A phase II study evaluating the effect of the addition of lenalidomide to R-CHOP for patients with newly diagnosed MYC positive DLBCL and BCL-U.

No registrations found.

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

Summary

ID

NL-OMON24704

Source
NTR

Brief title
HOVON 130 NHL

Health condition

Diffuse large B cell lymphoma, DLBCL, BCL-U, MYC

Sponsors and support

Primary sponsor: HOVON
Source(s) of monetary or material Support: HOVON, KWF, Celgene

Intervention

Outcome measures

Primary outcome

* Complete remission rate as determined by

- end-of-treatment PET-CT scan

- end-of-treatment negative bone marrow examination in case of localization of DLBCL or BLC-U at diagnosis

For complete remission, patients should have been treated with ¡Ý 3 cycles of R2CHOP. If the patient was in CR at mid-treatment PET-CT, but has to go off protocol after cycle 4 or 5 because of toxicity, end-of-treatment PET-CT has to show CR.

Secondary outcome

*Event Free Survival (EFS), defined as time from registration until no CR on protocol, relapse or death from any cause, whichever comes first

* Overall survival (OS), calculated from registration until death from any cause. Patients still alive or lost to follow up are censored at the last date known to be alive.

* Disease free survival (DFS) from time of complete remission. DFS is defined as duration from start of CR to relapse or death from any cause, whichever comes first, and applies only to patients who achieved CR.

* The relationship between mid-treatment 18F-FDG PET-CT result and end-of-treatment 18F-FDG PET-CT result.

Study description

Background summary

Patients with diffuse large B cell lymphoma (DLBCL) and with B-cell lymphomas, unclassifiable with features intermediate between diffuse large B cell lymphoma and Burkitt lymphoma (BCL-U) that harbor a MYC rearrangement (MYC+ DLBCL) have a dismal prognosis following treatment with standard therapy (R-CHOP). Lenalidomide is able to down-regulate MYC and its target genes and proteins in B cells that harbor a MYC rearrangement. The addition of lenalidomide to R-CHOP (R2CHOP) has been shown to be safe and might improve the prognosis of these patients.

Eligible patients will receive lenalidomide 15 mg on day 1-14 in addition to standard therapy with R-CHOP.

Treatment will consist of 6 cycles of R-CHOP with lenalidomide and two additional cycles of rituximab. Cycles will be given every 3 weeks. Total treatment duration is 24 weeks.

Subsequently patients will be followed until 5 years from registration

Study objective

Patients with diffuse large B cell lymphoma (DLBCL) and with B-cell lymphomas, unclassifiable with features intermediate between diffuse large B cell lymphoma and Burkitt lymphoma (BCL-U) that harbor a MYC rearrangement (MYC+ DLBCL) have a dismal prognosis following treatment with standard therapy (R-CHOP). Lenalidomide is able to down-regulate MYC and its target genes and proteins in B cells that harbor a MYC rearrangement. The addition of lenalidomide to R-CHOP (R2CHOP) has been shown to be safe and might improve the prognosis of these patients.

Study design

Prior to therapy, mid treatment and after completion of therapy.

Intervention

Eligible patients will receive lenalidomide 15 mg on day 1-14 in addition to standard therapy with R-CHOP.

Contacts

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Eligibility criteria

Inclusion criteria

* DLBCL or BCL-U, histologically confirmed according to the WHO classification 2008 with a MYC rearrangement as determined by FISH comprising:

- single hit (SH MYC+ lymphoma, not fulfilling the criteria for Burkitt Lymphoma) or

- double hit lymphoma (DH) MYC+/BCL2+ or MYC+/BCL6+ or

- triple hit lymphoma (TH)MYC+/BCL2+/BCL6+

* Age ¡Ý 18 year

* No prior treatment except

- local radiation or short course (max 7 days) steroids (max 100 mg/day)

- 1 course of R-CHOP in case MYC positivity became evident during first cycle of treatment

* WHO performance status (PS) 0-3, status 4 only if disease related (see appendix C)

* Ann Arbor stage II-IV

* Measurable disease: on CT scan at least 1 lesions/node with a long axis of >1.5 cm and at least one positive lesion on 18F-FDG PET scan.

* Negative pregnancy test at study entry

* Patient is willing and able to adhere to the requirements of the lenalidomide Pregnancy Prevention Risk Management Program

* Written informed consent

* Patient is capable of giving informed consent

Exclusion criteria

* All histopathological diagnoses other than DLBCL or BCL-U according to the WHO classification 2008, like Burkitt lymphoma, irrespective of the presence of MYC rearrangement

* Known history of indolent lymphoma. If during screening localization of an indolent lymphoma in the bone marrow biopsy is diagnosed, the patient is eligible.

* Inadequate renal function or creatinine clearance < 30 mL/min (after rehydration). Creatinine clearance may be calculated by Cockcroft –Gault formula:

CrCl = (140 - age [in years]) x weight [kg] (x 0.85 for females)/(0.815 x serum creatinine [ìmol/L])

* Inadequate hepatic function: bilirubin > 3 times ULN (total) except patients with Gilbert's syndrome as defined by > 80% unconjugated bilirubin

* Inadequate hematological function: ANC < 1.0x109/L or platelets < 75x109 /L unless lymphoma related

* CNS localization of the lymphoma

* Female subject pregnant or breast-feeding

* History of active malignancy during the past 5 years with the exception of basal carcinoma of the skin or stage 0 cervical carcinoma

* Active symptomatic ischemic heart disease, myocardial infarction, or congestive heart failure within the past year. If echo or MUGA is obtained the LVEF should exceed 40%

* Concurrent severe and/or uncontrolled medical condition (e.g. uncontrolled diabetes, infection, hypertension, cancer, etc.) that would jeopardize the patient's ability to receive the regimen with reasonable safety

* HIV positivity

* Active Hepatitis B or C infection as defined by positive serology and transaminitis. Non-active Hepatitis B carriers may be included if protected with lamivudine (see 9.4 of protocol)

* Severe pulmonary dysfunction (CTCAE grade III-IV, see appendix D of protocol)

* Severe neurological or psychiatric disease

* Current participation in another clinical trial interfering with this trial

* Any psychological, familial, sociological and geographical condition potentially hampering compliance with the study protocol and follow-up schedule

* Claustrophobia to the extent that PET-CT is impossible

Study design

Design

Study type:	Interventional
Intervention model:	Other
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	14-04-2015
Enrollment:	72
Type:	Anticipated

Ethics review

Positive opinion

Date:	30-06-2015
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	NL5038
NTR-old	NTR5267
Other	2014-002654-39 : HOVON 130 NHL

Study results