Abstract *80P*: A Phase I Trial of Optimized Autologous Tumor-Infiltrating Lymphocyte Therapy Without Exogenous IL-2 in Patients with Advanced Non-Small Cell Lung Cancer

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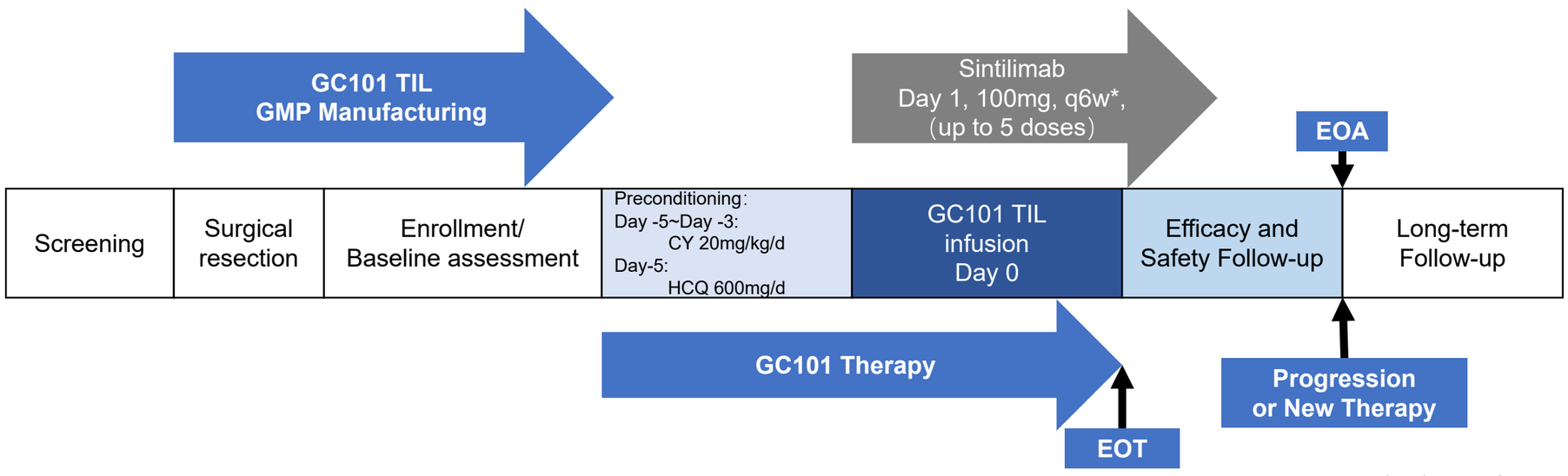
Background:

- Tumor-infiltrating lymphocyte (TIL) therapy is a promising approach for advanced non-small cell lung cancer (NSCLC) who failed to standard therapy[1]. However, the application of TIL therapy has been limited by the requirement for a high-intensity lymphodepletion consisting of high-dose cyclophosphamide (CY) and fludarabine, combined with interleukin-2 (IL-2) administered at high doses. These treatments are associated with significant toxicity[2].
- We explored GC101 TIL with a low-intensity preconditioning regimen, consisting of CY 20 mg/kg/day from day –5 to day –3 and a single 600 mg oral dose of hydroxychloroquine (HCQ) on day –5, combined with IL-2–free TIL infusion. Preliminary results from a prior phase 1 trial in patients with gynecological cancers indicated promising efficacy and tolerability[3].
- This trial evaluated a modified natural TIL regimen using low-intensity preconditioning and no IL-2 administrations in advanced NSCLC.

Methods:

This multicenter, open-label phase I trial (NCT05417750) enrolled patients with stage III/IV NSCLC who were refractory to standard therapy and had adequate organ function. Tumor tissues were resected and transported to a GMP facility for the manufacturing of the cryopreserved infusion product, which was then shipped back to the clinical center. All Patients received three consecutive daily infusions of cyclophosphamide (20 mg/kg/day) from day -5 to day -3, and oral administration of hydroxychloroquine (600 mg once) on day -5. On day 0, within 50 to 70 minutes following the administration of anti PD-1 antibody (100mg, sintilimab, Innovent), patients received a single intravenous adoptive transfer of GC101 TIL in 30 to 120 minutes. Primary endpoint was safety; secondary endpoints included objective response rate (ORR), disease control rate (DCR), duration of response (DOR), progression-free survival (PFS), and overall survival (OS) (Figure 1).



Endpoints:	
Primary endpoint	Safety
Secondary endpoints	ORR; DCR; PFS; OS.

Figure 1. Treatment Schema

Results:

Between August 2022 and September 2025, 12 patients were enrolled and received treatment. The median age was 56.5 years, 67% were female, and 83.3% had oncogenic driver alterations. The median number of prior lines of therapy was 3, which included chemotherapy(75%), anti-PD-(L)1 (41.7 %), and targeted therapy (75%). Median infused TIL dose was 37.7×10^9 cells (range $6.0–53.8\times10^9$). With a median follow-up of 13.0 months (range: 1.5–31.0), Grade 3–4 treatment-related adverse events (TRAEs) occurred in 3 of 12 patients (25.0%). Serious adverse events (SAEs) were reported in 2 patients. No cytokine release syndrome or treatment-related deaths occurred. ORR was 41.7% (5/12, 95% CI 15.2–72.3%). Disease control rate was 66.7% (8/12, 95% CI 34.9-90.1%, 5 PR and 3 SD). Median DOR was not reached. EGFR mutation appeared to be a risk factor for reduced PFS, and the median PFS in the non-EGFR mutation subgroup was not reached. Median OS was not reached, with a 12-month OS rate of 66.7% (95% CI 33.7–86.0%).

Table 1. Characteristics of Baseline

Characteristic	Value
Age, years, Mean ± SD	55.8 ± 10.6
Number of Prior Systemic Therapies, n (%)	
1	2 (16.7%)
2	3 (25.0%)
3	5 (41.7%)
4	2 (16.7%)
Number of Prior Systemic Therapies, n, Median (Range)	3 (1 - 4)
Number of Prior Chemotherapies, n (%)	
0	3 (25.0%)
1	5 (41.7%)
2	3 (25.0%)
3	1 (8.3%)
History of PD-1 Inhibitor Therapy, n (%)	
Yes	5 (41.7%)
No	7 (58.3%)
EGFR Mutation, n (%)	
Yes	5 (41.7%)
No	7 (58.3%)
Infused Cell Count ($\times10^9$), Median, range	37.7 (6.0–53.8)

Table 2. Treatment-Related Adverse Events (Grade≥3)

Grade ≥3 TRAEs, n (%)	Grade 3	Grade 4	Total
	3(25.0)	3(25.0)	3(25.0)
Leukopenia	2(16.7)	1(8.3)	3(25.0)
Neutropenia	0	2(16.7)	2(16.7)
Lymphopenia	1(8.3)	0	1(8.3)
Thrombocytopenia	1(8.3)	0	1(8.3)

Table 3. Best Overall Response

Clinical Response	n (%)	95% CI
Best Overall Response (BOR)		
Complete Response (CR)	0 (0.0)	-
Partial Response (PR)	5 (41.7)	-
Stable Disease (SD)	3 (25.0)	-
Progression Disease (PD)	4 (33.3)	-
Objective Response Rate (ORR)	5 (41.7)	15.2 - 72.3
Disease Control Rate (DCR)	8 (66.7)	34.9 - 90.1
Time to Response (TTR), months, Mean ± SD	1.7 ± 0.7	-

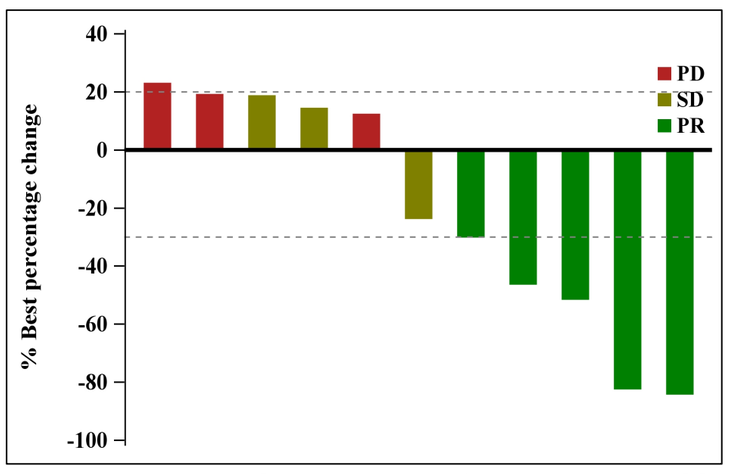


Figure 2. Best Percentage Change From Baseline in Target Lesion SOD

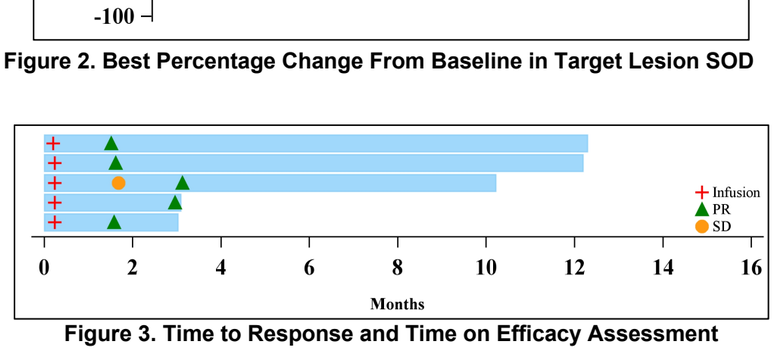


Figure 3. Time to Response and Time on Efficacy Assessment

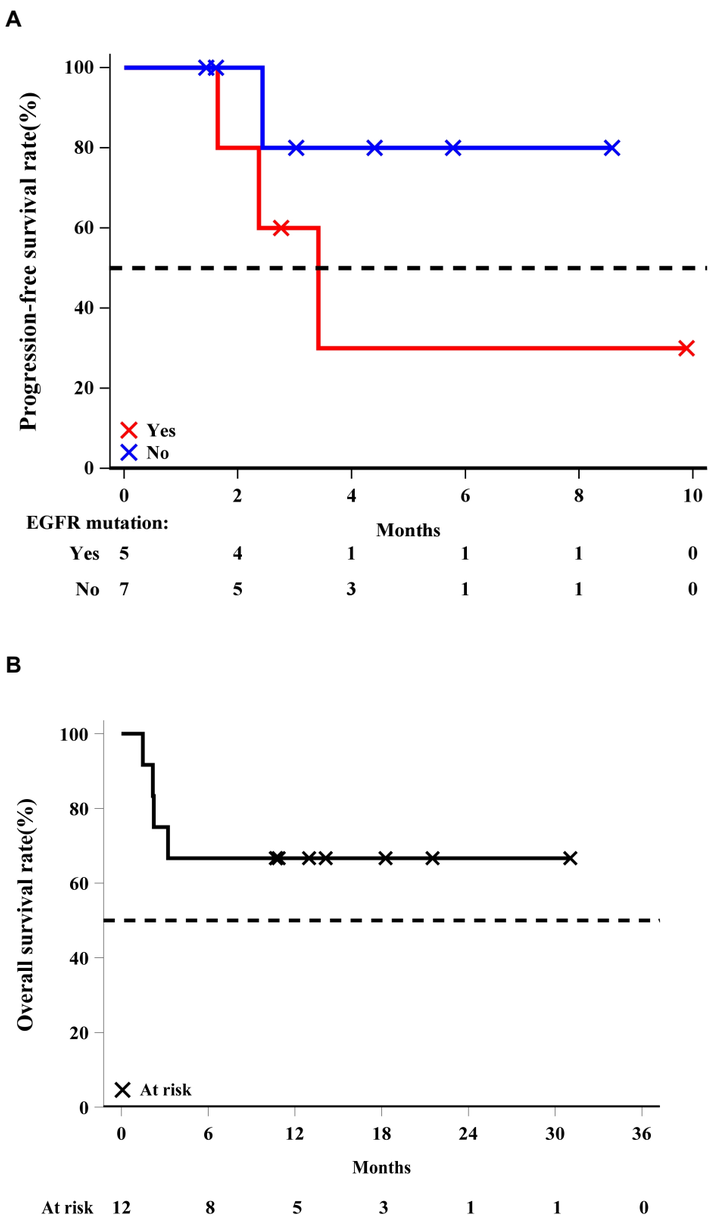


Figure 4. A, Progression-free survival (PFS) according to EGFR mutation status. B, Overall survival (OS), the median OS was not reached.

Conclusion:

Optimized autologous TIL therapy demonstrates manageable toxicity and encouraging activity in heavily pretreated NSCLC. These findings support further exploration of TIL-based strategies in combination with immune-modulatory agents to enhance durability of response.

Abbreviations

AE, adverse event; CY, cyclophosphamide; DCR, disease control rate; DoR, duration of response; ECOG, Eastern Cooperative Oncology Group; EOA, end of assessment; EOS, end of study; EOT, end of treatment; GMP, good manufacturing practice; HCQ, hydroxychloroquine; IL-2, interleukin-2; NCI-CTCAE, national cancer institute common terminology criteria for adverse events; ORR, objective response rate; OS, overall survival; PD, progressive disease; PD-1, programmed cell death protein 1; PFS, progression-free survival; SAE, serious adverse event; TIL, tumor infiltrating lymphocyte.

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