



# TCR Repertoire Biomarkers and Multimodal AIR-BERT Modeling in First-Line Tislelizumab plus EP for ES-SCLC: A Prospective Study

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## INTRODUCTION

- PD-1/PD-L1 inhibitors combined with etoposide and platinum (EP) have become the standard first-line treatment for extensive-stage small cell lung cancer (ES-SCLC). Tislelizumab, a PD-1–targeting monoclonal antibody, in combination with EP, has been approved in China and Europe for the first-line treatment of ES-SCLC<sup>1</sup>. However, clinically actionable biomarkers that can identify patients most likely to benefit from first-line chemo-immunotherapy are lacking in SCLC.
- High-throughput T-cell receptor (TCR) repertoire sequencing provides a minimally invasive method to quantify immune diversity and clonal dynamics and has shown potential as a biomarker for immune checkpoint inhibitor outcomes in NSCLC<sup>2-4</sup>, but prospective evidence with standardized sampling during first-line chemo-immunotherapy in ES-SCLC remains limited.
- This study evaluates whether baseline and on-treatment changes in peripheral blood TCR repertoire metrics are associated with clinical benefit from first-line tislelizumab plus EP. The study also explores whether a multimodal machine-learning framework (Multimodal-AIR-BERT) can improve prediction of neoantigen-specific TCR features by integrating TCR sequencing with HLA-I typing and tumor neoantigen information.

## REFERENCES & ACKNOWLEDGEMENTS

### Acknowledgments

We sincerely acknowledge all participating investigators for their dedicated efforts, and we extend our deepest gratitude to the patients who volunteered for this trial.

### Artificial Intelligence (AI) Use Disclaimer

We used OpenAI's GPT to assist with language polishing the abstract specifically, it was used to refine English grammar, syntax, wording, and overall clarity/organization. All scientific content were created by the authors; no data were generated or altered by AI.

### References

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## METHODS

- This is an ongoing prospective observational biomarker study (ChiCTR2500101752, [Figure 1](#)) planning to enroll 40 treatment-naïve ES-SCLC patients. Patients receive induction tislelizumab plus chemotherapy every 21 days for 4-6 cycles followed by tislelizumab maintenance per standard practice. Peripheral blood (3 mL) is collected pre-treatment and at 3 months after treatment initiation for TCR sequencing.
- To date, 23 patients have been enrolled, with 23 baseline blood samples available and 18 blood samples collected at 3 months post-treatment; TCR sequencing has been successfully completed, and 14 cases have been analyzed.
- Analyses will evaluate: (1) the correlation between pre-treatment TCR parameters and treatment efficacy; (2) associations between longitudinal changes in TCR parameters and efficacy; and (3) exploratory prediction of neoantigen-specific TCR repertoires using the Multimodal-AIR-BERT model integrating TCR repertoire features with HLA-I typing and tumor neoantigen data when available.
- The primary endpoint is progression-free survival (PFS); secondary endpoints include objective response rate (ORR), overall survival (OS), and PFS rates at 6 and 12 months. Time-to-event endpoints will be summarized using Kaplan–Meier methods with exploratory Cox regression analyses for biomarker associations, and ORR will be summarized with Clopper–Pearson exact 95% confidence intervals.

**Figure 1 . Study Flowchart**

### 1. Study Population & Treatment

#### Eligibility (N=40)

- Histologically/cytologically confirmed ES-SCLC
- No prior systemic treatment
- ECOG PS 0–1
- Age ≥ 18 years

#### Induction Treatment (4 cycles)

- Tislelizumab 200 mg D1+
- Etoposide 75 mg/m<sup>2</sup> D1–3 + Carboplatin AUC 5 D1

#### Maintenance Treatment

- Tislelizumab 200 mg, Q3W, continue until progression or unacceptable toxicity

### 2. Sample Collection

#### Baseline (pre-treatment):

- Archival tumor tissue
- Peripheral blood

#### 3 months post-treatment:

- Peripheral blood

### 3. Laboratory & Analytical Pipeline

- ↓ Isolate DNA from baseline and 3-month post-treatment peripheral blood → TCR repertoire sequencing;
- ↓ Analyze baseline peripheral blood DNA: TCR repertoire profiling, tissue gene panel-derived neoantigen repertoire, and HLA class I typing;
- ↓ Multimodal-AIR-BERT model: Predict tumor-reactive TCR repertoire by integrating TCR, HLA-I, and neoantigen data.

### 4. Statistical Analyses

- Correlate baseline/longitudinal TCR changes with clinical efficacy(PFS,ORR,OS);
- Identify efficacy-associated TCR
- Identify tumor-reactive TCR parameters.