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.

Gepubliceerd: 02-09-2011 Laatst bijgewerkt: 18-08-2022

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

Ethische beoordeling	Positief advies
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON23278

Bron
NTR

Verkorte titel
HOVON 109 CLL

Aandoening

Advanced previously untreated Chronic Lymphocytic Leukemia

Ondersteuning

Primaire sponsor: Stichting Hemato-Oncologie voor Volwassenen Nederland (HOVON)
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Overige ondersteuning: Stichting Hemato-Oncologie voor Volwassenen Nederland (HOVON),
Celgene
Roche

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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.

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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

Onderzoeksopzet

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.

Onderzoeksproduct en/of interventie

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

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	07-09-2011
Aantal proefpersonen:	62
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	02-09-2011
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL2906

Register	ID
NTR-old	NTR3052
Ander register	EudraCT / HOVON : 2010-022294-34 / 109 CLL;
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten
N/A