# READ IT BEFORE YOUR PATIENTS

## Palliation

## Stereotactic body radiotherapy versus conventional external beam radiotherapy in patients with painful spinal metastases: an open-label, multicentre, randomised, controlled, phase II/III trial.

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### BACKGROUND

Conventional external beam radiotherapy is the standard palliative treatment for spinal metastases; however, complete response rates for pain are as low as 10-20%. Stereotactic body radiotherapy delivers high-dose, ablative radiotherapy. We aimed to compare complete response rates for pain after stereotactic body radiotherapy or conventional external beam radiotherapy in patients with painful spinal metastasis.

### METHODS

This open-label, multicentre, randomised, controlled, phase II/III trial was done at 13 hospitals in Canada and five hospitals in Australia. Patients were eligible if they were aged 18 years and older, and had painful (defined as ≥2.0 points with the Brief Pain Inventory) MRI-confirmed spinal metastasis, no more than three consecutive vertebral segments to be included in the treatment volume, an Eastern Cooperative Oncology Group performance status of 0.0-2.0, a Spinal Instability Neoplasia Score of less than 12, and no neurologically symptomatic spinal cord or cauda equina compression. Patients were randomly assigned (1:1) with a web-based, computer-generated allocation sequence to receive either stereotactic body radiotherapy at a dose of 24 Gy in two daily fractions or conventional external beam radiotherapy at a dose of 20 Gy in five daily fractions using standard techniques. Treatment assignment was done centrally by use of a minimisation method to achieve balance for the stratification factors of radiosensitivity, the presence or absence of mass-type tumour (extraosseous or epidural disease extension, or both) on imaging, and centre. The primary endpoint was the proportion of patients with a complete response for pain at 3 months after radiotherapy. The primary endpoint was analysed in the intention-to-treat population and all safety and quality assurance analyses were done in the as-treated population (i.e, all patients who received at least one fraction of radiotherapy). The trial is registered with ClinicalTrials.gov, NCT02512965.

### FINDINGS

Between 4 Jan 2016, and 27 Sept 2019, 229 patients were enrolled and randomly assigned to receive conventional external beam radiotherapy (n=115) or stereotactic body radiotherapy (n=114). All 229 patients were included in the intention-to-treat analysis. The median follow-up was 6·7 months (IQR 6·3-6·9). At three months, 40 (35%) of 114 patients in the stereotactic body radiotherapy group, and 16 (14%) of 115 patients in the conventional external beam radiotherapy group had a complete response for pain (risk ratio 1·33, 95% CI 1·14-1·55; p=0·0002). This significant difference was maintained in multivariable-adjusted analyses (odds ratio 3·47, 95% CI 1·77-6·80; p=0·0003). The most common grade 3.0-4.0 adverse event was grade 3.0 pain (four [4.0%] of 115 patients in the conventional external beam radiotherapy group vs five (5%) of 110 patients in the stereotactic body radiotherapy group). No treatment-related deaths were observed.

## INTERPRETATION

Stereotactic body radiotherapy at a dose of 24 Gy in two daily fractions was superior to conventional external beam radiotherapy at a dose of 20 Gy in five daily fractions in improving the complete response rate for pain. These results suggest that use of conformal, image-guided, stereotactically dose-escalated radiotherapy is appropriate in the palliative setting for symptom control for selected patients with painful spinal metastases, and an increased awareness of the need for specialised and multidisciplinary involvement in the delivery of end-of-life care is needed.