BRENTUXIMAB VEDOTIN ASSOCIATED WITH CHEMOTHERAPY IN UNTREATED PATIENTS WITH STAGE I/II UNFAVOURABLE HODGKIN LYMPHOMA - A RANDOMIZED PHASE II LYSA-FIL-EORTC INTERGROUP STUDY
BREACH

Published: 26-05-2015
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Primary objective:To improve the PET negativity after two cycles of immuno-chemotherapyPrimary efficacy endpoint:PET 2 assessment according to the five-point scale Deauville criteria (Negative = 1, 2, 3 and Positive = 4, 5), based on central review....

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

Summary

ID

NL-OMON55642

Source
ToetsingOnline

Brief title
BREACH STUDY

Condition

- Lymphomas Hodgkin's disease

Synonym
CHEMOTHERAPY, UNFAVOURABLE HODGKIN LYMPHOMA

Research involving
Human

Sponsors and support

Primary sponsor: LYSARC
Source(s) of monetary or material Support: LYSARC

Intervention

Keyword: (>= 18 years to <= 60 years), Brentuximab, Hodgkin Lymphoma, Randomization

Outcome measures

Primary outcome

Primary objective:

To improve the PET negativity after two cycles of immuno-chemotherapy

Primary efficacy endpoint:

PET 2 assessment according to the five-point scale Deauville criteria (Negative

=1, 2, 3 and Positive = 4, 5), based on central review.

Secondary outcome

Secondary objectives:

Secondary efficacy endpoint:

- CR rate (according to Cheson 2007) at the end of treatment

- Progression-free survival (PFS)

- Overall survival

Secondary safety endpoint:

- Toxicity of brentuximab vedotin in combination with combined modality

treatment

Study description

Background summary

Hodgkin Lymphoma (HL) is a neoplasm of lymphoid tissue that is defined histopathologically by the presence of malignant Hodgkin Reed-Sternberg (RS) cells. CD30 expression has been well established on RS cells in fresh tumor biopsies and on established in vitro cell lines.
Chemotherapy alone or combined with radiotherapy produces a durable remission rate of approximately 70% in patients with newly-diagnosed HL.
Patients with limited stage disease do particularly well, and most of them with favorable prognostic factors can be cured. The future challenge for this group of patients is to determine the minimum amount of treatment that is necessary to achieve cure. Radiotherapy and multi-agent chemotherapy may contribute to the incidence of late complications that are seen and may be responsible for excess mortality in this population. Recent studies have shown that the amount of chemotherapy and the field and dose of radiotherapy can be reduced safely.

Study objective

Primary objective:
To improve the PET negativity after two cycles of immuno-chemotherapy
Primary efficacy endpoint:
PET 2 assessment according to the five-point scale Deauville criteria (Negative = 1, 2, 3 and Positive = 4, 5), based on central review.
Secondary objectives:
Secondary efficacy endpoint:
- CR rate (according to Cheson 2007) at the end of treatment
- Progression-free survival (PFS)
- Overall survival
Secondary safety endpoint:
- Toxicity of brentuximab vedotin in combination with combined modality treatment

Study design

Multicentric, open-label, randomized phase II trial
Arm A: 4 cycli van ABVD (elke 28 dagen) Radiotherapie op het einde van de chemotherapie: 30 Gy INRT zonder boost.
Arm B: 4 cycli van AVD / Brentuximab vedotin (elke 28 dagen) Radiotherapie eind immuno-chemotherapie: 30 Gy zonder INRT boost.

Intervention

Arm A:

4 cycles of ABVD (every 28 days) * Radiotherapy at the end of chemotherapy: 30 Gy INRT without boost.
Arm B:
4 cycles of AVD/Brentuximab vedotin (every 28 days) Radiotherapy at the end of immuno-chemotherapy: 30 Gy INRT without boost.

Study burden and risks

Physical examination, blood tests, heart and lung-function tests, a CT scan (with intravenous contrast) and PET scan
Administration of treatments: ABVD (arm A) or AVD + Brentuximab vedotin (arm B)
The rhythm and mode of administration are the same in each arm: by intravenous infusion in four 28-day cycles, at D1 and D15 of each cycle.
Radiotherapy (RT): This starts from 3 to 4 weeks after the last cycle of chemotherapy, and will last for about 3 weeks. You get a total standard dose of 30 Gy (Grays), spread over multiple sessions, the areas that were initially affected by Hodgkin lymphoma.
If the patient is one of the first 21 patients who started the radiotherapy, the doctor will every week contact him to the visit by the end of treatment to document all the events that have been observed during the radiotherapy.
The chemotherapy may be associated with known undesirable effects. Nausea and vomiting, Neurological disorders in the arms or legs, fatigue, gastrointestinal problems possible risks to the unborn child.

Contacts

Public
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Scientific
LYSARC

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

* Histologically confirmed CD30+ classical Hodgkin lymphoma according to local evaluation
* Supradiaphragmatic Ann Arbor clinical stage I or II
* Previously untreated
* PET scan without IV contrast at diagnosis available for central review with at least one hypermetabolic lesion

Exclusion criteria

* Histological diagnosis different from classical Hodgkin Lymphoma. Nodular lymphocyte predominant subtypes (nodular paragranuloma or Poppema paragranuloma) are excluded.
* Known cerebral or meningeal disease of any etiology, including signs or symptoms of PML

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	28-04-2016
Enrollment:	14
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Bleomycine
Generic name:	Bleomycine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Brentuximab Vedotin
Generic name:	Adcetris
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Dacarbazine
Generic name:	Carboxamide
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Vinblastine
Generic name:	Vinblastine
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	26-05-2015
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-12-2015

Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	06-01-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-07-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-07-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2013-000182-37-NL
CCMO	NL51979.078.15