Prostate

Outcomes of Observation vs. Stereotactic Ablative Radiation for Oligometastatic Prostate Cancer: The ORIOLE Phase 2 Randomised Clinical Trial.

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IMPORTANCE:

Complete metastatic ablation of oligometastatic prostate cancer may provide an alternative to early initiation of androgen deprivation therapy (ADT).

OBJECTIVE:

To determine if stereotactic ablative radiotherapy (SABR) improves oncologic outcomes in men with oligometastatic prostate cancer.

DESIGN, SETTING, AND PARTICIPANTS:

The Observation vs. Stereotactic Ablative Radiation for Oligometastatic Prostate Cancer (ORIOLE) phase 2 randomised study accrued participants from three US radiation treatment facilities affiliated with a university hospital from May 2016 to March 2018 with a data cut-off date of May 20, 2019, for analysis. Of 80 men screened, 54 men with recurrent hormone-sensitive prostate cancer and one to three metastases detectable by conventional imaging who had not received ADT within six months of enrolment or three or more years total were randomised.

INTERVENTIONS:

Patients were randomised in a 2:1 ratio to receive SABR or observation.

MAIN OUTCOMES AND MEASURES:

The primary outcome was progression at six months by prostate-specific antigen level increase, progression detected by conventional imaging, symptomatic progression, ADT initiation for any reason, or death. Predefined secondary outcomes were toxic effects of SABR, local control at six months with SABR, progression-free survival, Brief Pain Inventory (Short Form)-measured quality of life, and concordance between conventional imaging and prostate-specific membrane antigen (PSMA)-targeted positron emission tomography in the identification of metastatic disease.

RESULTS:

In the 54 men randomised, the median (range) age was 68 (61-70) years for patients allocated to SABR and 68 (64-76) years for those allocated to observation. Progression at six months occurred in 7 of 36 patients (19%) receiving SABR and 11 of 18 patients (61%) undergoing observation (P =0.005). Treatment with SABR improved median progression-free survival (not reached vs. 5.8 months; hazard ratio, 0.30; 95% CI, 0.11-0.81; P =0.002). Total consolidation of PSMA radiotracer-avid disease decreased the risk of new lesions at six months (16% vs. 63%; P =0.006). No toxic effects of grade 3 or greater were observed. T-cell receptor sequencing identified significant increased clonotypic expansion following SABR and correlation between baseline clonality and progression with SABR only (0.082085 vs. 0.026051; P =0.03).

CONCLUSIONS AND RELEVANCE:

Treatment with SABR for oligometastatic prostate cancer improved outcomes and was enhanced by total consolidation of disease identified by PSMA-targeted positron emission tomography. SABR induced a systemic immune response, and baseline immune phenotype and tumour mutation status may predict the benefit from SABR. These results underline the importance of prospective randomised investigation of the oligometastatic state with integrated imaging and biological correlates.