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Avelumab-cetuximab-radiotherapy versus standards of care in patients with locally advanced squamous cell carcinoma of head and neck (LA-SCCHN): Randomized phase III GORTEC-REACH trial

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Background

Based on a potential synergistic effect of anti–PD-L1 avelumab plus cetuximab and radiotherapy (RT), this combination was tested in a randomized phase III trial against 2 standards of care (SOC) in LA-SCCHN.

Methods

The trial comprised 2 cohorts of patients (pts) fit for cisplatin (3 cycles of 100 mg/m^2, Q3W) or unfit for cisplatin. The SOC was IMRT 70 Gy / 6.5 weeks with cisplatin in fit pts and with cetuximab in unfit pts (*Bonner, 2006*). In both cohorts, experimental arm (Exp) was 70 Gy / 6.5 weeks plus weekly cetuximab and avelumab 10 mg/kg at Day-7 and every 2 weeks during RT followed by avelumab for 12 months. The primary endpoint was progression-free survival (PFS). In Unfit pts, 115 events were needed / 277 pts to detect a HR of 0.62 (1-sided 0.05 type I error; power 80%). In Fit pts, 166 events were needed / 430 pts to detect a HR of 0.64 (2-sided 0.05 type I error; power 80%).

Results

Between 2017 and 2020, 707 pts were randomized. *For cisplatin unfit pts*, out of 277 pts, the number of PFS events was reached. Median age 67 years, 88% smokers, 61% oropharyngeal tumors (35% p16+), 24% stage III, 76% stage IV. Grade >= 3 AEs were 80% in both arms (p=0.91). Median follow-up was 21 months (IQR 15-28). PFS rate at 2 years (95%CI) was 44% (35%-53%) in Exp vs 31% (23%-40%) in Cetux-SOC (HR 0.85; p=0.15). Loco-regional progression at 2 years (95%CI) was 34% (26%-43%) in Exp vs 44% (35%-53%) in Cetux-SOC (HR = 0.83; p=0.34). Distant metastasis rate was lower in Exp (HR = 0.31, p=0.007). The 2-year OS rate (95%CI) was 58% (48%-67%) in Exp *vs* 54% in SOC (44%-64%) (HR 1.08; p-=0.69). *For cisplatin fit pts*, out of 430 pts, the number of PFS events was not reached. The interim analysis for futility based on 89 events in 317 first pts showed a 1-year PFS rate (95%CI) of 64% (54%-72%) in Exp *vs* 73% in SOC-cisplatin (65%-81%): HR 1.27 (95%CI 0.83-1.93), crossing the futility boundary.

Conclusions

In cisplatin-Unfit pts, a favorable effect of adding avelumab to cetuximab was seen on PFS, local-regional control, distant metastases, but the primary endpoint on PFS was not met. In cisplatin-Fit pts, the futility boundary for efficacy was crossed, favoring SOC cisplatin.

Clinical trial identification

NCT02999087.

Legal entity responsible for the study

GORTEC.

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Disclosure

All authors have declared no conflicts of interest.