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

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON25322

Source
NTR

Brief title
HOVON 129 PCL

Health condition

Multiple myeloma (Kahler's disease)

Sponsors and support

Primary sponsor: Stichting Hemato-Oncologie voor Volwassenen Nederland (HOVON)
Source(s) of monetary or material Support: Stichting Hemato-Oncologie voor Volwassenen Nederland (HOVON), Celgene, Onyx, KWF

Intervention

Outcome measures

Primary outcome

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

Secondary outcome

• 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 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

Background of the study:

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.

Objective of the study:
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

Study population:
Previously untreated patients with plasma cell leukemia with ISS staging between I and III, and 18 years or orlder.

Intervention (if applicable):
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.

Primary study parameters/outcome of the study:
Progression-free survival (PFS, i.e. time from registration until progression or death, whichever comes first)

Secundary study parameters/outcome of the study (if applicable):

- 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

Nature and extent of the burden and risks associated with participation, benefit and group relatedness (if
applicable):

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

Study objective

Based on 1) the improvement in survival of both younger and elderly pPCL patients by incorporation of novel agents (especially proteasome inhibitors and lenalidomide) and 2) improvement in survival for younger patients by using auto-SCT in treatment schedules, combined with the lower relapse rate with allo-SCT in pPCL, we here propose a new study to further improve the outcome of both transplant eligible (younger) and non-transplant eligible (elderly) pPCL patients.

Study design

• At entry: before start of treatment (results from diagnostic tests may be used, provided that they are no older than 4 weeks prior to registration)

• After 4 induction treatment cycles for younger patients and after 4 and 8 induction treatment cycles for elderly patients

• After stem cell collection (if applicable): 4 weeks after start cyclophosphamide i.v.

• After each HDM (if applicable): 8 weeks after each course of HDM

• After CRd consolidation : 4 weeks after start of the 2nd CRd consolidation cycle for younger patients with donor; and after 4th CRd for younger patients without donor

• After RIC allo-SCT (if applicable): 8 weeks after RIC allo-SCT

• During maintenance/follow up: every 2 months (after progression every 6 months)

Intervention

Patients with age 18-65 years will receive 4 cycles of CRd followed by HDM and auto-SCT, then consolidation therapy with 2 cycles of CRd, and subsequently if eligible and a suitable donor is available then allo-SCT, the latter involving semi-intensive conditioning with busulfan + fludarabine. After allo-SCT patients will receive carfilzomib maintenance. Eight months after allo-SCT lenalidomide will be added to carfilzomib maintenance. The immunomodulatory agent lenalidomide is added at a later stage after allo-SCT in order to prevent the development of GvHD.

In case no donor can be identified OR if patient is ineligible to proceed with allo-SCT after the first auto-SCT OR if patient does not want to undergo allo-SCT, a second course of high dose melphalan and auto-SCT will be administered between 2 and 3 months after the first course when the patient achieved at least PR. This will be followed by 4 cycles CRd consolidation and subsequently carfilzomib-lenalidomide maintenance.

Patients with age ≥66 years will receive 8 cycles of CRd followed by carfilzomib-lenalidomide maintenance until progression.

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Eligibility criteria

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 > 5 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 contraception during the study. Sperm could be frozen from men with child wish before start of treatment

• Negative pregnancy test at entry (if applicable)

• Patient is willing and able to adhere to the requirements of the lenalidomide Pregnancy Prevention Program (PPP)

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)

• 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)

• 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 type:	Interventional
Intervention model:	Parallel
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	10-08-2015

Enrollment:	116
Type:	Anticipated

Ethics review

Positive opinion Date:	12-08-2015
Application type:	First submission

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
NTR-new	NL5202
NTR-old	NTR5350
Other	MEC/CCMO : 2014.456/NL47727.029.14

Study results