

# Clinical Trial Protocol

## Iranian Registry of Clinical Trials

01 Mar 2021

### Evaluation of the effectiveness of intrathecal injection of allogeneic umbilical cord derived mesenchymal stem cells in the phenotypic changes of Spinal Muscular Atrophy type I, II and III in comparison with control group, A Clinical trial phase I, II

#### Protocol summary

##### Study aim

Evaluation of the efficacy of intrathecal injection of umbilical cord derived mesenchymal stem cells in the phenotypic changes of SMA I, II and III

##### Design

Randomized double blind clinical trial phase 1-2 with control group .60 confirmed SMA patients ( 20 cases from each type) recruited in this study , After explanation about side effects and its probable effectiveness and taking of parent's informed consent, each type of disease will be divided accidentally in two group of 10 patients of intervention or control .

##### Settings and conduct

Clinical exams and baseline electrodiagnostic tests were done. Patients will be admitted in Children's Medical Center and after injection will be monitored for 24 hours. After taking of 2 ml fluid, cellular suspension will be injected. With simulation of intrathecal injection in control group, patients and clinical evaluators will not be aware about two groups. Clinical evaluations and electrodiagnostic tests will be continued for a year.

##### Participants/Inclusion and exclusion criteria

inclusion criteria :Genetically confirmed SMA patients and its type, Minimum age of 6 months and maximum age of 16 years, Ventilator independent, Absence of other organs disorders Exclusion criteria : Age under 6 months and over 16 years, Ventilator dependent at the beginning of intervention, Serious diseases of other organs

##### Intervention groups

In the intervention group 3 sessions of intrathecal injection of 20 millions mesenchymal cells will be done every 2 weeks. In the control group 3 sessions of intrathecal injection simulation without any injection will be done every 2 weeks.

##### Main outcome variables

Evaluation of effectiveness of mesenchymal stem cells in life expectancy and probable muscle strength of SMA type 1 .Evaluation of effectiveness of mesenchymal stem cells in muscle strength of SMA type 2 and 3.

#### General information

##### Reason for update

##### Acronym

MSCSMA

##### IRCT registration information

IRCT registration number: **IRCT20110628006907N15**

Registration date: **2020-03-17, 1398/12/27**

Registration timing: **prospective**

Last update: **2020-03-17, 1398/12/27**

Update count: **0**

##### Registration date

2020-03-17, 1398/12/27

##### Registrant information

##### Name

Mahmoudreza Ashrafi

##### Name of organization / entity

##### Country

Iran (Islamic Republic of)

##### Phone

+98 21 6612 9252

##### Email address

ashrafim@tums.ac.ir

##### Recruitment status

**recruiting**

##### Funding source

##### Expected recruitment start date

2020-04-20, 1399/02/01

**Expected recruitment end date**

2021-04-20, 1400/01/31

**Actual recruitment start date**

empty

**Actual recruitment end date**

empty

**Trial completion date**

empty

**Scientific title**

Evaluation of the effectiveness of intrathecal injection of allogeneic umbilical cord derived mesenchymal stem cells in the phenotypic changes of Spinal Muscular Atrophy type I, II and III in comparison with control group, A Clinical trial phase I, II

**Public title**

Effects of umbilical cord derived mesenchymal stem cells injection in the treatment of Spinal Muscular Atrophy (SMA)

**Purpose**

Treatment

**Inclusion/Exclusion criteria****Inclusion criteria:**

Genetically confirmed deletion of SMN1 gene for the diagnosis of SMA disease, SMN2 gene copy number count for the diagnostic classification of disease type, Minimum age of 6 months in type I, Ventilator independent patients at the beginning of treatment in type I, Maximum age of 16 years in type II and III, Ventilator independent patients in type II and III, Absence of brain damage, Absence of liver disease, Absence of renal disease, Absence of hematological disease, Informed consent of patients and their parents

**Exclusion criteria:**

Acquired brain damage including hypoxia, Structural and functional brain disorders, Acute infections such as( HCV, HIV,HBV), Malignancies, Hemorrhagic diathesis, Severe anemia ( Hb less than 8 gram/dl), Renal dysfunction, Hepatic dysfunction

**Age**

From **6 months** old to **16 years** old

**Gender**

Both

**Phase**

N/A

**Groups that have been masked**

- Participant
- Care provider
- Outcome assessor
- Data analyser

**Sample size**

Target sample size: **60**

**Randomization (investigator's opinion)**

Randomized

**Randomization description**

The patients are randomly allocated using a balanced block randomization technique, into two groups of intervention and control (30 cases of intervention with injection of umbilical cord derived Mesenchymal cells, 10 cases in each type of disease and 30 cases of control

group without injection, 10 cases in each type of disease) . Randomization will be done by using of blocks of 6 and 9. All subjects randomly allocated with online randomization software to generate random-number sequences. Coordinator of randomization and clinical evaluators will not be aware of patients of each group .

**Blinding (investigator's opinion)**

Double blinded

**Blinding description**

This study is double blind therefore, in the control group after insertion of the needle into the skin with an appearance simulating lumbar puncture, needle will be removed without any injection. This technique will be repeated three times every two weeks, similar to intervention groups. Patients and their parents and clinical evaluators will not be aware of this subject. At the end of the study if safety and effectiveness of cell therapy will be proved in the intervention groups, for the ethical consideration stem cell injections will be performed for control groups .

**Placebo**

Used

**Assignment**

Parallel

**Other design features**

First study about intrathecal cell therapy in SMA disease in comparison with control group in IRAN - First study about cell therapy by using of mesenchymal stem cells in SMA disease in IRAN

**Secondary Ids**

empty

**Ethics committees****1****Ethics committee****Name of ethics committee**

Tehran University of Medical Sciences

**Street address**

No 226, Central organization of Tehran University of Medical Sciences, Ghods Street, Keshavarz Blvd

**City**

Tehran

**Province**

Tehran

**Postal code**

1417653761

**Approval date**

2020-02-04, 1398/11/15

**Ethics committee reference number**

IR.TUMS.VCR.REC.1398.899

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

Spinal Muscular Atrophy Type 1-2 3

**ICD-10 code**

G12

## ICD-10 code description

Spinal muscular atrophy and related syndromes

## Primary outcomes

### 1

#### Description

Evaluation of effectiveness of umbilical cord derived mesenchymal stem cells in increasing life expectancy of SMA type 1

#### Timepoint

Before intervention and then every 2 months till 1 year

#### Method of measurement

Questionnaire and clinical exams

### 2

#### Description

Evaluation of effectiveness of umbilical cord derived mesenchymal stem cells in increasing muscle strength of SMA type 1

#### Timepoint

Before intervention and then every 2 months till 1 year

#### Method of measurement

Hammersmith Infant Neurological Examinations (HINE) ,Children's Hospital of Philadelphia Questionnaire (CHOP intent )

### 3

#### Description

Evaluation of effectiveness of umbilical cord derived mesenchymal stem cells in increasing muscle strength of SMA type 2

#### Timepoint

Before intervention and then every 4 months till 1 year

#### Method of measurement

Expanded Hammersmith Functional Motor Scale(HFMSE) WHO Motor Mile stones (WMM) questionnaire , Upper limb Module Scale (ULMS)

### 4

#### Description

Evaluation of effectiveness of umbilical cord derived mesenchymal stem cells in increasing muscle strength of SMA type 3

#### Timepoint

Before intervention and then every 4 months till 1 year

#### Method of measurement

Expanded Hammersmith Functional Motor Scale(HFMSE) WHO Motor Mile stones (WMM) questionnaire, Upper limb Module Scale (ULMS) questionnaire, 6 Minute Walk Test (6MWT)

## Secondary outcomes

### 1

#### Description

Improvement of Electrodiagnostic evaluative indexes of SMA patients

#### Timepoint

Before intervention , 2 months after last injection and then every 4 months till 1 year of first injection

#### Method of measurement

Motor unit number estimation (CMAP scan)

### 2

#### Description

Number of participants experiencing adverse effects and serious adverse effects

#### Timepoint

First 24 hours after injection and then any time if occurred

#### Method of measurement

Questionnaire , parents report and periodic planned clinical evaluations

## Intervention groups

### 1

#### Description

Intervention group 1: Type 1 SMA patients that will receive three intrathecal injections of mesenchymal stem cells derived from umbilical cord, prepared by Royan stem cell Technology Company and Cell Thec Pharmed company. Intrathecal injections will be done under anesthesia via lumbar puncture. After taking 2 milliliters of cerebrospinal fluid, 2 milliliters suspension that contains 20 million stem cells will be injected with a syringe. The patient will be admitted for one day of probable adverse reactions monitoring . One year followup and evaluations with regular and similar rehabilitative therapy will be done .

#### Category

Treatment - Drugs

### 2

#### Description

Intervention group 2 : Type 2 SMA patients that will receive three intrathecal injections of mesenchymal stem cells derived from umbilical cord, prepared by Royan stem cell Technology Company and Cell Thec Pharmed company. Intrathecal injections will be done under anesthesia via lumbar puncture. After taking 2 milliliters of cerebrospinal fluid, 2 milliliters suspension that contains 20 million stem cells will be injected with a syringe. The patient will be admitted for one day of probable adverse reactions monitoring . One year followup and evaluations with regular and similar rehabilitative therapy will be done .

#### Category

Treatment - Drugs

### 3

#### Description

Intervention group 3 : Type 3 SMA patients that will receive three intrathecal injections of mesenchymal stem

cells, derived from umbilical cord prepared by Royan stem cell Technology Company and Cell Thec Pharmed company. Intrathecal injections will be done under anesthesia via lumbar puncture. After taking 2 milliliters of cerebrospinal fluid, 2 milliliters suspension that contains 20 million stem cells will be injected with a syringe. The patient will be admitted for one day of probable adverse reactions monitoring . One year followup and evaluations with regular and similar rehabilitative therapy will be done .

**Category**

Treatment - Drugs

**4****Description**

Control group 1: Type 1 SMA patients that after insertion of needle into the skin, without entrance to cerebrospinal fluid space, needle will be removed without any injection . In this group only intrathecal injection will be simulated, without patients or their parents awareness . The patient will be admitted for one day of probable adverse reactions monitoring . One year followup and evaluations with regular and similar rehabilitative therapy will be done .

**Category**

Placebo

**5****Description**

Control group 2: Type 2 SMA patients that after insertion of needle into the skin, without entrance to cerebrospinal fluid space, needle will be removed without any injection . In this group only intrathecal injection will be simulated, without patients or their parents awareness . The patient will be admitted for one day of probable adverse reactions monitoring . One year followup and evaluations with regular and similar rehabilitative therapy will be done .

**Category**

Placebo

**6****Description**

Control group 3: Type 3 SMA patients that after insertion of needle into the skin, without entrance to cerebrospinal fluid space, needle will be removed without any injection . In this group only intrathecal injection will be simulated, without patients or their parents awareness . The patient will be admitted for one day of probable adverse reactions monitoring . One year followup and evaluations with regular and similar rehabilitative therapy will be done .

**Category**

Placebo

**Recruitment centers****1****Recruitment center****Name of recruitment center**

Children's Medical Center Hospital

**Full name of responsible person**

Reza Shervin Badv

**Street address**

Children's Medical Center Hospital, No 62, Gharib Street, end of keshavarz Blvd

**City**

Tehran

**Province**

Tehran

**Postal code**

1419733151

**Phone**

+98 21 6692 9234

**Fax**

+98 21 6612 9252

**Email**

drbadv@gmail.com

**Sponsors / Funding sources****1****Sponsor****Name of organization / entity**

Tehran University of Medical Sciences

**Full name of responsible person**

Mohammad Ali Sahraeian

**Street address**

No 226, Central organization of Tehran University of Medical Sciences, Ghods Street, Keshavarz Blvd

**City**

Tehran

**Province**

Tehran

**Postal code**

1417653761

**Phone**

+98 21 8898 7381

**Email**

msahrai@tums.ac.ir

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

Yes

**Title of funding source**

Tehran University of Medical Sciences

**Proportion provided by this source**

1

**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

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

ROYAN stem cell technology Co

**Full name of responsible person**

Morteza zarrabi

**Street address**

No. 24, East Hafez Alley, Bani Hashim Square, Resalat Highway

**City**

Tehran

**Province**

Tehran

**Postal code**

1665666311

**Phone**

+98 21 8978 1307

**Email**

info@rsct.ir

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

Yes

**Title of funding source**

ROYAN stem cell technology Co

**Proportion provided by this source**

99

**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**

Persons

**Person responsible for general inquiries****Contact****Name of organization / entity**

Tehran University of Medical Sciences

**Full name of responsible person**

Morteza Heidari

**Position**

Assistant Professor

**Latest degree**

Subspecialist

**Other areas of specialty/work**

Neurology

**Street address**

Children's Medical Center Hospital, No 62, Gharib Street, End of Keshavarz Blvd

**City**

Tehran

**Province**

Tehran

**Postal code**

1419733151

**Phone**

+98 21 6612 9252

**Email**

mortezah93@gmail.com

**Person responsible for scientific inquiries****Contact****Name of organization / entity**

Tehran University of Medical Sciences

**Full name of responsible person**

Mahmoud Reza Ashrafi

**Position**

Professor

**Latest degree**

Subspecialist

**Other areas of specialty/work**

Neurology

**Street address**

Children's Medical Center Hospital, No 62, Gharib Street, End of Keshavarz Blvd

**City**

Tehran

**Province**

Tehran

**Postal code**

1419733151

**Phone**

+98 21 6612 9252

**Fax**

+98 21 6612 9252

**Email**

mr\_ashrafi@yahoo.com

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

Tehran University of Medical Sciences

**Full name of responsible person**

Anahita Majmaa

**Position**

Fellowship of PICU

**Latest degree**

Specialist

**Other areas of specialty/work**

Pediatrics

**Street address**

Children's Medical Center Hospital, No 62, Gharib Street, End of Keshavarz Blvd

**City**

Tehran

**Province**

Tehran

**Postal code**

1419733151

**Phone**

+98 21 6612 9252

**Email**

majmaaa911@yahoo.com

## Sharing plan

### Deidentified Individual Participant Data Set (IPD)

Yes - There is 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

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

Undecided - It is not yet known if there will be a plan to

make this available

### Title and more details about the data/document

All collected data deidentified can be shared

### When the data will become available and for how long

Availability of data starting 6 months after publication, without time limitation

### To whom data/document is available

Researchers working in academic institutions and people working in businesses

### Under which criteria data/document could be used

Documents will be shared for replication of study in other Medical universities

### From where data/document is obtainable

Email addresses

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

Request by email addresses

### Comments