# 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

No registrations found.

| | |
|---|---|
| **Ethical review** | Positive opinion |
| **Status** | Recruitment stopped |
| **Health condition type** | - |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON23842

**Source**
NTR

**Brief title**
HOVON 143 MM

**Health condition**

Multiple Myeloma, unfit or frail patients, Ixazomib, Daratumumab

### Sponsors and support

**Primary sponsor:** Stichting Hemato-Oncologie voor Volwassenen Nederland (HOVON)
**Source(s) of monetary or material Support:** HOVON; Millennium: The Takeda Oncology Company; Jansen Pharmaceutica

## Intervention

## Outcome measures

### Primary outcome

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

### Secondary outcome

- To determine the tolerability, defined as discontinuation rate due to treatment related toxicity, of 9 cycles of ixazomib, daratumumab and low dose dexamethasone

- To determine adverse events of CTCAE grade 2-4

- To determine complete response (CR) and very good partial response (VGPR) after 9 induction cycles

- To determine complete response (CR) and very good partial response (VGPR) on protocol

- To determine immunophenotypic complete response after 9 induction cycles

- To determine immunophenotypic complete response on protocol

- To determine the flow Minimal Residual Disease negative complete remission

- To determine the imaging plus flow MRD negative complete remission

- To determine progression free survival (PFS)

- To determine overall survival (OS)

- To determine efficacy of therapy determined as time to response and the time to best response

- To determine the effect of maintenance therapy with ixazomib and daratumumab in terms of improvement of response during maintenance

- To determine the tolerability of maintenance therapy, defined as discontinuation rate due to treatment related toxicity of ixazomib and daratumumab

- To determine time to next treatment

- To determine PFS2

- To evaluate quality of life (QoL)

# Study description

### Background summary

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

### Study objective

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

### Study design

- 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.

### Intervention

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.

# Contacts

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# Eligibility criteria

## Inclusion criteria

• 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

## Exclusion criteria

• 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.

# Study design

## Design

| | |
|---|---|
| Study type: | Interventional |
| Intervention model: | Other |
| Allocation: | Non controlled trial |
| Masking: | Single blinded (masking used) |
| Control: | N/A , unknown |

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 19-06-2017 |
| Enrollment: | 132 |

Type: Actual

### IPD sharing statement

**Plan to share IPD:** Undecided

## Ethics review

Positive opinion
Date: 06-04-2017

Application type: First submission

## 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 |
|---|---|
| NTR-new | NL6142 |
| NTR-old | NTR6297 |
| Other | EudraCT number : 2016-002600-90 |

## Study results