Clinical Trial Protocol
Iranian Registry of Clinical Trials

18 Sep 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

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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
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Province
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Approval date
2020-02-29, 1398/12/10
Ethics committee reference number
IR.ACECR.ROYAN.REC.1398.261

2

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Postal code
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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 reservare 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
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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
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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No.99, Mehran dead end alley, Sheikh Bahaei street, Mollasadra street, Tehran
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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

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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
-