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REPLY: We thank Adams and Kwee for their critical review of our paper (*1*). We clarify that, as implied by the title, the paper reports marrow involvement by large B-cell lymphoma in cases presenting with diffuse large B-cell lymphoma (DLBCL). Only 2% (2/87) of cases with positive marrow histology had small cell lymphoproliferative disease identified as the sole infiltrate. We also clarify that as marrow was assessed on the staging PET examination, this was before any steroid, chemotherapy, or growth factor was given.

The authors are incorrect in stating that we report neither the prognostic significance of ^{18}F-FDG PET–positive marrow disease alone nor the incremental value of PET-positive together with bone marrow biopsy (BMB)–positive involvement over BMB-positive involvement alone. Our cohort of 327 cases was large enough to explore, in a multivariate model including the International Prognostic Index components, the prognosis of marrow disease identified by PET alone, BMB alone, and PET and BMB together. We report, in Table 4, that compared with cases with no marrow involvement, PET-positive marrow disease alone has no significant effect on survival ($P = 0.46$), nor does BMB-positive marrow disease alone ($P = 0.49$). In contrast, marrow disease identified by both PET and BMB does have a significant impact on survival ($P = 0.05$) (*1*).

In their own research, Adams and Kwee focus on the argument as to whether either BMB or ^{18}F-FDG PET is best at assessing for marrow involvement, for the clinical purpose of predicting prognosis and guiding treatment. Their recent publications present conflicting views; on the one hand they "support the omission of BMB for routine staging of newly diagnosed DLBCL," and on the other hand they state that "visual 18-FDG PET/CT bone marrow status has no prognostic value. . .and cannot replace BMB in newly diagnosed DLBCL" (*2,3*).

Their dichotomous focus leads them to overlook the clinical relevance of our report, which, with the benefit of 327 prospectively collected cases, examines this conundrum from the perspective of the treating clinician's decision making and the patient's overall benefit.

The message of our paper is both practical and simple. All centers having this debate will be doing staging PET or PET/CT scans on all DLBCL patients; hence, assessment of abnormal ^{18}F-FDG uptake in marrow is routinely available for all cases. The data from our large cohort demonstrate that those with PET-negative marrow gain no clinical benefit, in terms of altered prognosis, from a routine iliac crest biopsy. These patients, 74% of the cohort, can therefore omit and avoid the pain and distress of this procedure. However, those with PET-positive marrow do gain clinically important additional information from a biopsy, whether ^{18}F-FDG uptake is focal or diffuse.

Diffuse ^{18}F-FDG uptake was quite clearly defined in the methods, contrary to Adams' and Kwee's statement, and the definition was based on previously reported criteria, namely diffuse homogeneous ^{18}F-FDG uptake throughout the marrow space, with intensity greater than uptake in normal liver and with no anatomic changes to suggest alternative benign bone pathology or spread from a contiguous nonskeletal site (*1,4*). We agree that diffuse ^{18}F-FDG uptake in marrow is difficult to assess (though assessment improves with experience) and that, consequently, marrow showing diffuse uptake should always undergo biopsy (*1,5,6*).

Focal marrow involvement identified by PET together with marrow biopsy histology showing large cell lymphoma does confer a worse prognosis than PET-positive/marrow histology–negative marrow disease, as shown in Figure 3 (*1*). Hence derives our statement that both biopsy and PET together have a role to play in the staging of DLBCL but that the addition of a marrow biopsy when PET data are already available is useful in only a minority of patients.

Although Adams and Kwee conclude that the prognostic potential of marrow assessment in DLBCL by PET has not yet been proven, our study does clarify the distinct and separate roles of PET and marrow biopsy for predicting outcome and hence influencing treatment decisions.

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