Abstract: S225

Title: THE RANDOMIZED STUDY GHSG HD21 SHOWS SUPERIOR TOLERABILITY AND EFFICACY OF BRECADD VERSUS BEACOPP IN ADVANCED STAGE CLASSICAL HODGKIN LYMPHOMA

Abstract Type: Oral Presentation

Session Title: Hodgkin lymphoma

Background:

We hypothesized that therapy with the novel BrECADD regimen (brentuximab vedotin, etoposide, cyclophosphamide, doxorubicin, dacarbazine, dexamethasone) guided by positron emission tomography after two cycles (PET2) could improve the treatment of advanced-stage classical Hodgkin lymphoma (AS-cHL). The HD21 trial aimed at demonstrating superiority over the intensified BEACOPP regimen (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone) in terms of treatment-related morbidity (TRMB) and non-inferiority (NI) in terms of progression-free survival (PFS). TRMB has been established recently, showing a relative risk for a TRMB event of 0.72 (95% CI, 0.65-0.79) in favor of BrECADD with consistent, highly significant benefit in all relevant subgroups. Improved tolerability allowed full dose treatment at cycle 4 in 58.5% of patients in the eBEACOPP group compared to 77.8% in the BrECADD group. Confirmatory superiority testing of efficacy was planned after non-inferiority was established.

Aims:

Here, we report the final confirmative analysis of the HD21 trial testing for superiority of PFS.

Methods:

HD21 is an international, open-label, randomized phase III trial including AS-cHL patients 18-60 years at diagnosis. Patients were randomized to receive individualized 4 or 6 cycles of either BEACOPP or BrECADD guided by PET2 results. The co-primary endpoints included TRMB and PFS, which had been successfully established recently. Testing for superiority was planned with follow-up of four years. An adjusted alpha level of 0.047 was required to cross the efficacy boundary for superiority. The trial was conducted in accordance with ICH-GCP (NCT02661503) and supported by a research grant from Takeda Oncology.

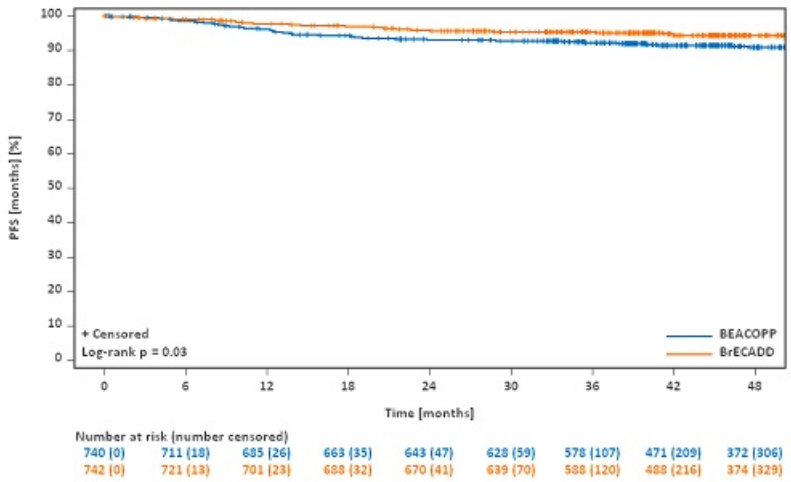
Results:

The ITT (intention-to-treat) cohort for the efficacy analysis consisted of 1482 patients, of which 742 were randomized to receive BrECADD and 740 to BEACOPP. Median age was 31.1 years (range 18 to 60), 44% were female. PET2 was negative in 424 (57.5%) and 426 (58.2%) patients for BrECADD or eBEACOPP, respectively, and these were scheduled for 4 treatment cycles. With median follow-up of 48 months, 4y-PFS was 94.3% for BrECADD (95%-CI 92.6-96.1), and 90.9% for BEACOPP (95%-CI 88.7-93.1). The hazard ratio was 0.66 [95% CI 0.45-0.97], p=0.035). PFS benefit of BrECADD was driven by a reduction in early treatment failures, i.e., primary progression within 3 months (5 vs. 15) or early relapse between months 3 and 12 (11 vs. 23) and observed across all investigated subgroups including, age, gender, and IPS (International Prognostic Score) risk groups. PET2-negative patients in the BrECADD group reached a 4-year PFS of 95.5%, and PET2-positive patients 92.5%. 4-yearOS was 98.5% for BrECADD and 98.2% for BEACOPP.

Summary/Conclusion:

BrECADD is significantly more effective than BEACOPP and is associated with an unprecedentedly high 4-year PFS, reducing the risk of progression/relapse by a third. Together with an abbreviated treatment duration for the majority of patients and a favorable tolerability and feasibility profile, treatment with PET2-individualized BrECADD sets a new benchmark for the treatment of adult patients with AS-cHL.

Figure 1:



Keywords: Phase III, Hodgkin’s lymphoma, B cell lymphoma, Outcome