Randomising Patients into Trials of Thoracic Cancer Surgery: An Analysis of Patient and Cancer Team Behaviour

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Background

Pulmonary Metastasectomy in Colorectal Cancer (PulMiCC) is a multicentre trial funded by Cancer Research UK. In Stage 1 participants were invited to consent for further evaluation within the PulMiCC protocol and if eligible were offered randomisation (Stage 2) to lung metastasectomy or continued active monitoring.

Noting a decreasing rate of randomisation during 2016, the Data Monitoring Committee recommended that the reasons for this should be investigated.

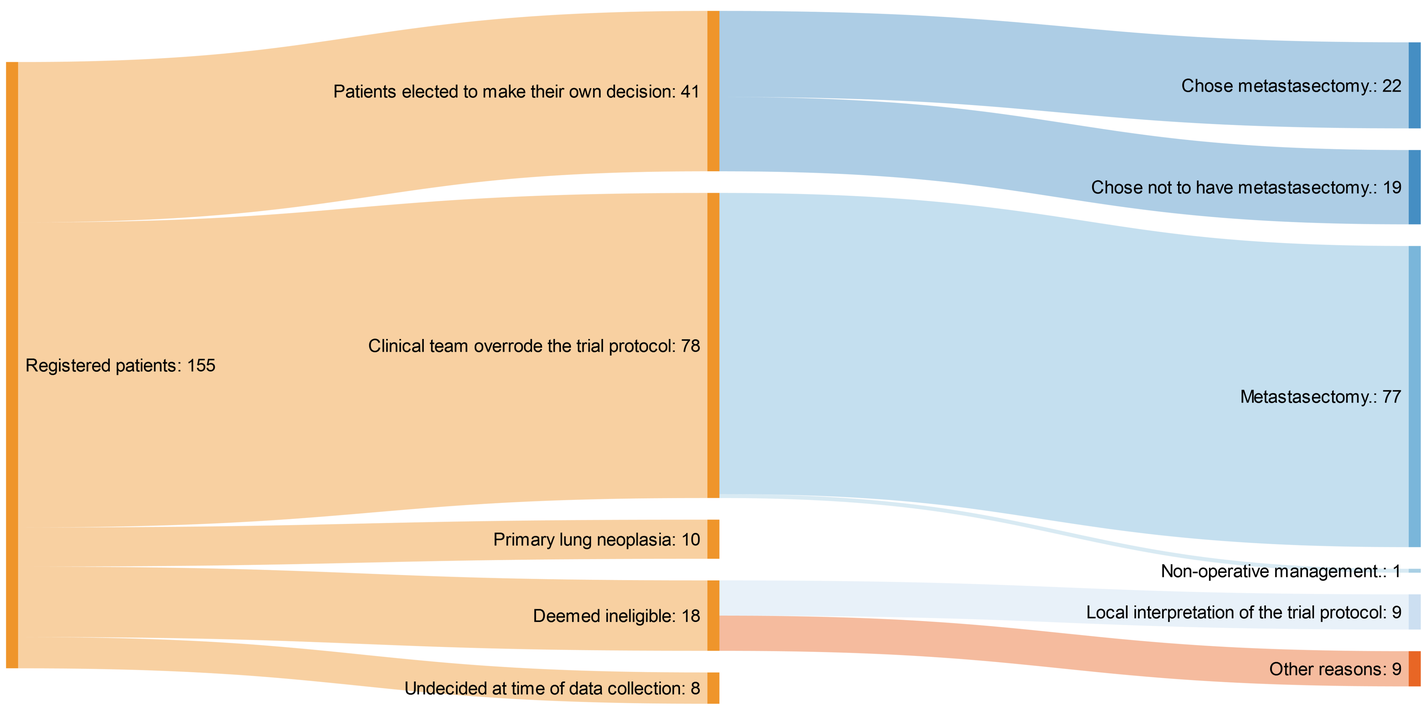
Method

The three most actively recruiting centres were approached and asked to provide reasons for patients in Stage 1 not being randomised into Stage 2 and to provide data according to the fields in the first column of the table.

We sought to discover who made the decision not to randomise and to establish what clinical management was then followed. If participants were deemed ineligible we asked for the reason.

Result

Of 155 patient participants consented into Stage 1 of the trial, and after full information and counselling during the period of assessment, 41 elected to make their own decision. The split to have or not have metastasectomy was 22:19. When the clinicians made the decision 77/78 (99%) patients had metastasectomy. (Sankey Flow Diagram) Ten patients had other pathology, nine lung cancer and one carcinoid. The protocol placed no constraint on the number of metastases but one unit set its own limits at 2-4 deeming patients outside as not eligible for randomisation but as suitable for metastasectomy.



Conclusions

At trial closure, of 512 patients in Stage 1, 82% were not randomised resulting in an inconclusive result despite the efforts of many doctors, nurses and scientists and the participation of a large number of patients.

In the sample of 155 drawn from the three most active centres:

- 78 patients deemed eligible had the decision made for them by the clinical team
- At least 56% of the patients were lost to randomisation by clinicians' decisions.
- Of the 18 deemed ineligible but not randomised, half of the reasons were not aligned with the written protocol
- 41/155 patients who elected to make their own decision, to have or not have metastasectomy, did so in numbers which better reflected equipoise.

The difficulty faced by clinicians in declaring uncertainty is well recognised. In PulMiCC this resulted in exclusion of many patients who had given their informed consent. Learning from this and similar experiences, later UK trials of thoracic oncology (MARS-2, VIOLETS) have recruited well after specific training in the QuinteT method for randomisation into surgical trials.

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