

Clinical Trial Protocol

Iranian Registry of Clinical Trials

29 Jul 2026

: The Safety Evaluation of Ex vivo Activated Haploidentical Natural Killer Cells (NK) in patients with Recurrent Glioblastoma Multiform and resistant/recurrent malignant brain tumor (Clinical Trial Phase I)

Protocol summary

Study aim

The Safety Evaluation of Ex vivo Activated Natural Killer Cells (NK) for tumor-targeting inpatient with Recurrent Glioblastoma Multiform and resistant/recurrent malignant brain tumor

Design

Five patients with recurrent glioblastoma or malignant brain tumor and one haploidentical donor for each patient will be selected by a clinical trial team and will enter the Phase 1 single-group clinical trial study.

Settings and conduct

Workplace: Royan Institute Study process: 1- Blood sampling and isolation of mononuclear cells (from sick patients) 2- Isolation of CD56 + cells 3- Activation of cells by IL-15 4- Assessment of lethality and surface marker of NK cells 5- Evaluation of sterility tests in activated cells 6- Preparing patients 7- Cell injection into the tumor cavity before radiotherapy or chemotherapy 8- Safety analysis of the method after injection

Participants/Inclusion and exclusion criteria

Inclusion criteria: patients with recurrent Glioblastoma Multiform (GBM) or brain tumor, being at the age of 3-65 Year, both sexes, Lansky/karnofsky performance statue of 70-100%, Life span expectation > 6 months. Non-inclusion criteria: Patients whose MRI or MRS view of the brain is in favor of radionecrosis, the patient can't tolerate the new treatment due to emergency conditions, Insufficient number of NK cells produced for treatment, appearance new neurological ulcers after the first injection

Intervention groups

Intervention process: 1- selection of 5 patients and their haploidentical donor; 2- peripheral blood collection, isolation of the CD56+ cells and cell activation with IL-15; 3- Doing control quality tests before cell injection; 4-Injection in the tumor cavity or CSF.

Main outcome variables

Fever, hysteria, new neurological symptoms, tumor size

General information

Reason for update

Because we realized at the beginning of the study that adult patients could also be included in the study and that the cell could be injected into the cerebrospinal fluid. According to studies to activate killer cells, only interleukin-15 could be examined.

Acronym

IRCT registration information

IRCT registration number: **IRCT20170122032121N5**

Registration date: **2020-06-11, 1399/03/22**

Registration timing: **prospective**

Last update: **2021-06-21, 1400/03/31**

Update count: **1**

Registration date

2020-06-11, 1399/03/22

Registrant information

Name

Marzieh Ebrahimi

Name of organization / entity

Royan Institute

Country

Iran (Islamic Republic of)

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Email address

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2020-07-10, 1399/04/20

Expected recruitment end date

2021-07-23, 1400/05/01

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

: The Safety Evaluation of Ex vivo Activated Haploidentical Natural Killer Cells (NK) in patients with Recurrent Glioblastoma Multiform and resistant/recurrent malignant brain tumor (Clinical Trial Phase I)

Public title

Nk cell therapy for recurrent GBM (Glioblastoma Multiform)

Purpose

Treatment

Inclusion/Exclusion criteria**Inclusion criteria:**

Age: 3-65 Year Sex: Both Lansky/Karnofsky performance statue: 7-100% Life span expectation: >6 months Hemoglobin: > 10.0 g/dL AGC > 1,500/mm³ Platelet count > 100,000/mm³ Serum total bilirubin < 1.5 times upper limit of normal(ULN) ALT and AST < 2.5 times ULN Serum creatinine < 1.5 times ULN

Exclusion criteria:

Patients whose MRI or MRS view of the brain is in favor of radio necrosis Due to emergency conditions, the patient can not tolerate the new treatment Insufficient number of NK cells produced for treatment appearance new neurological ulcers after the first injection (after the wound heals, subsequent injections will be given if the patient is in good condition) diagnosis of any other invasive cancer within the past 5 years. Closing the reservare for the next injection (if this problem is solved, the injections will be done again. concurrent serious medical or psychiatric illness that may interfere with giving informed consent or conducting this study

Age

From **3 years** old to **65 years** old

Gender

Both

Phase

1

Groups that have been masked

No information

Sample size

Target sample size: **5**

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**

Ethics committee of the Royan Institute

Street address

Royan institute, Royan alley, Banihashem street, Resalat highway

City

Tehran

Province

Tehran

Postal code

1665659911

Approval date

2020-02-29, 1398/12/10

Ethics committee reference number

IR.ACECR.ROYAN.REC.1398.261

2**Ethics committee****Name of ethics committee**

Ethics committee of the Royan Institute

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Approval date

2021-02-17, 1399/11/29

Ethics committee reference number

IR.ACECR.ROYAN.REC.1398.261

Health conditions studied**1****Description of health condition studied**

Recurrent Glioblastoma Multiform(GBM) and resistant/recurrent malignant brain tumor

ICD-10 code

C71.9

ICD-10 code description

Malignant neoplasm of brain, unspecified

Primary outcomes**1****Description**

fever

Timepoint

After cell injection, every 2 hours up to 48 hours after cell injection

Method of measurement

Fever meter

2

Description

hysteria

Timepoint

After cell injection, control the symptom up to 48 hours.

Method of measurement

Patient checkup

3

Description

New neurological symptoms which not related to the tumor

Timepoint

Up to 48 hours after surgery, up to one week after cell injection

Method of measurement

Physical examination and recording of symptoms

Secondary outcomes

1

Description

Tumor size

Timepoint

One week after injection, every 2 weeks up to 3 months

Method of measurement

MRI and MRS

2

Description

patient's survival

Timepoint

Every month up to 6 months

Method of measurement

Communicate with patients

Intervention groups

1

Description

Intervention group: 5 patients with recurrent glioblastoma and resistant/recurrent malignant brain tumor are included in the study according to the inclusion criteria. The peripheral blood of one parent is obtained with his/her consent. Then the NK cells are isolated and activated by the cliniMACS device. Microbial tests and cell quality control are performed. 7 days after surgery, MRI is ordered then, two million cells per 0.5 cc (cell count is variable depend on tumor size) are injected into the tumor cavity or CSF removed by surgery via a reservoir which fixes in the patient's cranium. This

injection is given again in the second and third weeks after the surgery with an increasing trend in the number of cells and before the start of radiotherapy. With the diagnosis of the physician, the number of injections can be increased.

Category

Treatment - Other

Recruitment centers

1

Recruitment center

Name of recruitment center

Children's Medical Center and Imam Khomeini Hospital

Full name of responsible person

Dr.Marzieh Ebrahimi

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity

Iranian academic center for education culture and research

Full name of responsible person

Dr. Parvaneh Afsharian

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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

Iranian academic center for education culture and research

Proportion provided by this source

25

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**

Other

2**Sponsor****Name of organization / entity**

Parsian Lotus Investment Bank

Full name of responsible person

Mojtaba jahangiri

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Web page address**Grant name****Grant code / Reference number****Is the source of funding the same sponsor organization/entity?**

Yes

Title of funding source

Parsian Lotus Investment Bank

Proportion provided by this source

75

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****Name of organization / entity**

Iranian academic center for education culture and

research

Full name of responsible person

Niloufar Shayan Asl

Position

Research assistant

Latest degree

Master

Other areas of specialty/work

Others

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Full name of responsible person

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Position

Associated professor

Latest degree

Ph.D.

Other areas of specialty/work

Immunology

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Person responsible for updating data**Contact****Name of organization / entity**

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Latest degree

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Other areas of specialty/work

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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

Yes - There is a plan to make this available

Statistical Analysis Plan

Yes - There is a plan to make this available

Informed Consent Form

Yes - There is a plan to make this available

Clinical Study Report

Yes - There is a plan to make this available

Analytic Code

Yes - There is a plan to make this available

Data Dictionary

Yes - There is a plan to make this available

Title and more details about the data/document

The research results with the publication of the article
will be provided to researchers.

When the data will become available and for how long

-

To whom data/document is available

-

Under which criteria data/document could be used

-

From where data/document is obtainable

-

What processes are involved for a request to access data/document

-

Comments

-