Clinical Trial Protocol
Iranian Registry of Clinical Trials

27 Oct 2026

Safety and feasibility of autologous cytokine induced killer (CIK) cells infusion as an adjuvant therapy in post resection hepatocellular carcinoma (HCC) patients

Protocol summary

Study aim

The primary objective of the study is to evaluate the safety of CIK cell infusion. Secondary objectives include assessment of feasibility, Recurrence-Free Survival, Overall Survival, and Cancer-Specific Survival.

Design

The study is designed as a prospective clinical trial involving CIK cell infusion.

Settings and conduct

The study will be conducted at the Liver Transplant Center of Imam Khomeini Hospital.

Participants/Inclusion and exclusion criteria

Inclusion Criteria: 1- Age between 18 and 80 years. 2- Patients with documented hepatocellular carcinoma at BCLC stage 0–A who have undergone surgical tumor resection. 3- Confirmation of cancer-free status one month after surgery. 4- Provision of written informed consent. 5- Laboratory eligibility criteria including: Leukocyte count > 3×10^9 cells/L. Absolute neutrophil count (ANC) ≥ 1000 cells/μL. Hemoglobin ≥ 8.5 g/dL. Platelet count > 50×10^9/L. Blood urea nitrogen (BUN) and serum creatinine ≤ 1.5 × upper limit of normal. Exclusion Criteria: 1-Presence of active infection or uncontrolled viremia 2- Receipt of any cell therapy or immunotherapy within the past six months, or participation in another clinical study. 3- Presence of another malignancy (previous or concurrent) with a different primary site or histological characteristics from HCC. 4- History of clinically significant cardiovascular disease 5- History of organ transplantation. 6- Primary or secondary immunodeficiency, or presence of active autoimmune disease. 7- Severe allergic disorders or history of anaphylactic reactions. 8- Pregnancy or breastfeeding at the time of study entry. 9- Women who intend to become pregnant.

Intervention groups

Eligible patients will receive adjuvant autologous CIK cells following tumor resection.

Main outcome variables

The primary outcome is the evaluation of the safety of autologous CIK cell infusion.

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20201229049871N1**
Registration date: **2026-05-30, 1405/03/09**
Registration timing: **prospective**

Last update: **2026-05-30, 1405/03/09**
Update count: **0**

Registration date

2026-05-30, 1405/03/09

Registrant information

Name

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Name of organization / entity

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Iran (Islamic Republic of)

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Recruitment status

recruiting

Funding source

Expected recruitment start date

2026-07-23, 1405/05/01

Expected recruitment end date

2028-07-22, 1407/05/01

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

Safety and feasibility of autologous cytokine induced killer (CIK) cells infusion as an adjuvant therapy in post resection hepatocellular carcinoma (HCC) patients

Public title

Safety and feasibility of autologous cytokine-induced killer (CIK) cell injection as adjuvant therapy in hepatocellular carcinoma

Purpose

Treatment

Inclusion/Exclusion criteria

Inclusion criteria:

Age between 18-80 Patients with Documented HCC in BCLC stage 0-A who have undergone surgical resection of the tumor. • Single or ≤ 3 nodules ≤ 3cm. • Liver function level according to Child Pugh Score A-B. • Patient performance level according to ECOG criteria 0-1 Establishment of Cancer free state one month after surgery Obtaining of Informed Consent Leukocyte count is bigger than (3 billion cells/L) Absolute Neutrophil Count (ANC) is bigger than or equal to 1,000/µL Hemoglobin is bigger than or equal to 8.5 g/dL Thrombocyte count is bigger than (50 billion cells/L) BUN and serum Creatinine is less than or equal to 1.5 multiply normal upper-limit

Exclusion criteria:

Receiving any cellular or immunotherapy treatment in the past six months or participation in another study Concomitant (previous or concurrent) that differs from HCC in primary site or histological features. History of clinically significant cardiovascular disease (such as heart failure, serious arrhythmias, or symptomatic coronary artery disease) History of organ trnasplant Primary or secondary immunodeficiency, or active autoimmune diseases Having a severe allergic disorder or a history of anaphylactic reaction Presence of active infection or uncontrolled viremia (especially HBV, HCV, or HIV) Pregnancy or breastfeeding at the time of study entry Women of childbearing age who are planning to become pregnant

Age

From **18 years** old to **80 years** old

Gender

Both

Phase

1

Groups that have been masked

No information

Sample size

Target sample size: **6**

Randomization (investigator's opinion)

N/A

Randomization description

Blinding (investigator's opinion)

Not blinded

Blinding description

Placebo

Not used

Assignment

Single

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Research Ethics Committee of Royan Research Institute

Street address

3th Floor, Block A, Ministry of Health and Medical Education Headquarters, Simaye Iran Street, between South Falamak and Zarafshan, Shahrak-e Gharb

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Tehran

Province

Tehran

Postal code

4364 - 14155

Approval date

2026-02-17, 1404/11/28

Ethics committee reference number

IR.ACECR.ROYAN.REC.1404.049

Health conditions studied

1

Description of health condition studied

Hepatocellular Carcinoma

ICD-10 code

C22.0

ICD-10 code description

Liver cell carcinoma

Primary outcomes

1

Description

Safety: Safety is defined as the frequency, type, severity, and suspected relatedness of adverse events associated with intravenous infusion of autologous CIK cells. All adverse events (AEs) and serious adverse events (SAEs) will be recorded from the time of the first infusion until the end of the follow-up period and will be graded according to the Common Terminology Criteria for Adverse Events (CTCAE), version 5.0.

Timepoint

Safety assessment and determination of possible adverse events (systemic, local, short-term, and serious) after intravenous injection of autologous cytokine-induced killer cells (CIK) will be performed at weeks 1, 2,

3, 4, 5, 6, 7, 8, 9, and 10, and at months 3 and 6 after injection.

Method of measurement

Safety assessment and determination of possible adverse events will be performed by taking history and examination according to the Common Terminology Criteria for Adverse Events (CTCAE) v5.

Secondary outcomes

1

Description

Recurrence-Free Survival (RFS): Defined as the time interval from the date of study enrollment to the occurrence of the first tumor recurrence (intrahepatic or extrahepatic) or death from any cause, whichever occurs first.

Timepoint

Recurrence-Free Survival (RFS) will be assessed during a 6-month follow-up period according to the study schedule, which includes regular clinical evaluations and imaging every 3 months. Time to recurrence or death will be measured from the date of study enrollment.

Method of measurement

Recurrence will be determined based on standard imaging findings (MRI and CT scan) and clinical assessment, and the date of the event will be recorded.

2

Description

Overall Survival (OS): Defined as the time interval from the date of study enrollment to the date of death from any cause.

Timepoint

Overall survival will be assessed at study enrollment and subsequently during regular follow-up according to the study schedule until the end of the follow-up period. Survival status will be recorded at each visit (weeks 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10, and months 3 and 6 after infusion).

Method of measurement

Survival status will be documented through clinical follow-up, review of medical records, and telephone contact if necessary.

3

Description

Cancer-Free Survival (CFS): Defined as the time interval from the date of study enrollment to the first occurrence of cancer recurrence (intrahepatic or extrahepatic) or death from any cause, whichever occurs first.

Timepoint

At study enrollment (baseline) and subsequently during regular follow-up according to the study schedule until the end of the follow-up period; recurrence or reappearance of cancer will be assessed and recorded at each follow-up visit (weeks 1 through 10 after treatment initiation, and then at months 3 and 6) through clinical evaluation and periodic imaging at 3 months interval.

Method of measurement

Recurrence will be determined based on standard imaging findings (MRI or CT scan) and clinical assessment, and the date of the event will be recorded.

Intervention groups

1

Description

Intervention group: In this study, patients with hepatocellular carcinoma (HCC) who have undergone successful surgical resection of the liver tumor will receive adjuvant therapy with autologous cytokine-induced killer (CIK) cells in addition to standard postoperative care.For cell preparation, patients mononuclear cells will be used. Peripheral blood mononuclear cells (PBMCs) are cultured under sterile, Good Manufacturing Practice (GMP) conditions and activated with interferon-gamma (IFN-γ), anti-CD3 antibody, and interleukin-2 (IL-2) for approximately 2–3 weeks to generate the effective CIK cell population. After completing culture, the final product undergoes quality control tests for sterility, cell viability, and phenotype. Only products meeting predefined quality criteria will be used for infusion.The CIK cells will be administered through six intravenous infusions — the first three given weekly and the subsequent three every two weeks. Before each infusion, the patient’s clinical condition and basic safety laboratory results (CBC and liver enzymes) will be reviewed. All infusions will be performed in a clinical setting under supervision of the research team, and patients will be monitored for any adverse events or infusion-related reactions.The objective of this intervention is to evaluate the safety, feasibility, and potential efficacy of adjuvant CIK therapy in reducing disease recurrence following tumor resection in HCC patients.

Category

Treatment - Other

Recruitment centers

1

Recruitment center

Name of recruitment center

Liver transplant and surgery research center, Imam Khomeini Hospital, Tehran University of Medical S

Full name of responsible person

Dr. Mohsen Nassiri-Toosi

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Sponsors / Funding sources

1

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Grant name
Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
Yes
Title of funding source
Royan Institute
Proportion provided by this source
10
Public or private sector
Public
Domestic or foreign origin
Domestic
Category of foreign source of funding
empty
Country of origin
Type of organization providing the funding
Academic

2

Sponsor
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Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
Yes
Title of funding source
Bahar Tashkhis Teb
Proportion provided by this source
45
Public or private sector
Private
Domestic or foreign origin
Domestic
Category of foreign source of funding
empty
Country of origin
Type of organization providing the funding
Other

3

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Grant name
Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
Yes
Title of funding source
Kian Immune Cell
Proportion provided by this source
45
Public or private sector
Private
Domestic or foreign origin
Domestic
Category of foreign source of funding
empty
Country of origin
Type of organization providing the funding
Other

Person responsible for general inquiries

Contact
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Royan Institute
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Sharing plan

Deidentified Individual Participant Data Set (IPD)
Undecided - It is not yet known if there will be a plan to make this available
Study Protocol
Undecided - It is not yet known if there will be a plan to make this available
Statistical Analysis Plan
Undecided - It is not yet known if there will be a plan to make this available
Informed Consent Form
Undecided - It is not yet known if there will be a plan to make this available
Clinical Study Report
Undecided - It is not yet known if there will be a plan to make this available
Analytic Code
Undecided - It is not yet known if there will be a plan to make this available
Data Dictionary
Undecided - It is not yet known if there will be a plan to make this available