Does end-of-treatment FDG-PET improve outcomes in follicular lymphoma?

Authors' reply

Hugo Adams and colleagues respond to our Article, involving several hundred patients with PET-CT scans in the GALLIUM study,[1] challenging the value of end-of-induction PET in follicular lymphoma. They acknowledge the data demonstrating that end-of-induction PET is prognostic for outcome: patients who achieved a complete metabolic response had improved progression-free survival and overall survival 2·5 years after induction, compared with those who did not have a complete metabolic response. Adams and colleagues note that only 14 deaths were due to progressive lymphoma; however, we wish to highlight that nine (64%) of these deaths occurred in the minority (69 [13%]) of 519 patients who did not obtain complete metabolic response. Therefore, at this early timepoint after induction, 13% of these 69 patients have died of lymphoma, compared with only 5 (1%) of 450 patients who achieved complete metabolic response.

We do not agree with the data interpretation and clinical assumptions provided by Adams and colleagues. Progression-free survival is a widely accepted clinical endpoint after first-line treatment of follicular lymphoma, a disease with a median overall survival beyond 15 years. Several studies have shown that time to next treatment usually closely follows progression. Therapy de-escalation is indeed possible after induction immunochemotherapy in follicular lymphoma. Such an approach is being investigated in the FOLL12 study (EUDRACT 2012-003170-60), which has completed recruitment of 810 patients, as well as the PET Response-Adapted therapy trial (PETReA; EUDRACT 2016-004010-10), in which patients who obtain complete metabolic responses are randomly assigned to rituximab maintenance therapy or observation. PETReA will quantify the progression-free survival benefit of maintenance rituximab, and assess the trade-off with toxicity in this low-risk (PET-negative) population. Similarly, a trial of therapeutic escalation, comparing the addition of lenalidomide to maintenance rituximab with rituximab alone, is appropriate in the 12% of patients who do not obtain a complete metabolic response, for whom we have shown a 45% risk of progression within only 30 months after induction and a 16% risk of early death.

Given the robust results of GALLIUM[1] and several other studies,[2–5] we are confident that end-of-induction PET status is an appropriate platform for study of response-adapted therapy in this common, usually indolent disease. We hope the FOLL12 and PETReA studies succeed in improving outcomes for all patients with follicular lymphoma.

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