**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**

**Authors:** Surbhi Sidana¹, MD, Andriyana K. Bankova¹, MD, Hitomi Hosoya¹, MD PhD, Shaji K. Kumar², MD, John Tamaresis², PhD, Anne Le¹, Lori S. Muffly¹, MD, MS Laura Johnston³, MD, Sally Arai¹, MD, Robert Lowsky¹, MD, Everett Meyer¹, MD PhD, Andrew Rezvani¹, MD, Wen-Kai Weng², MD PhD, Matthew J. Frank¹, MD PhD, Parveen Shiraz¹, MD, Doug Girgenti⁴, MD, Kevin A. Goncalves⁴, PhD, Veit Schmelmer⁴, PhD, John C Davis⁴, MD, Ying Lu³, PhD, Judith Shizuru¹, MD PhD, and David B. Miklos,¹ MD PhD.

**Affiliations:** 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;

**Category:** 711. Cell Collection and Processing

**Character Limit:** 3800 without spaces.

**Background:** MGTA-145, a CXCR2 agonist, has shown promising activity for hematopoietic stem cell (HSC) mobilization with plerixafor in pre-clinical models and healthy volunteers. It has the potential to become the first GCSF free regimen for HSC mobilization/apheresis in preparation for transplant, with fewer side effects, better patient experience and optimal resource utilization.

**Methods:** We conducted a 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 10⁶ CD34+ cells/kg in up to 2 days of mobilization/apheresis. Secondary endpoints were collection of 4 and 6 x 10⁶ CD34+ cells/kg, safety and engraftment. 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 10⁶ 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:** Median age was 62 years, 52% were female, 24% had ISS stage 3, 57% had high-risk FISH (primarily gain1q). Induction therapy was VRD in 68% (17), daratumumab VRD in 24% (6), CyBorD in 8% (2) patients. Median duration of induction was 4 months (3-6) and median lenalidomide exposure was 5 cycles (1-8), with ≥ VGPR in 88% of patients. (Table 1)

Plerixafor 0.24 mg/kg was given in 24 (96%) patients. Median pre-apheresis CD34 count was day 1, 24/uL (3-99) & day 2, 15/uL (5-46). Median total HSC cell yield (CD34+ cells/kg x 10⁶) was 5.0 (1.1-16.2), day 1 yield was 3.4 (0.3-16.2) and day 2 yield was 1.9 (0.5-4.6) (Fig1). 88% (n=22) of patients met the primary endpoint of collecting sufficient HSCs in < 2 days of mobilization + apheresis to proceed to transplant, 68% (17) in 1 day (2 x 10⁶ CD34+ cells/kg). 3 patients who did not meet primary endpoint successfully collected HSCs with standard GCSF + plerixafor dosing & 2-3 apheresis sessions. Secondary endpoints of 4 and 6 x 10⁶ CD34+ cells/kg in ≤ 2 days were met in 68% (17) and 40% (10) patients.
MGTA-145+plerixafor was well tolerated. At least 1 treatment emergent AE (TEAE) with MGTA-145 was seen in 60% of patients (grade 1, n= 14, grade 2, n=1). Pain (all grade 1) was most common, seen in 44% (11), with 38% (9) patients experiencing acute onset transient bone pain with MGTA-145 (duration: 7 minutes, range: 3-28). Using the validated Brief Pain Inventory, 56% (14) patients self-reported pain with mobilization vs 40% (10) at baseline. 7/15 patients without baseline pain reported pain with mobilization. An increase for worst pain was seen on mobilization day 1, that returned to the baseline, but no difference for aggregate score of pain severity/interference (linear mixed effects model).

At last follow-up, 18 patients have completed transplant with MGTA-145 mobilized graft, with melphalan 200 mg/m² in 15 (83%) patients. Median of 3.5 (2.2-8.1) x 10⁶ CD34+ cells/kg were infused. All patients have engrafted. Median time to neutrophil engraftment of 12 days (range: 11-15) & platelet engraftment (platelets > 20,000, no transfusion in 7 days) of 17.5 days (15-33) are comparable to historical data (DiPersio et al. 2009). RBC transfusion was needed in 3 (17%) patients. 14 patients have day 100 follow-up, all with durable engraftment.

MGTA-145 + plerixafor mobilized grafts had a favorable graft composition. We observed high enrichment for CD90+CD45RA- among CD34+ cells, a CD34 subset of long term engrafting HSCs (median: 36% of CD34+ cells, range 10-66%, N=25). 74% (17 of 23) grafts were minimal residual disease negative with next generation flow cytometry.

Conclusions: This is the first study to evaluate the novel G-CSF-free regimen of MGTA-145 + plerixafor for HSC cell mobilization & collection for hematologic malignancies. The study cohort was representative of transplant eligible patients with MM, with 88% patients meeting the primary endpoint. The regimen was well tolerated. Patients achieved timely & durable engraftment. Our data support further development of this regimen for rapid HSC mobilization.
Table 1: Baseline Characteristics and Myeloma Treatment

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N(%) or median (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>62 years (35-68)</td>
</tr>
<tr>
<td>Sex, female</td>
<td>13 (52%)</td>
</tr>
<tr>
<td>Race (White, AA, Asian, Other/not known)</td>
<td>18,3,2,2</td>
</tr>
<tr>
<td>ISS stage 1,2,3,Not known</td>
<td>6,10,6,3</td>
</tr>
<tr>
<td>High-risk cytogenetics* (NA in 4)</td>
<td>12 of 21 (57%)</td>
</tr>
<tr>
<td>Renal Insufficiency at diagnosis</td>
<td>7 (28%)</td>
</tr>
</tbody>
</table>

Myeloma Treatment

Induction Chemotherapy:**
- VRD (bortezomib, lenalidomide, dex) 17 (68%)
- Daratumumab VRD 6 (24%)
- CyBorD (cyclophosphamide, bortezomib, dex) 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 therapy for myeloma 5 (20%)

*High-risk cytogenetics: Deletion 17p/monosomy 17; t(4;14), t(14;16), t(14;20) and gain 1q
**3 patients started with CyBorD and switched to DaraVRD (1) or VRD (2)

Figure 1: Stem Cell Mobilization Yields with MGTA-145+ Plerixafor in Each Patient on Mobilization Days 1 and 2