Pregnancies and childbirth following advanced-stage HL treatment with BrECADD or eBEACOPP in the GHSG randomized phase III HD21 trial

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INTRODUCTION

The GHSG-HD21 trial in adult patients with newly diagnosed advanced-stage classical Hodgkin lymphoma (AS-cHL) compares BrECADD (Brentuximab vedotin, etoposide, cyclophosphamide, doxorubicin, dacarbazine, dexamethasone) to eBEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procar¬bazine, prednisone). Superior treatment-related morbidity (TRMB) and at least non-inferior efficacy of BrECADD with high progression-free survival (PFS) rates after three years were presented previously. Fertility following chemotherapy is a major concern for these mostly young AS-HL patients.

AIM

We aimed to analyze pregnancies and childbirth rates reported in HD21.

METHODS

This international open-label phase III trial included adult patients aged ≤ 60 yrs with AS-cHL. Patients were randomized in a 1:1 ratio to PET2-guided 4-6 cycles of either eBEACOPP or BrECADD. PET2 and PFS events were assessed by blinded panel review. Frequency of pregnancies among patients or their partners were analyzed in all female patients below 40 years and male patients below 50 years included in the ITT cohort for the safety endpoint TRMB. Descriptive statistics were used to report pregnancy rates. The trial was registered at clinicaltrials.gov (NCT02661503) and conducted according to ICH-GCP guidelines.

RESULTS

Between July 2016 and August 2020, we enrolled 1,500 patients from 9 countries and 233 trial sites. The final cohort for this analysis comprised 1200 patients (496 women and 704 men; 80.1% of ITT). Baseline characteristics were well balanced between treatment arms and median follow-up for this analysis was 46 months. 55.6% of the patients had cryocpreservation prior to chemotherapy (46.1% women, 76.4% men). Recovery of FSH in the first year of FU was higher following BrECADD in both females (**figure 1**) and males (**figure 2**). At time of this analysis, there were 124 reported pregnancies during follow-up. Data was incomplete in 11 cases, and these were excluded from analysis.

Overall, 100 (8.3%) patients had at least one documented pregnancy; 42 (7.0%) and 58 (9.7%) in eBEACOPP and BrECADD arm, respectively. Ten patients had more than one pregnancy. Pregnancy rates following BrECADD were higher in males (6.3% vs. 2.8%) and females (16.8% vs. 15.9%), see **table 1**. 8.0% of patients with reported pregnancy made use of cryopreservation. 82.3% of all pregnancies resulted in childbirth and 17.7% ended early (3.5% due to induced abortion; 14.2% due to abortion). Among patients with reported childbirth, there was a greater proportion of female patients vs. partners of male patients (66.7% vs. 33.3%); otherwise there were no notable differences between baseline characteristics or total cycles of chemotherapy in patients with reported pregnancy compared to the rest of the cohort. Median time from last day of chemotherapy until date of birth was 32 months (range 4-61). **Figure 3** shows a cumulative incidence plot for first parenthood separated by trial arm.

Figure 1 Recovery of FSH in females (18-39), mean Fu12-Fu24

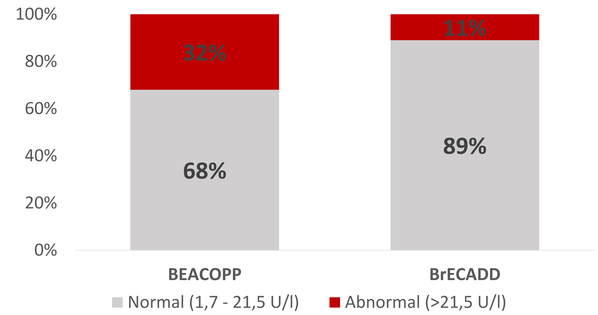


Figure 2 Recovery of FSH in males (18-49), mean Fu12-Fu24

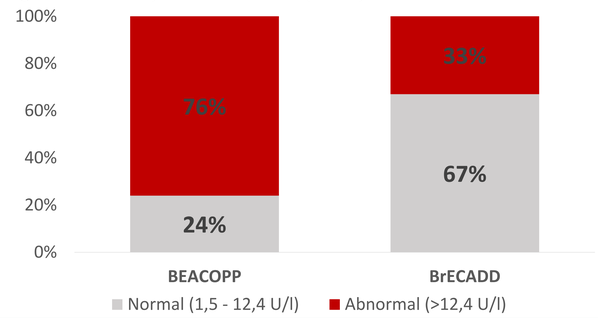
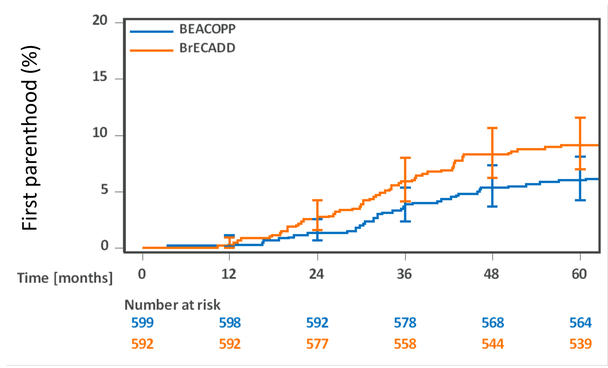


Table 1 Pregnancy rate (%) at 46 months of median follow up

Pregnancy rate (%)	Male (n= 704)	Female (n=496)
BEACOPP	2.8	15.9
BrECADD	6.3	16.8

Figure 3 Cumulative Incidence plot of first parenthood in HD21



CONCLUSIONS

- At time of analysis (46 mFU), approximately **one in ten patients have reported pregnancies in HD21**.
- Pregnancy rates were **twofold higher in partners of men** who received BrECADD and slightly higher in women. Numerically, childbirth rates were higher following BrECADD.
- Together with unparalleled primary cure rates achieved with BrECADD, **our data supports its use in young patients with a desire to have children**.

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