The gap narrows but shifts. Response to Comment on: "Mind the gap: anti–PD-1 salvage before autologous transplantation in classical Hodgkin lymphoma"

Tharmaseelan and von Tresckow provide a valuable update to the discussion around salvage treatment based on anti-programmed cell death protein 1 (PD-1) in classical Hodgkin lymphoma (cHL).[1-3] The European Commission approval of nivolumab plus brentuximab vedotin (BV) for patients aged 5-30 years with relapsed or refractory cHL after one prior line of therapy, based on the findings of CheckMate-744, is the first immunotherapy-based salvage regimen licensed in Europe for this setting and directly addresses the regulatory gap identified in both the original analysis and the editorial.[4]

Notably, CheckMate-744 excluded patients with prior exposure to anti–PD-1 antibodies or BV.[4] This exclusion has growing practical relevance as frontline regimens increasingly incorporate these agents. In Europe, BrECADD (BV, etoposide, cyclophosphamide, doxorubicin, decarbazine, dexamethasone) is emerging as a preferred advanced-stage option, particularly in German-speaking countries, replacing escalated BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone) and introducing BV into first-line treatment.[5] In the United States, the recent Food and Drug Administration approval of nivolumab plus AVD (doxorubicin, vinblastine, dacarbazine) based on the results of the SWOG S1826 trial shifts frontline exposure toward anti–PD-1 therapy.[6] Whether patients relapsing after BV- or anti–PD-1-containing frontline regimens respond to nivolumab plus BV with comparable efficacy is unknown, and such patients may not clearly fall within the scope of the current approval. The practical window in which the CheckMate-744-based indication applies, that is, patients within the age range who relapse after frontline therapy without BV or anti–PD-1 exposure, remains sizable today, particularly after limited-stage treatment with ABVD (doxorubicin, bleomycin, vinblastine, dacarbazine) or AVD, but will narrow as frontline practice continues to evolve.

At the same time, the anti–PD-1 plus chemotherapy combinations that dominate salvage practice in adults beyond the approved age range and that produced complete response rates exceeding 85% in phase II studies remain unapproved in the second-line transplant-eligible setting.[7-9] The post-consolidation data from the original multicenter analysis by Tharmaseelan *et al*. add a useful nuance here: the pre-transplant complete response rate was 47.7%, yet 97% of evaluable patients achieved complete response after transplant consolidation, including seven of eight patients who had only a partial remission after anti–PD-1 monotherapy.[1] This does not diminish the value of achieving deep remissions before transplant, but it suggests that the post-consolidation outcome, rather than the induction complete response rate alone, may be the more appropriate benchmark when comparing salvage regimens. If confirmed in larger cohorts, this perspective could temper cross-trial comparisons of induction complete response rates between approaches such as nivolumab plus BV and anti–PD-1 plus multi-agent chemotherapy, provided transplant consolidation remains part of the strategy. For patients in whom transplant is not intended, the CheckMate-744 low-risk cohort offers preliminary evidence that nivolumab plus BV followed by involved-site radiotherapy can achieve durable remissions without high-dose chemotherapy, although the small sample size and the restriction to a younger, lower-risk population limit generalizability.[10] Closing the remaining gap will require randomized trials comparing anti–PD-1-based salvage against standard platinum-based regimens in transplant-eligible adults without age restriction, ideally stratified by prior frontline exposure.

Author

Daniel Noerenberg

Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt Universität zu Berlin, and Berlin Institute of Health, Department of Hematology, Oncology, and Cancer Immunology, Berlin, Germany

Correspondence:
D. Noerenberg - daniel.noerenberg@charite.de

https://doi.org/10.3324/haematol.2026.301293

Received: May 22, 2026.
Accepted: May 27, 2026.
Early view: June 4, 2026.

©2026 Ferrata Storti Foundation
Published under a CC BY-NC license

Disclosures

No conflicts of interest to disclose.

References

1. Tharmaseelan H, Sgonina LM, Bühnen I, et al. Anti–programmed cell death protein 1–based salvage therapy for relapsed and refractory Hodgkin lymphoma: a multicenter real-world analysis. Haematologica. 2026;111(11):3645-3654.
2. Noerenberg D. Mind the gap: anti–PD-1 salvage before autologous transplantation in classical Hodgkin lymphoma. Haematologica. 2026;111(11):3893-3894.
3. Tharmaseelan H, von Tresckow B. On closing the gap: anti-PD-1-based salvage in relapsed/refractory classical Hodgkin lymphoma. Comment on: "Mind the gap: anti-PD-1 salvage before autologous transplantation in classical Hodgkin lymphoma". Haematologica. 2026;111(11):3891-3892.
4. Harker-Murray P, Mauz-Körholz C, Leblanc TM, et al. Nivolumab, brentuximab vedotin, +/- bendamustine for R/R Hodgkin lymphoma in children, adolescents, and young adults. Blood. 2023;141(17):2075-2084.
5. Borchmann P, Ferdinandus J, Schneider G, et al. Assessing the efficacy and tolerability of PET-guided BrECADD versus eBEACOPP in advanced-stage, classical Hodgkin lymphoma (HD21): a randomised, multicentre, parallel, open-label, phase 3 trial. Lancet. 2024;404(10450):341-352.
6. Herrera AF, LeBlanc M, Castellino SM, et al. Nivolumab+AVD in advanced-stage classic Hodgkin's lymphoma. N Engl J Med. 2024;391(15):1379-1389.
7. Moskowitz AJ, Shah G, Schöder H, et al. Phase II trial of pembrolizumab plus gemcitabine, vinorelbine, and liposomal doxorubicin as second-line therapy for relapsed or refractory classical Hodgkin lymphoma. J Clin Oncol. 2021;39(28):3109-3117.
8. Bryan LJ, Casulo C, Allen PB, et al. Pembrolizumab added to ifosfamide, carboplatin, and etoposide chemotherapy for relapsed or refractory classic Hodgkin lymphoma. JAMA Oncol. 2023;9(5):683-691.
9. Mei MG, Lee HJ, Palmer JM, et al. Response-adapted anti-PD-1-based salvage therapy for Hodgkin lymphoma with nivolumab alone or in combination with ICE. Blood. 2022;139(25):3605-3616.
10. Daw S, Cole PD, Hoppe BS, et al. Transplant-free approach in relapsed Hodgkin lymphoma in children, adolescents, and young adults: a nonrandomized clinical trial. JAMA Oncol. 2025;11(3):249-257.