Clinical Trial Protocol
Iranian Registry of Clinical Trials

31 May 2026

A phase III, randomized, parallel, two-arm, double-blind, multi-center, active-controlled, non-inferiority clinical trial to compare efficacy and safety of daratumumab (produced by CinnaGen Co.) versus the reference daratumumab (Darzalex®, produced by Janssen Biotech, Inc.) in relapsed or refractory multiple myeloma patients

Protocol summary

Study aim

To assess the non-inferiority, efficacy, safety, and immunogenicity of daratumumab (manufactured by CinnaGen Co.) in comparison with Darzalex® (manufactured by Janssen Biotech, Inc.) in relapsed or refractory multiple myeloma patients

Design

A phase III, randomized, parallel, two-arm (with 1:1 ratio), double-blind (patients and evaluators), multi-center, active-controlled, non-inferiority clinical trial

Settings and conduct

Patients with relapsed or refractory multiple myeloma will be randomly assigned to the groups. Then, over the course of 24 visits (52 weeks), the therapeutic intervention (DRd regimen) will be administered in both groups according to the study protocol. Laboratory assessments and, if necessary, imaging studies will also be performed at each scheduled visit in accordance with the protocol.

Participants/Inclusion and exclusion criteria

Eligible patients are adults ≥18 years with informed consent, a confirmed diagnosis of multiple myeloma per IMWG criteria, one or two prior lines of therapy, prior response (Partial Response or better), and progressive disease. Exclusion applies to prior anti-CD38 therapy, refractoriness to lenalidomide, or other concurrent conditions that may compromise safety or study integrity.

Intervention groups

Intervention group: Daratumumab (manufactured by CinnaGen Co.); Control group: Darzalex®. Both arms receive DRd regimen for 14 28-day cycles. This regimen consists of daratumumab 16 mg/kg intravenous infusion once weekly (cycles 1-2), every two weeks (cycles 3-6), and every four weeks (cycles 7 and beyond); lenalidomide 25 mg orally once daily, on days 1-21 of each 28-day cycle; and dexamethasone 40 mg orally once weekly.

Main outcome variables

The proportion of subjects who achieve Very Good Partial Response (VGPR) or better per International Myeloma Working Group criteria, within one year after treatment initiation

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20150303021315N38**
Registration date: **2025-10-28, 1404/08/06**
Registration timing: **prospective**

Last update: **2025-10-28, 1404/08/06**
Update count: **0**

Registration date

2025-10-28, 1404/08/06

Registrant information

Name

Nassim Anjidani

Name of organization / entity

Orchid Pharmed

Country

Iran (Islamic Republic of)

Phone

+98 21 4347 3000

Email address

amini@orchidpharmed.com

Recruitment status
recruiting
Funding source

Expected recruitment start date
2025-11-22, 1404/09/01
Expected recruitment end date
2026-11-23, 1405/09/02
Actual recruitment start date
empty
Actual recruitment end date
empty
Trial completion date
empty

Scientific title
A phase III, randomized, parallel, two-arm, double-blind, multi-center, active-controlled, non-inferiority clinical trial to compare efficacy and safety of daratumumab (produced by CinnaGen Co.) versus the reference daratumumab (Darzalex®, produced by Janssen Biotech, Inc.) in relapsed or refractory multiple myeloma patients

Public title
A comparison of the efficacy and safety of daratumumab (produced by CinnaGen Co.) versus the reference daratumumab (Darzalex®, produced by Janssen Biotech, Inc.) in relapsed or refractory multiple myeloma patients
Purpose
Treatment
Inclusion/Exclusion criteria
Inclusion criteria:
Age of at least 18 years old at the time of randomization Willingness for signing and having signed the written informed consent form Diagnosis of multiple myeloma per IMWG criteria:3.1. Clonal bone marrow plasma cells ≥10% at some point in their disease history or presence of a biopsy-proven plasmacytoma3.2. Measurable disease as defined by any of the following:3.2.1. IgG multiple myeloma: Serum monoclonal paraprotein (M-protein) level ≥1.0 g/dL or urine M-protein level ≥200 mg/24h3.2.2. IgA, IgM, IgD, or IgE multiple myeloma: serum M-protein level ≥0.5 g/dL or urine M-protein level ≥200 mg/24h Subject must have received at least one prior line of therapy for multiple myeloma.A line of therapy consists of 1 complete cycle of a single agent, a regimen consisting of a combination of several drugs, or a planned sequential therapy of various regimens (eg, 3-6 cycles of initial therapy with bortezomib-dexamethasone followed by stem cell transplantation, consolidation, and lenalidomide maintenance is considered 1 line). Subject must have achieved a response (Partial Response or Better based on investigator's determination) to at least one prior regimen. Subject must have progressive disease, based on investigator's determination, on or after their last regimen Eastern Cooperative Oncology Group (ECOG) performance status score of 0, 1, or 2
Exclusion criteria:
Subject has received daratumumab or other anti-CD38 therapies previously. Subject's disease shows evidence of refractoriness to any dose of lenalidomide, defined either:2.1. Subjects whose disease progresses within 60 days of the last dose of lenalidomide; or2.2. Subjects whose disease is nonresponsive while on lenalidomide. Nonresponsive disease is defined as either failure to achieve at least a Minimal Response or development of PD while on lenalidomide. Subject has received anti-myeloma treatment within 2 weeks before the date of randomization. The only exception is emergency use of a short course of corticosteroids (equivalent of dexamethasone 40 mg/day for a maximum 4 days) before treatment. Subject has received more than two prior lines of therapy for multiple myeloma. Subject has received autologous stem cell transplant within 12 weeks before the date of randomization, or subject has previously received an allogeneic stem cell transplant (regardless of timing) Subject in need of stem cell transplant during the study period (in investigator's opinion), or planning to undergo a stem cell transplant prior to disease progression in this study, ie, these subjects should not be enrolled in order to reduce disease burden prior to transplant. A history of malignancy (other than multiple myeloma) within 5 years before the date of randomization, with the exception of squamous and basal cell carcinomas of the skin, carcinoma in situ of the cervix, or a malignancy that in the opinion of the investigator is considered cured with minimal risk of recurrence within 5 years Subject has known meningeal involvement of multiple myeloma Known chronic obstructive pulmonary disease (COPD) of grade GOLD 3 (severe) or GOLD 4 (very severe) based on Global Initiative for Chronic Obstructive Lung Disease (GOLD) Current uncontrolled persistent asthma in time of screening (per American Lung Association's classification) Human immunodeficiency virus (HIV), hepatitis B virus (HBV), or hepatitis C virus (HCV) seropositivity; This criterion is assessed via HBs-Ag, HBc-Ab, HCV-Ab, and HIV-Ab tests at screening. Subject has any of the following laboratory test results during the Screening Phase:12.1. Aspartate aminotransferase (AST) or alanine aminotransferase level (ALT) ≥ 2.5 times the upper limit of normal (ULN)12.2. Alkaline phosphatase level ≥ 2.5 × ULN12.3. Total bilirubin level ≥ 1.5 × ULN, (except for Gilbert Syndrome: direct bilirubin 1.5 × ULN) Subject has known hypersensitivity to monoclonal antibodies or human proteins Subject has plasma cell leukemia (> 2.0 × 109/L circulating plasma cells by standard differential), Waldenström's macroglobulinemia, POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, and skin changes), monoclonal gammopathy of undetermined significance (MGUS), smoldering myeloma, or amyloidosis Pregnant or nursing women, or female/male subject planning to become pregnant while enrolled in this study, within 4 weeks after the last dose of lenalidomide, or within 12 weeks after the last dose of daratumumab. Female and male subjects in the reproductive age must use reliable methods of contraception. Subject has received an investigational drug within 4 weeks before randomization (except for investigational anti-myeloma agents, which cannot be taken within 2 weeks prior to randomization, as described in exclusion criterion #3) Subject has had major surgery within 2 weeks before randomization, or

will not have fully recovered from surgery, or has surgery planned during the time the subject is expected to participate in the study or within 2 weeks after the last dose of study treatment. Note: subjects with planned surgical procedures to be conducted under local anesthesia may participate. Kyphoplasty or vertebroplasty are not considered major surgery. Has had a plasmapheresis within 28 days before randomization Radiation therapy (with the exception of palliative radiation therapy) within 14 days before randomization Subject has any concurrent medical condition or disease (eg, active systemic infection) that is likely to interfere with study procedures or results, or that in the opinion of the investigator would constitute a hazard for participating in this study

Age

From **18 years** old

Gender

Both

Phase

3

Groups that have been masked

- Participant
- Care provider
- Investigator
- Outcome assessor
- Data analyser

Sample size

Target sample size: **128**

Randomization (investigator's opinion)

Randomized

Randomization description

Randomization of patients will be conducted using Stata software (v. MP 18, StataCorp, US.), utilizing block randomization (with size 2 and 4) stratified by disease stage (I, II or III) and number of prior lines of therapy (1 or 2) for a total of 128 patients (with a 1:1 ratio). Prior to the start of the study, the generated randomization series, along with the seed used for generating random numbers. The randomization process will be performed centrally, meaning that each patient will be allocated to one of these strata upon entering the study based on their conditions. Then, by contacting the unit responsible for randomization, they will be assigned to a treatment group using the random list corresponding to that stratum. Each randomized patient will be assigned a unique identification code for the duration of the study. The assigned code will consist of four letters (the first two letters of the first name and the first two letters of the last name), three numbers (the center code), three letters representing the generic drug name (which is DRT), and three digits (corresponding to the randomization code), forming the patient code. For example: ABCD001 DRT-001. The randomization numbers will be assigned sequentially.

Blinding (investigator's opinion)

Double blinded

Blinding description

Both vials of daratumumab (manufactured by SinaGen Research and Production Company) and Darzalex® (manufactured by Janssen Biotech, Inc.) used in the study were indistinguishable to patients and study staff, as they were completely identical in shape, size, material, and color, and therefore the brand of the drug could not be identified by appearance. The drug containers of daratumumab (manufactured by SinaGen Research and Production Company) and Darzalex® (manufactured by Janssen Biotech, Inc.) were also placed in identical packaging, making them visually indistinguishable. Randomization will not be disclosed to the study investigators. Individuals responsible for data review and analysis will remain blinded to patient group allocation.

Placebo

Not used

Assignment

Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Dr. Shariati Educational, Research and Clinical Center Ethics Committee, TUMS

Street address

Dr. Shariati Educational, Research and Clinical Center, Opposite to Faculty of Economics, Jalal Al Ahmad Crossroad, North Kargar Street, Tehran, Iran

City

Tehran

Province

Tehran

Postal code

1411713135

Approval date

2025-10-01, 1404/07/09

Ethics committee reference number

IR.TUMS.SHARIATI.REC.1404.077

Health conditions studied

1

Description of health condition studied

Relapsed or Refractory Multiple Myeloma

ICD-10 code

C90.0

ICD-10 code description

Multiple myeloma

Primary outcomes

1

Description

The proportion of subjects who achieve Very Good Partial Response (VGPR) or better per IMWG criteria, within one year after treatment initiation

Timepoint

From randomization up to 12 months

Method of measurement

Response, based on International Myeloma Working Group (IMWG) criteria

Secondary outcomes

1

Description

Duration of Response (DOR): The duration from the first documented VGPR or better per IMWG criteria, to the date of first documented progressive disease per IMWG criteria

Timepoint

From randomization up to 12 months

Method of measurement

Response, based on International Myeloma Working Group (IMWG) criteria

2

Description

Overall Survival (OS): Time from the randomization date to the date of the subject’s death due to any cause

Timepoint

From randomization up to 12 months

Method of measurement

Recording of the duration from the date of randomization to the date of the subject’s death due to any cause

3

Description

Overall Response Rate (ORR): The proportion of subjects who achieve Partial Response (PR) or better per IMWG criteria, within one year after treatment initiation

Timepoint

From randomization up to 12 months

Method of measurement

Response, based on International Myeloma Working Group (IMWG) criteria

4

Description

Time to Response (TTR): Time from the randomization date to VGPR or better per IMWG criteria

Timepoint

From randomization up to 12 months

Method of measurement

Response, based on International Myeloma Working Group (IMWG) criteria

5

Description

Time to progression (TTP): Time from the randomization date to progressive disease per IMWG criteria

Timepoint

From randomization up to 12 months

Method of measurement

Response, based on International Myeloma Working Group (IMWG) criteria

6

Description

Progression-Free Survival (PFS): The duration from the date of randomization to either progressive disease per IMWG criteria, or death, whichever occurs first

Timepoint

From randomization up to 12 months

Method of measurement

Response, based on International Myeloma Working Group (IMWG) criteria

7

Description

Evaluation of incidence of daratumumab adverse events

Timepoint

During all visits including screening visit; up to one month after the last injection; before, during, and after each intervention (until the next intervention is received)

Method of measurement

Assessment of the adverse events reported by the patient or physician, and evaluation of severity, seriousness and causal relationship of adverse events with daratumumab based on international guidelines, such as the guidelines of the World Health Organization

8

Description

Assessment of anti-daratumumab antibody development in patients.

Timepoint

At screening visit and weeks 24 and 52 after inititation of treatment with daratumumab

Method of measurement

Blood sampling for the evaluation of anti-daratumumab antibody serum using ELISA method

Intervention groups

1

Description

Intervention group:- Daratumumab (manufactured by CinnaGen Co.) 16 mg/Kg intravenous infusion once weekly (cycles 1-2), every two weeks (cycles 3-6), and every four weeks (cycles 7 and beyond) - Lenalidomide 25 mg orally once daily, on days 1-21 of each 28-day cycle- Dexamethasone 40 mg orally once weekly

Category

Treatment - Drugs

2

Description

Control group:- Daratumumab (Darzalex®,

manufactured by Janssen Biotech, Inc.) 16 mg/kg intravenous infusion once weekly (cycles 1-2), every two weeks (cycles 3-6), and every four weeks (cycles 7 and beyond) - Lenalidomide 25 mg orally once daily, on days 1-21 of each 28-day cycle- Dexamethasone 40 mg orally once weekly

Category

Treatment - Drugs

Recruitment centers

1

Recruitment center

Name of recruitment center

Taleghani Hospital

Full name of responsible person

Dr. Sayeh Parkhideh/ Dr. Sahar Parkhideh/ Dr. Mojtaba Ghadiany/ Dr. Mahshid Mehdizadeh

Street address

4th Floor, Ayatollah Taleghani Hospital, next to Shahid Beheshti University of Medical Sciences, Shahid Arabi Street, Yemen Street, Shahid Chamran Highway, Tehran

City

Tehran

Province

Tehran

Postal code

1985711151

Phone

+98 21 2293 7031

Email

ghadianymojtaba@yahoo.com

Web page address

https://taleghani.sbmu.ac.ir/

2

Recruitment center

Name of recruitment center

Shariati Hospital

Full name of responsible person

Dr. Sahar Tavakkoli Shiraji/ Dr. Mohammad Vaezi/ Dr. Soroush Rad/ Dr. Maryam Barkhordar

Street address

Shariati Educational, Research, and Clinical Center, Jalal-Al-Ahmad Junction, North Kargar Street, Tehran

City

Tehran

Province

Tehran

Postal code

1411713135

Phone

+98 21 8490 1000

Email

sahar.ts78@yahoo.com

Web page address

https://shariati.tums.ac.ir/

3

Recruitment center

Name of recruitment center

Firoozgar Hospital

Full name of responsible person

Dr. Seyd Mohsen Razavi

Street address

Firoozgar Hospital, Beafarin Street, Karim Khan Zand Street, Valiasr Square,Tehran

City

Tehran

Province

Tehran

Postal code

1593748711

Phone

+98 21 8214 1000

Email

drsmrazavi@gmail.com

Web page address

https://firoozgar.iums.ac.ir/

4

Recruitment center

Name of recruitment center

Naft Hospital

Full name of responsible person

Dr. Behrouz Gharib

Street address

Naft Hospital, Sarhang Sokhaei Street, Hafez Street, Tehran

City

Tehran

Province

Tehran

Postal code

1136774114

Phone

+98 21 6670 0023

Email

gharib.behrooz@yahoo.com

Web page address

https://teh.piho.ir/fa/bimarestanfoghetakhasosi

5

Recruitment center

Name of recruitment center

Rasht Hospital, Rasht

Full name of responsible person

Dr. Sirous Gharib/ Dr. Fatemeh Nejatifar

Street address

Razi Hospital, Sardar Jangal Street, Rasht

City

Rasht

Province

Guilan

Postal code

4144895655

Phone

+98 13 3354 1001

Email
dr.cygharib@gmail.com
Web page address
https://razi.gums.ac.ir/

6

Recruitment center
Name of recruitment center
Baghaei Hospital, Ahvaz
Full name of responsible person
Dr. Mehran Hoseinzadeh/ Dr. Tina Vosoughi/ Dr. Ahmad Ahmadzadeh
Street address
Shahid Baghaei Hospital, Golestan Road, Ahvaz
City
Ahvaz
Province
Khouzestan
Postal code
6138933333
Phone
+98 61 3375 0000
Email
vosoughi.hto@gmail.com
Web page address
https://h-baghaei2.ajums.ac.ir/

7

Recruitment center
Name of recruitment center
Namazi Hospital, Shiraz
Full name of responsible person
Dr. Alireza Rezvani/ Dr. Abolfazl Khalafi-nezhad / Dr. Vahid Mohammad karimi
Street address
Namazi Hospital, Namazi Square, Zand Street, Shiraz
City
Shiraz
Province
Fars
Postal code
7193613311
Phone
+98 71 3612 5000
Email
ar.rezvani@hotmail.com
Web page address
https://namazi.sums.ac.ir/

8

Recruitment center
Name of recruitment center
Seyed Al-Shohada Hospital
Full name of responsible person
MehranSharifi AlirezaSadeghi AliDerakhshande ValiolahMehrzad MohamadRezaKhosravi AliHajigholami
Street address
Seyyed Al-Shohada Hospital, Nahrfarshadi Neighborhood, Khayyam Highway, Isfahan
City
Esfahan
Province
Isfehan
Postal code
8168733333
Phone
+98 31 3235 0210
Email
valimehrzad@yahoo.com
Web page address
https://omid.mui.ac.ir/fa

9

Recruitment center
Name of recruitment center
Imam Khomeini Hospital, Sari
Full name of responsible person
Dr. Ehsan Zaboli/ Dr. Mohammad Eslami Jouibari
Street address
Beginning of Valiasr Highway, Imam Square, Sari
City
Sari
Province
Mazandaran
Postal code
4816633131
Phone
+98 11 3304 4000
Email
paya_1358@yahoo.com
Web page address
https://imamhospital.mazums.ac.ir

10

Recruitment center
Name of recruitment center
Ghaem Hospital, Mashhad
Full name of responsible person
Dr. Abolghasem Allahyari/Dr. Sajad Ataei/Dr. Mostafa Kamandi/Dr. Mohammad Moeini/Dr. Hossein Rahimi
Street address
Beginning of Ahmadabad Street, Dr. Ali Shariati Square, Mashhad
City
Mashhad
Province
Razavi Khorasan
Postal code
9176699199
Phone
+98 51 3840 0000
Email
allahyari@yahoo.com
Web page address
https://quaem.mums.ac.ir

11

Recruitment center
Name of recruitment center

Afzalipour Hospital, Kerman

Full name of responsible person
Dr. Behjat Kalantari/ Dr.Naeim Nikpoor

Street address
Afzalipour Educational and Clinical Center, next to Shahid Bahonar University, Imam Khomeini Highway, Kerman

City
Kerman

Province
Kerman

Postal code
7616913355

Phone
+98 34 3132 8000

Email
dkalantarikhandani@gmail.com

Web page address
https://ah.kmu.ac.ir/fa

12

Recruitment center

Name of recruitment center
Shahid Ghazi Hospital

Full name of responsible person
Dr. Ali Esfahani/Dr. Seyed Hadi Chavoshi/Dr.Babak Nejati

Street address
Hematology and Oncology Research Center, Shahid Ghazi Hospital, Golgasht Street, Daneshgah Street, Tabriz

City
Tabriz

Province
East Azarbaijan

Postal code
5166614731

Phone
+98 41 3334 3626

Email
ali_sfhn@yahoo.com

Web page address
https://horc-fa.tbzmed.ac.ir/

Sponsors / Funding sources

1

Sponsor

Name of organization / entity
CinnaGen Company

Full name of responsible person
Mehran Montajabi Niyat

Street address
Simin Dasht Industrial Park, Karaj, Alborz, Iran

City
Karaj

Province
Alborz

Postal code
3165933155

Phone
+98 26 3667 0980

Email
cinnagen@cinnagen.com

Web page address
https://www.cinnagen.com

Grant name

Grant code / Reference number

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

Title of funding source
CinnaGen Company

Proportion provided by this source
100

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
Industry

Person responsible for general inquiries

Contact

Name of organization / entity
Orchid Pharmed Co.

Full name of responsible person
Dr. Hamidreza Kafi

Position
Medical Department Manager

Latest degree
Ph.D.

Other areas of specialty/work
Medical Pharmacy

Street address
No 42, Attar St., Vanak Sq, Tehran, Iran

City
Tehran

Province
Tehran

Postal code
1994766411

Phone
+98 21 4347 3000

Email
Kafi.H@orchidpharmed.com

Web page address

Person responsible for scientific inquiries

Contact

Name of organization / entity
Tehran University of Medical Sciences

Full name of responsible person
Dr. Sahar Tavakoli Shiraji

Position
Assistant Professor

Latest degree
Subspecialist
Other areas of specialty/work
Hematology
Street address
Shariati Educational, Research, and Clinical Center, Jalal-Al-Ahmad Junction, North Kargar Street, Tehran
City
Tehran
Province
Tehran
Postal code
1411713135
Phone
+98 21 8490 1000
Email
sahar.ts78@yahoo.com

Person responsible for updating data

Contact
Name of organization / entity
Orchid Pharmed Co.
Full name of responsible person
Dr. Hamidreza Kafi
Position
Medical Department Manager
Latest degree
Ph.D.
Other areas of specialty/work
Medical Pharmacy
Street address
No 42, Attar St., Vanak Sq, Tehran, Iran
City
Tehran
Province
Tehran
Postal code
1994766411
Phone
+98 21 4347 3000
Email
Kafi.H@orchidpharmed.com

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
Undecided - It is not yet known if there will be a plan to make this available
Statistical Analysis Plan
Not applicable
Informed Consent Form
Undecided - It is not yet known if there will be a plan to make this available
Clinical Study Report
Undecided - It is not yet known if there will be 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