Prostate

Adjuvant radiotherapy versus early salvage radiotherapy plus short-term androgen deprivation therapy in men with localised prostate cancer after radical prostatectomy (GETUG-AFU 17): a randomised, phase III trial.

Sargos P, Chabaud S, Latorzeff I, Magné N, Benyoucef A, Supiot S, Pasquier D, Abdiche MS, Gilliot O, Graff-Cailleaud P, Silva M, Bergerot P, Baumann P, Belkacemi Y, Azria D, Brihoum M, Soulié M, Richaud P.

Lancet Oncol. 2020 Oct;21(10):1341-1352. doi: 10.1016/S1470-2045(20)30454-X.

BACKGROUND

Adjuvant radiotherapy reduces the risk of biochemical progression in prostate cancer patients after radical prostatectomy. We aimed to compare adjuvant versus early salvage radiotherapy after radical prostatectomy, combined with short-term hormonal therapy, in terms of oncological outcomes and tolerance.

METHODS

GETUG-AFU 17 was a randomised, open-label, multicentre, phase III trial done at 46 French hospitals. Men aged at least 18 years who had an Eastern Cooperative Oncology Group performance status of 1 or less, localised adenocarcinoma of the prostate treated with radical prostatectomy, who had pathologically-staged pT3a, pT3b, or pT4a (with bladder neck invasion), pNx (without pelvic lymph nodes dissection), or pN0 (with negative lymph nodes dissection) disease, and who had positive surgical margins were eligible for inclusion in the study. Eligible patients were randomly assigned (1:1) to either immediate adjuvant radiotherapy or delayed salvage radiotherapy at the time of biochemical relapse. Random assignment, by minimisation, was done using web-based software and stratified by Gleason score, pT stage, and centre. All patients received six months of triptorelin (intramuscular injection every three months). The primary endpoint was event-free survival. Efficacy and safety analyses were done on the intention-to-treat population. The trial is registered with ClinicalTrials.gov, NCT00667069

FINDINGS

Between 7 March 2008, and 23 June 2016, 424 patients were enrolled. We planned to enrol 718 patients, with 359 in each study group. However, on 20 May 2016, the independent data monitoring committee recommended early termination of enrolment because of unexpectedly low event rates. At database lock on 19 December 2019, the overall median follow-up time from random assignment was 75 months (IQR 50-100), 74 months (47-100) in the adjuvant radiotherapy group and 78 months (52-101) in the salvage radiotherapy group. In the salvage radiotherapy group, 115 (54%) of 212 patients initiated study treatment after biochemical relapse. 205 (97%) of 212 patients started treatment in the adjuvant group. Five-year event-free survival was 92% (95% CI 86-95) in the adjuvant radiotherapy group and 90% (85-94) in the salvage radiotherapy group (HR 0·81, 95% CI 0·48-1·36; log-rank p=0·42). Acute grade 3 or worse toxic effects occurred in six (3%) of 212 patients in the adjuvant radiotherapy group and in four (2%) of 212 patients in the salvage radiotherapy group. Late grade 2 or worse genitourinary toxicities were reported in 125 (59%) of 212 patients in the adjuvant radiotherapy group and 46 (22%) of 212 patients in the salvage radiotherapy group. Late genitourinary adverse events of grade 2 or worse were reported in 58 (27%) of 212 patients in the adjuvant radiotherapy group versus 14 (7%) of 212 patients in the salvage radiotherapy group (p<0·0001). Late erectile dysfunction was grade 2 or worse in 60 (28%) of 212 in the adjuvant radiotherapy group and 17 (8%) of 212 in the salvage radiotherapy group (p<0·0001).

INTERPRETATION

Although our analysis lacked statistical power, we found no benefit for event-free survival in patients assigned to adjuvant radiotherapy compared with patients assigned to salvage radiotherapy. Adjuvant radiotherapy increased the risk of genitourinary toxicity and erectile dysfunction. A policy of early salvage radiotherapy could spare men from overtreatment with radiotherapy and the associated adverse events.