MULTIPLEXED ION BEAM IMAGING (MIBI) UNCOVERS ADAPTIVE IMMUNE RESPONSES ASSOCIATED WITH CLINICAL OUTCOMES IN ORAL CAVIARY SQUAMOUS CELL CARCINOMA TREATED WITH NEOADJUVANT PD-1 INHIBITOR

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Background Oral cavity squamous cell carcinoma (OCSCC) is a subset of head and neck cancer with high recurrence rates. Recent evidence suggests that effective anti-tumor immunity can be induced by neoadjuvant immunotherapy in subsets of head and neck cancer patients, though immune mechanisms of response remain unclear. CD26, a novel costimulatory molecule, marks T cells with potent antitumor activity; therefore, we hypothesized that tumor infiltration by CD26+ T cells and other immune subsets may be related to treatment responsiveness. Here, using Multiplexed Ion Beam Imaging (MIBI), we report a first-in-class analysis of CD26 expression in relation to the immune and spatial architecture of the OCSCC microenvironment in patients treated with neoadjuvant nivolumab.

Methods Surgical pathology specimens from 8 OCSCC patients treated with pre-surgical nivolumab were stained with a panel of 31 metal-labeled antibodies. Tissues were imaged using MIBITM, and single cell segmentation was performed using a machine learning based tool that enabled downstream enumeration of 35 cell populations and quantitative analyses of both the costimulatory protein CD26 and immune checkpoint proteins as well as their spatial distribution. Cell population, protein expression, and spatial architectural differences were compared between patients with progressive disease and those with partial response.

Results A higher density of proliferating tumor cells was found in tumors from patients with progressive disease (p=0.01). Conversely, tumors from patients with partial response contained higher densities of cytotoxic T cells (p=0.004), particularly the activated and CD26+ cytotoxic T cell subsets. Evaluation of checkpoint expression across all populations showed that CD26 was predominantly expressed on T cells although a few of the myeloid subsets also expressed high CD26, particularly in patients with partial response. Finally, spatial analysis revealed pronounced interaction between tumor cells and cytotoxic T cells, notably of the activated cytotoxic T cell phenotype, in the samples from patients with partial response.

Conclusions MIBITM offers high-parameter tissue imaging, with a sensitivity and resolution suited to understanding the differences in the tumor immune landscape between patients with varied responsiveness to immunotherapies. In this study, OCSCC tumors from patients with partial response to neoadjuvant PD-1 inhibition showed evidence of adaptive immune responses with significant increases in infiltration of activated cytotoxic T cells and CD26+ cytotoxic T cells as well as greater interaction between activated cytotoxic T cells and tumor cells.