Abstract 5552: A phase I single-arm, open-label trial of engineering tumor-infiltrating lymphocytes with membrane-bound IL-7 for recurrent ovarian cancer

Jing Guo[1], Yuliang Wu[1], Chen Huang[2], Wei Huang[1], Jinye Ding[1], Yao Ge[1], Jihui Zhu[1], Weihui Shi[1], Guihai Ai[1], Shupeng Liu[1], Weina Wang[1], Ning Luo[1], Caixia Li[1], Rong Chen[1], Binghui Zhao[3], Huajun Jin[2], Zhongping Cheng[1]

[1]. Department of Obstetrics and Gynecology, Shanghai Tenth People's Hospital; [2]. Shanghai Juncell Therapeutics Co., Ltd.; [3]. Department of Radiology, Shanghai Tenth People's Hospital.

Background:

Tumor-infiltrating lymphocytes (TILs) therapy has shown limited success in patients with recurrent ovarian cancer (OC).

To improve TIL antitumor activity, we designed glycosylphosphatidylinositol-anchored membrane-bound interleukin-7 (mbIL-7-GPI) to engineer TILs (mbIL-7-TILs, GC203 TILs) through piggyBac transposon system (Figure 1).

This study aimed to investigate the safety and efficacy of GC203 TIL in recurrent OC patients.

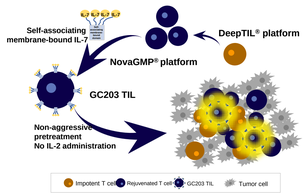

Figure 1. Schematic Diagram of membrane-bound IL-7 Tumor-Infiltrating Lymphocytes (mbIL-7-TILs, GC203 TIL)

Methods:

This is a single-center, investigator-initiated, open-label, single-arm phase 1 trial (NCT05468307). Tumor tissues were resected and transported to a GMP facility in a manufacturing cycle of 22-26 days (Figure 2). The cryopreserved infusion product was then shipped back to 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 GC203 TIL in 30 to 120 minutes (Figure 3).

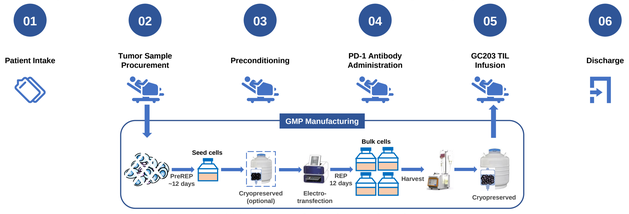

Figure 2. GC203 TIL Manufacturing and Patient Journey

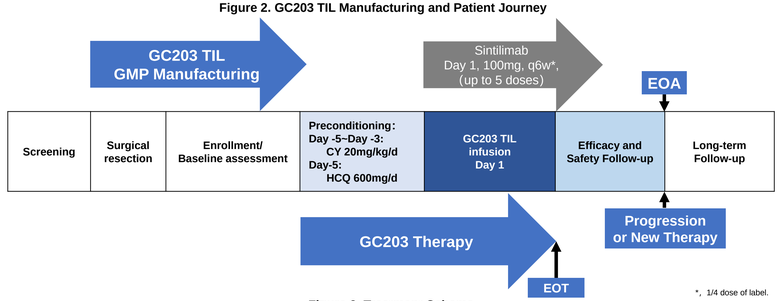

Figure 3. Treatment Schema

Endpoints:

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

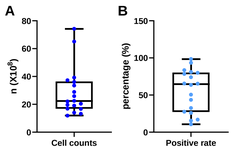

Figure 4. A, Total Cell Dose; B, Positive Rate of GC203 TIL. The median number of GC203 TILs infused was 26.5 ×10^8 cells (11.9 to 74.2), with a median proportion of engineered cells at a rate of 53.8% (10.7% to 98.53%).

Results:

Table 1. Characteristics of participants

Characteristics	N=18
Age, years, median (range)	52 (32-70)
Median time from initial diagnosis to enrollment, months (range)	35.3 (13.6-50.7)
ECOG PS, No. (%)	
1	10 (55.6)
2	8 (44.4)
FIGO stage at initial diagnosis, No. (%)	
IC2	1 (5.6)
IIB	1 (5.6)
IIIA2	1 (5.6)
IIIB	2 (11.2)
IIIC	11 (61.1)
IVB	2 (11.2)
Histology, No. (%)	
GCT	1 (5.6)
HGSOC	12 (66.7)
LGMOC	1 (5.6)
OCCC	2 (11.1)
OEC	2 (11.1)
Recurrent/metastatic site, No. (%)	
Local infiltration	9 (50.0)
Lymph node	8 (44.4)
Hematogenous spread	8 (44.4)
Peritoneal implantation	6 (33.3)
Recurrent/metastatic lesions≥3, No. (%)	9 (50.0)
Target Lesion size, mm (range)	57 (13-146)
Lesion size<60 mm, No. (%)	9 (50.0)
Lesion size≥60 mm, No. (%)	9 (50.0)
Previous systemic therapy, No. (%)	
Radiotherapy/Chemotherapy	18 (100)
Targeted therapy	16 (88.9)
Immunotherapy (ICIs, ACT)	3 (16.7)
No. of previous systemic therapies, median (range)	5 (2-11)
No. of previous surgical interventions	
2, No. (%)	10 (55.6)
3, No. (%)	6 (33.3)
4, No. (%)	2 (11.1)
Platinum-resistant, No. (%)	11 (61.1)

Table 2. Treatment Emergent Adverse Events (≥30%, Grade≥3)

Adverse events	Grade 3	Grade 4
Leukopenia	7 (38.9%)	2 (11.1%)
Lymphopenia	5 (27.8%)	2 (11.1%)
Neutropenia	4 (22.2%)	2 (11.1%)

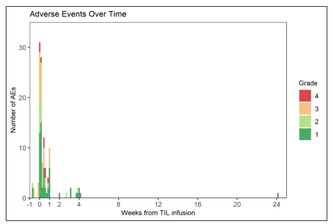

Figure 5. Adverse Events

Table 3. Best Overall Response

Clinical Response	N=18	95% CI
ORR	6 (33.3%)	16.3- 56.3
CR	2 (11.1%)	
PR	4 (22.2%)	
SD	9 (50%)	
PD	3 (16.7%)	
DCR	15 (83.3%)	60.8- 94.2
Median PFS (month)	5.1	(range, 1.0-13.9)
6-month OS rate (%)	75.60%	57.4-99.6
12-month OS rate (%)	68.80%	49.3-95.9

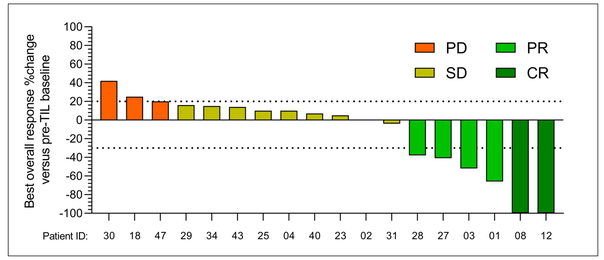

Figure 6. Best Percentage Change From Baseline in Target Lesion SOD

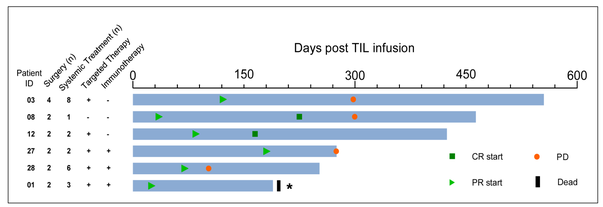

Figure 7. Time to Response and Time on Efficacy Assessment for Confirmed Responders (PR or Better). *, Patient 01 got COVID-19 infection before death.

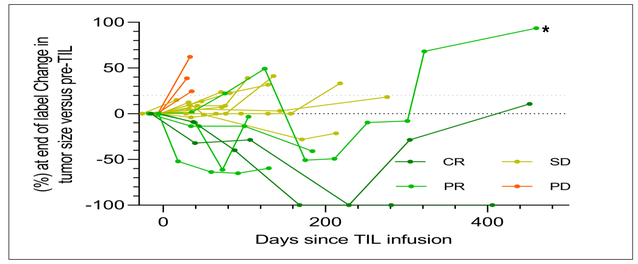

Figure 8. Percentage Change From Baseline in Target Lesion SOD. *, Patient 03 received only one dose of chemotherapy after PD, tumor size reduced 60% 5 months later (below baseline again, this also suggests that GC203 may have changed the TME).

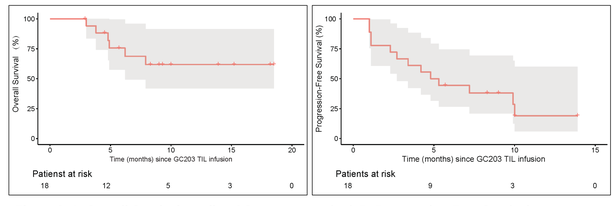

Figure 9. A. Overall Survival, median OS was not reached. B, Progression-Free Survival.

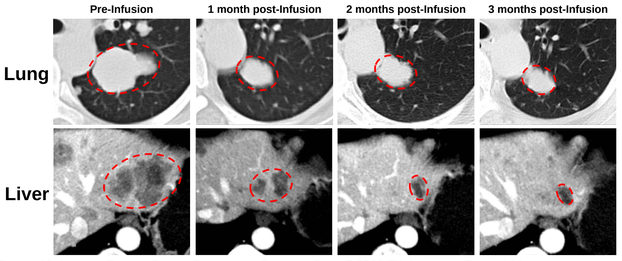

Figure 10. Images From a Partial Responder Pre- and Post-GC203 TIL Infusion. Patient 01, ovarian endometrioid cancer, progression after 5 lines of systemic treatment including chemotherapy and PARPis, 2022/6/16 received 19.1×10^8 cells with 25.9% positive rate, 2022/7/14 achieved PR with 66% shrinkage of target lesions.

Conclusion:

In this study, we successfully engineered TILs with membrane-bound IL-7 and GPI structure (mbIL-7-TIL, GC203 TIL) using nonviral vectors. And we performed the first-in-human evaluation of GC203 TIL in patients with metastatic OC. Our results indicated that GC203 TIL infusion has acceptable safety and potent efficacy in recurrent OC patients with limited treatment options.

Abbreviations

ACT, adoptive cell therapy; ALT, alanine amino transferase; AST, glutamic aspartate amino transferase; CR, complete response; CRP, C-reactive protein; DCR, disease control rate; ECOG PS, Eastern Cooperative Oncology Group performance status; EOA, end of assessment; EOT, end of TIL therapy; FIGO, Federation Internationale Of Gynecologie And Obstetrigue; GCT, granulosa cell tumor; GGT, gamma-glutamyl transpeptidase; GMP, good manufacturing practice; HGSOC, high-grade serous ovarian cancer; ICI, immune checkpoint inhibitor; IL-2, interleukin-2; LDH, lactate dehydrogenase; LGMOC, Low grade mucinous ovarian cancer; mbIL-7-GPI, glycosylphosphatidylinositol-anchored membrane-bound interleukin-7 ; mbIL-7-TIL, mbIL-7-GPI engineered TILs; OC, ovarian cancer ; OCCC, ovarian clear cell carcinoma; OEC, ovarian endometrial cell ; ORR, objective response rate; OS, overall survival; PARPi, poly(ADP-ribose) polymerase inhibitor; PD, progressive disease; PD-1, programmed cell death protein 1; PFS, progression-free survival; PR, partial response; REP, rapid expansion protocol; SD, stable disease; SOD, sum of diameters; TBA, total bile acid; TIL, tumor infiltrating lymphocyte.

Disclosures

Chen Huang: Employment: Shanghai Juncell Therapeutics. Leadership: Shanghai Juncell Therapeutics. Stock or Stock Options: Shanghai Juncell Therapeutics. Honoraria: Shanghai Juncell Therapeutics. Consulting or Advisory Role: Shanghai Juncell Therapeutics.
Huajun Jin: Employment: Shanghai Juncell Therapeutics. Leadership: Shanghai Juncell Therapeutics. Stock or Stock Options: Shanghai Juncell Therapeutics. Honoraria: Shanghai Juncell Therapeutics. Consulting or Advisory Role: Shanghai Juncell Therapeutics. Speakers' Bureau: Shanghai Juncell Therapeutics. Research Funding: Shanghai Juncell Therapeutics.

Corresponding author: Jing Guo. jguo12@foxmail.com