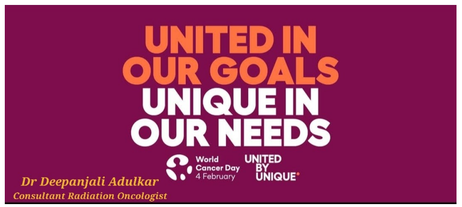

6th Knowledge Series for Genitourinary Cancers - Best of 2024

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ASCO Genitourinary Cancers Symposium

Metastases-directed therapy in addition to standard systemic therapy in oligometastatic castration resistant prostate cancer: A randomized phase II trial (GROUQ-PCS 9)

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Clinical Trials.gov identifier: NCT02685397
This study was supported by Astellas Canada

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Background:

- ADT and Enzalutamide is one of the standard options for ARPi naïve mCRPC patients.

- PCS 9 was designed to evaluate the role of MDT (SBRT) to the standard of care to provide a new treatment option for oligometastatic CRPC (omCRPC).

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Limitations

- Originally designed as adaptive Phase II/III randomized study
- ARPI → standard of care for mHSPC
- Trial was halted at the phase II
- Results reported on 100 omCRPC

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PCS-9 Study Design

Patient population
- 1L mCRPC
- 1-5 metastases
- Docetaxel allowed at mHSPC stage
- No prior NHAs
- Ongoing ADT
- ECOG 0–1

Stratification factors
- Site of distant metastases
- Number of mets <4 vs 4+

1:1

Enzalutamide 160 mg + Androgen Deprivation therapy

N=48

Enzalutamide 160 mg + Androgen Deprivation therapy + MDT (SBRT)

N= 52

Primary endpoint
- Radiographic progression or death (rPFS) by investigator assessment

Key secondary endpoint
- Biochemical Progression Free survival or death (bPFS)
- Time to subsequent therapy
- Health-related quality of life
- Safety and tolerability
- Overall survival

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PCS-9 Baseline patient and disease characteristics:
Well-balanced between arms

	Enzalutamide + ADT (n=48)	Enzalutamide + ADT + SBRT (n=52)
Median (range) age, years	72.5 (54–85)	72.1 (49–84)
ECOG performance status, n (%) 0 1	 31(67.4) 15 (32.6)	 41 (82) 9 (18)
Gleason 8+ n (%)	**29 (61.7)**	**25 (50)**
History of prostatectomy, n (%)	21 (43.8)	22 (42.3)
Prior radiotherapy to the prostate/prostate bed , n (%)	**37 (77.1)**	**45 (86.5)**
Number of mets <4 vs 4+	43 (89.6) vs. 5 (10)	44 (84.6) vs 8 (15.4)
Location of mets:		
Lymph node only	**10(21)**	**17 (32.5)**
Bone	**36 (75)**	**32 (61.5)**
Lung	**1 (2)**	**4 (6)**
Soft tissue	**1 (2)**	**0 (0.0)**

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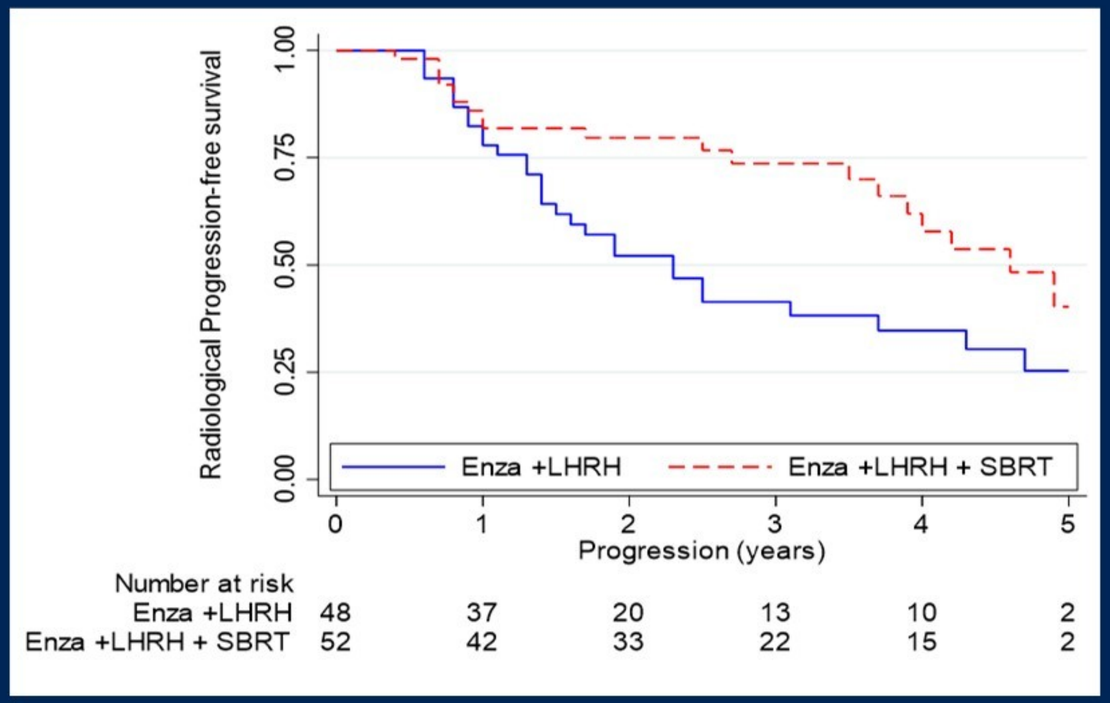
PCS-9 Primary endpoint: rPFS by investigator- assessment

52% risk reduction of radiological progression or death with SBRT



	Enza + ADT (n=48)	Enza + ADT + SBRT (n=52)
Events, n (%)	30 (62.5)	19 (36.5)
Median rPFS (years)	2.3	4.6
HR (95% CI)	0.48 (0.27–0.86); *P*=0.014	

Pre-specified 2-sided alpha: 0.05

Median rPFS improvement of 2.3 YEARS favors SBRT + Enzalutamide + ADT

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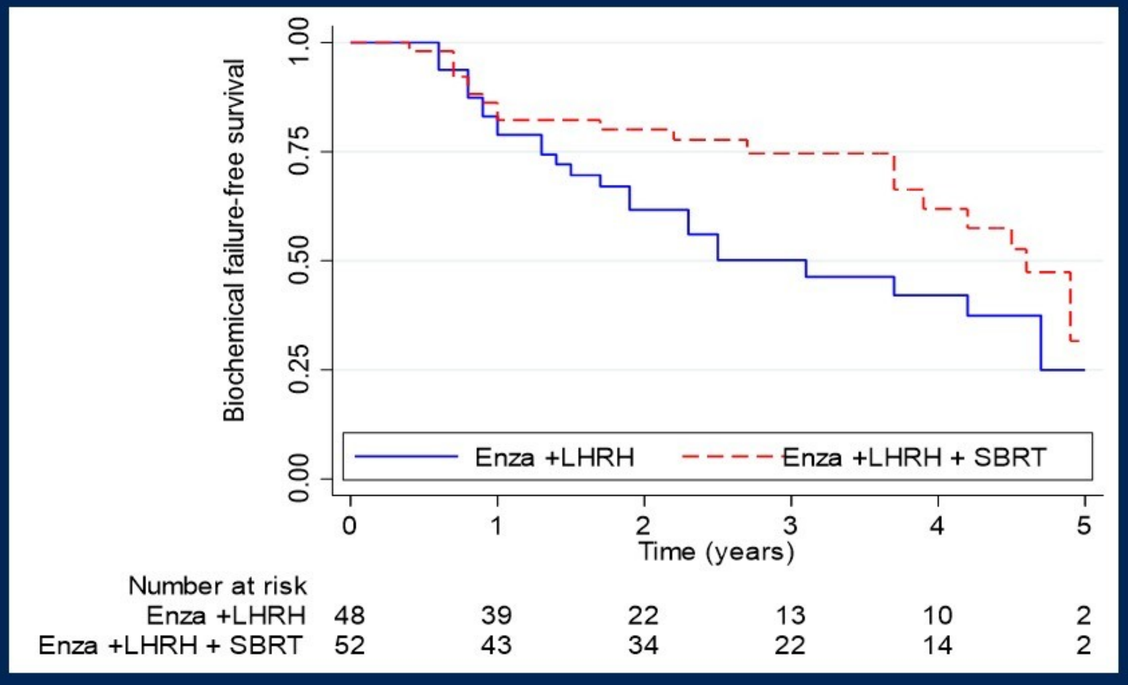
PCS-9 secondary endpoint of interest: bPFS

42% risk reduction of biochemical progression or death with SBRT



	Enza + ADT (n=48)	Enza + ADT + SBRT (n=52)
Events, n (%)	27 (59)	20 (40)
Median bPFS (years)	3.1	4.6
HR (95% CI)	0.58 (0.32–1.03); *P*=0.065	

Pre-specified 2-sided alpha: 0.05

Median bPFS improvement of 1.5 YEARS favors SBRT + Enzalutamide + ADT

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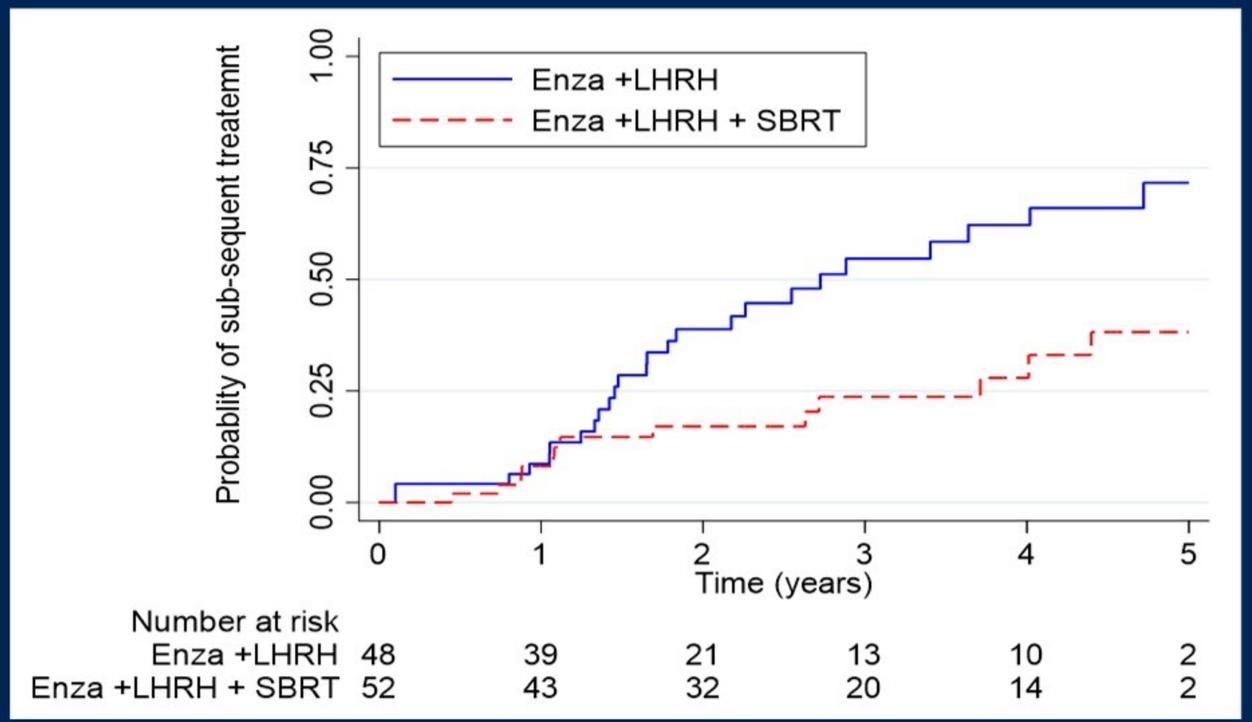
PCS-9 secondary endpoint of interest: subsequent line of therapy

58% risk reduction in time to subsequent line of therapy with SBRT



	Enza + ADT (n=48)	Enza + ADT + SBRT (n=52)
Events, n (%)	26 (54)	14 (27)
Median time to subsequent therapy (yrs)	2.9	5.1
HR (95% CI)	0.42 (0.22–0.8); *P*=0.009	

Pre-specified 2-sided alpha: 0.05

Median time to subsequent therapy delayed by 2.2 YEARS
favors SBRT + Enzalutamide + ADT

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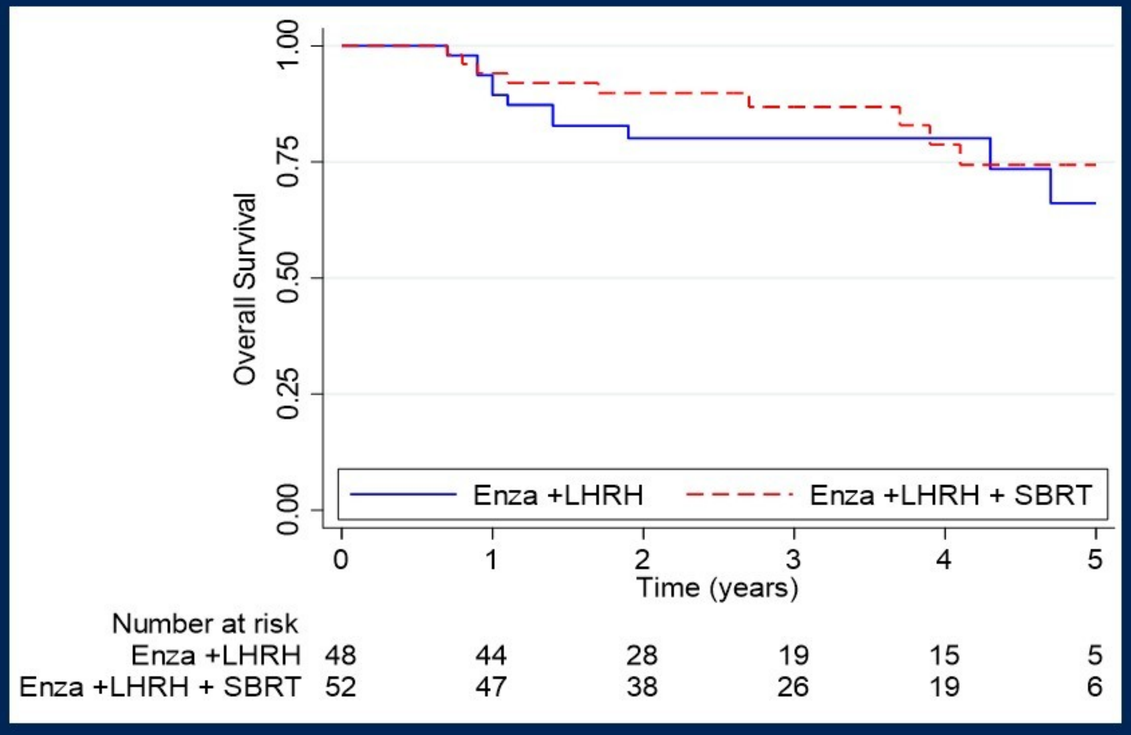
PCS-9 secondary endpoint of interest: Overall Survival

29% risk reduction of death with SBRT



	Enza + ADT (n=48)	Enza + ADT + SBRT (n=52)
Events, n (%)	13 (27)	11(21)
Median OS (years)	NR	NR
HR (95% CI)	0.71 (0.31–1.59); *P*=0.407	

Pre-specified 2-sided alpha: 0.05

Although not statistically significant 29% risk risk reduction of death favors SBRT + Enzalutamide + ADT

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PCS-9: most common adverse events

AE profile was consistent with the known toxicity profile of Enzalutamide

	Level	Enza +LHRH (N = 48)	Enza +LHRH + SBRT (N = 52)	P-Value
Grade 1 or Higher Event	Any, n (%)	40 (83.3%)	45 (86.5%)	0.781
Grade 2 or Higher Event	Any, n (%)	21 (43.8%)	19 (36.5%)	0.542
Arthritis	Any, n (%)	8 (16.7%)	6 (11.5%)	0.568
Hypertension	Any, n (%)	5 (10.4%)	1 (1.9%)	0.102
Fatigue	Any, n (%)	33 (68.8%)	31 (59.6%)	0.407
Fracture	Any, n (%)	2 (4.2%)	4 (7.7%)	0.679
Pain at SBRT Site	Any, n (%)	0 (0%)	4 (7.7%)	0.119
Asymptomatic Pneumonitis	Any, n (%)	0 (0%)	1 (1.9%)	1.000

Safety was assessed through the reporting of AEs according to the Common Terminology Criteria for Adverse Events version: 4.3

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PCS-9 Conclusions:

- **The addition of SBRT in oligometastatic CRPC** led to a statistically and clinically meaningful **improvement in rPFS (HR 0.48 [95% CI 0.27–0.86])** over Enzalutamide and ADT alone: **4.6 years vs. 2.3 years**
- Secondary and exploratory endpoints support the treatment benefit of SBRT + Enzalutamide/ADT over Enzalutamide/ADT alone.
- The safety profile of SBRT with Enzalutamide/ADT was **consistent with the safety profile of ENZA/ADT**
- MDT using SBRT should strongly be considered for CRPC patients with oligometastases (omCRPC).

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