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High Density of Tumor-Associated Macrophage Staining Correlates with Poor Clinicopathologic Markers in Head and Neck Squamous Cell Carcinoma: A Meta-Analysis

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High density of tumor-associated macrophage staining correlates with poor clinicopathologic markers in head and neck squamous cell carcinoma: A Meta-Analysis

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Background: Head and neck squamous cell carcinoma (HNSCC) develops within a complex cellular microenvironment that promotes tumor growth, but also represents many potential therapeutic targets. Macrophage presence within that environment has been implicated in the growth, aggression, and persistence of HNSCC. Current literature reports variable degrees of association between tumor-associated macrophage (TAMs) density and clinicopathologic markers of disease. Inconsistent findings may result from grouping of TAM subtypes, which include both M1 (pro-inflammatory) and M2 (immunosuppressive). Our aim is to define the prognostic significance of the phenotypes of tumor-associated macrophages in HNSCC.

Methods: We conducted a meta-analysis of the existing publications investigating the relationship between TAMs (total and M2 subtype) and T stage, nodal involvement, vascular invasion, lymphatic invasion, and tumor differentiation. Forest plots and risk ratios were generated to report overall effect.

Results: Higher density of both total and M2 subtype of TAMs in the tumor microenvironment is associated with advanced T stage, increased rates of nodal positivity, presence of vascular invasion, and presence of lymphatic invasion ($p < 0.0001$). There is no significant association between either total or M2 TAM density and tumor differentiation.

Conclusion: Increased density of TAMs, including those of the M2 phenotype, correlates with poor clinicopathologic markers in HNSCC, and therefore poor clinical prognosis. It is unknown whether

this relationship is causative or correlative. Additional investigation into the mechanisms behind TAM recruitment and differentiation, and effect of TAM population manipulation on tumor behavior will help define the feasibility of TAM-targeted therapies.