Prostate

Intensity-modulated fractionated radiotherapy versus stereotactic body radiotherapy for prostate cancer (PACE-B): acute toxicity findings from an international, randomised, open-label, phase 3, non-inferiority trial.


BACKGROUND

Localised prostate cancer is commonly treated with external-beam radiotherapy. Moderate hypofractionation has been shown to be non-inferior to conventional fractionation. Ultra-hypofractionated stereotactic body radiotherapy would allow shorter treatment courses but could increase acute toxicity compared with conventionally fractionated or moderately hypofractionated radiotherapy. We report the acute toxicity findings from a randomised trial of standard-of-care conventionally fractionated or moderately hypofractionated radiotherapy versus five-fraction stereotactic body radiotherapy for low-risk to intermediate-risk localised prostate cancer.

METHODS

PACE is an international, phase 3, open-label, randomised, non-inferiority trial. In PACE-B, eligible men aged 18 years and older, with World Health Organization (WHO) performance status 0-2, low-risk or intermediate-risk prostate adenocarcinoma (Gleason 4 + 3 excluded), and scheduled to receive radiotherapy were recruited from 37 centres in three countries (UK, Ireland, and Canada). Participants were randomly allocated (1:1) by computerised central randomisation with permuted blocks (size four and six), stratified by centre and risk group, to conventionally fractionated or moderately hypofractionated radiotherapy (78 Gy in 39 fractions over seven to eight weeks or 62 Gy in 20 fractions over four weeks, respectively) or stereotactic body radiotherapy (36·25 Gy in five fractions over one to two weeks). Neither participants nor investigators were masked to allocation. Androgen deprivation was not permitted. The primary endpoint of PACE-B is freedom from biochemical or clinical failure. The coprimary outcomes for this acute toxicity substudy were worst grade 2 or more severe Radiation Therapy Oncology Group (RTOG) gastrointestinal or genitourinary toxic effects score up to 12 weeks after radiotherapy. Analysis was per protocol. This study is registered with ClinicalTrials.gov, NCT01584258. PACE-B recruitment is complete and follow-up is ongoing.

FINDINGS

Between 7 August 2012 and 4 January 2018, we randomly assigned 874 men to conventionally fractionated or moderately hypofractionated radiotherapy (n=441) or stereotactic body radiotherapy (n=433). Four hundred and thirty-two (98%) of 441 patients allocated to conventionally fractionated or moderately hypofractionated radiotherapy and 415 (96%) of 433 patients allocated to stereotactic body radiotherapy received at least one fraction of allocated treatment. Worst acute RTOG gastrointestinal toxic effect proportions were as follows: grade 2 or more severe toxic events in 53 (12%) of 432 patients in the conventionally fractionated or moderately hypofractionated radiotherapy group versus 43 (10%) of 415 patients in the stereotactic body radiotherapy group (difference -1.9 percentage points, 95% CI -6.2 to 2.4; p=0.38). Worst acute RTOG genitourinary toxicity proportions were as follows: grade 2 or worse toxicity in 118 (27%) of 432 patients in the conventionally fractionated or moderately...
hypofractionated radiotherapy group versus 96 (23%) of 415 patients in the stereotactic body radiotherapy group (difference -4·2 percentage points, 95% CI -10·0 to 1·7; p=0·16). No treatment-related deaths occurred.

INTERPRETATION

Previous evidence (from the HYPO-RT-PC trial) suggested higher patient-reported toxicity with ultrahypofractionation. By contrast, our results suggest that substantially shortening treatment courses with stereotactic body radiotherapy does not increase either gastrointestinal or genitourinary acute toxicity.