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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.

Legal entity responsible for the study
Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital.
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Disclosure

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