Prostate

Prostate Radiotherapy With Adjuvant Androgen Deprivation Therapy (ADT) Improves Metastasis-Free Survival Compared to Neoadjuvant ADT: An Individual Patient Meta-Analysis

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PURPOSE

There remains a lack of clarity regarding the influence of sequencing of androgen deprivation therapy (ADT) and radiotherapy (RT) on outcomes in prostate cancer (PCa). Herein, we evaluate the optimal sequencing of ADT with prostate-directed RT in localised PCa.

METHODS

MEDLINE (1966-2018), Embase (1982-2018), ClinicalTrials.gov, and conference proceedings (1990-2018) were searched to identify randomised trials evaluating the sequencing, but not duration, of ADT with RT. Two randomised phase III trials were identified, and individual patient data were obtained: Ottawa 0101 and NRG Oncology's Radiation Therapy Oncology Group 9413. Ottawa 0101 randomly assigned patients to neoadjuvant or concurrent versus concurrent or adjuvant short-term ADT. Radiation Therapy Oncology Group 9413, a 2 × 2 factorial trial, included a random assignment of neoadjuvant or concurrent versus adjuvant short-term ADT. The neoadjuvant or concurrent ADT arms of both trials were combined into the neoadjuvant group, and the arms receiving adjuvant ADT were combined into the adjuvant group. The primary end point of this meta-analysis was progression-free survival (PFS).

RESULTS

The median follow-up was 14.9 years. Overall, 1,065 patients were included (531 neoadjuvant and 534 adjuvant). PFS was significantly improved in the adjuvant group (15-year PFS, 29% v 36%, hazard ratio [HR], 1.25 [95% CI, 1.07 to 1.47], P = .01). Biochemical failure (subdistribution HR [sHR], 1.37 [95% CI, 1.12 to 1.68], P = .002), distant metastasis (sHR, 1.40 [95% CI, 1.00 to 1.95], P = .04), and metastasis-free survival (HR, 1.17 [95% CI, 1.00 to 1.37], P = .050) were all significantly improved in the adjuvant group. There were no differences in late grade ≥ 3 gastrointestinal (2% v 3%, P = .33) or genitourinary toxicity (5% v 5%, P = .76) between groups.

CONCLUSION

The sequencing of ADT with prostate-directed RT has significant association with long-term PFS and MFS in localised PCa. Our findings favor use of an adjuvant over a neoadjuvant approach, without any increase in long-term toxicity.