

Trial in progress: A Pivotal Phase 2, Randomized, Controlled, Open-Label, Trial (MIZAR-003) to Assess the Efficacy and Safety of GC101 TIL, an Autologous Tumor-Infiltrating Lymphocyte (TIL) Cell Therapy, for Patients with Advanced Anti-PD-1 Refractory Melanoma in Later-Line Therapy

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Background

- Immune checkpoint inhibitors (ICIs) and targeted therapies have transformed the treatment landscape for advanced (unresectable or metastatic) melanoma. Nevertheless, most patients receiving frontline ICIs experience disease progression within one year [1-3].
- Furthermore, 40%–65% of patients exhibit primary resistance to ICIs, while 30%–40% develop secondary resistance [4-6].
- Autologous tumor-infiltrating lymphocyte (TIL) therapy has demonstrated clinically meaningful efficacy in patients with advanced melanoma following ICI treatment [7,8].
- However, the application of TIL therapy in advanced melanoma has been limited by the need for intensive lymphodepletion, using high-dose cyclophosphamide (CY) and fludarabine, along with high-dose interleukin-2 (IL-2), which are associated with significant toxicity.
- We explored GC101 TIL with a low-intensity preconditioning regimen, consisting of CY and hydroxychloroquine (HCQ), combined with IL-2-free TIL infusion. This regimen showed promising outcomes in a prior phase 1 trial [9].
- MIZAR-003 (NCT04943913) is a pivotal phase 2, multicenter, randomized, open-label, parallel-group, treatment study to assess the efficacy and safety of GC101 TIL therapy in melanoma patient refractory to programmed cell death protein 1 (PD-1) antibodies.

Trial Design

Figure 1. MIZAR-003 Study Design

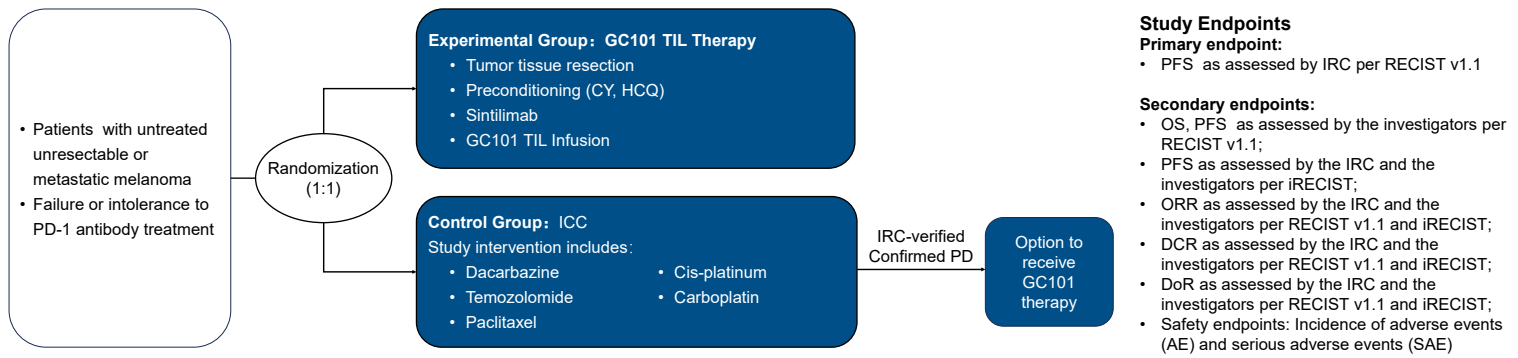
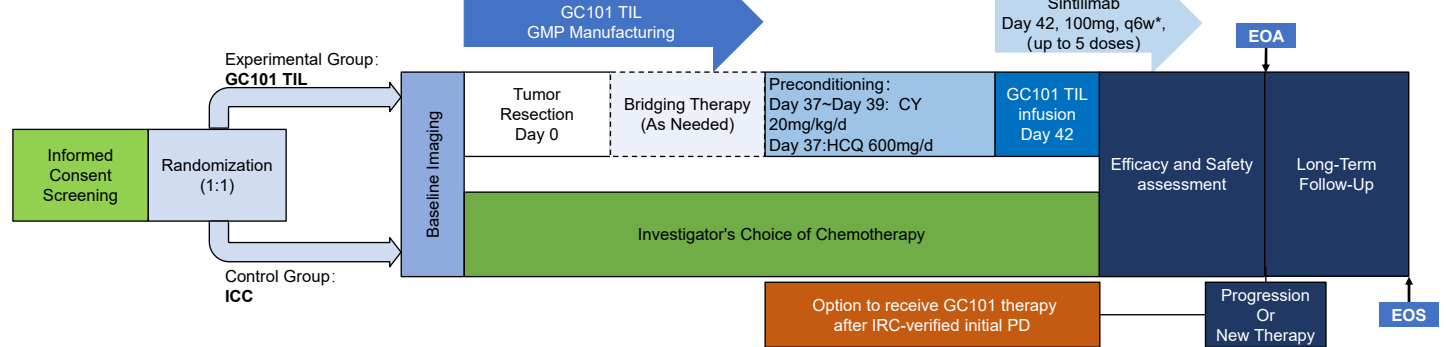


Figure 2. MIZAR-003 Treatment Schema



Key Eligibility Criteria

Inclusion Criteria

- Age ≥ 18 years and ≤ 75 years, gender not restricted;
- Patients with unresectable advanced, recurrent or metastatic melanoma (excluding uveal melanoma);
- At least one of the following has occurred: failure of PD-1 antibody treatment or intolerance (if carrying BRAF V600 mutation, failure of BRAF and MEK inhibitors treatment; if carrying NRAS mutation, failure of toremifene treatment);
- Have a feasible tissue region for tumor resection/puncture to isolate TILs;
- According to RECIST 1.1 criteria, at least one measurable lesion remain after tissue sampling and tumor resection;
- ECOG score 0-1;
- Expected survival period greater than 3 months.

Exclusion Criteria

- Melanoma of uveal/ocular origin;
- Participated in other clinical trials of drug or biological therapy within the past 4 weeks;
- Two or more types of malignant tumors;
- Have signed the informed consent form or plan to receive attenuated live vaccine during the study;
- Have not recovered to ≤ Grade 1 according to the National Cancer Institute - Common Toxicity Criteria Version 5.0 (NCI-CTCAE 5.0) (except for toxicities such as alopecia judged by the investigator to be without safety risks);
- Any form of primary or acquired immunodeficiency.

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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; ICC, investigator's choice of chemotherapy; ICI, immune checkpoint inhibitor; IL-2, interleukin-2; IRC, independent review committee; 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.

Acknowledgments:

- The authors would like to the investigators and study site team members who are participating in the study.
- This study is sponsored by Shanghai Juncell Therapeutics Co., Ltd.