909P Immunoscore-IC predicts nivolumab efficacy as adjuvant treatment after salvage surgery in head and neck cancer squamous cell carcinoma: The ADJORL1 trial

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Background: Locoregional failures or second primary in head and neck squamous cell carcinoma (HNSCC) have a 2 year DFS from 10 to 30% and OS from 30 to 60% with conventional therapies (reirradiation or wait and see strategy). Adjuvant anti-PD1 immunotherapy after salvage surgery could be an alternative to reirradiation and provide better survival with less toxicities. Biomarkers could help select patients who will benefit. Immunoscore Immune Checkpoint (Immunoscore IC® test, Veracyte ; IS-IC) is an in vitro quantification of CD8+ and PDL1+ expressing cells in the tumor environment. In non-small cell lung cancers and colorectal cancers, a high IS-IC score is associated with better outcomes. We aimed to identify if IS-IC and CPS (Combined positive score) could predict better outcomes for local relapses of HNSCC treated with adjuvant anti-PD1.

Methods: This multicentric phase II trial was conducted between 2018 and 2021. Inclusion criteria were recurrence or second primary of HNSCC in irradiated area, operated by salvage surgery. Pathological bad prognosis factors justifying adjuvant treatment were needed, with no distant metastases. Adjuvant treatment with Nivolumab was given for 6 months. Primary endpoint was two-year DFS. IS-IC and CPS performed on relapsing tumor material to identify biomarkers predictive of outcomes.

Results: 57 patients were treated. The 2-years DFS and 2-years OS were respectively 46.6%, 90%CI [36.1-57.5%] and 67.3%, 95%CI [54.2-78.2%]. IS-IC was available for 48 patients. A high IS-IC was associated with an improved OS compared to a low IS-IC (HR=0.12 [95%CI, 0.03-0.40]). High IS-IC was also associated with an improved DFS compared to a low IS-IC (HR=0.22 [95%CI, 0.09-0.51]). A high CPS was significantly associated with an improvement of DFS. For patients with a CPS <1, [1-19] and >19, the 2-years DFS were respectively 12.5% IC95%[2.2;47.1], 43.5% IC95%[25.0;64.0] and 63.6% IC95%[43.0;80.3].

Conclusions: These results show that IS-IC and CPS informs on the prognosis of relapsing HNSCC patients treated with anti-PD1 and could be used to select patients who will benefit from adjuvant immunotherapy after salvage surgery.

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910P Multi-omics analysis of tislelizumab plus nab-paclitaxel and cisplatin as neoadjuvant immunochemotherapy for locally advanced hypopharyngeal squamous cell carcinoma: A prospective single-arm phase II trial

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Background: Hypopharyngeal squamous cell carcinoma (HPSCC) suffers poorest prognosis among head and neck subtypes. The efficacy, safety, and biomarkers of neoadjuvant immunochemotherapy for HPSCC warrant further investigation.

Methods: This prospective phase II trial enrolled untreated locally advanced HPSCC pts and utilized tislelizumab plus nab-paclitaxel and cisplatin as neoadjuvant therapy. The primary endpoints were ORR and pCRR. The secondary endpoints were DCR, PFS, OS, DFS, and safety. PD-L1 expression was evaluated through IHC. Genomic alteration was detected via targeted sequencing. Plasma biomarker analysis was performed using Olink proteomics assay.

Results: From May 2022 to Nov 2023, 45 pts were included. The ORR, DCR, and pCRR were 62.2%, 100%, and 21.4%. Two pts with radiological SD were ultimately confirmed pCR. With a median follow-up of 11.6 months, the median PFS, DFS, and OS were not reached. The 12-month PFS, DFS, and OS rates were 69.8%, 81.6%, and 77.4%. The 12-month larynx preservation rate was 91.9%. AEs were mostly G1-2, with a 31% incidence of $\geq$G3 AEs, primarily neutropenia (18%). Pts who had undergone surgery had significantly better PFS (HR=0.24, P=0.03) and OS (HR=0.21, P=0.04) compared to others. Pts with PD-L1 CPS$\geq$5 had significantly better PFS (HR=0.20, P=0.03) and OS (HR=0.09, $P<0.01$) than those with PD-L1 CPS$<$5. Genomic alteration was not associated with tumor response or survival. Olink proteomics assay revealed that baseline protein levels of GZMH, GZMA, KLRD1, IL12RB1, CD244, NCR1, CXCL10, CXCL13, LAG3, IL10, MCP-3, CCL20, CD8A, and TWEAK were significantly higher in pts with tumor shrinkage of $<$50% compared to those with tumor shrinkage of $\geq$50%.

Conclusions: Tislelizumab plus nab-paclitaxel and cisplatin as neoadjuvant therapy demonstrated manageable safety and promising efficacy in HPSCC. Pts with radical surgery achieved PFS and OS benefit. PD-L1 CPS$\geq$5 is an indicator for better PFS and OS. The discordance between radiological and pathological assessments deserves further exploration. Plasma proteins show promising predictive value for predicting the deep response to immunochemotherapy in HPSCC.

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911P Association of genomic landscape and plasma protein dynamic changes with clinical outcome in patients with R/M HNSCC treated with pembrolizumab with nab-paclitaxel and platinum

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Background: The predictive effects of immunotherapy biomarkers are still limited in clinical practice. We evaluated the tumor genomic landscape and dynamic changes in plasma circulating biomarkers in R/M HNSCC pts receiving immunochemotherapy.

Methods: The clinical data were obtained from R/M HNSCC pts treated with pembrolizumab, nab-paclitaxel and platinum from the phase II clinical trial (NCT04857164). Tissue and blood specimens were collected for multi-omics analyses,