MGTA-145 + Plerixafor Provides GCSF-Free Rapid and Reliable Hematopoietic Stem Cell Mobilization for Autologous Stem Cell Transplant in Patients with Multiple Myeloma: A Phase 2 study

Surbhi Sidana[1], MD, Andriyana K. Bankova[1], MD, Hitomi Hosoya[1], MD PhD, Shaji K. Kumar[2], MD, John Tamaresis[3], PhD, Anne Le[1], Lori S. Muffly[1], MD, MS Laura Johnston[1], MD, Sally Arai[1], MD, Robert Lowsky[1], MD, Everett Meyer[1], MD PhD, Andrew Rezvani[1], MD, Wen-Kai Weng[1], MD PhD, Matthew J. Frank[1], MD PhD, Parveen Shiraz[1], MD, Doug Girgenti[4],MD, Kevin A. Goncalves[4], PhD, Veit Schmelmer[4], PhD, John C Davis[4], MD, Ying Lu[3], PhD, Judith Shizuru[1], MD PhD, and David B. Miklos,[1] MD PhD.

1: Division of BMT and Cellular Therapy, Stanford University School of Medicine, Stanford, California, USA; 2: Division of Hematology, Mayo Clinic, Rochester, MN, USA; 3: Dept of Biomedical Data Science, Stanford University School of Medicine, 4: Magenta Therapeutics, Boston, MA, USA

INTRODUCTION

- MGTA-145 (GroβT): CXCR2 agonist with promising activity for rapid HSC mobilization with plerixafor in pre-clinical models and healthy volunteers.
- Phase 2 single center, investigator-initiated trial of MGTA-145+plerixafor for HSC mobilization in patients with MM.
- First study to evaluate MGTA-145 + plerixafor for HSC mobilization in hematologic malignancies.

AIMS

- Single center phase 2 trial of MGTA-145 + plerixafor for HSC mobilization in patients with multiple myeloma (MM), NCT04552743.
- Primary endpoint was collection of ≥2 x 10^6 CD34+ cells/kg in up to 2 days of mobilization/apheresis.
- Secondary endpoints were collection of 4 and 6 x 10^6 CD34+ cells/kg, safety and engraftment.

METHODS

- Patients with MM, 18-70 years of age, within 1 year of starting treatment & CrCl > 30 ml/min were eligible.
- Patients received plerixafor 0.24 mg/kg (0.16 mg/kg if renal dysfunction) SQ, followed 2 hours later by MGTA-145 (0.03 mg/kg) IV over 3-10 minutes and apheresis within 30 minutes.
- Mobilization and collection were repeated for a second consecutive day if day 1 yield was < 6 x 10^6 CD34+ cells/kg.
- The study was open-label single arm trial of 15 patients. If 13 or more patients met primary endpoint, an expansion cohort of 10 patients was planned. The trial has 85% power at a 5% one-sided type I error rate. **Our analysis is based on aggregated results from total cohort of 25 patients**.

RESULTS

Table 1: Baseline and Treatment Characteristics, N=25

	N (%) or median (range)
Age	62 years (35-68)
Sex, female	13 (52%)
Race (White, AA, Other)	18/3/4 (72%/12%/16%)
ISS stage 1,2,3,Not known	6/10/6/3 (24/40/24/12)
High-risk cytogenetics* (NA in 4)	12/21 (57%)
Renal insufficiency at diagnosis	7 (28%)
Prior chemotherapy/radiation before active MM diagnosis**	6 (24%)
Induction Chemotherapy:*** VRD DaraVRD CyBorD	 17 (68%) 6 (24%) 2 (8%)
Duration of induction, median (range)	4 months (3-6)
Lenalidomide exposure, N=23	5 cycles (1-8)
More than 2 months of cyclophosphamide	4 (16%)
Lines of Therapy Before Mobilization, 1 vs. 2	22, 3 (88%, 12%)
Radiation for MM	5 (20%)
Best response prior to mobilization, VGPR/CR	22 (88%)

*High-risk cytogenetics: Deletion 17p/monosomy 17; t(4;14), t(14;16), t(14;20) and gain 1q. ** Includes 1 patient with radioactive iodine ***Three patients started with cyclophosphamide, bortezomib and dex and switched to VRD (2) or DaraVRD (1)

Table 2: Mobilization with MGTA-145 + Plerixafor, N=25

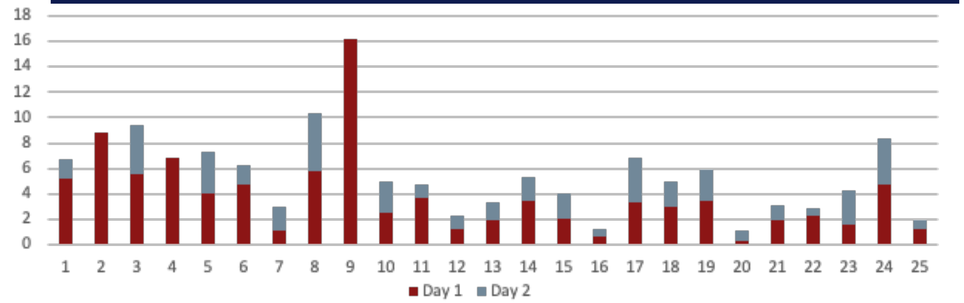
	N (%) or median, range
Plerixafor dose 0.24 mg/kg	24 (96%)
MGTA-145 infusion time, median (range)	4 minutes (3-10)
Intended dose given without interruption	100%

Tables 3a and 3b: Adverse Events

TEAEs Any grade	60% patients
Grade 1	
Pain	11 (50%), 9 acute pain after MGTA-145 infusion
AST/ALT increased	1 (4%)
Nausea	2 (8%)
Headache	1 (4%)
Hyperhidrosis	1 (4%)
Low platelet count	2 (4%)
Grade 2	
Vomiting	1 (4%)

Acute pain after MGTA-145, Day 1	9/25 (36%)
Location	Back:5 Hip:1 ; Sternum: 1 Generalized: 1
Severity of pain on scale of 1-10, median (range)	8 (3-10)
Onset, minutes after MGTA-145 infusion start; median (range)	5 minutes (3-10)
Duration of pain; median (range)	7 minutes (3-28)
Pain medication needed	1/9
Treatment interruption	0%
Recurrent pain with MGTA-145, Day 2	**2/22 (9%)**

Figure 1: Efficacy of Stem Cell Mobilization: CD34+ cells x 10^6/ kg, N=25



Mobilization Yield	Median (range)
Total Days of mobilization; 1 vs 2	12%, 88%
Total Stem Cell Collection	5 (1.1-16.2)
Day 1 apheresis yield, N=25	3.4 (0.3-16.2)
Day 2 apheresis yield, N=22	1.9 (0.5-4.6)

2 x 10^6 CD34+ cells/kg	88% (22)
4 x 10^6 CD34+ cells/kg	68% (17)
6 x 10^6 CD34+ cells/kg	40% (10)
2 x 10^6 CD34+ cells/kg on Day 1	68% (17)

Engraftment

Engraftment data N=18	Median (range) or n (%)
Engraftment	100%
Neutrophil engraftment, ANC ≥ 500 x 10^6/L	12 days (11-15)
Platelet engraftment ≥ 20,000 x 10^6/L without transfusion in 7 days	17.5 days (15-33)
RBC transfusions needed during ASCT	3/18 (17%)

- **At data cut-off, 13 patients completed day 100 visit post SCT. All with durable engraftment**

Stem Cell Graft Composition

- **Graft composition favorable for ASCT**
- Low residual disease with 74% grafts being MRD negative by next-generation flow cytometry
- Graft enriched for CD90+CD45RA- among CD34+ cells, a CD34 subset of long-term engrafting HSCs, median:36% of CD34+ cells (range 10-66%)

CONCLUSIONS

- **This is the first study to evaluate MGTA-145 + plerixafor for HSC mobilization and collection in a representative population of transplant eligible patients with multiple myeloma.**
- **88% efficacy in collecting enough cells in 1-2 days to proceed with SCT, with some variability in stem cell yield**
- **MGTA-145 was well-tolerated.**
- **MGTA-145 + plerixafor mobilized HSCs resulted in timely and durable engraftment in all patients who underwent transplant.**
- **Follow-up is ongoing**

Contact: Surbhi Sidana, MD. surbhi.sidana@stanford.edu