2021 ASCO ANNUAL MEETING

Stanford MEDICINE

PHASE 2 STUDY OF MGTA-145 + PLERIXAFOR FOR RAPID AND RELIABLE HEMATOPOIETIC STEM CELL (HSC) MOBILIZATION FOR AUTOLOGOUS STEM CELL TRANSPLANT IN MULTIPLE MYELOMA

Surbhi Sidana, Andriyana K. Bankova, Hitomi Hosoya, Lori S. Muffly, Shaji K. Kumar, Laura Johnston, Robert Lowsky, Everett Meyer, Andrew Rezvani, Wen-Kai Weng, Sally Arai, Matthew J. Frank, Parveen Shiraz, Haley Howell, Kevin A. Goncalves, Veit Schmelmer, John C Davis, Judith Shizuru and David B. Miklos

Presented by: Surbhi Sidana, MD

Division of BMT and Cell Therapy

Stanford University Medical Center

COI Disclosures

- Please refer to accompanying ASCO abstract for detailed COI information for each author
- This investigator-initiated trial was funded by Magenta Therapeutics.
- Surbhi Sidana: Research funding to institution: Magenta Therapeutics, Allogene, Janssen. Consultancy: Janssen
- John Davis, Veit Schmelmer, Kevin Goncalves and Haley Howell are employees of Magenta Therapeutics with stock ownership in Magenta Therapeutics

Background and Study Design

- MGTA-145 (GroβT): CXCR2 agonist with promising activity for rapid HSC mobilization with plerixafor in pre-clinical models and healthy volunteers.[1,2]
- 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.

Key Eligibility

- Diagnosis: Multiple Myeloma
- 18-70 years
- Within 1 year of treatment start
- ≤ 6 months of lenalidomide (6-8 cycles)
- At least partial response
- Eligible for ASCT
- Cr Cl ≥ 30 ml/min

Planned enrollment: 25 patients
Interim results: 15 patients

Mobilization + Apheresis (1-2 days)

Plerixafor 0.24 mg/kg SQ (renal dysfunction: 0.16 mg/kg)

↓ 2 hours

MGTA-145 (0.03 mg/kg) IV over 3-10 minutes

↓ Within 30 minutes

Same day apheresis

↓

Repeat on day 2 if yield < 6 million CD34+ cells/kg

ASCT

Melphalan 140-200 mg/m2 & ASCT per institutional standards

Follow-up for:
- Engraftment
- Disease outcomes
- Follow-up until day 100

If plan for delayed ASCT: Follow-up for 30 days

Endpoints

Primary:
≥2.0 x 10^6 CD34+ cells/kg in up to two days of apheresis

Secondary:
- ≥4.0 and ≥6 x 10^6 CD34+ cells/kg in up to two days of apheresis
- Engraftment
- Safety/AEs

Exploratory
- Graft composition: MRD & stem cell immunophenotype

[1]Hoggatt et al. Cell. 2018. PMID 29224778; [2]DiPersio et al. ASH 2019; Blood. 2019;134(Supplement_1):1961

Baseline Characteristics and Treatment

Interim data on first 15 of planned 25 patients, HSC mobilization from 11/2020 to 04/2021

	N (%) or median (range)
Age	62 years (46-68)
Sex, Female	9 (60%)
Race, White	10 (67%)
ISS stage 1/2/3 (N=14, N/A in 1)	4/5/5 (29%/36%/36%)
High-risk cytogenetics* (N=13, N/A in 2)	7 (47%)
Induction chemotherapy** Bortezomib/Lenalidomide/Dex Daratumumab/Bortezomib/Lenalidomide/Dex	 11 (73%) 4 (27%)
Duration of induction therapy	4 months (3-6)
Lenalidomide exposure, number of cycles	6 (1-7)
Lines of therapy before mobilization, 1;2	12;3 (80%;20%)
Any risk factors for poor mobilization***	5 (33%)
Best response prior to mobilization, at least VGPR	12 (80%)
Investigational Treatment: Mobilization	
MGTA-145 infusion time, median (range)	4 minutes (3-10), no interruptions
Plerixafor dose reduction to 0.16 mcg/kg for renal impairment	1 (7%)
Apheresis: Central line (vs peripheral access)	9 (60%)

Representative transplant eligible MM patient population

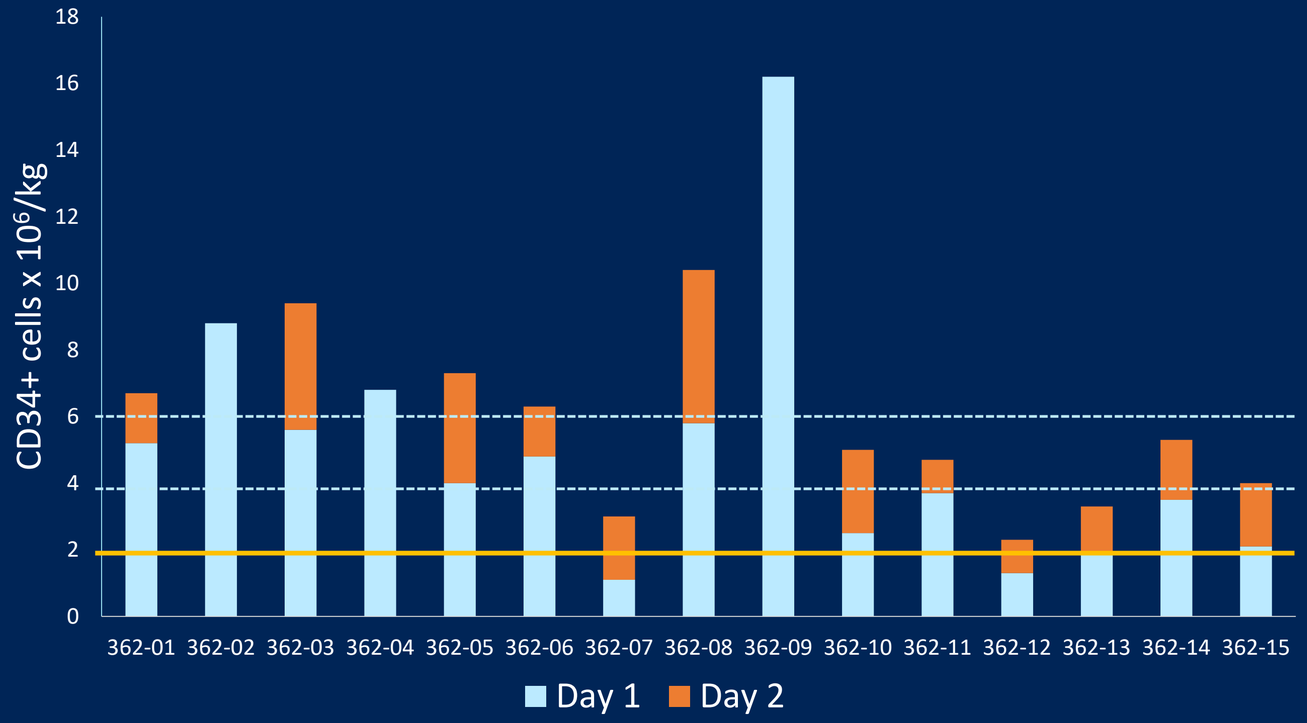
One-third of patients with risk factors that can unfavorably impact mobilization, in addition to lenalidomide exposure***

*High-risk cytogenetics: Deletion 17p/monosomy 17; t(4;14), t(14;16), t(14;20) and gain 1q
**Three patients started with cyclophosphamide, bortezomib and dex and switched to VRD (2) or DaraVRD (1)
*** Prior other cancer treated with chemotherapy and/or radiation (3), autoimmune disorder needing systemic therapy (1), daratumumab (4), alkylator exposure > 2 months (2). Patients may have > 1 RF

Efficacy: Stem Cell Collection

Total CD34+ cells collected, median (range): 6.3 x 10^6 cells/kg (2.3-16.2)

- All (15/15) patients collected sufficient cells for ASCT in 1-2 days
- Total number of days 1 vs. 2: 20% vs 80% (Day 2 needed only if day 1 yield < 6 x 10^6 CD34+ cells/kg)



Endpoints:

- **≥ 2 x 10^6 CD34+ cells/kg (Primary): 15 (100%)**
- **≥ 4 x 10^6 CD34+ cells/kg (Secondary): 12 (80%)**
- **≥ 6 x 10^6 CD34+ cells/kg (Secondary): 8 (53%)**

- Alternate mobilization needed for 2 patients:
  - 1 for collecting backup stem cells
  - 1 for complications with product during cell processing & cryopreservation after collection

Adverse Events

- MGTA-145, in combination with plerixafor, was well tolerated
- Treatment emergent adverse events, TEAEs (at least possibly related to MGTA-145): 60% of patients
- All grade 1, resolved before transplant in all patients
- No serious adverse events (SAEs) or unexpected AEs
- AE of special interest: acute, self limiting (i.e. no intervention) bone/musculoskeletal pain soon after MGTA-145 infusion (40% patients)

TEAEs (All grade 1)	n (%), N =15
Pain	7 (46%), 6 acute pain after MGTA-145 infusion
Nausea	1 (7%)
Hyperhidrosis	1 (7%)
Thrombocytopenia	2 (13%)

6 of 7 patients with pain had acute onset bone pain shortly after MGTA-145 infusion, 1 patient had mild shoulder pain during apheresis afterwards

Acute pain after MGTA-145 infusion	N=6 (40%)
Location	Back: 3; 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)	6 minutes (3-10)
Duration of pain; median (range)	5 minutes (3-10)
Intervention (pain medication/other)	0%
Treatment interruption	0%

Stem Cell Graft Composition

- **Low residual disease and enriched for long-term engrafting HSCs**
- **Graft composition favorable for ASCT**

MRD (Minimal Residual Disease) Testing, NGF (Next Generation Flow) Cytometry (Sensitivity > 1 x 10^5)

Apheresis graft (fresh) N=14	
MRD negative by NGF	10 (71%)
Events analyzed, median	1.92 x 10^6
Median clonal plasma cells in MRD positive patients	0.0001% (0.0001-0.0002)

Data from 14 patients with MGTA-145+plerixafor; one patient's cells were not viable at analysis due to transit delays

HSC Immunophenotyping: Flow Cytometry

MGTA-145+ plerixafor mobilized grafts: high enrichment for CD90+CD45RA- among CD34+ cells, a CD34 subset of long-term engrafting HSCs

Apheresis graft (cryopreserved + thawed), N=14	
CD34+CD90+ RA- proportion of CD34+ cells; median (range)	40% (18-66%)
Historical data with G-CSF alone[1]	6%

Data from 14 patients with MGTA-145+plerixafor; one patient with product loss issues during processing/cryopreservation excluded

[1]*Goncalves et al. ASTCT 2021*

Engraftment

- **12/12 (100%) patients transplanted with MGTA-145 + plerixafor-collected HSCs have successfully engrafted**
- Conditioning chemotherapy, melphalan 200 mg/m2: 10 patients (83%)
- CD34+ cells/kg infused, median (range): 4 x 10^6 CD34+ cells/kg (2.4-8.1)

Engraftment data N=12	Median (range) or n (%)
Engraftment	12 (100%)
Neutrophil engraftment, ANC $\geq$ 500 x 10^6/L	12.5 days (11-15)
Platelet engraftment $\geq$ 20,000 x 10^6/L without transfusion in 7 days	18 days (15-22)
RBC transfusions needed during ASCT	1 patient (8%)

Engraftment data comparable to historical institutional data and data from other published studies.[1,2]

[1]Johnsrud et al. TCT 2021, PMID 33915323; [2]DiPersio et al. Blood 2009 PMID 19363221

One patient used alternate mobilization due to issues with apheresis product during processing/cryopreservation after collection; pending data on one patient and one patient with plan for delayed ASCT

- **6 patients have completed day 100 follow-up, with durable engraftment.**

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.
- Preliminary results show 100% efficacy in collecting HSCs in 1-2 days to proceed with ASCT.
- MGTA-145 was well-tolerated.
- MGTA-145 + plerixafor mobilized HSCs resulted in timely and durable engraftment in all patients who underwent transplant.
- This regimen has the potential to replace G-CSF based regimens for rapid, safe HSC mobilization for autologous and allogeneic stem cell transplantation.

Acknowledgements

- Patients who participated in this study and their families
- Co-investigators, collaborators and members of the research team
- Stanford BMT and Cell Therapy Division; Stanford Cancer Institute
- Magenta Therapeutics

For Questions:
Surbhi Sidana, M.D.
surbhi.sidana@Stanford.edu
Twitter: @SurbhiSidanaMD