Carfilzomib and lenalidomide-based treatment for younger and elderly newly diagnosed primary plasma cell leukemia patients

Published: 07-10-2014
Last updated: 27-04-2024

The aim of this study is to improve the outcome of both younger and elderly primary plasma cell leukemia patients(pPCL) by using next generation novel agents and in case of younger patients also the tandem of auto-SCT and allo-SCT.

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

Summary

ID

NL-OMON50273

Source
ToetsingOnline

Brief title
HOVON 129 PCL

Condition

- Plasma cell neoplasms

Synonym
Plasma cell leukemia

Research involving
Human

Sponsors and support

Primary sponsor: HOVON

Source(s) of monetary or material Support: Amgen,Celgene Corporation,KWF kankerbestrijding

Intervention

Keyword: Carfilzomib, Plasma cell leukemia

Outcome measures

Primary outcome

Progression-free survival (PFS, i.e. time from registration until progression or death, whichever comes first)

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
- Overall response rate (at least PR) after the different phases of treatment
- (s)CR + VGPR ((stringent) complete and very good partial response) after the different phases of treatment
- Overall survival, defined as time from registration until death from any cause. Patients still alive at the date of last contact, will be censored
- Toxicity and tolerability of the different phases of treatment
- Explore the value of prognostic factors including including FISH abnormalities, β2-microgloublin, LDH, MRD-negativity, pPCL gene expression profiles and sequencing results on the overall response, overall survival and progression-free survival
- Frequency of second primary malignancies

Study description

Background summary

Primary plasma cell leukemia (pPCL) is the most aggressive form of the plasma cell dyscrasias. It is defined by the presence of >2x109/L peripheral blood plasma cells or plasmacytosis accounting for >20% of the differential white cell count, and does not arise from pre-existing multiple myeloma (MM.
The prognosis of pPCL is very poor, with a median overall survival (OS) of only 7 months with standard chemotherapy. The introduction of autologous stem cell transplantation (auto-SCT) and the novel agents, especially bortezomib, has recently improved outcome of patients with pPCL, but remains inferior when compared to MM. Therefore innovative treatment approaches which incorporate various modalities are required to improve outcome.

Lenalidomide with carfilzomib and dexamethasone (CRd) is a regimen that combines high efficacy with low rate of polyneuropathy and is therefore an attractive combination for induction treatment in pPCL.
Furthermore, allogeneic stem cell transplantation (allo-SCT) is a form of consolidation treatment, which by virtue of the graft-versus-tumor effect, results in a high rate of molecular remissions in plasma cell cancers. Several small studies reported successful results and long-term survival following allo-SCT in pPCL
.
In this study, the CRd regimen will be used as induction therapy. In case of younger transplant-eliglible patients (18-65 years), CRd will also be used as consolidation and maintenance treatment after high-dose therapy with autologous stem cell rescue and allogeneic stem cell transplantation. Elderly patients (>=66 years) with pPCL will receive carfilzomib and lenalidomide maintenance after induction therapy.

Study objective

The aim of this study is to improve the outcome of both younger and elderly primary plasma cell leukemia patients(pPCL) by using next generation novel agents and in case of younger patients also the tandem of auto-SCT and allo-SCT.

Study design

Multicenter, intergroup, phase 2 study

Intervention

Patients will be treated with a combinatin of carfilzomib, lenalidomide and

dexamethasone (CRd) followed by auto-stem cell transplantation and consolidation with CRd, or if possible an allo stem cell transplantation with CR in maintenance until progression.

Study burden and risks

Patients will be treated with a highly effective combination of drugs during induction, consolidation, and maintenance phases. Toxicity will be mainly hematologic.

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

- Patients with diagnosis of symptomatic pPCL (see appendix A)
- Measurable disease as defined by the presence of M-protein in serum or urine (serum M-protein > 10 g/l or urine M-protein > 200 mg/24 hours or abnormal FLC ratio with involved free light chain (FLC) > 100 mg/l) or proven plasmacytoma by biopsy)
- Age >=18 years
- WHO-performance status 0-3 (but WHO=3 is allowed only when caused by pPCL and not by co-morbid conditions)
- Written informed consent
- Patient capable of giving informed consent (patient is legally, physically and mentally capable of giving consent)
- All men and women of childbearing potential should use adequate highly effective contraception during the study. Men should be offered sperm banking before starting treatment (if applicable).
- Negative pregnancy test at entry (if applicable)
- Patient is willing and able to adhere to the requirements of the lenalidomide Pregnancy Prevention Program (PPP) throughout study treatment

Exclusion criteria

- Any current CNS involvement with disease refractory to intrathecal chemotherapy.
- Female patients who are pregnant or breast feeding.
- HIV positive patients
- Active malignancy other than pPCL requiring treatment, or a malignancy that has been treated with chemotherapy currently affecting bone marrow capacity
- Patients with active, uncontrolled infections
- Severe neurological or psychiatric disease
- Severe cardiac dysfunction (NYHA classification II-IV, see appendix E) - Myocardial infarction within 6 months, unstable angina, and cardiac arrhythmias which are not controlled by conventional treatment (including medications and cardiac devices)
- Severe pulmonary dysfunction
- Significant hepatic dysfunction (serum bilirubin or transaminases >= 3.0 times normal level), unless related to pPCL
- Patients with GFR < 15 ml/min
- Known history of allergy to Capsidol (a cyclodextrin derivative used to solubilize carfilzomib)
- Hypersensitivity to the active substances or to any of the excipients of the drug products
- Previous chemotherapy or radiotherapy except local radiotherapy in case of local myeloma progression or corticosteroids maximum 7 days for symptom control or stabilization(this includes dexamethasone 40 mg daily) or inthrathecal chemotherapy in case of CNS involvement
- Systemic AL amyloidosis

- Any psychological, 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
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	23-10-2015
Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Kyprolis
Generic name:	Carfilzomib
Product type:	Medicine
Brand name:	Revlimid
Generic name:	Lenalidomide
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	07-10-2014
Application type:	First submission

Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-08-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-12-2016
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:	09-06-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-06-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-07-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-03-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-05-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-11-2019
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-01-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-02-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-04-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-03-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-03-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-03-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-03-2024
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	EUCTR2013-005157-75-NL
CCMO	NL47727.029.14