GHSG-HD21

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

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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)

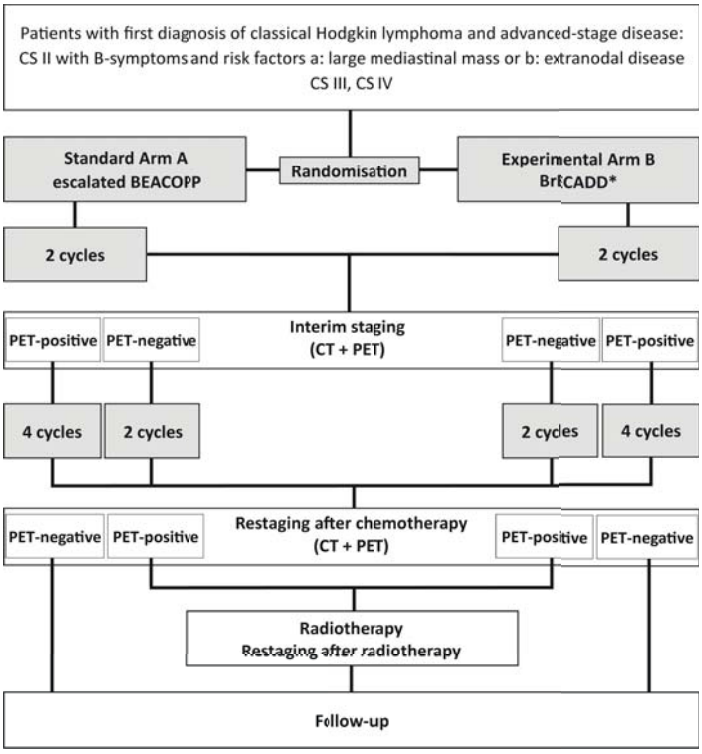
Duration: First patient in (FPI): Q3 2016 (D), Q2 2017 (A)
Last patient in (LPI): Q2 2020 (expected)
Last patient out (LPO): Q4 2025 (expected)

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



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/m^2 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 because of its higher potential for causing pulmonary toxicity.

Patients are randomized into one of the two treatment groups directly after their inclusion into the trial. Patients in the standard group receive escalated BEACOPP, patients in the experimental group receive BrECADD. After 2 cycles of chemotherapy, a restaging with ceCT (CT-2) and PET-2 is performed in all patients. PET-2 negative patients in both treatment groups receive additional 2 cycles of escalated BEACOPP or BrECADD respectively. PET-2 positive patients continue with additional 4 cycles of chemotherapy.

After completion of chemotherapy, ceCT (CT-4 or CT-6, respectively) is performed as staging examination. FDG PET/CT (PET-4 or PET-6) is obligatory for patients presenting with signs of active tumor, and optional in other cases. PET-4 positive or PET-6 positive patients will receive local radiotherapy with 30 Gy.

Recruitment (as of March 2019)

No	Site	Initiation	Patients
4150	PMU Salzburg / Innere Medizin III	13.04.2017	12
4151	UK Innsbruck / Innere Medizin V	22.06.2017	5
4152	Ordensklinikum Linz / Interne I	04.10.2017	11
4153	Klinikum Wels Grieskirchen / Innere Medizin IV	31.05.2017	0
4154	LKH Feldkirch / Innere Medizin II - Interne E	30.05.2017	3
4155	Kepler UK, Med Campus III. / UK Hämatologie	26.04.2017	0
0367	AKH MUW / Innere Medizin I - Hämatologie	20.07.2017	3
0461	Hanusch KH Wien / 3. Medizin	09.06.2017	14
4157	LKH Hochsteiermark / Dep. Hämato- Onkologie	25.04.2017	2
4158	LKH Steyr / Innere Medizin II	22.08.2017	2
	TOTAL		**52**

Inclusion Criteria (selected)

- Histologically proven classical Hodgkin lymphoma
- First diagnosis, no previous treatment for HL
- 18 to 60 years of age
- Stage IIB with large mediastinal mass and/or extranodal lesions, stage III or IV
- Normal organ function (except for HL-related functional disorders)
- Estimated life expectancy > 3 months

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
- Pregnancy, lactation
- Non-Compliance

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An academic clinical trial of GHSG, University of Cologne,
in cooperation with Arbeitsgemeinschaft medikamentöse Tumortherapie gemeinnützige GmbH,
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