BIOMARKER CORRELATES OF LETETRESGENE AUTOLEUCE (LETE-CEL; GSK3377794) RESPONSE IN PATIENTS WITH ADVANCED MYXOID/ROUND CELL LIPOSARCOMA (MRCLS)

Gurpreet Kapoor*, 1Stefan Zajic, 2Sunil Suchindran, 3Iaegil Kim, 4Uma Saxena, 1Ashwarya Bhaskar, 2Heather Kosynski, 4Michael Nathenson, 1Jonim D’Souza, 1Benjamin Rich, 2Sandra D’Angelo, 3Mihaela Druta, 4Brian Van Tine, 3Neeta Somaiah, 4David Liebner, 2Scott Schuetze, 7Ioanna Eleftheriadou, 1GluoSmithKline, Collegeville, PA, United States; 3Memorial Sloan Kettering Cancer Center, New York, NY, United States; 2Washington University in St. Louis, MO, United States; 3University of Texas MD Anderson Cancer Center, Houston, TX, United States; 4Washington University School of Medicine, St. Louis, MO, United States; 5The Ohio State University, Columbus, OH, United States; 6University of Michigan, Ann Arbor, MI, United States

Background NCT02992743 is an open-label pilot study of lete-CEL, a New York esophageal squamous cell carcinoma 1 (NY-ESO-1)-specific autologous T-cell therapy, expressing a high-affinity T-cell receptor (TCR) that recognizes the NY-ESO-1 antigen epitope in complex with specific human leukocyte antigen (HLA) alleles of group A*02. Lele-CEL exhibited anti-tumor activity and an acceptable safety profile in patients with advanced MRCLS1 Previously, the association of T-cell kinetics with response and elevated inflammatory cytokines levels has been shown in responders. This abstract presents additional data on potential biomarkers of response and non-response to lete-CEL in patients with advanced MRCLS.

Methods Twenty patients with advanced MRCLS received either reduced-dose (Cohort 1 [C1]; n=10; 30 mg/m2 fludarabine for 3 days + 600 mg/m2 cyclophosphamide for 3 days) or standard-dose (Cohort 2 [C2]; n=10; 30 mg/m2 fludarabine for 4 days + 900 mg/m2 cyclophosphamide for 3 days) lymphodepletion prior to lete-CEL infusion (median transduced T-cell dose = 4.6 × 109). Key eligibility criteria were: ≥18 years of age; HLA-A*02:01 and/or 05 and/or 06; advanced or metastatic NY-ESO-1-positive MRCLS (≥30% of cells 2+/3+ by immunohistochemistry); prior anthracycline treatment; and measurable disease. Investigator-assessed objective response rate by Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 was the primary efficacy endpoint. For T-cell kinetics, a quantitative polymerase chain reaction assay was used to assess transgene vector copies in DNA from peripheral blood mononuclear cells collected longitudinally during the trial. Serum cytokines were measured by Meso Scale Discovery platform. Whole-transcriptome sequencing was performed on pre- and post-infusion tumor samples. Statistical methods specific to data modalities were used for post-hoc correlative analyses.

Results T-cell persistence at Week 4 was significantly higher (P=0.0067) in responders (n=5) than in non-responders (n=13). Lele-CEL peak cell expansion was associated with maximum levels of interferon-γ (IFN-γ; r=0.56, P=0.03) and interleukin-15 (IL-15; r=0.55, P=0.02) post-infusion. Preliminary gene expression data from the tumors collected at baseline showed enrichment of metabolic pathways in responders and epithelial–mesenchymal transition and fibroblast activation in non-responders.

Conclusions These data suggest that higher lele-CEL persistence and the association of lele-CEL expansion with cytokine upregulation post-infusion, as well as tumor-intrinsic transcriptional features, may have a role in lete-CEL response in patients with advanced MRCLS.

Acknowledgements Editorial support in the form of copyediting was provided by Scion and was funded by GSK. This study (208469; NCT02992743) was funded by GSK.

Trial Registration NCT02992743

REFERENCES

Ethics Approval The study protocol and patient informed consent documentation were approved by center Institutional Review Boards (or Independent Ethics Committees and other site-level committees, as deemed appropriate by the institution).

Consent The study protocol and patient informed consent documentation were approved by center Institutional Review Boards (or Independent Ethics Committees and other site-level committees, as deemed appropriate by the institution).