

# Clinical Trial Protocol

## Iranian Registry of Clinical Trials

10 Jun 2026

### A randomized controlled trial comparing the effects of $\beta$ -D-Mannuronic acid and conventional Non-steroidal anti-inflammatory drugs on disease activity and inflammatory markers in patients with ankylosing spondylitis

#### Protocol summary

##### Summary

The aim of this study is to assess the safety and effectiveness of  $\beta$ -D mannuronic acid in patients with Ankylosing spondylitis.  $\beta$ -D mannuronic acid has shown therapeutic effects with the greatest tolerability and safety in various experimental models such as experimental autoimmune encephalitis, adjuvant induced arthritis, nephrotic syndrome and acute glomerulonephritis. In this randomized, controlled trial, thirty five patients with Ankylosing spondylitis fulfilling the modified New York criteria that have active disease (BASDAI score  $\geq 4$  and BASFI score  $\geq 4$ ) will be examined. Additionally, patients do not have other concomitant diseases (Hepatic, renal and cardiovascular) or malignancies. Written informed consent will be obtained. Patients will be randomly assigned to receive either  $\beta$ -D mannuronic acid (treatment group, 25 patients) 1500 mg/day (three 500 mg tablets/day) or conventional Non-steroidal anti-inflammatory drugs (control group, 10 patients) orally for 12 weeks. Medical history, physical examinations, BASDAI and BASFI scores, serum level of CRP, the frequencies of circulating Th17 cells and regulatory T cells, L- selectin expression and leukocyte function-associated antigen-1 (LFA-1) expression will be evaluated at baseline and 12 weeks after treatment.

#### General information

##### Acronym

##### IRCT registration information

IRCT registration number: **IRCT2013062213739N1**

Registration date: **2013-12-30, 1392/10/09**

Registration timing: **prospective**

Last update:

Update count: **0**

##### Registration date

2013-12-30, 1392/10/09

##### Registrant information

###### Name

Abbas Mirshafiey

###### Name of organization / entity

Tehran University of Medical Sciences

###### Country

Iran (Islamic Republic of)

###### Phone

+98 21 8895 4913

###### Email address

mirshafiey@tums.ac.ir

##### Recruitment status

###### Recruitment complete

##### Funding source

1- Vice-Chancellor for Research, Tehran University of Medical Sciences  
2- Rheumatology research center, Tehran University of Medical Sciences  
3- Research Center for Immunodeficiencies, Children's Medical Center, Tehran University of Medical Sciences

##### Expected recruitment start date

2014-04-20, 1393/01/31

##### Expected recruitment end date

2015-04-20, 1394/01/31

##### Actual recruitment start date

empty

##### Actual recruitment end date

empty

##### Trial completion date

empty

##### Scientific title

A randomized controlled trial comparing the effects of  $\beta$ -D-Mannuronic acid and conventional Non-steroidal anti-inflammatory drugs on disease activity and inflammatory markers in patients with ankylosing spondylitis

**Public title**

The therapeutic effects of  $\beta$ -D-Mannuronic acid in patients with ankylosing spondylitis

**Purpose**

Basic science

**Inclusion/Exclusion criteria**

Inclusion Criteria: Patients age 18-45 years old, Diagnosis of "Definite AS" as defined by the modified New York criteria, Disease activity equal to BASDAI score  $\geq 4$ , Functional activity equal to BASFI score  $\geq 4$ , Each patient must sign written informed consent. Exclusion Criteria: History of fever and Infectious diseases, Positive pregnancy test or Lactation, Other collagen-vascular diseases, Other auto-immune diseases, Malignancies, Patients have enrolled another clinical trial study within last 4 weeks, Other concomitant diseases (Hepatic, renal, haematological, gastrointestinal, endocrine, cardiovascular, pulmonary, neurological or cerebral disease)

**Age**

From **18 years** old to **45 years** old

**Gender**

Both

**Phase**

1-2

**Groups that have been masked**

No information

**Sample size**

Target sample size: **35**

**Randomization (investigator's opinion)**

Randomized

**Randomization description****Blinding (investigator's opinion)**

Double blinded

**Blinding description****Placebo**

Not used

**Assignment**

Parallel

**Other design features**

1- In this study the patients and outcomes assessor do not know which  $\beta$ -D mannuronic acid or conventional Non-steroidal anti-inflammatory drugs is being given (double-blind). 2- In this study randomization will be performed by stratified randomization method. 3-  $\beta$ -D mannuronic acid was extracted from Alginic acid sodium salt (Sigma, A2033-1Kg) as a reference sample. This extraction method is a modified procedure of acid hydrolysis method (Chhatbar et al. 2009) that is being performed in Immunology division of Department of pathobiology, School of Public Health, Tehran University of Medical Sciences.

**Secondary Ids**

empty

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

Ethics committee of Tehran University of Medical Sciences

**Street address**

6th floor, Headquarter for Tehran University of Medical Sciences, On the Corner of Keshavarz Blvd. and Qods Street, Keshavarz Blvd., Tehran, Iran.

**City**

Tehran

**Postal code****Approval date**

2013-10-12, 1392/07/20

**Ethics committee reference number**

130.1525.92.ص

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

Ankylosing spondylitis

**ICD-10 code**

M45

**ICD-10 code description**

Ankylosing spondylitis

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

The ASAS20 response criteria

**Timepoint**

12 weeks after intervention (at the end of study)

**Method of measurement**

Questionnaire

**2****Description**

Disease activity

**Timepoint**

At baseline and after 12 weeks of treatment

**Method of measurement**

Questionnaire

**3****Description**

Physical function

**Timepoint**

At baseline and after 12 weeks of treatment.

**Method of measurement**

Questionnaire

**Secondary outcomes****1****Description**

Serum level of CRP

**Timepoint**

At baseline and after 12 weeks of treatment

**Method of measurement**

Turbidometry

**2**

**Description**

The frequency of circulating Th17 cells

**Timepoint**

At baseline and after 12 weeks of treatment

**Method of measurement**

flow cytometry

**3**

**Description**

The frequency of circulating regulatory T (Treg) cells

**Timepoint**

At baseline and after 12 weeks of treatment

**Method of measurement**

flow cytometry

**4**

**Description**

L- selectin expression

**Timepoint**

At baseline and after 12 weeks of treatment

**Method of measurement**

flow cytometry

**5**

**Description**

LFA-1 expression

**Timepoint**

At baseline and after 12 weeks of treatment

**Method of measurement**

Real-time PCR

**6**

**Description**

Serum level of IL-6

**Timepoint**

At baseline and after 12 weeks of treatment

**Method of measurement**

Elisa

**7**

**Description**

Serum level of IL-10

**Timepoint**

At baseline and after 12 weeks of treatment

**Method of measurement**

Elisa

**8**

**Description**

Serum level of IL-17A

**Timepoint**

At baseline and after 12 weeks of treatment

**Method of measurement**

Elisa

**9**

**Description**

Serum level of TNF- $\alpha$

**Timepoint**

At baseline and after 12 weeks of treatment

**Method of measurement**

Elisa

**Intervention groups**

**1**

**Description**

Treatment group will receive 1500 mg/day (three 500 mg tablets/day) of  $\beta$ -D mannuronic acid orally for 12 weeks.

**Category**

Treatment - Drugs

**2**

**Description**

Control group will receive conventional Non-steroidal anti-inflammatory drugs orally for 12 weeks

**Category**

Treatment - Drugs

**Recruitment centers**

**1**

**Recruitment center**

**Name of recruitment center**

Rheumatology research center, Tehran University of Medical Sciences

**Full name of responsible person**

Dr. Mahdi mahmoudi (PhD- Assistant Professor)

**Street address**

Rheumatology research center, Dr. Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran

**City**

Tehran

**Sponsors / Funding sources**

**1**

**Sponsor**

**Name of organization / entity**

Vice-Chancellor for Research, Tehran University of Medical Sciences

**Full name of responsible person**

Dr. Masood younesian (MD, PhD, Vice-Chancellor for Research, Tehran University of Medical Sciences)

**Street address**

6th floor, Headquarter for Tehran University of Medical Sciences, On the Corner of Keshavarz Blvd. and Qods Street, Keshavarz Blvd., Tehran, Iran.

**City**

Tehran

**Grant name**

**Grant code / Reference number**

**Is the source of funding the same sponsor organization/entity?**

Yes

**Title of funding source**

Vice-Chancellor for Research, Tehran University of Medical Sciences

**Proportion provided by this source**

**Public or private sector**

*empty*

**Domestic or foreign origin**

*empty*

**Category of foreign source of funding**

*empty*

**Country of origin**

**Type of organization providing the funding**

*empty*

**2**

**Sponsor**

**Name of organization / entity**

Rheumatology research center, Tehran University of Medical Sciences

**Full name of responsible person**

Dr. Ahmad reza Jamshidi (MD, Professor)

**Street address**

Rheumatology research center, Dr. Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran

**City**

Tehran

**Grant name**

**Grant code / Reference number**

**Is the source of funding the same sponsor organization/entity?**

Yes

**Title of funding source**

Rheumatology research center, Tehran University of Medical Sciences

**Proportion provided by this source**

**Public or private sector**

*empty*

**Domestic or foreign origin**

*empty*

**Category of foreign source of funding**

*empty*

**Country of origin**

**Type of organization providing the funding**

*empty*

**3**

**Sponsor**

**Name of organization / entity**

Research Center for Immunodeficiencies, Tehran University of Medical Sciences

**Full name of responsible person**

Dr. Asghar Agha Mohammadi (MD, Professor)

**Street address**

Research Center for Immunodeficiencies, Children's Medical Center, Tehran University of Medical

Sciences, Tehran, Iran,

**City**

Tehran

**Grant name**

**Grant code / Reference number**

**Is the source of funding the same sponsor organization/entity?**

Yes

**Title of funding source**

Research Center for Immunodeficiencies, Tehran University of Medical Sciences

**Proportion provided by this source**

**Public or private sector**

*empty*

**Domestic or foreign origin**

*empty*

**Category of foreign source of funding**

*empty*

**Country of origin**

**Type of organization providing the funding**

*empty*

**Person responsible for general inquiries**

**Contact**

**Name of organization / entity**

Department of pathobiology, School of Public Health, Tehran University of Medical Sciences

**Full name of responsible person**

Dr. Abbas Mirshafiey

**Position**

Head of the Department of pathobiology (PHD - Professor)

**Other areas of specialty/work**

**Street address**

Department of pathobiology, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran

**City**

Tehran

**Postal code**

**Phone**

+98 21 8895 4913

**Fax**

**Email**

mirshafiey@tums.ac.ir

**Web page address**

**Person responsible for scientific inquiries**

**Contact**

**Name of organization / entity**

Department of pathobiology, School of Public Health, Tehran University of Medical Sciences

**Full name of responsible person**

Dr. Abbas Mirshafiey

**Position**

Head of the Department of pathobiology (PhD - Professor)

**Other areas of specialty/work**

**Street address**

Department of pathobiology, School of Public Health,

Tehran University of Medical Sciences, Tehran, Iran

**City**

Tehran

**Postal code**

**Phone**

+98 21 8895 4913

**Fax**

**Email**

mirshafiey@tums.ac.ir

**Web page address**

**Person responsible for updating data**

**Contact**

**Sharing plan**

**Deidentified Individual Participant Data Set (IPD)**

*empty*

**Study Protocol**

*empty*

**Statistical Analysis Plan**

*empty*

**Informed Consent Form**

*empty*

**Clinical Study Report**

*empty*

**Analytic Code**

*empty*

**Data Dictionary**

*empty*