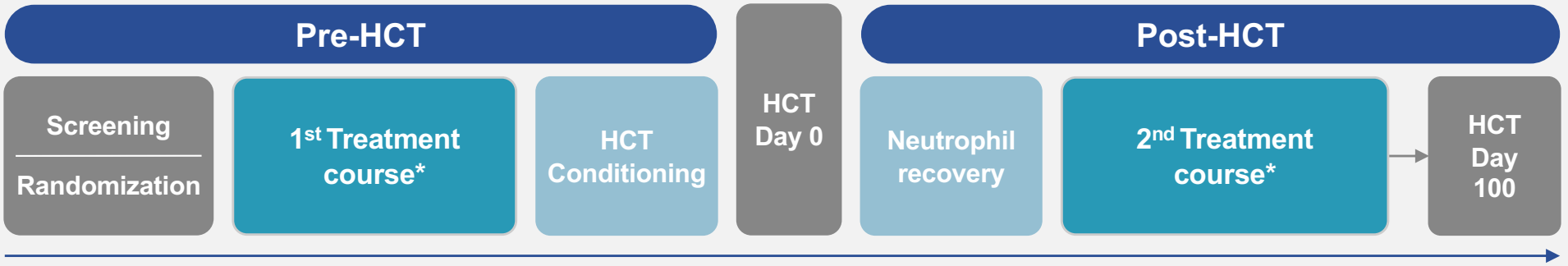


SER-155 strains selected to engraft in patients undergoing allo-HCT to reduce risk of BSI by:

- Inhibiting GI pathogens
- Promoting mucosal & epithelial barrier integrity
- Driving anti-inflammatory immune responses

U.S. FDA granted Breakthrough Therapy designation to SER-155 for reduction of BSIs in adults undergoing allo-HCT (December 2024)

SER-155-001: Randomized, Placebo-Controlled Design



Primary Endpoints

- Safety and tolerability evaluated through 6 months post-HCT
- SER-155 bacterial strain engraftment (PK)

Secondary Endpoints through HCT Day 100 ‡

- Incidence of BSIs
- Incidence of febrile neutropenia
- Incidence of acute GvHD ≥ Grade 2 (MAGIC criteria)
- Incidence of GI infections

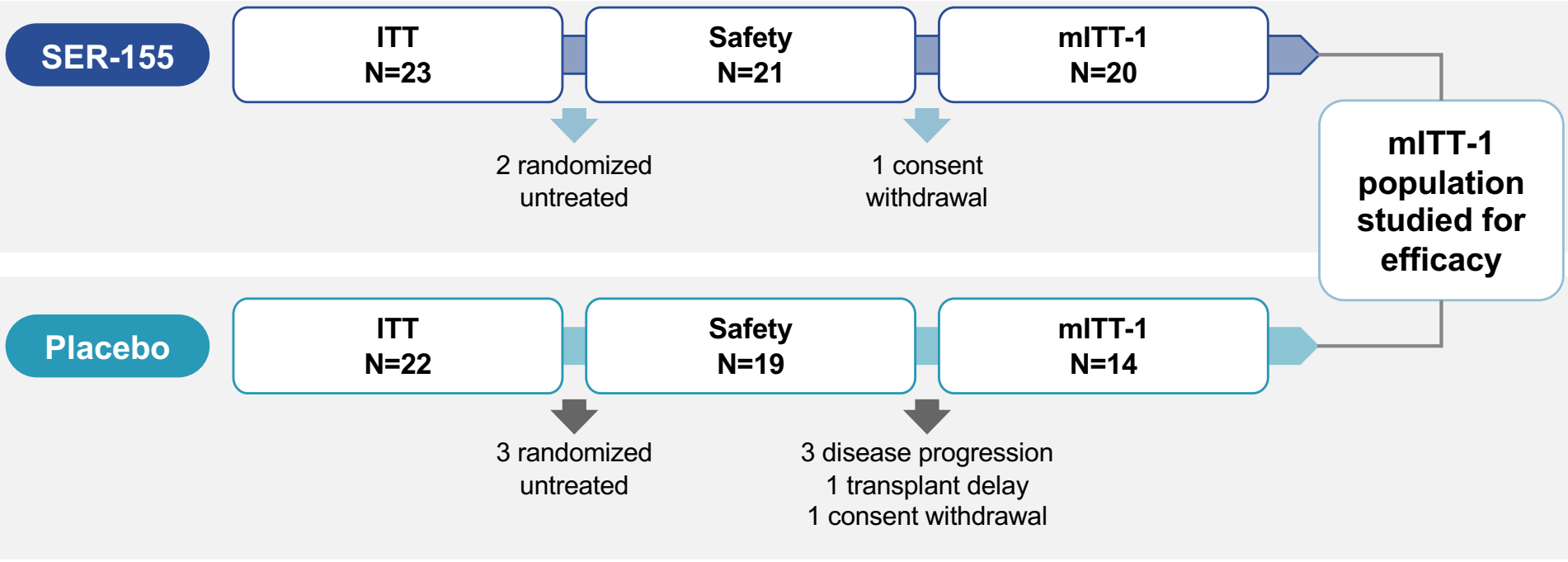
Exploratory Endpoints through HCT Day 100 ‡

- Antibacterial / antimycotic utilization
- Hospital utilization

*Oral vancomycin (125 mg, 4x daily for 4 days) / SER-155 (once daily for 10 days) or placebo/placebo

‡ Study was not powered for efficacy endpoints; no analyses were adjusted for multiplicity

Participant Disposition (N=45)



ITT (intent-to-treat): All enrolled participants

Safety: All participants who received any amount of study drug

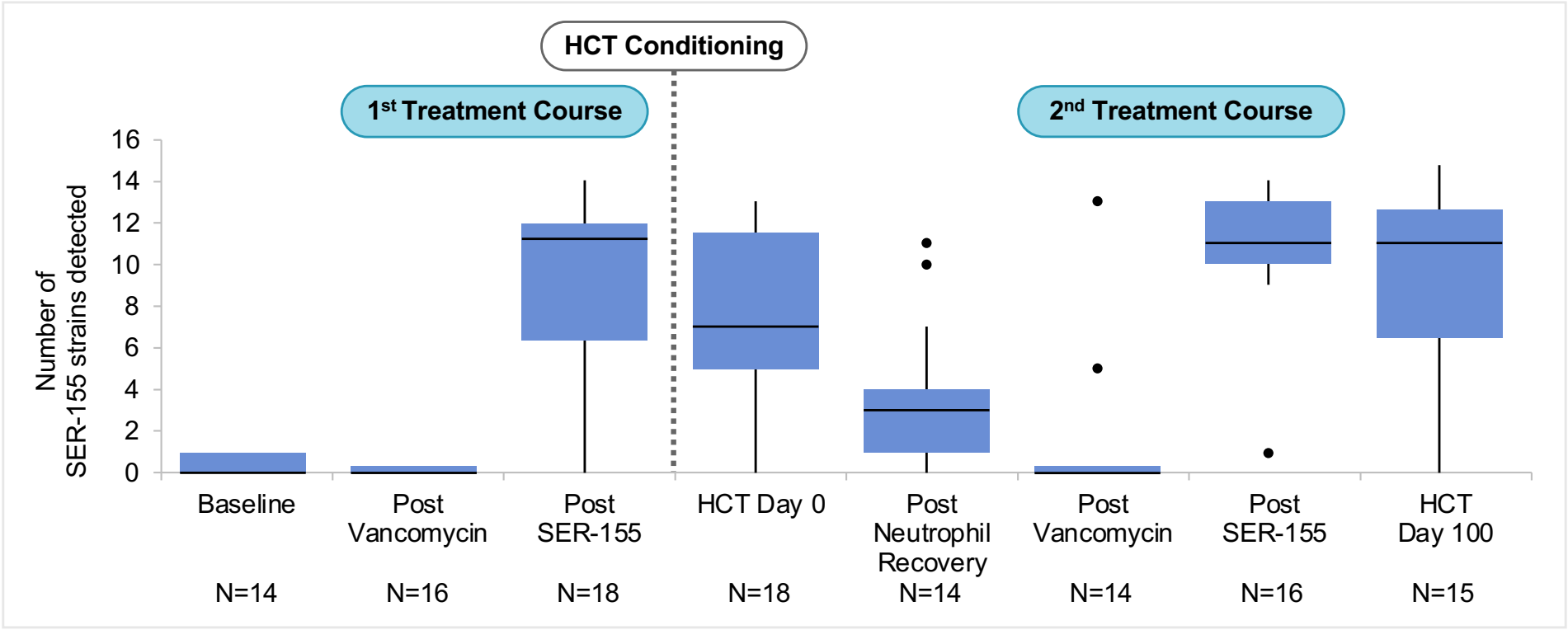
mITT-1 (modified intent-to-treat 1): All participants who received study drug in 1st course and underwent HCT

Demographics of Participants Who Received HCT are Representative of allo-HCT Patients and Mostly Balanced Between Arms

	SER-155 N=20	Placebo N=14	Total N=34
Age, years; Median (min, max)	62.5 (23, 75)	61.0 (25, 78)	**62.0 (23, 78)**
Sex: Male, n (%)	9 (45)	9 (64)	**18 (53)**
Race: White, n (%)	17 (85)	12 (86)	**29 (85)**
Disease diagnosis, n (%)			
AML	7 (35)	3 (21)	**10 (29)**
MDS	4 (20)	0	**4 (12)**
Myeloproliferative Neoplasms	1 (5)	4 (29)	**5 (15)**
ALL	3 (15)	3 (21)	**6 (18)**
CML	1 (5)	1 (7)	**2 (6)**
CLL	1 (5)	0	**1 (3)**
Other	3 (15)	3 (21)	**6 (18)**
Graft Source: Peripheral blood, n (%)	18 (90)	13 (93)	**31 (91)**
Stem cell donor source			
HLA-matched unrelated	13 (65)	7 (50)	**20 (59)**
HLA-matched related	4 (20)	3 (21)	**7 (21)**
Haploidentical related	2 (10)	3 (21)	**5 (15)**
HLA 1-antigen mismatched unrelated or related donor	1 (5)	1 (7)	**2 (6)**
HCT conditioning regimen: n (%)			
Reduced intensity	16 (80)	11 (79)	**27 (79)**
Myeloablative	3 (15)	3 (21)	**6 (18)**
Non-myeloablative	1 (5)	0	**1 (3)**
GvHD prophylaxis: PTCy-based	14 (70)	13 (93)	**27 (79)**

SER-155 Pharmacokinetics: Majority of SER-155 Strains Engrafted in the Majority of Participants

SER-155 Pharmacology: ePoster #A178 Infectious Complications



SER-155 was Generally Well-Tolerated

Participants with at Least One…	SER-155 N=21 (n%)	Placebo N=19 (n%)
Treatment-emergent adverse event (TEAE)	21 (100)	18 (95)
Vancomycin related TEAE	4 (19)	2 (11)
SER-155 related TEAE	1 (5)	2 (11)
Serious TEAE	11 (52)	8 (42)
Study drug-related serious TEAE	0	0
TEAE leading to treatment discontinuation	0	1 (5)
TEAE leading to study discontinuation	2 (10)	2 (11)
Grade 3 or higher TEAE	19 (91)	17 (90)
TEAE leading to death	2 (10)	2 (11)
Veno-occlusive disease	1 (5)	0
Idiopathic pneumonia syndrome (post Day 100)	1 (5)	0
Escherichia sepsis	0	1 (5)
Multiple organ dysfunction syndrome (secondary to life threatening staphylococcal sepsis)	0	1 (5)
Most common TEAEs (by preferred term) in SER-155 treated participants (≥50% and ≥5 percentage points greater than placebo)	6 (29)	8 (42)
Diarrhea	18 (86)	14 (74)
Nausea	13 (62)	10 (53)

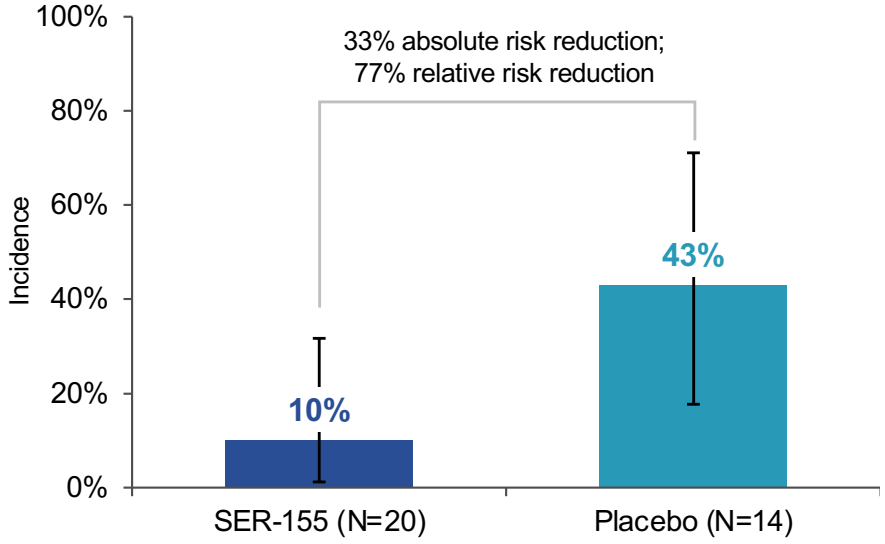
- Safety profile comparable between arms
- No treatment-related SAEs
- No SER-155 species identified in any clinical culture specimens
- Infection-related deaths observed only in placebo arm

Significantly Lower Incidence of Bloodstream Infections (BSI) in SER-155 Arm Compared with Placebo

HCT Day 0-100

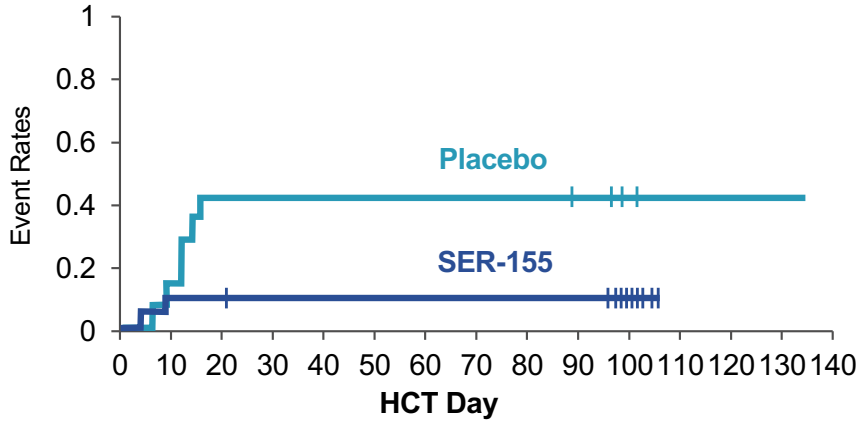
BSI Incidence

Odds Ratio 0.15 (95% CI, 0.01-1.13) *p*=0.0423



Time to First BSI

Hazard Ratio = 0.21; 95%CI:0.043-1.050 Log-rank *p*=0.04



No. of participants at risk

SER-155	20	18	18	17	17	17	17	17	17	17	11	0	-	-	-
Placebo	14	12	8	8	8	8	8	8	8	7	3	1	1	1	0

Note: Error bars represent 95% confidence intervals

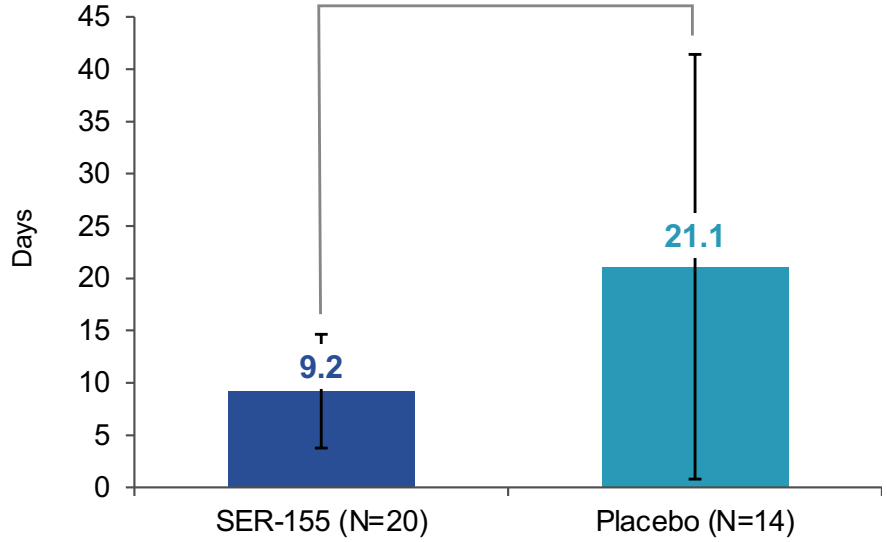
Adjusted for PTCy status, BSI incidence remained significantly lower in SER-155 vs placebo (p=0.0488; post hoc logistic regression)

Significantly Lower Utilization of Treatment Antibacterials / Antimycotics in SER-155 Arm Compared with Placebo

HCT Day 0-100

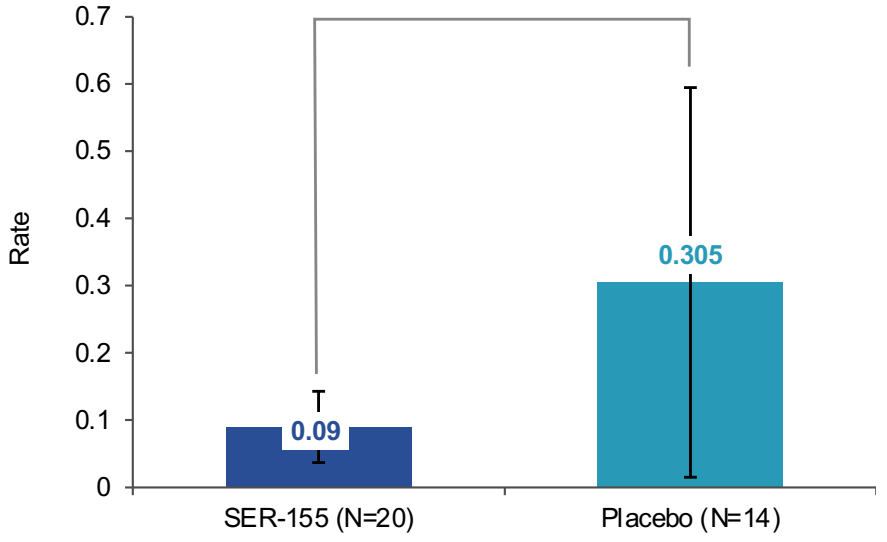
Mean Cumulative Utilization (Days)

Mean difference, -11.9 (95%CI, -23.85-0.04) *p*=0.0494



Mean Cumulative Utilization (Rate)*

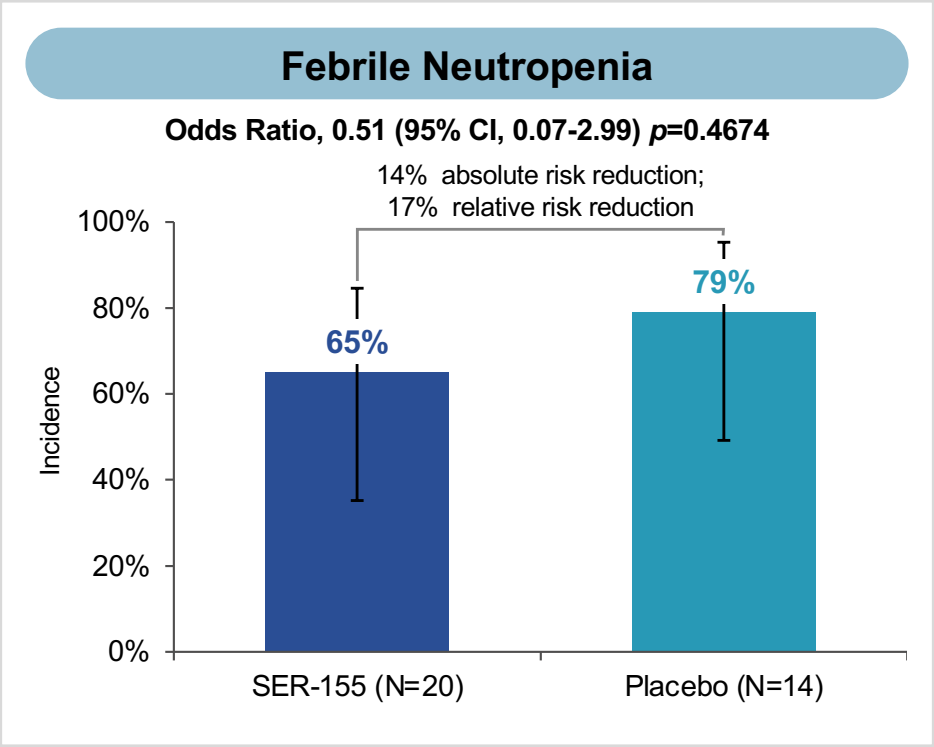
Mean difference, -0.2 (95% CI, -0.38-0.05) *p*=0.0163



*adjusted for time on study | Note: data presented are mean ± standard deviation

Numerically Lower Incidence of Febrile Neutropenia in SER-155 Arm Compared with Placebo

HCT Day 0-Neutrophil Engraftment; Day 0-30; Day 0-100 (Identical Results)



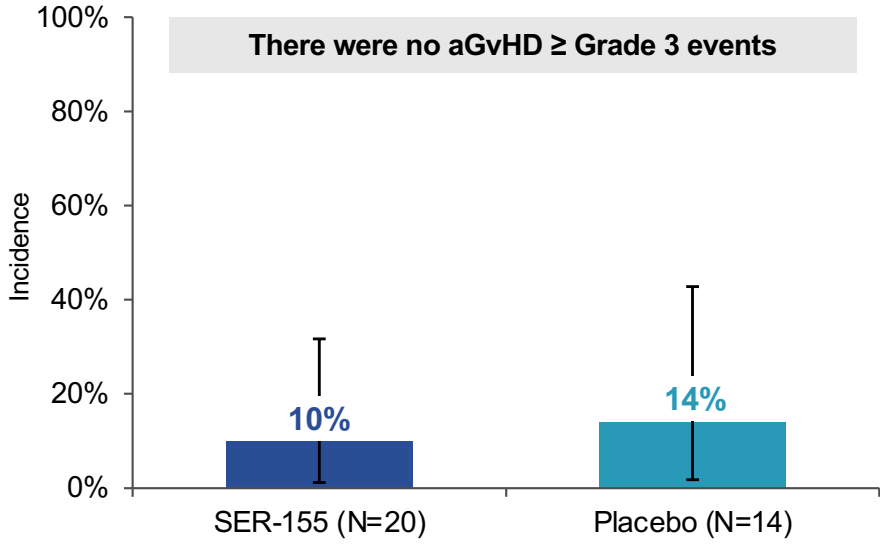
Note: Error bars represent 95% confidence intervals

Incidence of Acute GvHD ≥ Grade 2 and GI Infections

HCT Day 0-100

aGvHD ≥ Grade 2

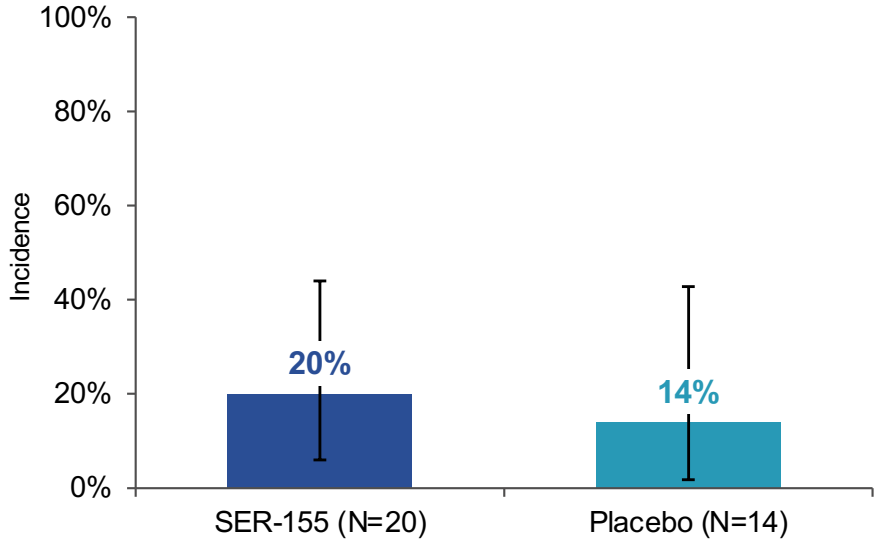
Odds Ratio, 0.67 (95% CI, 0.04-10.50) *p*=1.000



Note: Error bars represent 95% confidence intervals

GI Infections

Odds Ratio, 1.5 (95% CI, 0.18-18.97) *p*=1.000



Note: Error bars represent 95% confidence intervals

Conclusions

The majority of SER-155 strains engrafted in the GI tract

SER-155 was generally well-tolerated with a safety profile similar to placebo

- There were no SAEs related to SER-155
- There were no SER-155 strains identified in any clinical culture specimen

Treatment with SER-155 resulted in clinically meaningful and significantly lower incidence of BSI, fewer days in hospital, and less antibiotic utilization compared with placebo

These encouraging results support further development of SER-155 in allo-HCT

Thanks!

We are indebted to the patients and investigators for their participation; without them, none of this would be possible

For more on SER-155 pharmacology

ePoster #A178 Infectious Complications

EBMT