Efficacy and tolerability of ixazomib, daratumumab and low dose dexamethasone (IDd) followed by ixazomib and daratumumab maintenance therapy until progression for a maximum of 2 years in unfit and frail newly diagnosed multiple myeloma patients; an open-label phase II trial

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This study aims to assess: - the efficacy of 9 cycles of ixazomib, daratumumab and low dose dexamethasone in newly diagnosed unfit and frail multiple myeloma patients. - the value of geriatric assessments to predict both feasibility and...

Ethische beoordeling	Positief advies
Status	Werving gestopt
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON23842

Bron
NTR

Verkorte titel
HOVON 143 MM

Aandoening

Multiple Myeloma, unfit or frail patients, Ixazomib, Daratumumab

Ondersteuning

Primaire sponsor: Stichting Hemato-Oncologie voor Volwassenen Nederland (HOVON)
Overige ondersteuning: HOVON; Millennium: The Takeda Oncology Company; Jansen Pharmaceutica

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

To determine the efficacy, defined as overall response rate (ORR; ≥ partial response (PR)), of 9 cycles of ixazomib, daratumumab and low dose dexamethasone

Toelichting onderzoek

Achtergrond van het onderzoek

Study design: Prospective, multicenter, open-label phase II trial

Patient population: Previously untreated symptomatic patients with Multiple Myeloma age > 18 years, unfit and frail

Participating countries: The Netherlands, Belgium

Doel van het onderzoek

This study aims to assess:
- the efficacy of 9 cycles of ixazomib, daratumumab and low dose dexamethasone in newly diagnosed unfit and frail multiple myeloma patients.

- the value of geriatric assessments to predict both feasibility and efficacy

- the prognostic value of (PET)-CT to predict efficacy

Onderzoeksopzet

- At entry: before start of treatment (periperheral blood lab values within 2 weeks prior to start, bone marrow within 4 weeks and skeletal survey within 2 months)

-During induction therapy after 1, 2, 3, 5 ,7 and 9 cycles (just before start of the next cycle)

-During maintenance therapy after every maintenance cycle

-When patient is taken off protocol treatment

-During follow up every 8 weeks until second progression and every 6 months thereafter.

Onderzoeksproduct en/of interventie

The patients receive nine courses IxaDaraIDd ixazomib treatment (= ixazomib, daratumumab and low dose dexamethasone). (Ixazomib is the generic name Ninlaro; daratumumab is the generic name Darzalex). Each course lasts four weeks. The total duration of the treatment is 9 months (9 cycles of 4 weeks). Following induction therapy the patients will receive ixazomib and daratumumab as a maintenance therapy for a maximum of 2 years.

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

• Previously untreated patients with a confirmed diagnosis of multiple myeloma according to

IMWG criteria (see appendix A);

• Measurable disease according to the IMWG criteria;
(If plasmacytoma is the only measurable parameter, the patient is not allowed to be included in the study, because of difficult response evaluation)

• Patients who are either unfit or frail according to the IMWG criteria;

• Age 18 years or older;

• Absolute neutrophil count (ANC) ≥ 1.0 x109/l and platelet count ≥ 75x109/l , unless related to bone marrow infiltration by malignant plasma cells;

Platelet transfusions and G-CSF to help patients meet eligibility criteria are not allowed;

• Written informed consent, including consent for additional bone marrow and blood sampling and a skin biopsy (with the understanding that consent may be withdrawn by the patient at any time without consequences to future medical care);

• Patient is capable of giving informed consent;

• Negative pregnancy test at study entry (only for women of childbearing potential);

• Male patients and female patients of childbearing potential must agree to use adequate contraception from the time of signing the informed consent form through 90 days after the last dose of study drug

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

• Non-secretory MM;

• Plasma cell leukemia;

• Systemic Amyloid Light-chain (AL) amyloidosis;

• Central nervous system involvement;

• Known allergy to any of the study medications, their analogues, or excipients in the various formulations of any agent;

• Neuropathy, grade 1 with pain or grade ≥ 2;

• Severe cardiac dysfunction (NYHA classification III-IV, appendix D);

• Screening 12-lead ECG showing a baseline QT interval as corrected by Fridericia's formula (QTcF) >470 msec;

• Chronic obstructive pulmonary disease (COPD) with an Forced Expiratory Volume in 1 second (FEV1) < 50% of predicted normal. Note that FEV1 testing is required for patients suspected of having COPD and subjects must be excluded if FEV1 <50% of predicted normal;

• Moderate or severe persistent asthma within the past 2 years or currently uncontrolled asthma of any classification. (Note that subjects who currently have controlled intermittent asthma or controlled mild persistent asthma are allowed in the study);

• Significant hepatic dysfunction (total bilirubin ≥ 3 x ULN or transaminases ≥ 5 times normal level) except patients with Gilbert's syndrome as defined by > 80% unconjugated bilirubin;

• Creatinine clearance <20 ml/min or Calculated Glomerular Filtration Rate [ml/min/1.73m2] <20;

• Patients with active, uncontrolled infections;

• Patients known to be Human Immunodeficiency Virus (HIV)-positive;

• Known GI disease or GI procedure that could interfere with the oral absorption or tolerance of ixazomib including difficulty swallowing;

• Active malignancy other than MM requiring treatment or a malignancy that has been treated with chemotherapy currently affecting bone marrow capacity;

• Systemic treatment, within 14 days before the first dose of ixazomib, with strong CYP3A inducers (rifampin, rifapentine, rifabutin, carbamazepine, phenytoin, phenobarbital), or use of St. John's wort;

• Pre-treatment with cytostatic drug, immunomodulatory drugs (IMiDs) or proteasome inhibitors. Radiotherapy (provided the involved field is small and there are ≥ 7 days between radiotherapy and administration of ixazomib) or a short course of steroids (e.g. 4 day treatment of dexamethasone 40 mg/day or equivalent) are allowed;

• Major surgery within 14 days before enrollment;

• Any serious medical or psychiatric illness, or familial, sociological and geographical condition potentially hampering compliance with the study protocol and follow-up schedule;

• Participation in other clinical trials, including those with other investigational agents not included in this trial, within 30 days of the start of this trial and throughout the duration of this trial;

• Female patients who are lactating.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Anders
Toewijzing:	N.v.t. / één studie arm
Blindering:	Enkelblind
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	19-06-2017
Aantal proefpersonen:	132
Type:	Werkelijke startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Ethische beoordeling

Positief advies

Datum:	06-04-2017
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL6142
NTR-old	NTR6297
Ander register	EudraCT number : 2016-002600-90

Resultaten