HD21 for advanced stages: Treatment optimization trial in the first-line treatment of advanced stage Hodgkin lymphoma; comparison of 4-6 cycles of escalated BEACOPP with 4-6 cycles of BrECADD; a randomized phase III trial

Published: 13-03-2017
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This study has been transitioned to CTIS with ID 2024-518022-33-00 check the CTIS register for the current data. primary objective of the trial is to demonstrate non-inferior efficacy of 4-6 cycles of BrECADD compared to 4-6 cycles of escalated...

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

Summary

ID

NL-OMON50640

Source
ToetsingOnline

Brief title
HD21 (advanced stage)

Condition

- Lymphomas Hodgkin's disease
- Lymphomas Hodgkin's disease

Synonym
Hodgkin's disease; malignant lymphoma

Research involving
Human

Sponsors and support

Primary sponsor: Universitly of Cologne
Source(s) of monetary or material Support: KWF kankerbestrijding en Universiteit van Keulen,Millenium Pharmaceuticals

Intervention

Keyword: advanced stage, Hodgkin's disease

Outcome measures

Primary outcome

- Progression Free Survival (PFS).

- the rate of serious treatment- related toxicities during primary treatment.

New cohort for elderly 61-75 years:

- Complete response (CR) rate after chemotherapy

Secondary outcome

- CR rate

- Overall survival

- Infertility rate at 1 year (determined by hormone levels)

- second malignancies

- number of serious adverse events within 30 days after end of treatment.

- therapy adherence

- quality of life before, during and after therapy

Cohort elderly patients 61-75 years:

- Treatment related morbidity

- PFS and OS

- time to progression and HL-specific survival

Study description

Background summary

The German Hodgkin Study Group Center (GHSG) in Cologne is responsible for developing trials to improve the treatment of Hodgkin lymphoma. Improvements in radiotherapy and the introduction of polychemotherapy have contributed to the development of an incurable malignant disease into an oncological disease in adults that actually has the best prognosis of all. Relevant improvements in diagnostics and treatment are based on a stringent implementation of quality standards in the areas of pathology, radiology, nuclear medicine, radiotherapy and chemotherapy.

The standard treatment for patients with advanced stage is 4- 6 coureses of escalated BEACOPP chemotherapy every 3 weeks, followed by radiotherapy, when necessary.
This standard treatment is an intensive treatment with both acute and long term toxicity.

Therefore the GHSG had started this new trial to prove that the new chemotherapy regimen, BrECADD, is non-inferior to BEACOPP as first line treatment in advanced stage classical Hodgkin Lymphoma patients up to 60 years. The combination of conventional chemotherapy with brentuximab vedotin is designed to reduce the doses of certain conventional cytostatics in order to reduce the rate of adverse events while maintaining an equally good response to treatment.

Study objective

This study has been transitioned to CTIS with ID 2024-518022-33-00 check the CTIS register for the current data.

primary objective of the trial is to demonstrate non-inferior efficacy of 4-6 cycles of BrECADD compared to 4-6 cycles of escalated BEACOPP, each followed by radiotherapy on PET-positive residual lesions, in terms of progression free survival (efficacy objective).

If non-inferior efficacy can be shown, the co-primary objective is to further demonstrate reduced toxicity of the BrECADD treatment compared to the escalated BEACOPP treatment measured by treatment related morbidity (TRMB objective).

Study design

Open label, prospective, multicenter trial with two parallel groups and central statified randomization (minimization method).

Amendment March 2020: new cohort in this trial: older patients between 61-75 years.

Intervention

Patients are randomized to receive either 4-6 cycles of escalated BEACOPP regimen (standard group) or 4-6 cycles of BrECADD (experimental group).
After the first two cycles, a restaging is performed by contrast-enhanced computed tomography (ceCT) and FDG PET/CT in all patients in order to guide response-adapted continuation of therapy consisting of 4 or only 2 additional cycles of randomized chemotherapy in case of a PET positive or negative staging result, respectively.

So patients with negative PET-CT-scan after 2 cycles, will receive additional 2 cycles of chemotherapy.
Patients with a positive PET-CT-scan after 2 cycles, will receive 4 cycles of chemotherapy.

A second restaging will be performed after completion of chemotherapy; Patients with PET-positive residual disease will receive local irradiation, while patients in complete remission do not receive radiotherapy.

Amendment March 2020: all patients in the elderly cohort receive PET guided treatment with 4- 6 cycles of BrECADD +/- RT.

Study burden and risks

The benefit from participating in this trial is the chance of being treated with a new treatment approach that we hope to cause less side-effects compared to the current standard therapy.
The results of this trial may provide valuable knowledge for the treatment of Hodgkin Lymphoma in future.
However, it cannot be guaranteed that a patient will benefit from participating in this trial, and it cannot be ruled out with absolute certainty that participation in this trial, will not impair the success of the therapy in the long run.

Patients may suffer from side effects. Qualtiy of Life investigations can be part of the trial for a certain amount of patients.

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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 proven classical Hodgkin lymphoma
- First diagnosis, no previous treatment
- 18 to 60 years of age; cohort elderly: 61-75 years
- Stage IIB with large mediastinal mass and/or extranodal lesions, stage III or IV

Exclusion criteria

- Composite lymphoma or nodular lymphocyte-predominant Hodgkin lymphoma
-Previous malignancy (exceptions: basalioma, carcinoma in situ of the cervix uteri, completely resected melanoma TNMpT1)
- Prior chemotherapy or radiotherapy
- Concurrent disease which precludes protocol treatment
- Pregnancy, lactation
- Non-Compliance

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:	Recruiting
Start date (anticipated):	06-03-2018
Enrollment:	100
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Adcetris
Generic name:	brentuximab vedotin
Registration:	Yes - NL outside intended use
Product type:	Medicine

Brand name:	Cyclophosphamide
Generic name:	Cyclophosphamide
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Dacarbazine medac
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:	Toposin
Generic name:	Etoposide
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	13-03-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-07-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-10-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-10-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	25-04-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-05-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-02-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-02-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-02-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-02-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-09-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-01-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-01-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	01-03-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-02-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-03-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-07-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-02-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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
EU-CTR	CTIS2024-518022-33-00
EudraCT	EUCTR2014-005130-55-NL

Register	ID
ClinicalTrials.gov	NCT02661503
CCMO	NL59882.029.17