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

Judith Trotman and colleagues[1] recently investigated the value of end-of-treatment CT and 2-^{18}F-fluoro-2-deoxy-D-glucose-PET (^{18}F-FDG-PET) in predicting prognosis in patients with follicular lymphoma treated with various first-line regimens. The authors interpreted CT scans according to the International Harmonisation Project (IHP) criteria, whereas ^{18}F-FDG-PET scans were interpreted according to the IHP and Lugano 2014 criteria, the latter of which was superior in predicting prognosis. In this landmark analysis, 448 (88%) of 508 patients had a complete metabolic response at end-of-treatment ^{18}F-FDG-PET, whereas 60 (12%) patients did not, according to the Lugano criteria (as shown in figure 2).[1] Patients with a complete metabolic response had improved 2·5-year progression-free survival: 87·4% (95% CI 83·7–90·2) versus 54·9% (40·5–67·3) in those who did not completely respond (HR 0·2, 95% CI 0·1–0·3; p<0·0001). Patients with a complete metabolic response also had improved 2·5-year overall survival (96·9%, 95% CI 94·5–98·2) than those who did not (90·6%, 84·6–94·3). There were 37 deaths, of which only 14 patients died because of progressive lymphoma. Of these 14 lymphoma-related deaths, nine had an incomplete metabolic response, whereas five had a complete metabolic response. Trotman and colleagues[1] claimed end-of-treatment ^{18}F-FDG-PET provides a platform for the investigation of response-adapted therapeutic approaches.

However, we disagree with their conclusion. First, end-of-treatment ^{18}F-FDG-PET scans are done after the entire first-line treatment has been applied. As a result, therapy de-escalation is no longer possible, and treatment escalation is the only option. However, 54·9% of patients with an incomplete metabolic response after treatment were still progression-free after 2·5 years, which indicates that these patients would have been overtreated if treatment had been escalated. Of the 45·1% of patients who experienced the end of progression-free survival, it remains unknown how many patients actually required additional treatment within the first years after first-line treatment, because end of progression-free survival was defined as the time from randomisation to the first occurrence of progression or relapse. The first occurrence of progression or relapse, however, is not necessarily a requirement to initiate second-line therapy. Second, 2·5-year overall survival was 84·0% (95% CI 72·9–90·8) in the group of patients without a complete metabolic response, and the majority of deaths were due to other reasons than progressive lymphoma. The GALLIUM study showed that ^{18}F-FDG-PET-based response-adapted therapy in follicular lymphoma is unlikely to be feasible, given that the entire study population (n=508) required ^{18}F-FDG-PET, and a considerable number of patients (60 [12%]) needed intensified upfront treatment, to potentially prevent early death of only a small fraction of patients (maximum of nine [2%]), which is questionably justifiable.

We declare no competing interests.

*Hugo J A Adams, Thomas C Kwee
h.j.a.adams@gmail.com

Department of Radiology and Nuclear Medicine, Academic Medical Center, University of Amsterdam, 1105AZ Amsterdam, Netherlands (HJAA); and Department of Radiology, Nuclear Medicine and Molecular Imaging, University Medical Center Groningen, University of Groningen, Groningen, Netherlands (TCK)

1 Trotman J, Barrington SF, Belada D, et al. Prognostic value of end-of-induction PET response after first-line immunochemotherapy for follicular lymphoma (GALLIUM): secondary analysis of a randomised, phase 3 trial. *Lancet Oncol* 2018; **19:** 1530–42.