

Poster Session 1: Oncology – Prostate (Part 1)

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MP 1.1

Urologist-level variation in androgen deprivation therapy intensification in patients with metastatic hormone-sensitive prostate cancer: A retrospective, population-based cohort study in Ontario, Canada

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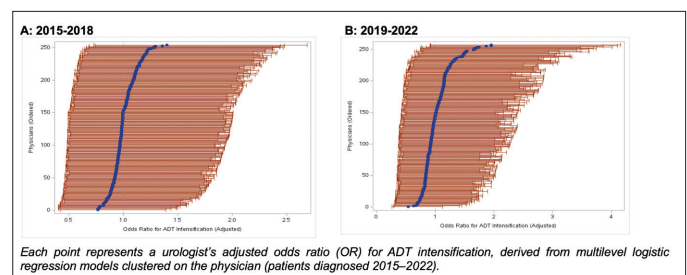
Introduction: Guidelines recommend androgen-deprivation therapy (ADT) intensification for individuals with de novo metastatic hormone-sensitive prostate cancer (mHSPC). Urologists frequently initiate ADT and influence early treatment decisions, yet the extent to which variation in intensification reflects physician practice vs. patient factors remains unclear.

Methods: We identified all patients diagnosed with de novo mHSPC and initiated on ADT by urologists in Ontario, Canada (2015–2022). For each urologist, we calculated the annual number and proportion of patients receiving treatment intensification. Intensification was attributed to the urologist if they either prescribed it directly or referred the patient to another specialist who subsequently intensified therapy, to capture appropriate referral practices. Multilevel logistic regression models clustered at the physician level were fit, and the variance partition coefficient (VPC) was used to estimate the proportion of variation in treatment intensification attributable to physician-level effects, adjusting for patient- and physician-level covariates. Caterpillar plots were constructed to visualize physician-specific random intercepts for ADT intensification.

Results: We included 332 urologists treating 3871 patients. Overall, physicians intensified therapy for an average of 23% of their patients (median 21%, IQR 0–33%). Mean annual proportion of intensification per urologist increased from 15% in 2016 to 59% in 2022. Physician-level clustering explained only 4.6% of variation in treatment intensification, with most variation attributable to patient characteristics. In a contemporary sub-cohort (2020–2022), physician clustering explained a larger share (VPC 7.8–8.5%). There was wide heterogeneity in physician-specific intercepts (Figure 1).

Conclusions: From 2015–2022, ADT intensification among patients initiated on therapy by urologists rose substantially. Most variation was explained by patient factors, although physician influence became more apparent in later years as early adopters drove uptake. These findings imply that accelerating equitable adoption of intensification may require system-level supports and targeted efforts to bring later adopters in line with evolving standards.

Acknowledgements: This abstract was presented at GU-ASCO 2026.



MP 1.1. Figure 1. Caterpillar plot of physician-specific random effects for ADT intensification. Each point represents a urologist's adjusted OR for ADT intensification, derived from multilevel logistic regression models clustered on the physician (patients diagnosed 2015–2022).

MP 1.2

Evolution of Canadian consensus forums on the management of prostate cancer

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Introduction: The Canadian consensus forum (CCF) series for prostate cancer convenes urologists, medical oncologists, and radiation oncologists to address areas of clinical uncertainty where evidence is insufficient to guide treatment decisions. This analysis compared trends across three CCFs (2020, 2022, 2025) to evaluate consensus and identify unresolved gaps across clinical themes.

Methods: Each forum used structured voting on predefined clinical questions, defining consensus as $\geq 75\%$ agreement, near-consensus as 50–74%, and non-consensus as $< 50\%$. Clinically relevant themes were classified as resolved, near-resolved, or unresolved, based on consensus results, enabling assessment of evolving perspectives and practice-changing trends.

Results: Three domains were evaluated: localized therapy, metastatic castration-sensitive prostate cancer (mCSPC), and the impact of genetic testing and novel imaging. Localized therapy shifted toward systemic intensification and short-course androgen deprivation therapy (ADT) with salvage radiotherapy, although nuances remain in patient selection and timing. mCSPC consensus evolution indicated that triplet therapy should be considered in select patients, considering alignment with disease characteristics and patient factors. Genetic testing became routine, and

prostate-specific membrane antigen-positron emission tomography (PSMA-PET) increasingly influences management where available. Consensus was established for PARP inhibitors in BRCA2/HRR-mutated metastatic castration-resistant prostate cancer (mCRPC) and for Lutetium-177 PSMA therapy post-chemotherapy, while optimal sequencing and treatment duration remain unresolved.

Conclusions: These CCFs provide a valuable platform for multidisciplinary alignment in prostate cancer care. By highlighting areas of progress and identifying where evidence is lacking, these forums help inform clinical practice, guide future research, and address remaining controversies, supporting ongoing improvements in disease management and patient outcomes.

MP I.3

Interim oncologic control and quality-of-life outcomes following focal irreversible electroporation for intermediate-risk prostate cancer in the WIRED clinical trial

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Introduction: Whole-gland treatment for intermediate-risk prostate cancer is effective but frequently associated with urinary and sexual morbidity. Focal therapy aims to preserve oncologic control while minimizing treatment-related toxicity by targeting the index lesion. Irreversible electroporation (IRE) is a non-thermal ablative modality that selectively disrupts cellular membranes while sparing adjacent critical structures. We report an interim analysis of prostate-specific antigen (PSA) kinetics and early biopsy outcomes from a prospective, pan-Canadian study evaluating focal IRE for intermediate-risk prostate cancer.

Methods: This is a prospective, non-randomized, multicenter study enrolling men with localized intermediate-risk prostate cancer treated with focal IRE using the NanoKnife system. All patients underwent standardized pre-treatment evaluation, including multiparametric magnetic resonance imaging and targeted plus systematic prostate biopsy to confirm an MRI-visible index lesion and exclude clinically significant disease outside the planned ablation zone. PSA and quality-of-life questionnaires were collected at baseline, three, six, nine, and 12 months post-treatment. Post-treatment biopsies were performed according to protocol or clinical indication. The primary effectiveness endpoint of the parent study is negative in-field biopsy at 12 months, defined as absence of clinically significant cancer (pattern 4 or higher). PSA kinetics were assessed descriptively as a secondary endpoint.

Results: This interim analysis reports on 22 patients who had complete PSA data at baseline, three months, and six months. Median baseline PSA was 7.6 ng/mL (range 1.2–15.4). Median PSA declined to 1.3 ng/mL at three months and remained stable at 1.3 ng/mL at six months, representing a median reduction of approximately 78% from baseline. Erectile function, assessed using the International Index of Erectile Function, demonstrated an expected early decline with median scores decreasing from 22 at baseline to 7.5 at one month, followed by recovery to 13.5 at three months and 14.5 at six months, with no evidence of progressive deterioration at the cohort level. Post-treatment biopsy data were available for the first eight patients. No clinically significant cancer was identified within the ablation zone in any patient. One patient developed clinically significant out-of-field disease, while all ablation-zone cores were negative.

Conclusions: Focal IRE was associated with a rapid and durable reduction in PSA and excellent early in-field oncologic control. These interim findings support the biologic effectiveness of focal irreversible electroporation for intermediate-risk prostate cancer and justify continued enrolment and longer-term followup to assess durability and functional outcomes.

MP I.4

Post-hoc Bayesian re-analysis of 21-year followup data from the Rotterdam section of the European Randomized Study of Screening for Prostate Cancer

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Introduction: The European Randomized Study of Screening for Prostate Cancer (ERSPC) demonstrated that prostate cancer (PCa) screening with a prostate-specific antigen (PSA) test reduces PCa-specific mortality (PCSM). Bayesian methods offer a complementary framework to frequentist analyses by directly estimating the probability of a clinically meaningful benefit and allowing explicit incorporation of prior beliefs. We conducted a post-hoc Bayesian reanalysis of the Rotterdam section of the ERSPC to quantify the benefit of PSA-based screening on PCSM and assess the robustness of findings under varying prior assumptions.

Methods: We analyzed patient-level data from the Rotterdam section of the ERSPC using Bayesian Poisson regression to estimate the effect of PSA screening on PCSM. Posterior rate ratios (RRs) and probabilities of clinically meaningful benefit (RR < 1.0, 0.9, 0.8, 0.75, 0.70) were calculated for the core age group (55–69), which represented the primary analysis of ERSPC, and for the full cohort (ages 55–74). Sensitivity analyses assessed robustness to flat (non-informative), neutral, skeptical, optimistic, pessimistic, and data-driven priors. Interaction analyses explored effect modification by age group.

Results: We included 42 374 participants with a median followup of 21 years. In the core age group (55–69 years, n=34,831), the posterior RR was 0.76 (95% credible interval [CrI] 0.63–0.90), with a 93% probability that RR < 0.9 and a 73% probability of a RR < 0.8. In the full cohort, the posterior RR for PCSM was 0.85 (95% CrI 0.73–0.99), with a 74% probability that RR < 0.9 and a 20% probability that RR < 0.8. Findings were robust across all priors, with probabilities that RR < 1 consistently ≥ 93%, although the data-driven prior was more conservative and showed higher probabilities for greater thresholds of PCSM benefit (2% probability that RR < 0.8 in the core age group). There was a negligible probability of any screening benefit among men older than 70 years of age at randomization.

Conclusions: In the Rotterdam section of the ERSPC, PSA screening was associated with a reduced risk of PCSM, with stronger evidence of benefit in the core screening age group. Our Bayesian analysis quantified clinically meaningful benefit probabilities and contextualized the findings following varying prior beliefs. The data-driven prior tempered support for larger effect sizes, providing a way to capture how a previous synthesis of evidence shaped beliefs at the time and, in turn, influenced interpretation. These results illustrate how Bayesian methods can complement conventional analyses by providing probabilistic estimates relevant for population health and policy decision-making for PCa screening.

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MP I.5

The effect of the Canadian Task Force on Preventive Health Care recommendation against prostate cancer screening: An interrupted, time-series analysis of change in opportunistic prostate-specific antigen testing in Ontario, Canada

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Introduction: In November 2014, the Canadian Task Force on Preventive Health Care (CTFPHC) issued recommendations against prostate cancer (PCa) screening using the prostate-specific antigen (PSA) test. The guideline strongly recommended against screening men younger than 55 years or 70 years and older, and

weakly against screening men aged 55–69 years. The influence of these recommendations, and similar national guidelines, on patterns and existing disparities in opportunistic PSA testing remains uncertain.

Methods: We conducted a population-based, interrupted time-series analysis using administrative health data for adult men between 40–85 in Ontario, Canada, from 2011–2019. Data were analyzed at the person-quarter level using generalized estimating equations with a Poisson distribution to estimate quarterly changes in PSA testing after vs. before the November 2014 recommendation. The primary analysis included PSA tests most likely performed for screening, excluding those associated with lower urinary tract symptoms or specialist visits. Effect modification was assessed by age group (per CTFPHC categories), primary care rostering status, rurality, and area-level income. A negative control analysis included men younger than 35 years, and sensitivity analyses included all PSA tests regardless of indication.

Results: We assessed the screening status of a median of 3 282 595 men per quarter. Following the 2014 CTFPHC recommendation, PSA testing showed an immediate decline (IRR 0.971, 95% CI 0.966–0.976). The post-guideline slope was 1% higher per quarter (IRR 1.010 per quarter; 95% CI 1.010–1.011) relative to the pre-guideline trend (IRR 0.989, 95% CI 0.987–0.988). Immediate relative declines were largest in rural, high-income, and less marginalized areas, and in older men (Table 1). PSA testing remained low and stable in the negative control group (<35 years), and sensitivity analyses, including all PSA tests, produced similar estimates.

Conclusions: The 2014 CTFPHC recommendation against PCa screening was associated with a decline in PSA testing. Disparities narrowed when stratified by income but widened when stratified by rurality, reflecting heterogeneous changes across area-level socioeconomic and geographic dimensions. The employed mar-

ginalization index encompasses multiple domains of deprivation and further analyses are needed to disentangle which domains most strongly influenced these patterns. These findings suggest that national recommendations lead to detectable changes in groups with higher baseline utilization and over-testing with smaller effects in populations with baseline reduced access to preventive care.

Funding: Movember Prostate Cancer Health Equity Initiative Grant, Bayer – CUASF – CUOG Prostate Research Award in Prostate Cancer

MP 1.6
5-α reductase inhibitors, treatment modality, and prostate cancer mortality: A population-based cohort study

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Introduction: 5-alpha reductase inhibitors (5-ARIs) reduce prostate cancer (PCa) incidence by approximately 25%, yet concerns regarding an increased risk of high-grade disease persist. Prior work from our group demonstrated no adverse impact of prediagnostic 5-ARI exposure on survival among men with PCa. Whether primary treatment modality modifies this association remains unknown.

Methods: We performed a population-based, retrospective cohort study using linked Ontario administrative databases (2003–2017). Men aged ≥65 years with

MP. 1.5. Table 1. Interrupted time-series effect estimates for the cohort of men between 40 and 85

Variable	Level	Post-guideline immediate level change* (IRR, 95% CI)	Post-guideline % immediate change in level*	Post-guideline quarterly slope change** (IRR, 95% CI)	Post-guideline % slope change over the entire post-period**
Cohort Wide		0.971 (0.966–0.976)	-2.9%	1.010 (1.01–1.011)	+1.0%
Age category	40-54	1.047 (1.039–1.055)	+4.7%	1.018 (1.017–1.018)	+1.8%
	55-69	0.939 (0.932–0.945)	-6.1%	1.010 (1.009–1.018)	+1.0%
	70-85	0.910 (0.901–0.919)	-9.0%	1.005 (1.004–1.006)	+0.5%
Primary care rostering	Rostered	0.970 (0.965–0.975)	-3.0%	1.011 (1.010–1.011)	+1.1%
	Not rostered	0.983 (0.960–1.007)	-1.7%	1.015 (1.013–1.017)	+1.5%
Rurality	Urban	0.976 (0.971–0.982)	-3.4%	1.011 (1.010–1.011)	+1.1%
	Rural	0.912 (0.898–0.925)	-8.8%	1.000 (0.999–1.001)	+0.0%
Median income (quintile)	1 (Lowest income)	0.974 (0.963–0.985)	-3.6%	1.012 (1.011–1.013)	+1.2%
	2	0.974 (0.963–0.985)	-3.6%	1.011 (1.010–1.011)	+1.1%
	3	0.973 (0.963–0.983)	-3.7%	1.010 (1.008–1.010)	+1.0%
	4	0.969 (0.959–0.978)	-3.1%	1.009 (1.008–1.010)	+0.9%
	5 (Highest income)	0.977 (0.968–0.986)	-2.3%	1.009 (1.009–1.010)	+0.9%
Ontario marginalization index (quintile)	5 (Most marginalized)	0.997 (0.986–1.01)	-0.3%	1.014 (1.013–1.015)	+1.4%
	4	0.989 (0.979–0.999)	-1.1%	1.012 (1.011–1.013)	+1.2%
	3	0.978 (0.968–0.988)	-2.2%	1.011 (1.010–1.011)	+1.1%
	2	0.965 (0.955–0.974)	-3.5%	1.008 (1.007–1.009)	+0.8%
	1 (Least marginalized)	0.949 (0.941–0.958)	-5.1%	1.008 (1.007–1.008)	+0.8%

*Relate to pre-intervention level (before November 2014). **Relative to pre-intervention slope (before November 2014). For example, a +1.0% change in slope represents a 1.0% quarterly increase of the slope compared to the pre-intervention slope. There are 20 quarters in our data following the intervention.

PCa were stratified by primary treatment: androgen deprivation therapy (ADT), radical prostatectomy (RP), radiation therapy (RT), and active surveillance (AS). Primary outcomes were all-cause mortality and PCa-specific mortality (PCSM). Interaction between primary treatment and 5-ARI exposure was evaluated; cause-specific hazard models incorporating stabilized inverse probability of treatment weighting (IPTW) and multivariable adjustment were applied within each subgroup.

Results: Among 19 938 patients, prior 5-ARI exposure was identified in 478 treated with ADT, 286 with RP, 695 with RT, and 653 managed with AS. Over a median followup of 8.96 years (IQR 6.28–12.17), 6053 patients (30.4%) died, including 1047 (5.3%) deaths attributable to PCa. A significant interaction between primary treatment modality and 5-ARI use for PCSM ($p=0.039$), but not all-cause mortality ($p=0.244$), was identified. Within treatment groups, 5-ARI use was not associated with either outcome among patients in ADT and AS subgroups. Among RP patients, 5-ARI users had lower all-cause mortality (HR 0.61, 95% CI 0.40–0.92, $p=0.020$), although PCSM could not be reliably estimated due to few cancer-specific events. In contrast, among RT patients, 5-ARI use was associated with higher all-cause mortality (HR 1.31, 95% CI 1.14–1.50, $p<0.001$) without a corresponding difference in PCSM (HR 0.93, 95% CI 0.62–1.40).

Conclusions: Prediagnostic 5-ARI exposure was not consistently associated with PCa-specific outcomes across treatment modalities. These findings provide novel treatment-stratified evidence regarding the oncologic safety of 5-ARIs and highlight differential survival patterns warranting prospective validation.

MP 1.7

From screening withdrawal to imaging-guided precision: A decade of evolution in prostate cancer diagnostics at Brightshores Health System

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Introduction: National recommendations discouraging PSA screening in the early 2010s led to widespread reductions in testing and biopsy rates across Canada. A 2017 study completed at Brightshores Health System (formerly Grey Bruce Health Services) documented a 43% decline in biopsy volume and a concurrent rise in malignancy yield from 53% to 70%, reflecting more selective referral and later disease presentation. Since 2017, the implementation of pre-biopsy multiparametric MRI (mpMRI) has reshaped diagnostic workflows by improving lesion localization and risk stratification. We evaluated how mpMRI integration influenced prostate cancer detection patterns at our institution, comparing outcomes in the MRI transition era (2017–2024) with the PSA-driven era (2009–2015). We examined changes in biopsy yield, PSA thresholds, histopathologic grade distribution, and MRI-biopsy spatial concordance to assess whether imaging restored diagnostic balance lost after the decline in screening.

Methods: All prostate biopsies from 2017–2024 were retrospectively reviewed. PSA at biopsy, MRI status, PI-RADS score, and Gleason grade group were recorded. MRI-biopsy concordance was defined as correct localization of at least one biopsy-positive region (right base, right mid, right apex, left base, left mid, left apex). Data were compared to institutional historical results (2009–2015) from Webster et al.

Results: MRI use increased from 1.3% of biopsies in 2021 to 55.3% by 2024. Overall malignancy yield rose from 78% to 86.5%, while benign biopsy rates declined to 1.3%. Median PSA decreased among MRI-guided biopsies (9.4 → 7.3 ng/mL) but increased among non-MRI cases (9.1 → 11.2 ng/mL). Concordance between MRI lesions and biopsy-positive sites remained high for PI-RADS 5 (82%) and PI-RADS 4 (72%), although approximately 25% of cancers lacked any MRI-predicted lesion. Compared to the 2009–2015 cohort, the MRI era maintained a high yield but at lower PSA thresholds with fewer low-grade (grade group 1) cancers.

Conclusions: Pre-biopsy MRI may have helped restore diagnostic precision lost during the PSA screening withdrawal period, enabling earlier detection while maintaining selectivity for clinically significant disease; however, incom-

plete lesion sensitivity and variable radiologic reporting highlight that systematic biopsy remains indispensable. The decade-long GBHS experience demonstrates an institutional evolution from broad PSA-driven screening to imaging-guided precision, emphasizing the need for standardized, region-based MRI templates to align radiologic, pathologic, and surgical communication.

MP 1.8

4th Canadian consensus forum on the management of prostate cancer

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Introduction: Introduction of novel therapeutic and diagnostic tools to improve prostate cancer (PCa) management and patient outcomes requires robust high-level evidence to guide clinical decisions. In October 2025, the Genitourinary Research Consortium (GURC) held its fourth Canadian consensus forum (CCF4) to provide guidance on key controversial areas of PCa management lacking level I evidence.

Methods: A committee of eight multidisciplinary physicians identified discussion topics by adapting relevant questions from the 2024 Advanced Prostate Cancer Consensus Conference. Questions focused on management of high-risk localized and locally advanced PCa, metastatic castration-sensitive PCa (mCSPC), and metastatic castration-resistant PCa; prostate-specific antigen (PSA) persistence and biochemical resistance; 177Lu-PSMA therapy; androgen receptor pathway inhibitor (ARPI) selection in special clinical contexts; systemic therapy side effects; bone protection; and genetics and genomics. During the live forum, 53 questions were voted on, with a predefined threshold of 75% set for consensus agreement.

Results: The final voting panel consisted of 24 physicians (11 urologists, 10 medical oncologists, three radiation oncologists). Consensus was reached for 25/53 questions (Table 1). Consensus was seen in duration of radiation and long-term androgen deprivation therapy + ARPI for two years in high-risk localized PCa and monitoring and early salvage therapy in patients with undetectable PSA post-surgery. Consensus was reached on the use of 177Lu-PSMA post-ARPI and taxane-based chemotherapy, use of denosumab as antiresorptive therapy, and routine germline and somatic testing for mCSPC.

Conclusions: CCF4 identified consensus agreement among a panel of multidisciplinary physicians, providing guidance on >20 practice scenarios for PCa management. These findings offer valuable guidance on areas of controversy in the absence of high-level evidence, underscoring the value of structured consensus initiatives in informing real-world practice.

MP 1.8. Table 1. CCF4 areas of consensus

Practice scenario questions	Consensus agreement	
In the majority of patients with high-risk localized prostate cancer (STAMPEDE definition) and NO MO on conventional imaging, with no extraprostatic extension seen, what is your recommended treatment?	92%	Radiation plus long-term ADT plus ARPI for 2 years
In the majority of patients with high-risk localized prostate cancer (STAMPEDE definition) and NO MO on conventional imaging, with definite extraprostatic extension seen on MRI, what is your recommended treatment?	96%	Radiation plus long-term ADT plus ARPI for 2 years
What is your preferred treatment recommendation for the majority of prostate cancer patients with cNO on conventional imaging but positive pelvic lymph nodes on PSMA-PET but no distant lesions (MO), and also meeting the STAMPEDE (high-risk, locally advanced MO) definition?	100%	Radiation therapy prostate plus pelvis plus long-term ADT plus ARPI for 2 years
For the majority of patients with pT3b pN0 following radical prostatectomy with extended PLND and ISUP grade group 4–5 and R1 and with undetectable postoperative PSA, what is your recommendation, provided the patient has regained continence?	88%	Monitoring and early salvage therapy (RT or systemic therapy or both) in case of a confirmed PSA rise
For the majority of patients with pT2/3 and 1–2 pathologically involved pelvic lymph nodes (pN1) following radical prostatectomy with extended PLND and ISUP grade group 4–5 and with undetectable postoperative PSA, what is your recommendation, provided the patient has regained continence?	93%	Monitoring and early salvage therapy (RT with ADT) in case of a confirmed PSA rise
In patients with (fully resected) positive nodes on pathology following radical prostatectomy who have an undetectable early PSA at 6 weeks, what is your systemic therapy approach in the majority of patients?	100%	Observe PSA serially with delayed treatment for PSA rise
For the majority of patients with slowly rising PSA (total PSA value 0.2 ng/ml) after radical prostatectomy and PSA-DT >1 year AND pathological ISUP grade group <4, do you recommend PSMA-PET imaging?	82%	Yes
In the majority of patients with a confirmed PSA rise after radical prostatectomy without prior salvage RT and PSA-DT ≤1 year or pathologic ISUP grade group 4 or 5 and 1–3 positive lymph nodes in the pelvis alone on PSMA-PET, what is your treatment recommendation regarding the radiation therapy?	80%	Radiation therapy prostate bed plus whole pelvis ± boost to positive nodes
For the majority of chemotherapy-fit, asymptomatic patients with PSMA imaging-positive mCRPC who meet PET criteria for 177Lu-PSMA therapy and have received one line of ARPI and no chemotherapy, what is your preferred treatment option, assuming treatments are readily available and there is no actionable molecular alteration?	86%	Docetaxel

MP 1.8. Table 1 (cont'd). CCF4 areas of consensus

Practice scenario questions	Consensus agreement	
For the majority of chemotherapy-fit patients with PSMA imaging-positive mCRPC who meet relevant PET criteria for 177Lu-PSMA therapy, who have received one line of ARPI and one line of taxane-based chemotherapy, what is your preferred treatment option, assuming treatments are readily available and there is no actionable molecular alteration?	88%	177Lu-PSMA
In the majority of patients that you evaluate for 177Lu-PSMA therapy eligibility, what imaging do you routinely recommend assuming all scans are readily available?	92%	PSMA-PET, bone scintigraphy, and CT scan and add FDG-PET selectively for equivocal cases
In the majority of patients with synchronous low-volume mCSPC on conventional imaging, do you recommend additional metastases-directed therapy (if technically feasible) of all lesions?	79%	Yes, but only if no relevant additional and/or untreatable lesions confirmed by next-generation imaging
In patients with synchronous low-volume mCSPC on conventional imaging, and if you use metastases-directed therapy, what is your recommendation regarding the duration of systemic therapy?	75%	Continuous lifelong treatment of ADT ± ARPI
In the majority of patients with synchronous low-volume mCSPC on next-generation imaging and negative recommendation (regardless of the decision about metastases-directed therapy and regardless of the addition of docetaxel)?	78%	ADT plus RT of the primary tumor ± ARPI
In patients with synchronous low-volume mCSPC on next-generation imaging and negative on conventional imaging, and if you use metastases-directed therapy, what is your recommendation regarding the duration of systemic therapy?	81%	Continuous treatment of ADT ± ARPI for 2–3 years
If you recommend systemic therapy in a patient with metachronous low-volume mCSPC on conventional imaging, what is your recommendation regarding systemic therapy?	96%	Continuous lifelong treatment of ADT ± ARPI
For the majority of patients with mCSPC with deep remission to systemic therapy (e.g., PSA <0.2 ng/ml) and complete radiologic response of measurable lesions (PCWG3 criteria), and no relevant side-effects, do you recommend treatment interruption?	100%	No, I recommend continuous therapy
If you use treatment interruption in patients with mCSPC with deep remission to systemic therapy (e.g., PSA <0.2 ng/ml), what is your trigger to restart systemic therapy in the absence of clinical progression and in the context of recovered testosterone?	91%	Based on PSA rise or imaging progression, whichever occurs first

MP 1.8. Table 1 (cont'd). CCF4 areas of consensus

Practice scenario questions	Consensus agreement	
In patients with synchronous mCSPC and presence of a pathogenic HRR alteration, does this information change your treatment recommendation for the patient?	83%	No
For the majority of patients with mCRPC with a pathogenic alteration in BRCA2, what is your treatment recommendation in the first-line mCRPC setting when they received ADT+ ARPI for mCSPC?	91%	PARP inhibitor monotherapy
For the majority of patients with mCRPC with a pathogenic alteration in BRCA2, what is your treatment recommendation in the first-line mCRPC setting when they received ADT+ ARPI + docetaxel for mCSPC?	96%	PARP inhibitor monotherapy
For the majority of patients with mCRPC ≥ 75 years of age, what is your ARPI of choice in any line with regards to efficacy and the safety profile in this patient population, assuming all options are available?	95%	Abiraterone acetate
If you recommend antiresorptive therapy in a patient with mCSPC on continuous ADT-based therapy, what do you recommend?	85%	Denosumab 60 mg q6 months subcutaneously
If you recommend antiresorptive therapy in a patient with high-risk localized/locally advanced prostate cancer on ADT-based therapy for 2-3 years, what do you recommend?	78%	Denosumab 60 mg q6 months subcutaneously
For the majority of patients with mCSPC, do you routinely recommend genetic evaluation (germline and/or somatic) (if not performed earlier)?	75%	Yes, both germline and somatic testing, independent of findings in somatic testing

MP 1.9
Real-world DARolutamide Observational (DAROL) study in patients with non-metastatic castration-resistant prostate cancer: Results from the North American region at prespecified interim analysis 4

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Introduction: Darolutamide is approved for the treatment of non-metastatic castration-resistant prostate cancer (nmCRPC) based on significant metastasis-free survival (MFS) and overall survival (OS) benefit vs. placebo, and a favorable safety profile in the phase 3 ARAMIS trial (NCT02200614). DAROL (NCT04122976) is assessing the real-world safety and effectiveness of darolutamide in nmCRPC. We report results from the North American (NA) region at prespecified interim analysis 4 (IA4).

Methods: DAROL is an ongoing, global, open-label, single-arm, non-interventional study in patients with nmCRPC for whom the decision to treat with darolutamide

was made pre-enrollment. The primary endpoint is safety. Secondary endpoints include MFS, OS, prostate-specific antigen (PSA) progression, and PSA response. IA4 was conducted when 799 patients completed ≥ 12 months' treatment (data cutoff July 8, 2024).

Results: Of the 799 patients, 228 were from NA (Canada n=86, U.S. n=142). Baseline patient and disease characteristics were generally similar to the overall population, except that Eastern Cooperative Oncology Group performance status 2/3 was more frequent in Canada (20.7%) vs. the NA (9.4%) and overall populations (6.3%), and fewer Canadian patients (7.0%) had baseline PSA < 2 ng/mL vs. the NA (20.6%) and overall populations (18.9%). Treatment-emergent adverse events (TEAEs) were more frequent in the NA (79.4%) vs. overall population (61.0%) (Table 1), with fatigue being the most frequently reported individual TEAE (33.3% vs. 15.8%); most TEAEs were grade 1/2 (48.7% vs. 38.0%). The 24-month event rates were similar between the NA and overall populations (MFS 72.4% vs. 77.0%, OS 83.9% vs. 87.1%, PSA progression-free 64.4% and 60.2%). PSA90 response rate was slightly higher in the NA (64.2%) vs. the overall population (58.7%).

Conclusions: Darolutamide consistently showed favorable safety and effectiveness profiles between the NA and overall populations at IA4, supporting its use as standard of care for patients with nmCRPC.

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Acknowledgement: Data from the overall population at DAROL IA4 were previously presented at the 2025 European Society for Medical Oncology (ESMO) Congress.

MP 1.9. Table 1. TEAEs in the North American and overall populations at DAROL prespecified interim analysis 4

TEAE, n (%)	North American population (n=228)	Overall population (n=799)
Any grade	181 (79.4)	487 (61.0)
Grade 1/2	111 (48.7)	304 (38.0)
Grade 3/4	50 (21.9)	138 (17.3)
Grade 5	17 (7.5)	29 (3.6)
Serious	57 (25.0)	152 (19.0)
Leading to darolutamide discontinuation	25 (11.0)	70 (8.8)
TEAEs in >5% of the North American population, n (%)		
Fatigue	76 (33.3)	126 (15.8)
Asthenia	11 (4.8)	52 (6.5)
Hot flush	19 (8.3)	50 (6.3)
Urinary tract infection	19 (8.3)	36 (4.5)
Constipation	17 (7.5)	35 (4.4)
Diarrhea	14 (6.1)	33 (4.1)
Hematuria	13 (5.7)	28 (3.5)
Anemia	16 (7.0)	28 (3.5)
Dizziness	16 (7.0)	23 (2.9)
Fall	17 (7.5)	22 (2.8)

Data from the overall population for DAROL IA4 were previously presented at the European Society for Medical Oncology (ESMO) Congress, Berlin, Germany, October 17-1, 2025.

MP 1.10

Tissue-based genomic markers of cabazitaxel response in castration-resistant prostate cancer

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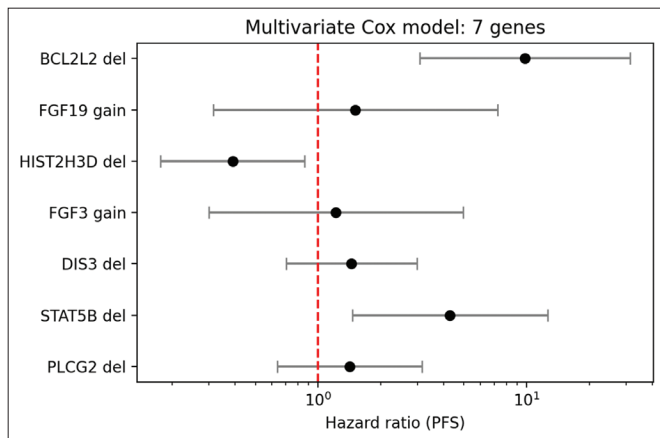
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Introduction: Cabazitaxel is a standard treatment for metastatic castration-resistant prostate cancer (mCRPC) patients who have progressed on androgen receptor pathway inhibitors (ARPIs) and docetaxel; however, the biomarkers associated with cabazitaxel's clinical outcomes are not yet fully elucidated.

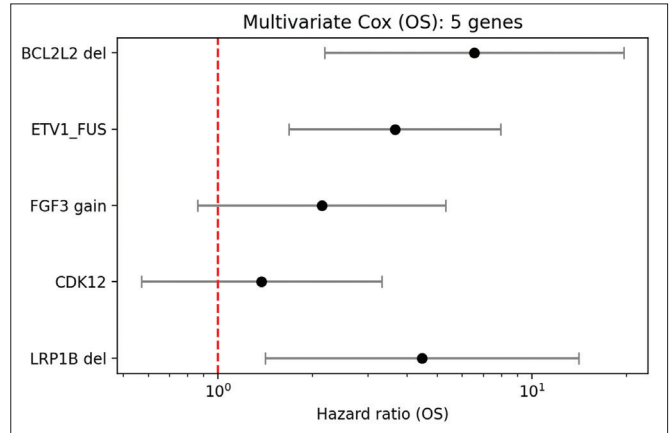
Methods: In this retrospective analysis, mCRPC patients treated with cabazitaxel after prior ARPI and/or docetaxel therapy were included. Univariate and multivariate Cox regression analyses were conducted to evaluate the association of clinical covariates and genetic alterations occurring in ≥5% of the cohort with progression-free survival (PFS) and overall survival (OS).

Results: A total of 73 patients with clinical and genetic data were included in the analysis. In multivariable analysis for PFS, BCL2L2 alteration (HR 9.79, 95% CI 3.07–31.27, p=0.0001) and FGF19 alteration (HR 4.28, 95% CI 1.46–12.57, p=0.0081) were associated with significantly shorter PFS. When adjusted for relevant clinical covariate (ECOG >1), BCL2L2 remained significant (HR 5.63, 95% CI 1.78–17.77, p=0.0032). Regarding OS, BCL2L2 (HR 6.55, 95% CI 2.19–19.63, p=0.0008), ETV1 (HR 3.66, 95% CI 1.68–7.94, p=0.001), and LRP1B (HR 4.47, 95% CI 1.42–14.08, p=0.0107) were associated with reduced OS. Even after adjusting for relevant clinical covariates for OS (PSA >72 ng/mL and liver metastasis), BCL2L2 (HR 5.06, 95% CI 1.60–16.03, p=0.0058) and ETV1 (HR 2.99, 95% CI 1.36–6.58, p=0.0065) were significantly associated with worse OS (Figures 1, 2).

Conclusions: In mCRPC patients receiving cabazitaxel, BCL2L2 was a robust prognostic biomarker for both PFS and OS. ETV1 was also independently associated with reduced OS. Further external validation to support clinical-genomic risk stratification models may facilitate a more personalized treatment approach.



MP 1.10. Figure 1. Multivariate Cox model: 7 genes.



MP 1.10. Figure 2. Multivariate Cox (OS): 5 genes.

MP 1.11

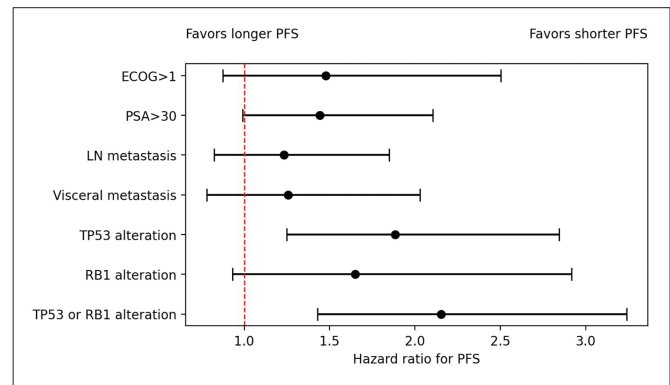
Cooperative TP53 and RBI alterations drive resistance to docetaxel in metastatic castration-resistant prostate cancer

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Introduction: Docetaxel remains a standard of care for mCRPC following resistance to androgen receptor pathway inhibitors (ARPIs); however, treatment outcomes are highly heterogeneous, and reliable genomic predictors of chemoresistance are lacking. TP53 and RBI, key tumor-suppressor genes involved in cell-cycle regulation and genomic stability, have been implicated in aggressive phenotypes and lineage plasticity in advanced prostate cancer. We investigated whether TP53 and/or RBI genetic alterations are associated with inferior clinical outcomes in mCRPC patients treated with docetaxel.

Methods: A retrospective analysis was conducted to evaluate the association between genetic alterations and docetaxel treatment outcomes. A total of 125 mCRPC patients who had progressed on ARPIs and subsequently received docetaxel were included. Genetic alterations were assessed using the TruSight Oncology 500 v2 panel (Illumina Inc., San Diego, CA, U.S.). Radiographic progression-free survival (rPFS) and overall survival (OS) were analyzed according to TP53 and RBI alteration status.

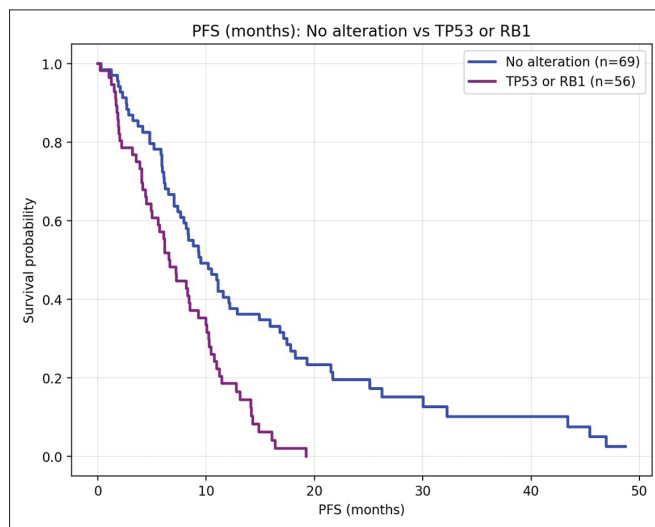


MP 1.11. Figure 1. Forest plot of hazard ratios for progression-free survival.

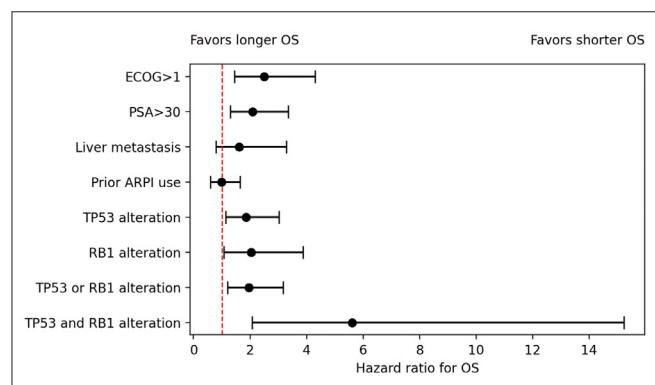
Results: Genetic alterations in TP53 were observed in 45 patients (36.0%), including 40 mutations and nine copy number losses. RB1 alterations were detected in 16 patients (12.8%), including two mutations and 16 copy number losses (Table 1). Patients with an alteration in either TP53 or RB1 had significantly shorter rPFS compared with those without alterations in both genes (median rPFS 6.6 vs. 9.5 months; HR 2.15, 95% CI 1.43–3.24, $p=0.0002$) (Figure 1). Although patients with co-alterations in both genes demonstrated shorter rPFS (median rPFS of 8.2 months), the difference was not statistically significant (Figure 2). For OS, patients with alterations in either TP53 or RB1 showed significantly shorter survival compared with those without alterations in both genes (median OS 18.1 vs. 32.2 months; HR 1.96, 95% CI 1.20–3.18, $p=0.0067$), while patients harboring co-alterations in both TP53 and RB1 genes experienced the poorest outcomes (median OS 11.4 months; HR 5.61, 95% CI 2.07–15.24, $p=0.0007$) (Figures 3, 4).

Conclusions: TP53 and RB1 genetic alterations are significant prognostic markers of poor survival outcomes following docetaxel therapy in mCRPC. These findings underscore the clinical relevance of genomic risk stratification and highlight the need for further exploration to support the development of therapeutic strategies to overcome TP53 and/or RB1-mediated docetaxel resistance

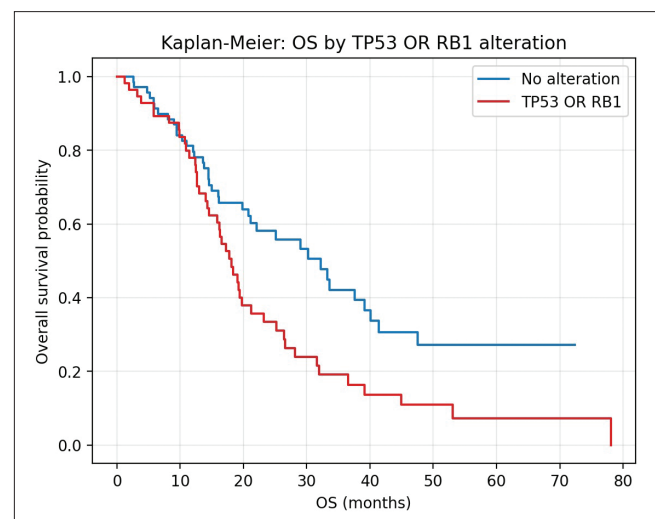
MP 1.11. Table 1. Baseline clinical and genomic characteristics of the patients	
Total patients (n=125)	
Median age, years (IQR)	68 (63–74)
ECOG performance status	
0	36 (28.8%)
1	66 (52.8%)
2	23 (18.4%)
Metastatic sites	
Bone	111 (88.8%)
Lymph node	50 (40.0%)
Lung	16 (12.8%)
Liver	11 (8.8%)
Adrenal gland	6 (4.8%)
Kidney	1 (0.8%)
Peritoneum	8 (6.4%)
PSA, ng/ml (IQR)	30.3 (11.4–99.6)
Previous ARPI	90 (72.0%)
Abiraterone	56 (44.8%)
Enzalutamide	40 (32.0%)
Apalutamide	2 (1.6%)
Prior lines of ARPI	
0	35 (28.0%)
1	82 (65.6%)
2	8 (6.4%)
TP53 alteration	45 (36.0%)
RB1 alteration	16 (12.8%)
TP53 and RB1 co-alteration	5 (4.0%)
Median followup, months (IQR)	18.0 (12.3–29)



MP 1.11. Figure 2. Kaplan-Meier analysis of progression-free survival.



MP 1.11. Figure 3. Forest plot of hazard ratios for overall survival.



MP 1.11. Figure 4. Kaplan-Meier Analysis of overall survival.

MP 1.12**Temporality and anatomical hierarchy of metastatic spread in high-grade prostate cancer after radical prostatectomy**

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Introduction: High-grade prostate cancer (HGPCa; ISUP 4–5) is characterized by poor outcomes, yet the temporal and anatomical sequence of metastatic spread to lymph nodes, bone, and visceral organs remains poorly defined. We aimed to reconstruct the natural history of metastatic dissemination from radical prostatectomy (RP) to radiologic metastases.

Methods: From 452 HGPCa patients who underwent RP, we retrospectively analyzed 145 patients that presented either pathologic nodal metastases (pN1) or radiologic metastases at followup. Patients were classified as harboring nodal (N1 or M1a), osseous (M1b), or visceral (M1c) metastases at first metastatic presentation or at followup. Time to each metastatic state and transitions between compartments were analyzed.

Results: At RP (mean age 66 years), 21 patients (14%) were pN0 and 124 (86%) pN1. Over a median followup of 6.5 years, 76/145 patients (52%) developed radiologic metastases, 72% of whom were initially pN1. Among these, N1/M1a, M1b, and M1c disease occurred in 56 (74%), 53 (70%), and 36 (47%) patients, respectively, with 73%, 74%, and 78% initially pN1. M1c spread mainly involved lung (n=19, 36%) and liver (n=17, 47%), while bone disease was predominantly axial (52/53). First radiologic metastases emerged at a median of 31 months and were nodal-only in 19 patients (25%), M1b in 47 (62%), and M1c in 16 (21%). Across the cohort, only 4% developed metastases without nodal pathologic or radiologic involvement, all as isolated M1b, while 100% of M1c cases showed nodal involvement at some point.

Conclusions: HGPCa follows a structured metastatic program in which lymph nodes act as the dominant gateway, bone as an intermediate expansion niche, and visceral organs as the terminal compartment. These findings define an ordered natural history of metastatic spread and identify anatomically and temporally distinct windows for therapeutic intervention, especially lymph node dissection or radiation.

MP 1.13**Efficacy of neoadjuvant hormonal therapy combined with robot-assisted radical prostatectomy for oligometastatic prostate cancer: A multicenter, retrospective study**

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Introduction: We aimed to evaluate the efficacy of neoadjuvant hormonal therapy (NHT) in patients with oligometastatic prostate cancer (OmPCa) treated with robot-assisted radical prostatectomy (RARP) and adjuvant androgen deprivation therapy (ADT).

Methods: In this multicenter, retrospective study, 160 OmPCa patients treated from five Chinese medical centers between May 2010 and May 2023 were included: 80 received NHT followed by RARP plus ADT, and 80 underwent RARP plus ADT alone. We evaluated perioperative and oncologic outcomes.

Results: Compared to the standard therapy group, the NHT group exhibited shorter operative time (p=0.030), less blood loss (p=0.022), lower positive surgical margin rate (p=0.005), and higher rates of pathologic downstaging in T-stage (p<0.001) and N-stage (p=0.003). More NHT patients achieved undetectable prostate-specific antigen (PSA) (p=0.007), with a shorter time to PSA nadir (p=0.002). After a median followup of 55 months, no significant differences were observed in biochemical progression-free survival (bPFS), radiologic progression-free survival (rPFS), or overall survival (OS) between groups; how-

ever, subgroup analysis revealed significant interaction effects between NHT and biopsy Gleason score ≥ 8 , seminal vesicle invasion, and clinical T stage $\geq T3$ (all p-interaction <0.05), with these subgroups showing significantly improved bPFS, rPFS, and OS. Furthermore, patients in the NHT group received fewer subsequent treatments (p=0.031), and the incidence of ADT-related adverse events was comparable between the two groups (all p>0.05).

Conclusions: NHT improves perioperative outcomes and may offer oncologic benefits in OmPCa patients undergoing RARP, particularly those with a biopsy Gleason score ≥ 8 or clinical T-stage $\geq T3$. It represents a safe and feasible neoadjuvant approach.

MP 1.14**Early PSA response and safety outcomes of irreversible electroporation (NanoKnife®) for localized prostate cancer: A single-center experience**

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Introduction: Irreversible electroporation (IRE) is a focal ablative therapy for localized prostate cancer that aims to preserve surrounding structures while achieving oncologic control. Early prostate-specific antigen (PSA) kinetics may provide an initial signal of treatment effect. We report early PSA response and safety outcomes following IRE.

Methods: We performed a retrospective analysis of patients undergoing IRE (NanoKnife®) for localized prostate cancer at a tertiary referral center. All patients had histologically confirmed conventional acinar adenocarcinoma without ductal or cribriform features. Baseline clinicopathologic variables, treatment parameters, perioperative outcomes, and PSA values were collected. The primary outcome was change in PSA at 12 months following treatment. Secondary outcomes included perioperative and early post-treatment safety outcomes.

Results: A total of 136 patients underwent IRE. Median age was 68 years (IQR 63–72) and median prostate volume was 34.3 cm³ (IQR 27.0–47.0). Most patients had intermediate-risk disease, with Gleason score 3+4 in 61.5% and 4+3 in 20.9% of cases. Among patients with evaluable PSA data at 12 months (n=42), median PSA decreased from 9.15 µg/L (IQR 6.5–13.7) pre-treatment to 2.85 µg/L (IQR 1.17–5.04) at 12 months, representing a median absolute reduction of 5.93 µg/L and a median percent reduction of 73.4%, with 95.2% demonstrating a PSA decline. No patients experienced immediate perioperative complications or postoperative complications within three months of the procedure.

Conclusions: IRE for localized prostate cancer demonstrates a substantial early PSA decline at 12 months with an excellent early safety profile. Postoperative MRI assessment and 12-month post-treatment biopsy data are forthcoming and will further inform oncologic outcomes. Longer followup is required to assess durability of cancer control.

MP 1.15**Randomized controlled trial of MRI-guided transurethral ultrasound ablation (TULSA) vs. radical prostatectomy: Six-month outcomes**

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Introduction: MRI-guided transurethral ultrasound ablation (TULSA) of the prostate has regulatory clearance in Canada and other countries based on single-arm studies in men with localized favorable-risk prostate cancer. CAPTAIN

is a randomized, controlled trial (NCT05027477) comparing MRI-guided TULSA vs. robotic prostatectomy (RP) for favorable and unfavorable intermediate-risk prostate cancer. We report on six-month outcomes, including the primary functional endpoint.

Methods: A total of 211 patients with ISUP 2–3 prostate cancer and PSA ≤ 20 ng/mL were treated across 20 high-volume prostatectomy centres in U.S., two in Canada, and one in Finland, with 2:1 randomization (148 TULSA, 63 RP) stratified for key baseline characteristics. The primary functional endpoint was preservation of pad-free continence (EPIC) and functional erections (IIEF Q2 \geq 2). The primary oncologic endpoint of freedom from additional prostate cancer treatment will be assessed at three years. Secondary data points available for assessment include treatment parameters, postoperative recovery, and 90-day complications.

Results: Baseline characteristics were balanced: median (IQR) age for TULSA vs. RP was 63 (58–68) vs. 65 (60–69) years; PSA 6.5 (4.9–9.6) vs. 7.2 (5.6–9.7) ng/mL; proportions with ISUP 2/3 prostate cancer were 76%/24% vs. 77%/23%. TULSA treatment plans included whole-gland (68%) and subtotal (32%) ablation, with a median treatment coverage of 78% (71–85) of the prostate volume. In

the RP cohort, nerve sparing was applied in 95% of cases (bilaterally in 89%), with lymph node dissection in 77%. Perioperatively, TULSA had zero blood loss vs. 150 (100–200) mL for RP; TULSA had no overnight stay (0.3 [0.2–0.3] days) vs. 1.1 [1.1–1.3] days for RP, and TULSA patients reported less pain in the first week (numerical rating scale). Positive surgical margins were found in 33% of RP patients. TULSA patients had less decline and faster recovery of EQ-5D overall health and required less time off from paid employment (10 [4–15] vs. 19 [10–41] days). The 90-day rate of hospitalization for complications was 0.7% after TULSA vs. 6.3% after RP. After RP, 1.6% required intensive care vs. 0% after TULSA. TULSA was superior to RP on the primary functional endpoint at six months, with 50% vs. 24% of patients preserving pad-free continence and erections sufficient for penetration (risk ratio 2.1).

Conclusions: In the first fully enrolled randomized, controlled trial comparing ablative vs. radical treatment of localized prostate cancer, TULSA was superior to RP for the primary functional endpoint of preserving pad-free continence and erectile function at six months. Oncologic endpoints will be reported with additional followup.

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