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

GU connect® POWERED BY COR2ED

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

	PROpel[1,2,3]	MAGNITUDE[4,5]	TALAPRO-2[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) Median OS: 42.1 (ola+abi) vs 34.7 months (abi+pbo) [Final analysis]	Compared to abiraterone, treatment with niraparib + abiraterone reduced progression or death by: • No effect in pts without a HRRm • 27% in HRRm pts (n=423) • 47% in *BRCA1/2* pts (n=225) Median OS: 30.4 (Nira +abi) vs 28.6 months (abi +pbo) [Final analysis]	Compared to enzalutamide, treatment with talazoparib + enzalutamide reduced progression or death by: • 37% in all patients (n=805) • 54% in HRRm pts (n=169) • 80% in BRCAm pts (n=69) Median OS: 36.4 months (tala +enza) vs NR (enza + pbo)	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**	**Effective in 'all-comer' mCRPC pts**	

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; abi, abiraterone; BICR, blinded independent central review; bid, twice a day; *BRCA*m, breast cancer susceptibility gene mutated; enza, enzalutamide; HRRm, homologous recombination repair gene mutation; mCRPC, metastatic castration-resistant prostate cancer; mCSPC, metastatic castration-sensitive prostate cancer; NHA, novel hormonal agent; Nira, niraparib; nmCRPC, non-metastatic castration-resistant prostate cancer; NR, not reached; ola, olaparib; OS, overall survival; PARP(i), poly (ADP-ribose) polymerase (inhibitor); pbo, placebo; pts, patients; QD, once a day; rPFS, radiographic progression-free survival; tala, talazoparib

1. Clarke N, et al. New Engl J Med Evid. 2022. DOI: 10.1056/EVIDoa2200043; 2. Saad F, et al. Annals of Oncology 2022; 33 (suppl_7): S616-S652 (ESMO 2022 oral presentation); 3. Saad F, et al. Lancet Oncology 2023;24: 1094-1108; 4. Chi K, et al. Journal of Clinical Oncology 2023; 41: 3339-3351; 5. Chi K, et al. Annals of Oncology 2023; 34 (suppl_2): S1254-S1335; 6. Agarwal A, et al. Lancet 2023;402: 291-303 (supplementary appendix); 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

Go to COR2ED.COM for more information and resources

The programme is supported by an independent educational grant from AstraZeneca. The programme is therefore independent; the content is not influenced by the supporter and is under the sole responsibility of the experts.

December 2023