An exploratory clinical trial on intra-lumbar injection of B7H3-specific allogeneic universal CAR-T Cells in patients with recurrent high-grade gliomas

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BACKGROUND

- No standard-of-care treatment was established for rHGGs yet
- T cell immunotherapy is becoming a powerful therapeutic strategy for hematological and solid malignancies and is a potential option for treatment of rHGGs
- Intrathecal infusion of autologous chimeric antigen receptor-T (CAR-T) cells has displayed potent anti-tumor activity in one patient (Brown et al. N Engl J Med 2016)
- We evaluated the safety, efficacy, pharmacokinetic (PK) and pharmacodynamic (PD) characteristics of B7H3-specific allogeneic universal CAR-T (B7H3 UCAR-T) cells (MT027) in patients with rHGGs (ChiCTR2100047968)

STUDY DESIGN

Dosage and administration

- 2.5×10^7 cells, intra-lumbar injection, every four weeks

Primary objectives

- Safety

Secondary objectives

- Efficacy (ORR, DCR, OS, PFS)
- PK

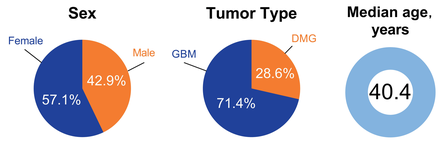
Patient population

- 18-70 years
- Life expectancy ≥ 3 months
- KPS ≥40
- Histologically- or cytologically-confirmed recurrent high-grade glioma
- Had been treated with SoC
- B7-H3 IHC positive score >50%

RESULTS (interim)

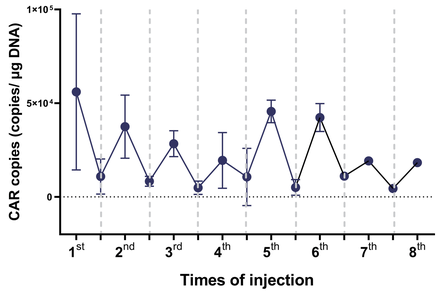
Patient characteristics

- As of January, 30, 2023, 7 patients were evaluable



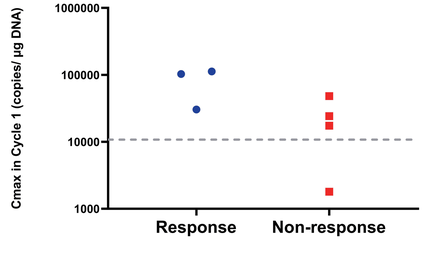
PK

- CAR copies were detected before each injection and 1 day after each injection
- Well expansion of 1 day and persistence of >30 days



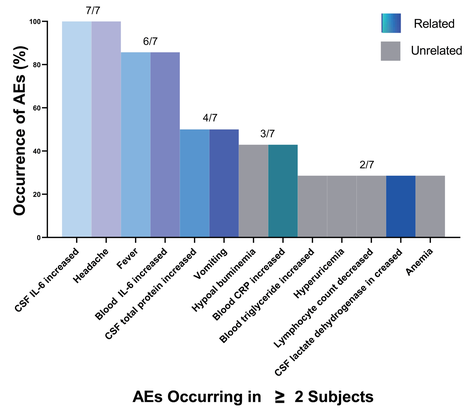
Exposure-response

- Response seems correlated with C_{max} of CAR copies after 1st injection

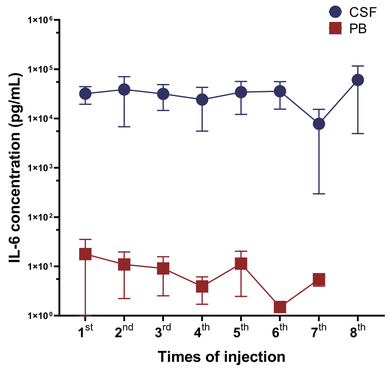


Safety

- Headache and fever were the most common symptoms
- Elevated CSF and Blood IL-6 were the most common abnormal laboratory tests
- No severe CRS or ICANS
- All of those AEs occurring in ≥2 subjects were Grade 1 or 2

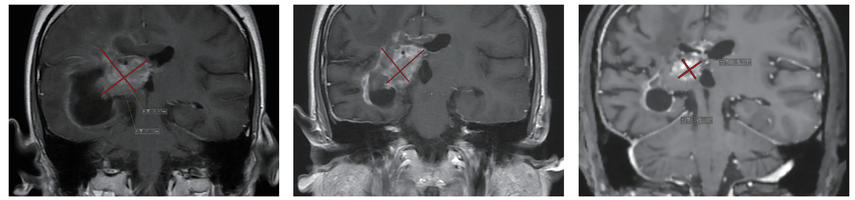


- Blood IL-6 concentration is low after administration



Efficacy (As of January, 30, 2023)

- 3 PR, 4 SD

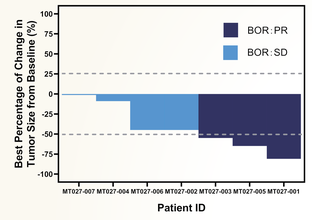


Pre-injection
Tumor size: 1422.78 mm²

40 weeks after injection
Tumor size: 1038.27 mm²

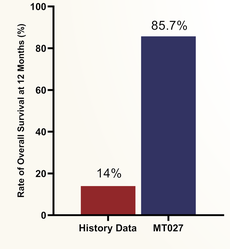
54 weeks after injection
Tumor size: 267.35 mm²

- ORR 42.9% (3/7), DCR 100% (7/7)

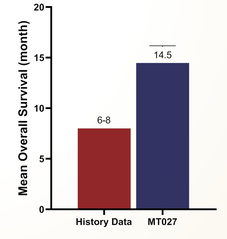


- PFS (month): Not available due to the COVID-19 pandemic

- 12m-OS: 85.7% vs. 14% (history data)



- OS (month): 2/7 died, median OS not reached, Mean 14.5 vs. 6-8 (history data)



CONCLUSION

In patients with rHGGs, B7H3 UCAR-T cells was not associated with any toxic effects of grade 3 or higher. B7H3 UCAR-T cells resulted in a significantly longer overall survival and a higher objective response rate than history data. B7H3 UCAR-T cells persist well in patients.

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