Prostate

Intensity-modulated radiotherapy versus stereotactic body radiotherapy for prostate cancer (PACE-B): two-year toxicity results from an open-label, randomised, phase III, non-inferiority trial.

Alison C Tree , Peter Ostler, Hans van der Voet, William Chu, Andrew Loblaw, Daniel Ford, Shaun Tolan, Suneil Jain, Alexander Martin, John Staffurth, John Armstrong, Philip Camilleri, Kiran Kancherla, John Frew, Andrew Chan, Ian S Dayes, Aileen Duffton, Douglas H Brand, Daniel Henderson, Kirsty Morrison, Stephanie Brown, Julia Pugh, Stephanie Burnett, Muneeb Mahmud, Victoria Hinder, Olivia Naismith, Emma Hall, Nicholas van As, PACE Trial Investigators.

Lancet Oncol. 2022 Sep 13;S1470-2045(22)00517-4. doi: 10.1016/S1470-2045(22)00517-4. Online ahead of print.

BACKGROUND

Localised prostate cancer is commonly treated with external beam radiotherapy and moderate hypofractionation is non-inferior to longer schedules. Stereotactic body radiotherapy (SBRT) allows shorter treatment courses without impacting acute toxicity. We report two-year toxicity findings from PACE-B, a randomised trial of conventionally fractionated or moderately hypofractionated radiotherapy versus SBRT.

METHODS

PACE is an open-label, multicohort, randomised, controlled, phase III trial conducted at 35 hospitals in the UK, Ireland, and Canada. In PACE-B, men aged 18 years and older with a WHO performance status 0.0-2.0 and low-risk or intermediate-risk histologically-confirmed prostate adenocarcinoma (Gleason 4 + 3 excluded) were randomly allocated (1:1) by computerised central randomisation with permuted blocks (size four and six), stratified by centre and risk group to control radiotherapy (CRT; 78 Gy in 39 fractions over 7.0-8.0 weeks or, following protocol amendment on 24 March 2016, 62 Gy in 20 fractions over four weeks) or SBRT (36·25 Gy in five fractions over 1.0-2.0 weeks). Androgen deprivation was not permitted. Co-primary outcomes for this toxicity analysis were Radiation Therapy Oncology Group (RTOG) grade 2.0 or worse gastrointestinal and genitourinary toxicity at 24 months after radiotherapy. Analysis was by treatment received and included all patients with at least one fraction of study treatment assessed for late toxicity. Recruitment is complete. Follow-up for oncological outcomes continues. The trial is registered with ClinicalTrials.gov, NCT01584258.

FINDINGS

We enrolled and randomly assigned 874 men between 7 August 2012 and 4 January 2018 (441 to CRT and 433 to SBRT). In this analysis, 430 patients were analysed in the CRT group and 414 in the SBRT group; a total of 844 (97%) of 874 randomly assigned patients. At 24 months, RTOG grade 2.0 or worse genitourinary toxicity was seen in eight (2%) of 381 participants assigned to CRT and 13 (3%) of 384 participants assigned to SBRT (absolute difference 1·3% [95% CI -1·3 to 4·0]; p=0·39); RTOG grade 2.0 or worse gastrointestinal toxicity was seen in 11 (3%) of 382 participants in the CRT group versus six (2%) of 384 participants in the SBRT group (absolute difference -1·3% [95% CI -3·9 to 1·1]; p=0·32). No serious adverse events (defined as RTOG grade 4.0 or worse) or treatment-related deaths were reported within the analysis timeframe.

INTERPRETATION

In the PACE-B trial, two-year RTOG toxicity rates were similar for five fraction SBRT and conventional schedules of radiotherapy. Prostate SBRT was found to be safe and associated with low rates of side-effects. Biochemical outcomes are awaited.