# Real-world (TW) Genomic Landscape, PARP-inhibitor (PARPi) Treatment Patterns and Adverse Events (AE) in Advanced Prostate Cancer: The National *CanaDNA* Study

**Authors**: S. Yip[1], K. Takemura[2], R. Gagnon[3], A. Gibson[1], K. Vo[4], M. Kolinsky[5], D. Heng[6], J.D. Ruether[6], S. North[7], N. Alimohamed[6], S. Karim[6], A. Kinnaird[8], T. Tucker[9], T. Xu[1], M. Dean[1], M. Murali[1], S. Selvarajah[10], K.N. Chi[11], P. Bose1, S. El Hallani[12]

***Institutional Affiliations***: 1: Precision Oncology and Experimental Therapeutics (POET) program, Cumming School of Medicine, University of Calgary, Canada. 2: Genitourinary Oncology, The Cancer Institute Hospital of JFCR, Japan. 3: BC Cancer, Canada; Medical Oncology, University of British Columbia, Canada. 4: Faculty of Medicine & Dentistry, University of Alberta, Canada. 5: Faculty of Medicine & Dentistry, University of Alberta, Canada. 6: Medical Oncology, Arthur JE Child Comprehensive Cancer Center, Canada. 7: Medical Oncology Department, University of Alberta Cross Cancer Institute, Canada. 8: Department of Surgery, University of Alberta, Canada. 9: Pathology and Laboratory Medicine, BC Cancer Agency, Canada. 10: Clinical Laboratory Genetics Dept, University Health Network, Princess Margaret Cancer Centre, Canada. 11: Department of Medical Oncology, BC Cancer Agency, Canada. 12: Pathology and Lab Medicine, University of Alberta, Canada

## Background

- The genomic landscape of advanced prostate cancer continues to be defined.
- The landscape of biomarker-driven treatment approaches in advanced prostate cancer is rapidly evolving.
- Thus, the national genomic profiling, targeted treatment patterns and their associated adverse events were examined and analyzed in this real-world study.

## Methods

- Western Canadian (Alberta, British Columbia) patients with advanced prostate cancer (metastatic castration-sensitive [mCSPC] or castration-resistant prostate cancer [mCRPC]) who underwent comprehensive genomic profiling were included.
- For Alberta patients, cell-free concordance analysis was conducted (130-gene custom in-house NGS panel vs. FoundationOne Liquid CDx).
- Clinical characteristics, treatment patterns, and outcomes were derived from the POET Clinical Database.
- Clinical and genomic data were used to examine:
  - Impact of presence (+) or absence (0) of HRR alterations on outcomes (e.g. time to castration resistance).
  - Treatment patterns, use of PARPi therapy, and response to therapy including adverse events, progression-free survival (PFS), and overall survival (OS), in patients with HRR+ disease of patients in Alberta, Canada.

POET PRECISION ONCOLOGY EXPERIMENTAL THERAPEUTICS

UNIVERSITY OF CALGARY

## This real-world analysis offers valuable insights into the genomic landscape PARPi-treatment outcomes for advanced prostate cancer in Western Canada.

- 1 in 4 RW patients had an HRR+ detected on two testing panels (100% concordance for clinical actionability).
- In RW patients, PARPi use achieved survival outcomes comparable to those of HRR- patients, despite often poorer prognosis.
- In real-world HRR+ patients, PARPi were used infrequently and later in the treatment course, yielding poorer clinical outcomes (response to therapy; duration of disease control) compared to clinical trial findings, despite similar duration of PARPi use.

**Equitable standard-of-care genomic testing in advanced prostate cancer is necessary to enable earlier PARPi access and improve outcomes.**

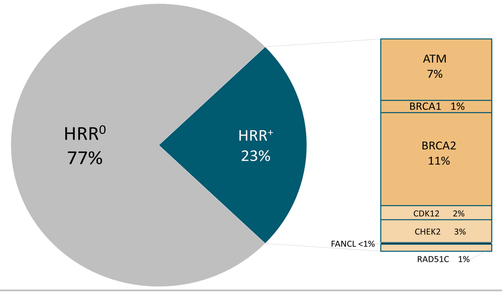
## Results

A cohort of 486 (Alberta n=236; British Columbia: n=250) were identified.

Median age was 68 years, 62% had a Gleason Score ≥ 8.
41% had high volume disease (15% visceral involvement).
58% had de novo mCSPC. 57% developed mCRPC a median 28.5 months post-androgen therapy initiation.

### Genomic Landscape and Impact on Outcomes

HRR alterations were identified in 23% of the Western Canadian cohort




High concordance was observed between an in-house NGS panel and FoundationOne Liquid CDx

- 98% Analytical Concordance
- 100% Clinical Actionability

Patients with HRR alterations progressed to mCRPC significantly faster than those without (log rank p <0.001; HR 1.52 [95% CI: 1.2 – 2.0])

**HRR⁺** 22.2 months

**HRR⁰** 31.2 months

### PARPi Therapy Outcomes

PARPi was used in 46% (51/111) of HRR+ patients in the 2nd (28% 20/51), 3rd 23% (12/51), 4th 23% (12/51) or 5th (13% 7/51) palliative intent systemic therapy line.

47% (24/51) received a taxane-based cytotoxic chemotherapy prior to PARPi.


Median survival post-mCRPC was similar between HRR⁰ patients and HRR⁺ patients receiving PARPi

**HRR⁰** 24.9 months

**HRR⁺ with PARPi** 24.0 months

Log-rank p = 0.4;
HR: 1.2; [95% CI: 0.8 – 1.7]

Among HRR+ patients without PARPi, 46% (11/24) received ≥1 line of cytotoxic chemotherapy.

| PARPi Received for HRR+ Disease (n=51) | n (%) or months [95% CI] |
|---|---|
| **ECOG at PARPi-initiation** | |
| ≤ 1 | 38 (75) |
| ≥ 2 | 13 (25) |
| **PSA decline ≥ 50%** | 13 (25) |
| **Objective Response Rate** | 3 (6) |
| **Disease Control Rate** | 24 (47) |
| **Progression-Free Survival** | |
| Biochemical | 4.0 [2.7 - 6.3] |
| Radiographic | 5.4 [3.3 – 7.7] |
| **Duration of Tx** | 4.8 |
| **PARPi ≥ 30 days post radiological progression** | 29 (58) |
| **PARPi-related AE** | 24 (50) |
| Tx modification required | 17/24 (71) |
| Tx termination required | 7/24 (29) |
| **Management(s) post-PARPi** | 23 (45) |
| Taxane-based CTx | 20/23 (87) |
| Platinum-based CTx | 3/23 (13) |

Median survival post-PARPi initiation:
7.0 months [3.7 – 9.1]

## Future Directions

The CanaDNA Study is ongoing and aims to enroll 1000 patients to build a pan-Canadian database characterizing the genomic landscape of advanced prostate cancer.

In addition to genomic profiles, the CanaDNA study's collection of clinical management and outcomes will help establish a knowledge base on advanced prostate cancer care prior to the widespread adoption of standard-of-care genomic testing in Canada.

*This research received Externally Sponsored Research funding from AstraZeneca*

**Corresponding Author**: Dr. Steven Yip

Steven.Yip@albertahealthservices.ca

Dr. Yip declares associations with AstraZeneca, Janssen, Merck, Oncohelix, Pfizer, Synnovation

**POET Program:** poetoncology.ca

POET ONCOLOGY
poetoncology.com

*Final Publication Number: 2451P*