454 ANALYSIS OF NY-ESO-1 EXPRESSION IN SPECIMENS FROM A PHASE I/II NY-ESO-1 T-CELL THERAPY CLINICAL TRIAL IN NON-SMALL CELL LUNG CANCER AND FROM EXPLORATORY STUDIES IN MULTIPLE TUMOR TYPES

[1]Bryan Barnes*, [1]Ming Shan, [1]Kristin Blouch, [2]Mehmet Altan*, [1]Jaegil Kim, [1]Natalia Ramos-Hernandez, [1]Ellie Corigliano. *[1]GlaxoSmithKline, Collegeville, PA, USA; [2]MD Anderson Cancer Center, Houston, TX, USA*

Background This analysis evaluates an NY-ESO-1 immunohistochemistry (IHC) clinical trial assay in multiple tumor types for the identification of patients who may be eligible for NY-ESO-1 TCR T-cell targeted therapy. We provide an analysis of NY-ESO-1 expression and prevalence in non-small cell lung carcinoma (NSCLC) tumor samples from a patient cohort of an early Phase I/II clinical trial assessing NY-ESO-1 TCR T-cell therapy. Furthermore, we describe exploratory analyses of NY-ESO-1 prevalence and expression in a preliminary set of multiple tumor types to identify new indications for NY-ESO-1 TCR T-cell therapy.

Methods An IHC assay was developed to detect NY-ESO-1 expression in formalin-fixed paraffin-embedded (FFPE) specimens utilizing an anti-NY-ESO-1 monoclonal antibody, clone E978. NY-ESO-1 protein expression levels and diagnostic status were determined by pathological evaluation under light microscopy to capture the percentage of tumor cell staining across all tumor cells in specimens at staining intensities 0, 1+, 2+ and 3+. NY-ESO-1 expression data were assessed for: prevalence using a $\geq$10% cutoff at $\geq$ 1+ intensity to assign positivity, and prevalence across classification (primary and metastatic) and subtype (adenocarcinoma and squamous cell carcinoma) for the NSCLC specimens.

Results The overall prevalence for NSCLC specimens from the Phase I/II trial was 15% (49/325) for NY-ESO-1. A prevalence of 15% (29/191) for primary and 14% (19/132) for metastatic samples, 13% (20/159) for adenocarcinoma, and 14% (5/35) for squamous cell carcinoma was observed. No significant difference was observed between subtype or%Tumor at each intensity. The preliminary set of indications used in exploratory studies had an observed prevalence as follows: gastric adenocarcinoma, 14 (4/28)%; esophageal adenocarcinoma & gastric esophageal junction, 9% (3/35); urothelial, 19% (6/31); head and neck squamous cell carcinoma, 10% (3/30); triple negative breast, 10% (3/30); hepatocellular carcinoma, 3%(1/30); and melanoma, 11% (3/27). NY-ESO-1 protein expression was localized in the cells' nuclei and surrounding cytoplasm.

Conclusions Multiple indications assessed by the IHC clinical trial assay demonstrated similar NY-ESO-1 expression across the range of staining intensities and percentage of positive tumor observed as that in NSCLC, therefore warranting further development and validation of an IHC assay for NY-ESO-1 detection in these additional tumor types for use in clinical trials. These data support the use of IHC as a tool for the identification of patients whose tumors upregulate NY-ESO-1 in NSCLC and further encourage the investigation of multiple tumor types that may upregulate NY-ESO-1 as potential targets for NY-ESO-1 TCR T-cell therapies.

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REFERENCES

1. Thomas R, et al. *Front Immunol* 2018;**9**:947

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