An Open-Label, 2-Arm, Multicenter, Randomized Phase 3 Study To Evaluate The Efficacy And Safety of Elranatamab (PF-06863135) + Daratumumab + Lenalidomide Versus Daratumumab + Lenalidomide + Dexamethasone in Transplant-Ineligible Participants With Newly-Diagnosed Multiple Myeloma

Published: 07-03-2023
Last updated: 16-11-2024

This study has been transitioned to CTIS with ID 2024-514139-50-00 check the CTIS register for the current data. Part 1PrimaryTo assess dose limiting toxicities (DLTs) of EDR to select an RP3D for the combination to be used in Part 2 of this study….

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Plasma cell neoplasms
Study type	Interventional

Summary

ID

NL-OMON53326

Source
ToetsingOnline

Brief title
MagnetisMM-6

Condition

- Plasma cell neoplasms

Synonym
multiple myeloma

Research involving
Human

Sponsors and support

Primary sponsor: Pfizer
Source(s) of monetary or material Support: Pfizer Inc

Intervention

Keyword: Elranatamab, Multiple Myeloma, Phase 3, Transplant-Ineligible Participants

Outcome measures

Primary outcome

Part 1

DLTs during the DLT observation period:

• For all Dose Level (DLs) except DL F: From the first priming dose of

elranatamab in the 2 Step-Up Priming Dose Period until 28 days (± visit

windows) from the first administration of the EDR combination.

• For DL F: 28 days (± visit windows) from the day of the first full dose of

elranatamab (76 mg) in combination with daratumumab (D) and lenalidomide (R).

Part 2

• Sustained MRD negativity rate (central lab) for at least 12 months per IMWG

as assessed via next generation sequencing (NGS)

• PFS by blinded independent central review (BICR) per IMWG

Secondary outcome

Part 1

• Adverse events (AEs) as characterized by type, frequency, severity (as graded by National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE v5.0), timing, seriousness, and relationship to study treatment. Severity of cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) will be graded according to American Society for Transplantation and Cellular Therapy (ASTCT) criteria.

• Laboratory abnormalities as characterized by type, frequency, severity (as graded by NCI CTCAE v5.0), and timing.

• Objective response rate (ORR) and complete response rate (CRR), per International Myeloma Working Group (IMWG) response criteria as determined by investigator.

• Time to event endpoints: time to response (TTR), duration of response (DOR), duration of complete response (DOCR) and progression-free survival (PFS) per IMWG response criteria as determined by investigator, and overall survival (OS);

• Minimal residual disease (MRD) negativity rate (central laboratory) per IMWG sequencing criteria.

• Predose and post dose concentrations of elranatamab

• Anti-drug antibodies (ADAs) and neutralizing antibodies (Nabs) against elranatamab

• Predose concentrations of daratumumab and lenalidomide

Part 2

Key Secondary:

• OS

Secondary:

• Overall MRD negativity rate per IMWG

• Duration of MRD negativity per IMWG

• PFS and progression-free survival on next line of therapy (PFS2) by investigatorper IMWG

• ORR, CRR, TTR, DOR, and DOCR by BICR per IMWG

• AEs as characterized by type, frequency, severity (as graded by NCI CTCAE v5.0), timing, seriousness, and relationship to study treatment.

The severity of CRS and ICANS will be graded according to ASTCT criteria ((Lee et al, 2019).

• Laboratory abnormalities as characterized by type, frequency, severity (as graded by NCI CTCAE v5.0), and timing.

• Predose and post dose concentrations of elranatamab

• ADAs and NAbs against elranatamab

• MY20European Organisation for Research and Treatment of Cancer (EORTC) Core Quality of Life Questionnaire (QLQ-C30) and Myeloma Module 20 (MY20

Study description

Background summary

This is an open-label, 2-arm, multicenter, randomized Phase 3 study to evaluate the efficacy and safety of elranatamab (PF-06863135) + daratumumab + lenalidomide (EDR) versus daratumumab + lenalidomide + dexamethasone (DRd) in transplant-ineligible participants with newly-diagnosed multiple myeloma (NDMM). The randomized Phase 3 part of the study (Part 2 in participants with NDMM) will be preceded by Part 1 to select the optimal recommended Phase 3 dose (RP3D) of EDR and to assess the safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD), and preliminary efficacy of elranatamab in combination

with daratumumab and lenalidomide in participants with NDMM and relapsed/refractory multiple myeloma (RRMM). Part 1 of the study will inform the RP3D of elranatamab and lenalidomide to be used in combination with daratumumab in Part 2 of the study. Participants with RRMM will have received 1 to 2 prior lines of therapy and will not be refractory to an anti-CD38 monoclonal antibody (mAb). Part 2 of the study will evaluate whether EDR can provide superior clinical benefit compared to standard of care therapy (DRd) in transplant-ineligible participants with NDMM. Participants with NDMM will be transplant-ineligible as defined by age >=65 years or transplant-ineligible as defined by age <65 years with comorbidities impacting the possibility of transplant.

Study objective

This study has been transitioned to CTIS with ID 2024-514139-50-00 check the CTIS register for the current data.

Part 1
Primary
To assess dose limiting toxicities (DLTs) of EDR to select an RP3D for the combination to be used in Part 2 of this study.

Secondary
• To evaluate the overall safety profile of EDR to select an RP3D for the combination to be used in Part 2 of this study.
• To evaluate the efficacy of EDR to select an RP3D for the combination to be used in Part 2 of this study.
• To evaluate the PK of elranatamab when used in combination with daratumumab and lenalidomide
• To evaluate the immunogenicity of elranatamab when used in combination with daratumumab and lenalidomide
• To evaluate the PK of daratumumab and lenalidomide when used in combination with elranatamab

Part 2
Primary
• To compare the efficacy of EDR (Arm A) vs DRd (Arm B) as measured by MRD status and PFS

Key Secondary
• To compare the efficacy of EDR (Arm A) vs DRd (Arm B) as measured by OS

Secondary
• To evaluate the efficacy of Arm A and Arm B
• To determine the safety and tolerability of elranatamab when used in combination with daratumumab + lenalidomide
• To evaluate the PK of elranatamab when used in combination with daratumumab +

lenalidomide
• To evaluate the immunogenicity of elranatamab when used in combination with daratumumab and lenalidomide
• To evaluate the impact of treatment on participant health-related quality of life (HRQoL)

Study design

Study C1071006 is a Phase 3, open-label, 2-arm, multicenter, randomized study to evaluate the efficacy and safety of experimental therapy in Arm A (EDR) versus control therapy in Arm B (DRd) in transplant-ineligible participants with NDMM (See Figure 1 of the protocol). The randomized Phase 3 part of the study (Part 2 in participants with NDMM) will be preceded by Part 1 to select the optimal RP3D of EDR and to assess the safety, tolerability, PK, PD, and preliminary efficacy of elranatamab in combination with daratumumab and lenalidomide in participants with NDMM and RRMM.
In Part 2, approximately 870 participants will be enrolled using a 1:1 randomization ratio to the experimental Arm A (EDR) or the control Arm B (DRd), stratified by Revised International Staging System (R-ISS) (I/II vs III), region (North America (NA) vs Europe (EU) vs Rest of World (ROW)) and age (< 75 vs >=75 years old).

Intervention

The design of Part 1 allows evaluation of the safety and tolerability of 3 dose schedules (76 mg QW, 76 mg Q2W, 76 mg Q4W) of elranatamab when used in combination with daratumumab and with up to 2 doses of lenalidomide (15 mg, 25 mg) to allow selection of an appropriate RP3D for Part 2 of the study.
Part 1 of the study is composed of a dose-finding phase and an expansion phase. The Sponsor, together with participating investigators, will evaluate the available safety data after at least 3 evaluable participants have been enrolled in a dose level and each participant has been followed during the DLT period. The RP3D of EDR to be further evaluated in Part 2 will be determined by the Sponsor based on an assessment of the totality of the available data including safety, tolerability, PK, PD and preliminary anti-myeloma activity
Study interventions are outlined in Table 9 of the protocol.
Once the RP3D is identified in Part 1, participants will be randomized into experimental Arm A (EDR) and control Arm B (DRd) for Part 2

Study burden and risks

The study is expected to last up to 6 years in total. Patients will continue to receive the study drug until tests show that the multiple myeloma has worsened, the study doctor thinks patients are no longer benefiting from the study drug, patients have unacceptable side effects, the study ends, or patients choose to stop taking part in the study.

The study consists of a screening period, a treatment period and a follow-up period.

Study treatment is broken up into 28-day cycles. During the treatment period, patients assigned to Treatment Arm A will be hospitalized 2 days for the first elranatamab administration (Day 1 and Day 2). A third day of hospitalization is required on Day 4 of C0. This study will require patients to visit the study doctor every week for the first 6 months of therapy, and then possibly every 2 weeks thereafter, to undergo study procedures. Study visits will last about 30 minutes to 3 hours.

The following procedures will be done no matter which arm patients will be assigned to:
• Patients will have an electrocardiogram (ECG).
• Patients will provide blood samples for laboratory and safety testing.
• Patients will give urine samples to measure how your cancer is responding to the study drug.
• For women of childbearing potential, urine pregnancy tests will be taken.
• Scans of patients' body will be made to measure how their cancer is responding to the study drug.
• Gene testing: Samples of patients' saliva, blood and bone marrow aspirates will be collected for testing genes that may be related to their cancer.

The study doctor may ask patients to come in for additional tests, procedures and assessments, if necessary.

During the follow-up period, patients will have an end of treatment visit within 14 days from last dose and then a follow-up visit approximately 1 month after the last dose of study drug. Thereafter, depending on their response to the study drug, they will have visits approximately every month to continue to monitor their disease, or the study team will contact them by telephone about every 3 months to ask them about their health and medications until the sponsor determines the study is complete, which may take many years, or until they withdraw their consent to be contacted. The study team may ask patients to come back for a visit to check on their well-being. If they decide they do not want to participate in the study procedures, information about their survival status will be collected.

Patients' participation may help future patients by increasing our understanding of elranatamab in treating multiple myeloma. It is possible that patients' condition or health may improve, worsen, or stay the same.

Taking part in the study can have these cons:
o Patients may experience the side effects or adverse effects of the study drug, as described in Section 6.
o There may be some discomfort from the measurements during the study. For example: taking a blood sample can be a little painful. Or patients could get a

bruise as a result.
o Taking part in the study will cost patients extra time.
o Patients need to be hospitalized for longer than usual.
o Patients have to comply with the study agreements.

Risks of study drugs are outlined in the Risk Section of the Informed Consent Document

Risks of study procedures outlined in the Informed Consent Document are summarized below:
• Bone marrow aspirate/biopsy: The risks of a bone marrow aspirate/biopsy can include bleeding, bruising, pain, nerve damage, and infection. To reduce these risks, the site of the sample collection will be numbed, and sterile techniques will be used. The numbing drug used may cause a burning feeling, rash, allergic reaction, redness or soreness where patients receive the shot.
• Blood draw: A blood draw may cause faintness, inflammation of the vein, pain, bruising, or bleeding at the site of puncture. You may feel dizzy, or you may faint. There is also a slight chance of infection.
• Blood Pressure: The test is usually painless, however as the blood pressure cuff squeezes patients arm while it inflates it may be uncomfortable. This feeling lasts only a few seconds.
• COVID-19 testing: Since the nasal swab will be going from your nostril to just about where your ear is, it can be uncomfortable. It may make patients gag or cough briefly. In some cases, people can get a nosebleed after the test.
• CT, PET-CT Scan: A CT scan exposes patients to a small dose of radiation, between 3.5 and 20.1 mSV. Although all radiation patients receive builds up over their lifetime, this amount of radiation should not create a significant risk to their health. Contrast dye is usually injected when patients get a CT scan. The contrast dye may cause pain or burning when it is injected and may worsen kidney function if patients already have kidney disease or who are dehydrated. The contrast dye may also cause an allergic reaction, which could be severe and life-threatening.
• Demographic Questions: While collection of demographic information does not expose patients to physical risk, collection of such information may result in a loss of their privacy if the information is lost or stolen.
• ECG: The risks from an ECG can include skin irritation and a rash from the gel that is used or from wearing or removing the sticky patches.
• Echocardiogram: Patients may feel some discomfort from the transducer being held very firmly against their chest.
• Health and Medication Questions: These questions may be sensitive in nature. Patients may refuse to answer any question that makes them feel uncomfortable. If patients have concerns after responding to these questions,they should tell the study doctor.
• MRI or magnetic resonance imaging: There are risks from an MRI if patients are pregnant or have one of the following, for example: an artificial heart valve, pacemaker, metal plate, pin, or other metallic objects in their body

(including from a gunshot or shrapnel). Patients may also become anxious from the loud noise or lying in a tight space without moving. The MRI scan does not cause any pain and does not expose patients to x-ray radiation.
• MUGA or multi-gated radionuclide angiography (scan using a radiotracer): The level of radioactivity produced by the tracer material and camera is extremely low and isn*t known to cause any short-term or long-term damage to patients body. It is possible to have an allergic reaction to the radioactive tracer material.
• Questionnaires: A questionnaire may contain questions that are sensitive in nature. Patients may refuse to answer any question that makes them feel uncomfortable.
• Study Diary: While collection of study diary information does not expose patients to physical risk, collection of such information may result in a loss of their privacy if the information contained in the study diary is lost or stolen.
• Testing of DNA and/or RNA: This may include analyzing all of patients genetic information (called *whole genome sequencing*). While collection of genetic information does not expose patients to physical risk, collection of such information may result in a loss of their privacy if their genetic information is lost or stolen.
• There is a very small chance that patients' genetic information could be misused by people not involved with the research, including to discriminate against them. However, steps are in place to prevent a particular result from being linked to patients and to prevent unauthorized people from even knowing genetic research was done.
• X-ray: Patients may be concerned about radiation exposure from chest X-rays, especially if they have them regularly, but the amount of radiation from an X-ray is low - even lower than what patients exposed to through natur

Contacts

Public
Pfizer

Rivium Westlaan 142
Capelle a/d IJssel 2909LD
NL
Scientific
Pfizer

Rivium Westlaan 142
Capelle a/d IJssel 2909LD
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Participants must meet the following inclusion criteria to be eligible for enrollment into the study. Criteria are for both Part 1 and Part 2 unless otherwise specified: Age and Sex: 1. Participant*s age >=18 years (or the minimum country specific age of consent if >18) at Visit 1 (Screening). Type of Participant and Disease Characteristics: 2. Diagnosis of multiple myeloma (MM) as defined according to IMWG criteria, Measurable disease based on IMWG criteria as defined by at least 1 of the following (as assessed by the central laboratory for Part 2): o Serum M-protein >=0.5 g/dL; o Urinary M-protein excretion >=200 mg/24 hours; o Involved Free Light Chain (FLC) >=10 mg/dL (>=100 mg/L) AND abnormal serum immunoglobulin kappa to lambda FLC ratio (<0.26 or >1.65). 3. Part 1 only: Participant with NDMM or RRMM. NDMM participant must be transplant-ineligible as defined by age >=65 years or transplant-ineligible as defined by age <65 years with comorbidities impacting the possibility of transplant. Participants with RRMM must have received 1-2 prior lines of MM therapy including at least one immunomodulatory drug (IMiD) and one proteasome inhibitor (PI). Part 2 only: Participant has NDMM and is transplant-ineligible as defined by age >=65 years or is transplant-ineligible as defined by age <65 years with comorbidities impacting the possibility of transplant.
4.Eastern Cooperative Oncology Group (ECOG) performance status <=2.
5. Adequate hepatic, renal, and bone marrow (BM) function absolute neutrophil count and [ANC], platelet count, hemoglobin).
6. Corrected serum calcium <=14 mg/dL (<=3.5 mmol/L), or free ionized calcium <=6.5 mg/dL (<=1.6 mmol/L).
7. Resolved acute effects of any prior therapy to baseline severity or CTCAE Grade <=1.

Exclusion criteria

Medical Conditions:
1. Smoldering MM
2. Monoclonal gammopathy of undetermined significance (MGUS)
3. Plasma cell leukemia
4. Waldenstro*ms Macroglobulinemia 5. Systemic light chain amyloidosis
6. Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal gammopathy, and Skin abnormalities (POEMS) Syndrome.
7. Impaired cardiovascular function or clinically significant cardiovascular diseases within 6 months prior to enrollment
8. Ongoing Grade 3 or higher peripheral sensory or motor neuropathy, history of Guillain-Barré syndrome (GBS) or GBS variants, or history of any Grade >3 peripheral motor polyneuropathy.
9. Active, uncontrolled bacterial, fungal, or viral infection, including (but not limited to) coronavirus disease 2019 (COVID-19) / severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), hepatitis B virus (HBV), hepatitis C virus(HCV), and known human immunodeficiency virus (HIV) or acquired immunodeficiency syndrome (AIDS)-related illness. Active infections must be resolved at least 21 days prior to enrolment.
Participants treated with systemic anti-infective agents within 28 days prior to enrolment are not eligible. Prophylactic use of systemic agents is permitted.

10. Any other active malignancy within 3 years prior to enrollment, except for adequately treated basal cell or squamous cell skin cancer, or carcinoma in situ, or Stage 0/1 with minimal risk of recurrence per investigator.
11. Participants with known or suspected hypersensitivity to the study interventions or any of their excipients.
12. Participants with known or suspected central nervous system (CNS) or clinical signs of myelomatous meningeal involvement.
13 Other surgical (including major surgery within 14 days prior to enrollment), medical or psychiatric conditions including recent (within the past year) or active suicidal ideation/behaviour or laboratory abnormality that may increase the risk of study participation or, in the investigator*s judgment, make the participant inappropriate for the study. • Active inflammatory gastrointestinal disease, chronic diarrhea, known diverticular disease or previous gastric resection or lap band surgery. Gastroesophageal reflux disease under treatment with proton pump inhibitors is allowed (assuming no drug interaction potential).

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):	24-07-2024
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	DARZALEX 1800 mg solution for injection
Generic name:	Daratumumab
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Dexamethasone 20 mg
Generic name:	Dexamethasone
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Elranatamab
Generic name:	Elranatamab
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Lenalidomide 10 mg
Generic name:	Lenalidomide
Registration:	Yes - NL outside intended use
Product type:	Medicine

Brand name:	Lenalidomide 5 mg
Generic name:	Lenalidomide
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	07-03-2023
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-05-2023
Application type:	First submission
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:	04-12-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-12-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-01-2024
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	

Date:	26-03-2024
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-03-2024
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	CTIS2024-514139-50-00
EudraCT	EUCTR2021-000803-20-NL
ClinicalTrials.gov	NCT05623020
CCMO	NL83523.056.23