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Ethnic diversity and disparities in access to genetic testing impact prostate cancer development and treatment

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More than 1.4 million men were diagnosed with prostate cancer in 2020 globally, but the molecular characteristics of the disease remain

unexplored for the majority of patients around the world. In the final days of the Movember campaign, which every year in November aims to raise awareness of men's health issues such as prostate cancer, testicular cancer and men's mental health, in concomitance with the forthcoming ESMO Asia Congress 2022 in Singapore, December 2–4, two studies emphasize the need for ethnically diverse prostate cancer genomics data and accessible genetic testing.

Prostate cancer is well-established as a BRCA-gene associated malignancy which can develop as a consequence of a hereditary cancer syndrome, and predisposition to the disease is known to vary across different ethnicities, with men of African and Caribbean descent being at increased risk.

Only just beginning to be understood, however, is the impact of ancestry on the somatic mutations arising in the tumor, likely as a result of both genetic and non-genetic, societal-environmental factors linked to ethnicity.

"Such race-related differences can condition the behavior of the disease and its treatment, yet our current knowledge of prostate cancer genomics is largely limited to data from Europe and the U.S., in which Asian and other non-Caucasian ethnicities are scarcely represented," said Dr. Rodrigo Dienstmann, Grupo Oncoclínicas, Sao Paulo, Brazil, and Vall d'Hebron Institute of Oncology, Barcelona, Spain, an expert not involved in the research.

A study has now confirmed the existence of variations in the genomic landscape of prostate cancer in Chinese men, by performing targeted genetic sequencing on the tumors of 1,016 Chinese patients and comparing the results with publicly available genomic data from The Cancer Genome Atlas (TCGA), Memorial Sloan Kettering Cancer Center and Stand Up to Cancer (SU2C) cohorts representative of

Caucasian men.

"The most important differences we observed were concentrated in castration-sensitive disease and included lower mutation rates in prostate cancer driver genes such as TP53 and PTEN among Chinese patients compared to the Western cohorts, which may partially account for the better prognosis observed in Asian men in this setting," reported study author Dr. Yu Wei, Fudan University Shanghai Cancer Center, China.

According to Wei, this raises the question of whether the benefits demonstrated by current standard therapies in clinical trials with Western patients can be translated to the Asian population given the varying treatment responses induced by different driver mutations.

In the castration-resistant setting, genetic testing for a group of 15 genes responsible for DNA damage and repair (DDR) including BRCA1 and BRCA2 entered clinical practice in 2020 with the approval of PARP inhibitor olaparib, which achieved a 30% reduction in the risk of death for patients with metastatic disease. The Chinese study found mutation rates in genes predictive of response to these therapies to be similar across the races, regardless of disease stage.

"This suggests that Chinese patients can equally benefit from PARP inhibitors provided they can obtain access to the treatment, which is why we propose that all Asian men with metastatic prostate cancer should receive genomic testing," Wei stated.

Commenting on the results, Dienstmann observed, "The genomic heterogeneity we see in metastatic, refractory prostate cancer can be understood as the result of tumor evolution under the pressure of therapy over several years, but it is noteworthy that variation between ethnicities was also observed in the primary tumor, confirming the existence of baseline differences in cancer development across races. These findings

are consistent with other recent research on Asian and African populations and underline the importance of increasing the diversity in prostate cancer genomics databases to better understand the molecular epidemiology and thus the testing strategies that need to be implemented in countries around the world."

The ESMO Clinical Practice Guidelines for prostate cancer recommend germline genetic testing for BRCA2 and other DDR genes in all patients with metastatic prostate cancer alongside or following tumor testing, but also in individuals with a family history of cancer to allow the early identification of mutation carriers and contribute to the prevention and early diagnosis of tumors in relatives. Far from being a reality, however, access to testing could become a factor in deepening health disparities in the future.

From equal representation to equitable access to treatment

The recommended technology in prostate cancer molecular testing as per the ESMO Precision Medicine Working Group is multi-gene next-generation sequencing, which is costly and requires high-quality testing and complex interpretation. As emerged in the preliminary results of a recent ESMO survey on the Availability and Accessibility of Biomolecular Technologies in Oncology in Europe, this is currently available only in selected academic cancer centers, and scarcely at all in low and middle-income countries. Developing the necessary infrastructure, which also includes resources and workflows for sample acquisition, preparation and storage, is a sizeable undertaking likely to require multi-stakeholder involvement.

"Support programs from companies like the one exemplified in a survey of physician testing patterns in India are a good and necessary starting

point for increasing patient access to testing. Moving forward, insights from these programs should be made public to allow better understanding of local gaps in access to testing, as well as the prevalence of driver mutations in different patient cohorts. However, these programs are not sustainable in the long term, and the study authors themselves report that post-test implications, such as drug affordability and availability of genetic counselors, remain major barriers in India," said Dienstmann.

"National testing programs will need to be implemented to support access to the medicines, and companies must increasingly engage in public-private partnerships, not just to facilitate the analysis of samples abroad, but to help build the local laboratory ecosystems that can make testing affordable and available to entire patient populations."

More information: Abstract 162MO 'Genomic Characterization Revealed from Prospective Clinical Sequencing of 1016 Chinese Prostate Cancer Patients' will be presented by Yu Wei during the Genitourinary Tumours Mini Oral Session on Friday 2 December, 16:15–17:45 SGT in Hall 407

Abstract 167P 'Genetic Testing for Prostate Cancer: The Indian Scenario' will be presented by Ganesh Bakshi during the Poster Viewing Session on Saturday 3 December, 18:00–19:00 SGT in the Exhibition Area

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