VIRTUAL ESMO congress 2020

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.

Legal entity responsible for the study

Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital.

Funding

Bristol Myers-Squibb.

Disclosure

L. Zuur: Spouse/Financial dependant: Mosadex U.A.; Spouse/Financial dependant: Obvious Pharmaceuticals BV. M.W. van den Brekel: Research grant/Funding (institution), Travel/Accommodation/Expenses: ATOS Medical. S.M. Willems: Research grant/Funding (institution): Roche; Research grant/Funding (institution): Pfizer; Research grant/Funding (institution): MSD; Research grant/Funding (institution): Bayer; Research grant/Funding (institution): Amgen; Research grant/Funding (institution): BMS; Research grant/Funding (institution): Nextcure. T.N. Schumacher: Full/Part-time employment: Kite Pharma; Leadership role: Kite Pharma; Shareholder/Stockholder/Stock options: AIMM Therapeutics; Shareholder/Stockholder/Stock options: Allogene; Shareholder/Stockholder/Stock options: Merus; Shareholder/Stockholder/Stock options: Kite Pharma; Shareholder/Stockholder/Stock options: Neon Therapeutics; Shareholder/Stockholder/Stock options: Neogene Therapeutics; Shareholder/Stockholder/Stock options: Scenic Biotech; Advisory/Consultancy: AIMM Therapeutics; Advisory/Consultancy: Allogene; Advisory/Consultancy: Merus; Advisory/Consultancy: Neon Therapeutics; Advisory/Consultancy: Neogene Therapeutics; Advisory/Consultancy: Scenic Biotech; Research grant/Funding (self): Merck KgGA; Research grant/Funding (self): MSD; Licensing/Royalties: Kite Pharma; Licensing/Royalties: Neon Therapeutics; Licensing/Royalties: Scenic Biotech; Licensing/Royalties: Immatics. C.U. Blank: Honoraria (self), Paid to the institute: BMS; Honoraria (self), Paid to the institute: MSD; Honoraria (self), Paid to the institute: Roche; Honoraria (self), Paid to the institute: Novartis; Honoraria (self), Paid to the institute: GSK; Honoraria (self), Paid to the institute: AZ; Honoraria (self), Paid to the institute: Pfizer; Honoraria (self), Paid to the institute: Lilly; Honoraria (self), Paid to the institute: Genmab; Honoraria (self), Paid to the institute: Pierre Fabre; Honoraria (self), Paid to CUB: Third Rock Ventures; Shareholder/Stockholder/Stock options: Uniti Cars; Shareholder/Stockholder/Stock options: Immagene BV; Research grant/Funding (self), Paid to the institute: BMS; Research grant/Funding (self), Paid to the institute: Novartis; Research grant/Funding (self), Paid to the institute: NanoString. J.P. de Boer: Advisory/Consultancy: MSD; Research grant/Funding (self), Paid to the institute: Merck KgGa; Travel/Accommodation/Expenses: MSD. J.B.A.G. Haanen: Shareholder/Stockholder/Stock options: Neogene Therapeutics; Research grant/Funding (institution): BMS; Research grant/Funding (institution): MSD; Research grant/Funding (institution): GSK; Research grant/Funding (institution): Neon. All other authors have declared no conflicts of interest.