Year 1, N°2

June 2018

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**.

Contents

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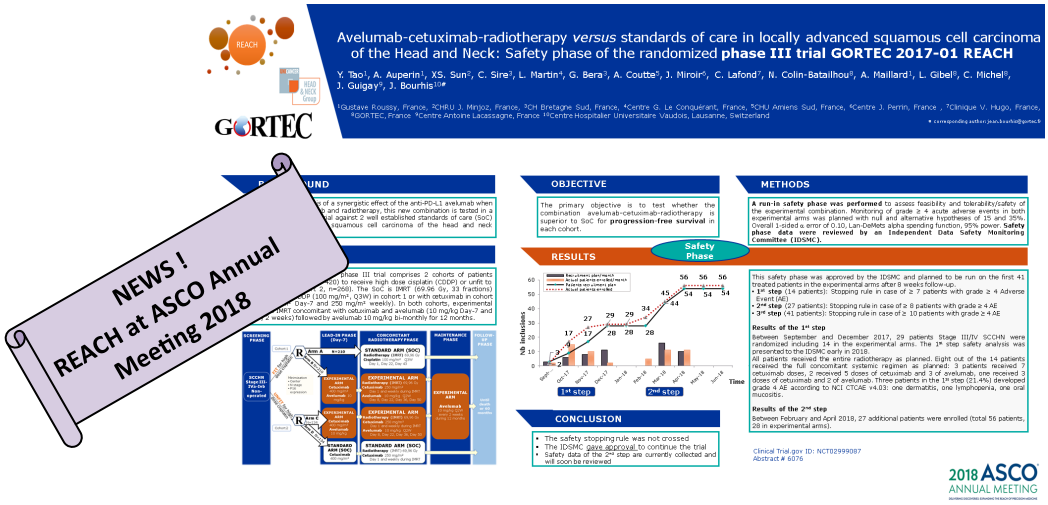
Dr Yungan TAO,
Pr Joël GUIGAY
Study coordinators

& Pr Jean BOURHIS
Study Global Coordinator



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	-

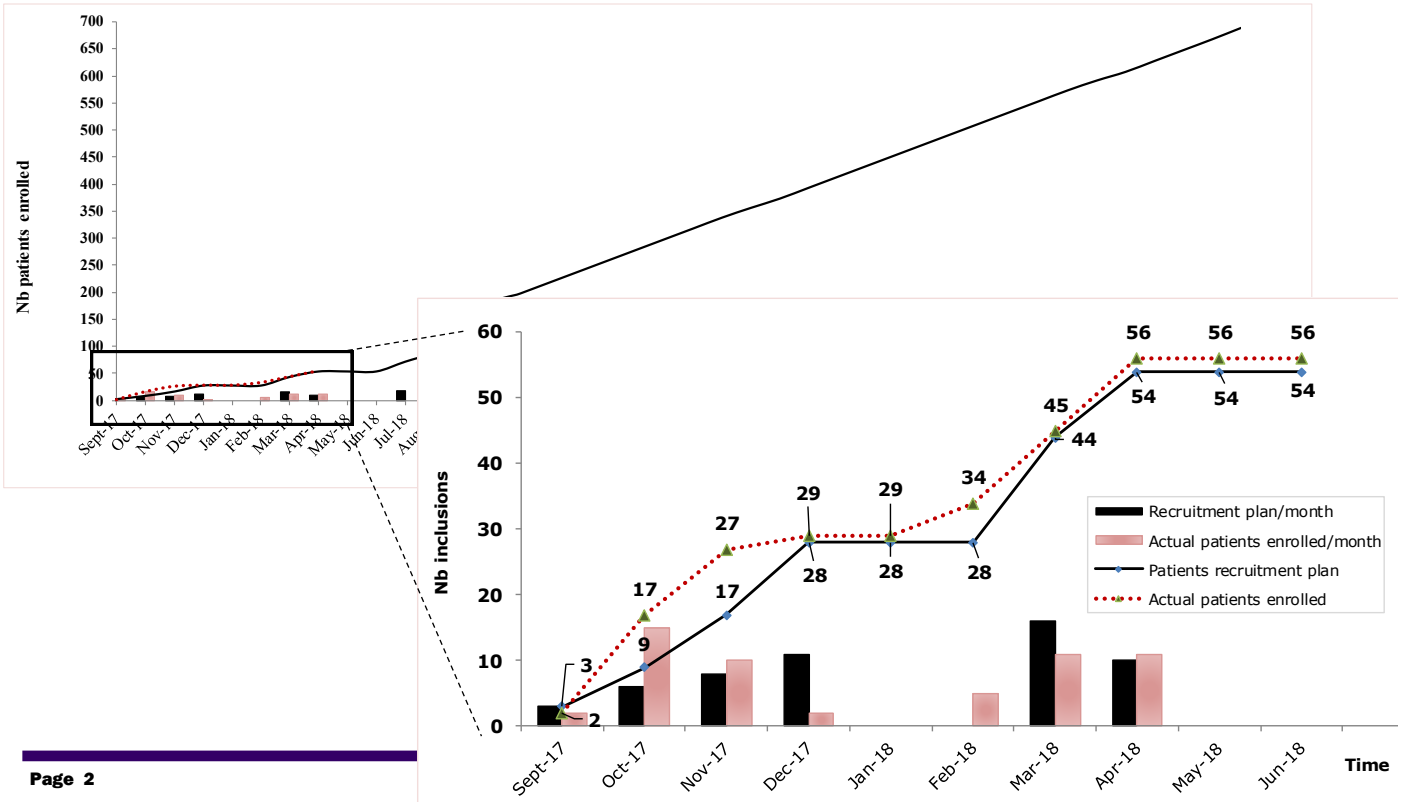
Our 2018 study milestones are to:

⇒ 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**
Centre Oscar Lambret (DrsAbdeddaim, Lefebvre)**:** **2 patients**
Clinique Victor Hugo (Dr Lafond)**:** **1 patient**
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	1st 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 m² **Subsequent cycles (100 mg/m²)**: same dose as 1st 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 1st 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

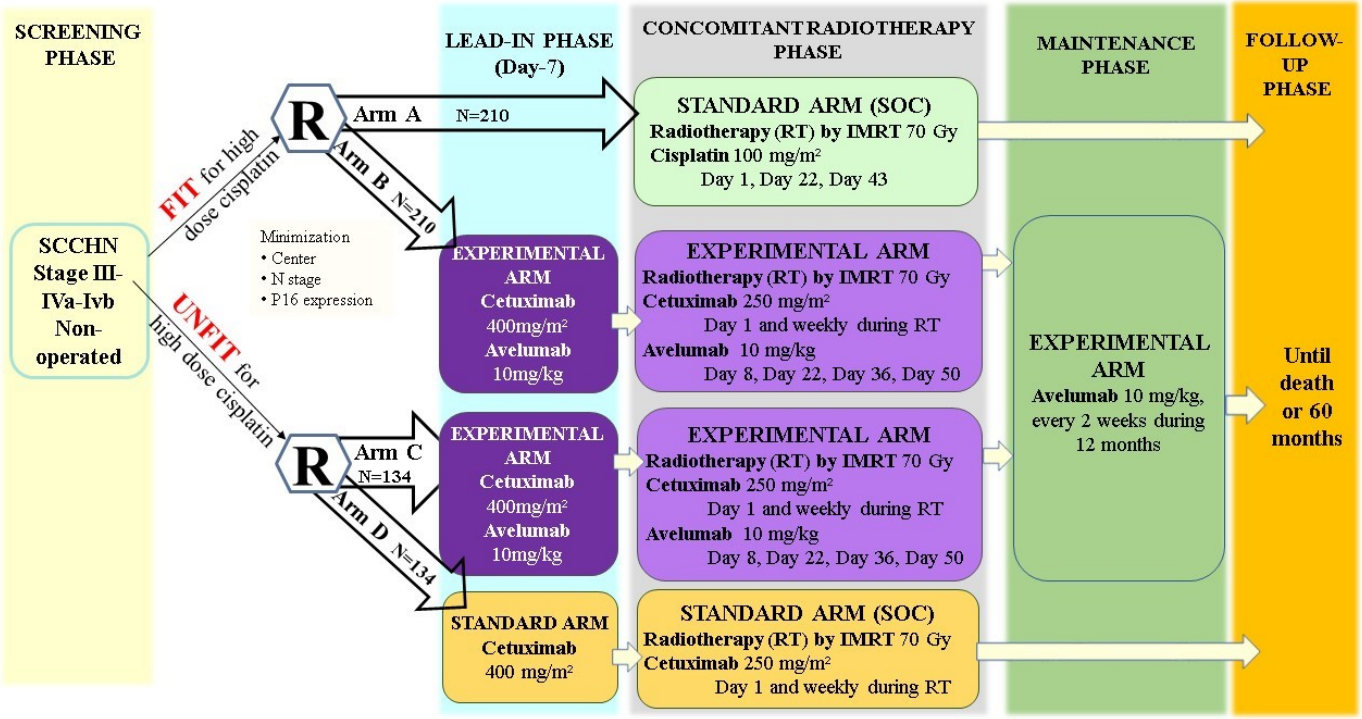
Avelumab - Maintenance Phase (Arms B & C)

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
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