A Phase 3 Study Comparing Daratumumab, Lenalidomide, and Dexamethasone (DRd) vs Lenalidomide and Dexamethasone (Rd) in Subjects with Previously Untreated Multiple Myeloma who are Ineligible for High Dose Therapy

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The primary objective is to compare the efficacy of daratumumab when combined with lenalidomide and dexamethasone (DRd) to that of lenalidomide and dexamethasone (Rd), in terms of progression-free survival (PFS) in subjects with newly diagnosed...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Haematological disorders NEC
Study type	Interventional

Summary

ID

NL-OMON54750

Source
ToetsingOnline

Brief title
MMY3008 MAIA

Condition

- Haematological disorders NEC
- Miscellaneous and site unspecified neoplasms benign

Synonym

bone marrow cancer, Kahler disease

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Multiple Myeloma, Randomized, Untreated

Outcome measures

Primary outcome

The primary endpoint is PFS, which is defined as the duration from the date of randomization to either progressive disease, or death, whichever occurs first. Disease progression will be determined according to the IMWG criteria.

Secondary outcome

Time to disease progression (TTP) is defined as the time from the date of randomization to the date of first documented evidence of PD, as defined in the IMWG criteria. For subjects who have not progressed, data will be censored at the date of the disease evaluation before the start of any subsequent anti-myeloma therapy.

*

CR rate, defined as the percentage of subjects achieving CR, as defined:

* -Negative immunofixation of serum and urine, and

* -Disappearance of any soft tissue plasmacytomas, and

* -<5% plasma cells (PCs) in bone marrow

* -For those subjects with negative serum M-protein quantitation by

electrophoresis (SPEP) and suspected daratumumab interference on immunofixation, a reflex assay using anti-idiotype antibody will be utilized to confirm daratumumab interference and rule out false positive immunofixation. Patients who have confirmed daratumumab interference, but meet all other clinical criteria for CR or sCR, will be considered CR/sCR.

MRD negativity rate, defined as the proportion of subjects assessed as MRD negative, at any timepoint
after the date of randomization.

Progression-free Survival on Next line of Therapy (PFS2), defined as the time from randomization to progression on the next line of treatment or death, whichever comes first. Disease progression will be based on investigator judgment. For those subjects who are still alive and not yet progressed on the next line of treatment, they will be censored on the last date of follow-up.

Overall survival (OS), measured from the date of randomization to the date of the
subject*s death. If the subject is alive or the vital status is unknown, then the subject*s data will be
censored at the date the subject was last known to be alive.

*

Time to next treatment, defined as the time from randomization to the start of the next-line treatment.

sCR rate, defined as the percentage of subjects achieving CR in addition to having a normal free light
chain (FLC) ratio and an absence of clonal cells in bone marrow by immunohistochemistry,
immunofluorescence, 2-4 color flow cytometry

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Overall response rate (ORR), defined as the proportion of subjects who achieve CR or PR, according to the IMWG criteria, during or after the study treatment.

*

Proportion of subjects who achieve VGPR or better, defined as the proportion of subjects achieving VGPR and CR (including sCR) according to the IMWG criteria during or after the study treatment at the time of data cutoff.

Time to response, defined as the time between the randomization and the first efficacy evaluation that
the subject has met all criteria for PR or better. For subjects without response, data will be censored
either at the date of progressive disease or, in the absence of progressive disease, at the last disease
evaluation before the start of subsequent anti-myeloma therapy.

*

Duration of response, calculated from the date of initial documentation of a response (CR or PR) to the date of first documented evidence of progressive disease, as defined in the IMWG criteria. For subjects who have not progressed,

data will be censored at the last disease evaluation before the start of any

subsequent anti-myeloma therapy.

To evaluate clinical efficacy of DRd in high risk molecular subgroups compared

to Rd alone.

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To evaluate the impact of DRd compared to Rd on patient-reported perception of

global health.

Study description

Background summary

Multiple myeloma is a heterogeneous disease, with a course that varies on the basis of both disease- and host-related factors (eg, age, renal function, stage, chromosomal abnormalities). Multiple myeloma causes significant morbidity and mortality.
For those not considered suitable for high-dose chemotherapy and ASCT, longer-term treatment with multi-agent combinations including alkylators, high-dose steroids, and novel agents are currently considered as standards of care.

Study objective

The primary objective is to compare the efficacy of daratumumab when combined with lenalidomide and dexamethasone (DRd) to that of lenalidomide and dexamethasone (Rd), in terms of progression-free survival (PFS) in subjects with newly diagnosed myeloma who are not candidates for high dose chemotherapy and autologous stem cell transplant

Study design

This is a randomized, open-label, active controlled, parallel-group, multicenter study

Intervention

Daratumumab (16 mg/kg) will be administered by IV infusion to subjects in Arm B initially once every week for 8 weeks; then once every other week for 16 weeks; thereafter once every 4 weeks until documented progression, unacceptable toxicity, or study end.
Lenalidomide will be self-administered at a dose of 25 mg PO each day on Days 1 through 21 of each 28 day cycle.
Dexamethasone (or equivalent in accordance with local standards) will be administered at a total dose of 40 mg weekly.

Study burden and risks

The primary hypothesis of this study is that daratumumab in combination with Rd will prolong PFS as compared with Rd alone in subjects with newly diagnosed multiple myeloma who are ineligible for high dose chemotherapy and autologous stem cell transplant.

Contacts

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Adults (18-64 years)

Inclusion criteria

Participant must have documented multiple myeloma and measurable disease defined as: 1) monoclonal plasma cells in the bone marrow greater than or equal to (>=) 10 percent (%) or presence of a biopsy proven plasmacytoma; 2) measurable disease as defined by any of the following: (a) immunoglobulin (Ig) G myeloma (serum monoclonal paraprotein [M-protein] level >=1.0 gram/deciliter [g/dL] or urine M-protein level >=200 milligram[mg]/24 hours[hrs]; or (b) IgA, IgM, IgD, or IgE multiple myeloma (serum M-protein level >=0.5 g/dL or urine M-protein level >=200 mg/24 hrs); or (c) light chain multiple myeloma (serum immunoglobulin free light chain >=10 mg/dL and abnormal serum immunoglobulin kappa lambda free light chain ratio), - Participant must have an Eastern Cooperative Oncology Group (ECOG) performance status score of 0, 1, or 2 - Participants who are newly diagnosed and not considered for high-dose chemotherapy due to: being age >=65 years; or participants less than (<) 65 years with presence of important comorbid condition(s) likely to have a negative impact on tolerability of high dose chemotherapy with stem cell transplantation. Sponsor review and approval of participants below 65 years of age is required before randomization, - Women of childbearing potential must commit to either abstain continuously from sexual intercourse or to use 2 methods of reliable birth control simultaneously as deemed appropriate by the Investigator. Contraception must begin 4 weeks prior to dosing, - Man, who is sexually active with a woman of child-bearing potential and has not had a vasectomy, must agree to use an adequate contraception method as deemed appropriate by the Investigator, and must also agree to not donate sperm during the study and for 4 weeks after last dose of lenalidomide and 4 months after last dose of daratumumab

Exclusion criteria

Participant has a diagnosis of primary amyloidosis, monoclonal gammopathy of undetermined significance (presence of serum M-protein <3 g/dL; absence of lytic bone lesions, anemia, hypercalcemia, and renal insufficiency related to the M-protein), or smoldering multiple myeloma (asymptomatic multiple myeloma with absence of related organ or tissue impairment end organ damage), - Participant has a diagnosis of Waldenström*s disease, or other conditions in which IgM M protein is present in the absence of a clonal plasma cell infiltration with lytic bone lesions, - Participant has a history of malignancy (other than multiple myeloma) within 5 years before the date of randomization (exceptions are squamous and basal cell carcinomas of the skin and carcinoma in situ of the cervix, or malignancy that is considered cured with minimal risk of recurrence within 5 years), - Participant has prior or current systemic therapy or SCT for multiple myeloma, with the exception of an emergency use of a short

course (equivalent of dexamethasone 40 mg/day for a maximum 4 days) of corticosteroids before treatment, - Participant has had radiation therapy within 14 days of randomization, - Participant has known chronic obstructive pulmonary disease (COPD) (defined as a forced expiratory volume in 1 second [FEV1] <60% of predicted normal), persistent asthma, or a history of asthma within the last 2 years (intermittent asthma is allowed).
Participants with known or suspected COPD or asthma must have a FEV1 test during Screening
- Participant is known to be seropositive for history of human immunodeficiency virus (HIV) or known to have active hepatitis B or hepatitis C

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:	Recruitment stopped
Start date (anticipated):	10-03-2015
Enrollment:	13
Type:	Actual

Medical products/devices used

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

Brand name:	JNJ-54767414
Generic name:	Daratumumab
Product type:	Medicine
Brand name:	Revlimid
Generic name:	Lenalidomide
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	19-02-2015
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	12-05-2015
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	26-05-2015
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	17-07-2015
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	09-10-2015
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	13-10-2015
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	23-12-2015

Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	12-01-2016
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	11-04-2016
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	08-06-2016
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	09-08-2016
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	16-08-2016
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	24-01-2017
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	22-02-2017
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	22-03-2017
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	23-08-2017

Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	23-03-2018
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	16-04-2018
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	29-08-2018
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	27-09-2018
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	14-05-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	22-05-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	31-07-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	06-08-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	25-03-2020

Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	26-03-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	28-04-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	07-06-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	10-10-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	28-10-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	02-04-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	12-05-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	18-07-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	25-07-2022

Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	04-03-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	21-03-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	05-05-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	01-06-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	24-01-2024
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	09-02-2024
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)

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
EudraCT	EUCTR2014-002273-11-NL
ClinicalTrials.gov	NCT02252172
CCMO	NL52584.028.15