Real-world patient characteristics, treatment patterns, and overall survival (OS) in metastatic hormone-sensitive prostate cancer (mHSPC): insights by *PTEN* status

Dana Rathkopf[1], MD; Danni Zhao[2], PhD, MScGH; Lana Kovacevic[2], PhD; Jenna Collins[2], MPH; Eunice Hankinson[2], MSN, FNP-C; Helen Marshall[3], MSc; Aaron Springford[4], PhD; Simran Shokar[4], MPH; Hélène von Bandemer[5], MSc; and Weiyan Li[5], PhD

[1]Memorial Sloan Kettering Cancer Centre, New York, NY; [2]Flatiron Health, New York, NY, USA; [3]AstraZeneca contracted through Phastar, Cambridge, United Kingdom; [4]AstraZeneca, Mississauga, ON, Canada; [5]AstraZeneca, Gaithersburg, MD, USA

Objectives

- To characterize real-world clinical and demographic characteristics, treatment patterns, and survival outcomes of patients with mHSPC by their tumor *PTEN* status.
- To discuss the prognostic significance of *PTEN* alterations in mHSPC.

Conclusions

- This study found that, among patients with mHSPC, worse survival outcomes were observed in patients with tumors harboring *PTEN* alterations relative to patients with tumors without *PTEN* alterations.
- Future survival analyses will account for potential differences between *PTEN* groups, such as patient race and the co-occurrence of other biomarker alterations.

Plain language summary

Why did we perform this research?
This study was performed to describe patient characteristics, treatment patterns, and survival outcomes of patients with mHSPC by *PTEN* status.

How did we perform this research?
We used a US-based database derived from electronic health record data collected during routine clinical care from predominantly community oncology settings that are linked to comprehensive genomic testing, which includes patients that had *PTEN* testing.

What were the findings of this research?
Among 1,508 patients whose tumors were tested, 516 (34.2%) had *PTEN*-altered tumors. Patients with *PTEN*-altered tumors showed worse survival compared to patients with *PTEN*-non-altered tumors. This finding held across all first-line treatments received for mHSPC, as well as for patients with de novo mHSPC.

What are the implications of this research?
Approximately a third of patients with mHSPC had *PTEN*-altered tumors. Worse survival was consistently seen in patients with mHSPC whose tumors harbor a *PTEN* alteration.

Limitations

- The study data are primarily drawn from community oncology centers in the US. In addition, patients included in the FH-FMI CGDB database are required to have undergone CGP testing. These factors may limit the generalizability of these data to the broader mPC population in the US.

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References: 1. SEER. Cancer of the prostate - cancer stat facts. Accessed April 22, 2025. https://seer.cancer.gov/statfacts/html/prost.html. 2. Schoen MW, et al. *JAMA Netw Open*. 2024;7(3):e241970. 3. Roychowdhury S, Chinnaiyan AM. *J Clin Oncol*. 2013;31(15):1866-73. 4. de Bono JS, et al. *Eur Urol*. doi:10.1016/j.eururo.2024.12.015. 5. Turnham DJ, et al. *Cells*. 2020;9(11):2342. 6. Jamaspishvili T, et al. *Nat Rev Urol*. 2018;15:222-234. 7. Flatiron Health. Database Characterization Guide. Accessed April 8, 2025. https://flatiron.com/database-characterization. 8. Singal G, et al. *JAMA*. 2019;321(14):1391-99. 9. Milbury CA, et al. *PLoS One*. 2022;17(3):e0264138. 10. Frampton GM, et al. *Nat Biotechnol*. 2013;31(11):1023-103.

[†]Clinical data from the Flatiron Health Research Database are linked to genomic data, derived from FMI's CGP tests FoundationOne® and FoundationOne®CDx in the FH-FMI CGDB by deterministic matching, providing a deidentified dataset.

[‡]Reported as or consistent with a confirmed pathogenic somatic mutation in COSMIC or other literature source, or so assessed by FMI scientists.

Poster

Narrated poster video

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Corresponding author email address: simran.shokar@astrazeneca.com

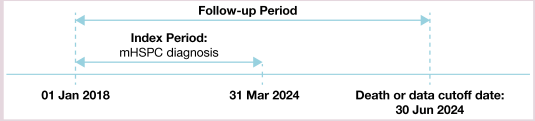
Introduction

- In general, survival for metastatic prostate cancer (mPC) remains poor (5-year survival of 37.9%), with an estimated median OS of 30 months for patients with mHSPC[1,2]
- Genomic alterations of phosphatase and tensin homologue (*PTEN*), such as mutations or deletions, occur more frequently in the mPC setting and can be one mechanism leading to reduced or absent PTEN function[3-5]
- Multiple mechanisms can affect PTEN function; thus, genomic alterations may not directly correlate with the level of PTEN protein deficiency[6]
- Loss of function of the *PTEN* gene is associated with an increased risk of recurrence and poor clinical outcomes in patients with mPC[6]
- Patient characteristics and survival outcomes for patients with mHSPC with *PTEN*-altered tumors receiving standard of care therapies have not been well investigated in a real-world setting

Methods

- This longitudinal cohort study used secondary data from the US-based FH-FMI CGDB[†] (data cutoff date: 30 Jun 2024; **Figure 1**)[7-10]
- Eligible male patients had a mPC adenocarcinoma dx date between 01 Jan 2018 and 31 Mar 2024 before evidence of castration-resistant dx date (if relevant); exclusion criteria included receipt of an investigational drug before mHSPC dx
- Patients were required to have ≥1 solid tissue specimen that underwent CGP with a panel that included a valid result for *PTEN*. This criteria was further restricted to a solid tissue specimen collection date in the mHSPC setting
- *PTEN*-altered group included patients with a tumor harboring a homozygous deletion (copy number variant = 0) or mutation (known or likely pathogenic short variant alterations or rearrangements).[‡] All other patients were included in the *PTEN*-non-altered group
- **Analysis:** Patient characteristics and treatment patterns were descriptively analysed. K-M estimates for real-world OS (unadjusted) by *PTEN* status were estimated for all patients, by treatment type in the 1L mHSPC setting, and for the de novo subgroup (i.e. patients with M1 stage at initial PC dx). K-M survival estimates were adjusted for left truncation using the risk set adjustment method. K-M curves were truncated at 60 months

Figure 1. Study design diagram



Results

- Among the 1,630 included patients with mHSPC, 1,508 patients had ≥1 mHSPC solid tissue collection date for the final analytic sample (**Table 1**)
- Of the 1,508 patients, 34.2% had tumors with *PTEN* alterations
- Mean (SD) age was 68.8 (9.1) years; at initial dx, 67.2% had a Gleason Score of 8-10 and 1,050 (69.6%) patients had de novo mHSPC
- The *PTEN*-altered group had a lower proportion of Black or African American patients (6.2% vs. 13.6%) and a lower median PSA (IQR, ng/mL) level at metastatic dx (45.7 [9.5-199.5] vs. 68.7 [14.6-331.2]) compared to the *PTEN*-non-altered group
- HRR (Non-*BRCA* and *BRCA1*/*BRCA2*) mutations were less frequent in *PTEN*-altered tumors relative to *PTEN*-non-altered tumors; *TP53* and *RB1* mutations were more frequent in *PTEN*-altered tumors relative to *PTEN*-non-altered tumors (*TP53*: 48.3% vs. 33.1%; *RB1*: 9.9% vs. 4.4%)

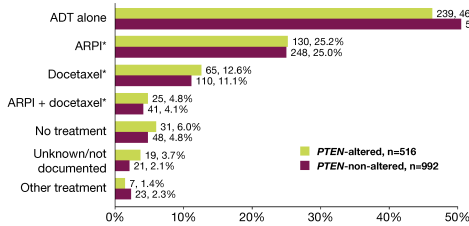
Table 1. Patient characteristics by *PTEN* status

Patient Characteristic	Overall N = 1,508	*PTEN*-altered n = 516 (34.2%)	*PTEN*-non-altered n = 992 (65.8%)
Age at mHSPC dx (y), mean (SD)	68.8 (9.1)	68.3 (9.0)	69.0 (9.2)
Race, n (%)			
White	941 (62.4)	339 (65.7)	602 (60.7)
Black or African American	167 (11.1)	32 (6.2)	135 (13.6)
Other race	154 (10.2)	51 (9.9)	103 (10.4)
Unknown/missing	246 (16.3)	94 (18.2)	152 (15.3)
Practice type, n (%)			
Community	1,078 (71.5)	393 (76.2)	685 (69.1)
Academic	332 (22.0)	98 (19.0)	234 (23.6)
Both	98 (6.5)	25 (4.8)	73 (7.4)
Metastasis stage at initial dx, n (%)			
M0	368 (24.4)	132 (25.6)	236 (23.8)
M1	1,050 (69.6)	348 (67.4)	702 (70.8)
Unknown/not documented/missing	90 (6.0)	36 (7.0)	54 (5.4)
Gleason Score at initial dx, n (%)			
≤6	27 (1.8)	12 (2.3)	15 (1.5)
7 (4+3, 3+4, 7)	177 (11.7)	69 (13.4)	108 (10.9)
8-10	1,013 (67.2)	345 (66.9)	668 (67.3)
Unknown/not documented/missing	291 (19.3)	90 (17.4)	201 (20.3)
PSA at metastatic dx, ng/mL, median (IQR)	58.5 (12.8-272.7)	45.7 (9.5-199.5)	68.7 (14.6-331.2)
Presence of other biomarker alterations, n (%)			
BRCA1/BRCA2	169 (11.2)	46 (8.9)	123 (12.4)
Non-*BRCA* HRR[a]	286 (19.0)	68 (13.2)	218 (22.0)
TP53	577 (38.3)	249 (48.3)	328 (33.1)
RB1	95 (6.3)	51 (9.9)	44 (4.4)
AKT1	42 (2.8)	7 (1.4)	35 (3.5)
PIK3CA	97 (6.4)	45 (8.7)	52 (5.2)

[a]Non-*BRCA* HRR biomarkers tested include: *ATM, ATR, BARD1, BRIP1, CDK12, CHEK1, CHEK2, FANCA, FANCL, MLH1, MRE11A, NBN, PALB2, RAD51B, RAD51C, RAD51D, RAD54L*.

Abbreviations: ADT, androgen deprivation therapy; ARPI, androgen receptor pathway inhibitor; CGP, comprehensive genomic profiling; dx, diagnosis; FH-FMI CGDB; Flatiron Health-Foundation Medicine Clinico-Genomic Database; HRR, homologous recombination repair; IQR, interquartile range; K-M, Kaplan Meier; PSA, prostate-specific antigen; rwOS, real-world overall survival; SD, standard deviation; y, years.

Figure 2. Treatment patterns in 1L mHSPC, by *PTEN* status



ARPI includes abiraterone, darolutamide, enzalutamide, apalutamide.
ADT includes goserelin, leuprolide, triptorelin, degarelix, relugolix, nilutamide, flutamide, bicalutamide.
*Patients who received these treatments are assumed to have received ADT. Although ADT treatments are not included in the standard Flatiron Health line of therapy (LOT) rules, they were incorporated into the study-specific LOT algorithm for the purpose of identifying ADT use in 1L mHSPC setting.

Figure 3. rwOS among patients with mHSPC, by *PTEN* status

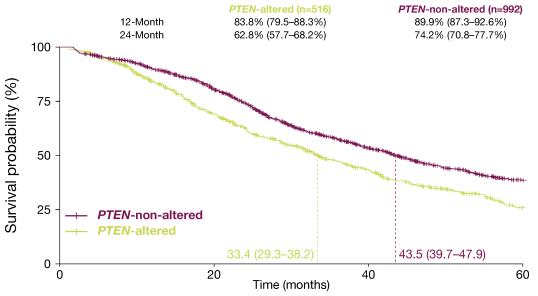
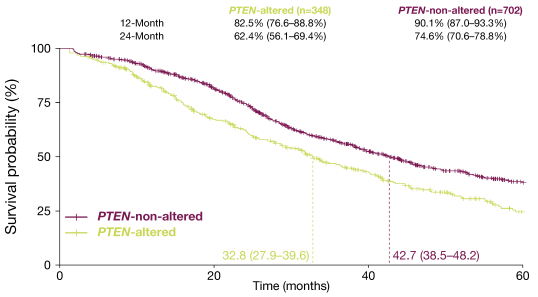


Figure 4. rwOS among patients with mHSPC, de novo subgroup by *PTEN* status



- The most common 1L treatments received by patients with both *PTEN*-altered and *PTEN*-non-altered tumors were ADT alone and ARPI (**Figure 2**)
- Overall, patients with *PTEN*-altered tumors had a lower survival probability relative to patients with *PTEN*-non-altered tumors (**Figure 3**); median (95% CI) rwOS was 33.4 (29.3, 38.2) months and 43.5 (39.7, 47.9) months, respectively; similar trends were observed for patients with de novo mHSPC (**Figure 4**)
- Patients with *PTEN*-altered tumors treated with ARPI, docetaxel, or ADT alone in the 1L mHSPC setting appeared to have worse rwOS than those without *PTEN* alterations (**Figure 5**)

Figure 5. rwOS in patients who received a) ARPI, b) docetaxel, or c) ADT alone in 1L mHSPC, by *PTEN* status

