

P3.124 – B7-H3 Universal CAR-T (MT027) for Refractory Lung Cancer Brain Metastases: Preliminary Phase I IIT Results

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Introduction: Lung cancer brain metastases (LCBM) occur in 30% to 50% of lung cancer patients, presenting a critical clinical challenge due to poor prognosis and limited treatment options that can effectively cross the blood-brain barrier. B7-H3 is highly expressed in a majority of lung cancers and their intracranial metastases. MT027 is an innovative, "off-the-shelf" allogeneic CAR-T cell therapy targeting B7-H3, designed to provide a readily available and affordable treatment for these high-need patients.

Methods: This prospective Phase I investigator-initiated trial (IIT) (ChiCTR2500107346) evaluates the safety and efficacy of MT027 in patients with refractory LCBM who have failed standard therapies. The product utilizes a unique CRISPR-based gene-editing strategy, knocking out TRAC and HLA-I to minimize the risk of Graft-versus-Host Disease (GvHD) and host-versus-graft rejection. MT027 is administered via intracerebroventricular (ICV) or lumbar cistern injection to deliver cells directly to the tumor site within the central nervous system. The study follows a dose-escalation design with a planned total of nine patients across two dose cohorts.

Results: As of the current analysis, five patients have been enrolled and treated. All subjects were heavily pre-treated with no further guideline-recommended options available. • **Safety:** The overall safety profile is favorable, with no drug-related Grade 3 or higher adverse events (AEs) and no observed GvHD. Reported AEs were primarily Grade 1-2 immune-inflammatory reactions, consistent with the mechanism of action of CAR-T cells in the central nervous system. • **Efficacy:** Among three evaluable patients with measurable lesions, early efficacy signals are highly promising. One patient achieved a Partial Response (PR) with approximately 80% tumor reduction. Two patients achieved Stable Disease (SD); notably, one SD patient experienced a 46% tumor reduction and has maintained a Progression-Free Survival (PFS) exceeding 8 months.

Conclusions: MT027 demonstrates a manageable safety profile and significant preliminary anti-tumor activity in patients with refractory lung cancer brain metastases. These results support the continued clinical development of MT027 as a potential breakthrough therapy for patients with high B7-H3-expressing intracranial malignancies. Further enrollment is ongoing to confirm these findings and establish the recommended Phase II dose.