

## Letters to the Editor

**Pulmonary Metastasectomy for Colorectal Cancer: Randomized Controlled Trial**

From

Norman R. Williams, PhD,\* Tom Treasure, MD,<sup>†</sup> and Fergus Macbeth, DM<sup>‡</sup>Clinical and Interventional Trials Unit\* and Clinical Operational Research Unit,<sup>†</sup> University College London, Gower Street, London WC1E 6BT, England  
e-mail: [tom.treasure@gmail.com](mailto:tom.treasure@gmail.com)Centre for Trials Research, Cardiff University, Cardiff, Wales<sup>‡</sup>**Editor:**

We were interested in the study by Dr Hasegawa and colleagues (1) regarding radiofrequency ablation (RFA) for pulmonary metastases and the accompanying editorial by Dr Gemmete (2), who kindly referred to our pulmonary metastasectomy for colorectal cancer (PulMiCC) trial. To our knowledge, this is the only randomized trial (RCT) comparing pulmonary metastasectomy to active monitoring in patients with colorectal cancer that is now published (3). It was designed as an ambitious noninferiority trial but failed to recruit the intended number of patients. With 93 patients randomized, it showed no difference in survival between the two groups, out to 5 years (hazard ratio, 0.93; 95% CI: 0.65, 1.56) and 5-year survival in both arms around 30%. But, importantly, it has enough statistical power to show that survival in the control arm is unlikely to be less than 5%, as is so widely quoted and believed. Two randomized phase II trials (4,5) have reported on the use of RFA ( $n = 119$ ) and stereotactic radiation therapy ( $n = 99$ ) for metastases. Unlike PulMiCC, they both had significant imbalance in key prognostic factors favoring intervention, but even so, the 5-year survival in the control arms was between 25% and 30% and neither showed a convincing survival benefit (4,5).

As with any RCT, the patients in the PulMiCC trial were selected by entry criteria and researcher choice, but key characteristics are well balanced and similar to those in the many published observational studies. The observational study of Dr Hasegawa and colleagues appeared to show impressive results, but this was clearly a highly selected group of patients and, without any control group, it is impossible to draw meaningful conclusions about overall effectiveness.

We fully accept that it is possible that there may be a survival benefit for selected patients from pulmonary metastasectomy, but the current evidence does not suggest that this is as great as generally believed. A large RCT comparing pulmonary metastasectomy, whether surgical or by RFA or stereotactic radiation therapy, to active monitoring (ie, no treatment) is still needed to show whether there is benefit and if so for whom. If, as Dr Gemmete remarked, RFA is ready for “prime time,” this should not mean routine practice, but as a comparator in such an RCT.

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**References**

- Hasegawa T, Takaki H, Kodama H, et al. Three-year Survival Rate after Radiofrequency Ablation for Surgically Resectable Colorectal Lung Metastases: A Prospective Multicenter Study. *Radiology* 2020;294(3):686–695.
- Gemmete JJ. Percutaneous Radiofrequency Ablation Is Ready for Prime Time in the Treatment of Colorectal Pulmonary Metastases. *Radiology* 2020;294(3):696–697.
- Milosevic M, Edwards J, Tsang D, et al. Pulmonary Metastasectomy in Colorectal Cancer: updated analysis of 93 randomized patients - control survival is much better than previously assumed. *Colorectal Dis* 2020. 10.1111/codi.15113. Published online May 9, 2020 <https://doi.org/10.1111/codi.15113>.
- Ruers T, Van Coevorden F, Punt CJ, et al. Local Treatment of Unresectable Colorectal Liver Metastases: Results of a Randomized Phase II Trial. *J Natl Cancer Inst* 2017;109(9):dix015 <https://doi.org/10.1093/jnci/dix015>.
- Palma DA, Olson R, Harrow S, et al. Stereotactic ablative radiotherapy versus standard of care palliative treatment in patients with oligometastatic cancers (SABR-COMET): a randomised, phase 2, open-label trial. *Lancet* 2019;393(10185):2051–2058.

