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Letters to the Editor

Randomized Controlled Trial of Pulmonary Metastasectomy in Colorectal Cancer: PulMiCC International Is Open in Italy

MARCELLO MIGLIORE,[a] BELINDA LEES,[b] TOM TREASURE,[c] LESLEY J. FALLOWFIELD[d]

[a]Thoracic Surgery, Policlinico Hospital, Catania, Italy; [b]Clinical Trials and Evaluation Unit, Royal Brompton Hospital, Imperial College School of Medicine, London, United Kingdom; [c]Clinical Operation Research Unit, University College London, London, United Kingdom; [d]Sussex Health Outcomes Research & Education Centre, Brighton and Sussex Medical School, Brighton, United Kingdom

Disclosures of potential conflicts of interest may be found at the end of this article.

While reporting a comparative analysis of 409 patients with pulmonary metastases because of colorectal cancer, Tampellini and colleagues write: "To solve the debate, a phase III, prospective, randomized clinical trial ... has been advocated" [1]. The trial cited [2] is PulMiCC (Pulmonary Metastasectomy in Colorectal Cancer). At the time of writing, 123 U.K. patients have been recruited and 36 of them have been randomized to either pulmonary metastasectomy or not, with both groups being actively monitored. PulMiCC International is open for recruitment in Catania, Italy.

We are running the trial because we agree with the statement of Tampellini and colleagues, "From a statistical point of view, our findings are insufficient to definitively solve the question of whether or not surgery is beneficial in resectable patients because this can be demonstrated only with a prospective, randomized, phase III trial" [1]. They nicely show the statistical limitations of observational data. They identified 1,411 patients with metastatic colorectal cancer between 1994 and 2010. Of these patients, 409 (29%) had pulmonary metastases and in 154 (11%), metastases were confined to the lung; 50 patients (3.5%) were selected to have pulmonary metastasectomy. This illustrates the problem of the shrinking denominator in selection of patients for pulmonary metastasectomy. As the authors state, this information is not generally captured in surgical follow-up studies where the starting point is a retrieved list of patients who had pulmonary metastasectomy. Exceptions include reports from the U.S. Department of Veterans Affairs [3] and a Cleveland Clinic study of liver and lung versus lung only metastasectomy [4], which showed a similarly high degrees of selection.

If we consider the 154 patients with lung-only metastases, 50 (32%) were selected for surgery (group 3) while the remaining 104 (group 2) were selected to not have surgery [1]. The groups are very different on critical baseline characteristics. Compared with the 104 patients in group 2, the 50 patients selected for pulmonary metastasectomy had far fewer metastases (median 1, range 1–5 vs. 5, 1–15) and a much longer interval before metastases were evident (median 24 months, range 0–119 months vs. 5, 0–76). These are well-established factors associated with survival variation in patients with pulmonary metastases, irrespective of whether they do or do not have metastasectomy [5]. So, to ask the 30-year-old question [6], is it the selection rather than the surgery that explains the difference?

We agree with the authors' final conclusion: "From a medical oncology point of view, however, our results add evidence to the debate on whether or not such a study is still necessary." Their data, which show the large differences in selection criteria between those who did and did not have pulmonary metastasectomy, emphasize the need for an even-handed comparison. PulMiCC is designed so that patients and clinical teams can decide for or against pulmonary metastasectomy. If, after standard clinical assessment, the better course of action is uncertain, then treatment allocation is made by randomization [7, 8].

Author Contributions

Conception and design: Tom Treasure, Marcello Migliore, Belinda Lees, Lesley J. Fallowfield
Provision of study material or patients: Tom Treasure, Marcello Migliore, Belinda Lees, Lesley J. Fallowfield
Collection and/or assembly of data: Tom Treasure, Belinda Lees, Lesley J. Fallowfield
Data analysis and interpretation: Tom Treasure, Belinda Lees, Lesley J. Fallowfield
Manuscript writing: Tom Treasure, Lesley J. Fallowfield
Final approval of manuscript: Tom Treasure, Marcello Migliore, Belinda Lees, Lesley J. Fallowfield

Disclosures

Lesley J. Fallowfield: Cancer Research UK (CRUK) (RF). The other authors indicated no financial relationships.
(C/A) Consulting/advisory relationship; (RF) Research funding; (E) Employment; (H) Honoraria received; (OI) Ownership interests; (IP) Intellectual property rights/inventor/patent holder; (SAB) Scientific advisory board

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Correspondence: Tom Treasure, M.D., University College London, Clinical Operational Research Unit, 4 Taviton Street, London ME13 0NZ, United Kingdom. E-Mail: tom.treasure@gmail.com Received December 20, 2012; accepted for publication February 13, 2013. ©AlphaMed Press 1083-7159/2013/$20.00/0 http://dx.doi.org/10.1634/theoncologist.2012-0476