915P Longer OS and RFS for CD3high/PD-L1+ head and neck squamous cell carcinoma (HNSCC) patients

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Background: T cell infiltrates are associated with longer survival in HNSCC. For PD-L1 expression, aside of treatment targeting the PD1/PD-L1 axis, published data are equivocal. In this analysis, we combined CD3 density and PD-L1 expression in a cohort of HNSCC patients treated with surgery and risk-adapted adjuvant therapy.

Methods: IHC for CD3 and PD-L1 (E1L3N) was performed in a TMA with 457 HNSCC (triplicates). Digital image analysis (QuPath) was performed to measure CD3 densities (cells/mm^2). PD-L1 expression was assessed in tumor and immune cells analogue to CPS. Overall survival (OS) and recurrence-free survival (RFS) in months were calculated using the Kaplan-Meier method and were compared by log-rank tests. A multivariable cox regression analysis was performed for T-, N-, HPV-status and CD3/PD-L1 (hot vs. cold).

Results: CD3 densities compared by primary tumor site were significantly different, whereas PD-L1 CPS were not. Median CD3 density of the respective primary site was used for binarization (CD3$^{high/low}$). 343 patients (pt) were evaluable for OS and 324 for RFS. CD3^{high} pt had longer median OS ($p<0.001$; not reached vs. 52.0 Mo) and RFS ($p<0.001$; 111,3 vs. 43.3 Mo) compared to CD3^{low}. Pt with PD-L1 expression CPS=1-19 and CPS20 had longer OS ($p=0.009$) and longer RFS ($p=0.019$) than pt with CPS<1 (CPS=1-19 vs CPS20 = ns). Binarization by CPS1 resulted in longer median OS ($p=0,002$; 111,3 vs. 49,3 Mo) and RFS ($p=0.006$; 98.3 vs. 41.0 Mo) compared to CPS<1. OS and PFS were significantly longer for CD3^{high}/CPS1 compared to all other combinations ($p<0.001$). CD3^{low}/CPS<1, CD3^{low}/CPS and CD3^{high}/CPS<1 did not differ significantly for OS or RFS. CD3^{high}/CPS1 (*hot*) was grouped against CD3^{low}/CPS<1, CD3^{low}/CPS and CD3^{high}/CPS<1 combined (*cold*). In a multivariable cox regression for OS, N-status (hazard ratio (HR) = 1.95), HPV-status (HR = 0.422) and "hot" (HR = 0.403) were independent prognostic markers. For RFS only "hot" was an independent prognostic marker (HR = 0.526).

Conclusions: The combination of CD3-density and PD-L1 expression performed superiorly in comparison to CD3 or PD-L1 alone. This may explain the equivocal impact of PD-L1 on OS and RFS. CD3-density combined with PD-L1 expression may identify patients who could benefit most from immunotherapy.

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