The H10 EORTC/GELA randomized Intergroup trial on early FDG-PET scan guided treatment adaption versus standard combined modality treatment in patiënts with supradiaphragmatic stage I/II Hodgkin's lymphoma

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To evaluate whether chemotherapy alone is as effective -but less toxic-, as combined modality treatment in terms of progression-free survival (PFS), in patients with stages I/II Hodgkin*s lymphoma who are FDG-PET scan negative after two cycles of...

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

Summary

ID

NL-OMON29848

Source
ToetsingOnline

Brief title
EORTC H10

Condition

- Lymphomas Hodgkin's disease

Synonym
Hodgkin's disease

Research involving

Human

Sponsors and support

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

Intervention

Keyword: combined modality, CS I/II, FDG-PET, Hodgkin lymphoma

Outcome measures

Primary outcome

To find out whether investigational treatments (without radiotherapy) are non inferior to the standard treatments in patients with a negative PET scan after 2 cycles of ABVD. This will be separately evaluated in patients with an initially favorable prognosis (Group A), and in patients with an initially unfavorable prognosis (Group B).

With a standard 5 years progression free survival of 95% and 85% in the experimental arm (non radiotherapy and expectance of 10 -15% less long term toxicity) 608 patients will be needed in the F and 720 in the U group

In PET positive patients, the objective is to find out whether progression free survival can be improved by treatment intensification (investigational treatment) as compared to standard therapy. The favorable and unfavorable patients will be grouped for this analysis (group C). A total of 248 will be simultaneously accrued in group C (55/year). At the time of the final analysis, 77 events will be recorded in those patients. The final analysis will provide a 77% power to detect a 20% improvement (from 50% to 70%) in 5 years progression free survival rate with the investigational arm.

Secondary outcome

Not applicable

Study description

Background summary

The H10-trial aims at reducing toxicity while maintaining efficacy in patients with early stage HL who experience an excellent tumor-free outcome with standard combined modality treatment. However, the long-term serious adverse events of treatment ask for modification of primary treatment burden. This randomized phase III trial aims at identifying the group of patients that will enjoy long-term tumor free survival with less intensive treatment and thus -according to our hypothesis- less serious long-term adverse events. The identification of the *good-risk*-group will be based upon the early response to ABVD (after two cycles) analyzed by FDG-PET scan. When according to FDG-PET scanning no viable tumor is left after two cycles of ABVD (both in the abinitio favorable (F) as well as unfavorable subgroup (U)), we will withhold RT for these patients and complete the treatment with chemotherapy alone whereas the patients in the standard combined modality arm will receive additional cycles of ABVD + involved node RT (IN-RT) irrespective of the result of the FDG-PET scan. Notably, in the standard arm FDG-PET scan after 2 cycles of ABVD is mandatory as well, but the result will be used for documentation purposes only. When according to FDG-PET scanning viable tumor is still present after two cycles of ABVD (both in the ab initio favorable (F) as well as unfavorable subgroup (U)), we will change chemotherapy from
ABVD to a more intense schedule e.g. escalated BEACOPP for two cycles followed by IN-RT. By doing this we are aiming at improving the PFS for this subgroup of patients whereas the patients in the standard combined modality arm will receive additional cycles of ABVD + IN-RT.

Study objective

To evaluate whether chemotherapy alone is as effective -but less toxic-, as combined modality treatment in terms of progression-free survival (PFS), in patients with stages I/II Hodgkin*s lymphoma who are FDG-PET scan negative after two cycles of ABVD. This question will be addressed in the group of patients with favorable stages I/II disease as well as in those with unfavorable stages I/II disease.
Evaluate whether early change of chemotherapy from ABVD to escalated BEACOPP improves the progression-free survival of patients who are FDG-PET-positive after two cycles of ABVD, as compared with those who continue on standard ABVD in both favorable as well as unfavorable subsets of patients.

Confirm that early response to FDG-PET scan can predict the outcome of patients with stage I/II Hodgkin*s lymphoma. This will be evaluated in the patients randomized in the standard arm.

Study design

Fase III, randomized, open, multicenter intergroup trial

Intervention

ABVD and FDG-PET followed by ABVD or escalated BEACOPPin combination with radiotherapy depending on the outcome of the FDG-PET.

Study burden and risks

FDG-PET

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

Histologically confirmed Hodgkin's lymphoma (HL), except for nodular lymphocyte predominant subtype (nodular paragranuloma)
Supradiaphragmatic Ann Arbor clinical stage I or II
Previously untreated
Clinical stages I/II
Age 15-70 years
WHO performance 0-3
FDG-PET scan prospectively planned after two cycles of ABVD in all patients
Informed consent

Exclusion criteria

No FDG-Pet scan facilities available
Inadequate liver-renal function (bili>2,5x uln or creat >2,5x uln
Unstable diabetes mellitus (because of FDG-PET scan

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):	01-09-2006
Enrollment:	500
Type:	Anticipated

Ethics review

Approved WMO Date:	11-07-2006
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	26-11-2007
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-02-2008
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	11-02-2009
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	21-10-2009
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	24-08-2010
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	12-04-2012
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2005-002765-37-NL
CCMO	NL12065.091.06