



# Liquid TIL (L-TIL) Plus Tislelizumab for Anti-PD-1-Resistant Advanced NSCLC: A Multicenter Single-Arm Phase II Trial

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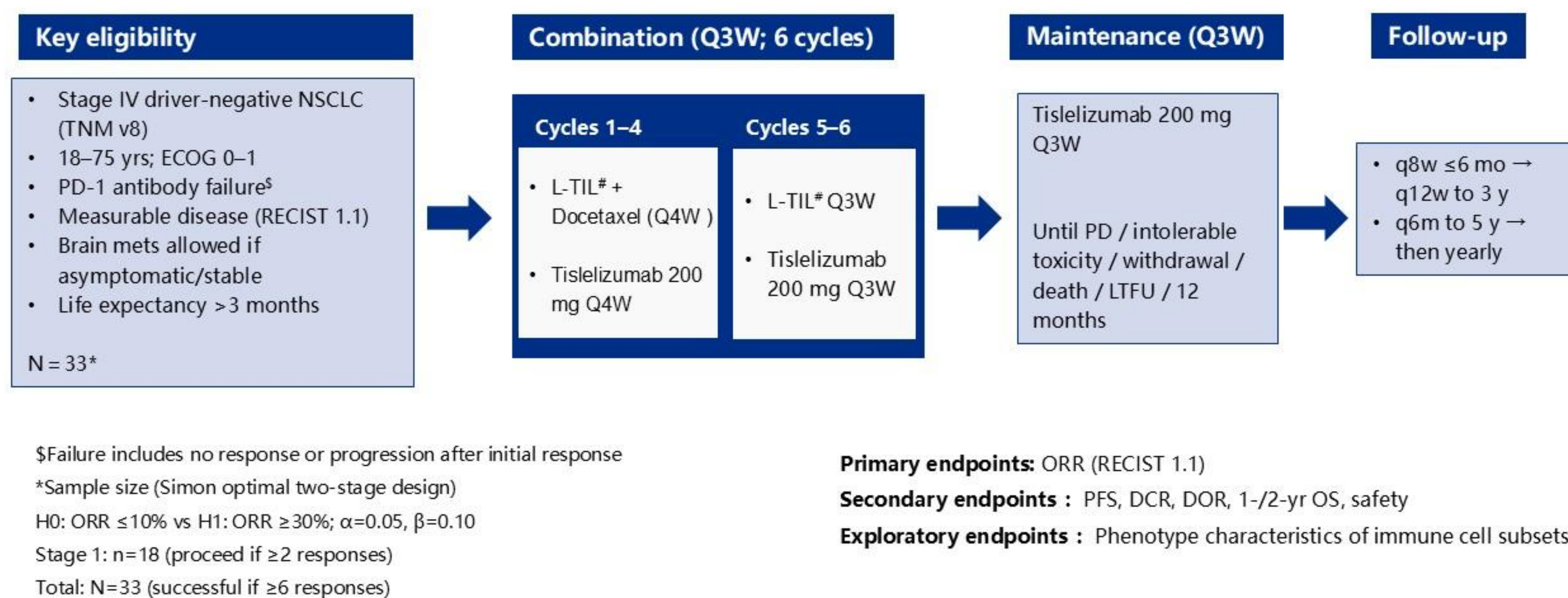
## INTRODUCTION

- PD-(L)1 inhibitors have significantly improved outcomes of driver gene-negative advanced non-small cell lung cancer (NSCLC). However, resistance to PD-1 is common and effective second-line treatment regimen remains limited.
- Tumor-infiltrating lymphocyte (TIL) therapy has been approved by the FDA for previously PD(L)-1 inhibitor treated unresectable or metastatic melanoma on Feb 24, 2024. Randomized phase III study has shown that TIL achieved higher ORR (49% vs 21%) and longer median PFS (7.2 vs 3.1 months; HR 0.50) than ipilimumab therapy<sup>1</sup>. Additionally, TIL therapy can bring durable responses across solid tumors. Data from a single-arm phase I study in advanced NSCLC patients who had progressed from nivolumab demonstrated that 2 of 13 patients achieved sustained complete response (CR) for over 1.5 years by TIL therapy, the remaining 11 experienced a reduction in tumor burden<sup>2</sup>. Nonetheless, conventional tissue-derived TIL faces numerous challenges, including but not limited to tissue inaccessibility, culture failure, and risk of adverse events<sup>3</sup>.
- Our team develops liquid TIL (L-TIL), generating by isolated and expanded peripheral blood PD-1+ T cells, which exhibits a consistent repertoire of tumor-reactive clones compared to tissue-originated TIL<sup>4</sup>. Earlier findings supported that PD-1 antibody can enhance L-TIL ex vivo expansion, with promising clinical effectiveness and safe signals (unpublished). Despite this, L-TIL combined with PD-1 antibody has not been prospectively studied in anti-PD-1 refractory advanced NSCLC.

## METHODS

- This is an ongoing multicenter, prospective, single-arm phase II trial (NCT05878028; Figure 1). The primary endpoint is ORR by RECIST v1.1; secondary endpoints include PFS, DCR, DOR, 1-year OS and safety; exploratory endpoint is the phenotype characteristics of immune cell subsets.
- Given that no appropriate contemporaneous control for baseline estimation, this study uses a Simon optimal two-stage design for sample size determination: the null hypothesis is ORR  $\leq 10\%$  and the alternative hypothesis is ORR  $\geq 30\%$ , with one-sided type I error  $\alpha=0.05$  and type II error  $\beta=0.10$ ; 18 patients will be enrolled in stage 1 and the trial will proceed to stage 2 if  $\geq 2$  responses are observed, with an additional 15 patients enrolled (total N=33); the regimen will be considered promising if  $\geq 6$  responses are observed in the total population.
- ORR will be summarized with Clopper-Pearson exact 95% confidence intervals, and time-to-event endpoints (PFS, OS) will be analyzed using Kaplan-Meier methods.

**Figure 1. Study schema**



## REFERENCES & ACKNOWLEDGEMENTS

### Acknowledgments

We thank all participating investigators for their valuable contributions and are deeply grateful to the patients enrolled in this trial.

### Artificial Intelligence (AI) Use Disclaimer

GPT-4.0 was used only to improve the English linguistic clarity of the abstract; all substantive content, data and analyses were created and validated exclusively by the authors.

### References

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