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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	[ ] Prospectively registered [ ] Protocol
Registration date 24/01/2020	**Overall study status** Ongoing	[ ] Statistical analysis plan [ ] Results
Last Edited 08/09/2023	**Condition category** Cancer	[ ] Individual participant data [ ] 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: 0.6-1.5×10^7 cells/kg;
2. Dose level two: 1.8-3.6×10^7 cells/kg;
3. Dose level three: 4-6×10^7 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

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
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

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
No participant information sheet available

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: 0.6-1.5×10^7 cells/kg;
2. Dose level two: 1.8-3.6×10^7 cells/kg;
3. Dose level three: 4-6×10^7 cells/kg.
Before CAR-T infusion, all participants will receive a preconditioning therapy suggested as: Fludarabine 30 mg/m^2×6d, Cyclophosphamide 300 mg/m^2×6d or Cyclophosphamide 600 mg /m^2×6d. 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 particpants. 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 measure
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

Secondary outcome measures
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

Overall study start date
01/02/2019

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 ≥45%
f. No clinically significant ECG findings
g. Baseline oxygen saturation >90% on room air
7. Recovered from acute toxic effects of prior chemotherapy ≥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

Age group
Not Specified

Sex
Both

Target number of participants
15

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, Shut-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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Sponsor type
Research organisation

Website
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Funder(s)

Funder type
Industry

Funder Name
Gracell Biotechnology Ltd

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal

Intention to publish date
30/06/2026

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