A Phase 3 Randomized Study Comparing Talquetamab in Combination with Daratumumab (SC) and Pomalidomide (Tal-DP) or Talquetamab (SC) in combination with Daratumumab SC (Tal-D) versus Daratumumab SC, Pomalidomide and Dexamethasone (DPd), in Participants With Relapsed or Refractory Multiple Myeloma who Have Received at Least 1 Prior Line of Therapy

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This study has been transitioned to CTIS with ID 2023-503467-41-00 check the CTIS register for the current data. The purpose of the study is to compare the efficacy of talquetamab subcutaneous(ly) (SC) in combination with daratumumab SC and...

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

Summary

ID

NL-OMON53729

Source
ToetsingOnline

Brief title
MonumenTAL-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: de opdrachtgever

Intervention

Keyword: Multiple Myeloma, Refractor, Relapsed, Talquetamab

Outcome measures

Primary outcome

Progression-Free Survival (PFS)

PFS is defined as time from the date of randomization to the first

documentation of disease progression, or death due to any cause, whichever is

reported first.

Secondary outcome

Overall Response (Partial Response [PR] or Better)

Overall response (PR or better) is defined as percentage of participants who

have a PR or better per International Myeloma Working Group (IMWG) criteria.

Very Good Partial Response (VGPR) or Better Rate

VGPR or better rate is defined as the percentage of participants who achieve a

VGPR or better according to IMWG response criteria.

Complete Response (CR) or Better Rate

CR or better rate is defined as the percentage of participants who achieve CR or better according to IMWG response criteria.

Overall Minimal Residual Disease (MRD) Negative CR

MRD-negative CR is defined as proportion of participants with CR or stringent CR who achieve MRD negativity at a threshold of 10^-5 at any timepoint after the first dose of study drug and before disease progression or start of subsequent antimyeloma therapy.

Overall Survival (OS)

OS is defined as the time from the date of randomization to the date of the participant's death.

Progression-free Survival on Next-line Therapy (PFS2)

PFS2 is defined as the time interval between the date of randomization and date of event, which is defined as progressive disease as assessed by investigator on the first subsequent line of antimyeloma therapy, or death from any cause, whichever occurs first.

Time to Next Therapy (TTNT)

TTNT is defined as the time from randomization to the start of subsequent antimyeloma treatment.

Number of Participants with Adverse Events (AEs)

An AE is any untoward medical occurrence in a participant participating in a clinical study that does not necessarily have a causal relationship with the pharmaceutical/biological agent under study.

Number of Participants with AEs by Severity

Severity will be graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE).

Serum Concentrations of Talquetamab

Serum concentrations of talquetamab will be reported.

Serum Concentrations of Daratumumab

Serum concentrations of daratumumab will be reported.

Number of Participants with Presence of Anti-Drug Antibodies (ADAs) to Talquetamab

Number of participants with presence ADAs to talquetamab will be reported.

Number of Participants With Presence of Anti-Drug Antibodies (ADAs) to Daratumumab

Number of participants with presence of ADAs to daratumumab will be reported.

Time to Worsening in Symptoms, Functioning, and Overall Health-Related Quality

of Life (HRQoL) as Assessed by Multiple Myeloma Symptom and Impact Questionnaire (MySIm-Q)

The MySIm-Q is a disease-specific PRO assessment complementary to the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core-30 item (EORTC-QLQ-C30).

Time to Worsening in Symptoms, Functioning, and HRQoL as Assessed by PROMIS Short Form Version 2.0 -Physical Functioning 8c

The Patient-reported Outcomes Measurement Information System (PROMIS) Short Form Version 2.0 -Physical Function 8c is an 8-item fixed--length short form derived from the PROMIS Physical Function item bank.

Time to Worsening in Symptoms, Functioning, and HRQoL as Assessed by EORTC-QLQ-C30

Time to worsening in symptoms, functioning, and HRQoL as assessed by EORTC-QLQ-C30 will be reported.

Time to Worsening in Symptoms, Functioning, and HRQoL as Assessed by PRO-CTCAE

The National Cancer Institute's (NCI) PRO-CTCAE is an item library of common AEs experienced by people with cancer that are appropriate for self-reporting of treatment tolerability.

Time to Worsening in Symptoms, Functioning, and HRQoL as Assessed by EuroQol Five Dimension Questionnaire 5-Level (EQ-5D-5L)

The EQ-5D-5L is a generic measure of health status. For purposes of this study, the EQ-5D-5L will be used to generate utility scores for use in cost-effectiveness analyses.

Time to Worsening in Symptoms, Functioning, and HRQoL as Assessed by Patient Global Impression - Severity (PGI-S)
The PGI-S will be used as an anchor, external criterion, to determine meaningful change in scores for the MySIm-Q and PROMIS SF PF 8c in this population.

Change From Baseline in Symptoms, Functioning, and Overall HRQoL as Assessed by Multiple Myeloma Symptom and Impact Questionnaire (MySIm-Q)
The MySIm-Q is a disease-specific PRO assessment complementary to the EORTC-QLQ-C30.

Change from Baseline in Symptoms, Functioning, and HRQoL as Assessed by PROMIS Short Form Version 2.0 -Physical Functioning 8c
The Patient-reported Outcomes Measurement Information System (PROMIS) Short Form Version 2.0 -Physical Function 8c is an 8-item fixed-length short form derived from the PROMIS Physical Function item bank.

Change from Baseline in Symptoms, Functioning, and HRQoL as Assessed by EORTC-QLQ-C30
Time to worsening in symptoms, functioning, and HRQoL as assessed by

EORTC-QLQ-C30 will be reported.

Change from Baseline in Symptoms, Functioning, and HRQoL as Assessed by PRO-CTCAE

The National Cancer Institute's (NCI) PRO-CTCAE is an item library of common AEs experienced by people with cancer that are appropriate for self-reporting of treatment tolerability.

Change from Baseline in Symptoms, Functioning, and HRQoL as Assessed by EuroQol Five Dimension Questionnaire 5-Level (EQ-5D-5L)

The EQ-5D-5L is a generic measure of health status. For purposes of this study, the EQ-5D-5L will be used to generate utility scores for use in cost-effectiveness analyses.

Change from Baseline in Symptoms, Functioning, and HRQoL as Assessed by Patient Global Impression - Severity (PGI-S)

The PGI-S will be used as an anchor, external criterion, to determine meaningful change in scores for the MySIm-Q and PROMIS SF PF 8c in this population.

Study description

Background summary

Multiple myeloma is a malignant plasma cell disorder that accounts for approximately 10 percent (%) of all hematologic cancers, making it the second

most common hematologic malignancy. Overall rationale of study is that combination treatments of talquetamab, daratumumab, pomalidomide and dexamethasone may lead to enhanced clinical responses in treatment of relapsed or refractory multiple myeloma through multiple mechanisms of action.

Study objective

This study has been transitioned to CTIS with ID 2023-503467-41-00 check the CTIS register for the current data.

The purpose of the study is to compare the efficacy of talquetamab subcutaneous(ly) (SC) in combination with daratumumab SC and pomalidomide (Tal-DP) and talquetamab SC in combination with daratumumab SC (Tal-D), respectively, with daratumumab in combination with pomalidomide and dexamethasone (DPd).

Study design

The study is divided into 3 phases: screening, treatment (until confirmed progressive disease, death, intolerable toxicity, withdrawal of consent, or end of the study, whichever occurs first), and posttreatment follow-up (until death, withdrawal of consent, loss to follow-up, or end of the study, whichever occurs first). Efficacy, safety (physical examinations, neurologic examinations, Eastern Cooperative Oncology Group [ECOG] performance status, clinical laboratory tests, vital signs, and AE monitoring), pharmacokinetics (PK), immunogenicity, and biomarkers will be assessed at specified time points. Total duration of study will be up to 6 years 6 months.

Intervention

Arm A: Talquetamab Subcutaneous (SC) in Combination With Daratumumab SC and Pomalidomide (Tal-DP) - Participants will receive talquetamab and daratumumab as SC injections; pomalidomide will be self-administered as a single dose orally; dexamethasone may be given orally or intravenously as a pre-treatment medication and study drug.

Arm B: Daratumumab in Combination With Pomalidomide and Dexamethasone (DPd) - Participants will receive daratumumab as SC injection; pomalidomide will be self-administered as a single dose orally; dexamethasone may be given orally or intravenously as a pre-treatment medication and study drug.

Arm C: Talquetamab SC in Combination With Daratumumab SC (Tal-D) - Participants will receive talquetamab and daratumumab as injection SC injection; dexamethasone may be given orally or intravenously as a pre-treatment medication and study drug.

Study burden and risks

The following adverse reactions have been observed with administration of talquetamab to patients at various doses, either alone or in combination with other drugs:
Occur very frequently: Cytokine inflammatory response, Fever, Skin problems, Skin rash, Nail problems, Dysgeusia (altered taste), Dry mouth, Dysphagia (difficulty swallowing) , Weight loss, Upper respiratory tract infection, Viral infections & Neutropenia (low white blood cell count).

Occur frequently: Palmar-plantar erythrodysesthesia syndrome (hand-foot syndrome), Stomatitis (sore mouth), Pneumonia, Febrile neutropenia (low white blood cell count with fever) , Immuno-effector cell-associated neurotoxicity syndrome (ICANS) , Encephalopathy (abnormal brain function).

Collection of blood: the subject may experience bruising or irritation at the site where the needle enters the skin. Some patients may faint and, in rare cases, get an infection.
Ecg (electrocardiogram): There is usually no risk associated with undergoing an ecg. The stickers may pull on the subject's skin or cause redness or itching.
Bone marrow aspirate: During and after the procedure, the subject may experience pain and discomfort. There is also a risk of infection and bleeding at that site. The subject may also have an allergic reaction to the anesthetic.
MRI scan: There are no known risks or side effects of an MRI scan. If a contrast agent is used, the investigator will inform the subject of possible side effects or an allergic reaction.
CT scan: CT scans emit some radiation, so there is a small risk of causing cancer and other conditions. Each individual scan carries a small risk.
Spirometry test: There are generally few complications that can occur during or after a spirometry test. Immediately after the test is done, the subject may feel a little dizzy or short of breath.

Contacts

Public
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NL
Scientific
Janssen-Cilag

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Breda 4837 DS
NL

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: a) Multiple myeloma diagnosis according to the International Myeloma Working Group (IMWG) diagnostic criteria and b) Measurable disease at screening as defined by any of the following: i) Serum M-protein level greater than or equal to (>=) 0.5 grams per deciliter (g/dL) (central laboratory); ii) Urine M-protein level >= 200 milligram (mg)/24 hours (central laboratory); iii) Light chain multiple myeloma without measurable M-protein in the serum or the urine: serum immunoglobulin free light chain >= 10 milligram per deciliter (mg/dL) (central laboratory), and abnormal serum immunoglobulin kappa lambda free light chain ratio
- Relapsed or refractory disease as defined by: i) Relapsed disease is defined as an initial response to prior treatment, followed by confirmed progressive disease by IMWG criteria greater than (>) 60 days after cessation of treatment; ii) Refractory disease is defined as less than (<) 25 percent (%) reduction in monoclonal paraprotein (M-protein) or confirmed progressive disease by IMWG criteria during previous treatment or less than or equal to (<=) 60 days after cessation of treatment.
- Received at least 1 prior line of antimyeloma therapy including a proteasome inhibitor (PI) and lenalidomide. Participants who have received only 1 prior line of antimyeloma therapy must be considered lenalidomide-refractory (that is, have demonstrated progressive disease by IMWG criteria on or within 60 days of completion of lenalidomide-containing regimen). Participants who have received >=2 prior lines of antimyeloma therapy must be considered lenalidomide exposed
- Documented evidence of progressive disease based on investigator*s

determination of response by the IMWG criteria on or after their last regimen
- Have an Eastern Cooperative Oncology Group (ECOG) performance status score of 0, 1, or 2 at screening and immediately prior to the start of administration of study treatment

Exclusion criteria

- Contraindications or life-threatening allergies, hypersensitivity, or intolerance to study drug excipients
- Disease is considered refractory to an anti-cluster of differentiation 38 (CD38) monoclonal antibody as defined per IMWG consensus guidelines (progression during treatment or within 60 days of completing therapy with an anti-CD38 monoclonal antibody)
- Received prior pomalidomide therapy
- A maximum cumulative dose of corticosteroids to >=140 milligrams (mg) of prednisone or equivalent within 14-day period before the first dose of study drug
- Known active central nervous system (CNS) involvement or exhibits clinical signs of meningeal involvement of multiple myeloma. If either is suspected, negative whole brain magnetic resonance imaging (MRI) and lumbar cytology are required
- Plasma cell leukemia (per IMWG criteria) at the time of screening, Waldenström's macroglobulinemia, polyneuropathy, organomegaly, endocrinopathy, M-protein, and skin changes (POEMS syndrome), or primary amyloid light chain amyloidosis

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):	14-03-2023
Enrollment:	25
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Daratumumab
Generic name:	Daratumumab
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Dexamethasone
Generic name:	Dexamethasone
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Pomalidomide
Generic name:	Pomalidomide
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Talquetamab
Generic name:	Talquetamab
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	23-07-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-09-2022

Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-12-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-12-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-04-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-08-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-08-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	13-11-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-03-2024
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	27-03-2024
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	CTIS2023-503467-41-00
EudraCT	EUCTR2021-000202-22-NL
CCMO	NL81800.056.22