Carfilzomib in combination with Thalidomide and Dexamethasone for remission induction and consolidation of Multiple Myeloma at first presentation

Published: 03-02-2010
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To assess the feasibility and efficacy of Carfilzomib in combination with Thalidomide and Dexamethasone in a phase II trial.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Miscellaneous and site unspecified neoplasms benign
Study type	Interventional

Summary

ID

NL-OMON46962

Source
ToetsingOnline

Brief title
The Carthadex trial

Condition

- Miscellaneous and site unspecified neoplasms benign

Synonym
Multiple Myeloma

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: farmaceutische industrie,Onyx

Pharmaceuticals

Intervention

Keyword: carfilzomib, kahlers disease, multiple myeloma

Outcome measures

Primary outcome

To establish the response, in patients with Multiple Myeloma at first presentation, to carfilzomib in combination with thalidomide and dexamethasone.

Secondary outcome

To investigate the clinical efficacy and toxicity of carfilzomib in combination with thalidomide and dexamethasone in remission induction of Multiple Myeloma at first presentation.

To investigate the clinical efficacy and toxicity of carfilzomib in combination with thalidomide and dexamethasone in consolidation treatment of Multiple Myeloma at first presentation.

To assess the stem cell harvest following carfilzomib in combination with thalidomide and dexamethasone.

To assess Progression-free survival (PFS).

Study description

Background summary

Thalidomide and bortezomib combined with dexamethasone and a third agent (alkylating agent or anthracycline) are now recognized as the most active drugs for remission induction in transplant candidates. In elderly patients they are combined with Melphalan/Prednisone (MP) in first line treatment. Both drugs share the disadvantage of inducing peripheral polyneuropathy which is dose limiting in 50% of patients and leads to premature termination of treatment in

25%.

Replacing bortezomib by carfilzomib would associate effective proteasome inhibition with lack of neuropathy, thereby improving the proportion of patients who are able to complete the planned treatment and reducing the rate of serious adverse events, in particular polyneuropathy. In view of the recently reported high response rates with Bortezomib containing regimens (VD, VRD, VCD, VTD, PAD) prior and after high-dose therapy, a regimen with Carfilzomib combining less polyneuropathy with similar efficacy would be a likely candidate for standard induction in the future. Equally, such regimen could be used for short consolidation treatment after high-dose therapy

Study objective

To assess the feasibility and efficacy of Carfilzomib in combination with Thalidomide and Dexamethasone in a phase II trial.

Study design

This trial will establish the feasibility and efficacy of Carfilzomib, in combination with Thalidomide and Dexamethasone as an induction therapy prior to therapy with High Dose Melphalan (HDM) and Autologous Stem Cell Transplantation (ASCT) in previously untreated patients with Multiple Myeloma. Stem cell harvest will be performed using high-dose Cyclophosphamide and standard G-CSF. In addition, the efficacy of a short (4 cycles) post-transplant consolidation schedule of Carfilzomib, in combination with lower dose Thalidomide and Dexamethasone will be investigated. The study will be conducted as a Phase II trial.

Fifty patients will be included in the study cohort. Molecular (FISH) characterization and gene expression profiling of the myeloma tumor cells will be performed at inclusion. All patients will be followed closely for toxicities and response assessment, as indicated. After completion of treatment, all patients will be followed two-monthly until relapse or progression.

Intervention

The treatment is composed of the standard therapy for patient with Multiple Myeloma at first presentation. Instead of giving, in the consolidation & induction phase, Thalidomide, Dexamethason and a third agent (i.e. Bortezomib) , Carfilzomib will be administered in combination with Thalidomide and Dexamethasone.

Study burden and risks

Carfilzomib has been given as monotherapy ans also in combination with

Lenalidomide and dexamethsone but not with this peticular antimyeloma standard chemotherapy regimen. So unexpected toxicites are possible.
A *first-dose* effect has been seen, which is notable for fever, chills, rigors, and/or dyspnea occurring during the evening following the first day of infusion and an increase in creatinine on Day 2, which may be the clinical sequelae of rapid tumor lysis and/or cytokine release.
At time of the normal bone marrow punctions a limited amount of extra bone marrow will be collected via the same needle.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Patients with a confirmed diagnosis of multiple myeloma stage II or III according to the Salmon & Durie criteria;

- Age 18-65 years inclusive;
- WHO performance status 0-3 (WHO<=3 is allowed only when caused by MM and not by co-morbid conditions);
- Negative urine pregnancy test at inclusion if applicable;
- Written informed consent.

Exclusion criteria

- Known intolerance of Thalidomide;
- Previous chemotherapy or radiotherapy except 2 cycles of Melphalan/Prednisone or local radiotherapy in case of local myeloma progression;
- Severe cardiac dysfunction;
- Creatinine clearance <30cc/min;
- ANC < 1,0 x109/L, platelets < 75 x109/L, Hb < 4.9 mmol/L;
- Patients with neuropathy, CTC grade 3 or higher or grade 2 painful peripheral neuropathy;
- Patients with a history of active malignancy during the past 5 years with the exception of basal carcinoma of the skin or stage 0 cervical carcinoma;

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-08-2010
Enrollment:	145
Type:	Actual

Medical products/devices used

Product type:	Medicine

Brand name:	Carfilzomib
Generic name:	Carfilzomib Lyophilisate
Product type:	Medicine
Brand name:	Decadron
Generic name:	Dexamethasone
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Thalidomide
Generic name:	Thalidomide

Ethics review

Approved WMO Date:	03-02-2010
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-07-2010
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	22-03-2011
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-03-2011
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-12-2011
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam

	(Rotterdam)
Approved WMO Date:	22-05-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	04-06-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-01-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-01-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-12-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-12-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-10-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	25-11-2014

Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	14-01-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-02-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	03-04-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-04-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-11-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-02-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-03-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	06-04-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-04-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-05-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-06-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-06-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-07-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2009-014922-40-NL
CCMO	NL29308.078.10