

XXXIII CONGRESSO NAZIONALE AIRO

# AIRO2023

BOLOGNA,  
27-29 OTTOBRE 2023

PALAZZO DEI CONGRESSI

Radioterapia Oncologica: l'evoluzione al servizio dei pazienti

## **CEMIPLIMAB COMBINED WITH RADIOTHERAPY IN ADVANCED CUTANEOUS SQUAMOUS CELL CARCINOMA: A SINGLE INSTITUTION EXPERIENCE**

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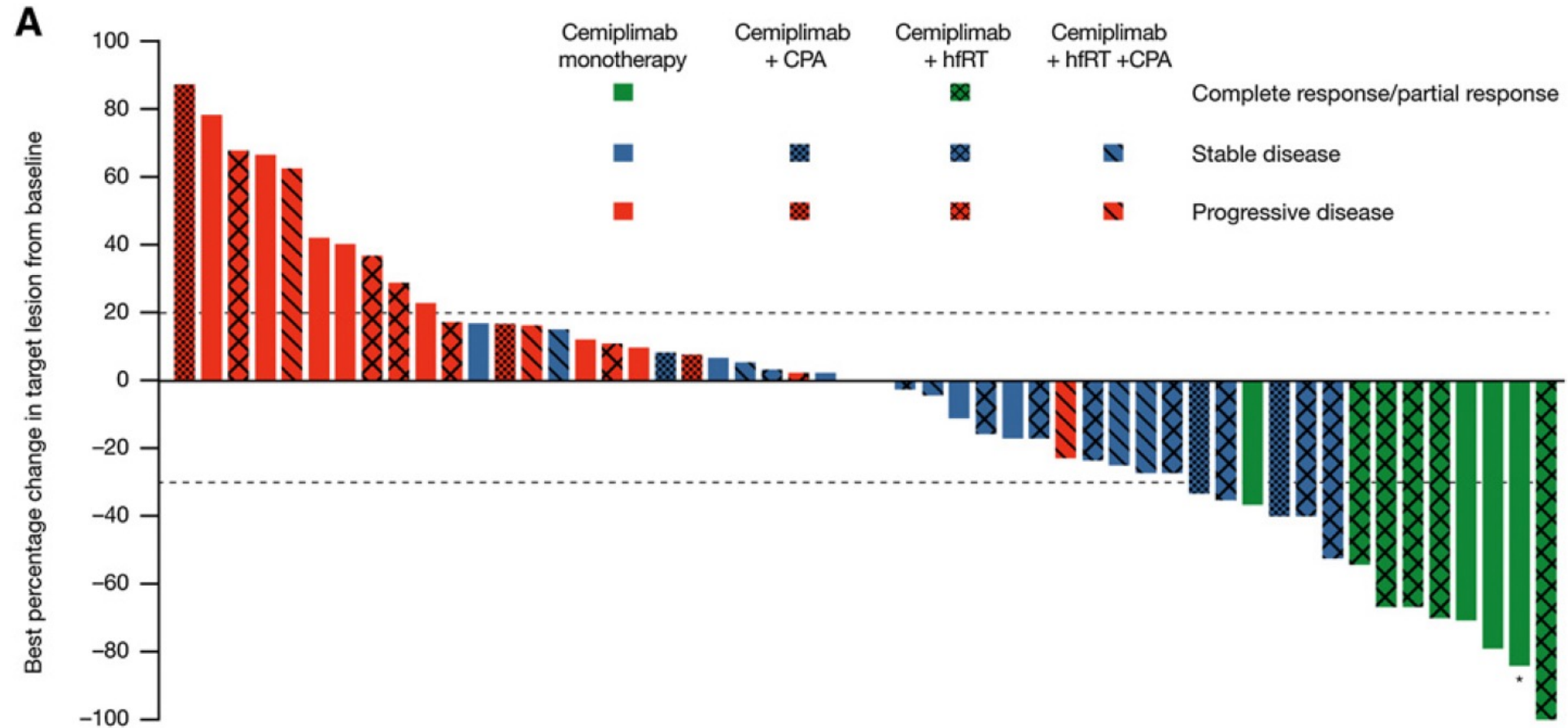
Associazione Italiana  
Radioterapia e Oncologia clinica

## Potential of Radiotherapy as a Synergistic Modality to Improve Response Rate to Immunotherapy in Patients with cSCC

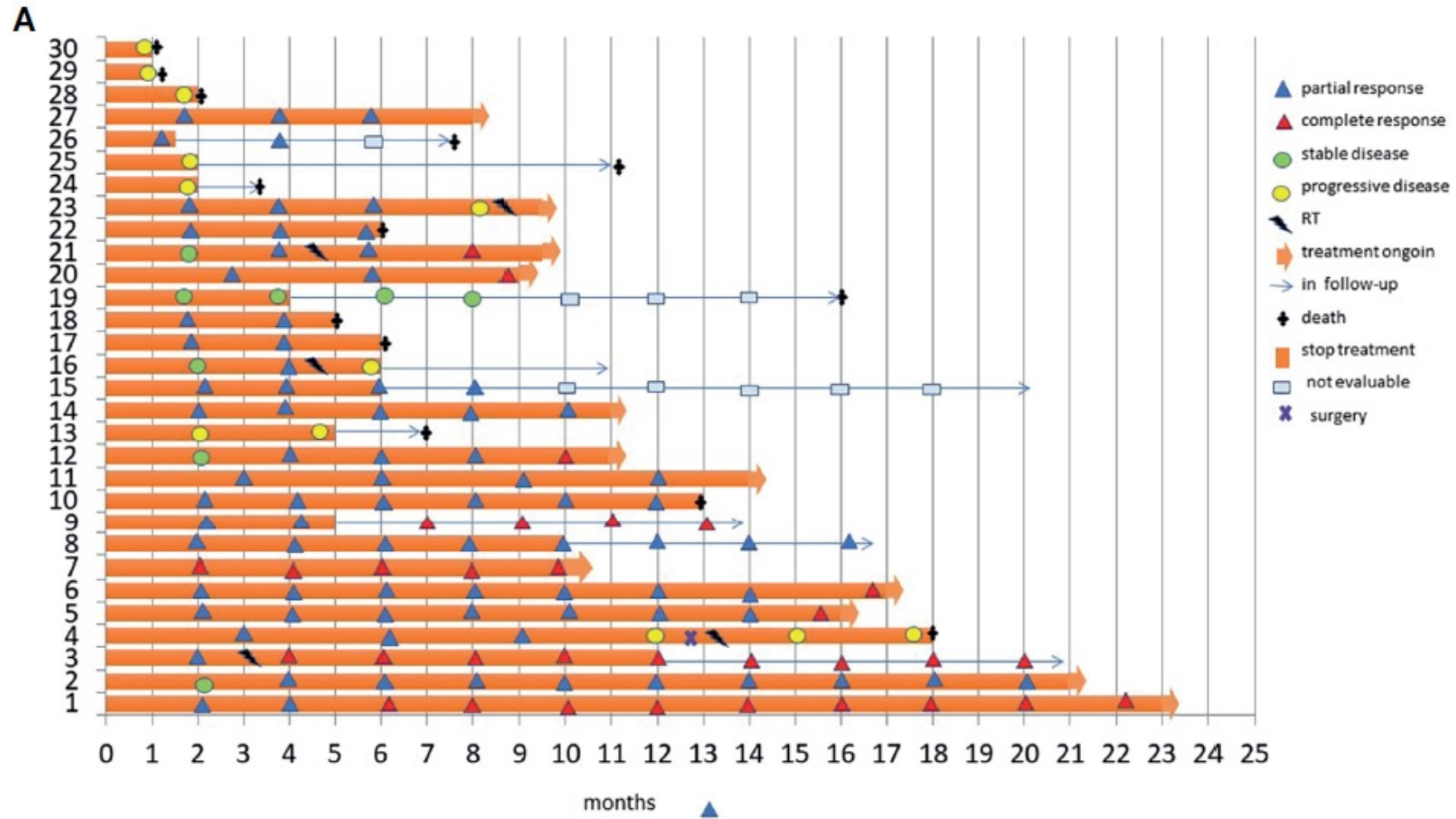
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- ✓ Even though PD-L1 is not a perfect biomarker to predict tumor response to CPIs, high PD-L1 expression defined as 50% or more or a high tumor proportion score (TPS) often indicates a high response to immunotherapy regardless of tumor histology
- ✓ Through a complex mechanism which involves a DNA damage signaling pathway, interferon (IFN) signaling, the cyclic GMP–AMP synthase–stimulator of interferon genes (cGas–STING) pathway, and the epidermal growth factor receptor (EGFR) pathway, the PD-L1 in the tumor cells is upregulated
- ✓ As a result, following radiotherapy, PD-L1 expression increases significantly in proportion to the dose of radiation delivered both in the in vitro and in vivo setting
- ✓ The increase in PD-L1 expression following irradiation reflects a protective mechanism of the tumor to escape cell death from infiltrating T cells, which are attracted into the tumor microenvironment by radiation induced inflammation
- ✓ Thus, it could be used as a clinical strategy to enhance response to immunotherapy

## Early clinical evidence of combining radiotherapy to immunotherapy in cSCC



# Early clinical evidence of combining radiotherapy to immunotherapy in cSCC



## Methods

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- ✓ We performed a retrospective analysis of patients treated by cemiplimab combined with radiotherapy from 2020 to 2022 at our institution for advanced cutaneous squamous cell carcinoma after multidisciplinary discussion and evaluation (including always both radiation oncologists and dermatologists)
- ✓ Cemiplimab was always started before radiotherapy
- ✓ The total dose and the fractionation schedule of radiotherapy treatments were tailored according to the radiation target and clinical patient's conditions (total dose range from 20 Gy to 55 Gy)
- ✓ The infusions were always continued in short course schedules of radiotherapy; whereas in the case of long course radiotherapy one infusion was postponed in order not to be concomitant
- ✓ All patients were evaluated after radiotherapy treatment in multidisciplinary follow-up visits, in order to investigate the clinical benefits and side effects



## Results

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- ✓ We identified 13 patients, with a majority of males (males 85%, females 15%), and an average age of 82 years (range 70-90)
- ✓ In 92% of the patients the clinical target volume (either primary tumour or lymph nodes metastasis) was located at the head and neck region
- ✓ The average number of infusions before radiotherapy was 4 cycles
- ✓ All clinical responses were evaluated by restaging the patients by imaging (CT or MRI) using the iRECIST and the overall response rate was 77%, with a complete response rate of 46%
- ✓ No G3 or higher skin acute side effects were observed

# Recent clinical evidence of combining radiotherapy to immunotherapy in cSCC

Table 1. Patient characteristics.

	Cemiplimab (n = 21)	Cemiplimab/RT (n = 12)
Age (years)	75.1 ± 11.8	77.2 ± 12.5
<65 yo	2 (9.5)	3 (25.0)
65–75 yo	5 (23.8)	1 (8.3)
>75 yo	14 (66.7)	8 (66.7)
Gender		
Male	17 (81)	11 (91.7)
Female	4 (19)	1 (8.3)
ECOG status		
0	2 (9.5)	1 (8.4)
1	8 (38.1)	7 (58.3)
2	10 (47.6)	4 (33.3)
3	1 (4.8)	0
Previous cSCC		
No	8 (38.1)	6 (50)
Yes	13 (61.9)	6 (50)
Immunodepression		
No	16 (76.2)	8 (66.7)
Yes	5 (23.8)	4 (33.3)
Lymphopenia		
No	14 (66.7)	7 (58.3)
Yes	7 (33.3)	5 (41.7)
Staging		
LacSCC	3 (14.3)	1 (8.3)
mcSCC	18 (85.7)	11 (91.7)
Locoregional metastasis	11 (61.1)	7 (63.6)
Distant metastasis	7 (38.9)	4 (36.4)
Site		
Face	16 (76.2)	6 (50)
Scalp	2 (9.5)	0
Cervical	0	2 (16.7)
Trunk	2 (9.5)	1 (8.3)
Arm or leg	1 (4.8)	3 (25)

Table 1. Cont.

	Cemiplimab (n = 21)	Cemiplimab/RT (n = 12)
Size (mm)	35.4 ± 24.2	48.1 ± 33.4
Previous lines of therapy		
No	19 (90.5)	11 (91.7)
Yes	2 (9.5)	1 (8.3)
Previous radiotherapy		
No	7 (33.3)	11 (91.7)
Yes	14 (66.7)	1 (8.3)
Histological features		
Degree of differentiation		
Well	9 (52.9)	5 (41.7)
Moderate	6 (35.3)	4 (33.3)
Poor	2 (11.8)	3 (25)
PNI		
No	6 (66.7)	5 (100)
Yes	3 (33.3)	0
Bone erosion		
No	10 (66.7)	8 (88.9)
Yes	5 (33.3)	1 (11.1)
Invasion beyond subcutaneous fat		
No	6 (50)	2 (33.3)
Yes	6 (50)	4 (66.7)
Dose of cemiplimab		
3 mg/kg/2 weeks	5 (23.8)	0
350 mg/3 weeks	14 (66.7)	12 (100)
Both #	2 (9.5)	0
Intent of radiotherapy		
Curative		8 (66.7)
Palliative		4 (33.3)
Site of radiotherapy		
Primary tumour		2 (16.7)
Metastasis		10 (83.3)
Dose per fractions (Gy)		4.0 ± 1.7
Fractions		16.2 ± 12.6
Prescribed dose		45.5 ± 22.6
BED		60.5 ± 26.0

Results are expressed as mean ± standard deviation or number (%). The patient characteristics were compared between the two groups. ECOG: Eastern Cooperative Oncology Group; cSCC: cutaneous squamous cell carcinoma; La: locally advanced; m: metastatic; PNI: perineural invasion; Gy: grey; BED: biologically effective dose. #: patients who received the two dosages.

➤ Five patients received two sequences of radiotherapy

## Recent clinical evidence of combining radiotherapy to immunotherapy in cSCC

The combination of cemiplimab and radiotherapy allows

- for a quicker objective clinico-radiological response than with cemiplimab in monotherapy with a median time to response of 3 months in the concomitant group versus 5.5 months in the cemiplimab group
- No increase in AE occurrence

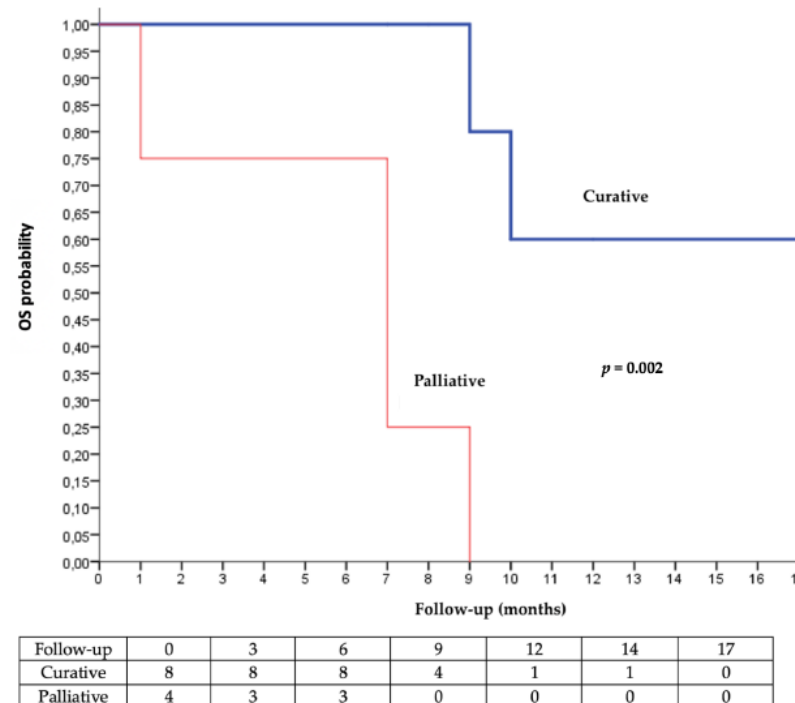


Figure 2. Kaplan–Meier analysis of overall survival according to the intent of radiotherapy (palliative vs. curative).



March 2021



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March 2021

COMORBIDITIES:

- Mild mitral and tricuspid insufficiency
- COPD, pulmonary emphysema, chronic respiratory failure
- Chronic AF
- Bilateral carotid atheromasia
- Multi-infarct encephalopathy with cortical atrophy
- Prostate adenocarcinoma diagnosed in 2019 (Gleason 6, 3+3), for which he had no treatment
- Polyposis of the vocal cords
- Depression of mood tone
- Multinodular goiter in mild hyperthyroidism
- Hyperparathyroidism secondary to hypovitaminosis D
- Osteoporosis
- Right adrenal adenoma
- Peptic ulcer
- Chronic HCV and HBV-related hepatopathy

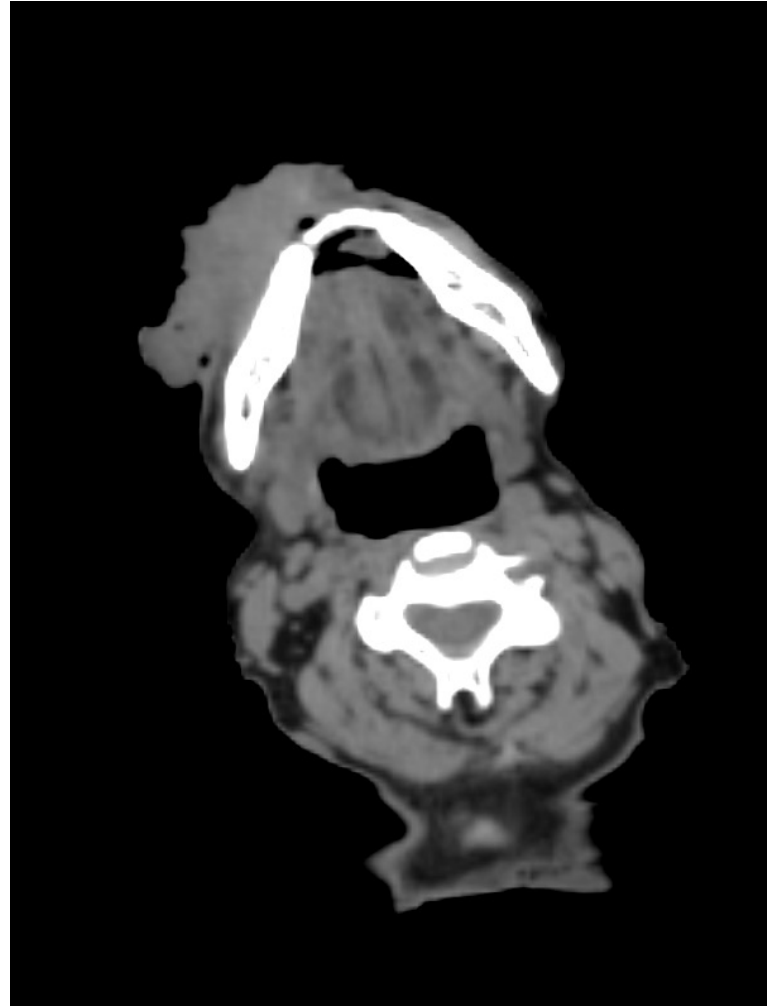
October 2021



11th infusion of Cemiplimab

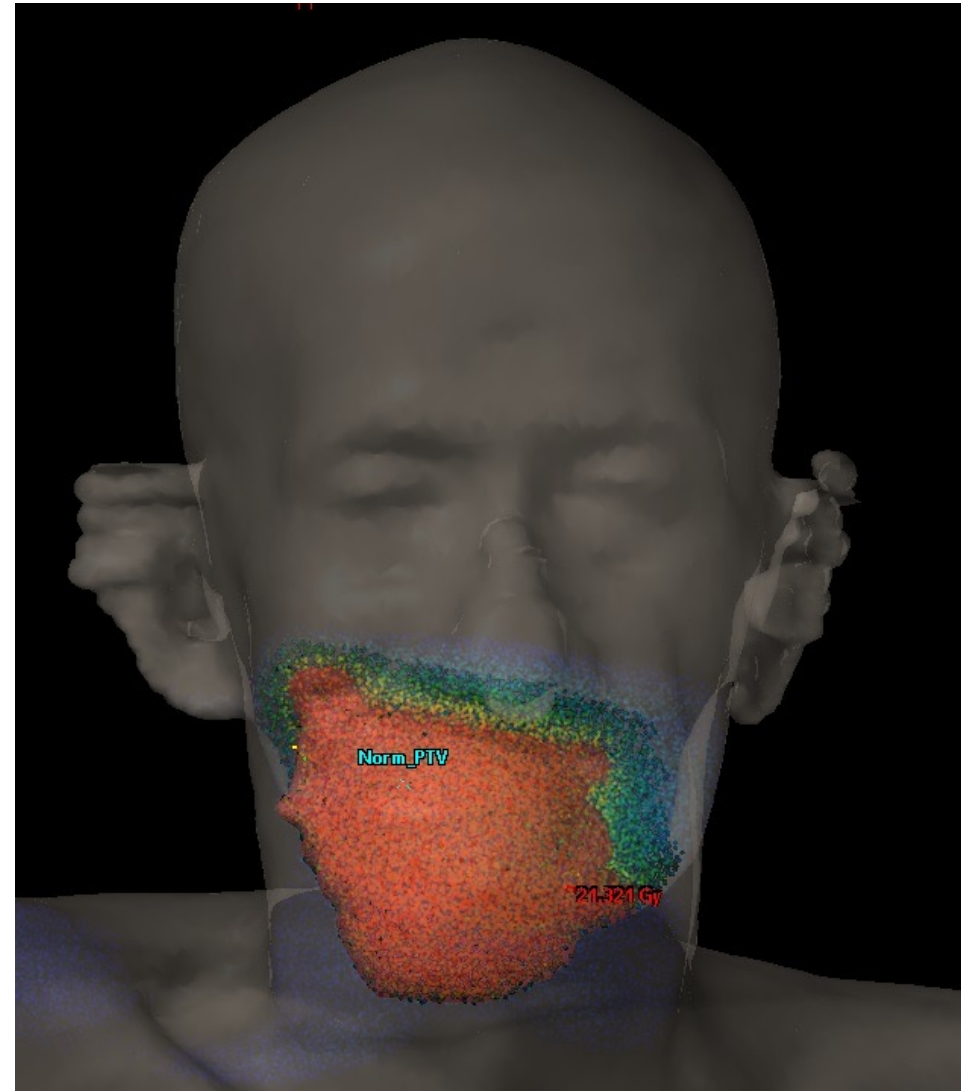
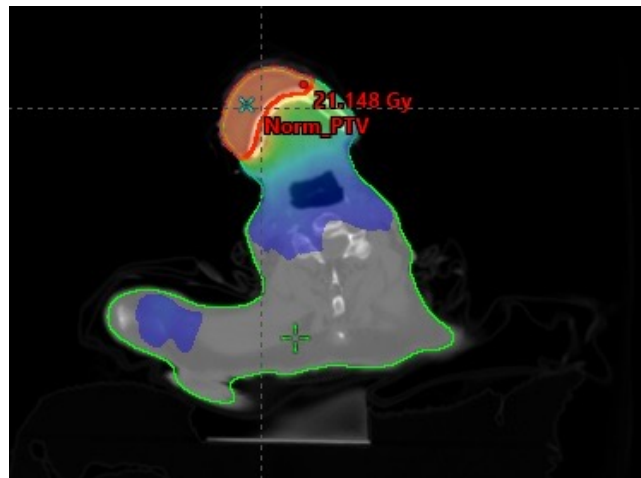
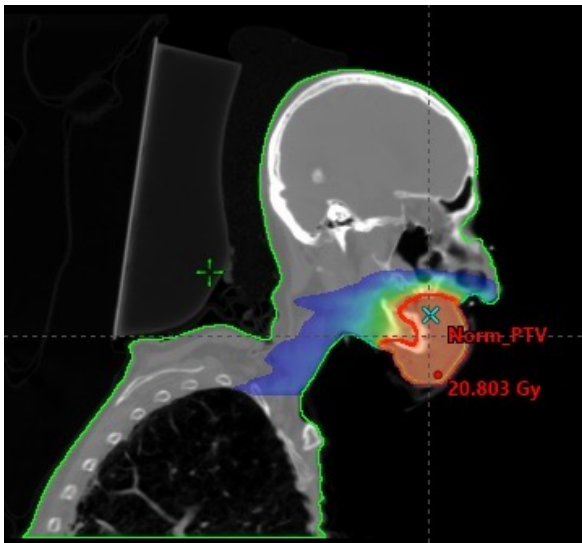
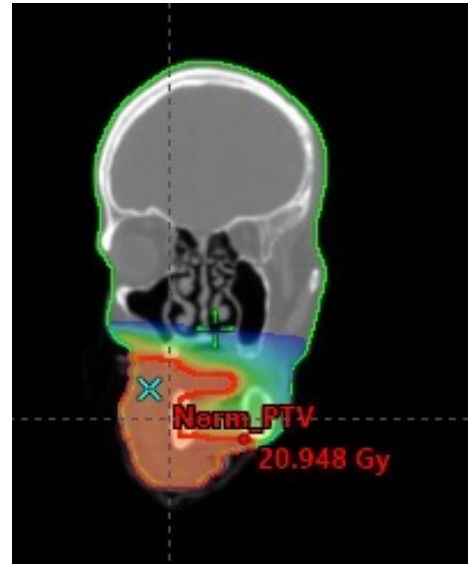
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## CT scan



November 2021

RT 400 cGy x 5 in VMAT  
(only primary lesion,  
no elective neck irradiation)



December 2021



January 2022

June 2022

March 2023

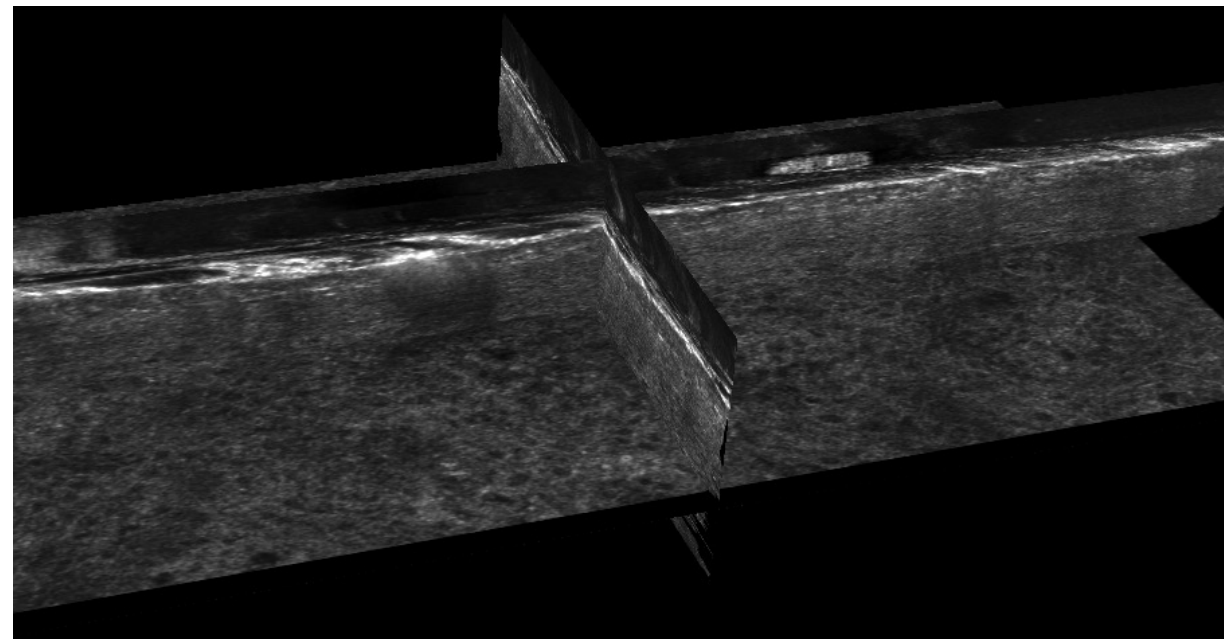
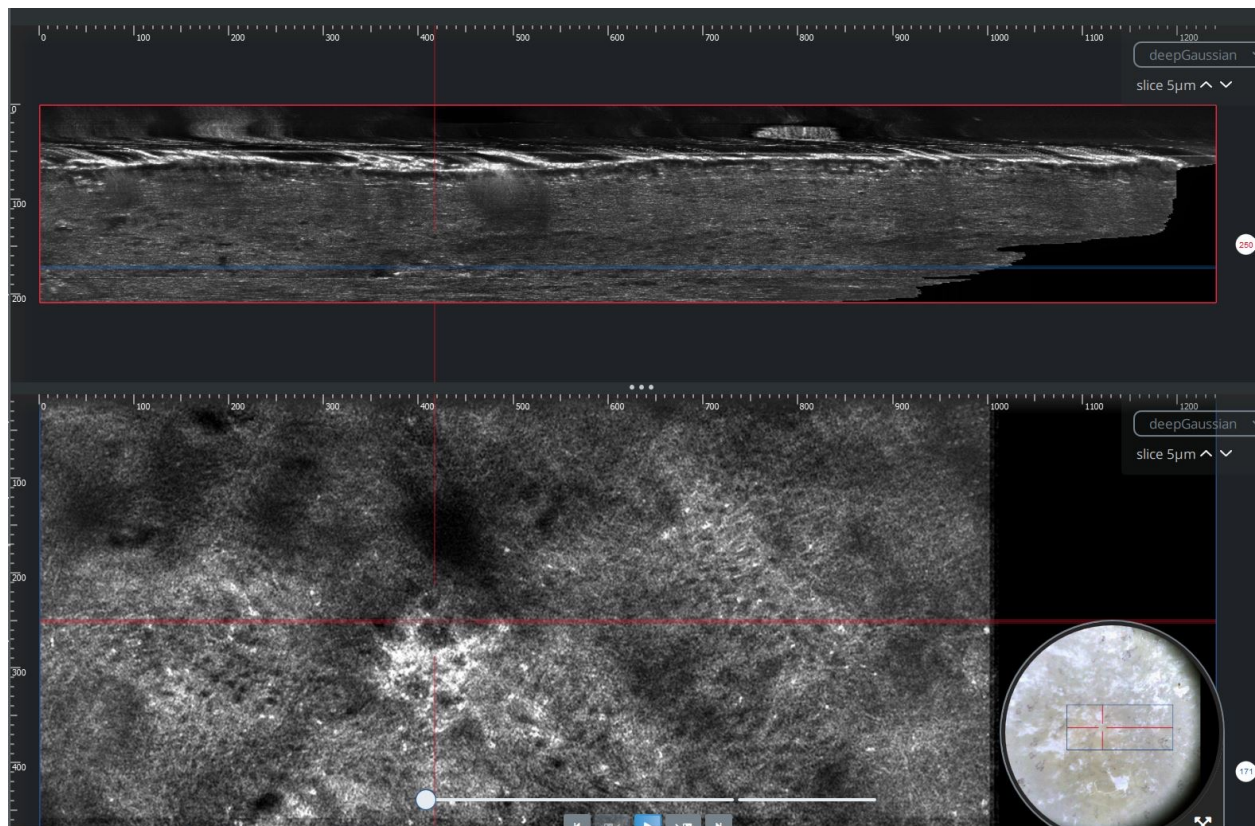


20th infusion of Cemiplimab



SARS-CoV2 infection

# LC-OCT





RT+immunotherapy



# Thank you for your attention

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