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Pembrolizumab versus cetuximab, concomitant with radiotherapy (RT) in locally advanced head and neck squamous cell carcinoma (LA-HNSCC): Results of the GORTEC 2015-01 “PembroRad” randomized trial


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Background
Based on the hypothesis of a potential synergistic effect of the anti-PD1 pembrolizumab when combined with RT, this new combination was tested in a randomized trial against the well-established standard of care (SOC) cetuximab-RT in LA-HNSCC.

Methods
In this phase II randomized trial, patients with non operated stage III-IVa-b SCC of oral cavity, oropharynx, hypopharynx and larynx and unfit for receiving high dose of cisplatin were enrolled. Patients received once-daily IMRT up to 69.96 Gy concomitant with cetuximab (Cetux-RT arm: 400 mg/m$^2$ loading dose and 250 mg/m$^2$ weekly) or pembrolizumab (Pembro-RT arm: 200 mg Q3W during RT). The primary endpoint was 15-month Loco-Regional Control (LRC) rate and secondary endpoints included Progression-free survival (PFS), Overall Survival (OS) and tolerance. To detect a difference between arms of 60% to 80% in 15-month LRC, inclusion of 66 patients per arm was required to achieve a power of at least 0.85 at 2-sided significance level of 0.20.

Results
Between May 2016 and October 2017, 131 patients were randomized and treated by 27 centers: 65 patients in Cetux-RT arm and 66 patients in Pembro-RT arm. The median age was 65 years, 92% were smokers, 60% of oropharynx (46% p16+), 41% of N2a-N3 with 25%, 56% and 19% of stage III, IVa and IVb respectively. Median follow-up was 25 months in both arms. Acute toxicity was lower in Pembro-RT arm than Cetux-RT arm: 74% vs 92% patients with at least one grade ≥ 3 acute adverse events (p=0.006), mainly due to dermatitis in radiation field, mucositis and cutaneous rash. LRC at 15 months were 59% in Cetux-RT arm and 60% in Pembro-RT arm, not significantly different: OR=1.05 (95%CI: 0.43-2.59, p=0.91). 2-year PFS rate was 40% in the Cetux-RT arm vs 42% in the Pembro-RT arm. There was no significant difference between arms for PFS: HR=0.83 (95%CI 0.53-1.29, p=0.41). 2-year OS rate was 55% in the Cetux-RT arm vs 62% in the Pembro-RT arm. OS was not significantly different between arms: HR=0.83 (95%CI: 0.49-1.40, p=0.49).

Conclusions
Compared to the SOC cetuximab-RT, the anti-PD1 pembrolizumab concomitant with RT did not improve carcinologic outcomes but appeared less toxic.

Clinical trial identification
NCT 02707588.

Legal entity responsible for the study
GORTEC.

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GORTEC.
Disclosure

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