SABR versus conventional fractionation regimens in NSCLC

Authors' reply

We thank Alfredo Addeo and Lucio Buffoni, as well as Nuradh Joseph and Ananya Choudhury, for their interest in, and their comments on, our recently published CHISEL trial.[1] In answer to the suggestion that overall survival might have been driven by subsequent treatments, we do not have detailed information about post-relapse treatment since the primary endpoint was local failure. Although a slightly larger proportion of patients with non-squamous histology were randomly assigned to stereotactic ablative body radiotherapy (SABR) than to standard radiotherapy (66% *vs* 54%), it seems unlikely that there would have been an excess of patients with actionable mutations influencing survival in the SABR group, given that in our population the incidence of such mutations is around 20%.

Joseph and colleagues state that, based on the biological effective dose model, 50 Gy (62·5 Gy_{10}) is "clearly suboptimal" compared with 66 Gy (72·4 Gy_{10}). We would, however, be wary of making such assertions based on a theoretical model, as demonstrated in the RTOG 0617 trial in which the lower dose (60 Gy) was superior in terms of local control and survival compared with 74 Gy.[2] In CHISEL, there was no randomisation between 66 Gy and 50 Gy; rather, the decision to treat patients with 50 Gy or 66 Gy was based on institutional preference. Comparisons between 66 Gy and SABR thus lose the benefit of randomisation. The limited power of a comparison between 66 Gy and SABR to show an effect has already been acknowledged by the correspondents.

Recognising these limitations, analyses testing for association between freedom from local failure and treatment (66 Gy *vs* SABR) and between overall survival and treatment were done. The sample size was 66 (SABR) plus 23 (66 Gy). The hazard ratio for freedom from local failure was 0·31 (95% CI 0·12–0·80; p=0·010). For overall survival, the hazard ratio was 0·60 (95% CI 0·32–1·14; p=0·12).

We declare no competing interests.

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1 Ball D, Mai GT, Vinod S, et al. Stereotactic ablative radiotherapy versus standard radiotherapy in stage 1 non-small-cell lung cancer (TROG 09.02 CHISEL): a phase 3, open-label, randomised controlled trial. *Lancet Oncol* 2019; **20:** 494–503.

2 Bradley JD, Paulus R, Komaki R, et al. Standard-dose versus high-dose conformal radiotherapy with concurrent and consolidation carboplatin plus paclitaxel with or without cetuximab for patients with stage IIIA or IIIB non-small-cell lung cancer (RTOG 0617): a randomised, two-by-two factorial phase 3 study. *Lancet Oncol* 2015; **16:** 187–99.