Avelumab-cetuximab-radiotherapy *versus* standards of care in locally advanced squamous cell carcinoma of the Head and Neck: Safety phase of the randomized **phase III trial GORTEC 2017-01 REACH**

1118PD Abstract **#4934**

Y. Tao[1], A. Auperin[1], XS. Sun[2], C. Sire[3], L. Martin[4], A. Coutte[5], C. Lafond[6], J. Miroir[7], X. Liem[8], F. Rolland[9], A. Maillard[1], N. Colin-Batailhou[10], C. Michel[10], J. Thariat[11], J. Guigay[12], J. Bourhis[13]

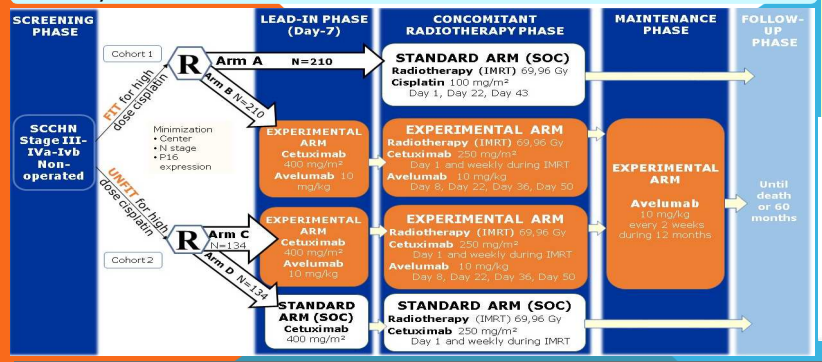
[1]Gustave Roussy, Villejuif, [2]Hopital Nord Franche-Comté de Montbéliard & CHRU de Besançon, [3]Centre Hospitalier de Lorient , [4]Centre G. Le Conquérant, Le Havre, [5]CHU Amiens Sud, France, [6]Centre Jean Bernard, Le Mans, [7]Centre Jean PERRIN, Clermont-Ferrand, [8]Centre Oscar Lambret, Lille, [9]ICO Rene-Gauducheau, Nantes, [10]GORTEC, Tours, [11]Centre Francois Baclesse, Caen [12] Centre Antoine Lacassagne, Nice ; all above in FRANCE; [13]CHUV Lausanne, SWITZERLAND

BACKGROUND

Based on the hypothesis of a synergistic effect of the anti-PD-L1 avelumab when combined with cetuximab and radiotherapy, this new combination was tested in a large scale randomized trial against 2 well established standards of care (SoC) in locally advanced (LA) squamous cell carcinoma of the head and neck (SCCHN).

DESIGN

This randomized multicenter phase III trial comprised 2 cohorts of patients deemed fit (Cohort 1, n=420) to receive high dose cisplatin (CDDP) or unfit to receive CDDP (Cohort 2, n=268). The SoC was IMRT (69.96 Gy, 33 fractions) combined with CDDP (100 mg/m², Q3W) in cohort 1 or with cetuximab in cohort 2 (400 mg/m² Day-7 and 250 mg/m² weekly). In both cohorts, experimental (exp) arms were IMRT concomitant with cetuximab and avelumab (10 mg/kg Day-7 and every 2 weeks) followed by avelumab 10 mg/kg bi-monthly for 12 months.



OBJECTIVE

The primary objective was to test whether the combination avelumab-cetuximab-radiotherapy is superior to SoC for progression-free survival in each cohort.

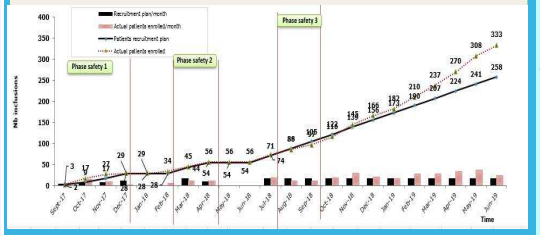
METHODS

A safety phase was designed by monitoring grade ≥ 4 acute adverse events (AE) in both experimental arms. The acceptable and unacceptable grade ≥ 4 AE rates were 15% and 35%. Monitoring was done in 3 steps with overall 1-sided alpha error of 0.10, Lan-DeMets alpha spending function and 95% power. It ran on the first 41 treated patients (pts) in the exp arms after 8 weeks follow-up.

Safety phase data were reviewed by an Independent Data Safety Monitoring Committee (IDSMC).

The stopping rules at each step were:

- **1st step** in 14 patients: ≥ 7 patients with grade ≥ 4 AE
- **2nd step** in 27 patients: ≥ 8 patients with grade ≥ 4 AE
- **3rd step** in 41 patients: ≥ 10 patients with grade ≥ 4 AE



RESULTS

Between 09/2017 and 08/2018, 82 LA SCCHN pts were randomized: 41 in the exp arms (21 in arm B, 20 in arm C).

In the exp arms:

All pts received the entire RT, except one pt of arm C with early stop after 55 Gy.

36 pts (88%) and 31 pts (76%) received the expected number of avelumab and cetuximab administrations during RT.

The most common grade ≥3 AEs were radiation dermatitis, mucositis and dysphagia.

The thresholds of the safety monitoring rule were not crossed at any of the 3 steps.

At the last step, grade ≥4 AEs occurred in 5/41 (12%) pts in the exp arms (all in arm C), in 3/21 (14%) pts in arm A and 2/20 (10%) in arm D. One grade 5 AE occurred in arm A.

The grade 4 AE in the exp arms were radiation dermatitis, mucositis, lymphopenia, anemia (colon polyp bleeding), gastrointestinal perforation on ileocolic anastomosis.

Table 1: Initial characteristics

	Arm A n=21	Arm B n=21	Arm C n=20	Arm D n=20
Oropharynx	16 (76%)	15 (71%)	14 (70%)	15 (75%)
Hypopharynx	3 (14%)	5 (24%)	3 (15%)	3 (15%)
Oral cavity	1 (5%)	0 (0%)	1 (5%)	1 (5%)
Larynx	1 (5%)	1 (5%)	2 (10%)	1 (5%)
Oropharynx p16 positive	8 (38%)	7 (33%)	7 (35%)	6 (30%)
Stage				
III	2 (10%)	3 (14%)	2 (10%)	7 (35%)
IVa	15 (71%)	13(62%)	17(85%)	8 (40%)
IVb	4 (19%)	5 (24%)	1 (5%)	5 (25%)

Table 2: Skin toxicity

	Arm A (N=21)	Arms B+C (N=41)	Arm D (N=20)
Dermatitis radiation			
Grade 1	11 (52%)	8 (20%)	1 (5%)
Grade 2	7 (33%)	11 (27%)	7 (35%)
Grade 3	4 (19%)	20 (49%)	11 (55%)
Grade 4	0	1 (2%)	0
Rash			
Grade 1	0	15 (37%)	7 (35%)
Grade 2	0	16 (39%)	6 (30%)
Grade 3	0	2 (5%)	3 (15%)
Grade 4	0	0	0

CONCLUSIONS

The combination of avelumab, cetuximab and RT was tolerable for patients with LA-SCCHN in the safety phase of this ongoing phase 3 trial and an approval to continue the trial was given by IDSMC.

Clinicaltrial.gov: NCT02999087