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

Published: 23-10-2014
Last updated: 15-05-2024

Maintenance treatment- To compare progression free survival between maintenance therapy with Ixazomib versus placebo, both following induction therapy with ixazomib citrate * thalidomide * low dose dexamethasone Induction treatment-To determine...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Haematopoietic neoplasms (excl leukaemias and lymphomas)
Study type	Interventional

Summary

ID

NL-OMON50234

Source
ToetsingOnline

Brief title
HOVON 126 MM/ NMSG 21.13

Condition

- Haematopoietic neoplasms (excl leukaemias and lymphomas)

Synonym
Multiple Myeloma

Research involving
Human

Sponsors and support

Primary sponsor: HOVON
Source(s) of monetary or material Support: Millennium Pharmaceuticals,stichting HOVON;Millenium pharmaceuticals

Intervention

Keyword: Ixazomib citrate, Maintenance tratment, Multiple Myeloma

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

Standard of care in Europe for newly diagnosed MM patients who are not eligible for autologous stem cell transplantation is melphalan-prednisone-bortezomib. Hematological toxicity and increased rate of second primary malignancies with alkylating agents justifies the investigation of a triplet combination therapy omitting alkylating agents. A triplet combination without alkylating agents combining an IMiD (thalidomide or lenalidomide), a proteasome inhibitor (bortezomib) and corticosteroids have been found to be very effective indeed. In view of In view of a high incidence of peripheral neuropathy in the current protocol bortezomib will be replaced with the oral proteasome inhibitor ixazomib. Importantly, this is an oral regimen, especially being convenient in an elderly population. The hypothesis is that the response rate will be superior, with less hematological and painful neural toxicity as compared to standard therapy. In addition, a role for maintenance therapy with bortezomib has been suggested in non-head to head comparisons. Therefore, the efficacy of Ixazomib maintenance therapy will be investigated by randomizing maintenance treatment with Ixazomib versus placebo.

Study objective

Maintenance treatment
- To compare progression free survival between maintenance therapy with Ixazomib versus placebo, both following induction therapy with ixazomib citrate * thalidomide * low dose dexamethasone
Induction treatment

-To determine overall response* rate of induction therapy with ixazomib citrate * thalidomide * low dose dexamethasone
* overall response will be defined as (stringent) complete response, very good partial
response and partial response

Study design

Phase II trial

Intervention

Induction treatment with Ixazomib, Thalidomide and Dexamethasone. Following induction therapy half of the patients will receive 4 mg of Ixazomib capsules as a maintenance therapy until progression and the other half of patients will receive placebo capsules as a maintenance therapy until progression

Study burden and risks

The burden will be that following induction therapy, maintenance therapy will be given until progression. Although a benefit with respect to prolongation of PFS is expected, the extent is currently unknown. Patients may suffer from side effects, although these are generally mild with ixazomib citrate. Moreover, 50% of patients receive a placebo. There are no additional procedures required as compared to standard care. Patients will only be requested to participate in Quality of Life studies and will be asked to give extra blood and marrow for future research.

Contacts

Public
HOVON

VUMC, HOVON Centraal Bureau, De Boelelaan 117
Amsterdam 1081 HV
NL
Scientific
HOVON

VUMC, HOVON Centraal Bureau, De Boelelaan 117
Amsterdam 1081 HV
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Previously untreated patients with a confirmed diagnosis of symptomatic multiple myeloma according to IMWG criteria
- 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).
- 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
- Absolute neutrophil count (ANC) * 1.0 x109/l and platelet count * 75x109/l , unless related to bone marrow infiltration by malignant plasmacells .
- Written informed consent.
- Patient gives consent for extra bone marrow and blood sampling.
- Negative pregnancy test at study entry or at least 1 year post-menopausal or surgically sterile before study entry
- Patients must use adequate contraception as specified in the protocol (all men and all women of childbearing potential)

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) except patients with Gilbert*s syndrome as defined by > 80% unconjugated bilirubin
- Creatinine clearance <30 ml/min or Calculated Glomerular Filtration Rate [ml/min/1.73m2] <30
- Systemic treatment, within 14 days before the first dose of ixazomib, with strong CYP3A inducers (rifampin, rifapentine, rifabutin, carbamazepine, phenytoin, phenobarbital), or use of Ginkgo biloba or St. John*s wort.
- 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 radiotherapy, 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 citraat 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 21days 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

Study phase: 2

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	26-11-2014
Enrollment:	71
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	n.v.t.
Generic name:	Ixazomib citrate

Ethics review

Approved WMO Date:	23-10-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-11-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-12-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-01-2015

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-04-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-04-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-09-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-11-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-03-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-03-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-04-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-05-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-12-2017

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-02-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-07-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-07-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-01-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-01-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-02-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 29252
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2013-003266-14-NL
CCMO	NL45340.029.14
OMON	NL-OMON29252