# HD 18 for advanced stages: treatment optimization trial in the first line treatment of advanced stage Hodgkin Lymphoma; treatment stratification by means of FDG-PET.

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| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Lymphomas Hodgkin's disease |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON46958

**Source**
ToetsingOnline

**Brief title**
HD 18

### Condition

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

**Synonym**
malignant lymphoma; Hodgkin's disease

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Vrije Universiteit Medisch Centrum
**Source(s) of monetary or material Support:** Ministerie van OC&W

## Intervention

**Keyword:** Advanced stage, Hodgkin lymphoma

## Outcome measures

### Primary outcome

Progresion Free Survival (PFS).

### Secondary outcome

Overall survival

Acute and late toxicity of treatment

Quality of Life

Secondary maligancy rate

CR rate

HL-specific death rate

Prognostic value of the PET-2 examination

# 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 8 coureses of

escalated BEACOPP chemotherapy every 3 weeks, followed by radiotherapy, when necessary.
This standard treatment is an intensive and long treatment with both acute and long term toxicity.
Therefore the GHSG had started this new trial to investigate if the experimental therapy (4x BEACOPP escalated) for patients who are PET negative after 2 cycles of chemotherapy is non-inferior to standard treatment with respect to the primary endpoint of progression free survival.
Also the GHSG investigates if the experimental therapy for patients who are PET positive after 2 cycles of chemotherapy: standard treatment with Rituximab, is superior to standard treatment alone.
In July 2011amendement 2: the standard therapy will be 6 courses of BEACOPP escalated in stead of 8 courses. This was the outcome of the results of the HD 15 study.
Also randomisation for PET-2 positive patients was closed, because inclusion for arm B has been ended. They have already included the number of patients.

**Study objective**

The aim of the trial is to individualize treatment for each patient by adapting it to early response and thus to continue intensive treatment only with those patients wo show an inadequate treatment response.
For patients who show a good initial response to treatment (PET-2 negative patients) the primary aim of the trial is to reduce toxicity while maintaining tumor control.
For patients who show a poor initial response to treatment (PET-2 positive patients), the primary aim of the trial is to improve PFS by means of adding Rituximab to treatment.

**Study design**

Prospective, randomized and unblinded multicenter study with treatment stratification by means of FDG-PET-scan performed after 2 courses of chemotherapy.

**Intervention**

For PET-2 negative patients:
one group with in total 8x escalated BEACOPP cycles (standard arm)
one group with in total 4x escalated BEACOPP cycles (experimental arm)

For PET-2 positive patients:
one group 8x escalated BEACOPP and 30 Gy radiotherapy on residual tumor (standard arm)
one group 8x escalated BEACOPP with Rituximab and 30 Gy radiotherapy on residual tumor (experimental arm)

July 2011amendement 2:
For PET-2 negative patients:
one group with in total 6x escalated BEACOPP cycles.
one group with in total 4x escalated BEACOPP cycles.

For PET-2 positive patients: 6x escalated BEACOPP cycles and 30 Gy radiotherapy on residual tumor.

**Study burden and risks**

In the experimental arm Rituximab will be added to the treatment in cycle 4 - 8. This may induce a larger decrease of the serum immunoglobulines. This may result in a larger risk for infections. In the protocol are described mandatory measurements to prevent complications.

Amendement 2 is submitted that the experimental arm with Rituximab is closed because the necessary number of patient has been achieved.

# 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

1.Histologically proven primary diagnosis of Hodgkin lymphoma;
2. Stage:
2.1 CS (PS) IIB with one or both of the following risk factors:
a) Large mediastinal mass (><= 1/3 of the maximum transverse diameter of the thorax),
b) Extranodal lesions (see definition in section 14.3.4);
2.2 CS (PS) III, IV;
3. Patient had no previous treatment for HL;
4. Age at entry: 18 - 60 years;
5. 6. Normal organ function (except HL-related);
6. Negative HIV test
7. In women: negative pregnancy test
8. Life expectancy > 3 months.

## Exclusion criteria

1. Incomplete diagnosis of the disease stage;
2. Prior or concurrent disease that prevents treatment according to protocol;
3. HL as composite lymphoma;
4. Prior chemotherapy or radiation;
5. Malignant disease within the last 5 years (exceptions: basalioma, carcinoma in situ of the cervix uteri, completely resected melanoma TNMpT1);
6. Pregnancy, lactation;
7. WHO activity index > 2;
8. Long-term ingestion of corticosteroids (e.g. for chronic polyarthritis) or antineoplastic drugs (e.g. methotrexate)

# Study design

## Design

Study phase: 3

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

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 30-11-2009 |
| Enrollment: | 40 |
| Type: | Actual |

## 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: | Cyclophosphamide |
| Registration: | Yes - NL intended use |
| Product type: | Medicine |
| Brand name: | Doxorubicine |
| Generic name: | Doxorubicin |
| Registration: | Yes - NL intended use |
| Product type: | Medicine |
| Brand name: | Etoposide |
| Generic name: | Etoposide |
| Registration: | Yes - NL intended use |
| Product type: | Medicine |
| Brand name: | Prednisone |
| Generic name: | Prednisone |

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| Registration: | Yes - NL intended use |

## Ethics review

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| Approved WMO Date: | 17-07-2009 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 02-09-2009 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 26-04-2012 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 03-05-2012 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 11-02-2013 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 12-02-2013 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 29-06-2018 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 16-10-2018 |
| 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 |
|---|---|
| EudraCT | EUCTR2007-003187-22-NL |
| Other | ISRTCN 00515554 |
| CCMO | NL25542.029.09 |