Oligometastatic

Stereotactic ablative radiotherapy versus standard-of-care palliative treatment in patients with oligometastatic cancers (SABR-COMET): a randomised, phase 2, open-label trial.

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BACKGROUND

The oligometastatic paradigm suggests that some patients with a limited number of metastases might be cured if all lesions are eradicated. Evidence from randomised controlled trials to support this paradigm is scarce. We aimed to assess the effect of stereotactic ablative radiotherapy (SABR) on survival, oncological outcomes, toxicity, and quality of life in patients with a controlled primary tumour and one to five oligometastatic lesions.

METHODS

This randomised, open-label, Phase 2 study was done at 10 hospitals in Canada, The Netherlands, Scotland, and Australia. Patients aged 18 or older with a controlled primary tumour and one to five metastatic lesions, Eastern Cooperative Oncology Group score of 0-1, and a life expectancy of at least six months were eligible. After stratifying by the number of metastases (1-3 vs 4-5), we randomly assigned patients (1:2) to receive either palliative standard-of-care treatments alone (control group), or standard-of-care plus SABR to all metastatic lesions (SABR group), using a computer-generated randomisation list with permuted blocks of nine. Neither patients nor physicians were masked to treatment allocation. The primary endpoint was overall survival. We used a randomised Phase 2 screening design with a two-sided α of 0·20 (wherein $p<0·20$ designates a positive trial). All analyses were intention to treat. This study is registered with ClinicalTrials.gov, number NCT01446744.

FINDINGS

A total of 99 patients were randomised between 10 Feb, 2012, and 30 Aug, 2016. Of 99 patients, 33 (33%) were assigned to the control group and 66 (67%) to the SABR group. Two (3%) patients in the SABR group did not receive allocated treatment and withdrew from the trial; two (6%) patients in the control group also withdrew from the trial. Median follow-up was 25 months (IQR 19-54) in the control group versus 26 months (23-37) in the SABR group. Median overall survival was 28 months (95% CI 19-33) in the control group versus 41 months (26 not reached) in the SABR group (hazard ratio 0·57, 95% CI 0·30-1·10; p=0·090). Adverse events of Grade 2 or worse occurred in three (9%) of 33 controls and 19 (29%) of 66 patients in the SABR group (p=0·026), an absolute increase of 20% (95% CI 5-34). Treatment-related deaths occurred in three (4·5%) of 66 patients after SABR, compared with none in the control group.

INTERPRETATION

SABR was associated with an improvement in overall survival, meeting the primary endpoint of this trial, but three (4·5%) of 66 patients in the SABR group had treatment-related death. Phase 3 trials are needed to show conclusively an overall survival benefit, and to determine the maximum number of metastatic lesions wherein SABR provides a benefit.