ISRCTN17901467 https://doi.org/10.1186/ISRCTN17901467

Safety and feasibility of CD19 CAR-T cells in adults with recurrent and hard-to-treat B cell blood cancers

Submission date
25/04/2024

Recruitment status
Recruiting

Registration date
27/04/2024

Overall study status
Ongoing

Last Edited
13/11/2024

Condition category
Cancer

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

Plain English summary of protocol

Background and study aims
This study aims to investigate the safety and feasibility of using modified T cells from either the patient themselves (autologous) or from matched donors (allogeneic) that have been changed to target the CD19 protein on B cells. This treatment will be given to adults with CD19-positive recurrent and refractory (hard-to-treat) B cell blood cancer after the patient receives chemotherapy to deplete their lymphocytes. The main goal is to assess the safety of this treatment and document any side effects in adults with certain types of cancer, such as acute lymphoblastic leukemia (ALL) and non-Hodgkin lymphoma (NHL), in a Thai adult population. Additionally, the researchers hope to show that they can produce enough of these modified T cells at the point of care to meet the required standards for treatment.

Who can participate?
Men and women aged 18-70 years old diagnosed with CD19-positive leukemia or lymphoma (blood cancer) who have recurrent and refractory disease

What does the study involve?
Patients will receive the CAR-T cell infusion after lymphodepletion chemotherapy. The infusion may be split into 2-3 days to reduce the side effects.

What are the possible benefits and risks of participating?
Several CD19 CAR-T cell products have demonstrated impressive effectiveness in the treatment of various forms of relapsed/refractory B cell cancer. However, this is the first study using the point-of-care manufactured SiCF-019 cells. As cell products, patients, and disease characteristics may differ, the benefits associated with this treatment are mainly unknown. Taking part in this study may lead to stable disease control and improve clinical outcomes, but these clinical benefits are not guaranteed. The potential risks of CD19 CAR-T cell therapy include cytokine release syndrome (a systemic inflammatory response caused by the rapid release of cytokines), neurotoxicity (damage to the nervous system), and B cell aplasia (a condition where there is a deficiency or absence of B cells).

Where is the study run from?
Faculty of Medicine Siriraj Hospital (Thailand)

When is the study starting and how long is it expected to run for?
August 2019 to November 2025

Who is funding the study?
Siriraj Foundation (Thailand)

Who is the main contact?
Prof. Surapol Issaragrisil, surapol.iss@mahidol.ac.th

Contact information

Type(s)
Principal Investigator

Contact name
Prof Surapol Issaragrisil

ORCID ID
http://orcid.org/0000-0002-8924-0646

Contact details
Division of Hematology, Department of Medicine
Faculty of Medicine Siriraj Hospital, Mahidol University
2 Siriraj Hospital, Wanglang Road
Siriraj, Bangkoknoi
Bangkok
Thailand
10700
+66 (0)2419 4446
surapol.iss@mahidol.ac.th

Type(s)
Public

Contact name
Dr Sudjit Luanpitpong

ORCID ID
http://orcid.org/0000-0002-1639-4935

Contact details
Siriraj Center of Excellence for Stem Cell Research
Faculty of Medicine Siriraj Hospital, Mahidol University
2 Siriraj Hospital, Wanglang Road
Siriraj, Bangkoknoi
Bangkok
Thailand
10700

+66 (0)2419 2907
sudjit.lua@mahidol.edu

Type(s)
Scientific

Contact name
Dr Smith Kungwankiattichai

ORCID ID
http://orcid.org/0000-0001-6072-4025

Contact details
Division of Hematology, Department of Medicine
Faculty of Medicine Siriraj Hospital, Mahidol University
2 Siriraj Hospital, Wanglang Road
Siriraj, Bangkoknoi
Bangkok
Thailand
10700
+66 (0)2419 4448
smith.kun@mahidol.ac.th

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
SiRB 472/2562(EC1)

Study information

Scientific Title
A pilot study: evaluation of efficacy and safety of autologous or graft HLA-matched donor-derived CD19 CAR-T cells for the treatment of CD19-positive recurrent and refractory B cell malignancies in adults

Study objectives
1. To successfully produce CAR T-cells at a minimum target dose of 1 million cells/kg
2. The researchers anticipate a similar adverse event profile and recommended dose as CAR T-cell products previously reported in clinical trials

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 27/11/2020, Siriraj Institutional Review Board (Human research protection unit, Faculty of Medicine Siriraj Hospital, Mahidol University. His Majesty the King's 80th Birthday Anniversary 5th December 2007 Building, 2nd floor, Room 210. 2 Wang Lang Road, Bangkok, 10700, Thailand; +66 (0)2419 2667 - 72; siethics@mahidol.ac.th), ref: 472/2562(EC1)

Study design
Single-arm open-label single-center study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Medical and other records, University/medical school/dental school

Study type(s)
Safety, Efficacy

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

Health condition(s) or problem(s) studied
CD19-positive recurrent and refractory B cell malignancies

Interventions
Biologic: Autologous CD19-specific chimeric antigen receptor (CAR)-T cells or allogeneic CD19 CAR-T cells from prior HLA-matched stem cell transplant donor

Other agents: Fludarabine, Cyclophosphamide

Patients will receive conditioning lymphodepletion chemotherapy and CAR-T cell infusion within a 14-day period. CAR-T cells at a dosing range of 0.1-1×10^7 CAR-T cells/kg will be administered intravenously in an inpatient setting with emergency equipment and emergency medications available at the bedside per institutional cellular therapy infusion SOP. Dose fractions of CAR-T cells over 2–3 days instead of a single dose infusion may be administered.

Intervention Type
Biological/Vaccine

Pharmaceutical study type(s)
Pharmacokinetic, Pharmacodynamic, Dose response

Phase
Phase I

Drug/device/biological/vaccine name(s)

SiCF-019

Primary outcome measure
1. Proportion of products successfully manufactured meeting the established release criteria with a goal of at least 1 million cells/kg at the end of culture, which typically takes 12 days, measured using recorded data about the combinations of the following metrics at the end of the manufacturing process:
- Identity and quantity: immunophenotyping, cell counting, viability
- Purity: immunophenotyping
- Sterility: USP<71>, blood culture system
- Safety: replication-competent lentivirus (RCL), vector copy number (VCN), mycoplasma, endotoxin
- Potency: CAR expression, cytotoxicity towards target tumor cells, cytokine production
2. Incidence and severity of adverse events and dose-limiting toxicity (DLT) measured using physical and neurologic examination and routine labs at baseline, days 1–8 (daily), day 14, day 21, and 1, 3, 6, and 12 months post-infusion. The National Cancer Institute Common Terminology Criteria for Adverse Events version 5.0 and ASTCT Consensus Grading for Cytokine Release Syndrome and Neurologic Toxicity Associated with Immune Effector Cells 2019 will be applied.

Secondary outcome measures
1. Complete response (CR) rate measured using data recorded in medical records at 1, 3, and 6 months post-infusion
For B-cell lymphoma, the Lugano response criteria for non-Hodgkin lymphoma will be used. CR is defined as the complete disappearance of all detectable clinical evidence of disease, and disease-related symptoms if present prior to the therapy. For B-acute lymphoblastic leukemia (B-ALL), the criteria are based upon the NCCN guidelines version 4.2023 acute lymphoblastic leukemia. Definition of CR is as follows:
- No circulating lymphoblasts or extramedullary disease: no lymphadenopathy, splenomegaly, skin/gum infiltration, testicular mass, CNS involvement
- Trilineage hematopoiesis (TLH) and < 5% blasts
- Absolute neutrophil count (ANC) ≥ 1000/μL
- Platelets ≥100,000/μL
2. MRD status measured using flow cytometry for B-ALL MRD at 1 month post-infusion. Not available for lymphoma.
3. Overall and event-free survival measured using the definition from the National Cancer Institute (NCI) at 1 year
- Overall survival (OS) is the length of time from either the date of diagnosis or the start of treatment for a disease, such as cancer, that patients diagnosed with the disease are still alive.
- Relapse-free survival (RFS) is the length of time after primary treatment for a cancer ends that the patient survives without any signs or symptoms of that cancer.
4. Amount of SiCF-019 in blood measured using antigen-based detection by flow cytometry at days 0, 7, 14, 21 and 1, 3, 6, and 12 months post-infusion

Overall study start date
02/08/2019

Completion date
30/11/2025

Eligibility

Key inclusion criteria
1. Adult patients with CD19-positive recurrent and refractory B cell malignancies, aged 18-70 years old
2. Karnofsky Performance Status (KPS) score ≥60, expected survival ≥3 months
3. Platelet count (PLT) ≥30 × 10^9/L
4. Lymphocyte count (LYM) ≥0.15 × 10^9/L
5. Serum alanine aminotransferase (ALT) ≤100 U/mL
6. Total bilirubin (T-BIL) ≤30 μmol/L
7. Creatinine ≤200 μmol/L
8. Women of childbearing age are negative for the urine pregnancy test before the start of dosing and agree to take effective contraceptive measures
9. Voluntary participation, good compliance: willing to take part in studies and cooperate with clinical observations and follow-up plan

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
70 Years

Sex
Both

Target number of participants
20

Key exclusion criteria
1. Clinically diagnosed as central nervous system leukemia
2. Patients with hyperleukocytosis (WBC ≥50 × 10^9/L), or the researcher judges that the patient cannot receive a complete treatment cycle due to his rapid disease progress
3. Patients with fungi, bacteria, viruses or other uncontrolled infections or requiring isolation
4. Patients with positive HIV, HBV, and HCV
5. Patients with central nervous system diseases such as stroke, epilepsy, dementia or autoimmune neurological disorders
6. Patients with myocardial infection, cardiac angiography or stent, active angina or other obvious clinical symptoms, or with cardiac asthma or cardiovascular lymphocytic infiltration within 12 months prior to enrollment
7. Patients who are receiving anticoagulant therapy or who have severe coagulation disorders (aPTT >70)
8. Patients who receive medication that may affect the safety and efficacy of CAR-T cell product
9. Patients with a history of allergies to the biologics used in this project
10. Pregnant or lactating women
11. Patients who use systemic steroids within 2 weeks prior to treatment (except for inhaled steroids)
12. Patients with other uncontrolled diseases who are considered to be unsuitable to anticipate

in the research by researchers
13. Any conditions that researchers believe may increase the risk to patient safety or may interfere with the overall outcome

Date of first enrolment
01/02/2023

Date of final enrolment
30/08/2025

Locations

Countries of recruitment
Thailand

Study participating centre
Mahidol University
Faculty of Medicine Siriraj Hospital
2 Siriraj Hospital
Wanglang Road
Siriraj
Bangkoknoi
Bangkok
Thailand
10700

Sponsor information

Organisation
Siriraj Hospital

Sponsor details
Faculty of Medicine Siriraj Hospital, Mahidol University
2 Siriraj Hospital, Wanglang Road
Siriraj, Bangkoknoi
Bangkok
Thailand
10700
+66 (0)2419 4448-50
siiro@mahidol.ac.th

Sponsor type
Hospital/treatment centre

Website

http://www.si.mahidol.ac.th/en/

ROR
https://ror.org/0331zs648

Funder(s)

Funder type
Charity

Funder Name
Siriraj Foundation

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
Thailand

Results and Publications

Publication and dissemination plan
1. Peer-reviewed scientific journals
2. Internal report
3. Conference presentation

Intention to publish date
30/11/2026

Individual participant data (IPD) sharing plan
The datasets generated and/or analyzed during the current study during this study will be published as a supplement to the results publication

IPD sharing plan summary
Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		05/11/2024	13/11/2024	Yes	No