

Glossary

AKT

Also known as “protein kinase B”, a serine/threonine kinase involved in cell growth, proliferation, metabolism and survival; part of the PI3K/AKT pathway, which is frequently activated in cancer.¹⁻³ See also the below definition for PI3K/AKT pathway.

Androgen deprivation therapy (ADT)

A therapy for prostate cancer that directly lowers testosterone levels and other androgens.⁴

Androgen receptor (AR) pathway

A signaling pathway central to the growth and survival of prostate cancer cells and the target of hormonal therapies.⁵

Androgen receptor pathway inhibitor (ARPI)

Therapy that inhibits the androgen receptor function and/or the hypothalamic/pituitary/end-organ axis.⁴

Biomarker

A biological molecule (eg, gene, protein) found in blood or tissues that is a sign of a normal or abnormal process, or of disease; may be used for patient risk stratification (prognostic biomarker) or to help guide treatment decisions (predictive biomarker).⁶

Biomarker-driven approaches

Strategies that use specific biological markers (or “biomarkers”) to guide patient risk stratification and treatment optimization, as part of precision oncology.⁶

Castration resistance

A state in which prostate cancer continues to grow despite suppression of androgen levels.⁷

De novo metastatic hormone-sensitive prostate cancer (de novo mHSPC)

Disease that is already metastatic at first presentation/diagnosis. De novo mHSPC is linked with more aggressive disease, including earlier development of castration resistance and poorer overall survival, compared with recurrent mHSPC.⁸ See also the below definition for ‘mHSPC’.

Doublet and triplet combination strategies

Treatment regimens combining two or three therapies to improve outcomes in metastatic prostate cancer.⁹

Fluorescence in situ hybridization (FISH)

A molecular technique that detects chromosomal abnormalities or gene amplifications/deletions in tissue or cells.^{10,11}

Gene alterations

Changes in the DNA sequence of a gene, including mutations, deletions, amplifications, and rearrangements, that may impact cancer behavior, prognosis and treatment response; detectable by genomic analyses, including NGS and FISH.^{10,12}

Germline testing

Genetic testing on normal tissue (e.g., blood or saliva) to identify inherited mutations that may increase cancer risk/impact cancer behavior.^{13,14} Different from “somatic tumor testing”—see also the below definition.

Immunohistochemistry (IHC)

A common lab technique used to visualize protein expression in tissue samples using specific antibodies; by detecting changes in protein levels, whether driven by genetic or non-genetic mechanisms, IHC can detect tumor alterations that genomic analyses alone may miss.^{11,15}

Glossary (Cont'd)

Metastatic castration-resistant prostate cancer (mCRPC)

Prostate cancer that has spread beyond the prostate and advanced despite ADT.⁴

Metastatic hormone-sensitive prostate cancer (mHSPC)

Prostate cancer that has spread beyond the prostate but remains responsive to ADT. May be seen elsewhere referred to as "metastatic castration-sensitive prostate cancer (mCSPC)".⁴

Metastatic prostate cancer

Prostate cancer that has spread beyond the prostate to other parts of the body. The most common sites of metastasis are the lymph nodes and the axial skeleton. However, in more aggressive or advanced cases, the cancer may also spread to other organs such as the liver and lungs.¹⁶

Multidisciplinary team (MDT)

Used to manage complex diseases like prostate cancer by bringing together specialists to coordinate care, assess risk, and deliver multimodal treatments. They aim to provide evidence-based, patient-centered care and support shared decision-making when multiple treatment options are available.¹⁷

Next-generation sequencing (NGS)

A high-throughput method for sequencing DNA or RNA to detect mutations, copy number changes, and other genomic alterations.¹⁸

PI3K/AKT pathway

A critical intracellular signaling pathway regulating cell growth, proliferation, metabolism and survival; overactivation is common in various cancers, contributing to disease progression and treatment resistance, and may be a therapeutic target.¹⁹

PI3K/AKT pathway activation

A key oncogenic event that promotes cellular proliferation, survival, and motility; this pathway is often overactivated in prostate cancer due to loss or downregulation of PTEN, a key negative regulator of PI3K/AKT signaling.^{8,20,21}

Precision medicine

A medical model using characterization of individuals' disease phenotypes and genotypes (e.g., molecular profiling, medical imaging, lifestyle data) for tailoring the right therapeutic strategy for the right patient at the right time.¹¹

Predictive biomarker

A biological molecule that indicates the likely benefit from a specific therapy, guiding treatment selection.^{6,15}

Prognostic biomarker

A biological molecule that indicates the likely course or outcome of a disease, independent of treatment, guiding patient risk stratification and management.^{6,15}

Phosphatase and tensin homolog (PTEN)

A key tumor suppressor protein that modulates signaling of the PI3K/AKT pathway by preventing AKT activation; encoded by the *PTEN* gene.^{8,22}

PTEN alteration

Changes in the DNA sequence of the *PTEN* gene, including mutations, deletions, amplifications, and rearrangements, that may affect PTEN protein expression and tumor suppressive function. Detectable by genomic analyses, such as NGS or FISH.^{8,20,23}

Glossary (Cont'd)

PTEN deficiency

Reduced levels of the PTEN protein. PTEN deficiency is a biomarker of PI3K/AKT pathway activation in prostate cancer and is associated with worse survival compared with PTEN proficiency.⁸

PTEN proficiency

Normal levels of the PTEN protein as detected by IHC; typically associated with intact regulation of the PI3K/AKT pathway in prostate cancer.⁸

RB1

A commonly mutated tumor suppressor gene which regulates cell cycle progression; alteration of this gene is associated with aggressive cancer phenotypes.²⁴

Recurrent mHSPC

Metastatic disease identified after first presentation/diagnosis and treatment for metastatic prostate cancer, and remains responsive to ADT despite prior treatment.²⁵

Somatic tumor testing

Biomarker testing performed on tumor tissue to identify molecular (e.g., gene, protein) changes acquired during cancer development. PTEN deficiency testing is one example of this. Sequential somatic testing may be offered when there has been a meaningful change in the patient's status or treatment plan, especially if prior tests were negative or uninformative.^{13,14}

TP53

A commonly mutated tumor suppressor gene which is involved in apoptosis; alteration of this gene is associated with poor prognosis.^{24,26}

Wnt pathway

A signaling pathway involved in cell growth and differentiation; dysregulation is implicated in cancer development.¹²

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