IN BRIEF

RADIOTHERAPY

SABR improves outcomes in men with recurrent oligometastatic prostate cancer

Stereotactic ablative radiotherapy (SABR) is superior to observation for preventing disease progression in men with recurrent hormone-sensitive oligometastatic prostate cancer, according to results from the phase II ORIOLE trial. Fifty-four patients were randomly allocated (2:1) to receive SABR or undergo observation. The primary outcome measure was progression at 6 months, defined by PSA increase, conventional imaging, symptomatic progression, initiation of androgen deprivation therapy or death. Progression occurred in 19% of patients receiving SABR compared with 61% undergoing observation ($P = 0.005$), and SABR improved median progression-free survival compared with observation (not reached vs 5.8 months; HR 0.30, 95% CI 0.11–0.81; $P = 0.002$).

ORIGINAL ARTICLE Phillips, R. et al. Outcomes of observation vs stereotactic ablative radiation for oligometastatic prostate cancer. *JAMA Oncol.* https://doi.org/10.1001/jamaoncol.2020.0147 (2020)

PROSTATE CANCER

Oral ADT demonstrates greater efficacy than existing injectable treatment

A new oral androgen deprivation therapy (ADT) could be an alternative to injectable ADT, following the results of a phase II randomized trial. Relugolix, an oral gonadotropin-releasing hormone receptor antagonist, was compared with degarelix, an injectable control, in 103 men with prostate cancer undergoing external beam radiotherapy (randomization 3:2). Castration rates between weeks 4 and 24 (primary outcome, testosterone <1.73 nmol/l; secondary outcome, testosterone <0.7 nmol/l) were 95% and 82% for patients treated with relugolix compared with 89% and 68% for those treated with degarelix. Time to castration for both treatments was rapid: 4 days for relugolix and 3 days for degarelix. At 3 months after treatment discontinuation, 52% of men on relugolix but only 16% on degarelix recovered testosterone levels to baseline (>9.8 nmol/l).

ORIGINAL ARTICLE Dearnaley, D. P. et al. The oral gonadotropin-releasing hormone receptor antagonist relugolix as neoadjuvant/adjuvant androgen deprivation therapy to external beam radiotherapy in patients with localised intermediate-risk prostate cancer: a randomised, open-label, parallel-group phase 2 trial. *Eur. Urol.* https://doi.org/10.1016/j.eururo.2020.03.001 (2020)

PROSTATE CANCER

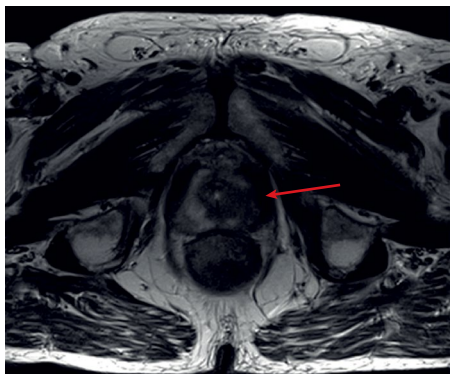
Novel PDL1 regulation mechanism provides opportunity for prostate cancer treatment

A new study in *Oncogene* describes an epigenetic mechanism of PDL1 regulation by cancer cells and a therapeutic approach to enhance efficacy of PDL1 blockade in prostate cancer. The researchers showed that the histone acetyltransferases p300 and CBP were recruited to the promoter of *CD274* (encoding PDL1) by transcription factor IRF1, which resulted in acetylation of histone H3 at the *CD274* promoter and subsequent *CD274* transcription. The p300/CBP inhibitor A485 blocked transcription of *CD274* and stopped exosomal PDL1 secretion. Upregulation of PDL1 expression is a resistance mechanism to antibody-based PDL1 blockade in prostate cancer. Cutting off PDL1 secretion at transcription by inhibiting p300/CBP combined with anti-PDL1 antibodies demonstrated increased efficacy in a syngeneic mouse model of prostate cancer (TRAMP-C2).

ORIGINAL ARTICLE Liu, J. et al. p300/CBP inhibition enhances the efficacy of programmed death-ligand 1 blockade treatment in prostate cancer. *Oncogene* https://doi.org/10.1038/s41388-020-1270-z (2020)

PROSTATE CANCER

MRI, TRUS or both?



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The majority of men with suspected prostate cancer undergo 12-core biopsy sampling guided by transrectal ultrasonography (TRUS); however, this procedure often leads to false-negative diagnoses and can result in undertreatment and/or the need for further clinical monitoring. Now, prospective data from a large cohort of men requiring diagnostic investigations for suspected prostate cancer demonstrate the potential of MRI-targeted prostate biopsy, either alone or in combination with TRUS-guided sampling, to overcome these limitations.

A total of 2,180 men with an elevated serum prostate-specific antigen level or an abnormal digital rectal examination (DRE), with MRI-visible lesions, underwent combined biopsy sampling, involving both TRUS-guided and MRI-guided approaches. Among the 2,103 patients whose data were eligible for analysis, 408 underwent radical prostatectomy.

Both methods resulted in a diagnosis of prostate cancer in approximately half of all men (52.5% with TRUS-guided sampling and 51.5% with MRI-guided sampling). However, MRI-guided procedures resulted in significantly fewer diagnoses of low-grade disease (Gleason grade group 1; $P = 0.01$) and significantly more diagnoses of high-grade disease (Gleason grade groups 3, 4 and 5; $P = 0.004$, $P < 0.001$ and $P = 0.003$, respectively) than the TRUS-guided approach.

Addition of data from MRI-guided sampling to that obtained with TRUS resulted in a diagnosis of prostate cancer in an additional 208 men (9.9%), of whom 59 were diagnosed with clinically significant disease (defined as Gleason grade group ≥3). This combination also resulted in 74 new diagnoses of clinically insignificant prostate cancer (Gleason grade group 1) and 134 men with grade group 1 disease being reclassified as having grade group ≥2 disease.

A total of 404 men subsequently underwent radical prostatectomy, of whom 58 (14.4%) had their grade group upgraded on examination of the surgical specimen, including upgrading to clinically significant disease in 3.5%. When classified using only a single diagnostic procedure, 41.6% and 16.8% of patients with prostate cancer diagnosed using only TRUS-guided biopsy required upgrading and upgrading to clinically significant disease, respectively, compared with 30.9% and 8.7% for MRI-targeted sampling ($P \leq 0.002$ for all comparisons). Fewer than 4% of patients diagnosed using any modality required downstaging following radical prostatectomy.

These findings support the use of combined biopsy sampling, which provides the lowest level of diagnostic uncertainty. When only one diagnostic procedure is possible, MRI-targeted biopsy seems to be superior to the TRUS-guided approach. Nonetheless, a subset of clinically significant cancers will continue to go undetected using MRI-targeted biopsy alone.

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ORIGINAL ARTICLE Ahdoot, M. et al. MRI-targeted, systematic, and combined biopsy for prostate cancer diagnosis. *N. Engl. J. Med.* **382**, 917–928 (2020)
RELATED ARTICLE Stabile, A. et al. Multiparametric MRI for prostate cancer diagnosis: current status and future directions. *Nat. Rev. Urol.* **17**, 41–61 (2020)