

## Supplementary

### Appendix 1

#### Methods

##### Inclusion criteria:

- ◆ Bronchoscopic biopsy confirmed as tracheal squamous cell carcinoma (SCC) by pathological examination;
- ◆ PET-CT confirmed no metastasis;
- ◆ ECOG physical status score 0-1;
- ◆ Bronchoscopy, chest CT is evaluated as locally advanced tracheal SCC, and radical surgery is expected to be feasible or after neoadjuvant therapy;
- ◆ Age  $\geq 18$  years;
- ◆ Have one measurable lesion at least;
- ◆ Good function of other major organs (liver, kidney, blood system, etc.): -absolute neutrophil count (ANC)  $\geq 1.5 \times 10^9$ , platelet  $\geq 100 \times 10^9$ , hemoglobin  $\geq 90$ g/L; note: patients shall not receive blood transfusion or growth factor support within 14 days before blood collection during the screening period; -international standardized ratio (INR) or prothrombin time (PT)  $\leq 1.5 \times$ normal upper limit (ULN); -activated partial thromboplastin time (APTT)  $\leq 1.5 \times$ ULN; -serum total bilirubin  $\leq 1.5 \times$ ULN (Gilbert syndrome patients with total bilirubin must be  $<3 \times$ ULN). Fertile female patients with aspartate and alanine amino transferase (AST and ALT)  $\leq 2.5 \times$ ULN, or liver metastasis with AST and ALT  $\leq 5 \times$  ULN;
- ◆ Fertile female patients must voluntarily take effective contraceptive measures more than 120 days after chemotherapy or the last administration of Toripalimab, whichever is later, and the urine or serum pregnancy test results less than 7 days before entering the group were negative. Unsterilized male patients must voluntarily take effective contraceptive measures  $\geq 120$  days after chemotherapy or the last administration of Toripalimab, whichever is the later;
- ◆ Sign informed consent.

##### Exclusion criteria:

- ◆ Systemic anticancer therapy for tracheal SCC, including radiotherapy, chemotherapy, targeted therapy, immunotherapy, and experimental therapy;

- ◆ Any Chinese herbal medicine used to control cancer used within 14 days before the first administration of the study drug;
- ◆ Patients with other malignant tumors in the 5 years before the start of this trial;
- ◆ Complicated with unstable systemic disease, including active infections, uncontrolled hypertension, unstable angina pectoris, congestive heart failure (higher than II New York college of cardiology), severe arrhythmias, liver, kidney or metabolic diseases;
- ◆ Active, known or suspected autoimmune diseases, or autoimmune paraneoplastic syndrome requiring systemic treatment;
- ◆ Any infection treated with antibiotics within 4 weeks before the start of the trial;
- ◆ A history of active bleeding or embolism within 6 months, or received thrombolysis or anticoagulation therapy, or the researchers believe that there is an obvious tendency of gastrointestinal bleeding (such as esophageal varices have the risk of bleeding, local active ulcer lesions, etc.)
- ◆ Had or is suffering from nephrotic syndrome;
- ◆ Has been or is suffering from chronic obstructive pneumonia, bronchiectasis, or interstitial lung disease;
- ◆ Allergic to experimental drugs;
- ◆ Complicated with HIV infection or active hepatitis;
- ◆ Vaccination within 4 weeks before the start of the trial;
- ◆ Those who had undergone other major operations or severe injuries within the previous 2 months;
- ◆ Pregnant or lactating women;
- ◆ Those with neurological diseases or mental disorders;
- ◆ Participated in another therapeutic clinical study at the same time;
- ◆ Other conditions that researchers did not consider it appropriate to enroll in the group.

## Case presentation

### Patient 1

Jan 2021 43y, male presented with hemoptysis

Biopsy: Squamous cell carcinoma  
cT4N0M0 stage IV

Feb 2021 Toripalimab + Gemcitabine + Carboplatin  
3 cycles

Apr 2021 Radiological response: **PR**, ycT2N0M0 stage II

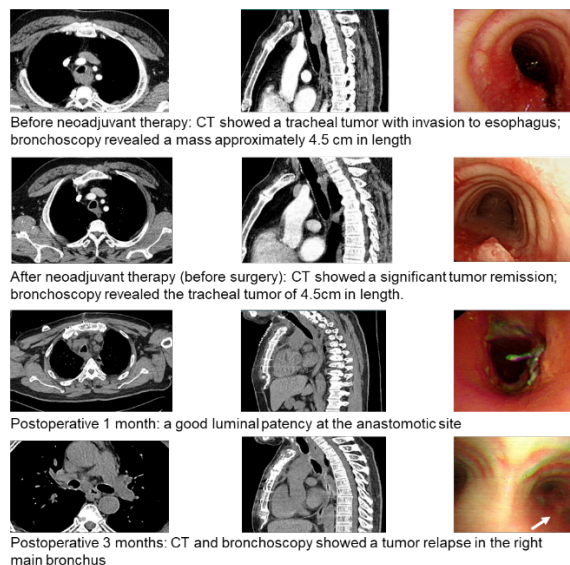
Operation: bilateral hilar + laryngeal release and  
tracheal segmental resection (**R1 resection**)

Pathology: **40%** residual surviving tumor cells at  
resection

July 2021 Re-examinations: a new neoplasm was identified at  
the right main bronchus

Tissue biopsy confirmed tumor recurrence

Nov 2021 The patient refused further treatment and eventually  
died



## # Patient 2

Dec 2022 22y, female presented with cough and  
expectoration

Biopsy: Squamous cell carcinoma  
cT3N0M0 stage III

Jan 2023 High-frequency electrotherapy and metal stent  
placement under bronchoscopy  
Toripalimab + Paclitaxel + Carboplatin  
2 cycles

Mar 2023 Radiological response: **CR**, ycT0N0M0 stage 0

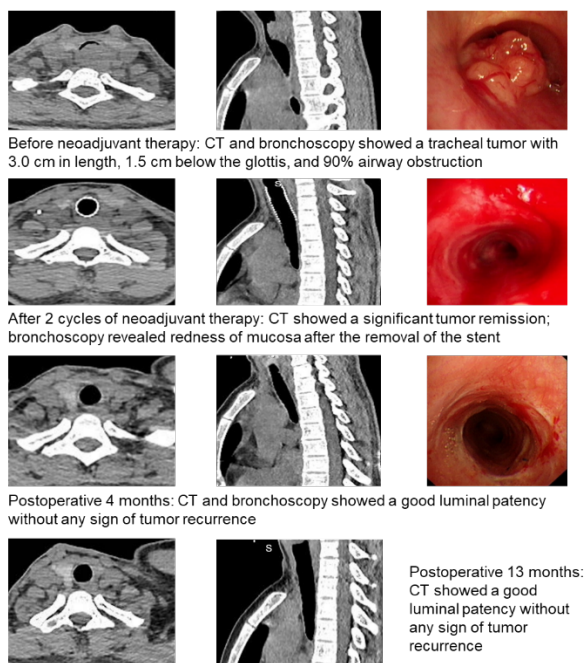
Operation: Tracheal segmental resection + left  
thyroid lobectomy (**R0 resection**)

Pathology: 0% residual surviving tumor cells at  
resection (**pCR**)

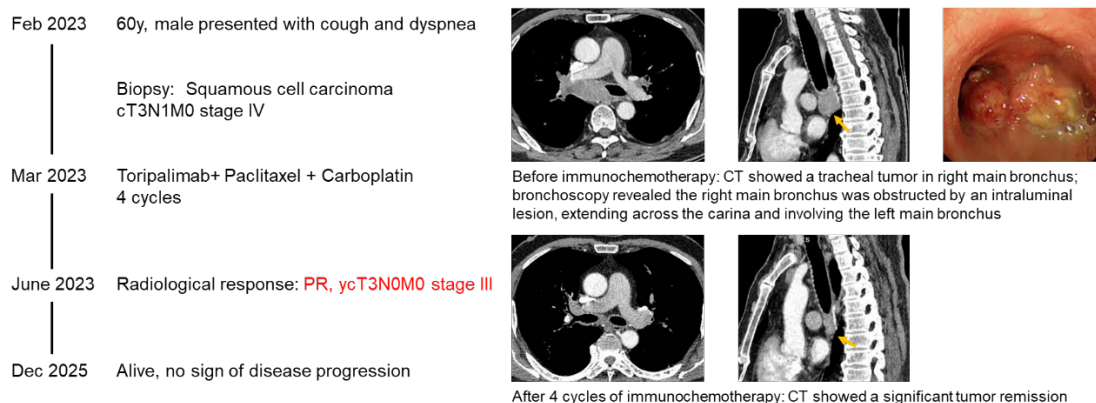
Apr 2023 Adjuvant immunochemotherapy: Toripalimab +  
Paclitaxel + Carboplatin 2 cycles

July 2023 Tumor evaluation

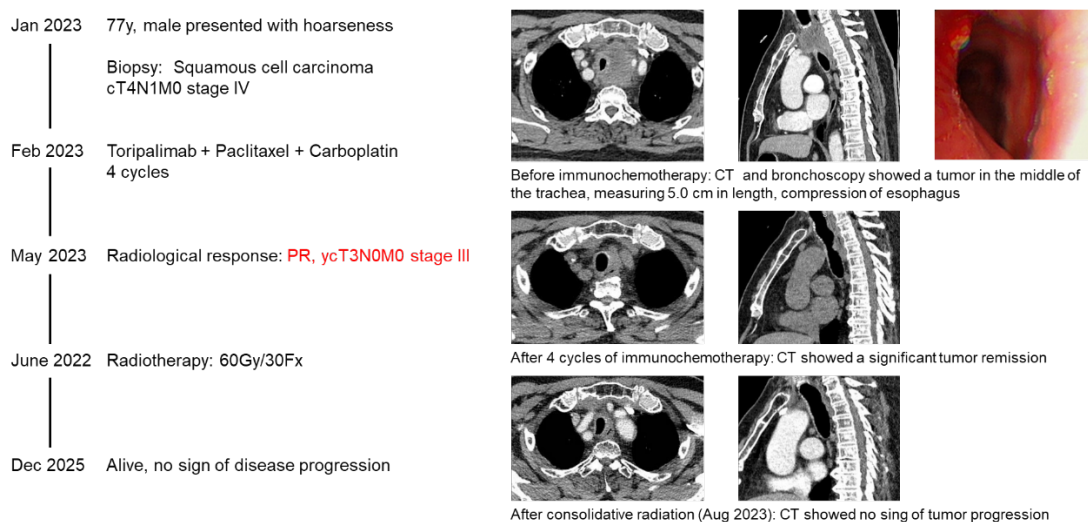
Jan 2025 Alive, no sign of disease recurrence



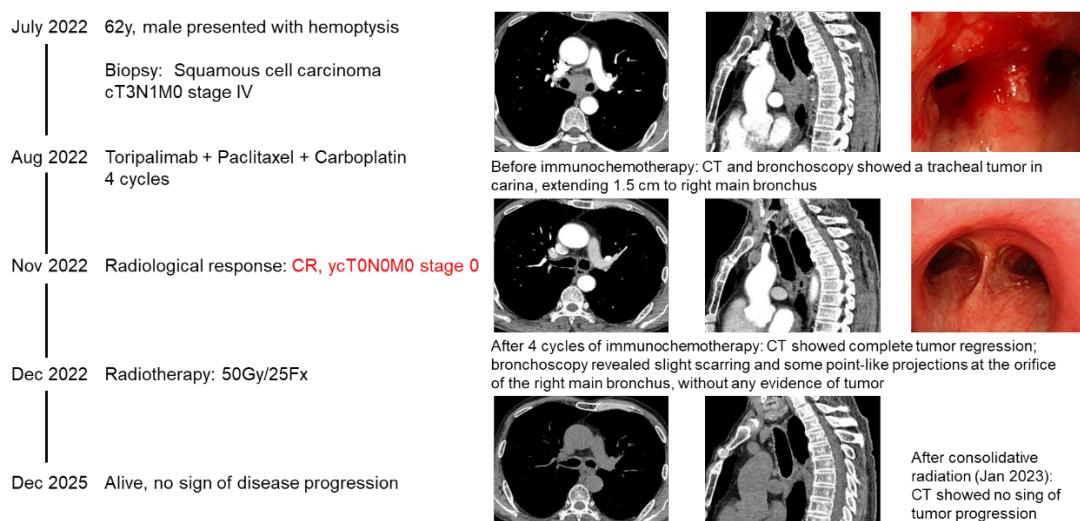
## Patient 3



## Patient 4



## Patient 5



## Patient 6

Jan 2022 61y, male presented with cough and hoarseness

Biopsy: Squamous cell carcinoma  
cT4N1M0 stage IV

Feb 2022 Toripalimab + Paclitaxel + Carboplatin  
4 cycles

June 2022 Radiological response: PR, ycT3N0M0 stage III

July 2022 Radiotherapy: 50Gy/25fx

Dec 2025 Alive, no sign of disease progression



Before immunochemotherapy: CT and bronchoscopy revealed a neoplasm in the mid-to-lower right side of the trachea (the length of tumor invasion: 40.3 mm).



After 4 cycles of immunochemotherapy and radiation: CT showed a significant tumor remission; bronchoscopy revealed slight scarring without any evidence of tumor



After definitive immunochemotherapy and radiation: CT showed no sign of tumor progression