VOLUME 34 · NUMBER 29 · OCTOBER 10, 2016

JOURNAL OF CLINICAL ONCOLOGY

CORRESPONDENCE

Reply to T.P. Vassilakopoulos et al

We thank Vassilakopoulos and Johnson[1] 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]

Francesco Merli
Hematology, Arcispedale Santa Maria Nuova-IRCCS, Reggio Emilia, Italy

Massimo Federico
University of Modena and Reggio Emilia, Modena, Italy

Stefano Luminari
Hematology, Arcispedale Santa Maria Nuova-IRCCS, Reggio Emilia; and University of Modena and Reggio Emilia, Modena, Italy

ACKNOWLEDGMENT

Written on behalf of Fondazione Italiana Linfomi.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at www.jco.org.

REFERENCES

1. Vassilakopoulos TP, Johnson PWM: Re: HD2000 update in Hodgkin lymphoma—ABVD or BEACOPP? J Clin Oncol (in press).
2. Merli F, Luminari S, Gobbi PG, et al: Long-term results of the HD2000 trial comparing ABVD versus BEACOPP versus COPP-EBV-CAD in untreated patients with advanced Hodgkin lymphoma: A study by Fondazione Italiana Linfomi. J Clin Oncol 34:1175-1181, 2016
3. Viviani S, Zinzani PL, Rambaldi A, et al: ABVD versus BEACOPP for Hodgkin's lymphoma when high-dose salvage is planned. N Engl J Med 365: 203-212, 2011
4. Mounier N, Brice P, Bologna S, et al: ABVD (8 cycles) versus BEACOPP (4 escalated cycles ≥ 4 baseline): Final results in stage III-IV low-risk Hodgkin lymphoma (IPS 0-2) of the LYSA H34 randomized trial. Ann Oncol 25:1622-1628, 2014
5. Carde P, Karrasch M, Fortpied C, et al: Eight cycles of ABVD versus four cycles of BEACOPPescalated plus four cycles of BEACOPPbaseline in stage III to IV, International Prognostic Score ≥ 3, high-risk Hodgkin lymphoma: First results of the phase III EORTC 20012 Intergroup Trial. J Clin Oncol 34:2028-2036, 2016

DOI: 10.1200/JCO.2016.68.7749; published online ahead of print at www.jco.org on August 15, 2016.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Reply to T.P. Vassilakopoulos et al

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or jco.ascopubs.org/site/ifc.

Francesco Merli
Honoraria: Roche
Consulting or Advisory Role: Roche, Celgene, TEVA Pharmaceuticals Industries
Research Funding: Roche

Massimo Federico
No relationship to disclose

Stefano Luminari
Honoraria: Roche
Consulting or Advisory Role: Celgene, Roche, TEVA Pharmaceutical Industries
Travel, Accommodations, Expenses: Takeda Pharmaceuticals, Celgene