Patient-Reported Chemotherapy-Induced Peripheral Neuropathy (CIPN) in Advanced-Stage Classic Hodgkin Lymphoma Treated with BrECADD and eBEACOPP: Data with longer follow-up from HD21 Trial

HL - 1012

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Background

- German Hodgkin Study Group (GHSG) HD21 study, a phase 3 open-label randomized trial, showed better efficacy and safety of BrECADD compared to escalated BEACOPP (eBEACOPP) as first-line treatment for patients with newly diagnosed advanced-stage classic Hodgkin lymphoma (AS-cHL)[1].
- Chemotherapy-induced peripheral neuropathy (CIPN) is a frequent, dose-limiting toxicity that can adversely affect heath-related quality of life (HRQoL).
- Despite increasing use of intensive combination regimens, their cumulative neurotoxic effects are not completely understood[2]. Patient-reported outcomes (PROs) may provide insight on the burden of CIPN.
- This post-hoc analysis explores patients' experience of CIPN sensory symptoms when being treated with BrECADD vs. eBEACOPP for AS-cHL using longer-term follow-up (FU) data.

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) and Quality of Life Questionnaire – 20-item Chemotherapy-Induced Peripheral Neuropathy module (QLQ-CIPN20).
  - Scores range from 0 to 100, with higher scores indicating better functioning/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-month, 6-month, then every 6-month 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 analyses

- Item-level responses and meaningful deterioration from baseline (change ≤ -3.7)[3] to the QLQ-CIPN20 Sensory symptom scale were described longitudinally across treatment arms.
- The association of the QLQ-C30 Global health/Quality of life score (GH/QL), identified as a key concept that could be negatively impacted by CIPN, and participants' experience of CIPN sensory symptoms was explored. Groups of participants were defined as no symptom (answering 'Not at all' to a given QLQ-CIPN20 Sensory symptom scale item) versus any symptom severity (answering at least 'A little' to a given QLQ-CIPN20 Sensory symptom scale item).

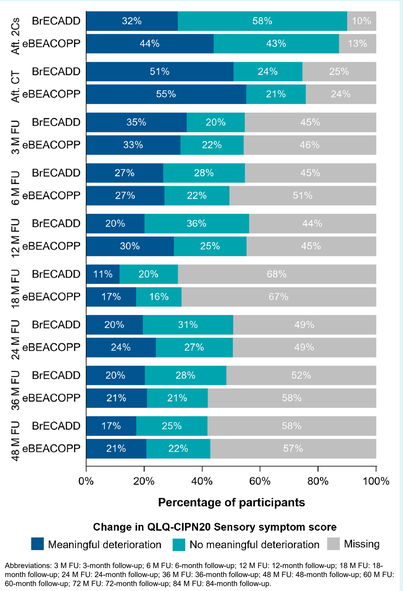
Results

Demographics

Table 1: PRO population demographics and disease characteristics

Characteristics	BrECADD N=370	eBEACOPP N=375
Age, median (range), in years	31 (18-60)	31 (18-60)
Sex, male, n (%)	195 (53%)	210 (56%)
Ann Arbor Stage, n (%)		
IIb	79 (16%)	71 (14%)
IIIa	90 (18%)	104 (21%)
IIIb	103 (21%)	109 (22%)
IVa	67 (14%)	81 (16%)
IVb	159 (32%)	132 (27%)
IPS score, n (%)		
0-2	271 (54%)	279 (56%)
3-7	227 (46%)	218 (44%)
ECOG-PS at baseline, n (%)		
0-Fully active	243 (66%)	265 (71%)
1-Symptoms ambulatory	120 (32%)	106 (28%)
2-In bed <50% of daytime	7 (2%)	4 (1%)

Figure 2: Percentage of participants with a meaningful deterioration in EORTC QLQ-CIPN20 Sensory symptom score across arms over time

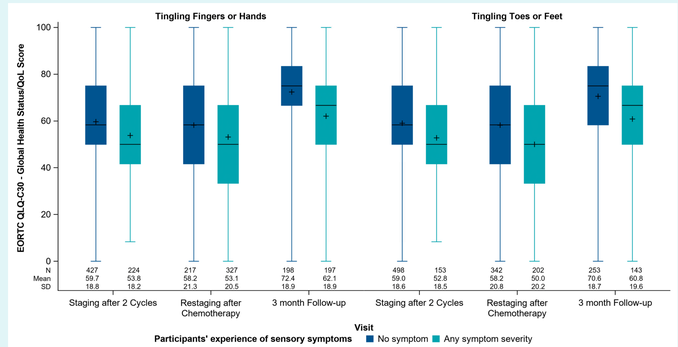


Abbreviations: 3 M FU: 3-month follow-up; 6 M FU: 6-month follow-up; 12 M FU: 12-month follow-up; 18 M FU: 18-month follow-up; 24 M FU: 24-month follow-up; 36 M FU: 36-month follow-up; 48 M FU: 48-month follow-up; 60 M FU: 60-month follow-up; 72 M FU: 72-month follow-up; 84 M FU: 84-month follow-up.

Association of CIPN sensory symptoms with participants' HRQoL

- Participants reporting tingling in fingers/hands and tingling in toes/feet had lower QLQ-C30 GH/QL scores, indicating poorer overall health, than participants who did not experience these symptoms (Figure 3):
  - At RaC, the mean QLQ-C30 GH/QL score in participants with vs. without symptom was 53.1 vs. 58.2 for tingling in fingers/hands, and 50.0 vs. 58.2 for tingling in toes/feet, respectively.
  - At 3-month FU, the mean QLQ-C30 GH/QL score in participants with vs. without symptom was 62.1 vs. 72.4 for tingling in fingers/hands, and 60.8 vs. 70.6 for tingling in toes/feet.

Figure 3: Description of the EORTC QLQ-C30 GH/QL score according to participants' experience of CIPN sensory symptoms as assessed by the QLQ-CIPN20 items

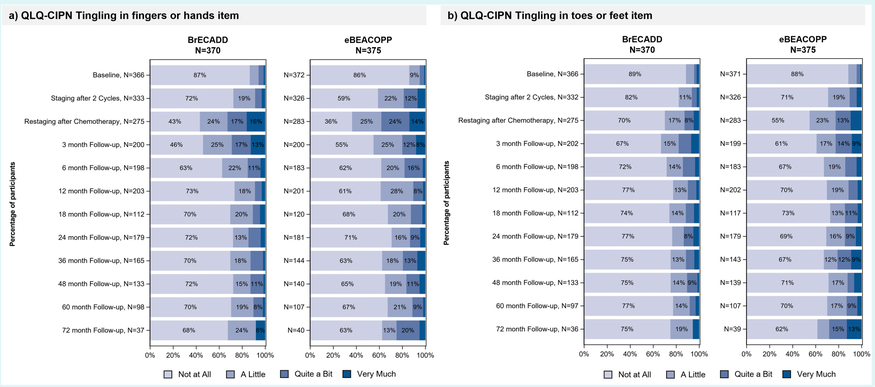


Legend: The box represents the interquartile range (first-third quartiles); +: mean; –: median; bottom and top bars (whiskers): minimum and maximum observed scores.
A higher EORTC QLQ-C30 GH/QL score indicates better general health/quality of life.

Participants' experience of CIPN sensory symptoms over time across arms

- Tingling in fingers/hands and in toes/feet were the most frequently reported CIPN sensory symptoms by the participants in both arms.
- Participants reported tingling in fingers/hands and in toes/feet in an overall similar manner over time in both arms, with an increased percentage of the participants reporting these symptoms at restaging after chemotherapy (RaC; end of treatment) and 3-month FU, before this percentage decreased (Figure 1):
  - Fewer participants reported these symptoms in the BrECADD arm compared to the eBEACOPP arm at most timepoints.
    - Tingling in fingers or hands (Figure 1a): 28% vs. 41% at staging at 2 cycles, 57% vs. 64% at RaC, and 54% vs. 45% at 3-month FU in BrECADD vs. eBEACOPP, respectively.
    - Tingling in toes or feet (Figure 1b): 18% vs. 29% at staging after 2 cycles, 30% vs. 45% at RaC, and 33% vs. 39% at 3-month FU in BrECADD vs. eBEACOPP, respectively.
- A similar pattern was seen in both arms over time in the percentage of participants who had a meaningful deterioration in the QLQ-CIPN20 Sensory symptom score (Figure 2):
  - The percentage of participants with a meaningful deterioration in their score in BrECADD vs. eBEACOPP increased from 32% vs. 44% at staging after 2 cycles to 51% vs. 55% at RaC.
  - During FU, this percentage in BrECADD vs. eBEACOPP decreased from 35% vs. 33% at 3-month FU to 20% vs. 24% at 24-month FU, respectively.

Figure 1: Tingling in fingers/hands (a) and Tingling in toes/feet (b) reported by participants across arms over time



Limitations

- This is a post-hoc analysis providing descriptive insights on the experience of CIPN symptoms in patients with AS-cHL only, and results should be interpreted with caution.
- The dynamics of CIPN was only captured partially by the PRO data from the HD21 study: PRO data was collected infrequently (3 months apart during the follow-up phase) and was missing for an increasing percentage of participants over time. Conclusions on the experience of participants with CIPN should therefore be considered carefully as the symptomatic experience of participants with missing PRO data was unknown (risk of selection bias).

Conclusions

- Tingling in fingers/hands and in toes/feet were experienced by participants in both treatment arms, especially at the end of treatment and early follow-up periods. Participants treated with BrECADD were less likely to experience symptoms affecting upper and lower extremities compared to eBEACOPP.
- The percentage of participants experiencing a meaningful deterioration in their CIPN sensory symptoms was similar between arms, increasing during treatment period before decreasing during follow-up.
- Tingling in fingers/hands and in toes/feet were associated with deteriorated general health/quality of life compared to participants without these symptoms.
  - The observed differences in mean QLQ-C30 GH/QL score between participants with these symptoms and those without may be considered small, but not trivial (4-10 points difference)[4].
- This suggest that multiagent regimens for newly diagnosed AS-cHL associated with fewer CIPN sensory symptoms such as BrECADD may contribute to better general health/quality of life.

References

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Abbreviations

AS-cHL: advanced-stage classic Hodgkin lymphoma; CIPN: Chemotherapy-induced peripheral neuropathy; eBEACOPP: escalated BEACOPP; ECOG-PS: Eastern Cooperative Oncology Group Performance Status; EORTC: European Organisation for Research and Treatment of Cancer; FU: Follow-up; GH/QL: Global health/quality of life; GHSG: German Hodgkin Study Group; IPS: international prognostic score; PRO: Patient-reported outcome; QLQ-C30: Quality of Life questionnaire – Core 30 items; QLQ-CIPN20: Quality of Life Questionnaire – 20-item Chemotherapy-Induced Peripheral Neuropathy module; RaC: Restaging after chemotherapy; SD: standard deviation.

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