# Ixazomib citrate-thalidomide-low dose dexamethasone induction followed by maintenance therapy with ixazomib citrate or placebo in newly diagnosed multiple myeloma patients not eligible for autologous stem cell transplantation; a randomized phase II trial.

No registrations found.

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

## Summary

### ID

NL-OMON29252

**Source**
NTR

**Brief title**
HOVON 126 MM

**Health condition**

Multipel Myeloom, Ixazomib, elderly patients

### Sponsors and support

**Primary sponsor:** Stichting HOVON
**Source(s) of monetary or material Support:** Stichting HOVON
Millennium: The Takeda Oncology Company

## Intervention

## Outcome measures

### Primary outcome

Maintenance treatment

- Progression free survival (PFS) from randomization, defined as time from randomization to progression or death from any cause, whichever comes first

Induction treatment

- Response rate defined as sCR, CR, VGPR or PR

### Secondary outcome

- Safety and toxicity as defined by type, frequency and severity of adverse events as defined by the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE), version 4

- PFS from registration

- Overall survival (OS) from registration, measured until death from any cause. Patients alive will be censored at the date of last contact

- OS from randomization.

- Quality of response during maintenance, measured as improvement of response (from start maintenance till progression)

- Time to maximum response, defined as time from registration to maximum response

- Time to death from progression (after initial response), measured from time of first relapse/progression

- Time to next treatment

- PFS from the start of second line therapy

- Quality of life as defined by the EORTC QLQ-C30 and QLQ-MY20 definitions.

- Second Primary Malignancies

# Study description

### Background summary

Study design:
Prospective, multicenter, randomized double blind placebo controlled phase II

Patient population:
Previously untreated symptomatic patients with MM age > 66 years or patients < 65 years and ineligible for high dose therapy and peripheral stem cell transplantation

Participating countries:
The Netherlands, Denmark, Norway, Sweden

### Study objective

This study aims to assess the efficacy and feasibility of this triple combination induction therapy with Ixazomib as a proteasome inhibitor, Thalidomide as an IMiD and low dose Dexamethasone. Moreover, the merits and feasibility of MLN9708 (Ixazomib) maintenance will be determined.

### 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, 3, 5 ,7 and 9 cycles (just before start of the next cycle)

-During maintenance therapy after every maintenance cycle during the first year, thereafter every 8 weeks

-When patient is taken off protocol treatment

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

### Intervention

Following induction therapy half of the patients will receive 4 mg of ixazomib citrate capsules as a maintenance therapy until progression and the other half of patients will receive placebo capsules as a maintenance therapy until progression.

# Contacts

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# Eligibility criteria

## Inclusion criteria

- Previously untreated patients with a confirmed diagnosis of symptomatic multiple myeloma according to IMWG criteria (see appendix A)

- Measurable disease according to the IMWG criteria (see appendix A)

(If plasmacytoma is the only measurable parameter, the patient is not allowed to be included in the study, because of difficult response evaluation).
- Age > 66 years or patients <65 years not eligible for ASCT

- WHO performance status 0-3 for patients <75 years and WHO performance status 0-2 for patients > 75 years (see appendix D)

- Absolute neutrophil count (ANC) >1.0 x109/l and platelet count >75x109/l , unless related to bone marrow infiltration by malignant plasmacells.

Platelet transfusions to help patients meet eligibility criteria are not allowed within 3 days before study enrollment

- Written informed consent

- Negative pregnancy test at study entry or at least 1 year post-menopausal or surgically sterile before study entry

- A female patient of childbearing potential, agrees to practice 2 effective methods of contraception, at the same time, from the time of signing the informed consent through 90 days after the last dose of study drug, AND must also adhere to the guidelines of any treatment-specific pregnancy prevention program (for thalidomide) OR agrees to completely abstain from heterosexual intercourse. (Periodic abstinence (eg, calendar, ovulation, symptothermal, post-ovulation methods) and withdrawal are not acceptable methods of contraception)

- Male patients, even if surgically sterilized, (i.e., status post vasectomy) must agree to practice effective barrier contraception during the entire study period and through 90 days after the last dose of study drug, AND must also adhere to the guidelines of any treatment-specific pregnancy prevention program (for thalidomide), OR agrees to completely abstain from heterosexual intercourse (Periodic abstinence (eg, calendar, ovulation, symptothermal, post-ovulation methods] and withdrawal are not acceptable methods of contraception.)

## Exclusion criteria

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

- Systemic AL amyloidosis

- Polyneuropathy, grade 3 or higher or grade 2 with pain on clinical examination during the screening period

- Evidence of current uncontrolled cardiovascular conditions, including uncontrolled hypertension, uncontrolled cardiac arrhythmias, symptomatic congestive heart failure, unstable angina, or myocardial infarction within the past 6 months

- Severe pulmonary dysfunction (Modified Medical Research Counsil dyspnea scale classification III-IV)

- Significant hepatic dysfunction (total bilirubin >1.5 x ULN or transaminases >3 times normal level)

- Creatinine clearance <30 ml/min

- Systemic treatment with strong inhibitors of CYP1A2 (fluvoxamine, enoxacin, ciprofloxacin), strong inhibitors of CYP3A (clarithromycin, telithromycin, itraconazole, voriconazole, ketoconazole, nefazodone, posaconazole) or strong CYP3A inducers (rifampin, rifapentine, rifabutin, carbamazepine, phenytoin, phenobarbital), or use of Ginkgo biloba or St. John's wort within 14 days before registration in the study

- Pre-treatment with cytostatic drug, IMIDs or proteasome inhibitors. Radiotherapy or a short course of steroids (e.g. 4 day treatment of dexamethasone 40 mg/day or equivalent) are

allowed. Radiotherapy should not be given within 14 days before enrollment. In case of palliative radiotherapy for pain control and if the involved field is small, 7 days will be considered a sufficient interval between treatment and administration of the ixazomib citrate

- Not able and/or not willing to use adequate contraception

- Female patients who are lactating or have a positive serum pregnancy test during the screening period

- Major surgery within 14 days before enrollment

- Central nervous system involvement

- Ongoing or active systemic infection, active hepatitis B or C virus infection, or known human immunodeficiency virus (HIV) positive

- Known GI disease or GI procedure that could interfere with the oral absorption or tolerance of ixazomib citrate including difficulty swallowing.

- Diagnosed or treated for another malignancy within 2 years before study enrollment or previously diagnosed with another malignancy and have any evidence of residual disease. Patients with nonmelanoma skin cancer or carcinoma in situ of any type are not excluded if they have undergone complete resection.

- Participation in other clinical trials, including those with other investigational agents not included in this trial, within 21 days of the start of this trial and throughout the duration of this trial.

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

# Study design

## Design

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|---|---|
| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Double blinded (masking used) |
| Control: | Placebo |

### Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruiting |
| Start date (anticipated): | 24-11-2014 |
| Enrollment: | 142 |
| Type: | Anticipated |

## Ethics review

Positive opinion

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|---|---|
| Date: | 18-11-2014 |
| Application type: | First submission |

## Study registrations

### Followed up by the following (possibly more current) registration

ID: 50234
Bron: ToetsingOnline
Titel:

### Other (possibly less up-to-date) registrations in this register

No registrations found.

### In other registers

| Register | ID |
|---|---|
| NTR-new | NL4772 |
| NTR-old | NTR4910 |
| CCMO | NL45340.029.14 |
| OMON | NL-OMON50234 |

## Study results