PARP INHIBITORS COMBINED WITH NHAs ARE AN EFFECTIVE FIRST-LINE TREATMENT FOR mCRPC PATIENTS

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PARP inhibitors + Novel hormonal agents → Combination benefit in 1L mCRPC pts

	PROpel[1,2]	MAGNITUDE[3]	TALAPRO-2[4,5,6]	CASPAR[7,8]
	olaparib + abiraterone vs abiraterone[a]	niraparib + abiraterone vs abiraterone[a]	talazoparib + enzalutamide vs enzalutamide[b]	rucaparib + enzalutamide vs enzalutamide[b]
Dose of PARPi	olaparib 300 mg bid	niraparib 200 mg QD	talazoparib 0.5 mg QD	rucaparib 600 mg bid
Prior therapies	Prior docetaxel for mCSPC/locally advanced prostate cancer No prior abiraterone Other prior NHA for pre-mCRPC allowed if stopped ≥12 months before randomisation	≤4 months prior abiraterone at mCRPC Prior to mCRPC: enzalutamide, apalutamide, darolutamide, taxane chemotherapy allowed	No prior systemic cancer treatment initiated at nmCRPC or mCRPC Prior docetaxel or abiraterone allowed in mHSPC	No prior treatment for mCRPC Prior abiraterone, darolutamide or apalutamide in non-mCRPC setting is allowed
Primary endpoint	rPFS in unselected patients (by investigator assessment)	rPFS (BICR) in patients with and without HRRm	rPFS (BICR) in patients with HRRm and unselected patients	rPFS and OS in unselected patients
Key Results	Compared to abiraterone, treatment with olaparib + abiraterone reduced progression or death by: 34% in all pts (n=796) 50% in HRRm pts (n=226) 77% *BRCA*m pts (n=85)	No effect in pts without a HRRm Compared to abiraterone, treatment with niraparib + abiraterone reduced progression or death by 27% in HRRm pts (n=423) and by 47% in *BRCA1/2* pts (n=225)	Initial results suggest talazoparib plus enzalutamide provides a rPFS benefit compared with enzalutamide in first-line mCRPC patients Awaiting presentation of full dataset	Trial ongoing
Safety	The safety profile of all PARPi + NHA combinations was consistent with that of the individual treatments			
Clinical Message	**Effective in 'all-comer' mCRPC pts**	**Effective in mCRPC pts with HRRm**	**Awaiting presentation of full dataset**	

a. abiraterone acetate given as 1000 mg QD with prednisone/prednisolone 10 mg/day; **b.** enzalutamide used at a dose of 160 mg QD

1L, first-line; BICR, blinded independent central review; bid, twice a day; *BRCA*m, breast cancer susceptibility gene mutated; HRRm, homologous recombination repair gene mutation; mCRPC, metastatic castration-resistant prostate cancer; mCSPC, metastatic castration-sensitive prostate cancer; NHA, novel hormonal agent; nmCRPC, non-metastatic castration-resistant prostate cancer; OS, overall survival; PARP(i), poly (ADP-ribose) polymerase (inhibitor); pts, patients; QD, once a day; rPFS, radiographic progression-free survival

1. Clarke N, et al. New Engl J Med Evid. 2022. DOI: 10.1056/EVIDoa2200043; **2.** Saad F, et al. Ann Oncol. 2022;33 suppl 7:S616-52 (ESMO 2022 oral presentation); **3.** Chi KN, et al. J Clin Oncol. 2022;40 suppl 6:12 (ASCO GU 2022 oral presentation); **4.** Agarwal N, et al. J Clin Oncol. 2020;38 15_suppl:TPS5598 (ASCO 2020 poster presentation); **5.** TALAPRO-2. ClinicalTrials.gov identifier: NCT03395197. Accessed October 11, 2022. https://clinicaltrials.gov/ct2/show/NCT03395197; **6.** https://www.pfizer.com/news/press-release/press-release-detail/pfizer-announces-positive-topline-results-phase-3-talapro-2. Accessed October 13, 2022; **7.** CASPAR. ClinicalTrials.gov identifier: NCT04455750. Accessed October 11, 2022. https://clinicaltrials.gov/ct2/show/NCT04455750; **8.** Rao A, et al. J Clin Onc. 2022;40 6_suppl:TPS194

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