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Metastatic hormone-sensitive prostate cancer: Strategies to evaluate risk and potential for precision treatment approaches in US veterans

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Initial diagnosis and genomic testing in a high-risk patient

Vietnam veteran, aged 67 years, was diagnosed with high grade (GG4) prostate cancer after experiencing a rapid rise in PSA (3 to 58 in <2 years).

- Imaging revealed metastatic disease to multiple sites involving the lymph nodes and bone (cT2aN1M1)

- As part of a comprehensive work-up through the Veterans Health Administration, the patient underwent genomic testing of his primary tumor
  - Genomic testing is recommended in patients diagnosed with stage M1 prostate cancer in both VA Clinical Oncology Pathways as well as national guidelines (ie, the National Comprehensive Cancer Network® (NCCN®)[1]
  - Veterans can obtain somatic tumor testing free of charge through the Veterans Affairs National Precision Oncology Program

Somatic tumor testing revealed a pathogenic *PTEN* alteration (splice site 210-1G>T).

GG4, Gleason Grade Group 4; NGS, next-generation sequencing; PSA, prostate-specific antigen; PTEN, phosphatase and tensin homolog; VA, Veterans Affairs.
This presentation is informed by the speaker's clinical expertise and is intended for educational purposes only.

Potential prognostic implications of PTEN

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The patient was started on combination therapy with Androgen Deprivation Therapy and an anti-androgen with interval decrease in all metastatic lesions except for a lesion in the right iliac bone.

Repeat imaging demonstrated progression of the right iliac bone metastasis. The patient underwent stereotactic beam radiation therapy of the bone lesion with excellent response.

The presence of PTEN is informative in this case because it suggests that precision oncology treatment options targeting the PTEN pathway may be considered by the patient and his care team in the future, should disease progression occur.

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PTEN, phosphatase and tensin homolog.
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Using *PTEN* alterations to guide risk assessment and shared decision-making

Veterans with HSPC receiving care in the VA Healthcare System **are eligible for somatic tumor sequencing at no cost to them.**[1] They may also receive other molecular testing, such as tissue immunohistochemistry, if additional information is needed or if NGS testing is not feasible.

- **A panel of tumor genes was assessed that could provide prognostic and/or predictive information.** One of the genes included on the panel, *PTEN*, was found to have a pathogenic alteration (splice site 210-1G>T)
- Studies of **veterans with metastatic prostate cancer** undergoing somatic tumor testing have revealed that some **harbor pathogenic *PTEN* alterations**[2]
- Preliminary analysis suggests that **metastatic prostate cancer cases with *PTEN* alterations have a worse prognosis** compared to metastatic cases that have no genomic alterations identified[3]

The knowledge that a patient has a tumor with a pathogenic *PTEN* alteration, which is often associated with worse outcomes, **is helpful to the care team, allowing better informed shared decision-making with the patient** when considering the risks and benefits of upfront combination therapy and/or metastasis-directed therapy.

HSPC, hormone-sensitive prostate cancer; NGS, next-generation sequencing; PTEN, phosphatase and tensin homolog; VA, Veterans Affairs.
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1. Kelley MJ, *Fed Pract.* 2020:37(Suppl. 4):S22–S27; 2. Valle LF, et al. *JAMA Netw Open.* 2025;8:e249119 and supplement; 3. Schoen SA, et al. Unpublished results.

Reflecting on the role of *PTEN* in clinical practice

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This case highlights the **utility of somatic tumor testing** and **why it is recommended across national guidelines** for metastatic prostate cancer patients.

Identification of pathogenic alterations, like *PTEN*, and/or other unfavorable genomic alterations in somatic tumors compels the medical care team to take pause and consider the following:

- The prognosis may be worse, therefore, intensification of treatment using combination therapies as well as close monitoring may be warranted after engaging in shared decision-making that accounts for patient preferences and co-morbidities
- There may be targeted therapies available to the patient, depending on the specific alteration identified and the clinical scenario

It is important that physicians are aware of the trends in the populations that they treat, including:

- What is the frequency of alterations like *PTEN* in patients with mHSPC?
- What is the prognosis of these patients compared to those with mHSPC and no alterations?
- Is there evidence, from the profiles and outcomes of the population that the physician treats, to support treatment intensification in patients with *PTEN* alterations?
- What precision oncology options may be available to these patients?

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mHSPC, metastatic hormone-sensitive prostate cancer; PTEN, phosphatase and tensin homolog.
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Key takeaways: PTEN and prognostic biomarker insights in mHSPC

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Recommendations and clinical guidance

Numerous **clinical guidelines** affirm that the **standard of care for patients diagnosed with mHSPC includes tumor testing** so that genomic alterations with prognostic and/or predictive implications may be identified[1,2]

The identification of somatic tumor alterations, such as *PTEN*, provides important prognostic implications, which may influence upfront treatment selection and follow-up given the relatively poor prognosis[3]

VA Healthcare System-specific insights

Veterans treated in the VA Healthcare System are at higher risk of prostate cancer diagnosis, across all stages including mHSPC[4]
- **Black Veterans** have the **highest incidence** of prostate cancer in the Veteran Healthcare population[5]

Veterans treated within the VA Healthcare System diagnosed with mHSPC have free access to somatic tumor testing to identify genomic alterations, like *PTEN*

Over 5,000 veterans with metastatic prostate cancer have been tested through the National Precision Oncology Program.[3,6,7] However, **many veterans who are eligible for testing, have not yet undergone testing**, and it is estimated that **genomic testing occurs in approximately 20% of eligible veterans**[8]

VA data suggest that approximately 25% of metastatic prostate cancer cases have tumors with *PTEN* alterations, and these patients appear to have worse outcomes compared with patients with tumors without *PTEN* alterations[3,6]

mHSPC, metastatic hormone-sensitive prostate cancer; NGS, next-generation sequencing; PTEN, phosphatase and tensin homolog; VA, Veterans Affairs.
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2. Yu EY, et al. *J Clin Oncol*. 2025;43:748–758; 3. Schoen SA, et al. Unpublished results; 4. Bailey A, et al. Unpublished results. 5. Yamoah K, et al. *JAMA Net Open*. 2022;5:e2144027; 6. Valle LF, et al. *JAMA Netw Open*. 2025;8:e249119 and supplement; 7. Kelley MJ, *Fed Pract*. 2020:37(Suppl. 4):S22–S27; 8. Hung A, et al. *Semin Onc*. 2023;50:11–24.

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