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LBA40 Neoadjuvant nivolumab and nivolumab plus ipilimumab induce (near-) complete responses in patients with head and neck squamous cell carcinoma: The IMCISION trial

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Background: Nivolumab (NIVO) alone or with ipilimumab (COMBO) immune checkpoint blockade (ICB) prior to curative surgery has shown promising results in multiple tumor types. We completed a phase Ib/II study with neoadjuvant NIVO or COMBO in resectable head and neck squamous cell carcinoma (HNSCC) and show safety, efficacy and correlative biomarker results.

Methods: 32 stage II-IVB HNSCC patients indicated for curative (salvage) surgery were treated with NIVO (240mg, weeks 1&3, N=6) or NIVO (240mg, weeks 1&3) + IPI (1mg/kg, week 1, N=26) prior to surgery in week 5. Imaging was performed at baseline and week 4. AEs were reported in terms of CTCAE. Pathological response (pR) was defined as % change in viable tumor cells from baseline to on-treatment; ≥90% pR was considered (near-) complete response (pCR). WES and RNAseq were performed on paired tumor biopsies.

Results: 32 (31 HPV-negative) patients started treatment (stage II n=3, III n=8, IVA-B n=11, recurrent disease n=10). 6 patients included with recurrent disease had had previous (C)RT. 1 patient discontinued ICB after one course due to patient's preference. Surgery was not postponed in any patient. 3/32 patients did not undergo surgery: 1 due to unresectable PD and 2 due to reasons unrelated to ICB or disease. Grade 3-4 irAEs in 11/32 patients were well manageable. (Near-)pCR in the primary tumor was seen in 9/29 evaluable patients (31%). Another 31% of patients had 20-89% pR. At 14 months median FU, RFS for patients with (near-)pCR was 100%, significantly better than patients with <90% pR (p=<0.05). Metabolic response assessment with FDG-PET (week 4) was able to identify (near-)pCRs. A baseline AID/APOBEC-associated tumor mutational profile was correlated with (near)pCR (p=<0.05). Finally, (near)pCR tumors were characterized by a decrease in hypoxia gene expression after ICB.

Conclusions: Neoadjuvant ICB was feasible in HNSCC and induced (near)pCR in 31% of evaluable patients at time of surgery, which was accompanied by 100% RFS. Baseline AID/APOBEC-related mutations, on-treatment FDG-PET and resolution of hypoxia need future validation to discover their potential role as biomarkers for (near)pCR after ICB in HNSCC.

Clinical trial identification: NCT03003637.

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