

The Latest Efforts in Precision Oncology for Advanced Prostate Cancer

Precision techniques are becoming more broadly applied for men with advanced prostate cancer.

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The management of advanced prostate cancer is rapidly evolving with the application of precision treatments based on genomic testing of tumors' altered DNA. With recent biomarker-driven drug approvals and increased clinical use of genomic testing, there are a number of opportunities to expand upon this framework. Researchers are calling for increased collaboration and new strategies.

“The field is moving fast, and it is quite encouraging, but we still have a lot to learn on how to optimize testing and the application of precision medicine for patients,” says [Himisha Beltran, MD](#), a prostate cancer specialist in Dana-Farber's [Lank Center for Genitourinary Oncology](#). Beltran is senior author of a report in *Nature Cancer* that represents the perspective of a large number of specialists in the field.

Current advanced prostate cancer treatment

Prostate cancer detected early can often simply be observed if it is an indolent form, and if it progresses can be cured, but cancer that has metastasized tends to become treatment-resistant and lethal.

There is an array of treatment options available for patients with metastatic prostate cancer. The principal treatment is agents that inhibit male hormones feeding the tumor, but over time the tumor becomes resistant to this hormonal blockade.

Other modalities include the addition of more potent hormonal drugs, chemotherapy, radium-223; the treatment vaccine sipuleucel-T; the immune checkpoint inhibitor pembrolizumab for a subset of advanced prostate tumors that have a specific mutational profile, hyper-mutation, or microsatellite instability; and PARP inhibitors such as olaparib or rucaparib for tumors with deficiencies in specific homologous-recombination genes. Despite these options, patient responses are extremely variable.

The role of precision techniques

Precision techniques are becoming more broadly applied for men with potentially lethal prostate cancer to test if they may be eligible for these genomic-driven therapies. These assays are also identifying mechanisms of resistance.

The researchers' goal is to speed and expand the use of genomic testing to discover prognostic biomarkers, identify new actionable drug targets, and improve the selection of therapies for individual patients, the scientists say in the article published in *Nature Cancer*.

"A number of barriers still exist, including the difficulty of obtaining suitable tumor samples for testing, questions concerning what to test for, a still-limited understanding of the role of co-occurring alterations and rare alterations that speaks to the complex nature of prostate cancer itself, and understanding the impact of genomics in diverse populations. In order to make significant progress we really do need to work together," explains Beltran.

In addition, she says, traditional genomic study designs aren't geared toward investigating the clinical significance of low-prevalence genomic alterations in prostate tumors.

"If precision medicine is to make a difference for patients with prostate cancer, it is the duty of clinicians and researchers to define the optimal timing and type of genomic testing and application of test results for the treatment of patients," the authors of the report say.

What is needed — and envisioned — the authors say, is a global, collaborative network of learning and understanding the clinical impact of rare biologically important molecular alterations and response and resistance to therapies. Building on the findings of such research will help establish a framework for future biomarkers and guidelines for molecular profiling in prostate cancer.

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