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Standard versus fractionated high dose cisplatin concomitant with radiotherapy in locally advanced head & neck squamous cell cancer (LA-HNSCC): Results of the GORTEC 2015-02 CisFRad randomized trial

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Background

Chemo-radiation (CRT) with high dose cisplatin (Cis) 100 mg/m^2 q3w (3 cycles) is the standard of care (SOC) in LA-HNSCC. Cumulative delivered dose of Cis is prognostic of survival, even beyond 200 mg/m^2 (P Strojan 2016) but high toxicity compromises its delivery. Fractionated dose of Cis allows decreasing the serum concentration peak and toxicity. No direct comparison was done of SOC vs. fractionated high dose Cis (FHD Cis) leading the GORTEC to conduct a randomized phase II.

Methods

The trial, stratified on postoperative or definitive CRT, compares SOC to FHD Cis (25 mg/m^2/d d1-4 q3w (3 cycles)) concomitantly to definitive (70 Gy/7 weeks) or postoperative (66 Gy/6.5 weeks) RT. The primary endpoint was the cumulative delivered Cis dose.

Results

A total of 124 patients (pts) were randomized at 10 sites in France: 65 in SOC arm and 59 in FHD Cis arm. Median age: 60, Male: 85%, ECOG 0: 50%, Stage IV: 77%, definitive CRT: 58%, oropharynx: 51% (p16+: 43%), smoking history 89% of pts (median of 40 pack-years), all well balanced between the 2 arms. The median cumulative Cis dose was 291 mg/m^2 (interquartile [IQ]: 256-298) for FHD Cis vs. 280 mg/m^2 (IQ: 199-295) for SOC (p=0.03). 84% of pts with FHD Cis received the third cycle of Cis vs. 67% with SOC (p=0.03). Overall, 50 (35%) grade III-IV acute toxicities occurred with FHD Cis vs. 91 (65%) with SOC (p<0.001) leading to 19 SAEs with FHD Cis vs. 32 with SOC, including one toxic death with pneumonitis and febrile neutropenia (p=0.07). With a median follow-up of 2.2 years (yrs) (0-3.4), the 2-yr loco-regional failure-free survival (LRFFS) was 61% with FHD Cis vs. 58% with SOC (hazard ratio [HR]=0.97, 95%CI: 0.54-1.74, p=0.91). The 2-yr progression-free and overall survival FHD Cis / SOC were: 54%/ 54% (HR=1.05, 95%CI: 0.60-1.81, p=0.87) and 69%/ 68% (HR=0.88, 95%CI: 0.48-1.66, p=0.67) respectively.

Conclusions

FHD Cis allowed significantly more Cis to be delivered, with significantly lower toxicity, when compared to SOC. LRFFS, PFS and OS were not significantly different between the two arms. FHD Cis concomitantly with RT is a treatment option which deserves further consideration.

Clinical trial identification

EudraCT: 2015-001928-29.

Legal entity responsible for the study

GORTEC Group.

Funding

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Disclosure

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