Efficacy and safety of first-line therapy with chlorambucil, rituximab and lenalidomide (Revlimid®) (CR2) in elderly patients and young frail patients with advanced Chronic Lymphocytic Leukemia (CLL): A phase II trial.

No registrations found.

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

Summary

ID

NL-OMON23278

Source
NTR

Brief title
HOVON 109 CLL

Health condition

Advanced previously untreated Chronic Lymphocytic Leukemia

Sponsors and support

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

Intervention

Outcome measures

Primary outcome

For part I of the study:

Dose-limiting toxicity (DLT), maximum tolerated dose (MTD) and recommended part II dose (RDL) of Chlorambucil when combined with Rituximab and Lenalidomide.

For part II of the study: CR+PR rate.

Secondary outcome

For part I of the study:

To evaluate toxicity, especially tumor lysis syndrome (TLS), tumor flare reaction (TFR) and clinically relevant hematologic toxicity.

For part II of the study:

1. To evaluate the efficacy of Lenalidomide monotherapy in patients without progressive disease after 6 cycles of CR2;

2. To evaluate toxicity, especially tumor lysis syndrome (TLS), tumor flare reaction (TFR) and clinically relevant hematologic toxicity;

3. To evaluate progression free survival;

4. To evaluate event-free survival;

5. To evaluate overall survival.

Study description

Background summary

Chronic lymphocytic leukemia (CLL) is the most common leukemia in the western world mainly affecting the elderly. Although recently novel regimes containing the chemotherapeutic agents fludarabine and cyclophosphamide in combination with the monoclonal antibody rituximab (FCR) has shown improved progression free and overall survival, this regimen is considered too toxic for elderly patients. For the standard treatment of this patient group, chlorambucil, response rates and duration are limited. A recent study showed that addition of rituximab to chlorambucil improved the overall response rate but level of responses remained poor. Lenalidomide, a novel immunomodulating agent is thought to act by interaction in crosstalk between the microenvironment and leukemic cells and has promising clinical activity in CLL. This study will test the hypothesis that addition of lenalidomide to chlorambucil and rituximab will result in improved response rates for elderly and young FCR unfit patients with acceptable toxicity.

In this phase I/II prospective multicenter trial elderly (≥ 65 years) patients and FCR unfit patients <65 years with advanced previously untreated CLL will be treated with 6 cycles of chlorambucil at the maximum tolerated dose, rituximab and lenalidomide followed by 6 cycles of lenalidomide monotherapy. Target number of patients during phase I and II will be 12 and 50 respectively. Expected duration of accrual will be 2 years. Main study endpoints during phase I are: Dose-limiting toxicity (DLT), maximum tolerated dose (MTD) and recommended phase II dose (RDL) of chlorambucil when combined with rituximab and lenalidomide, and during phase II: overall and complete response rates.

Study objective

Does addition of lenalidomide to chlorambucil and rituximab result in better response rates with acceptable toxicity.

Study design

1. At entry;

2. Weekly during cycle I and cycle II;

3. Every 2 weeks during cycle III-VI;

4. Prior to each cycle;

5. At day 7 following the first cycle of lenalidomide dose escalation;

6. End of protocol;

7. Follow up: At 15, 18, 21, 24, 27, 30, 33, 36, 42, 48, 54 and 60 months after start treatment;

8. At progressive disease.

Intervention

Patients will be treated with 6 cycles of chlorambucil, rituximab and lenalidomide followed by 6 cycles of lenalidomide monotherapy.

Contacts

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Eligibility criteria

Inclusion criteria

1. Diagnosis of CLL without prior treatment;

2. Patients with symptomatic (according to IWCLL guidelines) stage A or stage B or stage C;

3. Age ≥ 65 years at the time of signing the informed consent form, or age < 65 years and CIRS ≥ 7;

4. Able to adhere to the study visit schedule and other protocol requirements;

5. WHO performance status of ≥ 2;

6. Laboratory test results within these ranges: absolute neutrophil count ≥ 1.0 x 10^9/l, platelet count ≥ 30 x 10^9/l, creatinine clearance ≤ 60 ml/min, total bilirubin ≤ 25 umol/L, AST & ALT ≤ 2 x ULN;

7. Females of childbearing potential must have a negative serum or urine pregnancy test within 10 - 14 days prior to and again within 24 hours of starting lenalidomide;

8. Patients who are willing and capable to use adequate contraception during the therapy (all men, all pre-menopausal women). Patients must be able to adhere to the requirements of the Lenalidomide Pregnancy Prevention Risk Management Plan;

9. Written informed consent.

Exclusion criteria

1. Patients that are unable or unwilling to adhere to the requirements of the Lenalidomide Pregnancy Prevention Risk Management Plan;

2. Intolerance of exogenous protein administration;

3. Hepatitis B Ag positive, Hepatitis C positive and/or HIV positive patients;

4. Patients with uncontrolled Autoimmune Hemolytic Anemia (AIHA) or autoimmune thrombocytopenia (ITP);

5. Active fungal, bacterial, and/or viral infection;

6. Pregnant or breast-feeding females (lactating females must agree not to breast feed while taking lenalidomide);

7. Use of any other experimental drug or therapy within 28 days of baseline;

8. Known hypersensitivity and/or serious adverse reactions to lenalidomide or similar drugs;

9. Any prior use of lenalidomide;

10. Concurrent use of other anti-cancer agents or treatments;

11. Uncontrolled hyperthyroidism or hypothyroidism;

12. Patients with history of idiopathic deep venous thrombus and/or pulmonary embolism within last three years;

13. Neuropathy ≥ grade 2;

14. History of active malignancy during the past 5 years with the exception of basal carcinoma of the skin; squamous cell carcinoma of the skin, carcinoma in situ of the cervix, carcinoma in situ of the breast, prostate cancer (TNM stage of T1a or T1b);

15. Current inclusion in other clinical trials;

16. 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 controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	07-09-2011
Enrollment:	62
Type:	Anticipated

Ethics review

Positive opinion

Date:	02-09-2011
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	NL2906
NTR-old	NTR3052
Other	EudraCT / HOVON : 2010-022294-34 / 109 CLL;
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A