A multicenter, phase II study of bortezomib and dexamethasone as induction treatment followed by high dose melphalan (HDM) and autologous stem cell transplantation (SCT) in patients with de novo amyloid light chain (AL) amyloidosis

Published: 22-11-2010
Last updated: 04-05-2024

* To determine the efficacy of bortezomib plus dexamethasone induction therapy followed by HDM and auto-SCT in patients with newly diagnosed AL amyloidosis who are 18-70 years inclusive.* To asses the safety of bortezomib plus dexamethasone as...

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

Summary

ID

NL-OMON39975

Source
ToetsingOnline

Brief title
HOVON 104 AL amyloidosis

Condition

- Plasma cell neoplasms

Synonym
AL amyloidosis

Research involving
Human

Sponsors and support

Primary sponsor: HOVON
Source(s) of monetary or material Support: Johnson & Johnson Pharmaceutical,KWF;Johnson & Johnson

Intervention

Keyword: AL amyloidosis, Bortezomib

Outcome measures

Primary outcome

* Hematological CR rate 6 months after auto-SCT. Patients are considered a success if they received HDM and auto-SCT and are in CHR at 6 months, all other patients are considered a failure.

Secondary outcome

* Overall survival measured from the time of registration. Patients still alive or lost to follow up ace censored at the day they were last known to be alive
* Progression Free Survival, (hematological), i.e. time from registration until hematological progression, relapse or death, whichever occurs first.
* Hematological response rate rate after induction therapy
* Response Rate, hematological and organ
* Time to response, hematological and organ
* Duration of response, hematological and organ
* Time to next AL amyloidosis therapy
* Safety (type, frequency, and severity of adverse events (AE) and relationship of AE to study drug

* Exploratory assessment of multiparameter flow cytometry quantification of

bone marrow plasma cells and change in amyloid deposition in abdominal fat

aspiration samples

* Evaluation of prognostic factors for survival included in the hematological

and organ response criteria

Study description

Background summary

The aim of the current study is to investigate the efficacy of induction treatment consisting of bortezomib and dexamethasone followed by HDM and auto-SCT to improve the hematological response rate and especially the CHR of patients with de novo AL amyloidosis. Considering the potent effect in relapsed AL amyloidosis patients and the improvement in response rates achieved when used as the first line treatment of MM patients, it is expected that the use of bortezomib will also improve the response rate in first line treatment of AL amyloidosis patients.

With the use of induction therapy the TRM of the auto-SCT procedure is < 5% and the hematological response after the treatment is long-lasting. Because hematological response rate is closely related with survival in this patient population a better response rate will translate into better overall survival.

Study objective

* To determine the efficacy of bortezomib plus dexamethasone induction therapy followed by HDM and auto-SCT in patients with newly diagnosed AL amyloidosis who are 18-70 years inclusive.
* To asses the safety of bortezomib plus dexamethasone as induction treatment followed by HDM and auto-SCT in patients with newly diagnosed AL amyloidosis who are 18-70 years inclusive.

Study design

This is a multi-center, open label, 1 arm phase II study.

Intervention

Treatment consists of bortezomib and dexamethasone followed by stem cell mobilization, HDM and auto-SCT.

Study burden and risks

Patients are exposed to bortezomib and therefore to the side effects of the drug such as peripheral polyneuropathy, gastro-intestinal complaints and thrombocytopenia. If informed consent is given for participation in the experimental studies patients will undergo 4 additional abdominal fat aspiration procedures

Contacts

Public
HOVON

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NL
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

* Biopsy proven, systemic, untreated AL amyloidosis requiring systemic chemotherapy,
* Age 18 -70 years inclusive at the time of signing the informed consent form,
* Measurable plasma cell dyscrasia, defined as a detectable M-protein with serum electrophoresis and/or level of involved FLC> 50 mg/L,
* Life expectancy > 3 months,
* WHO performance status 0-2,
* NYHA stage 1-2,
* Negative pregnancy test at inclusion for women of childbearing potential,
* Written informed consent.

Exclusion criteria

* Multiple Myeloma stage II and III (Durie and Salmon),
* Any serious medical condition, laboratory abnormality, or psychiatric illness that would prevent the subject from signing the informed consent form,
* Any psychological, familial, sociological and geographical condition potentially hampering compliance with the study protocol and follow-up schedule,
* Previous treatment for plasma cell dyscrasia
* Pregnant or breast feeding females.
* Presence of other active malignancy or a history of active malignancy during the past 5 years, with the exception of nonmelanoma skin cancer, stage 0 cervical carcinoma, or treated early-stage prostate cancer provided that prostate-specific antigen is within normal limits,
* Hypersensitivity to boron or mannitol,
* Uncontrolled infection,
* Symptomatic othostatic hypotension defined as a decrease in systolic blood pressure on standing of >20mmHg combined with symptoms like dizziness, cerebral and/or cardial ischemia,
*NT pro BNP level > 5000 pg/ml and Troponin T> 0.06 microgram/l (not high senstitivity assay) or NT proBNP level > 5000 pg/ml and Troponin I > 2 times ULN
* Symptomatic effusions, defined as pleural effusion or ascites needing drainage therapy,
* Positive for HIV or infectious hepatitis, B or C,
* Bilirubin > 2x upper limit of normal,
* Creatinin clearance < 30 ml/min (after rehydration),
* Absolute neutrophil count < 1.0 × 109/L,
* NCI CTCAE grade peripheral sensory neuropathy > grade 2,
* NCI CTCAE grade peripheral sensory neuropathy > grade 1 in the presence of neuropathic pain,
*NCI CTCAE grade peripheral motor neuropathy > grade 2
* Concurrent diagnosis of B-cel NHL or B-CLL,
* Previous organ transplantation.
* Unwilling or unable to use adequate contraception

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):	21-03-2012
Enrollment:	34
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Velcade
Generic name:	Bortezomib
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	22-11-2010
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	31-08-2011
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	25-11-2011

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	20-12-2011
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-06-2012
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	10-07-2012
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	17-01-2013
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	10-10-2013
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-02-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	27-03-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	06-05-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-09-2014

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	23-09-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	17-07-2015
Application type:	Amendment
Review commission:	METC NedMec

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	EUCTR2010-021445-42-NL
CCMO	NL33641.041.10
Other	NL33641.041.10

Study results

Date completed:	29-01-2021
Results posted:	28-12-2021
Actual enrolment:	40

Summary results
Trial is onging in other countries

First publication
06-12-2021