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Prostate & Spine

Observation versus screening spinal MRI and pre-emptive treatment for spinal cord compression in patients with castration-resistant prostate cancer and spinal metastases in the UK (PROMPTS): an open-label, randomised, controlled, phase III trial

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BACKGROUND

Early diagnosis of malignant spinal cord compression (SCC) is crucial because pretreatment neurological status is the major determinant of outcome. In metastatic castration-resistant prostate cancer, SCC is a clinically significant cause of disease-related morbidity and mortality. We investigated whether screening for SCC with spinal magnetic resonance imaging (MRI), and pre-emptive treatment if radiological SCC (rSCC) was detected, reduced the incidence of clinical SCC (cSCC) in asymptomatic patients with metastatic castration-resistant prostate cancer and spinal metastasis.

METHODS

We did a parallel-group, open-label, randomised, controlled, phase III, superiority trial. Patients with metastatic castration-resistant prostate cancer were recruited from 45 National Health Service hospitals in the UK. Eligible patients were aged at least 18 years, with an Eastern Co-operative Oncology Group performance status of 0-2, asymptomatic spinal metastasis, no previous SCC, and no spinal MRI in the past 12 months. Participants were randomly assigned (1:1), using a minimisation algorithm with a random element (balancing factors were treatment centre, alkaline phosphatase [normal vs raised, with the upper limit of normal being defined at each participating laboratory], number of previous systemic treatments [first-line vs second-line or later], previous spinal treatment, and imaging of thorax and abdomen), to no MRI (control group) or screening spinal MRI (intervention group). Serious adverse events were monitored in the 24 h after screening MRI in the intervention group. Participants with screen-detected rSCC were offered pre-emptive treatment (radiotherapy or surgical decompression was recommended per treating physician's recommendation) and 6-monthly spinal MRI. All patients were followed up every three months, and then at month 30 and 36. The primary endpoint was time to and incidence of confirmed cSCC in the intention-to-treat population (defined as all patients randomly assigned), with the primary timepoint of interest being one year after randomisation. The study is registered with ISRCTN, ISRCTN74112318, and is now complete.

FINDINGS

Between 26 Feb 2013, and 25 April 2017, 420 patients were randomly assigned to the control (n=210) or screening MRI (n=210) groups. Median age was 74 years (IQR 68 to 79), 222 (53%) of 420 patients had normal alkaline phosphatase, and median prostate-specific antigen concentration was 48 ng/mL (IQR 17 to 162). Screening MRI detected rSCC in 61 (31%) of 200 patients with assessable scans in the intervention group. As of data cutoff (April 23, 2020), at a median follow-up of 22 months (IQR 13 to 31), time to cSCC was not significantly improved with screening (hazard ratio 0·64 [95% CI 0·37 to 1·11]; Gray's test p=0·12). 1-year cSCC

rates were 6·7% (95% CI 3·8-10·6; 14 of 210 patients) for the control group and 4·3% (2·1-7·7; nine of 210 patients) for the intervention group (difference -2·4% [95% CI -4·2 to 0·1]). Median time to cSCC was not reached in either group. No serious adverse events were reported within 24 h of screening.

INTERPRETATION

Despite the substantial incidence of rSCC detected in the intervention group, the rate of cSCC in both groups was low at a median of 22 months of follow-up. Routine use of screening MRI and pre-emptive treatment to prevent cSCC is not warranted in patients with asymptomatic castration-resistant prostate cancer with spinal metastasis.