Phase 1b/2a study of autologous mRNA-engineered anti-B-cell maturation antigen (BCMA) chimeric antigen receptor (CAR) T-cells for treatment of severe generalized myasthenia gravis

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BCMA-positive plasma cells have not been a target of MG treatments to date

CAR-T cells are the most potent BCMA-targeting agents in the clinic

Toxicity of DNA-engineered CAR T-cells prohibits their use outside of oncology

Anti-BCMA CAR-T therapies approved for multiple myeloma

Descartes-08 eliminates BCMA+ plasma cells ex vivo

Successful manufacturing of potent CD8+ autologous CAR-T cells from patients on continuous immunosuppressive therapy

Primary objective: Safety, tolerability, and manufacturing feasibility of Descartes - 08

Secondary objective: Change in MG outcome measures, anti-MG antibody titers, immunoglobulin titers

Trial design

Exploratory objectives: Assessment of immunogenicity, pharmacokinetics, pharmacodynamics of Descartes-08

Part I: intra-patient Dose Escalation

Part II: Dose Expansion at MTD (52.5x10⁶ CAR+ T-cells) per dose

Key inclusion/exclusion criteria

- ≥18 years of age
- ≤12 years
- ≥ 16 patients with advanced MM

By substituting RNA for DNA, Descartes-08 constrains unchecked CAR-T cell activation

Descartes-08: mRNA-engineered autologous anti-BCMA CAR-T cells

Demonstrated safety and anti-tumor activity in 16 patients with advanced MM

Adverse Events

No dose-limiting toxicities, treatment-related SAEs, CRS, or neurotoxicity of any grade in 8 patients with gMG who have received at least one dose of Descartes-08 to date

All reported serious adverse events (per patient, Part I)

All reported serious adverse events (per patient, Part II)

Changes in MG disease severity scales

MGC, change from baseline

Part I (Dose Escalation)

Part II (Dose Expansion)

Active sites

- University of North Carolina (PI: Metin Kurtoglu)
- Oregon Health and Sciences University (PI: Michael M. Feinberg)
- University of California Irvine (PI: Adam Chowdhury)
- South Florida Neurology Associates (PI: Michael Benatar)
- Barrow Neurological Institute (PI: Volkan Granit)
- Biologics other than Eculizumab <8 weeks, IVIg/PLEX <4 weeks

MG-ADL

Clinical trial investigators, please contact:

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References

1. University of North Carolina, Florida, University of California Irvine, 3 University of North Carolina, Chapel Hill, 4 Cartesian Therapeutics, Maryland

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3. Toxicity of DNA-engineered CAR T-cells prohibits their use outside of oncology

4. Anti-BCMA CAR-T therapies approved for multiple myeloma

5. Demonstrated safety and anti-tumor activity in 16 patients with advanced MM

6. Adverse Events

7. Changes in MG disease severity scales

8. Active sites

9. Clinical trial investigators, please contact: