



# READ IT BEFORE YOUR PATIENTS

## Pulmonary metastases

### Single-Fraction vs Multifraction Stereotactic Ablative Body Radiotherapy for Pulmonary Oligometastases (SAFRON II): The Trans Tasman Radiation Oncology Group 13.01 Phase II Randomised Clinical Trial.

*Siva S, Bressel M, Mai T, Le H, Vinod S, de Silva H, Macdonald S, Skala M, Hardcastle N, Rezo A, Pryor D, Gill S, Higgs B, Wagenfuehr K, Montgomery R, Awad R, Chesson B, Eade T, Wong W, Sasso G, De Abreu Lourenco R, Kron T, Ball D, Neeson P; Stereotactic Ablative Fractionated Radiotherapy Versus Radiosurgery for Oligometastatic Neoplasia to the Lung (SAFRON) II Study Investigators.*

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#### IMPORTANCE

Evidence is lacking from randomised clinical trials to guide the optimal approach for stereotactic ablative body radiotherapy (SABR) in patients with pulmonary oligometastases.

#### OBJECTIVE

To assess whether single-fraction or multifraction SABR is more effective for the treatment of patients with pulmonary oligometastases.

#### DESIGN, SETTING, AND PARTICIPANTS

This multicenter, unblinded, phase II randomised clinical trial of 90 patients across 13 centers in Australia and New Zealand enrolled patients with one to three lung oligometastases less than or equal to 5.0 cm from any nonhematologic malignant tumours located away from the central airways, Eastern Cooperative Oncology Group performance status zero or one, and all primary and extrathoracic disease controlled with local therapy. Enrollment was from 1 January 2015, to 31 December 2018, with a minimum patient follow-up of two years.

#### INTERVENTIONS

Single fraction of 28 Gy (single-fraction arm) or four fractions of 12 Gy (multifraction arm) to each oligometastasis.

#### MAIN OUTCOMES AND MEASURES

The main outcome was grade three or higher treatment-related adverse events (AEs) occurring within one year of SABR. Secondary outcomes were freedom from local failure, overall survival, disease-free survival, and patient-reported outcomes (MD Anderson Symptom Inventory-Lung Cancer and EuroQol 5.0-dimension visual analog scale).

#### RESULTS

Ninety participants were randomised, of whom 87 were treated for 133 pulmonary oligometastases. The mean (SD) age was 66.6 [11.6] years; 58 (64%) were male. Median follow-up was 36.5 months (interquartile range, 24.8-43.9 months). The numbers of grade three or higher AEs related to treatment at one year were two (5.0%; 80% CI, 1.0%-13%) in the single-fraction arm and 1 (3.0%; 80% CI, 0.0%-10%) in the multifraction arm, with no significant difference observed between arms. One grade 5.0 AE occurred in the multifraction arm. No significant differences were found between the multifraction arm and single-fraction arm for freedom from local failure (hazard ratio [HR], 0.5; 95% CI, 0.2-1.3; P = .13), overall survival (HR, 1.5; 95% CI, 0.6-3.7; P = .44), or disease-free survival (HR, 1.0; 95% CI, 0.6-1.6; P > .99). There were no significant differences observed in patient-reported outcomes.

## CONCLUSIONS AND RELEVANCE

In this randomised clinical trial, neither arm demonstrated evidence of superior safety, efficacy, or symptom burden; however, single-fraction SABR is more efficient to deliver. Therefore, single-fraction SABR, as assessed by the most acceptable outcome profile from all end points, could be chosen to escalate to future studies.

