Prostate screening for people with inherited risk of developing aggressive prostate cancer: The PATROL study

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BACKGROUND:
Inherited (germline) pathogenic and likely pathogenic variants (gPV) in key genes associated with increased risk of prostate cancer (PrCa) now warrant more attentive prostate cancer screening in NCCN guidelines—e.g., *BRCA2 and HOXB13* among others, in some cases in association with more aggressive disease and worse outcomes. However, there remains uncertainty about degree of risk by gene and interest in optimizing screening. Data from the international IMPACT study of a targeted PrCa screening program used a PSA threshold to biopsy of >3.0ng/mL and supports initiating screening at the age of 40y. However, questions remain, such as optimal PSA threshold for biopsy, incorporation of MRI data, and the role of new and emerging biomarkers. In the PATROL study, we offer a prospective early detection study for people at risk for PrCa due to known or suspected cancer risk genes (rare variants of high or moderate penetrance), which also serves as infrastructure for engaging people at-risk for PrCa and as a framework to refine screening strategies and investigate novel biomarkers of early detection.

METHODS:
PATROL is a multicenter, prospective study for people who are at known or suspected increased risk for PrCa due to carrying a gPV in *BRCA2, HOXB13*, and additional genes to participate in a PrCa early detection study. The primary endpoint is to determine the positive predictive value of predefined age-directed PSA thresholds and prostate-specific imaging for biopsy. Other exploratory endpoints include characterizing clinico-pathologic characteristics of diagnosed PrCa, and understanding the impact of screening on patient-reported outcomes (e.g., anxiety and decisional regret). Biospecimens to be collected include germline DNA, urine, and tumor tissue to evaluate emerging clinical and research biomarkers. Key eligibility includes: people >/=40y who carry a gPV in a eligible gene, who have no prior diagnosis of PrCa, who do not have another active malignancy, and who provide informed consent. Study procedures include annual physical exam, PSA, and imaging per treating physician. In addition, study will collect annual clinical data, blood and urine, archival biopsy tissue, biomarkers (e.g., SelectMDx). Participants will undergo prostate biopsy per protocol recommendations: for any clinical concern, PSA >1.0 ng/mL if <50y; PSA >1.5 ng/mL if 50-59y; PSA >2.0 ng/mL if =/>60y). If PrCa is diagnosed, clinical care will be determined by the participant and their treating physician. If opting for active surveillance, study procedures will continue to be collected annually for 10 yrs or until definitive treatment. If/when opting for definitive treatment, study procedures will continue to be collected for one additional year. Long-term clinical PrCa outcomes will be collected annually until the study closes. (clinicaltrials.gov: NCT04472338)

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Conflicts of Interest Disclosure Statement: Authors have no conflicts of interest to declare.

Commented [HC1]: Culled this since NCCN is in the process of trying to harmonize across risk guidelines.

PATROL PATIENTS ENROLLMENT		
	n	**%**
Enrollment by Site (n, %)	**n = 129**	
University of Pennsylvania	78	60%
University of Washington	48	37%
Oregon Health and Sciences University	3	2%
Current Age (n, %)	**n = 129**	
< 50 years	50	39%
50 - 59 years	33	26%
≥ 60 years	46	36%
Self-Identified Race (n, %)	**n = 129**	
White	118	91%
Black or African American	2	2%
Asian	6	5%
Unknown	2	2%
More than one gene	1	1%
Ethnicity (n, %)	**n = 129**	
Non-Hispanic/Latino	121	94%
Hispanic/Latino	4	3%
Unknown	4	3%
Genetic Test Results (n, %)	**n = 75**	
BRCA2	64	50%
BRCA1	26	20%
ATM	4	3%
CHEK2	2	2%
HOXB13	3	2%
MLH1	2	2%
MSH2	1	1%
MSH6	5	4%
PALB2	4	3%
PMS2	2	2%
RAD51D	1	1%
TP53	5	4%
Other	1	1%
More than one gene	9	7%
Patient Status (n, %)	**n = 129**	
Screening for PCa	122	95%
Active Surveillance	3	2%
Definitive Treatment	4	3%