Autologous HER2 CMV bispecific CAR T cells are safe and demonstrate clinical benefit for glioblastoma in a Phase I trial.

Nabil Ahmed1*, Vita Brawley2, Meenakshi Hegde2, Kevin Bielamowicz2, Amanda Wakefield1, Alexia Ghazi1, Aidin Ashoori1, Oumar Diouf3, Claudia Gerken1, Daniel Landi1, Mamta Kalra1, Zhongzhen Yi2, Cliona Rooney1, Gianpietro Dotti1, Adrian Gee1, Helen Heslop2, Stephen Gottschalk1, Suzanne Powell4, Robert Grossman4, Winfried Wels5, Yzonne Kew4, David Baskin4, Jonathan Zhang4, Pamela New4, John Hicks4

From 30th Annual Meeting and Associated Programs of the Society for Immunotherapy of Cancer (SITC 2015)
National Harbor, MD, USA. 4-8 November 2015

Glioblastoma (GBM) remains incurable with current standard-of-care therapies. Adoptive T cell transfer holds the promise to improve outcomes for GBM patients. We report on the results of the Phase I clinical study, NCT01109095, administering autologous CMV.pp65 T cells grafted with a second generation HER2 chimeric antigen receptor (CAR) with a CD28.zeta signaling domain to patients with progressive GBM.

Seventeen CMV-seropositive patients with radiologically progressive HER2+ GBM were enrolled. The median age was 49 years (range 11 to 71; 6 children; 11 adults). Children enrolled had significantly larger tumor volumes at infusion. A cell product was successfully generated for all patients from a peripheral blood draw (maximum 90mL). A median of 67% (range: 46-82) of T cells expressed the HER2 CAR, and exhibited a median 985.5 (range 390 to 1292) CMV.pp65 reactivity in an IFN-γ Elispot assay (SFC/10^5 T cells). Infusions of 1x10^6/m^2-1x10^8/m^2 were well tolerated without severe adverse events or cytokine release syndrome. HER2 CMV T cells were detected in the peripheral blood for up to 12 weeks post infusion, as judged by rtPCR of a CAR-specific amplicon. Out of 16 evaluable patients, 8 had progressive disease, 8/16 patients had objective responses: 1 patient had a partial response with a ~62% reduction in tumor volume lasting 8 months, 7 patients had stable disease for more than 6 weeks (of these 5 were durable >10 weeks) and 3 subjects are currently with a follow up 24 to >30 months, after T cell infusion. The median survival was 11.6 months from infusion and 24.8 months from diagnosis. The median survival for adults was 30 months from diagnosis.

We conclude that systemically administered HER2 CAR CMV bispecific T cells are safe. A durable clinical benefit was observed in ~38% of patients.

Trial Registration
ClinicalTrials.gov Identifier NCT01109095.

Authors’ details
1Department of Pediatrics, Center for Cell and Gene Therapy, Baylor College of Medicine, Houston, TX, USA. 2Baylor College of Medicine, Houston, TX, USA. 3Baylor College of Medicine/Texas Children’s Hospital, Houston, TX, USA. 4Houston Methodist Hospital, Houston, TX, USA. 5CGT Frankfurt, Frankfurt, Germany.

Published: 4 November 2015

doi:10.1186/2051-1426-3-S2-O11
Cite this article as: Ahmed et al: Autologous HER2 CMV bispecific CAR T cells are safe and demonstrate clinical benefit for glioblastoma in a Phase I trial. Journal for ImmunoTherapy of Cancer 2015, 3(Suppl 2):O11.