

Therapeutic Decision-Making in Metastatic Hormone-Sensitive Prostate Cancer (mHSPC): The INTERACT RAND/UCLA Study on ARPi-Based Doublet and Triplet Therapies

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Conclusions

Our study helped to define the key drivers in the choice of treatment for mHSPC according to the most recent evidence.

Disclosures: The authors report the following COI: Maiorano BA: Speaker, advisor, consultant: Astellas, Astra Zeneca, Bayer, BMS, Eisai, IPSEN, Johnson & Johnson, Merck Serono, MSD, Novartis; Oderda M: Advisory boards: Johnson & Johnson, AstraZeneca, Bayer, Astellas, Novartis; Speaker honoraria: Johnson & Johnson, AstraZeneca, Bayer, Astellas, Esaote, Coloplast, Eisai, MSD, Eurobio; Scarcia M: Consultant for Astellas, Bayer, Astrazeneca, Recordati, Johnson & Johnson, Accord; Simone G: Consultant for Astellas, Bayer, Astrazeneca, Recordati, Johnson & Johnson, Janssen, Accord, ABMedica, Intuitive, Ipsen, MSD, Merck, Pfizer; Maruzzo M: Advisory Board: MSD, Merck Serono, BMS, Recordati, Astellas, Johnson & Johnson, IPSEN, AstraZeneca, Bayer; Speaker's Bureau: Astellas, Johnson & Johnson, IPSEN, AstraZeneca, Bayer. M.Portaro is an employee of J&J. All other authors declared no COI.

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Background



The treatment landscape of metastatic hormone-sensitive prostate cancer (mHSPC) is evolving rapidly¹; although several patients and disease-related factors can guide the choice among available treatments, controversy exists about the optimal regimen to be used.

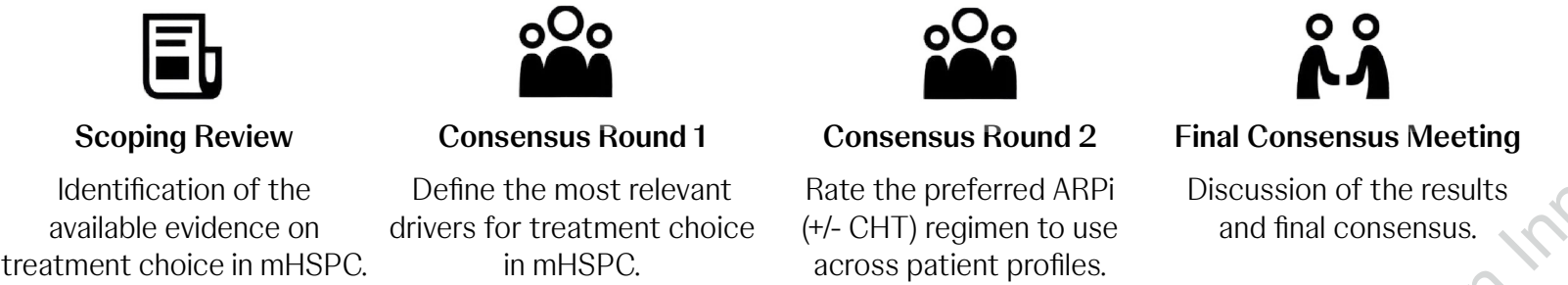


Through a RAND/UCLA appropriateness² study in the Italian clinical community, this work developed a consensus document guiding the use and choice of ARPIs + ADT, with or without docetaxel, by disease status and patient profile in mHSPC.

Method

Study design: RAND/UCLA appropriateness method

A structured, iterative process to define key drivers of treatment selection and identify the most appropriate ARPi-based regimens (+/- chemotherapy) across patient/disease profiles in mHSPC.



Identification of treatment selection drivers

Candidate drivers evaluated by expert voting

- Presence of visceral metastases
- Timing of metastatic disease
- ECOG Performance Status
- Extent of bone disease (number of bone metastases)
- Patient age
- Gleason Score



Selection of the most relevant drivers defining mHSPC patient profiles



Development of patient profiles for appropriateness assessment

Expert panel

16 Expert physicians



- 7 Medical Oncologists
- 5 Urologists
- 3 Radiation Oncologists
- 1 Nuclear Medicine Specialist

Experts working in different areas of Italy were invited to participate.

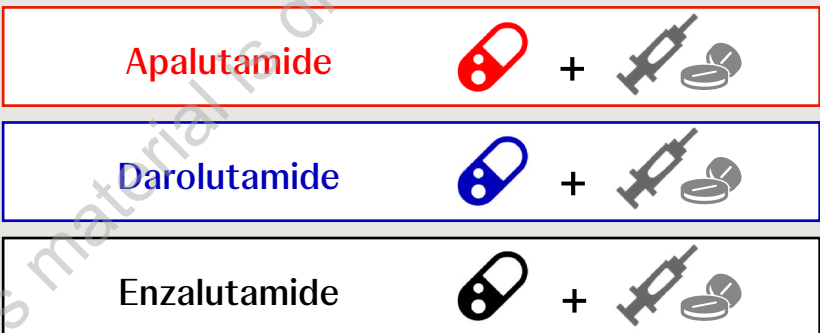
Rating of treatment appropriateness

In the second consensus round, experts rated the appropriateness of each regimen for every patient profile using a 1-9 scale.

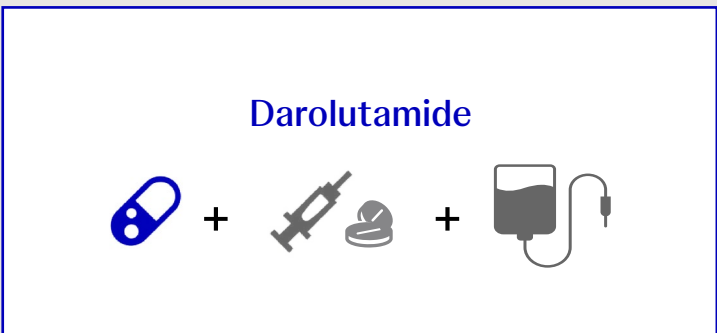


Treatment regimens

Doublet

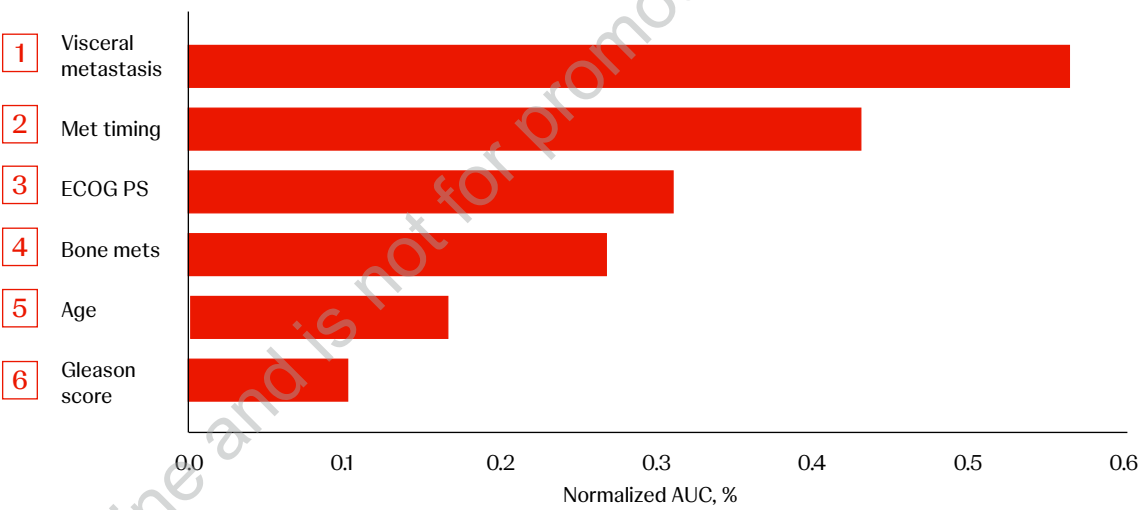


Triplet



Results

Round 1: Drivers Ranked by Cumulative Dominance (Normalized AUC)



Four key drivers emerged as most influential in treatment selection:

- Presence of visceral metastases,
- Timing of metastatic disease (synchronous vs metachronous),
- ECOG performance status (0–1 vs ≥2)
- Number of bone metastases (<4 vs ≥4).

The combination of these variables resulted in 16 patient profiles.

Round 2: Appropriateness of ARPi-Based Regimens and Level of Consensus

Patient profiles									Treatments (level of agreement-IQR)			
	1 Visceral metastasis	2 Metastasis at diagnosis	3 ECOG performance status		4 N° bone metastasis				Doublets		Triplets	
	YES	NO	Synchronous	Metachronous	0 o 1	≥2	<4	≥4	Apalutamide	Enzalutamide	Darolutamide	Daro + CHT
PP 1	x			x	x		x		8 (1)	7 (1)	6 (1)	8 (2)
PP 2	x		x		x		x		7 (1)	7 (2)	7 (2)	8 (1)
PP 3	x			x		x	x		8 (1)	7 (1)	7 (2)	6 (5)
PP 4	x			x	x			x	8 (1)	7 (0)	6 (1)	8 (1)
PP 5		x		x	x		x		8 (1)	8 (2)	8 (1)	3 (3)
PP 6		x	x		x		x		8 (1)	8 (1)	7 (2)	5 (3)
PP 7		x		x			x		8 (3)	7 (2)	7 (2)	2 (2)
PP 8		x		x	x			x	8 (1)	8 (1)	7 (2)	6 (2)
PP 9	x		x			x	x		7 (3)	7 (3)	6 (2)	6 (1)
PP 10	x		x			x		x	7 (1)	7 (0)	6 (2)	7 (3)
PP 11	x			x		x		x	7 (2)	7 (2)	6 (2)	7 (3)
PP 12	x		x		x			x	7 (1)	6 (1)	6 (1)	9 (0)
PP 13		x	x			x	x		8 (1)	7 (1)	7 (2)	5 (3)
PP 14		x	x			x		x	8 (1)	7 (1)	7 (2)	4 (4)
PP 15		x		x		x		x	8 (1)	7 (1)	7 (1)	5 (3)
PP 16		x	x		x			x	8 (2)	8 (1)	7 (1)	8 (3)

Doublet regimens therapy was judged appropriate in most clinical scenarios.

- Apalutamide and Enzalutamide (+ ADT) showed high appropriateness across nearly all patient profiles (100% and 94%, respectively), with the highest level of consensus (IQR ≤1) in 12/16 [75%] and 10/15 [66%], respectively.
- Darolutamide (+ ADT) was judged appropriate in 10/16 profiles (62%), while uncertainty was observed in 6/16 scenarios (38%). The highest level of consensus was reached in 6/16 patients profile (38%).
- PS 0–1 and visceral disease were considered the main drivers of treatment intensification with CHT, achieving the highest level of consensus in 3 out of 7 scenarios in which triplet therapy was considered appropriate (7/16 [43%]).

References:

1. Fizazi et al., Lancet Oncol 2022.
2. Brook, R. H., et al. (1986). A method for the detailed assessment of the appropriateness of medical technologies. International journal of technology assessment in health care, 2(1), 53-63.

Prostate Cancer

