GEN-009, A PERSONALIZED NEOANTIGEN VACCINE CANDIDATE, ELICITS DIVERSE AND DURABLE IMMUNE RESPONSES ASSOCIATED WITH CLINICAL EFFICACY OUTCOMES

Mara Shainheit*, Ece Bicak, Masoud Golshadi, Gabriella Santone, Syukri Shukor, Emily Tjon, Li Xue, Thomas Davis, Jessica Flechtner. *Genocea Biosciences, Cambridge, MA, USA*

Background GEN-009, a personalized vaccine candidate comprised of ATLAS™-prioritized neoantigens combined with Hiltonol®, is currently being evaluated in a Phase 1/2a clinical trial (NCT03633110). ATLAS™ is a cell-based recall assay that, without predictions, screens each patient's mutanome to identify neoantigens for vaccine inclusion and deleterious Inhibigens™ for exclusion. In the Part A monotherapy cohort, vaccine-specific immune responses were generated in all subjects, against 99% of administered peptides.¹ Here we characterize immune responses and their association with reduction in tumors in Part B of the study, in which patients were treated with GEN-009 combined with anti-PD-1-based checkpoint inhibitors (CPI).

Methods Fourteen adults with solid tumors were enrolled in the study. During the screening and manufacturing period, patients received standard of care anti-PD-1 CPI. Subsequently, patients were immunized with GEN-009 in combination with anti-PD-1. CPI refractory patients received salvage therapy prior to GEN-009. Peripheral blood mononuclear cells were collected at baseline, pre-vaccination (D1), as well as multiple days post first dose. The magnitude and durability of vaccine-induced immune responses were assessed by quantifying neoantigen-specific responses in fluorospot assays. Proliferation of neoantigen-specific T cells and T cell phenotypes were evaluated by flow cytometry. Circulating tumor DNA (ctDNA) levels were monitored pre- and post-GEN-009 dosing to assess its potential as a predictive biomarker.

Results GEN-009 immunization induced neoantigen-specific T cell responses in all evaluable patients, with ex vivo responses emerging as early as 1 month and persisting up to 366 days in some subjects. Comparing RECIST responders (PR, CR) to non-responders (SD, PD), the median breadth of statistically positive responses to vaccine antigens at day 50 was greater in non-responders ex vivo (29 vs. 75%, respectively), however, by IVS assay the proportions inverted (83% vs. 38%). Longitudinal evaluation of neoantigen-specific responses revealed an association between the magnitude and kinetics of cytokine secretion and increased activated and proliferating Ki-67+ T cells and TEM cells in both T cell subsets. Quantification of ctDNA in a subset of patients supported the RECIST readouts in association with the enhanced neoantigen-specific T cell responses.

Conclusions Vaccination with GEN-009 combined with anti-PD-1-based therapy induced early, durable, and neoantigen-specific CD4+ and CD8+ T cell responses with pronounced Ki-67+ and TEM cell populations. Overall, a greater breadth of response to vaccine neoantigens was associated with improved clinical benefit, which was further supported by ctDNA levels. These data support that GEN-009, in combination with checkpoint blockade, represents a unique approach to treat solid tumors.

REFERENCES

1. Lam H, et al. An empirical antigen selection method identifies neoantigens that either elicit broad anti-tumor response or drive tumor growth. *Cancer Discovery* 2021 March; **11**(3):696–713.

Ethics Approval ETHICS STATEMENT: This study was approved by Western Institutional Review Board, approval number 1-1078861-1

<http://dx.doi.org/10.1136/jitc-2021-SITC2021.521>