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

Submission date	**Recruitment status**	[X] Prospectively registered
07/01/2020	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
31/01/2020	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
31/01/2020	Cancer	[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
B cell malignancies mainly include B cell leukaemia and B cell lymphoma. For those with relapsed /refractory B cell malignancies, the prognosis is poor. Patients with relapsed/refractory B cell leukaemia or lymphoma have limited choices. CAR-T cells targeting CD19 have shown great effectiveness in the treatment of B cell tumor. Here we construct a new universal CAR-T design targeting CD7 and CD19, hoping to test its safety and efficiency in the treatment of relapsed /refractory B cell leukaemia and lymphoma.

Who can participate?
Patients diagnosed with relapsed/refractory B cell leukaemia or lymphoma. Both gender, aged 2-70 years old.

What does the study involve?
Participants are assigned into one of the three dose-specific groups after enrollment.
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 they receive CAR-T therapy, participants will have preconditioning therapy of one of several chemotherapy agents or other interventions that will help CAR-T cells expand better in the body. After completion of preconditioning therapy, a flexible tube will be put into a vein of the participants for receiving the liquid containing the GC197 cells and this must start within 1 week of the preconditioning therapy. Participants will receive GC197 once, and this will take 15-30 minutes. Blood tests will be arranged for the day before and 4, 7, 10 and 14 days after the CD197 treatment.

A clinical assessment will be used to judge the response of participants to the treatment at 4 and 12 weeks after GC197 infusion. 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 and CD19 may lead to disease control and long term survival.

The risks of participating include cytokine release syndrome (CRS) and CAR-T-cell-related encephalopathy syndrome (CRES).

Where is the study run from?
The 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?
January 2019 to October 2022

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
Prof Sanbin Wang

ORCID ID
https://orcid.org/0000-0002-4802-0292

Contact details
920th Hospital of Joint Logistics Support Force of People's Liberation Army of China
No.212 Daguan Road
Xishan District
Kunming, Yunnan Province
China
650100 P.R.China
+86 15398671578
Sanbin1011@163.com

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
GUB001

Study information

Scientific Title
A single-arm, open-label, single-center study of GC197 injection in relapse and refractory B cell malignancies

Acronym
Study of GC197 injection in Relapse and Refractory B cell malignancies.

Study objectives
The GC197 injection will be safe and effective in patients with relapse /refractory B cell malignancies

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 22/11/2019, Ethics Committee of 920th Hospital of Joint Logistics Support Force (No. 212 Daguan Road, Xishan District, Kunming, Yunnan Province, 650100 P.R.China; km920iec@163.com; +86 0871 64774287), ref: 2019-101(R) -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 B cell malignancies

Interventions

Once a participant is enrolled, He/She will be assigned to a dose-specific group. Three dose levels will be evaluated and the infusion dose of CAR-T cells will start at low dose then rise to a higher dose after completion of the 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

Preconditioning therapy before CAR-T infusion is needed. Suggested therapy includes: Fludarabine 30 mg/m^2×6d, Cyclophosphamide 300 mg/m^2×6d or Cyclophosphamide 600 mg /m^2×6d. Other interventions are allowed to be used as preconditioning therapy.

After completion of preconditioning therapy, the infusion of GC197 must start within 1 week. Participants will receive one intravenous infusion of GC197. The infusion should be completed within 15-30 minutes.

Infusion day is set as day 0. Blood tests are arranged for -1, 4, 7, 10 and 14 days. Additional blood tests may be required according to clinical demand. Response judgment is set at 4 weeks and 12 weeks after GC197 infusion (earlier judgment before the time point set is acceptable).

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)
GC197

Primary outcome measure
1. Presence of dose-limiting toxicity assessed by Common Terminology Criteria for Adverse Events (CTCAE v5.0) at 4 and 12 weeks following GC197 infusion
2. Overall response rate of patients who received GC197 infusion assessed by NCCN clinical practice guidelines in oncology: Acute Lymphoblastic Leukemia (2016.V2) for B-ALL response rate and Lugano 2014 for B-Lymphoma response rate at 24 weeks

Secondary outcome measures
1. Clinical benefit of GC197 infusion measured by progression-free survival (PFS), overall survival (OS) and duration of remission (DOR) assessed at 4 and 12 weeks.
2. Response to GC197 infusion measured by changes in peripheral blood and bone marrow, CAR-T cell flow cytometry in peripheral blood, peripheral blood serum cytokines, lymphocyte subsets, and anti-GC197 antibody levels at -1, 4, 7, 10 and 14 days

Overall study start date
06/01/2019

Completion date
01/10/2022

Eligibility

Key inclusion criteria
1. 2 to 70 years
2. Diagnosed with relapsed and refractory CD19+ B cell malignancies
3. Eastern cooperative oncology group (ECOG) performance status of 0 to 2
4. Life expectancy ≥12 weeks
5. 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
6. Agreement to the use of medical-approved-contraception during the period of trial and in 1 year after cell transfusion therapy
7. Quantifiable tumor burden
8. Informed consent given

Participant type(s)
Patient

Age group
All

Sex
Both

Target number of participants
15

Key exclusion criteria
1. Have other tumors (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 diseases 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 of pulmonary fibrosis
12. Involvement in other clinical trials ≤ 4 weeks prior to enrollment

13. Presence of concomitant disease that requires systemic steroids or other immune suppressive therapy during the study period in the researcher's judgment
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 the researcher thinks it is inappropriate for the subject to anticipate the trial

Date of first enrolment
01/02/2020

Date of final enrolment
01/10/2021

Locations

Countries of recruitment
China

Study participating centre
920th Hospital of Joint Logistics Support Force
No.212 Daguan road
Xishan district
Kunming , Yunnan Provience
China
650100 P.R.China

Sponsor information

Organisation
Gracell Biotechnologies Co., Ltd

Sponsor details
12th Floor
926 Yishan Road
XuHui District,
Shanghai
China
200030 P.R.China
+86-21-64031375
info@gracellbio.com

Sponsor type

Research organisation

Website
https://www.gracellbio.com/

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
01/12/2021

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
Data sharing statement to be made available at a later date