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Supplementary information

Personalized intensification of treatment for hormone-sensitive prostate cancer

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Supplementary Table 1 | Ongoing trials in patients with mHSPC

Trial	Disease setting	Intervention	Control treatment	Primary end points	Selected secondary end points and other notes	Study ID
PEACE6-Poor Responders (phase III)	De novo mHSPC; PSA >0.2 ng/mL at 6–8 months ADT after initiation	[^{177}Lu]-PSMA-617 (up to 4 cycles) + SOC (ADT + ARPI ± RT ± docetaxel)	SOC (ADT + ARPI ± RT ± docetaxel)	OS, rPFS by PCWG3 criteria.	CRPC-FS, PCSS, PSA response, SRE-FS	NCT06496581
PSMAddition (phase III)	mHSPC; PSMA-positive disease by central reader	[^{177}Lu]-PSMA-617 (6 cycles) + SOC (ADT + ARPI)	SOC (ADT + ARPI)	rPFS	OS, PSA90 response, time to mCRPC, PFS, PFS2	NCT04720157
STAMPEDE2, arm P (phase III)	mHSPC; >5 metastases or SABR ineligible	[^{177}Lu]-PSMA-617, (on day 1 + day 8 for 3 cycles) + SOC (ADT + ARPI ± RT ± docetaxel)	ADT + ARPI ± docetaxel ± prostate RT	rPFS, OS	FFS, PCSS, QOL, safety, toxicity	NCT06320067
EORTC GUCG 2238 De-Escalate (phase III)	mHSPC; PSA ≤0.2 ng/mL after 6–12 months of ADT + ARPI	Intermittent therapy: no treatment until significant PSA increase, with ADT + ARPI treatment reinitiated at investigator discretion	SOC (continuous ADT + ARPI ± RT ± docetaxel)	Co-primary (hierarchical): proportion of patients who did not restart intermittent-ADT treatment at 1 year; and OS	Occurrence of adverse events, time spent on treatment, time to next systemic therapy, magnitude of change in HRQOL, PCSS	NCT05974774
PEACE6-Vulnerable (phase III)	De novo mHSPC, not receiving docetaxel or ARPI	ADT + darolutamide	ADT + placebo	rPFS by PCWG3 criteria	CRPC-FS, clinical PFS, OS, complete PSA response at 6 months	NCT04916613
Oligo-PRESTO (phase III)	Oligometastatic mHSPC (≤5 metastases)	SBRT to metastases + SOC (ADT ± ARPI ± docetaxel ± prostate RT)	SOC (ADT ± ARPI ± docetaxel ± prostate RT)	CRPC-FS	OS, PCSS, time to mCRPC, time to next symptomatic skeletal event at the treated metastatic bone sites	NCT04115007
LIBERTAS (phase III)	mHSPC; PSA <0.2 ng/mL after 6 months of ADT + apalutamide	Apalutamide + intermittent ADT	Apalutamide + continuous ADT	18-month rPFS, severity of adjusted hot flash score at 18 months	OS, PCSS, duration of time on ADT	NCT05884398
A-DREAM (phase II)	mHSPC and PSA ≥5 ng/mL pre-ADT and <0.2 ng/mL after 18–24 months of ADT + ARPI	Interrupt ADT + ARPI, with reinitiation upon PSA ≥5 ng/mL, radiographic change (by PCWG3), or cancer-related symptoms	NA (single group assignment)	Proportion of patients treatment-free at 18 months with eugonadal testosterone	Time to eugonadal testosterone level, duration off therapy, QOL (FACT-P)	NCT05241860
ASPIRE (phase III)	High-volume or de novo low-volume mHSPC (prior treatment with ADT ± ARPI permitted within 120 days of registration); candidates for docetaxel; available NGS results	ADT + apalutamide + docetaxel	ADT + apalutamide	OS	Stratified by TSG-altered status, defined by any copy-number loss or deleterious mutation in one or more of *TP53*, *PTEN* or *RB1*	NCT06931340

TRIPLE-SWITCH (phase III)	mHSPC; PSA ≥0.2 ng/mL at enrolment after receiving ADT for 6–12 months and an ARPI ≥4 months; candidates for docetaxel	ADT + ARPI + docetaxel	ADT + ARPI	OS	PSA progression, PSA response (PCWG3), PSA kinetics (PSA90, <0.2 ng/ml and <0.02 ng/ml) and clinical progression; plasma ctDNA also being collected for biomarker analysis at registration, cycle 2 of docetaxel, post cycle 6 docetaxel, and at progression)	NCT06592924
CAPItello 281 (phase III)	De novo mHSPC; PTEN loss on central IHC testing	ADT + abiraterone + prednisone + capivasertib	ADT + abiraterone + prednisone + placebo	rPFS	OS	NCT04493853
AMPLITUDE (phase III)	mHSPC; germline or somatic HRR deficiency	ADT + abiraterone + prednisone + niraparib	ADT + abiraterone + prednisone + placebo	rPFS	OS, symptomatic PFS, time to subsequent therapy	NCT04497844
TALAPRO-3 (phase III)	mHSPC; germline or somatic HRR deficiency	ADT + enzalutamide + talazoparib	ADT + enzalutamide + placebo	rPFS	OS, objective response in measurable soft tissue disease, PSA response, time to PSA progression	NCT04821622
EvoPAR-PR01 (phase III)	mHSPC; HRR-gene mutated or non-HRR-gene mutated	ADT + abiraterone + prednisone + saruparib	ADT + abiraterone + prednisone + placebo	rPFS	OS, PFS2, time to first subsequent therapy or death, SRE-FS, time to castration-resistance	NCT06120491

ADT, androgen-deprivation therapy; ARPI, androgen receptor pathway inhibitor; CRPC-FS, castration-resistant prostate cancer-free survival; ctDNA, circulating tumour DNA; FACT-P, Functional Assessment of Cancer Therapy – Prostate; FFS, failure free survival; HRQOL, health-related quality of life; HRR, homologous recombination repair; IHC, immunohistochemistry; mCRPC, metastatic castration-resistant prostate cancer; mHSPC, metastatic hormone-sensitive prostate cancer; NA, not applicable; OS, overall survival; PCSS, prostate cancer-specific survival; PCWG3, Prostate Cancer Working Group 3; PFS, progression-free survival; PFS2, progression-free survival 2 (time from initial treatment randomization to the progression of disease on a second-line therapy or death from any cause); PSA, prostate-specific antigen; PSA90, ≥90% decline in serum PSA level; QOL, quality of life; rPFS, radiological progression-free survival; SBRT, stereotactic body radiotherapy; SOC, standard of care; SRE-FS, skeletal-related event-free survival; TSG, tumour-suppressor gene.