Clinical Trial Protocol
Iranian Registry of Clinical Trials

16 Sep 2026

Efficacy of the intrathecal injection of activated allogeneic natural killer cells in patients with High-grade gliomas; A multi-center phase II clinical trial

Protocol summary

Study aim
Evaluation of efficacy of intrathecal injection of activated allogenic NK cells in patients with high grade glioma

Design
Phase II clinical trial, controlled, randomized, non-blinded

Settings and conduct
Eligible patients will be allocated randomly in two stratum (adults and pediatrics) into intervention and control group in ratio of 3 to 1 and then they will receive NK cells intrathecally in 3 times in one of the recruiting hospitals.

Participants/Inclusion and exclusion criteria
New diagnosed patients with grade 3 or 4 brain tumor, which are included in the one of the following conditions: Astrocytoma IDH-mutant, Oligodendroglioma IDH-mutant, Glioblastoma IDH-wild type, Diffuse midline glioma, Diffuse hemispheric glioma, Diffuse pediatric-type high-grade glioma IDH-wild type Age range of 3 to 60 years old both sex Lansky/Karnofsky performance score above 60 Obtained informed consent of patients or parents or legal attendance in cases of pediatrics Hemoglobin above 10 gr/dL of blood AGC above 500 per microliter of blood Platelet count above 50000 per microliter of blood INR below 2 and PTT less than 1.5 times of maximum normal value Plasma bilirubin level less than 1.5 times of maximum normal value Plasma hepatic transaminases (ALT and AST) level less than 3 times of maximum normal value Plasma creatinine level less than 1.5 times of maximum normal value

Intervention groups
Intervention group: Patients will receive 200 millions NK cells via intrathecal injection for 3 times. Injection will be administered in period between radiotherapy to chemotherapy or in periods between chemotherapy courses. Control group: Patients in control group will receive no cell and just conventional treatments will be administered for them.

Main outcome variables
Efficacy

General information

Reason for update

Acronym

IRCT registration information
IRCT registration number: **IRCT20170122032121N7**
Registration date: **2023-07-22, 1402/04/31**
Registration timing: **registered_while_recruiting**

Last update: **2023-07-22, 1402/04/31**
Update count: **0**

Registration date
2023-07-22, 1402/04/31

Registrant information

Name
Marzieh Ebrahimi

Name of organization / entity
Royan Institute

Country
Iran (Islamic Republic of)

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+98 23562516

Email address
mebrahimi@royaninstitute.org

Recruitment status
Recruitment complete

Funding source

Expected recruitment start date
2023-06-22, 1402/04/01

Expected recruitment end date
2024-06-21, 1403/04/01

Actual recruitment start date
empty

Actual recruitment end date
empty
Trial completion date
empty

Scientific title
Efficacy of the intrathecal injection of activated allogeneic natural killer cells in patients with High-grade gliomas; A multi-center phase II clinical trial

Public title
Efficacy of allogenic NK cells IT injection in patients with high grade brain glioma
Purpose
Treatment
Inclusion/Exclusion criteria
Inclusion criteria:
New diagnosed patients with grade 3 or 4 brain tumor, based on WHO classification, which are included in the one of the following conditions: • Astrocytoma, IDH-mutant • Oligodendroglioma, IDH-mutant • Glioblastoma, IDH-wild type • Diffuse midline glioma • Diffuse hemispheric glioma • Diffuse pediatric-type high-grade glioma, IDH-wild type Age range of 3 to 60 years old both sex Lansky/Karnofsky performance score above 60 Obtained informed consent of patients or parents or legal attendance in cases of pediatrics Hemoglobin above 10 gr/dL of blood Absolute granulocyte count (AGC) above 500 per microliter of blood Platelet count above 50000 per microliter of blood INR below 2 and PTT less than 1.5 times of maximum normal value Plasma bilirubin level less than 1.5 times of maximum normal value Plasma hepatic transaminases (ALT and AST) level less than 3 times of maximum normal value Plasma creatinine level less than 1.5 times of maximum normal value
Exclusion criteria:
Evidence of radio necrosis in MRI or MRS Intolerance of new treatment due to emergency condition History of other malignancies History of any immunodeficiency diseases or any immune compromising conditions Rupture of cerebral shunt or unable to perform a lumbar puncture Pregnancy History of uncontrolled chronic diseases such as: Diabetes, CHF, liver cirrhosis, CKD, etc.
Age
From **3 years** old to **60 years** old
Gender
Both

Phase
2
Groups that have been masked
No information
Sample size
Target sample size: **40**
Randomization (investigator's opinion)
Randomized
Randomization description
In this trial, patients will be stratified in 2 level: first level patient under 18 y/o and second level above 18 y/o. For random allocation in each stratum, permuted-block randomization method will be used. Ratio of patients in intervention group to patients in control group would be 3 to 1 and for randomization 5 foursome blocks in each stratum would be selected. Each block contains one patient in control group and 3 patients in intervention group. Required blocks will be designed and randomly selected using Sealed Envelope software and the patients would be placed in houses of each block in order of date of recruitment.
Blinding (investigator's opinion)
Not blinded
Blinding description
Placebo
Not used
Assignment
Parallel
Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee
Name of ethics committee
Royan institute ethics committee
Street address
Royan ethics committee, Royan alley, Hafez street, Banihashem square, Banihashem street, Resalat highway, Tehran, Iran
City
Tehran
Province
Tehran
Postal code
1665659911
Approval date
2023-02-28, 1401/12/09
Ethics committee reference number
IR.ACECR.ROYAN.REC.1402.001

Health conditions studied

1

Description of health condition studied
High grade brain glioma
ICD-10 code
C71
ICD-10 code description
Malignant neoplasm of brain

Primary outcomes

1

Description
Response rate comparison between control and intervention groups
Timepoint
1 to 2 weeks after last injection with the follow up of 3, 6, and 12 months after last injection

Method of measurement
Using iRANO (Immunotherapy Response Assessment in Neuro-Oncology) checklist and using MRI and MRS

Secondary outcomes

1

Description
Safety
Timepoint
After each injection to next injection and 2 weeks after last injection
Method of measurement
Using CTCAEs (Common Terminology Criteria for Adverse Events) checklist

2

Description
Overall survival and progression-free survival
Timepoint
After the end of the study
Method of measurement
using Kaplan-Meier method

3

Description
Analysis of CSF including: hematology, biochemistry, culture, cytokine level and immunophenotype of cells
Timepoint
Before each injection, CSF sample will be taken from patients for analysis
Method of measurement
using microscope and slides, spectrophotometer, enzyme assay, ELISA and Flowcytometry

Intervention groups

1

Description
Intervention group: Patients in intervention group will receive 200 millions NK cells via intrathecal injection (LP or resorvor) for 3 times. In cases who have ongoing surgery or have been operated recently and have been planned for radiotherapy after surgery, if the patient condition would be suitable for IT injection, the first injection will be administered one or two weeks after the end of radiotherapy. The other doses would be injected in the period between courses of chemotherapy (one week after the end of last chemotherapy course). In cases who have passed surgery and radiotherapy and in the cases who are not eligible for surgery and radiotherapy (such as diffuse midline glioma cases) all three injections will be administered in the period between chemotherapy courses. CSF will be taken before each injection for intended assessments. The therapist physicians would be suggested to not prescribe corticosteroids or prescribe low dose of them from 3 days before to one week after NK cell injection to avoid their suppressing effects on NK cells. But this is not mandatory because of the risk of brain edema. Also therapist physicians would be suggested to prescribe immune checkpoint inhibitors if there is indication (PD-L1 expression or MSI) for prescription to intensify the cytotoxic effect of NK cells.
Category
Treatment - Other

2

Description
Control group: patients in control group will not receive any cells and just conventional treatments (surgery, radiotherapy and chemotherapy) will be ordered for them. Because of the risk of the adverse events, IT injection of the placebo will not be done for patients in control group. But if the study results 6 months after last injection of last patient would reveal that there is significant superiority in the intervention group, patients in the control group can be benefited with NK cell therapy for free. Patients in control group will be Followed-up till one year after recruitment for comparison with intervention group.
Category
Other

Recruitment centers

1

Recruitment center
Name of recruitment center
Rasoul Akram hospital
Full name of responsible person
Dr. Mohammad Faranoush
Street address
Pediatric oncology ward, floor 4, Rasoul Akram hospital, Niayesh street, Shahr Ara street, Sattar Khan vicinity, Tehran, Iran
City
Tehran
Province
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Postal code
1445613131
Phone
+98 21 6652 5328
Email
faranoush47@gmail.com

2

Recruitment center
Name of recruitment center
Children's medical center hospital
Full name of responsible person
Dr. Zohreh Habibi
Street address
Children’s Medical Center, No 63, Gharib Ave, Keshavarz Blv, and Tehran, Iran
City

تهران
Province
Tehran
Postal code
1419733151
Phone
+98 21 6692 9234
Email
mahdizadehmd@yahoo.com

3

Recruitment center
Name of recruitment center
Loghman e Hakim hospital
Full name of responsible person
Dr. Guive Sharifi
Street address
Loghman e Hakim hospital - Makhsoos street, Lashgar crossroad, Tehran
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Tehran
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Tehran
Postal code
1333635445
Phone
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Email
gsharifi@gmail.com

Sponsors / Funding sources

1

Sponsor
Name of organization / entity
Kian immune cell company
Full name of responsible person
Hassan Salehi Moghadam
Street address
Kian immune cell company, first floor, Royan RITAC center, Number 6, Keshvari alley, Banihashem square, Banihashem street, Resalat highway, Tehran, Iran
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tehran
Province
Tehran
Postal code
1665813339
Phone
+98 21 2233 8248
Email
kiacell.immune@gmail.com
Web page address
https://kiacell-immune.com
Grant name
Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
Yes
Title of funding source
Kian immune cell company
Proportion provided by this source
90
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

2

Sponsor
Name of organization / entity
Royan institute
Full name of responsible person
Marzieh Ebrahimi
Street address
Royan institute, Hafez street, Banihashem square, Banihashem street, Resalat highway, Tehran, Iran
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Postal code
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Phone
+98 21 2356 2000
Email
marzieh.ebrahimi@gmail.com
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

Person responsible for general inquiries

Contact
Name of organization / entity
Royan institute & Kian immune cell company
Full name of responsible person
Hamid Mahdizadeh
Position
Research assistant

Latest degree
Medical doctor
Other areas of specialty/work
Immunology
Street address
Kian immune cell company, first floor, Royan RITAC center, Number 6, Keshvari alley, Banihashem square, Banihashem street, Resalat highway, Tehran, Iran
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Tehran
Postal code
1665813339
Phone
+98 21 2233 8248
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Person responsible for scientific inquiries

Contact
Name of organization / entity
Royan institute & Kian immune cell company
Full name of responsible person
Hamid Mahdizadeh
Position
Research asisstant
Latest degree
Medical doctor
Other areas of specialty/work
Immunology
Street address
Kian immune cell company, first floor, Royan RITAC center, Number 6, Keshvari alley, Banihashem square, Banihashem street, Resalat highway, Tehran, Iran
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Postal code
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Email
mahdizadehmd@yahoo.com

Person responsible for updating data

Contact
Name of organization / entity
Royan institute & Kian immune cell company
Full name of responsible person
Hamid Mahdizadeh
Position
Research assistant
Latest degree
Medical doctor
Other areas of specialty/work
Immunology
Street address
Kian immune cell company, first floor, Royan RITAC center, Number 6, Keshvari alley, Banihashem square, Banihashem street, Resalat highway, Tehran, Iran
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Email
mahdizadehmd@yahoo.com

Sharing plan

Deidentified Individual Participant Data Set (IPD)
Yes - There is 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
Undecided - It is not yet known if there will be a plan to make this available
Data Dictionary
Not applicable
Title and more details about the data/document
After concealment of personal information of participants, data of eligibility, CRFs and measured outcomes can be shared in case of request
When the data will become available and for how long
After publishing results in a scientific journal with no deadline
To whom data/document is available
Just to academic PIs
Under which criteria data/document could be used
Any usage of data should be consulted and approved by the PIs
From where data/document is obtainable
Applicant should send an e-mail to Dr.Mahdizadeh and propose their detailed requirements of the study data
What processes are involved for a request to access data/document
After sending an e-mail to Dr.Mahdizadeh, he will assess the authenticity of the applicant in almost 2 weeks. Then he will plan a meeting (visual or attendance) for the applicant with Dr.Ebrahimi in next month. The applicant can obtain approval of data sharing in this meeting and the data will be sent in next 14 days
Comments