PERIPHERAL LYMPHOCYTES AND LACTATE DEHYDROGENASE CORRELATE WITH IMPROVED RESPONSE AND SURVIVAL IN HEAD AND NECK CANCER TREATED WITH IMMUNE CHECKPOINT INHIBITORS

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Background: Little is known regarding peripheral blood biomarkers (PBBMs) for oncologic outcomes in recurrent/metastatic head and neck squamous cell carcinoma (R/M HNSCC) treated with immune checkpoint inhibitors (ICIs). We explored associations of PBBMs with outcomes and toxicities in R/M HNSCC treated with ICIs.

Methods: In this single-institution retrospective cohort study, records of 186 adult patients with R/M HNSCC treated with ICIs between 08/2012–03/2021 were reviewed. Pretreatment PBBMs investigated included lactate dehydrogenase (LDH), platelets, neutrophils, lymphocytes, monocytes, eosinophils, neutrophil-to-lymphocyte ratio (NLR), and prognostic nutritional index (PNI). Percent (%) and absolute (abs) values for each cell type were examined. Cox regression was performed to explore associations with time-to-event outcomes, including overall survival (OS) and progression-free survival (PFS). Logistic regression was performed for binary outcomes, including objective response (ORR) by RECIST 1.1 and grade ≥3 toxicities (G ≥3AE) by CTCAEv5 within 100 days of treatment initiation. Multivariable models for each outcome were created using elastic net variable selection method.

Results: Median age was 64 (range 24–90), 145 (78%) were male, 149 (82%) had ECOG ≤1, 81 (44%) were never-smokers, and 60 (33%) had p16-positive tumors. Single-agent pembrolizumab or nivolumab was used in 140 (75%) patients. Combined positive score (CPS) was available in 33 patients, with median CPS 31 (range 0–100). Univariate analyses adjusted for ECOG, p16, and smoking revealed that baseline higher LDH (p=0.025), neutrophils (%: p=0.002, abs: p=0.001), monocytes (abs: p=0.043), and NLR (p<0.001), and lower lymphocytes (%: p=0.001, abs: p=0.005), eosinophils (%: p=0.046), and PNI (p=0.005) correlated with worse OS. Elevated platelets (p=0.010), neutrophils (%: p=0.010, abs: p=0.001), and NLR (p<0.001), and decreased lymphocytes (%: p<0.001) and PNI (p=0.007) correlated with worse PFS. No peripheral blood parameter reached significance for G ≥3AEs or ORR, although % lymphocytes, absolute neutrophils, and LDH were borderline significant for ORR (p=0.066, p=0.055, and p=0.069, respectively). Refitted multivariable models adjusted for ECOG, p16, and smoking confirmed that lower % lymphocytes and higher LDH and absolute neutrophils correlated with worse OS and PFS. Lower % lymphocytes and higher LDH also correlated with worse ORR.

Conclusions: In the largest cohort to date of R/M HNSCCs treated with ICIs, our variable selection method showed that baseline lower % lymphocytes and higher LDH and absolute neutrophils correlated with worse OS and PFS, and lower % lymphocytes and higher LDH correlated with worse ORR. PBBMs are promising prognostic tools for immunotherapy in HNSCC and warrant further investigation in a large, prospective study along with validation with CPS biomarker.