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MOLECULAR BIOMARKERS TO IDENTIFY PATIENTS WHO BENEFIT FROM DURVALUMAB (ANTI-PD-L1) ALONE OR WITH TREMELIMUMAB (ANTI-CTLA-4) IN RECURRENT/METASTATIC HEAD AND NECK SQUMOUS CELL CARCINOMA FROM THE HAWK AND CONDOR STUDIES

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Abstract No. S44

Introduction

• There is a growing need to identify biomarkers that will improve the selection of patients who will best respond to immuno-oncology (IO) therapy, further elucidate drug mechanisms of action, and help tailor regimens.

• Biomarkers being explored include serum proteins, tumor-specific receptor expression patterns, factors in the tumor microenvironment, circulating immune and tumor cells, and host genomic factors.

• Tumor mutation burden (TMB) is emerging as a useful biomarker for the identification of patients who will benefit from IO therapy.

• Limited data support TMB and human leukocyte antigen (HLA) genotyping as predictive biomarkers for IO therapy.

• We conducted a proof of concept study in recurrent/metastatic head and neck squamous cell carcinoma (R/M HNSCC) to systematically analyze the association of these biomarkers with clinical outcomes and their interactions with programmed cell death ligand-1 (PD-L1).

Methods

Study Objectives

• Retrospective analysis to evaluate TMB and other biomarkers for their predictive potential in patients benefiting from durvalumab (D) or tremelimumab (T) regimens.

• Defined as the total number of somatic mutations per coding area of a tumor genome.

• Limited data support TMB and human leukocyte antigen (HLA) genotyping as predictive biomarkers for IO therapy.

• Paired formalin-fixed, paraffin-embedded (FFPE) archival tumor and peripheral blood mononuclear cell (PBMC) samples (as germline reference) were collected from 103 evaluable patients from HAWK/CONDOR. PBMC samples were collected approximately 1 year prior to study enrollment.

• TMB correlated with smoking (ρ = 0.24).

• In the randomized, open-label, Phase II CONDOR trial, 7,673 patients were enrolled.

• In the HAWK and CONDOR trials, 153 patients had evaluable FFPE samples (Figure 1). TMB distributions were comparable between studies.

• TMB correlated with smoking (p = 0.02) but not with HPV status (p = 0.24).

• TMB also did not correlate with PD-L1 status (not shown).

Key conclusions

• TMB is a possible predictive biomarker of IO therapy for HNSCC.

• Data from the CONDOR study suggest that TMB may have greater predictive potential when PD-L1 expression is low.

• PD-L1 and TMB appear to be independent of each other with double negative patients having the worst outcomes.

• Combined analysis of NLR and TMB may provide data in addition to PD-L1 for evaluating patients most likely to have long-term benefit.

• TMB correlated with smoking (ρ = 0.24).

• Patients with low PD-L1 and low TMB had the shortest OS compared to other TMB subgroups (Figure 3).

• OS in patients with high NLR (median), TMB status did not appear to be associated (Figure 3).

• TMB is a possible predictive biomarker of IO therapy for HNSCC.

• Data from the CONDOR study suggest that TMB may have greater predictive potential when PD-L1 expression is low.

• PD-L1 and TMB appear to be independent of each other with double negative patients having the worst outcomes.

• Combined analysis of NLR and TMB may provide data in addition to PD-L1 for evaluating patients most likely to have long-term benefit.

Table 1. Association of TMB with smoking and HPV status.

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Figure 1. TMB Data availability from the HAWK and CONDOR studies.

Figure 2. Association of TMB with smoking and HPV status.

Figure 3. Association of TMB with OS in patients with low PD-L1.

Figure 4. Association of low PD-L1 and low TMB with OS in all evaluable patients from HAWK/CONDOR.

References


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