

Exploring the Role of PARP Inhibitors in Ovarian and Endometrial Cancers

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Abstract

endometrial cancers, particularly in patients with specific genetic vulnerabilities. This article explores the mechanisms of action of PARP inhibitors, emphasizing their role in exploiting defects in DNA repair pathways, such as those seen in BRCA1 and BRCA2 mutations. In ovarian nonmalignant conditions, PARP inhibitors are used as adjuvant therapies to enhance treatment outcomes, as well as stratification in clinical trials.

As the understanding of tumor biology evolves, the integration of PARP inhibitors into personalized treatment regimens holds promise for improving patient outcomes in gynecologic malignancies. This review highlights the current state of application.

Introduction

PARP is an enzyme that plays a critical role in the repair of single-strand DNA breaks through the base excision repair pathway. In cancer cells with mutations in genes responsible for homologous recombination repair, such as BRCA1 and BRCA2, the inhibition of PARP leads to the accumulation of DNA damage, resulting in cell death. The concept of synthetic lethality is central to the therapeutic efficacy of PARP inhibitors.

Mechanism of Action

When PARP is inhibited in cancer cells already compromised by BRCA mutations or other defects in homologous recombination repair, the cells cannot adequately repair DNA breaks. This leads to:

- Accumulation of DNA Damage:** As DNA damage accumulates, the cancer cells become unable to survive.
- Cellular Senescence or Apoptosis:** The inability to repair DNA triggers cellular senescence (a state of permanent cell cycle arrest) or programmed cell death (apoptosis).

PARP Inhibitors in Ovarian Cancer

Ovarian cancer, particularly high-grade serous ovarian cancer, is associated with mutations in the BRCA genes [2-5]. The following PARP inhibitors have been approved for use in ovarian cancer:

Key PARP Inhibitors

Olaparib (Lynparza):

- Indications:** Approved for the maintenance treatment of patients with recurrent ovarian cancer who have received at least two prior lines of chemotherapy and have BRCA mutations. It is also used

PARP Inhibitors in Endometrial Cancer

While the role of PARP inhibitors in endometrial cancer is less established than in ovarian cancer, recent studies indicate potential efficacy, particularly in specific subtypes:

Target Populations

Lynch Syndrome:

- Patients with Lynch syndrome often exhibit mismatch repair deficiency, making them candidates for PARP inhibitor therapy [6,7]. Early studies have suggested that these patients may benefit from PARP inhibition, especially when the tumors also exhibit HRD.

HRD-Positive Endometrial Cancer:

- Emerging evidence indicates that patients with HRD-positive endometrial tumors, regardless of BRCA status, may respond to PARP inhibitors. Clinical trials are underway to assess the effectiveness of PARP inhibitors in these populations.

Ongoing Research