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We have recently published the results of the PulMiCC trial (Pulmonary Metastasectomy in Colorectal Cancer).(1) We know that completing a randomised trial of interventions for 'oligometastatic' cancer is difficult and so we congratulate Palma and colleagues on publishing the results of SABR-COMET. (2) When more than 1000 radiation oncologists were asked about their practice and opinions concerning stereotactic ablative radiotherapy for metastatic cancer, 99% were already believers in the practice.(3) SABR-COMET will be welcomed by them and will be used to give hope to their patients. The Lancet commentators liken the SABR-COMET findings to the ancient sightings of comets "as harbingers of important events". But we question whether those findings really provide the robust evidence of the benefit of treating 'oligometastases' that is claimed.

As with the CLOCC trial of radiofrequency ablation for liver metastases (4) the two arms of SABR-COMET were not balanced for key prognostic factors. The number of metastases is the most powerful prognostic factor (5) but the greatest statistical effect is seen between solitary and multiple metastases with a hazard ratio of 2.04 (95% CI 1.72-2.41).(4) Palma et al set the stratification at between 1-3 and 4-5 metastases and could not adequately control for this confounding factor. Importantly there was a 10% excess of solitary metastases in the intervention group (46% versus 36%). In the CLOCC trial the imbalance in solitary metastases was more than double (25% versus 12%), again favouring the intervention.(5) In PulMiCC balance was ensured by including minimisation in randomisation.(6) SABR-COMET also had an imbalance in the cancer types with more breast and prostate, and fewer colorectal cancers, in the intervention arm, also probably biasing the survival outcome.

The improvement in survival seems impressive (HR.0.37) but is less so in the light of this prognostic factor imbalance and the fact that the upper limit of the 95% CI was 1.10. SABR-COMET also showed significant risks from the intervention with a 20% increase in Grade 2 or worse adverse events and 4.5% treatment-related deaths. This small randomised phase 2 trial is interesting but clearly does not provide strong enough evidence to reliably determine the value of SABR in 'oligometastatic' disease.

The authors note the better-than-expected survival in the control group which was also the important finding in PulMiCC.(1) The five-year survival of about 40%, consistently observed in observational follow-up studies of lung metastasectomy(4) is always attributed to the operation. The five-year survival of a comparable population of controls is generally assumed to be near zero. But for patients selected as suitable for metastasectomy, but randomly assigned to the control group of PulMiCC the five-year survival was about 30%. (Control N=32 compared with N=33 in SABR-COMET) The five-year survival was also about 30% in the control arm of the CLOCC trial of radiofrequency ablation for liver metastases.(5) Randomised trials fairly representing contemporary outcomes with best alternative management for patients *not* receiving the intervention are clearly needed.

As far as we are aware there have only been three randomised trials addressing in various ways the value of removing or ablating 'oligometastases', all small. Two (SABR-COMET and CLOCC) are potentially flawed by imbalances in key prognostic factors. PulMiCC shows no difference in survival. We believe that the question remains open and, despite all those with vested interests who might argue otherwise, larger definitive trials are still needed to determine whether this policy does in fact improve survival and, if so, in which patients.

Reference List

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