Very early FDG-PET/CT-response adapted therapy for advanced stage Hodgkin Lymphoma, a randomized phase III non-inferiority study of the EORTC Lymphoma Group and the Polish Lymphoma Research Group

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Ethical review	Approved WMO
Status	Pending
Health condition type	Lymphomas Hodgkin's disease
Study type	Interventional

Summary

ID

NL-OMON39829

Source
ToetsingOnline

Brief title
H11 / EORTC 20101-23101

Condition

- Lymphomas Hodgkin's disease

Synonym
Advanced stage Hodgkin Lymphoma

Research involving

Human

Sponsors and support

Primary sponsor: European Organisation for Research in Treatment of Cancer (EORTC)
Source(s) of monetary or material Support: EORTC

Intervention

Keyword: ABVD, BEACOPPesc, FDG-PET./CT, Hodgkin Lymphoma

Outcome measures

Primary outcome

Freedom from treatment failure (FFTF)

Secondary outcome

* Response at the end of therapy (chemotherapy and radiotherapy, whenever

applicable);

* Progression-free survival (PFS) ;

* Overall survival ;

* Serum TARC levels at baseline, during treatment and follow up;

* Frequency of acute toxicity and long-term toxicity in terms of second

malignancies, cardiovascular and pulmonary events.

Study description

Background summary

Escalated BEACOPP is currently considered to be the standard treatment in advanced Hodgkin Lymphoma in a large number of centers. Escalated BEACOPP is more effective than ABVD. However, the disadvantage of treating patients with escalated BEACOPP is the higher risk of serious acute and late side effects compared with ABVD. A clinical trial is therefore needed to identify those patients who can reliably be treated with the less intense ABVD schedule and those who need more intense treatment.

Study objective

The main objective of the trial is to show that ABVD-based response-adapted therapy for advanced-stage Hodgkin lymphoma, with treatment intensification (BEACOPP) in case of a positive FDG-PET after one cycle of ABVD, has non-inferior efficacy compared with the intensive BEACOPP regimen. Secondary objectives include the assessment of the prognostic value of PET after one cycle of BEACOPPesc; of the predictive and prognostic value of serum TARC levels as tumor marker; of treatment related toxicities with a focus on second malignancies, pulmonary toxicities and cardiotoxicity during therapy and during (long term) follow up.

Study design

All patients will have a baseline FDG-PET/CT and diagnostic quality CT scan prior to randomization. All patients will be randomized between:

1. An experimental arm (very early PET-response adapted), where all patients are initially treated with a single cycle of ABVD, followed by Very early FDG-PET/CT and if negative patients continue on ABVD therapy to a total of six cycles. Very early FDG-PET/CT-positive patients receive 3 cycles of BEACOPPesc followed by another 3 cycles of BEACOPPesc. Mid-treatment evaluation is performed after 4 cycles. In case of treatment failure (less than PR), the patient goes off protocol treatment.

2. A standard arm, where patients are treated with four cycles of BEACOPPesc followed by 2 cycles of BEACOPPesc. Very early PET/CT is performed after one cycle, but with no therapeutic consequences. Mid-treatment evaluation is performed after four cycles. In case of treatment failure (less than PR), the patient goes off protocol treatment.

Only patients with residual PET positive disease after chemotherapy will receive radiotherapy (36 Gy/18 fractions to the FDG-PET/CT positive residual mass (es).

Intervention

The standard arm is 6 cycli escBEACOPP
After cycle 1, after completion of chemotherapy and, if applicable after completion of radiotherapy a FDG-PET/CT scan is being made.

The experimentel arm is 1 cycle ABVD, followed by a PET-scan.
If the PET-scan after cycle 1 is negative, another 5 cycli of ABVD will follow.
If the PET-scan after cylce 1 is positive, another 6 cycli of escBEACOPP will follow.

After completion of chemotherapy and, if applicabele after completion of radiotherapy an other FDG-PET/CT scan will be made.

Study burden and risks

Both the ABVD scheme as escBEACOPP scheme is being used in the daily practice.Therefore it gives no extra risks.
FDG-PET/CT scan gives an extra radiation exposure.
From patients who participate in the side study extra blood will be taken during regular control. Patients will not have to undergo an extra puncture.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

* Previously untreated, histologically proven classical Hodgkin lymphoma
* Clinical stages III/IV (Ann Arbor, see Appendix F)
* Age 18-60
* WHO performance 0-2 (see Appendix C)
* FDG-PET/CT scan prospectively planned after one cycle of chemotherapy in all patients
* Adequate organ function:;* Heart:
New York Heart Association (NYHA) functional classification <= II (EF >= 50% or FS >= 25%)
No symptomatic coronary heart disease (stable angina pectoris is allowed),
No severe uncontrolled hypertension.;* Liver: Total Bilirubin <= 2 x UNL, alanine aminotransferase (ALT, SGPT) <= 3 x UNL, aspartate aminotransferase (AST, SGOT) <= 3 x UNL (exception: elevated values due to HL liver involvement).;* Kidney: creatinine clearance >= 60 ml/min (measured or calculated according to the method of Cockcroft), uric acid, calcium (all <UNL).;* Hematological: Hemoglobin >= 10 g/dl, Leukocyte concentration >= 3.0 x 109/L absolute neutrophil count >= 1.5 x 109/L, platelets >= 75 x 109 /L. (exception: reduced values related to HL (e.g. BM infiltration, splenomegaly));Patients with a buffer range from the normal values of +/- 10% for hematology and +/- 10% for biochemistry are acceptable.;* Patients of childbearing/reproductive potential should use adequate birth control measures during the whole duration of study treatment.;* Female subjects of childbearing potential (defined as any female subject unless she meets at least one of the following criteria: Age >=50 years and naturally amenorrheic for >= 1 year {amenorrhea following cancer therapy does not rule out childbearing potential}, premature ovarian failure confirmed by a specialist gynecologist, previous bilateral salpingo-oophorectomy or hysterectomy, XY genotype, Turner syndrome or uterine agenesis.) must:;* Agree to have a medically supervised pregnancy test with a minimum sensitivity of 25 mIU/ml not more than 3 days before the start of study medication. This requirement also applies to women of childbearing potential who practice complete and continued abstinence;* Male subjects must:;* Agree to use condoms throughout study drug therapy, during any dose interruption and for one week after cessation of study therapy if their partner is of childbearing potential and has no contraception.;* Agree not to donate semen during study drug therapy and for one week after end of study drug therapy.;* Written informed consent according to ICH/EU Good Clinical Practice, and national/local regulations

Exclusion criteria

No pregnancy or breast feeding
* No specific contraindications to BEACOPPesc therapy, so therefore:
* poorly controlled diabetes mellitus
* known HIV infection
* chronic active hepatitis B and/or hepatitis C
* concomitant or previous malignancies with the exception of basal cell skin tumors, adequately treated carcinoma in situ of the cervix and any cancer that has been in complete remission for > 5 years

* No psychological, familial, sociological or geographical condition potentially hampering compliance with the study protocol and follow-up schedule; those conditions should be discussed with the patient before randomization in the trial.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-02-2014
Enrollment:	190
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Bleomycin
Generic name:	Bleomycin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Cyclophosphamide
Generic name:	Endoxan
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Dacarbazine

Generic name:	Dacarbazine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Doxorubicin
Generic name:	Doxorubicin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Vinblastine
Generic name:	Vinblastine
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	23-01-2013
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	10-07-2013
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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
EudraCT	EUCTR2011-005473-22-NL
CCMO	NL42634.042.12