A Phase 3 Randomized Study Comparing Teclistamab in Combination with Daratumumab SC (Tec-Dara) versus Daratumumab SC, Pomalidomide, and Dexamethasone (DPd) or Daratumumab SC, Bortezomib, and Dexamethasone (DVd) in Participants with Relapsed or Refractory Multiple Myeloma

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This study has been transitioned to CTIS with ID 2023-503441-55-00 check the CTIS register for the current data. The primary objective is to compare the efficacy of Tec-Dara (Arm A) with DPd/DVd (Arm B) in participants who have received 1 to 3 prior…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Haematopoietic neoplasms (excl leukaemias and lymphomas)
Study type	Interventional

Summary

ID

NL-OMON54191

Source
ToetsingOnline

Brief title
MajesTEC-3

Condition

- Haematopoietic neoplasms (excl leukaemias and lymphomas)

Synonym
Multiple Myeloma

Research involving
Human

Sponsors and support

Primary sponsor: Janssen-Cilag
Source(s) of monetary or material Support: door de verrichter

Intervention

Keyword: DPd, DVd, Multiple myeloma, Teclistamab

Outcome measures

Primary outcome

The primary objective of this study is to compare the efficacy of teclistamab

in combination with daratumumab SC (Tec-Dara; Arm A) with that of an

investigator*s choice of DPd or DVd (Arm B; termed DPd/DVd hereafter) as

assessed by PFS

Secondary outcome

Key secondary objectives include further comparison of efficacy as assessed by

overall response (PR or better) rate, CR or better rate,MRD -negativity rate,

PFS2, Overall survival, Time to next treatment and duration of response.

Study description

Background summary

Although the treatment of patients with multiple myeloma is getting better, patients cannot be cured from the disease. That is why we are constantly looking for better treatment options. One of the possibilities is to treat people with so-called antibodies. One of the antibodies is the study drug teclistamab.

Teclistamab (also known as JNJ-64007957) is a humanized IgG4-PAA bispecific antibody that binds the CD3 receptor complex on T cells and BCMA on plasma cells. With its dual binding sites, teclistamab is able to draw myeloma cells in close proximity to CD3+ T cells, resulting in T cell activation and subsequent lysis of BCMA+ cells that is mediated by secreted perforin and various granzymes stored in the secretory vesicles of cytotoxic T cells.

Study objective

This study has been transitioned to CTIS with ID 2023-503441-55-00 check the CTIS register for the current data.

The primary objective is to compare the efficacy of Tec-Dara (Arm A) with DPd/DVd (Arm B) in participants who have received 1 to 3 prior lines of therapy, including a PI and lenalidomide.

Study design

A Phase 3 Randomized Study Comparing Teclistamab in Combination with Daratumumab SC (Tec-Dara)
versus Daratumumab SC, Pomalidomide, and Dexamethasone (DPd) or Daratumumab SC, Bortezomib,
and Dexamethasone (DVd) in Participants with Relapsed or Refractory Multiple Myeloma.
The study will be conducted in 3 phases: Screening, Treatment, and Follow-Up. Approximately 560 subjects will be randomized 1:1 to receive either standard therapy with DVd or DPd (Arm B) or to receive Tec-Dara (Arm A). Decision DVd or DPd treatment is by investigator's choice.

Intervention

Study treatment will be administered on 28-day cycles for Tec-Dara (Arm A) and DPd (Arm B). For DVd (Arm B), study treatment will be administered on 21-day cycles for Cycles 1 to 8 and 28-day cycles for Cycles 9+. Teclistamab will be administered subcutaneously using a weight-based dose schedule as detailed in the protocol.

Study burden and risks

Taking into account the measures taken to minimize risk to participants in this study, the potential risks identified for combination therapy of teclistamab and daratumumab are justified by the anticipated benefits that may be afforded to participants with relapsed/refractory multiple
myeloma. The addition of teclistamab to daratumumab SC offers a unique mechanism of action of T -cell redirection that could lead to synergistic antimyeloma effects. A short course of steroids may prevent long-term

steroid-induced toxicities.
There is potential risk for overlapping toxicities with the planned study drugs, specifically the unknown effect of daratumumab SC on CRS (which is the main toxicity of concern with teclistamab) and sARRs. The risk mitigation measures planned for the experimental arm:
- Implementation of step-up doses of teclistamab to reduce risk or severity of CRS
- Note that teclistamab has demonstrated mostly low-grade CRS in studies to date
- Staggered initiation of daratumumab SC and teclistamab therapy to reduce the risk of overlapping toxicity
- Implementation of pretreatment medications to reduce risk or severity of sARRs and CRS for the first 2 weeks of therapy
- Provision of specific monitoring guidelines for participants during the first few doses of teclistamab when CRS risk is highest
- SC administration of daratumumab reduces the risk of high-grade sARRs
- Note that sARRs have been observed at low frequency and low grade to date with participants treated with teclistamab in studies.
- Robust management strategies for potential toxicities

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- >=18 years of age.
- Documented multiple myeloma as defined by the criteria below:
a. Multiple myeloma diagnosis according to the IMWG diagnostic criteria
b. Measurable disease at screening as defined by any of the following:
1) Serum M-protein level >=0.5 g/dL (central laboratory); or
2) Urine M-protein level >=200 mg/24 hours (central laboratory); or
3) Serum immunoglobulin free light chain >=10 mg/dL (central laboratory) and abnormal serum immunoglobulin kappa lambda free light chain ratio.
- Received 1 to 3 prior line(s) of antimyeloma therapy (Appendix 6) including a PI and lenalidomide.
a. Participants who have received only 1 line of prior line of antimyeloma therapy must be lenalidomide refractory (ie, have demonstrated progressive disease by IMWG criteria during treatment or within 60 days of completion of lenalidomide-containing regimen). Progression on or within 60 days of the last dose of lenalidomide given as maintenance will meet this criterion.
- Documented evidence of progressive disease based on investigator*s determination of response by IMWG criteria on or after their last regimen.
- Have an ECOG performance status score of 0, 1, or 2 at screening and immediately prior to the start of administration of study treatment (Appendix 7).
- Have clinical laboratory values meeting the criteria specified in the protocol.

Exclusion criteria

- Contraindications or life-threatening allergies, hypersensitivity, or intolerance to any study drug or its excipients,
Additional exclusion criteria pertaining to specific study drugs include:
a. A participant is not eligible to receive DPd as control therapy if any of the following are present:
1) Contraindications or life-threatening allergies, hypersensitivity, or intolerance to pomalidomide (intolerance defined as prior therapy discontinued due to any AE related to pomalidomide)
2) Disease that is considered refractory to pomalidomide per IMWG (progression during treatment or within 60 days of completing treatment with pomalidomide).
b. A participant is not eligible to receive DVd as control therapy if any of

the following are present:
1) Contraindications or life-threatening allergies, hypersensitivity, or intolerance to bortezomib (intolerance defined as prior therapy discontinued due to any AE related to bortezomib)
2) Grade 1 peripheral neuropathy with pain or Grade >=2 peripheral neuropathy as defined by NCI-CTCAE Version 5.0
3) Disease that is considered refractory to bortezomib per IMWG (progression during treatment or within 60 days of completing treatment with bortezomib).
4) Received a strong CYP3A4 inducer (see Section 6.12.3.3) within 5 half-lives prior to randomization.
c. A participant is not eligible for this study if they are refractory to both pomalidomide and bortezomib.
- Received any prior BCMA-directed therapy.
- Has disease that is considered refractory to an anti-CD38 monoclonal antibody per IMWG (progression during treatment or within 60 days of completing therapy with an anti-CD38 monoclonal antibody).
- Received a cumulative dose of corticosteroids equivalent to >=140 mg of prednisone within 14 days before randomization.
- Received a live, attenuated vaccine within 4 weeks before randomization.
- Plasma cell leukemia at the time of screening, Waldenström*s macroglobulinemia, POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, M-protein, and skin changes), or primary amyloid light chain amyloidosis.

For a full list of exclusion criteria, please refer to section 5.2 of the study protocol

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	25-10-2021
Enrollment:	32
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	DARZALEX
Generic name:	Daratumumab
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	IMNOVID
Generic name:	Pomalidomide
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	JENAPHARM
Generic name:	dexamethasone
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Teclistamab
Generic name:	Teclistamab
Product type:	Medicine
Brand name:	VELCADE
Generic name:	bortezomib
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	14-09-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek

	(Assen)
Approved WMO Date:	12-10-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-11-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	13-12-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-03-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	13-06-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-07-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-08-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-11-2022

Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-01-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-02-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-03-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-07-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-08-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-11-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-02-2024
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	20-02-2024
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EU-CTR	CTIS2023-503441-55-00
EudraCT	EUCTR2020-004742-11-NL
ClinicalTrials.gov	NCT05083169
CCMO	NL78480.056.21