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A complete list of authors is available with the full text of this letter at NEJM.org.

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Disclosure forms provided by the authors are available with the full text of this letter at NEJM.org.

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Brentuximab Vedotin in Advanced Hodgkin's Lymphoma

TO THE EDITOR: For all studies of frontline therapy in which data on overall survival are provided, such as in the ECHELON-1 trial reported on by Ansell et al. (July 28 issue),[1] it is imperative to have clear reporting of postprotocol therapies and full transparency with regard to trial results so that readers can better interpret the findings and place them in context, especially as they relate to the standard of care. If these therapies do not meet the U.S. standard of care, it can be debated whether the results should be extrapolated to the U.S. population.

The tables of postprotocol results in the ECHELON-1 trial (provided in the Supplementary Appendix, available with the full text of the article at NEJM.org) contain many discrepancies, including the number of patients who had disease progression and the number of patients who received various types of postprotocol therapies such as radiation therapy. These differences raise questions about whether patients in the control group (i.e., those who received doxorubicin, bleomycin, vinblastine, and dacarbazine [ABVD]) received an adequate standard of care when they had disease progression.

Can the authors report the number of patients with disease progression who survived (excluding those who had had a noncomplete response after frontline therapy and who had received salvage chemotherapy or radiation therapy)? Of the patients who survived, how many received an additional line of therapy? Which therapies did patients receive on first disease progression? Also, how many patients had disease progression a second time, and which therapies did these patients then receive?

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Dr. Prasad reports receiving research funding from Arnold Ventures, consulting fees from Optum Health, UnitedHealthcare, and New Century Health, and revenue and royalties from Patreon, Substack, and YouTube,. No other potential conflict of interest relevant to this letter was reported.

1. Ansell SM, Radford J, Connors JM, et al. Overall survival with brentuximab vedotin in stage III or IV Hodgkin's lymphoma. N Engl J Med 2022;387:310-20.

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THE AUTHORS REPLY: We appreciate that data on postprotocol therapies are of interest, and we agree with Haslam and Prasad that the tables in the Supplementary Appendix of our article can be clarified. We have added explanatory foot-

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notes and further data on the use of subsequent chemotherapy to the Supplementary Appendix.

The ECHELON-1 trial was a large, global, randomized trial conducted at 218 sites in 21 countries by clinicians who had experience in the care of patients with advanced Hodgkin's lymphoma; a total of 1334 patients were enrolled between November 2012 and January 2016. These clinicians directed the postprotocol care for each patient. We acknowledge the concern that undertreatment of only patients who received ABVD could have affected the benefit observed with brentuximab vedotin plus doxorubicin, vinblastine, and dacarbazine. However, the use of subsequent therapy in both groups was consistent with the authors' collective clinical experience, guideline recommendations, and studies involving patients with advanced Hodgkin's lymphoma.[1]

Furthermore, because treatment patterns and access to supportive care vary worldwide, the ECHELON-1 trial was prospectively designed with geographic region as a stratification factor in the patient randomization and analyses. It is therefore unlikely that the effects of regional differences on postprotocol care were isolated to the ABVD group.

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Since publication of their article, Dr. Ansell reports receiving research funds paid to his institution from AstraZeneca, and Dr. Radford reports receiving consulting fees from Kite Pharma. No further potential conflict of interest relevant to this letter was reported.

1. Casasnovas R-O, Bouabdallah R, Brice P, et al. Positron emission tomography-driven strategy in advanced Hodgkin lymphoma: prolonged follow-up of the AHL2011 phase III Lymphoma Study Association study. J Clin Oncol 2022;40:1091-101.

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Anti-BDCA2 Antibody for Cutaneous Lupus Erythematosus

TO THE EDITOR: Werth et al. (July 28 issue)[1] report the efficacy of litifilimab in the treatment of cutaneous lupus erythematosus. New therapeutic targets for this complex disease are important, but the mechanism of action of litifilimab remains unclear. The rationale for the use of litifilimab was that blood dendritic cell antigen 2 (BDCA2) is exclusively expressed on plasmacytoid dendritic cells. However, the role of plasmacytoid dendritic cells in the pathogenesis of lupus is increasingly doubted. We found that in all patients who had positive results on antinuclear antigen testing without organ inflammation, plasmacytoid dendritic cells had impaired type I interferon production and antigen presentation. However, keratinocytes sustain the production of type I interferon.[2] In single-cell RNA sequencing, cutaneous plasmacytoid dendritic cells had an inert phenotype without the expression of type I interferon transcripts.[3] Furthermore, we found that BDCA2 was not exclusively expressed by plasmacytoid dendritic cells, since other peripheral-blood mononuclear cells (PBMCs) up-regulated BDCA2 after in vitro culture but lacked type I interferon production.[2]

A previous study showed that there was a reduction in interferon-stimulated genes after litifilimab therapy.[4] However, this finding does not show specific targeting of the cellular source of type I interferon. For example, activation of the interferon pathway was decreased in patients with systemic lupus erythematosus after treatment with bortezomib, a proteasome inhibitor that targets plasma cells.[5] Elucidating the mechanism of action of litifilimab is essential in order to know which patients will benefit from its use.

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