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REPLY

Reply

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The aim of this retrospective pilot study was to draw attention to a phenomenon that had only been reported episodically and only in adults: the large frequency of a high diffuse FDG uptake (greater than that of the liver) by at least one organ in 77 % (0.95 confidence interval = 58–90 %) of young patients with untreated Hodgkin's lymphoma. The classical approach is to take into account only focal FDG uptake and its early response to treatment. This diffuse uptake is also modified after two cycles of treatment, as shown by significant differences in univariate analysis. In response to the objection raised by R Kluge et al., we confirm that the 5 sites were selected on basis of previous reports and studies in adults (quoted references 13–15 in our article) or in children (reference 17). R Kluge et al. also object that practicing this type of multiple comparisons increases the statistical risk alpha and accurately suggest applying the Bonferroni correction. This correction, multiplying by five the p values (e.g. $p = 0.005$ instead of 0.001) for a comparison of five sites, will not change the conclusions drawn from Table 3, since most p values were very small: there is a significant decrease after two cycles of treatment in the FDG uptake of the thymus, bone marrow and spleen. Similarly, the increase in FDG liver uptake remains significant. This variation is likely to have consequences on the visual evaluation which is made on the interim PET with reference to the liver uptake. It will influence visual evaluation of diffuse organ uptake, as shown on Table 2, by a decrease in organ uptake which is only significant for diffuse spleen uptake. It will probably also influence the visual evaluation of uptake of lymphoma foci on interim PET while assessing the Deauville criteria.

We also decided to search for a potential value of the evolution of the diffuse FDG uptake to predict a refractory response to the scheduled therapy or recurrence. All the patients were those referred to us for performing FDG PET/CT and/or reading and for whom follow-up data could be obtained. Indeed, treatment was not uniform since it was modified from the standard schedule in those "refractory" patients. However, the treatment was identical for all patients during the first two cycles of chemotherapy, i.e. before the interim FDG PET; merging their results with those of other patients is, then, legitimate.

Concerning the variation of the spinal cord SUVmax, the standard deviation (SD, which was not given in Table 3) was 26 % and a variation of 5 % corresponds to one fifth of the SD, which seems not to be negligible. As illustrated by Table 4, this criterion appeared as a potential predictor of relapse, not of refractoriness. Finally, it seemed to us not useless to derive from this analysis an index that aims helping an early detection of those patients who are unlikely to reach complete response after standard treatment or are at a higher risk of relapse.

We agree that the sample size is limited and that a retrospective analysis may lead to bias. We also agree with Kluge et al. that the present results have to be confirmed by prospective large studies. The information that has been exploited in our pilot study was already present in the FDG PET/CTs that have been performed and this new approach does not request any complementary procedure to the standard baseline-interim PET/CT evaluation. So, it seems worthwhile performing a confirmation study on the data of a larger number of patients, which is underway.

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