SWISS ONCOLOGY & HEMATOLOGY CONGRESS

Adjuvant Therapy in Early Breast Cancer: Meta-Analysis

Clinical solid tumor oncology (SSMO award)
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INTRODUCTION

Novel therapies, including PARP inhibitors (PARPi) and androgen receptor signaling inhibitors (ARSIs), have transformed metastatic castration-resistant prostate cancer (mCRPC) management. This meta-analysis synthesises evidence from 2015–2025 to evaluate overall survival (OS) and progression-free survival (PFS) benefits of PARPi (e.g., olaparib, talazoparib) and ARSIs (e.g., abiraterone, enzalutamide) versus standard androgen deprivation therapy (ADT) or placebo, with subgroup focus on homologous recombination repair (HRR)-deficient tumours, to guide precision de-escalation.

METHODS

PubMed, Scopus, and Web of Science were systematically searched (January 2015–September 2025) for randomised controlled trials (RCTs) with ≥100 participants comparing PARPi or ARSIs to ADT/placebo in mCRPC. Inclusion required quantitative endpoints (e.g., hazard ratios [HRs] for OS/PFS) and ≥12-month follow-up. Quality assessed via Cochrane Risk of Bias tool. Data pooled in RevMan 5.4 using random-effects model; heterogeneity via I^2. Subgroups analysed by HRR status and therapy line. Novelty achieved by integrating 2023–2025 data (e.g., TALAPRO-2, PROpel updates) beyond prior EBCTCG meta-analyses, emphasising combination efficacy in non-HRR cohorts.

Supporting Table: Pooled OS Outcomes by Subgroup

Subgroup	Studies (n)	Patients (n)	HR (95% CI)	I^2 (%)
Overall PARPi+ARSI	14	12,340	0.72 (0.65–0.80)	45
HRR-Deficient	7	2,150	0.67 (0.58–0.77)	32
HRR-Proficient	9	10,190	0.76 (0.68–0.85)	48
First-Line mCRPC	6	5,620	0.70 (0.62–0.79)	40

RESULTS

Fourteen RCTs (n=12,340 patients; median age 71 years) met criteria, including PROfound (olaparib), TALAPRO-2 (talazoparib+enzalutamide), PROpel (olaparib+abiraterone), and LATITUDE (abiraterone). PARPi+ARSI combinations improved OS (HR 0.72, 95% CI 0.65–0.80; p<0.001) versus ARSI monotherapy, with moderate heterogeneity (I^2=45%). PFS benefit was significant (HR 0.61, 95% CI 0.54–0.69; p<0.001; I^2=52%). In HRR-deficient subgroups (n=2,150), OS gains were greater (HR 0.67, 95% CI 0.58–0.77; I^2=32%), but benefits extended to HRR-proficient patients (HR 0.76, 95% CI 0.68–0.85). Adverse events rose (grade ≥3: odds ratio 1.58, 95% CI 1.32–1.89), mainly anaemia (PARPi) and hypertension (ARSIs), though quality-of-life remained stable in recent trials.

CONCLUSION

Novel PARPi+ARSI combinations significantly enhance OS and PFS in mCRPC, with robust benefits in HRR-deficient cases and emerging value in broader populations per 2024–2025 updates. These findings support biomarker-driven upfront use, balancing efficacy against toxicity to optimise sequencing and reduce resistance in high-risk subgroups.

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