Health-Related Quality of Life of Patients with Advanced-Stage Classic Hodgkin Lymphoma Treated with BrECADD and eBEACOPP: Results from the HD21 Study

HL - 1010

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Background

- BrECADD showed improved progression-free survival and better safety over escalated BEACOPP (eBEACOPP) in the first-line treatment of participants with newly-diagnosed, advanced-stage classic Hodgkin lymphoma (AS-cHL) in the HD21 study.[1]
- Multiregimen combination chemotherapies can affect health-related quality of life (HRQoL) positively, through better disease control, and negatively, through its associated toxicity.
- This post-hoc analysis documents the benefit of BrECADD compared to eBEACOPP from the patient's perspective in the HD21 study using long-term follow-up (FU) data, final database lock.

Methods

Study design

- HD21 study (NCT02661503), a phase 3, multicenter, open-label trial, randomized 1,500 patients 1:1 to BrECADD or eBEACOPP, applied in four or six 21-day treatment cycles, according to an individualized positron emission tomography after 2 cycles (PET2)-guided approach.

Patient-Reported Outcome (PRO) data

- HRQoL was assessed using European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life questionnaire – Core 30 items (QLQ-C30).
  - Scores range from 0 to 100, with higher scores indicating better functioning and health for the functioning and overall health scales, and more symptoms for symptom scales.
- PRO data were collected at baseline, during the treatment period after 2 cycles and at the end of the treatment period (4 or 6 cycles), and during the FU period (3-months, 6-months, then every 6-months up to 24 months, then every year up to 60 months).
  - Participants had to provide informed consent to collect PRO questionnaires.
- The PRO population used in this analysis included participants with a PRO measurement at baseline and at least one post-baseline visit from all randomized patients who received at least 1 dose of any of the study medications.
- This research was conducted using the final database lock of October 1, 2025.

Statistical analysis

- Estimated change from baseline (with 95% confidence interval - CI) was estimated across arms using linear mixed-effect models with repeated measures for QLQ-C30 General health/quality of life (GH/QL), Physical functioning (PF), Fatigue (FA), and Dyspnea (DY), adjusted for baseline PRO, age, sex, and International Prognostic Score (IPS).

Results

- In both arms, participants' general health and physical functioning deteriorated during the treatment period and improved (general health) or reached the baseline level (physical functioning) during FU (Figure 1).
  - The estimated mean change in QLQ-C30 GH/QL score in BrECADD vs. eBEACOPP was -4.7 vs. -6.6 at restaging after chemotherapy (RaC), and between 6.5 vs. 6.9 at 3-month FU and 10.4 vs. 10.0 at 3 years FU, respectively.
    - Smaller decrease during treatment and greater improvement at several timepoints during FU were seen in BrECADD compared to eBEACOPP.
  - The estimated mean change in QLQ-C30 PF score in BrECADD vs. eBEACOPP was -9.1 vs. -11.8 at RaC, and between 1.3 vs. 0.3 at 3-month FU and 5.0 vs. 4.1 at 3 years FU, respectively.
    - After 6 months FU, greater improvement were observed in BrECADD versus eBEACOPP.

Figure 1: Estimated mean change from baseline in QLQ-C30 General health/quality of life and Physical functioning scores across arms over time

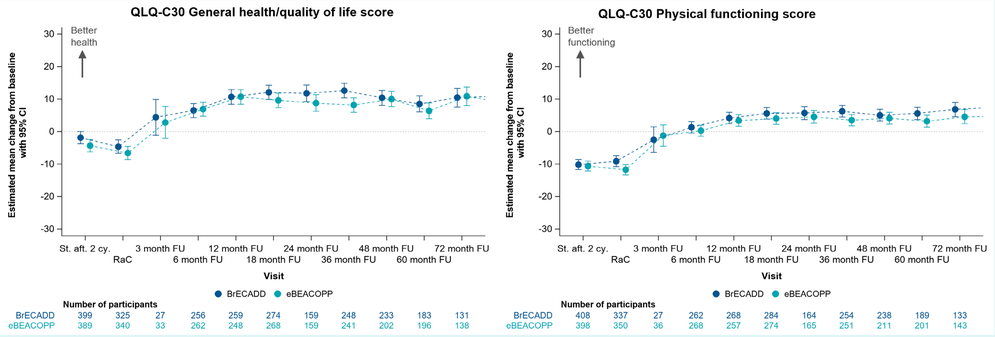

Figure 2: Estimated mean change from baseline in QLQ-C30 Fatigue and Dyspnea scores across arms over time

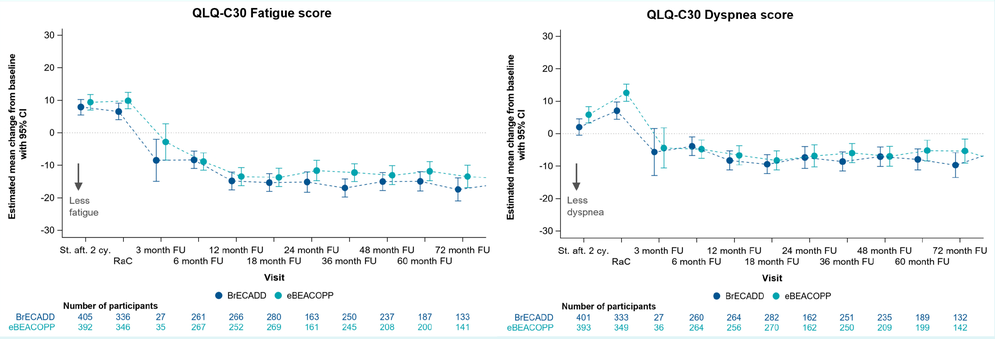

Table 1: PRO population demographics and disease characteristics

Characteristics	BrECADD N=498	eBEACOPP N=497
Age, median (range), in years	31 (18-60)	31 (18-60)
Sex, male, n (%)	270 (54%)	282 (57%)
Country, n (%)[a]		
Australia	30 (6%)	22 (4%)
Austria	26 (5%)	28 (6%)
Denmark	10 (2%)	11 (2%)
Germany	370 (74%)	375 (75%)
Netherlands	9 (2%)	7 (1%)
New Zealand	3 (1%)	4 (1%)
Norway	7 (1%)	9 (2%)
Sweden	7 (1%)	6 (1%)
Switzerland	36 (7%)	35 (7%)
Ann Arbor Stage, n (%)		
IIb	79 (16%)	71 (14%)
IIIa	90 (18%)	104 (21%)
IIIb	103 (21%)	109 (22%)
IVa	67 (13%)	81 (16%)
IVb	159 (32%)	132 (27%)
IPS, n (%)		
0-2	271 (54%)	279 (56%)
3-7	227 (46%)	218 (44%)
ECOG-PS at baseline, n (%)		
0-Fully active	337 (68%)	353 (71%)
1-Symptoms ambulatory	153 (31%)	137 (28%)
2-In bed <50% of daytime	8 (1%)	7 (1%)

[a] Percentages may not add up to 100% because of rounding.

- In both arms, participants' fatigue and dyspnea deteriorated during the treatment period and improved during FU, with smaller declines during treatment and greater improvement during FU observed in BrECADD versus eBEACOPP (Figure 2).
  - The estimated mean change in QLQ-C30 FA score in BrECADD vs. eBEACOPP was 6.6 vs. 9.9 at RaC, and between -8.3 vs. -8.8 at 3-month FU and -15.0 vs. -13.0 at 3 years FU, respectively.
  - The estimated mean change in QLQ-C30 DY score in BrECADD vs. eBEACOPP was 7.1 vs. 12.6 at RaC, and between -3.9 vs. -4.8 at 3-month FU and -7.1 vs. -7.0 at 3 years FU, respectively.

Limitations

- This post-hoc analysis provides a descriptive insight on patients' HRQoL, with no formal *a priori* hypothesis or control of type I error.
- Given the quick decrease in available PRO data during the follow-up, results should be interpreted cautiously due to the risk of selection bias.
  - Participants with post-treatment data may not be directly comparable to those at baseline. Participants still in the study with available PRO data may have better HRQoL than those who dropped out.
- Given these caveats, the PRO results presented here should be considered with caution and would need to be confirmed in further research.

Conclusions

- Transient deterioration in HRQoL, physical functioning and the core symptoms of fatigue and dyspnea was observed in patients with AS-cHL during treatment by both PET2-guided BrECADD and eBEACOPP in the HD21 study.
- However, this deterioration was no longer visible in the FU period for either treatment options. Better overall HRQoL and fatigue compared to baseline was even observed in participants during the FU period, suggesting possible long-term meaningful benefits for patients.
- BrECADD was associated with smaller decline in overall HRQoL and fatigue during treatment and greater improvement at multiple FU visits compared to eBEACOPP. Better long-term functioning was also seen in BrECADD vs. eBEACOPP.
  - These results are consistent with previous results obtained in German participants only.[1,2]
- These findings suggest that first-line treatment with PET2-guided BrECADD, while associated with transient deterioration during the treatment period in both BrECADD and eBEACOPP arms of the HD21 study, may provide better outcomes compared to eBEACOPP in the longer term.

References

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Abbreviations

AS-cHL: advanced-stage classic Hodgkin lymphoma; CI: confidence interval; DY: dyspnea; eBEACOPP: escalated BEACOPP; ECOG-PS: Eastern Cooperative Oncology Group Performance Status; EORTC: European Organisation for Research and Treatment of Cancer; FA: fatigue; FU: follow-up; GH/QL: general health/quality of life; HRQoL: health-related quality of life; IPS: International Prognostic Score; PET2: positron emission tomography after 2 cycles; PF: physical functioning; PRO: patient-reported outcome; QLQ-C30: Quality of Life questionnaire – Core 30 items; RaC: restaging after chemotherapy; St. aft. 2 cy.: staging after 2 cycles.

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