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Integration of IHC and NGS in identifying PTEN deficiency in mHSPC: A clinical insight case study

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Disclosures

Organizations	Type
Allessa GmbH, Amgen, AstraZeneca, Bayer, BMS, CG Oncology, Daiichi Sankyo, Dendreon, Ferring, J&J Medicine, Merck, Pfizer, Photocure, Sumitomo, Tutelix	Research/ consulting

Patient presentation and initial assessment

A 60-year-old healthy, asymptomatic male has a PSA of 21 ng/mL during routine testing by his primary care provider

- **Since no prior PSA results** were available, the PSA was repeated and confirmed
  - The DRE **demonstrated prostate** enlargement only. Once the PSA was repeated and confirmed, the patient was then referred for a urology consultation

Family history:
Uncle with prostate cancer and sister with breast cancer

Medical history:
Obesity, hypertension, and high cholesterol (hyperlipidemia)

- A prostate biopsy was performed and confirmed prostate cancer (6 out of 12 cores, Gleason Grade Group 4)
- **Baseline CBC/CMP** were within **normal limits**
- **Computed tomography and bone scan imaging** confirmed **four osteoblastic lesions** in the thoracic and lumbar spine and **one in the right acetabulum**
- **Prostate biopsy tissue sample was sent for NGS/IHC analysis**
  - Testing aimed to **identify potential genomic** or **molecular alterations** that could **inform prognosis** and **guide clinical decision-making**

CBC, complete blood count; CMP, comprehensive metabolic panel; DRE, digital rectal examination; IHC, immunohistochemistry; NGS, next-generation sequencing; PSA, prostate-specific antigen.
This presentation is informed by the speaker's clinical expertise and is intended for educational purposes only.

Genomic findings

NGS revealed no alterations in the *BRCA* genes or in any other homologous recombination repair genes; **however, the tumor was identified by NGS as being PTEN deficient**

- **PTEN deficiency** identified by NGS **was also confirmed by IHC testing**, which validated **loss of PTEN protein expression and demonstrated intratumoral heterogeneity**

This patient had **de novo mHSPC** with high-volume disease (five total bone metastases, including one in the appendicular skeleton)

Reflection for decision-making: What additional clinical or pathological information might support further risk stratification in this patient?

BRCA, breast cancer gene (*BRCA1/BRCA2*); IHC, immunohistochemistry; mHSPC, metastatic hormone-sensitive prostate cancer; NGS, next-generation sequencing; PTEN, phosphatase and tensin homolog.
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Rationale for assessing PTEN deficiency in metastatic prostate cancer

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- Traditional clinicopathologic factors such as Gleason Grade Group, number of biopsy cores, and PSA levels support risk stratification, but additional information could further enhance **diagnostic accuracy, thereby optimizing treatment decision-making**[1]
- Approximately **30% of patients** initially classified as low risk and managed by active surveillance may develop more aggressive disease within 1–2 years, highlighting the need for **additional prognostic biomarkers**[1]
- **PTEN** is a key tumor suppressor frequently lost in prostate cancer and may **improve risk stratification** by **differentiating indolent and aggressive tumors**[1]
- Given that **PTEN loss is often focal and subclonal**, *in situ* detection methods such as IHC may be more effective for identifying protein-level loss than sequencing-based approaches that assess copy number variation[2]
- The **integration of both somatic and germline testing** may be part of a comprehensive molecular characterization; however, these approaches remain **underutilized in clinical practice**
  - Due to its **simplicity, accessibility, and cost-effectiveness**, **IHC testing** offers a practical means for detecting PTEN deficiency in metastatic tumor samples[3–6]

IHC, immunohistochemistry; PSA, prostate-specific antigen; PTEN, phosphatase and tensin homolog.
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1. Kisiel F, et al. *Cancers*. 2025;17(17):2862; 2. Lotan TL, et al. *Oncotarget*. 2017;8(39):65566–65576; 3. Wise HM, et al. *Clin Sci (Lond)*. 2017;131(3):197–210; 4. Giunta EF, et al. *Cancers (Basel)*. 2021;13(19):4771; 5. Pulido R, et al. *Cold Spring Harb Perspect Med*. 2019;9(12):a036293; 6. Lotan TL, et al. *Mod Pathol*. 2016;29:904–914.

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Clinical Consideration: Approaches to biomarker testing in mHSPC

Given a patient with similar clinical features, how would you approach biomarker testing?

1. No further biomarker testing
2. Routine comprehensive testing (both germline and somatic)
3. Selective/targeted testing based on clinical indicators
4. Germline testing only
5. Somatic testing only
6. IHC testing only

IHC, immunohistochemistry; mHSPC, metastatic hormone-sensitive prostate cancer.
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Key takeaways and educational insights

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PTEN is the most commonly lost tumor suppressor in primary prostate cancer and is among the few **prognostic biomarkers** reproducibly associated with poor outcomes in affected patients[1]

Determining PTEN status in diagnostic biopsies may improve patient selection for active surveillance and identify those at increased risk for disease progression[1,2]

NGS and IHC testing offer complementary insights that can identify patients for **cascade family testing**, supporting evaluation of hereditary risk and informed clinical decisions[3]

Reflection point to consider: How could knowledge of a patient's PTEN status inform your clinical decision-making, guide conversations with the patient, and shape your overall management approach?

Explore the ***"Prognostic role of PTEN"*** and ***"PTEN testing strategies"*** pages to access key Pioneer Hub resources, offering deeper insights into PTEN deficiency and testing in metastatic prostate cancer

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1. Jamaspishvili T, et al. *Nat Rev Urol.* 2018;15:222–234; 2. Kisiel F, et al. *Cancers.* 2025;17(17):2862; 3. Caswell-Jin JL, et al. *J Natl Cancer Inst.* 2019;111:95–98.