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

Protokoll Nummer: HD 21
EudraCT Nummer: 2014-005130-55

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Protocol Synopsis:

Indication: Hodgkin Lymphoma of advanced stage

Study design: Open-label, prospective, multicenter trial with two parallel groups and central stratified randomization

Planned sample size: 60 Patients (Austria); 1500 (International)

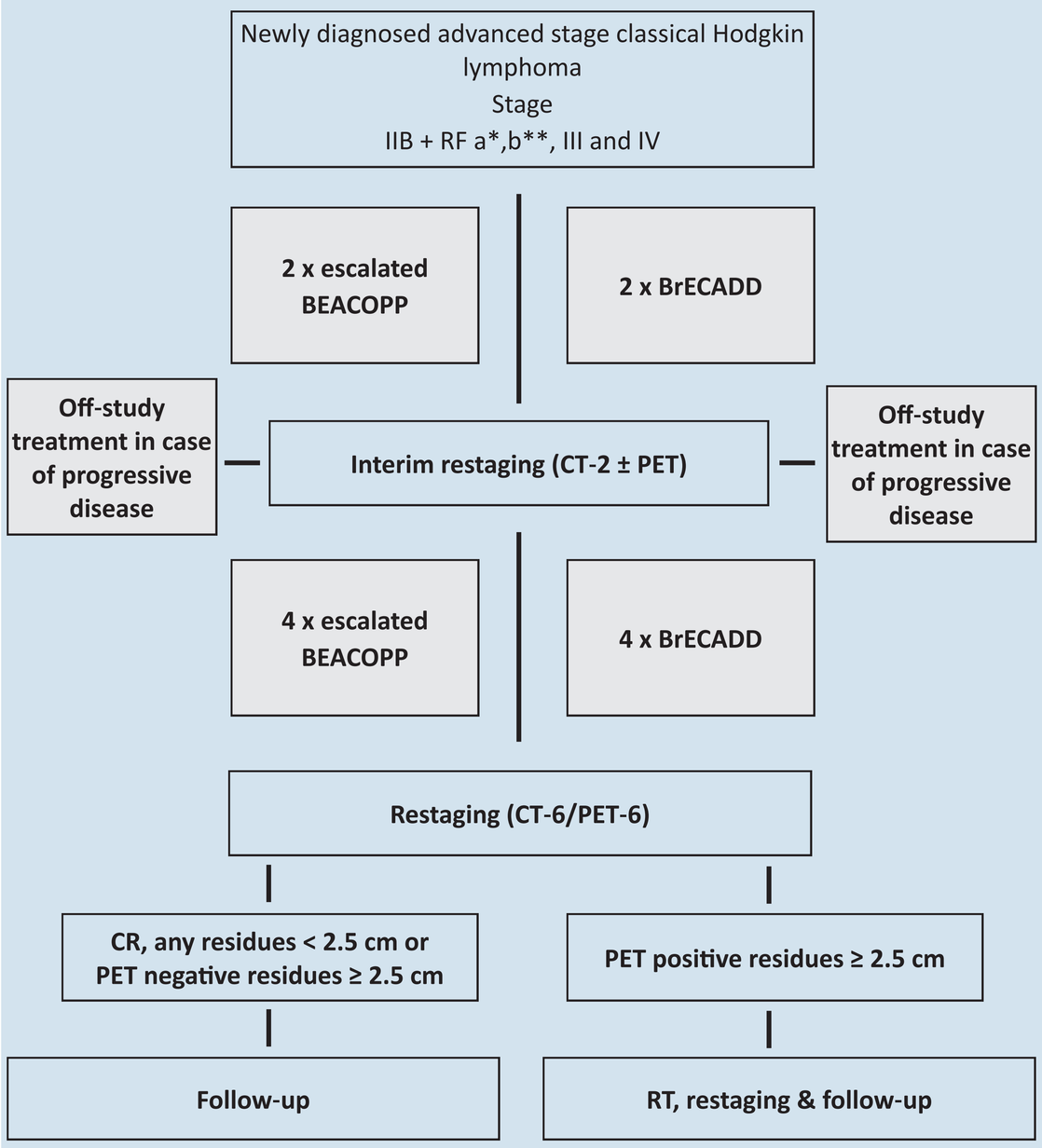
Duration:
First patient in (FPI): Q3 2016 (D), Q2 2017 (A, exp.)
Last patient in (LPI): Q2 2020 (expected)
Last patient out (LPO): Q4 2025 (expected)

Study medication: Brentuximab vedotin

Primary endpoints:
- Progression free survival (PFS)
- Treatment-related morbidity (TRMorbidity)

Secondary endpoints (selected):
- Tumor response (CR rate)
- Overall survival (OS)
- Infertility rate at 1 year (by hormone levels)
- Second malignancies
- Quality of life (QoL)

Study Design:



Risk factors
a* Large mediastinal mass (1/3 of the maximum transverse thoracic diameter)
b** Extranodal disease
BrECADD (Brentuximab, Etoposid,Cyclophosphamid, Doxorubicin, Dacarbazin, Dexamethason)

The aim of the HD21 trial is to prove that the new chemotherapy regimen, BrECADD, is non-inferior to BEACOPP as first-line treatment in advanced stage classical Hodgkin lymphoma patients aged ≤ 60. 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 effects while maintaining an equally good response to treatment.

All changes within the new treatment regimen are aimed to reduce the number of acute and late toxicities without impairing treatment success. Due to the implementation of brentuximab vedotin into the BEACOPP regimen with a maximum tolerated dose of 1.8 mg/kg as defined in the phase I trial, it is possible to dispense with the agent of vincristine. The etoposide dose is lowered to 150 mg/m2 while the anthracycline dose is increased moderately from 35 mg to 40 mg of adriamycin. 14-day prednisone therapy is replaced by 4-day dexamethasone therapy. Oral administration of procarbazine for 7 days is replaced by a 2-day intravenous therapy with dacarbazine on day 2 and on day 3 of each chemotherapy cycle. Besides, bleomycin is abandoned completely from the chemotherapy regimen.

Patients are randomized into one of the two treatment groups. Patients in the standard group receive 6 cycles of escalated BEACOPP, followed by local radiotherapy with 30 Gy if needed (see flow sheet). Patients in the experimental group receive 6 cycles of the new BrECADD regimen, radiotherapy is administered just as in the standard group.

Inclusion Criteria (selected):

- Histologically proven classical Hodgkin lymphoma
- First diagnosis, no previous treatment
- 18 to 60 years of age
- Stage IIB with large mediastinal mass and/or extranodal lesions, stage III or IV
- In women: negative pregnancy test at the time of trial entry

Exclusion Criteria (selected):

- 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

An academic clinical trial of GHSG, University of Cologne, in cooperation with
Arbeitsgemeinschaft medikamentöse Tumortherapie gemeinnützige GmbH, Clinical-Scientific Director: R. Greil