

NEWSLETTER REACH



HEAD AND NECK INTERGROUP GORTEC-GETTEC-GERCOR-UNICANCER

REACH Safety Phase

Dear Investigators,

The entire REACH team would like to recognize all the hard work done by everyone during the first steps of the safety phase.

Thanks to your active collaboration in patient enrollment and data collection, **IDSMB** will be able to examine safety data soon.

Results are encouraging with **no safety concerns**. Our new objective is to enroll **the last 26 patients of the safety phase within the summer**.

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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

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BACKGROUND

Aim: To evaluate the safety and efficacy of a synergistic effect of the anti-PD-L1 avelumab when combined with cetuximab and radiotherapy in locally advanced squamous cell carcinoma of the head and neck (LACC).

DESIGN

Phase III trial comparing 2 cohorts of patients (1:1) to receive high-dose cisplatin (100mg/m² or 40mg/m²) + cetuximab (500mg) + radiotherapy (70Gy) or standard of care (SOC) consisting of cisplatin (40mg/m²) + cetuximab (500mg) + radiotherapy (70Gy).

OBJECTIVE

The primary objective is to test whether the combination avelumab-cetuximab-radiotherapy is superior to SOC for progression-free survival in LACC.

METHODS

A run-in safety phase was performed to assess feasibility and tolerability of the experimental combination. Monitoring of grade 3-4 acute adverse events in both experimental arms was planned with full and alternative hypotheses of 30 and 20%.

RESULTS

The safety phase was approved by the IDEC and planned to be run on the first 41 treated patients in the experimental arms after 8 weeks follow-up.

1st Step (18 patients): Stopping rule in case of 2 patients with grade 4 Adverse Event (AE).

2nd Step (27 patients): Stopping rule in case of 2 patients with grade 4 AE.

3rd Step (45 patients): Stopping rule in case of 2 patients with grade 4 AE.

Results of the 1st step

Between September and December 2017, 29 patients (Stage III/IV, SCCN) were randomized including 14 in the experimental arms. The 1st step safety analysis was presented to the IDEC in early 2018. All patients required the entire radiotherapy as planned. Eight out of the 14 patients received the full concurrent systemic regimen as planned: 3 patients received 3 doses of cetuximab and 2 doses of avelumab; 3 patients received 2 doses of cetuximab and 2 doses of avelumab; 3 patients received 1 dose of cetuximab and 2 doses of avelumab. Three patients in the 1st step (21.4%) developed grade 4 AE according to NCI CTCAE v4.03: one dermatitis, one lymphopenia, one oral mucositis.

Results of the 2nd step

Between February and April 2018, 27 additional patients were enrolled (total 56 patients, 28 in experimental arms).

CONCLUSION

- The safety stopping rule was not crossed
- The IDEC gave approval to continue the trial
- Safety data of the 2nd step are currently collected and will soon be reviewed

IDSMB Meeting

27/06/2018

The second IDSMB Meeting will held in June, the 27th.

His responsibilities are:

- To guarantee the protection of the patients enrolled
- To ensure that the study conduct respects all ethical issues
- To ensure the independent review of scientific results during the study
- To assess the benefit/risks ratio

The 2nd meeting aimed to review toxicity data of the 28th first patients treated in the experimental arms and assess the inclusion resumption (step 2 of the safety analysis).

Regulatory Update

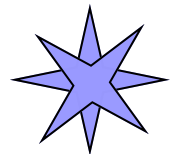
Country	Planned sites	Planned site initiation by 12/ 2018	Site Initiated	Approval Status	Patients Enrolled
France	59	59	11 4 sites planned during the summer	MSA2 Approved MSA3 Approved by ANSM (CPP pending)	56
Monaco	1	1	Planned in July	Approved	-
Switzerland	1	0	0	Not yet submitted	-

Our 2018 study milestones are to:

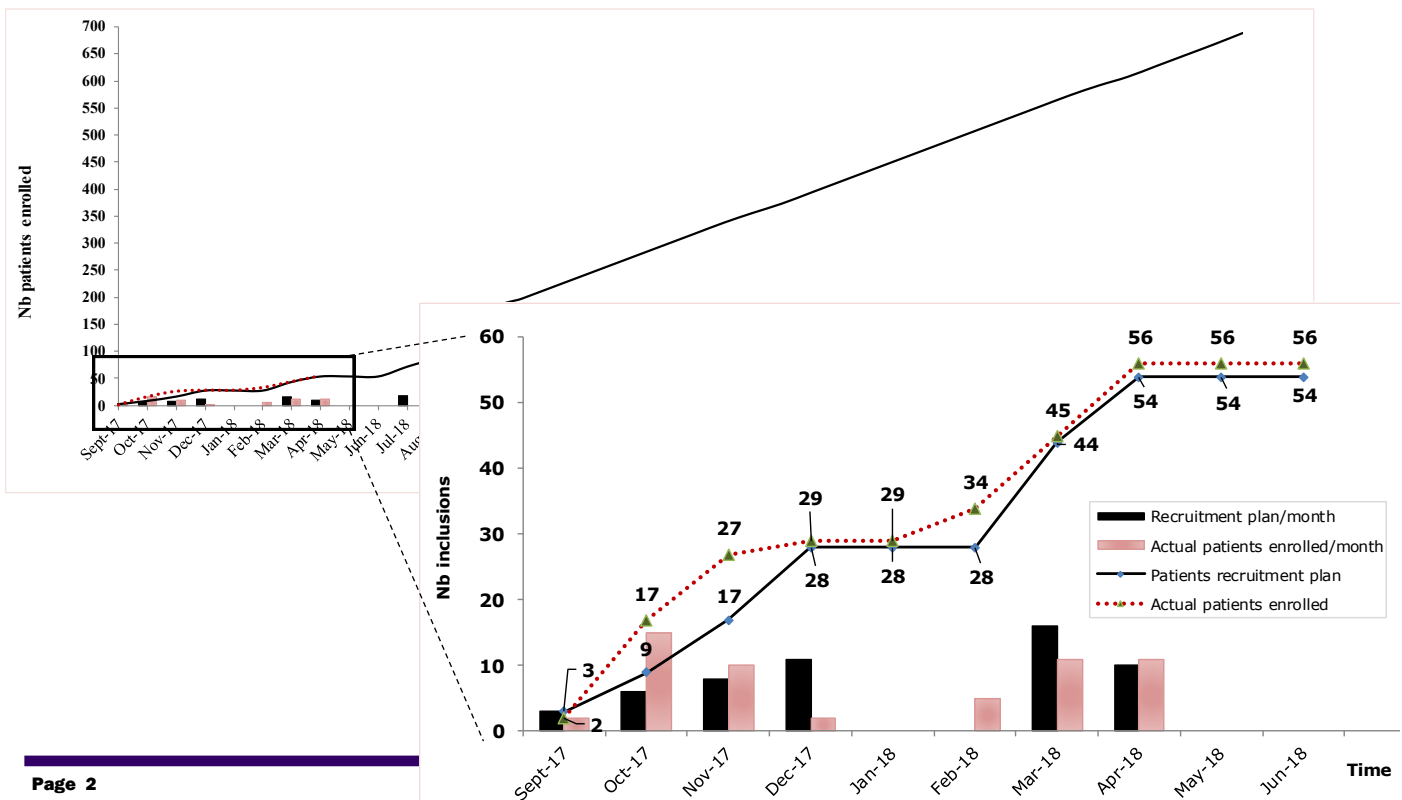
- ⇒ Run the 5 last safety centers during the summer: ICM, ICO Papin, Monaco, Institut Curie, CH Besançon
- ⇒ End the safety phase by end of Summer 2018.
- ⇒ Obtain health authorities and ethics committee approvals for Switzerland in 2019

THE FIRST 56 PATIENTS ENROLLED : THANKS TO STUDY CLINICAL TEAM !

Gustave Roussy—Villejuif (Dr Tao):	16 patients	
Hôp. Nord Franche Comté—Montbéliard (Dr Sun):	12 patients	
CH Bretagne Sud—Lorient (Drs Sire, Bera):	9 patients	
Centre Guillaume Le Conquérant (Dr Martin):	8 patients	
CHU Sud Amiens—Amiens (Pr Chauffert, Dr Coutte):	3 patients	
Centre Jean Perrin (Drs Miroir, Dillies):	2 patients	
Centre François Baclesse (Pr Thariat, Dr Johnson):	2 patients	Clinique Victor Hugo (Dr Lafond): 1 patient
Centre Oscar Lambret (Drs Abdeddaim, Lefebvre):	2 patients	ICO Gauducheau (Dr Rolland): 1 patient



Recruitment Update—Reach Safety Phase



Important Reminder

Main points related to cohort determination, modified at last protocol amendment:

- No sensorineural hearing loss (confirmed by audiogram): *investigator clinical judgment and presence/absence of patient complaint will prevail for evaluation even if an audiogram still shall be done*
- Addition of a new eligibility criterion: Age < 75 years. For patients aged 71-74-year-old, PS must be 0 and fit according to geriatric evaluation.
- In case of a patient presenting a non-eligibility criterion for cisplatin other than “sensorineural hearing loss”, the audiogram becomes optional.

Study treatments:

RT-CT Phase	Cisplatin (Arm A)	Cetuximab (Arm B / C / D)	Avelumab (Arm B / C)
Infusion rates Duration	120 minutes minimum	1 st infusion : 5 mg/min Subsequent infusions : 10 mg/min	1 hour (50-80 min)
Dose calculations	1st cycle (100 mg/m²): dose based on actual body weight with BSA ≤ 2 m ² Subsequent cycles (100 mg/m²): same dose as 1 st cycle as long as there's no change of ≥ 10% of baseline patient weight	1st infusion (400 mg/m²): dose based on actual body weight Subsequent infusions (250 mg/m²): dose based on actual body weight, reduction in case of weight loss ≥ 10% of baseline weight	1st infusion (10 mg/kg): dose based on actual body weight Subsequent infusions (10 mg/kg): same dose as 1 st infusion as long as there's no change of ≥ 10% of baseline patient weight
Infusion schedule	D1, D22, D43 21 (+/- 2) days between each infusion	Weekly: D-7 → D43 (D50 if RT still ongoing) 7 (+/-1) days between each infusion	Q2W: D-7 → D36 (D50 if RT still ongoing) 14 days between each infusion

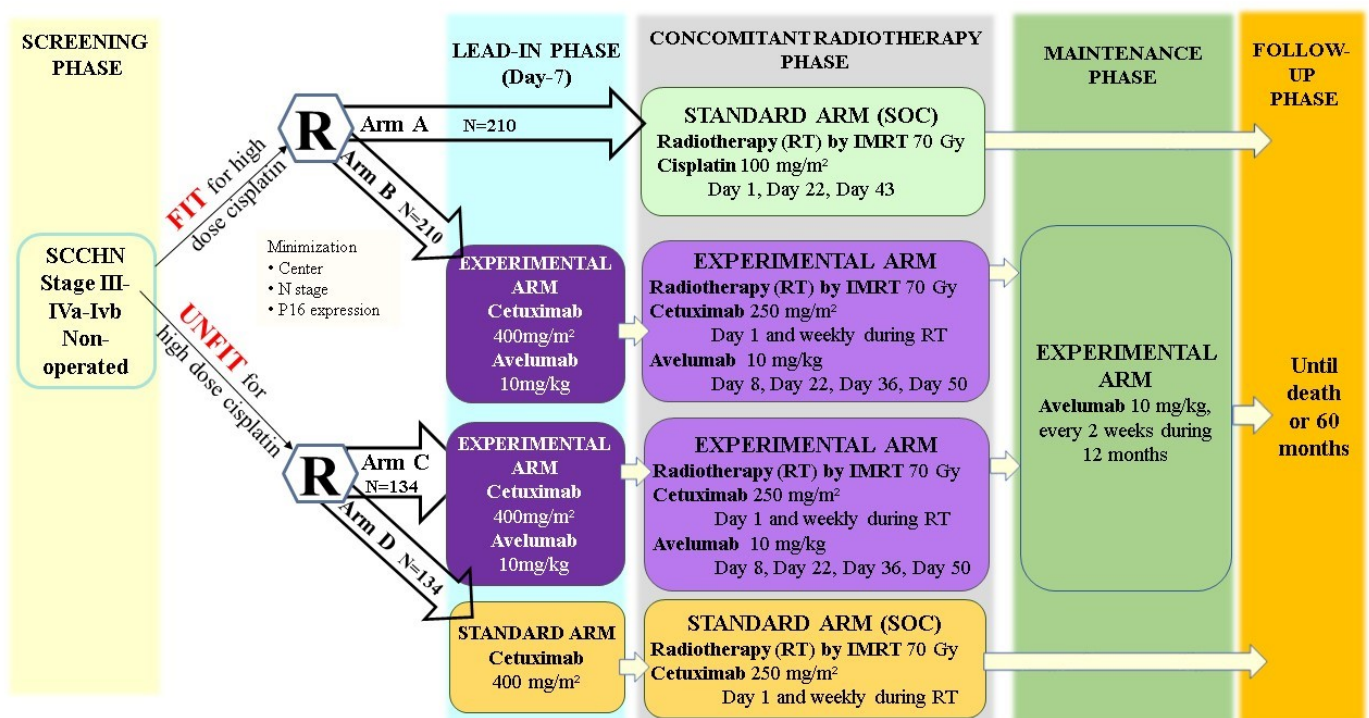
Avelumab - Maintenance Phase (Arms B & C)

If no infusion-related reactions are observed after the 4th avelumab infusion, **no further premedications** are required and the observation period can be shortened to **1-hour**

Study procedures:

- ✓ None of protocol specific procedure should be performed before informed consent signature
- ✓ Study treatment should start within maximum 10 days of randomization
- ✓ Paracetamol allowed until 3g/day (amendment pending)
- ✓ Audiogram mandatory before C2 and C3 cisplatin cycle treatment (amendment in progress)

Study Design



REACH

Contact Information



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