

 PROSTATE CANCER

An adaptive approach to therapy

Analysis of a mathematical model of an evolution-based strategy for two-drug therapy has shown it could improve outcomes in men with metastatic castration-resistant prostate cancer (mCRPC).

In this study, the authors developed an evolution-based approach in which therapies are divided into primary and secondary roles, termed primary–secondary therapy. In this approach, the drug that has the highest efficacy and/or the lowest toxic effects is the primary therapy. The only role of the secondary drug is to reduce the population of cells resistant to the primary drug. Specifically, the investigators considered the context of a clinical trial of treatment of mCRPC in which the administration of abiraterone was dependent on patient response and informed by an evolution-based mathematical model. The addition of docetaxel was investigated to reduce proliferation of androgen-independent, abiraterone-resistant cells. Thus, the primary–secondary strategy in this context comprised abiraterone as the primary drug and docetaxel as the secondary therapy. Using this context, the authors quantitatively investigated the hypothesized evolutionary dynamics of this strategy using mathematical modelling.

Simulations derived from a virtual patient using the mathematical model showed that time to progression was increased in circumstances in which the primary–secondary therapy approach was used compared with administration of treatment with no regard for evolutionary dynamics. The investigators then retrospectively applied the mathematical model to an ongoing adaptive therapy trial of abiraterone treatment for mCRPC using an evolution-based approach. Data from two patients included in this trial who had experienced progression were used as the model parameters. Simulations derived using these data suggested that administration of docetaxel according to the primary–secondary strategy would result in a considerably increased time to progression.

These results show that using mathematical models could improve patient outcomes in clinical trials of multidrug therapy by integration of evolutionary dynamics.

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ORIGINAL ARTICLE West, J. B. et al. Multidrug cancer therapy in metastatic castrate-resistant prostate cancer: an evolution-based strategy. *Clin. Cancer Res.* <https://doi.org/10.1158/1078-0432.CCR-19-0006> (2019)

 PROSTATE CANCER

⁶⁸Ga-PSMA-11 PET enables accurate detection of recurrent disease

Retrospective studies have shown that ⁶⁸Ga-labelled prostate-specific membrane antigen PET (⁶⁸Ga-PSMA-11 PET) imaging improves metastasis detection compared with conventional imaging (CT, MRI and bone scintigraphy) in biochemically recurrent prostate cancer. Findings from the first prospective trial in this setting have now been reported.

The single-arm multicentre trial enrolled 635 men with biochemically recurrent prostate cancer to undergo ⁶⁸Ga-PSMA-11 PET imaging. The final efficacy analysis included patients with adequate follow-up for lesion validation via histopathological analysis ($n = 93$) or a composite reference standard ($n = 223$; comprising conventional imaging and serum PSA follow-up).

The overall detection rate was 75%, and detection significantly increased with rising PSA, although PSA doubling time and nadir were not associated with detection rate. Both per-patient and per-region positive predictive values (PPVs) were 0.84 (95% CI 0.75–0.90 and 0.76–0.91, respectively)

by histopathological validation (the primary end point) and 0.92 (both 95% CI 0.88–0.95) by composite validation. The per-patient and per-region sensitivity by histopathological validation was 0.92 (95% CI 0.84–0.96) and 0.9 (95% CI 0.82–0.95), respectively. Regarding secondary end points, inter-reader agreement was substantial across regions and no grade ≥ 2 adverse events occurred.

These data illustrate the promise of ⁶⁸Ga-PSMA-11 PET for localization of recurrent disease, and data from an ongoing study (NCT03515577) comparing ⁶⁸Ga-PSMA-11 PET with the FDA-approved ¹⁸F-fluciclovine PET modality are eagerly awaited.

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ORIGINAL ARTICLE Fendler, W. P. et al. Assessment of ⁶⁸Ga-PSMA-11 PET accuracy in localizing recurrent prostate cancer: a prospective single-arm clinical trial. *JAMA Oncol.* <https://doi.org/10.1001/jamaoncol.2019.0096> (2019)
FURTHER READING Maurer, T. et al. Current use of PSMA-PET in prostate cancer management. *Nat. Rev. Urol.* **13**, 226–235 (2016)

 FROM THE MEETING

A deep dish of urology advances in Chicago for AUA2019

From 3 May until 6 May 2019, the urology community looked to Chicago where the 114th American Urological Association (AUA) Annual Meeting took place. The combination of an outstanding scientific programme, motivated delegates and a convenient conference layout resulted in a highly educational and interactive meeting with a broad scope to satisfy the wide-ranging professional interests of attendees.

Several new findings regarding prostate cancer care were among the highlights of AUA2019. The increasing range of available tracers and applications for prostate cancer PET imaging — a technique with particular utility in high-risk and advanced disease — was considered at a plenary panel discussion. In addition, the all-day International Prostate Forum session included highly informative talks on the costs and economics of various diagnosis and management strategies and the latest data on radiotherapy for prostate cancer. Another plenary session highlighted disparities in prostate cancer care

for African American men, which occur along the whole treatment continuum and result in poor outcomes. The meeting also featured the presentation of the AUA's first clinical guideline for diagnosis and treatment of testicular cancer, which focuses on early-stage disease.

The research programme of this year's AUA meeting featured interesting sessions on sex differences in urological health and disease and on the increasingly recognized roles of microbes in the urinary tract, specifically in prostate and bladder diseases, in both inflammatory processes and cancer. Another increasingly acknowledged topic was featured through several studies that examined the burden on the emotional and mental health of patients with urological disease, ranging from male factor infertility to effects of androgen deprivation therapy for prostate cancer.

Undoubtedly, meeting the therapy dogs of the Canine Therapy Corps (courtesy of the Urology Care Foundation) was another highlight for many AUA2019 delegates.

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