

A SYSTEMATIC REVIEW OF COMBINED POLY (ADP-RIBOSE) POLYMERASE INHIBITOR AND ANDROGEN RECEPTOR ANTAGONISTS IN METASTATIC CASTRATION-RESISTANT PROSTATE CANCER

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Background and Importance



- Poly (ADP-ribose) polymerase inhibitors (PARPi) and androgen deprivation therapy (ADT) may have synergistic efficacy for metastatic castration-resistant prostate cancer (mCRPC) patients.
- The effectiveness of PARPi and ADT was highly depended on mCRPC patients' heterogeneous gene status.

Aim and Objectives

 To conduct a systematic review and metaanalysis to estimate effectiveness of PARP inhibitors combined with ADT versus standard



ADT in the mCRPC patients with homologous recombination repair (HRR) positive and negative.

Materials and Methods

- Study design: Systematic review of RCTs
- Database: PubMed, Embase, Cochrane
- Duration: 2009 to September 2023
- No Searching restrictions
- Two independent review authors
- Assessed risk of bias
- Outcomes among all patients, HRR+ and HRR-:
 - 1. Progression-free survival (PFS)
 - 2. Overall survival (OS)

Overall patients – PFS



Overall patients – OS

| Study or Subgroup | log[Hazard Ratio] SE | Weight | Hazard Ratio IV, Fixed, 95% Cl | Hazard Ratio IV, Fixed, 95% Cl |
|---|---|--------|---|-----------------------------------|
| Olaparib phase 2 2018 | -0.0943 0.2125 | 12.3% | 0.91 [0.60, 1.38] | |
| Olaparib phase 3 2023 | -0.1165 0.1299 | 32.9% | 0.89 [0.69, 1.15] | |
| Talazoparib phase 3 2023 | -0.2107 0.1006 | 54.8% | 0.81 [0.67, 0.99] | |
| Total (95% CI) | | 100.0% | 0.85 [0.73, 0.98] | • |
| Heterogeneity: Chi ² = 0.46, o Test for overall effect: Z = 2.2 | if = 2 (P = 0.80); I² = 0% 22 (P = 0.03) | | 0.1 0.2 0.5 1 2 5 10 Favours PARPi Favours placebo | |

Subgroup : HRR+ patients – PFS

| | | | | Hazard Ratio | Hazard Ratio |
|---|---------------------------|--------|--------|-------------------|-------------------|
| Study or Subgroup | log[Hazard Ratio] | SE | Weight | IV, Fixed, 95% Cl | IV, Fixed, 95% Cl |
| Niraparib phase 3 2023 | -0.3147 | 0.1353 | 69.0% | 0.73 [0.56, 0.95] | |
| Olaparib phase 2 2018 | -0.3011 | 0.5337 | 4.4% | 0.74 [0.26, 2.11] | |
| Talazoparib phase 3 2023 | -0.7765 | 0.2181 | 26.6% | 0.46 [0.30, 0.71] | |
| Total (95% CI) | | | 100.0% | 0.65 [0.52, 0.81] | • |
| Heterogeneity: Chi ² = 3.30, d | df = 2 (P = 0.19); I² = 3 | | | | |

A fixed-effects meta-analysis was applied to pool hazard ratio (HR) with 95% confidence intervals (Cls).

Test for overall effect: Z = 3.89 (P = 0.0001)

Favours PARPi Favours placebo

Subgroup : HRR- patients – PFS



Conclusion and Relevance

• The combination of PARPi and ADT in patients with mCRPC to significantly improved both progression-free survival and overall survival rates, especially for HRR+ patients.



