Abstract: S228

Title: GONADAL FUNCTION RECOVERY AND FERTILITY IN THE PHASE III GERMAN HODGKIN STUDY GROUP HD21 TRIAL

Abstract Type: Oral Presentation

Session Title: Hodgkin lymphoma

Background:

Treatment for advanced-stage classical Hodgkin Lymphoma (AS-cHL) can cause gonadal function impairment with detrimental effect on fertility and quality of life. Especially patients with higher age and males face increased risk of persisting gonadal damage. BrECADD demonstrated unprecedented efficacy and improved acute tolerability compared to eBEACOPP for first-line treatment of AS-cHL, however its effect on gonadal function recovery and fertility remains unclear.

Aims:

To investigate the effects of BrECADD on gonadal function recovery and fertility.

Methods:

The phase III HD21 trial (NCT02661503) randomized patients between 18-60 years with newly diagnosed AS-cHL to receive four to six of cycles BrECADD or eBEACOPP. Women up to 40 and men up to 50 years of age without baseline gonadal dysfunction treated within HD21 were included in the Patients of Childbearing Potential (POCBP) cohort. Gonadal function impairment was defined as follicle-stimulating hormone (FSH) serum levels >25 U/L for women and >15 U/L for men. We defined time to gonadal function recovery (TT-GF) as time from end-of-treatment until the first measurement of FSH level below the aforementioned threshold or last FSH measurement (censored) and was analyzed TT-GF using survival analysis. Incidence of parenthood was compared using Fisher's exact test.

Results:

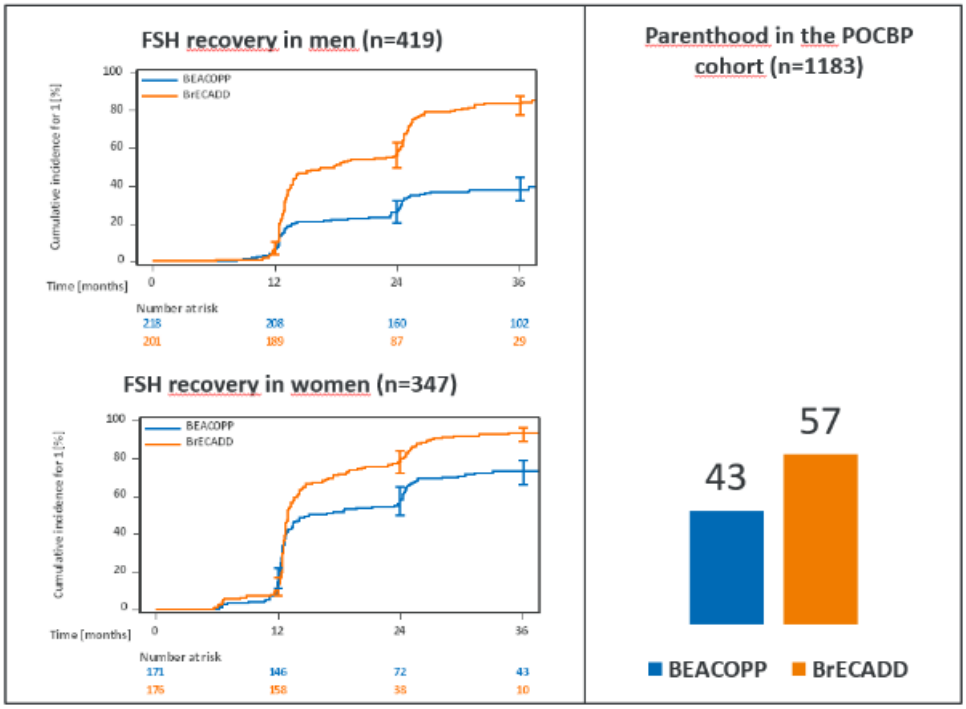
In total, 1183 (80%) out of 1482 patients from the intention to treat cohort were included in the POCBP cohort (491 women and 692 men) and FSH measurements were available for** 766 patients (419 men and 347 women). Women randomized to receive BrECADD had significantly higher recovery rates, with 94% vs. 73% ($p<0.0001$) three years after BrECADD vs. eBEACOPP, respectively. The greatest difference was observed in women older than 35 years with 3-year recovery rates of 83% vs. 23% ($p<0.0001$). Treatment with six vs. four cycles of BrECADD did not result in significantly different TT-GF (3-year recovery: 95% vs. 91%; $p = 0.1797$), however reduction from six to four cycles of eBEACOPP did so (3-year recovery: 64% vs. 79%; $p = 0.0494$). In men, BrECADD resulted in markedly improved TT-GF (3-year recovery: 84% vs. 38%; $p < 0.0001$). Following eBEACOPP, insufficient gonadal function recovery was observed irrespective of cycles received but most prominent in males >35 years. There were 103 reported cases of childbirth in 95 patients of the POCBP cohort: 57 patients in the BrECADD arm and 38 patients in the eBEACOPP arm. In men, the incidence of patients fathering at least one child was statistically higher in the BrECADD Group (7% vs. 3%, $p = 0.0253$). Similarly, in women a higher incidence of motherhood was observed after BrECADD (14% vs. 12%, $p = 0.3932$) but the difference was not statistically significant.

Summary/Conclusion:

BrECADD improves gonadal function recovery compared to eBEACOPP in patients treated for AS-cHL, especially in those who are at higher risk for persisting gonadal dysfunction. The gonadal function recovery observed with BrECADD is comparable to that of ABVD reported in the RATHL trial. [1] Remarkably, this led to significantly higher rates of parenthood in males and numerically higher rates in women receiving BrECADD in HD21. This supports the use of BrECADD as first-line therapy for AS-cHL in patients with ongoing desire to

have children. **

Figure: Gonadal function recovery and fertility in HD21



References :

[1] Anderson RA, Remedios R, Kirkwood AA, Patrick P, Stevens L, Clifton-Hadley L, Roberts T, Hatton C, Kalakonda N, Milligan DW, McKay P, Rowntree C, Scott FM, Johnson PWM. Determinants of ovarian function after response-adapted therapy in patients with advanced Hodgkin's lymphoma (RATHL): a secondary analysis of a randomised phase 3 trial. Lancet Oncol. 2018 Oct;19(10):1328-1337. doi: 10.1016/S1470-2045(18)30500-X. Epub 2018 Sep 13. PMID: 30220622; PMCID: PMC6167406.

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