Randomized phase III trial in elderly patients with previously untreated symptomatic Multiple Myeloma comparing MP-Thalidomide (MP-Thal) followed by thalidomide maintenance versus MP-Lenalidomide (MP-Len) followed by maintenance with lenalidomide

Published: 27-10-2008
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To compare efficacy, safety and quality of life of MP-Thal followed by thalidomide maintenance versus MP-Len followed by maintenance with lenalidomide

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

Summary

ID

NL-OMON50624

Source
ToetsingOnline

Brief title
HOVON 87 MM/NMSG 18

Condition

- Plasma cell neoplasms

Synonym

Kahlers disease, Multiple Myeloma

Research involving
Human

Sponsors and support

Primary sponsor: HOVON
Source(s) of monetary or material Support: KWF Kankerbestrijdding

Intervention

Keyword: Elderly patients, Lenalidomide, Multiple Myeloma, Thalidomide

Outcome measures

Primary outcome

- Progression free survival, defined as time from registration to progression

or death from any cause

- Response rate (sCR, CR or VGPR)

Secondary outcome

- Response rate (sCR, CR, VGPR or PR)

- Overall survival, measured from time of registration

- 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

- Safety and toxicity as defined by type, frequency and severity of adverse

events as defined by the National Cancer Institute (NCI) Common Terminology

Criteria (CTC), version 3.0

- Quality of life.

Study description

Background summary

Until recently melphalan/prednisone (MP) has been the standard combination of drug treatment for patients with Multiple Myeloma (MM) at an elderly age. With MP the response rate is approximately 50%, of which < 5 % are complete responses (CR). Addition of thalidomide to MP (MP-Thal) increases the overall response (OR), complete response (CR) and event-free survival (EFS) as demonstrated in two recent randomized trials. Moreover, a significant increase in survival has recently be found: 51.5 months in MPT treated patients versus 33.2 months in MP treated patients.However, despite these improvements, the majority of patients develop a relapse or progressive disease in relatively short time, as indicated by an EFS of 54% at two years in patients treated with MP-Thal. Therefore, there is a need to further explore the role of novel agents, such as Lenalidomide in the upfront treatment of MM. Lenalidomide has now been tested as single agent in MM, with clear clinical effects giving response in 25% of patients in heavily pretreated patients, including pretreatment with thalidomide. Responses up to 60% have been described in combination with dexamethasone or bortezomib in pretreated patients. In previously untreated patients, the combination of lenalidomide with MP was found to be feasible in an elderly population and resulted in response in all patients. Moreover, in contrast to thalidomide, lenalidomide has a safety profile which does not include central or peripheral neuropathy. However, hematological toxicity was found to be more frequent. As currently no data from randomized studies comparing MP-Thal versus MP-Lenalidomide are available, HOVON decided to initiate a Phase III randomized trial comparing MP-Thal versus MP-Len. In both treatment arms maintenance therapy will be given, either thalidomide or lenalidomide. Efficacy, toxicity and quality of life will be compared.

Study objective

To compare efficacy, safety and quality of life of MP-Thal followed by thalidomide maintenance versus MP-Len followed by maintenance with lenalidomide

Study design

Multicenter, randomized, phase III.

Intervention

Patients will be randomized between treatment with 9 cycles of MP-Thalidomide followed bij Thalidomide maintenance until relapse/progression or treatment with 9 cycles of MP-Lenalidomide followed by Lenalidomide maintenance until

relapse/progression

Study burden and risks

Toxicity, especially myelosuppression, polyneuropathy

Contacts

Public
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Scientific
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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, - Age > 65 years or patients * 65 not eligible for high dose chemotherapy and peripheral stem cell transplantation, - WHO performance status 0-3 for patients <75 years and WHO

performance status 0-2 for patients *75 years , - Measurable disease as defined by the presence of M-protein in serum or urine or proven plasmocytoma by biopsy, - Written informed consent

Exclusion criteria

- Non-secretory MM, - Known hypersensitivity to thalidomide, - Systemic AL amyloidosis , - Polyneuropathy, grade 2 or higher , - Severe cardiac dysfunction (NYHA classification II-IV) , - Severe pulmonary dysfunction , - Significant hepatic dysfunction (total bilirubin *30 umol/l or transaminases *3 times normal level), unless related to myeloma , - Creatinine clearance < 30 ml/min, - Patients with active, uncontrolled infections , - 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., - Patients known to be HIV-positive , - History of active malignancy during the past 5 years, except basal carcinoma of the skin or stage 0 cervical carcinoma , - Not able and/or not willing to use adequate contraception , - Pregnancy

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:	Recruitment stopped
Start date (anticipated):	12-03-2009
Enrollment:	500
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Revlimid
Generic name:	Lenalidomide
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Thalidomide
Generic name:	Thalidomide

Ethics review

Approved WMO Date:	27-10-2008
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-11-2008
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-06-2009
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-08-2009
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-03-2010
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-10-2010
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Approved WMO Date:	04-11-2010
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-04-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-08-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-08-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-12-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-12-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-03-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-04-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-02-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	02-03-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-07-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-01-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-02-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-07-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-07-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-05-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-05-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-03-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	28-03-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-07-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-07-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-07-2020
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

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2007-004007-34-NL
CCMO	NL24321.029.08