

Genomic Predictors of Overall Survival and PSA Response in PARP Inhibitor–Treated mCRPC: A Meta-Analysis from the PRECISION Registry

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Background: Outcomes in metastatic castration-resistant prostate cancer (mCRPC) vary substantially according to clinical and genomic characteristics. We evaluated the associations of genomic alterations and clinical factors with overall survival (OS) and prostate-specific antigen (PSA) response using data from the PRECISION real-world registry of patients with mCRPC treated with poly(ADP-ribose) polymerase inhibitors (PARPi).

Methods: Patient-level data from a multi-center real-world registry were analyzed, including demographic characteristics, clinical and treatment history, genomic alterations, and clinical outcomes. OS was defined as the time from PARPi initiation to death or last follow-up, and PSA response was defined as a confirmed $\geq 50\%$ decline from baseline PSA. BRCA alterations were defined as mutations in BRCA1 or BRCA2, while homologous recombination repair (HRR) alterations included mutations in BRCA1/2, ATM, BRIP1, CDK12, CHEK2, or PALB2. Within each study, Cox proportional hazards models were used to evaluate OS and logistic regression models were used to evaluate PSA response, with gene alterations treated as the primary exposures and adjustment for relevant clinical and treatment-history covariates. Study-specific estimates were subsequently combined using random-effects meta-analysis. Between-study heterogeneity was assessed using Cochran's Q test and the I^2 statistic.

Results: The combined dataset included 327 patients with mCRPC treated with PARPi. In the random-effects meta-analysis, BRCA alterations were associated with improved OS (HR 0.51, 95% CI 0.33–0.78) and an increased likelihood of PSA response (OR 3.58, 95% CI 1.83–6.99). Similarly, HRR alterations were associated with improved OS (HR 0.56, 95% CI 0.40–0.80) and increased odds of PSA response (OR 2.02, 95% CI 1.02–3.97). There was little evidence of substantial heterogeneity in effect estimates across studies.

Conclusions: BRCA and HRR alterations were associated with improved survival and PSA response among patients with mCRPC treated with PARPi. By synthesizing study-specific estimates, the meta-analytic approach provided an overall assessment of these associations, identifying significant pooled associations even when some individual study estimates were not statistically significant, while accounting for potential between-study heterogeneity.

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