

## PET-guided, BEACOPP<sup>escalated</sup> therapy in advanced Hodgkin lymphoma

Early assessment of response with interim <sup>18</sup>F-fluorodeoxyglucose (<sup>18</sup>F-FDG)-PET is increasingly being investigated in patients with advanced Hodgkin lymphoma.<sup>1</sup> Casasnovas and colleagues<sup>2</sup> reported on the findings of the AHL2011 trial, in which PET2 was done after patients had received two cycles of BEACOPP<sup>escalated</sup>. In the experimental group, patients were switched to ABVD if the PET2 result was negative, or continued on BEACOPP<sup>escalated</sup> treatment if the PET2 result was positive. In the control group, patients continued with BEACOPP<sup>escalated</sup> treatment, regardless of PET2 outcome. In both groups, <sup>18</sup>F-FDG-PET was repeated after four cycles (PET4). If the PET4 result was negative, two final chemotherapy cycles were administered. If the PET4 result was positive, salvage chemotherapy was administered.

The AHL2011 trial echoes the results of the HD18 trial,<sup>3</sup> which also used a de-escalation strategy, which consisted of limiting the number of BEACOPP<sup>escalated</sup> cycles to only four if the patient's PET2 result was negative, whereas patients with a positive PET2 result received the full number of BEACOPP<sup>escalated</sup> cycles, similar to the standard group (eight cycles, or six cycles after an amendment to the protocol). At the end of treatment, <sup>18</sup>F-FDG-PET was done if a residual lesion greater than 2.5 cm was identified by CT. Patients with a positive <sup>18</sup>F-FDG-PET score received radiotherapy.<sup>3</sup>

In a previous publication,<sup>4</sup> we pointed out that PET-2 is not sufficient for management of patients with advanced stage Hodgkin lymphoma who are being treated with ABVD. Two published studies<sup>2,3</sup> suggest that PET2 alone is also not sufficient for fine-tuning treatment in patients treated with BEACOPP. In

AHL2011, a positive PET2 score, but a negative PET4 score, was reported in 62 (8%) of 766 patients.<sup>2</sup> 5-year progression-free survival was superior in these 62 patients compared with the 43 patients who were positive for both PET2 and PET4 (75% vs 47%). Thus, PET4 allowed the investigators to determine whether the patient needed salvage therapy. Additionally, for most patients with positive PET2, but negative PET4, who experienced relapse, disease progression seemed to occur less than a year after inclusion,<sup>2</sup> raising the question of the potential utility of an end-of-chemotherapy assessment in this subgroup. In the HD18 trial, 35% (155 of 434 patients) of PET2 positive patients were offered radiotherapy as a result of having an FDG-positive residual mass, as well as a small proportion of PET2 negative patients who showed an FDG-positive residual mass.<sup>3</sup> This end-of-chemotherapy PET evaluation thus allowed the investigators to identify patients who needed additional therapy, and highlights the potential utility of radiotherapy directed to a residual PET-positive mass. In total, although assessment of disease after two cycles appears necessary, additional assessment is warranted. Furthermore, the question of optimal timing, whether after four cycles or at the end of treatment, remains to be settled.<sup>4</sup>

We declare no competing interests.

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- 1 Cheson BD, Fisher RI, Barrington SF, et al. Recommendations for initial evaluation, staging, and response assessment of hodgkin and non-hodgkin lymphoma: the lugano classification. *Clin Oncol* 2014; **32**: 3059–68.
- 2 Casasnovas RO, Bouabdallah R, Brice P, et al. PET-adapted treatment for newly diagnosed advanced Hodgkin lymphoma (AHL2011): a randomised, multicentre, non-inferiority, phase 3 study. *Lancet Oncol* 2019; **20**: 202–15.

- 3 Borchmann P, Goergen H, Kobe C, et al. PET-guided treatment in patients with advanced-stage Hodgkin's lymphoma (HD18): final results of an open-label, international, randomised phase 3 trial by the German Hodgkin Study Group. *Lancet* 2018; **390**: 2790–802.
- 4 Mesguich C, Bouabdallah K, Milpied N, Hindié E. Additional evidence that end-of-treatment fluorodeoxyglucose-positron emission tomography evaluation is necessary in advanced hodgkin lymphoma. *J Clin Oncol* 2018; **36**: 2124–25.