Prostate

Androgen deprivation therapy use and duration with definitive radiotherapy for localised prostate cancer: an individual patient data meta-analysis

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BACKGROUND

Randomised trials have investigated various androgen deprivation therapy (ADT) intensification strategies in men receiving radiotherapy for the treatment of prostate cancer. This individual patient data meta-analysis of relevant randomised trials aimed to quantify the benefit of these interventions in aggregate and in clinically relevant subgroups.

METHODS

For this meta-analysis, we performed a systematic literature search in MEDLINE, Embase, trial registries, the Web of Science, Scopus, and conference proceedings to identify trials with results published in English between 1 Jan 1962, and 30 Dec 2020. Multicentre randomised trials were eligible if they evaluated the use or prolongation of ADT (or both) in men with localised prostate cancer receiving definitive radiotherapy, reported or collected distant metastasis and survival data, and used ADT for a protocol-defined finite duration. The Meta-Analysis of Randomised trials in Cancer of the Prostate (MARCAP) Consortium was accessed to obtain individual patient data from randomised trials. The primary outcome was metastasis-free survival. Hazard ratios (HRs) were obtained through stratified Cox models for ADT use (radiotherapy alone vs radiotherapy plus ADT), neoadjuvant ADT extension (i.e., extension of total ADT duration in the neoadjuvant setting from 3.0-4.0 months to 6.0-9.0 months), and adjuvant ADT prolongation (i.e., prolongation of total ADT duration in the adjuvant setting from 4.0-6.0 months to 18-36 months). Formal interaction tests between interventions and metastasis-free survival were done for prespecified subgroups defined by age, National Comprehensive Cancer Network (NCCN) risk group, and radiotherapy dose. This meta-analysis is registered with PROSPERO, CRD42021236855.

FINDINGS

Our search returned 12 eligible trials that provided individual patient data (10 853 patients) with a median follow-up of 11·4 years (IQR 9·0-15·0). The addition of ADT to radiotherapy significantly improved metastasis-free survival (HR 0·83 [95% CI 0·77-0·89], p<0·0001), as did adjuvant ADT prolongation (0·84 [0·78-0·91], p<0·0001), but neoadjuvant ADT extension did not (0·95 [0·83-1·09], p=0·50). Treatment effects were similar irrespective of radiotherapy dose, patient age, or NCCN risk group.

INTERPRETATION

Our findings provide the strongest level of evidence so far to the magnitude of the benefit of ADT treatment intensification with radiotherapy for men with localised prostate cancer. Adding ADT and prolonging the portion of ADT that follows radiotherapy is associated with improved metastasis-free survival in men, regardless of risk group, age, and radiotherapy dose delivered; however, the magnitude of the benefit could vary and shared decision making with patients is recommended.