Optimal patient selection for stereotactic body radiotherapy

Authors' reply

We thank Amar Kishan and colleagues for their well informed letter regarding our Article on the acute toxicity seen in the PACE-B trial.[1] They raise an excellent point of interest; using the patient and treatment heterogeneity in the trial to draw new insights regarding associations between characteristics and toxicity outcomes. The questions raised regarding prostate volume, baseline toxicity, and fractionation are important and their analysis in multivariate frameworks capable of accounting for confounding factors, including dosimetry, is a current priority for our study group. To this end, we have been centrally accruing radiotherapy plan data (DICOM format) for all participants in PACE-B receiving trial radiotherapy. Our initial focus will be on predictors of acute toxicity for those receiving stereotactic body radiotherapy, given our prespecified interest in treatment platform effects after the trial protocol amendment (Oct 24, 2014) to allow conventional linear accelerator based stereotactic body radiotherapy.

Crucially, such post-hoc analyses of randomised controlled trials must be undertaken with due regard for confounding influence since the protective effect of randomisation is lost. We are therefore currently taking time to assure the quality of candidate predictive variables and will proceed with toxicity predictive modelling in due course.

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1 Brand DH, Tree AC, Ostler P, et al. Intensity-modulated fractionated radiotherapy versus stereotactic body radiotherapy for prostate cancer (PACE-B): acute toxicity findings from an international, randomised, open-label, phase 3, non-inferiority trial. *Lancet Oncol* 2019; **20:** 1531–43.