

Reply to T.P. Vassilakopoulos et al

We thank Vassilakopoulos and Johnson¹ for having addressed this important question on the long-term update of the HD2000 trial.² Actually, all time-dependent analyses were conducted with an intention-to-treat (ITT) approach, with the only exception of the assessment of late events and of second malignancies that were evaluated per protocol. We also conducted a per-protocol analysis of patients treated with doxorubicin, bleomycin, vinblastine, dacarbazine (ABVD, n = 113); bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone (BEACOPP, n = 89); and cyclophosphamide, lomustine, vindesine, melphalan, prednisone, epidoxorubicin, vincristine, procarbazine, vinblastine, and bleomycin (COPP-EBV-CAD; CEC, n = 93). Fifteen patients received ABVD in place of the randomly assigned arm (BEACOPP, n = 9; CEC, n = 6), and only one patient was randomly assigned to receive ABVD, but received CEC. The main reason for the treatment change was patient request or medical decision. Looking at survival data, the 10-year progression-free survival rates were 71% (95% CI, 61% to 79%) and 75% (95% CI, 64% to 83%) for ABVD and BEACOPP, respectively (P = .512). As observed with the ITT analysis, also in the per-protocol assessment, the proportionality of risk function was missing: the hazard ratio of BEACOPP against ABVD for progression-free survival was 0.50 (95% CI, 0.25 to 0.98) within the first 30 months of observation and 2.03 (95% CI, 0.83 to 4.98) after 30 months of follow-up. Again, no difference among the study arms was observed in the per-protocol analysis for overall survival (OS): 10-year OS was 85% (95% CI, 76% to 91%) and 84% (95% CI, 73% to 90%) for ABVD and BEACOPP, respectively.

In conclusion, even if some patients were treated with ABVD chemotherapy in place of the assigned intensified regimen after randomization, the per-protocol analysis confirmed the findings of the ITT analysis, showing better disease control with BEACOPP compared with ABVD, but higher frequency of late events with the intensified treatment, resulting

in the same OS rates. We are looking forward to reading the long-term results of the other studies that also compared BEACOPP and ABVD in advanced-stage Hodgkin lymphoma patients.³⁻⁵

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTERESTDisclosures provided by the authors are available with this article at www.jco.org.**REFERENCES**

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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