ReBeL study: A randomized phase I/II trial of lenalidomide and rituximab with or without bendamustine in patients ≥ 18 years with relapsed follicular lymphoma. A HOVON/GLSG study.

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

In this trial the efficacy and toxicity is tested of treatment with lenalidomide and rituximab (arm A), and lenalidomide, rituximab and bendamustine (arm B) in patients with relapsed follicular lymphoma (FL).

Ethische beoordeling	Positief advies
Status	Werving gestopt
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON22769

Bron
NTR

Verkorte titel
HOVON 110 FL / GLSG

Aandoening

Relapsed CD20+ follicular lymphoma

Ondersteuning

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

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

For the phase I part of the study: To determine the dose limiting toxicity (DLT) and recommended dose level (RDL) of lenalidomide and bendamustine given in combination with rituximab for the phase II part of the study.
For the phase II of the study: To determine the efficacy and toxicity of the two arms of the study (arm A: lenalidomide and rituximab, and arm B: lenalidomide, rituximab and bendamustine) in patients with relapsed follicular lymphoma (FL) and to identify the most promising of these two treatment arms.

Toelichting onderzoek

Achtergrond van het onderzoek

Follicular lymphoma (FL) is an indolent type of lymphoma. After diffuse large B cell lymphoma, it is the most frequently occurring type of lymphoma. In the Netherlands, 800 new cases are diagnosed yearly. Although the disease is exquisitely sensitive to both chemotherapy, immunotherapy and radiotherapy, there are no curative options. Currently, there is no standard treatment for patients with relapsed FL. Lenalidomide, rituximab and bendamustine have shown promising activity in FL, both in first line and in relapse. Since the toxicity of both drugs is relatively minor , combination of these drugs is an attractive option.The hypothesis is that both treatment arms will be effective with acceptable toxicity. This phase I/II prospective multicenter trial will be performed in the Netherlands and Germany. In the phase I part the optimal dose of bendamustine and lenalidomide will be established. In the phase II parts, patients aged 18 years or older with FL will be treated with 6 monthly cycles of lenalidomide and rituximab, with or without bendamustine, followed by 2 years of rituximab maintenance treatment (once every 3 months). Patients will be followed until 8 years after registration.The target number of patients during the phase I and II part will be 15-24 and 150 respectively. Expected duration of the study will be 11 years.
The primary endpoints for the phase I part are: Dose-Limiting toxicity (DLT) and recommended phase II dose (RDL) of lenalidomide and bendamustine given in combination

with rituximab. For the phase II part the primary endpoints are CR rate and severe toxicity during induction treatment.

Doel van het onderzoek

In this trial the efficacy and toxicity is tested of treatment with lenalidomide and rituximab (arm A), and lenalidomide, rituximab and bendamustine (arm B) in patients with relapsed follicular lymphoma (FL).

Onderzoeksopzet

1. At entry;

2. Prior to each cycle;

3. 6-8 weeks after start of induction cycle 6;

4. Before each administration of rituximab maintenance treatment;

5. After 12 and 24 months of maintenance treatment;

6. End of protocol treatment;

7. During follow up every 3 months for 2 years and every 6 months thereafter, up to 8 years after registration;

8. At progressive disease.

Onderzoeksproduct en/of interventie

All patients will be treated with 6 induction cycles followed by 2 years of maintenance treatment with Rituximab, once every three months.

In the induction cycles in the phase I part of the study, lenalidomide, rituximab and bendamustine are given using up to three dose levels of lenalidomide (10, 15 or 20 mg on day 3-21 of a 28-day schedule) with up to two dose levels of bendamustine (70 or 90 mg/m2 on day 1,2) and rituximab (375 mg/m2 on day 1), in order to establish the RDL of lenalidomide and bendamustine given in combination with rituximab for the phase II of the study.

In the phase II part of the study, in the induction cycles lenalidomide in combination with rituximab with or without bendamustine is given.

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Relapsed FL grade 1, 2, 3a;

2. Ann Arbor stage II-IV at relapse;

3. The lymphoma at relapse must be CD20+. To establish this, and to exclude transformation to aggressive lymphoma, a biopsy at relapse is strongly recommended;

4. A maximum of three prior treatment regimens (patients that have had a prior allogeneic SCT are excluded; prior autologous SCT (if > 1 year ago) is allowed);

5. Subjects must have an indication for treatment based on one or more of the following criteria:

A. Involvement of at least 3 nodal sites, each with a diameter > 3 cm;

B. Symptomatic splenomegaly;

C. Bulky disease at study entry according to the GELF criteria: nodal or extranodal mass (except spleen) > 7 cm in its greatest diameter;

D. B-symptoms (absence or presence of fever and/or night sweats and/or unexplained loss of 10% of body weight or more in the 6 months preceding diagnosis);

E. Hb < 10 g/dl (6.2 mmol/l) (if caused by bone marrow infiltration and not otherwise explained);

F. Thrombocytopenia: platelets < 100x109/l caused by bone marrow infiltration;

G. Organ compression syndrome (e.g. hydronephrosis caused by lymphadenopathy);

H. Pleural/peritoneal effusion;

I. Symptomatic extranodal manifestations.

6. Measurable disease as defined in appendix C (patients with only bone marrow involvement are therefore not eligible);

7. Age ≥ 18 years;

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

9. WHO performance status of 0-2;

10. Laboratory test results within these ranges: absolute neutrophil count ≥ 1.5x 109/l, platelet count ≥ 100x 109/l, creatinin clearance ≥ 50 ml/min, total bilirubin ≤ 30 µmol/l (1,75 mg/dl), AST & ALT ≤ 3x ULN;

11. 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 treatment;

12. Patients must be 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;

13. Written informed consent.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Rituximab-refractory patients (definition: progression during or within 6 months after rituximab containing immunochemotherapy or rituximab maintenance treatment);

2. Clinical or histologic signs of transformation;

3. Prior allogeneic SCT;

4. Prior autologous SCT less than one year ago;

5. Any prior use of lenalidomide or bendamustine;

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

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

8. Hepatitis B sAg positive, Hepatitis C positive and/or HIV positive patients;

9. Patients with uncontrolled autoimmune hemolytic anemia (AIHA) or autoimmune thrombocytopenia (ITP);

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

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

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

13. Intolerance of exogenous protein administration, or known allergy to murine products;

14. Uncontrolled hyperthyroidism or hypothyroidism;

15. Neuropathy ≥ grade 2 at time of inclusion;

16. Clinically symptomatic severe cardiac dysfunction (NYHA III-IV);

17. Clinically symptomatic severe pulmonary dysfunction;

18. Severe neurologic or psychiatric diseases.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	Geneesmiddel

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	05-09-2011
Aantal proefpersonen:	174
Type:	Werkelijke startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Ethische beoordeling

Positief advies

Datum:	18-08-2011
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	NL2882
NTR-old	NTR3028
Ander register	HOVON / METC : HO110 / 2011-000097-56;
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten
N/A