

Investigating the safety and efficacy of a Universal CAR-T cell immunotherapy in patients with relapse and refractory T-cell acute lymphoblastic leukemia and T lymphoblastic lymphoma

Submission date 07/01/2020	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 24/01/2020	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 08/09/2023	Condition category Cancer	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

Plain English summary of protocol

Background and study aims

T cells are a type of immune cell. Like other cells of the body, T Cells can develop cancer. T cell cancers mainly include T cell leukaemia and T cell lymphoma, both of which have a relatively poor prognosis. Currently, patients with relapsed/refractory type (the name given to cancer that reappears or grows again after a period of no changes or signs of cancer) of this leukaemia or lymphoma have limited choices for treatment. CAR-T cells are immune cells that are engineered to target specific cell markers. For example, CAR-T cells targeting the marker CD19 have shown great effectiveness in the treatment of B cell tumors that carry this marker. Here we construct a new universal CAR-T design targeting CD7 which is found on the cells of relapsed/refractory type T cell leukaemia and lymphoma and hope to test its safety and efficiency in the treatment of relapsed/refractory type T cell leukaemia and lymphoma.

Who can participate?

Patients diagnosed with relapsed/refractory T cell leukaemia or lymphoma. Both genders, aged 2-70 years old.

What does the study involve?

Enrolled participants are randomly chosen to receive one of three different dose levels of CAR-T cells called GC027.

1. Dose level one: $0.6-1.5 \times 10^7$ cells/kg;
2. Dose level two: $1.8-3.6 \times 10^7$ cells/kg;
3. Dose level three: $4-6 \times 10^7$ cells/kg.

Before CAR-T infusion, all participants will receive a preconditioning therapy including several chemotherapy agents or other interventions that are required to help the effect of the CAR-T cells. After completion of preconditioning therapy, infusion of the CAR-T cells via a tube into the vein needs to start within 1 week. Participants will receive one infusion of CAR-T cells which will

take between 15 and 30 mins. All participants will have a blood test before infusion and at 4, 7, 10 and 14 days following infusion to measure their response to the treatment and some further tests will be required in some participants. The clinicians involved in the trial will make judgments on participant response at 4 weeks and 12 weeks after the infusion (earlier judgment before the time point set is acceptable) on the basis of blood test results and other clinical measures. The total duration of follow-up is at least 12 weeks.

What are the possible benefits and risks of participating?

The universal CAR-T cells targeting CD7 may lead to durable disease control and long term survival. The main risks of participating include cytokine release syndrome (CRS) and CAR-T-cell-related encephalopathy syndrome (CRES).

Where is the study run from?

Haematology department of 920th Hospital of Joint Logistics Support Force of People's Liberation Army of China (China).

When is the study starting and how long is it expected to run for?

From February 2019 to December 2025

Who is funding the study?

Gracell Biotechnologies Co., Ltd (China)

Who is the main contact?

Prof. Sanbin Wang, Sanbin1011@163.com

Contact information

Type(s)

Public

Contact name

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Additional identifiers

Clinical Trials Information System (CTIS)

Nil known

Protocol serial number

GUT001

Study information

Scientific Title

A single-arm, open-label, single-center study of GC027 injection in relapse and refractory T-ALL or relapse and refractory T-LBL

Acronym

N/A

Study objectives

The GC027 injection will be safe and effective in patients with relapse and refractory T-ALL and T-LBL

Ethics approval required

Old ethics approval format

Ethics approval(s)

Approved 22/11/2019, the Ethics Committee of 920th Hospital of Joint Logistics Support Force (Kunming, Yunnan, 650100 P.R.China; km920iec@163.com; +86 871 64774287) ref: 2019-101 (research) -02

Study design

Interventional, single arm, open-label, single center study

Primary study design

Interventional

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Relapse and Refractory T cell acute lymphoblastic leukaemia (T-ALL), Relapse and Refractory T cell lymphoblastic lymphoma (T-LBL)

Interventions

Enrolled participants are allocated to one of three different dose levels of GC027. The infusion dose of CAR-T cells will start at low dose and then rise to higher dose after completion of low dose group.

1. Dose level one: $0.6-1.5 \times 10^7$ cells/kg;

2. Dose level two: $1.8-3.6 \times 10^7$ cells/kg;

3. Dose level three: $4-6 \times 10^7$ cells/kg.

Before CAR-T infusion, all participants will receive a preconditioning therapy suggested as: Fludarabine $30 \text{ mg/m}^2 \times 6\text{d}$, Cyclophosphamide $300 \text{ mg/m}^2 \times 6\text{d}$ or Cyclophosphamide $600 \text{ mg/m}^2 \times 6\text{d}$. After completion of preconditioning therapy, infusion of GC027 needs to start within 1 week. Participants will receive one infusion of GC027 which will take between 15 and 30 mins.

All participants will have a blood test at -1, 4, 7, 10 and 14 days following infusion to measure their response to the treatment and some further tests will be required in some participants. The clinicians involved in the trial will determine participant response at 4 weeks and 12 weeks (earlier judgment before the time point set is acceptable) according to National Comprehensive Cancer Network (NCCN) clinical practice guidelines in oncology: Acute Lymphoblastic Leukemia (2016.V2) for T-ALL response rate and Lugano 2014 for T-LBL response rate.

The total duration of follow-up is at least 12 weeks.

Intervention Type

Biological/Vaccine

Phase

Phase I/II

Drug/device/biological/vaccine name(s)

GC027

Primary outcome(s)

1. Dose-limiting toxicity assessed by Common Terminology Criteria for Adverse Events (CTCAE v5.0) at 4 and 12 weeks following GC027 infusion
2. Percentage of participants with adverse events measured by Common Terminology Criteria for Adverse Events (CTCAE v5.0) at 4 and 12 weeks following GC027 infusion
3. Overall response rate of patients, determined by National Comprehensive Cancer Network (NCCN) clinical practice guidelines in oncology: Acute Lymphoblastic Leukemia (2016.V2) for T-ALL response rate and Lugano 2014 for T-LBL response rate, at 24 weeks following GC027 infusion

Key secondary outcome(s)

1. Progression-free survival (PFS) determined from patient notes at 24 weeks following GC027 infusion
2. Overall survival (OS) determined from patient notes at 24 weeks
3. Duration of remission (DOR) determined from patient notes at 24 weeks
4. CD7 + T cells in peripheral blood at baseline (-1 days) and at 4, 7, 10, 14 days
5. CAR DNA copies measured by flow cytometry in peripheral blood and bone marrow at 4 and 12 weeks
6. CAR-T cell number measured by flow cytometry in peripheral blood and bone marrow at 4 and 12 weeks
7. Changes of peripheral blood serum cytokines measured by flow cytometry in peripheral blood and bone marrow at 4 and 12 weeks
8. Lymphocyte subsets measured by flow cytometry in peripheral blood and bone marrow at 4 and 12 weeks
9. Anti-GC027 antibody levels measured by flow cytometry in peripheral blood and bone marrow at 4 and 12 weeks

Completion date

31/12/2025

Eligibility

Key inclusion criteria

1. 2 to 70 years
2. Diagnosed with relapsed and refractory CD7 + T cell acute lymphocytic leukemia (T-ALL) or relapsed and refractory CD7 + T lymphoblastic lymphoma (T-LBL)
3. Quantifiable tumor burden
4. Eastern cooperative oncology group (ECOG) performance status of 0 to 2
5. Life expectancy ≥ 12 weeks
6. Adequate organ function defined as:
 - a. Serum ALT/AST ≤ 2.5 ULN
 - b. Creatinine clearance (as estimated by Cockcroft Gault) ≥ 60 mL/min
 - c. PT and APTT ≤ 1.5 ULN
 - d. Total bilirubin ≤ 1.5 ULN
 - e. Cardiac ejection fraction $\geq 45\%$
 - f. No clinically significant ECG findings
 - g. Baseline oxygen saturation $>90\%$ on room air
7. Recovered from acute toxic effects of prior chemotherapy \geq one week before entering this study
8. Agreement to use of medical-approved-contraception during the period of trial and in 1 year after cell transfusion therapy
9. Signed informed consent form

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Not Specified

Sex

All

Key exclusion criteria

1. Diagnosis of other malignancy (except non-melanoma and cervical carcinoma in situ, bladder cancer, breast cancer that have a disease-free survival of more than 5 years)
2. Severe mental disorders
3. History of hereditary diseases, including but not limited to: Fanconi anemia, Shu-Dai syndrome, Costman syndrome or any other known bone marrow failure syndrome
4. Grade 2-4 acute graft-versus-host disease (GVHD) (Glucksberg criteria) or extensive chronic GVHD (Seattle criteria)
5. Grade III-IV heart failure or myocardial infarction, angioplasty or stent placement, unstable angina pectoris, or other clinically prominent heart disease within one year before enrollment
6. History or presence of CNS disorder, including but not limited to: seizure disorder, cerebrovascular ischemia/hemorrhage, dementia, cerebellar disease, or any autoimmune disease with CNS involvement
7. Positive for any of the following etiological tests: HIV, HBV, HCV, TPPA
8. Presence of fungal, bacterial, viral, or other infection that is uncontrolled
9. Severe allergies
10. History of autoimmune disease resulting in end organ injury or requiring systemic immunosuppression/systemic disease modifying agents within the last 2 years
11. History or diagnosis of pulmonary fibrosis

12. Participation in other clinical trials ≤ 4 weeks prior to enrollment
13. Concomitant disease that require systemic steroids or other immune suppressive therapy during the study period in researcher's judgement
14. Patients who are contraindicated to cyclophosphamide, fludarabine, or melphalan
15. Allogeneic cell therapy (such as donor lymphocyte infusion, DLI) ≤ 6 weeks prior to enrollment
16. Poor adherence due to physical, family, social, geographic, and other factors, who cannot follow the research plan and follow-up plan
17. Pregnant and lactating women
18. Any other conditions that researcher think it is inappropriate for the subject to anticipate the trial

Date of first enrolment

20/01/2020

Date of final enrolment

31/12/2024

Locations

Countries of recruitment

China

Study participating centre

920th Hospital of Joint Logistics Support Force

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China

650100 P.R.China

Sponsor information

Organisation

Gracell Biotechnologies Co., Ltd

Funder(s)

Funder type

Industry

Funder Name

Gracell Biotechnology Ltd

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated and/or analyzed during the current study during this study will be included in the subsequent results publication

IPD sharing plan summary

Available on request