Feasibility and Efficacy of dose adjusted Melphalan - Prednisone - Bortezomib (MPV) in elderly patients >= 75 years of age with newly diagnosed Multiple Myeloma; a non-randomised phase II study

Published: 24-07-2013
Last updated: 25-04-2024

To assess the feasibility, defined as discontinuation rate, of a dose-adapted MPV scheme in MM patients >= 75 years

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

Summary

ID

NL-OMON47392

Source
ToetsingOnline

Brief title
HOVON 123 MM

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: Janssen-Cilag,KWF kankerbestrijding

Intervention

Keyword: Bortezomib, Elderly patients, Multiple Myeloma

Outcome measures

Primary outcome

Discontinuation rate, defined as the proportion of patients who received less

than 9 cycles of MPV according to protocol treatment

Secondary outcome

- Relative dose intensity of Melphalan, Prednisone and Bortezomib

- 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 4.0

- Overall response rate defined as sCR, CR, VGPR or PR

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

or death from any cause

- Overall survival, measured from time of registration

- Geriatric assessments

- Quality of life as defined by the EORTC QLQ-C30 and MY-20 definitions.

- Biomarkers for biological age

- Genetic polymorphism analysis of genes involved in drug metabolism and

related with bortezomib-induced PNP

- Cost efficacy analysis

Study description

Background summary

The prognosis of MM patients has increased significantly over the last decade with the availability of new drugs. This also accounts for the elderly patients with MM >65 years of age. However, toxicity of the treatment leading to discontinuation of therapy and an inferior outcome remains a concern. Especially in those patients over 75 years of age, because of vulnerability due to co-morbidities complicating the treatment of MM. Appropriate screening for vulnerability and an assessment of cardiac, pulmonary, renal, hepatic and neurologic functions at the start of therapy allows treatment strategies to be individualized an drug doses to be tailored to improve tolerability and optimize efficacy. However, there is a lack of information on geriatric assessments predicting the feasibility of MM treatment and the need for dose reductions preferably without hampering outcome in MM patients. Only recently a high risk vulnerability score based on PS and CCI was found to be associated with outcome in a retrospective analysis of a non-uniformly described group of MM patients. Therefore, currently applied treatment algorithms in the elderly are based on age (< versus >=75 years of age) and co-morbidities, not being precisely defined, are mainly based on expert opinions instead of based on clinical outcome. Adding the fact that geriatric assessments have currently not been implemented, current clinical practice is characterized by *individual physician impression-based dose adjustments*. As a consequence either irreversible toxicity as well as unnecessary loss of efficacy will occur, hampering QoL, duration of life and cost efficacy.
This study aims to assess the feasibility of a well defined dose-adjusted MPV scheme in patients >=75 years of age and to assess the additive value of geriatric assessments to predict both feasibility and efficacy. In addition, the value of new biomarkers reflecting biological age will be investigated. Finally, a QoL and cost-efficacy analysis will be performed. This will hopefully lead to a geriatric assessment-based treatment in MM patients in the near future.

Study objective

To assess the feasibility, defined as discontinuation rate, of a dose-adapted MPV scheme in MM patients >= 75 years

Study design

multi center phase 2 study

Intervention

The patients will be treated with the standard therapy for this patient population.

Study burden and risks

The specific side effects of the medication, participation in the geriatric assessment taking time of patients and a minor invasive skin biopsy will be performed.

Contacts

Public
HOVON

HOVON Centraal Bureau, VUMC, De Boelelaan 1117
Amsterdam 1081 HV
NL
Scientific
HOVON

HOVON Centraal Bureau, VUMC, De Boelelaan 1117
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
- Age >= 75 years
- WHO performance status 0-3, WHO 4 performance status is allowed when related to MM
- Measurable disease as defined by the presence of M-protein in serum or urine and/or abnormal free light chain (FLC) ratio with involved FLC. (If plasmacytoma is the only measurable parameter, the patient is not allowed to be included in the study, because of difficult response evaluation)
- Patient gives consent for extra bone marrow, blood and skin biopsy sampling
- Written informed consent

Exclusion criteria

- Non-secretory MM
- Systemic Amyloid Light-chain amyloidosis
- Polyneuropathy, grade 1 with pain or >= grade 2
- Severe cardiac dysfunction (NYHA classification IV)
- Severe pulmonary dysfunction defined as breathlessness at rest
- Significant hepatic dysfunction (total bilirubin >= 30 µmol/l or transaminases >= 3 times normal level), unless related to MM
- Renal insufficiency requiring dialysis
- 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
- Active malignancy requiring treatment or having been treated with chemotherapy currently affecting bone marrow capacity. Non-active previous malignancies are allowed.
- Any psychological, familial, sociological and geographical condition potentially hampering compliance with the study protocol and follow-up schedule
- Patients with plasma cell leukemia

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	04-02-2014
Enrollment:	240
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Alkeran
Generic name:	Melphalan
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Prednisone
Generic name:	Prednisone
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Velcade
Generic name:	Bortezomib
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	24-07-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-11-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-02-2014
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-02-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-03-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-04-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-06-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-06-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-06-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-12-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-12-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-06-2015
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-07-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-12-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-12-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-02-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-03-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-04-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-04-2016
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:	10-01-2017
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-02-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-11-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-12-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-07-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-07-2018
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	EUCTR2013□000320□33-NL
CCMO	NL43698.029.13