Int. J. Sci. R. Tech., 2025 2(8)
A Multidisciplinary peer-reviewed Journal
www.ijsrtjournal.com [ISSN: 2394-7063]

Original Article

Olaparib: A Magic Bullet in the Treatment of Ovarian Cancer

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ABSTRACT

Olaparib is an anti-cancer medication that belongs to the class of N-acyl piperazines. Olaparib works by inhibiting PRPA. Medication that is administered orally and starts working one to three hours after intake. The FDA has approved this medication for the treatment of ovarian, breast, prostate, and pancreatic cancers, among other cancers. Additionally helpful for several mutation problems, including the BRCA1/2 mutation, is olaparib. Olaparib is prescribed either alone or in combination following chemotherapy. Combination therapy is utilised in severe and advanced mutation disorders. We included narrative information about the action, treatment strategies, pharmacokinetics, dosage schedule, and resistance in this review paper. Here, we provide a brief overview of olaparib resistance mechanisms and treatment strategies for prostate, breast, and ovarian cancer.[1-4].

Keywords: Olaparib, anti-cancer, Treatment, Ovarian Cancer

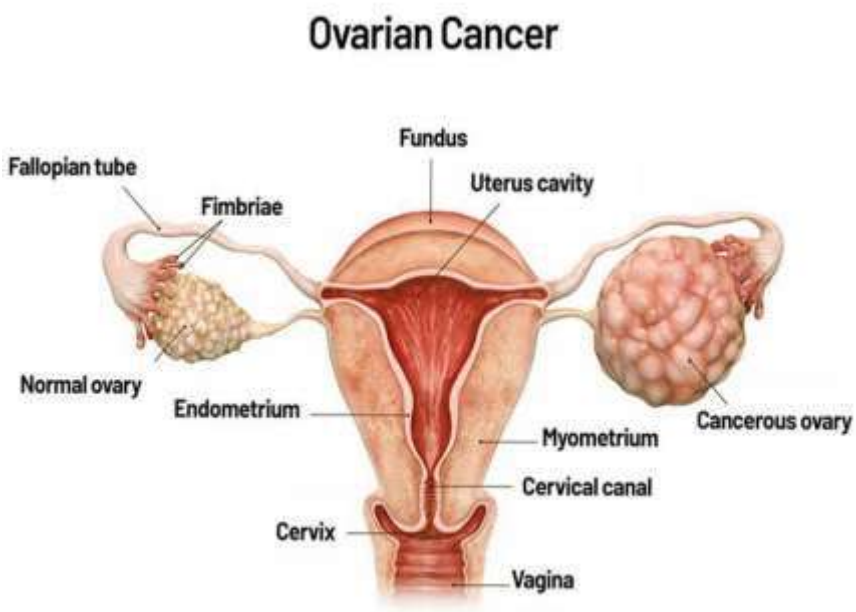
INTRODUCTION

In June 2014, the USFDA advisory committee sanctioned the accelerated approval of olaparib. In December 2014, the USFDA approved olaparib for the treatment of advanced ovarian cancer. In August 2017, olaparib was approved for the maintenance treatment of ovarian cancer. In January 2018, it was approved for use in metastatic breast cancer with germline BRCA mutations. In December 2018, the USFDA approved olaparib for maintenance treatment in BRCA-mutated advanced ovarian cancer in the first-line setting. In December 2019, olaparib was approved for use as first-line maintenance treatment in metastatic pancreatic cancer with germline BRCA mutations. In May 2020, it was approved as maintenance treatment for homologous recombination deficiency-positive advanced ovarian cancer in the first-line setting in combination with bevacizumab and as a single agent for metastatic castration-resistant prostate cancer with mutations in the homologous recombination repair genes. [5]

OVARIAN CANCER

DNA mutations that allow cells to grow and proliferate quickly, eventually resulting in a tumour, are the first step in the development of ovarian cancer, a disease in which malignant cells grow in the ovaries. These cancerous cells can infiltrate adjacent tissues and travel to different bodily areas. The type of ovarian cancer and the available treatments are determined by the type of cell from which the cancer starts. A malignant growth in one or both ovaries is known as ovarian cancer. Although there are many different kinds of ovarian cancer, the three most prevalent ones are the common epithelial type, which develops from the cells outside the ovary in 90% of cases; the germ cell type, which develops from the cells that produce eggs in 4% of cases; and the uncommon stromal type, which develops from the ovary's supporting tissues.

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.



CAUSES

- Age (risk increases for women over 50)
- Family history of ovarian cancer
- Changes in the genes BRCA1 or BRCA2
- Early onset of periods (before 12 years) and late menopause
- women who have not had children or had their first child after the age of 35
- Using oestrogen-only hormone replacement therapy or fertility treatment

SYMPTOMS

- Abdominal bloating.
- Difficulty eating or feeling full quickly.
- Frequent or urgent urination.
- Back, abdominal, or pelvic pain.
- Constipation or diarrhoea.
- Menstrual irregularities.
- Tiredness.
- Indigestion.

DIAGNOSIS

1. Physical examination

It involves the doctor checking your abdomen for lumps and performing an internal vaginal examination.

2. Blood tests

Blood tests are performed to check for CA125, a common tumour marker for ovarian cancer.

3. Pelvic ultrasound

Pelvic ultrasound is used to create an image of your ovaries and uterus using echoes from sound waves.

4. CT scan

A CT scan uses X-rays to take images of your inside body to check for cancer and determine whether it has spread.

5. PET scan

A PET scan identifies abnormal tissues in the body. A colonoscopy is for bowel problems.

Merits and Demerits of Api Merits

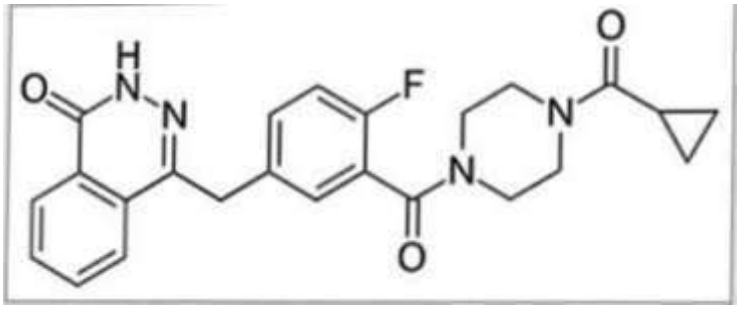
- Easy integration
- Save time and effort
- Automation
- Scalability
- Platform friendly

Demerits

- Security risks
- Hard to understand
- Depends on others
- Needs maintenance
- Can be slow

PHARMACOGENOMICS

Pharmacogenomics is the study of how a person's genes influence how they react to medications. In order to create safe, efficient treatments that may be administered based on a person's genetic composition, this field integrates pharmacology, the science of drugs, and genomics, the study of genes and their roles. The study of pharmacogenomics examines how a person's genetic composition may impact how their body metabolises specific drugs. Genetic testing is used to check for alterations in particular genes. The science of pharmacogenomics is expanding quickly.



Structure

Brand Names: Lynparza Generic Name: Olaparib

Drug class: antineoplastic, poly (ADP-ribose), polymerase (PAPR)inhibitor Drug Bank Accession Number: DB09074

Physicochemical Properties

Property	Value
Appearance	White to off white Solid
Solubility	Slightly soluble in water; soluble in DMSO, methanol, and ethanol.
Melting point	~196 – 196°c
Log P (partition coefficient)	~2.4
Pka	13.2 (weakly basic)
Hydrogen bond Donors	1

BCS Classification

In the Biopharmaceutical classification system, the Olaparib drug is classified as class IV due to its low solubility and bioavailability using a solid nanoemulsifying drug delivery system.

Class I High solubility High permeability	**Class II** Low solubility High permeability
Class III High solubility Low permeability	**Class IV** Low solubility Low permeability

• **Cmax (Maximum Plasma Concentration):**

The Cmax of Olaparib typically occurs about 2 to 3 hours after oral administration of a dose.

• **Tmax (Time to Reach Maximum Concentration):**

Tmax for Olaparib is generally around 2 to 3 hours post-dose.

• **Half-life:**

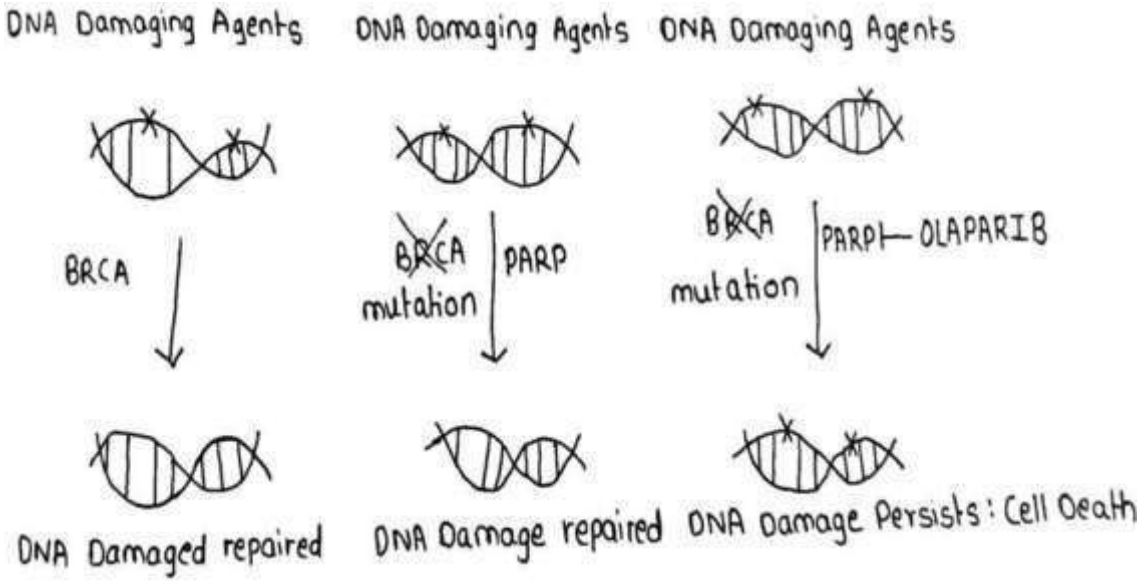
In patients with cancer, the mean half-life was 6- 10 hours. [6]

- Absorption: Olaparib is rapidly absorbed when ingested orally. Olaparib achieves peak plasma concentrations between 1 and 3 hours after administration. Fatty food can decrease the rate of absorption of olaparib but does not affect the systemic exposure. [7] The effect of food on olaparib pharmacokinetics is not deemed clinically significant. [8]

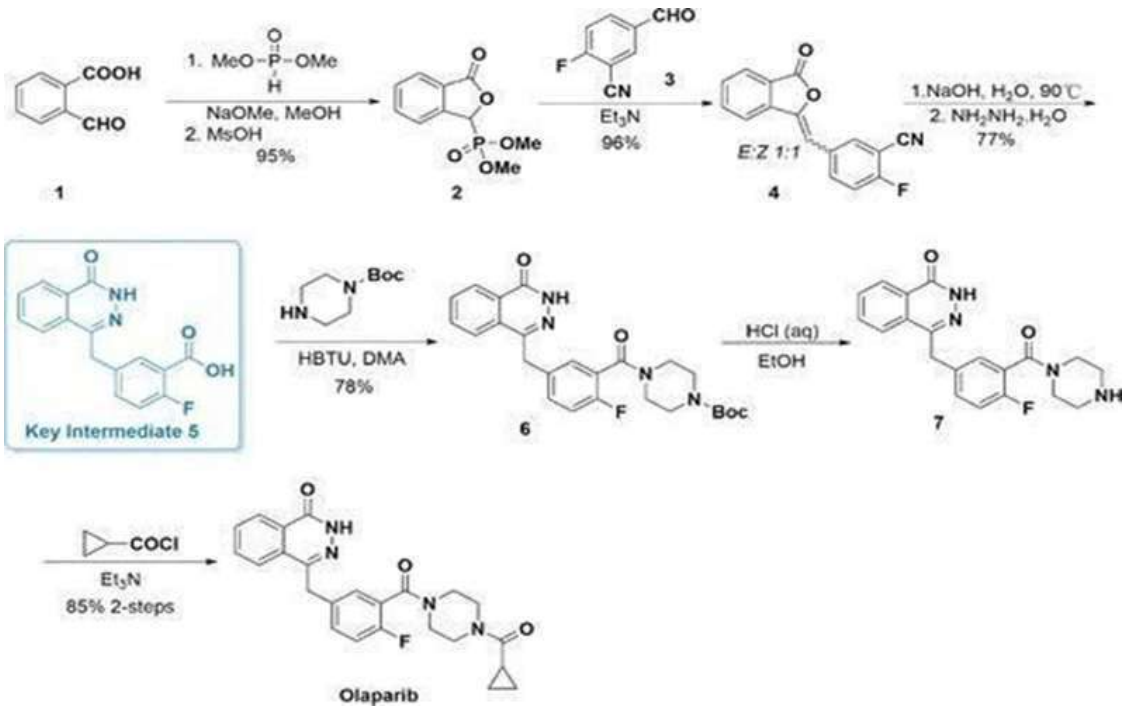
- Distribution: 82% of the Olaparib drug binds to the plasma proteins. Steady-state blood levels are achieved in 3–4 days with daily dosing.
- Metabolism: Olaparib is metabolized in the liver by the cytochrome P450 3A4 (CYP3A4) microsomal enzymes. The drug is largely metabolized by oxidation reactions, with several of the metabolites subsequently undergoing glucuronide or sulfate conjugation. The half-life of olaparib is 5–7 hours. [18] A Phase I study showed that the mean maximal extent of PARP inhibition in the mononuclear cells of the peripheral blood was 50.6% and in the tumor tissue was 70%. [9] Around 90% of the drug is excreted, 42% in the feces and 44% in the urine, mainly in the form of metabolites.
- Route of elimination: About 44% of the drug was excreted via the urine, and 42% of the dose was excreted via the feces. Following an oral dose of radiolabeled olaparib to female patients, the unchanged drug accounted for 15% and 6% of the radioactivity in urine and feces, respectively.

MECHANISM OF ACTION

Olaparib functions as an inhibitor of poly (ADP-ribose) polymerase (PARP) enzymes, specifically targeting PARP1, PARP2, and PARP3. These enzymes are essential components of the nucleotide base excision repair pathway, which is responsible for the repair of single-strand DNA breaks. [10,11] Inhibition of PARP compromises this repair Mechanism, resulting in the accumulation of single-strand breaks that subsequently progress to double-strand DNA breaks. Double-strand breaks are typically repaired through homologous recombination or non-homologous end joining. However, in tumors exhibiting homologous recombination deficiency—such as those harboring BRCA1 or BRCA2 mutations [12,13]—PARP inhibition prevents effective DNA repair. This ultimately leads to cell death, a process known as synthetic lethality. [14,15] Furthermore, the suppression of PARP enzymatic activity, along with the increased formation of PARP-DNA complexes, contributes to cytotoxicity and enhances the antitumor efficacy of olaparib.



Synthesis of Olaparib



MEDICINAL USE

1. Ovarian Cancer: Maintenance therapy for recurrent ovarian cancer.
2. Breast Cancer: Treatment of HER2-negative metastatic breast cancer with germline BRCA1/2 mutations.
3. Pancreatic Cancer: Maintenance therapy for metastatic pancreatic cancer with germline BRCA mutations.
4. Prostate Cancer: Treatment of metastatic castration-resistant prostate cancer.

ADVERSE EFFECTS

1. Anemia
2. Neutropenic
3. Nausea
4. Vomiting
5. Liver Toxicity
6. Skin rashes
7. Dizziness
8. Hypothyroidism

TREATMENT OF OVERDOSE

1. Immediate Medical Attention: The patient should be evaluated promptly in a healthcare setting.
2. Monitoring: Continuous monitoring of vital signs and organ function is essential. Particular attention should be given to hepatic, renal, and hematological parameters due to olaparib's known adverse effects.
3. Supportive Care: Administer intravenous fluids if necessary to maintain adequate hydration and renal perfusion.
4. Activated Charcoal: If the overdose is recent (within 1–2 hours), administration of activated charcoal may be considered to limit further absorption, depending on clinical judgment.
5. Dialysis: Olaparib is highly protein-bound (~82%) and has a relatively large volume of distribution, making dialysis unlikely to be effective in significantly removing the drug from systemic circulation

CONTRAINDICATIONS

1. Hypersensitivity: Olaparib is contraindicated in individuals with known hypersensitivity to the active pharmaceutical ingredient or any of its excipients.
2. Myelodysplastic Syndrome (MDS) and Acute Myeloid Leukemia (AML): The use of olaparib is contraindicated in patients diagnosed with MDS or AML due to the risk of exacerbating these hematological malignancies.
3. Severe Renal Impairment: Olaparib is contraindicated in patients with severe renal impairment, defined as a creatinine clearance of

less than 30 mL/min, owing to altered drug clearance and potential toxicity.

4. Severe Hepatic Impairment: The use of olaparib is contraindicated in individuals with severe hepatic impairment, classified as a Child-Pugh score greater than 8, due to the potential for increased systemic exposure and adverse effects.
5. Pregnancy and Lactation: Olaparib is contraindicated during pregnancy and breastfeeding, as it may pose a risk of teratogenicity or other harmful effects to the fetus or nursing infant.
6. Severe Hepatic Impairment: The use of olaparib is contraindicated in individuals with severe hepatic impairment, classified as a Child-Pugh score greater than 8, due to the potential for increased systemic exposure and adverse effects.
7. Pregnancy and Lactation: Olaparib is contraindicated during pregnancy and breastfeeding, as it may pose a risk of teratogenicity or other harmful effects to the fetus or nursing infant.

INTERACTION

1. Abametapir + Olaparib

The serum concentration of Olaparib can be increased when it is combined with Abametapir.

2. Abetacept +Olaparib

The metabolism of Olaparib can be increased when combined with Abatacept.

3. Acetyl Salicylic acid + Olaparib

The risk of bleeding can be increased when Acetyl salicylic acid is combined with Olaparib.

Conventional Marketed Formulation

1. Tablets: Olaparib tablets are available in 100mg and 150mg strengths, manufactured by AstraZeneca. The dose is about 300mg twice daily.
2. Casule: capsule formulation has been replaced by the tablet formulation due to improved bioavailability and reduced pill burden.

Novel Marketed Formulation

1. Tablets

Brand name: Lynparza Company: AstraZeneca

Dosage: 100 mg and 150 mg tablets 2. Capsules

Brand name: Lynparza Company: AstraZeneca Dosage: 50mg capsules

Patents

Drug used in	Drug patent number	Drug patent title	Drug patent expiry	Drug owner
Lynparza	US11970530	Methods of treating homologous Recombination-deficient cancer	October 25, 2041	AstraZeneca
Lynparza	US8859562	Use of RNAI inhibiting PARP activity for the manufacture of a medicament for the treatment of cancer	August 04, 2031	AstraZeneca
Lynparza	US8247416	pathalazinone derivative	September 24, 2028	AstraZeneca
Lynparza	US8071579	DNA damage repair inhibitors for the treatment of cancer	August 12, 2027	AstraZeneca

CONCLUSION

Olaparib represents a significant advancement in targeted cancer therapy, particularly for patients with BRCA1/2 mutations and homologous recombination deficiency. Its mechanism of action through PARP inhibition enables synthetic lethality in tumor cells with impaired DNA repair pathways. Olaparib has demonstrated efficacy in the treatment of various malignancies, including ovarian, breast, prostate, and pancreatic cancers, and is used either as monotherapy or in combination with chemotherapy, especially in advanced or mutation-driven cases. Understanding the pharmacokinetics, appropriate dosing strategies, and resistance mechanisms is crucial for optimizing therapeutic outcomes. Ongoing research into combination treatments and resistance management continues to enhance the clinical utility of olaparib in personalized cancer care. [16]

REFERENCE

1. Robson, M. L., Senkus, E., Olaparib for Metastatic Breast Cancer in Patients with a Germline BRCA Mutation. New England Journal of Medicine, (2017),377(6),523-533
2. Moore, K., Colombo, N., Scambia, G. Maintenance Olaparib in Patients with Newly Diagnosed Advanced Ovarian Cancer. New England Journal of Medicine, (2018)379(26),2495-2505
3. De Bono, J., Mateo, J., Fizazi, K. Olaparib for Metastatic Castration-Resistant Prostate Cancer. New England Journal of Medicine, (2020),382(22),2091-2102.
4. Golan, T., Hammel, P., Reni, M., Maintenance Olaparib for Germline BRCA-Mutated Metastatic Pancreatic Cancer. New England Journal of Medicine, (2019)381(4),317-327.
5. Ledermann, J, Harter, P., Gourley, C. Olaparib maintenance therapy in platinum-sensitive relapsed ovarian cancer. Lancet Oncol, (2014)15(8),852-861.
6. Rottenberg S., Jaspers, JE., Kersbergen, A. Van der Burg, E., Nygren, A., Zander, S.A., High sensitivity of BRCA1-deficient mammary tumors to the PARP inhibitor AZD2281 alone and in combination with platinum drugs. Proc Natl Acad Sci USA. (2008),105:17079-84.
7. Rolfo, C., Swaisland, H., Leunen, K., Rutten, A., Soetkouw, P., Salter, S. Effect of the food on the pharmacokinetics of olaparib after oral dosing of the capsule formulation in patients with advanced solid tumours. Adv Ther. (2015),32:510-22.
8. Bundred, N., Gardovskis, J., Jaskisewicz, J., Eglitis, J., Paramonov, V., McCormack, P. Evaluation of the pharmacodynamics and pharmacokinetics of the PARP inhibitor Olaparib: A Phase I multicentre trial in patients scheduled for elective breast Cancer surgery. Invest New Drugs. (2013),31:949-58.
9. Chen, Y., Zhang, L., Hao Q: Olaparib: a promising PARP inhibitor in ovarian cancer therapy. Arch Gynecon Obstet(2013) Aug, 288(2):367-74.
10. Rouleaux, M., Patel, A., Hendzen, MJ., Kaufmann, SH., Poirier, GG. PARP inhibition: PARP1 and beyond. Nat Rev Cancer. (2010),10:293-301
11. Baute, J., Depicker, A. Base excision repair and its role in maintaining genome stability. Crit Rev Viochem Mol Biol. (2008),43:239-76.
12. Gudmundsdottir, K., Ashwirth, A. The roles of DRCA1and DRCA2 and associated proteins in the maintenance of genomic stability, Oncogene. (206),25:5864-74.
13. McCabe, N., Turner, NC., Lord, CJ., Kluzek, K., Bialkowska, A., Swifp,S. Deficiency in the repair of DNA damage by homologous recombination and sensitivity to poly (ADP-ribose) polymerase inhibition Cancer Res. (296),66:8109-15
14. Ashworth, A. A synthetic lethal therapeutic approach: Poly (ADP) ribose polymerase inhibitors for the treatment of cancer deficient in DNA double-strand break repair. J. Clin Oncol. (2008),26:3785-90.
15. Nijman, SM. Synthetic lethality: General principles, utility and detection using genetic screens in human cells FEBS Lett. (2011),585:1-6.
16. Robson, M., Im, S.A., Senkus, E., Olaparib for Metastatic Breast Cancer in Patients with a Germline BRCA Mutation. New England Journal of Medicine. (2017),377(6),5023-533.

HOW TO CITE: Javane Nalini, Bhagyashri Randhawan*, Chaudhari Gauri, Damale Anjali, Munot Navinya, Mule Gayatri, Bhavar Pradnya, Maske Vaibhavi, Olaparib: A Magic Bullet in the Treatment of Ovarian Cancer, Int. J. Sci. R. Tech., 2025, 2 (8), 361-367. https://doi.org/10.5281/zenodo.16917622