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PARP Inhibitor Resistance in Ovarian Cancer: Mechanisms, Biomarkers, and Therapeutic Strategies

M Akhila^{1}, D Vyshnavi Neela¹, B Dharani¹, P Prasanthi¹, Dr. Shaik Farahan Subahan²*

¹Pharm D, Vijaya Institute of Pharmaceutical Sciences for women, Vijayawada, Andhra Pradesh, India.

²Associate Professor, Department of Pharmacy Practice, Vijaya Institute of Pharmaceutical Sciences for women, Vijayawada, Andhra Pradesh, India.

[Email Id: serviceheb@gmail.com](mailto:serviceheb@gmail.com)

ABSTRACT

Ovarian cancer remains a leading cause of gynecologic cancer mortality, largely due to the development of treatment resistance. Poly(ADP-ribose) polymerase (PARP) inhibitors have transformed the management of homologous recombination-deficient tumors, particularly those harboring BRCA mutations. However, both intrinsic and acquired resistance limit their long-term clinical benefit. This review summarizes key DNA damage repair pathways in ovarian cancer, the biological role of PARP enzymes, and the mechanistic basis of PARP inhibitor activity. We comprehensively discuss emerging molecular mechanisms of resistance, including restoration of homologous recombination, replication fork protection, and chromatin remodeling. Finally, we highlight biomarkers, combination strategies, and future precision-based approaches aimed at overcoming resistance and improving durable outcomes in ovarian cancer patients.

Keywords: Ovarian cancer; PARP inhibitors; Treatment resistance; DNA damage response; Homologous recombination deficiency; BRCA mutations; Replication fork protection; Precision oncology.

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