Phase III study comparing R-CODOX-M/R-IVAC versus dose-adjusted EPOCH-R (DA-EPOCH-R) for patients with newly diagnosed high risk Burkitt lymphoma

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The hypothesis to be tested is that the outcome in arm B is better than in arm A.

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

Samenvatting

ID

NL-OMON28081

Bron
Nationaal Trial Register

Verkorte titel
HOVON 127 BL

Aandoening

Non-hodgkin lymphoma, Burkitt lymphoma
Burkitt lymfoom

Ondersteuning

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

(HOVON)
- KWF

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

2 year PFS; defined as time from randomisation to disease progression, relapse or death, whichever comes first. Patients still alive or lost to follow up are censored at the date they were last known to be alive.

Toelichting onderzoek

Achtergrond van het onderzoek

Study phase: phase III

Study objectives:

Primary objective

- To confirm in a multicenter setting an improvement in PFS to 85% at 2 years of DA-EPOCH-R in patients with newly diagnosed high risk Burkitt lymphoma as compared to an expected PFS of 70% at 2 years for the control arm R-CODOX-M/R-IVAC.

Secondary objectives:

- To evaluate Overall Response Rate (ORR) end-of-treatment, Event Free Survival (EFS) and Overall Survival (OS) at 2 years
- To evaluate both regimens with respect to CTCAE grade ≥3 toxicity

- To evaluate both regimens with respect to hospitalisation days

Patient population: Patients with newly diagnosed high risk Burkitt lymphoma 18 -75 years

Study design: prospective, multi-center, randomized

Duration of treatment: Arm A: 16 weeks, Arm B: 18 weeks

Doel van het onderzoek

The hypothesis to be tested is that the outcome in arm B is better than in arm A.

Onderzoeksopzet

At entry, at mid treatment (after cycle 2 in arm A, after cycle 3 in arm B), at end of treatment, during follow-up (every 3 months until 6 months after completion of therapy, then every 6 months until 24 months after therapy, and then annually until 5 years after registration)

Onderzoeksproduct en/of interventie

Arm A: R-CODOX-M/R-IVAC

2 cycles of R-CODOX-M and 2 cycles R-IVAC
(alternately) total of 16 weeks (4 weeks per cycle)
R-CODOX-M consists of:

- rituximab i.v. (day 1,9: 375 mg/m^2/d)

- cyclophosphamide i.v. (day 1: 800 mg/m^2, day 2-5: 200 mg/m^2/d)

- vincristine i.v. (day 1,8: 1.5 mg/d)

- doxorubicin i.v. (day 1: 40 mg/m^2)

- methotrexate i.v.(day 10: 3000 mg/m^2 (<= 65 y), 1000 mg/m^2 (> 65 y))

R-IVAC consists of:

- rituximab i.v. (day 3,7: 375 mg/m^2/d)

- ifosfamide (day 1-5: 1500 mg/m^2/d (<=65 y), 1000 mg/m^2/d (>65 y))

- etoposide i.v. (day 1-5: 60 mg/m^2/d)

- cytarabine i.v. (day 1,2: 4000 mg/^2/d (<=65 y), 2000 mg/m^2/d (>65 y)

Both regimens also include supportive care and i.t. prophylaxis.

Arm B: DA-EPOCH-R

6 cycles, 3 weeks per cycle, total of 18 weeks

- etoposide i.v. (day 1-4: 50-124.4 mg/m^2/d continuous infusion, dose adjustment possible at every cycle)

- prednisolone p.o. (day 1-5 : 120 mg/m^2/d)

- vincristine i.v. (day 1-4: 0.4 mg/m^2/d continuous infusion)

- cyclophosphamide i.v. (day 5: 480-1866 mg/m^2/d dose adjustment possible at every cycle)

- doxorubicin i.v. (day 1-4 : 10-24.8 mg/m^2/d continuous infusion, dose adjustment possible at every cycle)

- rituximab i.v. (day 1,5: 375 mg/m^/d)

Also with supportive care and i.t. prophylaxis.

Contactpersonen

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

- First diagnosis of high risk Burkitt lymphoma (sporadic and HIV associated), histologically confirmed according to the WHO classification 2008. Upon its availability the WHO 2016 classification should be used, to replace the WHO 2008 classification;

- High risk disease; i.e. any of following: elevated LDH, WHO performance status ≥ 2, Ann Arbor stage III or IV, tumour mass ≥ 10 cm;

- Age 18-75 years inclusive;

- WHO performance status (PS) 0-3, WHO PS 4 only if disease related;

- Written informed consent.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

- All histopathological diagnoses other than Burkitt lymphoma according to the WHO classification 2008, irrespective of the presence of a MYC rearrangement. Upon its availability the WHO 2016 classification should be used, to replace the WHO 2008 classification;

- Patients with endemic Burkitt lymphoma;

- Patients with low risk Burkitt lymphoma (i.e. all of following: normal LDH, WHO performance status 0 or 1, Ann Arbor stage I or II, no tumour mass ≥ 10 cm);

- Patients with CNS localisation of Burkitt lymphoma;

- Prior treatment other than local radiation (max. 10 Gy) or short course (max 7 days) of steroids ≤ 1 mg/kg

or ≤100mg prednisolone (whichever is greater; or equivalent corticosteroid) for acute symptoms;

- Creatinine clearance < 50 ml/min unless lymphoma related;

- Inadequate hepatic function: bilirubin > 2.5 * ULN (total) except patients with Gilbert’s syndrome as defined by > 80% unconjugated;

- Inadequate haematological function ANC < 1x10^9/l and platelets < 75x10^9 /l unless lymphoma related;

- Severe pulmonary dysfunction (CTCAE grade 3-4);

- Severe neurological or psychiatric disease;

- Active symptomatic ischemic heart disease, myocardial infarction, or congestive heart failure within the past year. If an ultrasound or MUGA scan is obtained the LVEF should exceed 45%;

- All men and all women of child-bearing potential not willing or able to use an acceptable method of birth control for the duration of the study and one year beyond treatment completion;

- Female subject pregnant or breast-feeding;

- History of a prior invasive malignancy in the past 5 years with the exception of basal carcinoma of the skin or stage 0 cervical carcinoma;

- Serious concomitant medical illnesses that would jeopardise the patient's ability to receive the regimen with reasonable safety, including active hepatitis B (HBV) or hepatitis C (HCV) infection;

- Current participation in another clinical trial if interfering with HO127;

- 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:	Gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	Actieve controle groep

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	15-06-2014
Aantal proefpersonen:	260
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Ethische beoordeling

Positief advies

Datum:	20-05-2014
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	NL4429
NTR-old	NTR4602
Ander register	HOVON : HO127

Resultaten

Samenvatting resultaten
Not yet for this trial.