International Journal of Pharmaceutical research and Applications
Volume 8, Issue 5, Sep.-Oct. 2023, pp: 1711-1718 www.ijprajournal.com ISSN: 2456-4494

Role of PARP INIBHITORS on Ovarian Cancer Treatment

Bhumika Thakur*[1], Krititka Thakur[1], Reena Kumari[1], Manisha[1]
Shiva Institute of B. Pharmacy, Bilaspur, India

Date of Submission: 27-10-2023 Date of Acceptance: 08-11-2023

ABSTRACT
Poly-ADP-ribose polymerase (PARP) inhibitors typically exhibit an efficient response over this lethal disease that is ovarian cancer in females worldwide. These novel classes of medication target tumors with minor defects within the DNA repair pathways. Ovarian cancer disorders are majorly affected by the treatment process of these selective inhibitors. There are different kinds of novel PARP inhibitors but selective inhibitors like rucaparib, olaparib, and niraparib are undoubtedly the foremost used inhibitors in managing this infectious disease. For a more satisfactory clinical response, there is keenly a distinct need to typically achieve clinical improvements in these inhibitors types. Novel PARP inhibitors are one of the foremost used treatment processes in efficiently handling typical patients suffering terribly from ovarian cancer.

KEYWORDS: PARP inhibitors, Ovarian Cancer, High-Grade Serous Carcinomas, BRCA Gene.

I. INTRODUCTION

In properly treating ovarian cancer we primarily use Poly-ADP-ribose polymerase inhibitors (PARP). When selective PARP inhibitors combined with other agents may overcome resistance mechanisms[1]. Novel PARP inhibitors were typical of distinct types that were prominently used in the effective treatment of ovarian cancer, Olaparib, Niraparib, rucaparib, DNA(Deoxyribo nucleic acid) repair defects were caused by specific BRCA genes (Breast Cancer Gene) mutations. The key source for cell death was due to breakage in DNA strands, caused by selective PARP inhibitors leading synthetic lethality[2]. Inadequate or defective DNA repair by homologous recombination pathway leads to the selective activation of specific PARP inhibitors in that particular cell. DNA repair or DNA repair pathways typically provide the crucial grounds for typically triggering various cancers and to cope adequately with these humanitarian problems. Ovarian cancer needs improved medical results, acquired only by typically practicing targeted therapies[3].

II. MECHANISM OF ACTION OF PARP INHIBITORS:

PARPs are a typical family of 17 nucleoproteins, in which most PARP members could transfer only a mono-ADP ribose (mono-Adinosine Diphosphate Ribosylation) group to their target protein. While others just added repeated ADP-ribose units, thus generating long PARP chains [4, 5]. Its insidious nature and ineffectiveness of screening tests for early detection, EOC (Epithelial ovarian cancer) was undoubtedly the most lethal gynecological disease[6]. PARP inhibitors were the most active therapies approved for typically treating epithelial ovarian cancer[7]. Understanding cancer genome and complex cancer development process led to considerable variation in its treatment processes and, molecular alteration of its possible pathways was directly targeted. A specific capability that helps to accurately differentiate between a typical cell and tumor cell and tumor cell naturally provides the potential to typically mark or target the tumors cells. Novel PARP inhibitors typically serve as the leading illustration of this specific mechanism[8].

International Journal of Pharmaceutical research and Applications
Volume 8, Issue 5, Sep.-Oct. 2023, pp: 1711-1718 www.ijprajournal.com ISSN: 2456-4494

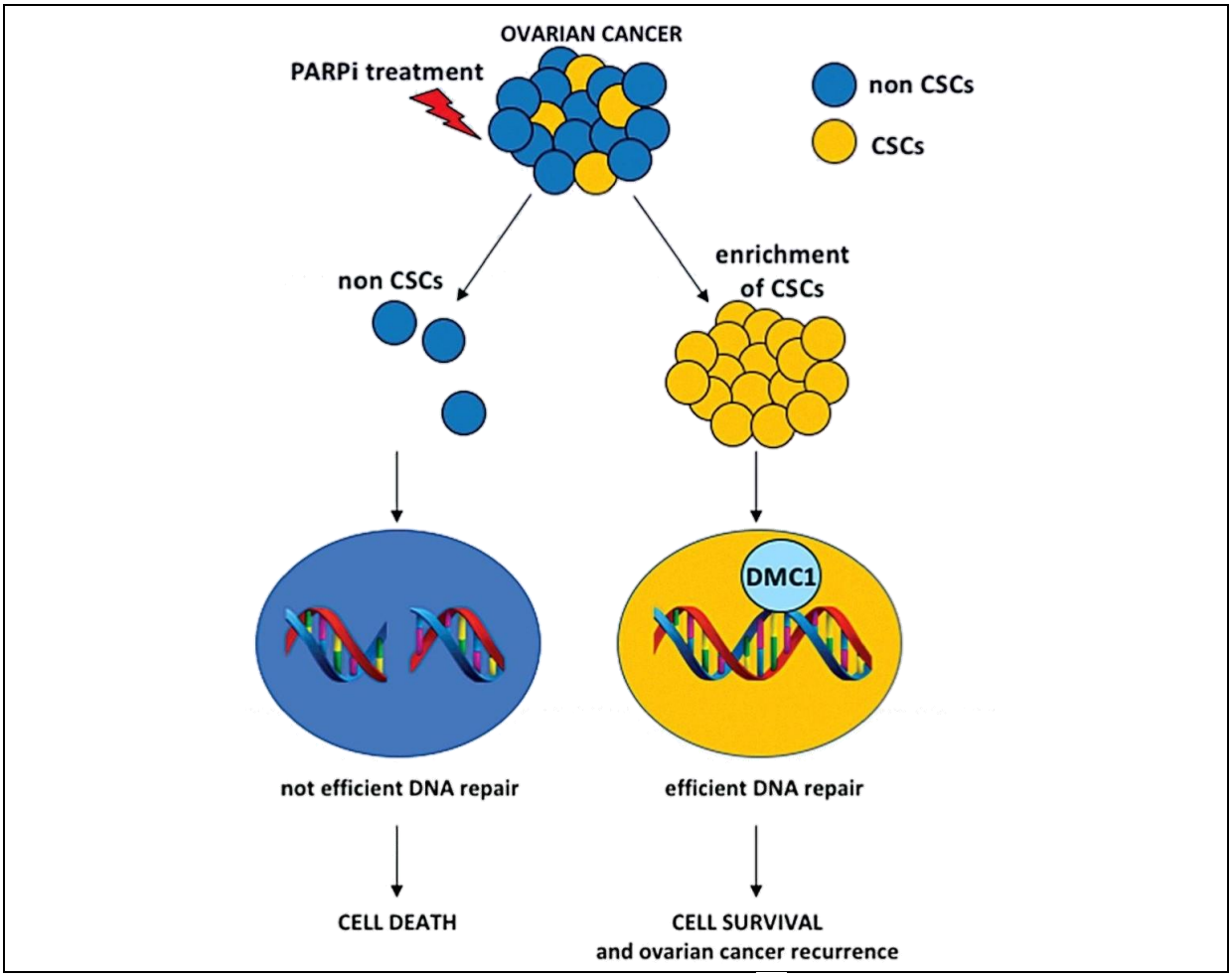

Fig. 1: Mechanism of action of PARP inhibitors [4]

According to Sir Spencer Wells I n 1872 ovarian surface epithelial (OSE) cells naturally stimulate ovarian cancer which rests controversial for more than a millennium. Dubeau in 1999 discarded the prevailing theory provided by wells and stated that secondary Mullerian tract structures were responsible for specific cancer. Several published observations over the last decade had typically shown that considering ovarian cancer as a single disease entry was unsuitable. Cancerous tumors at the distal end of the fallopian tube were typically obtained from BRCA1 and BRCA2 mutation carriers, in prophylactic salpingectomy specimen [9].

Ovarian cancer was critically the biggest prevailing cancer in females and over two hundred thousand new patients were detected every twelve months worldwide [10].Ovarian cancer was one of the most crucial causes of confirmed fatality in females. However, various critical advances and doctoral researches in this specialized field had typically prevented and eliminated this infectious disease a lot [11].There were typically two main genes responsible for abundantly showing their impact over ovarian cancer, these responsible genes were BRCA1 (breast cancer gene 1) and BRCA2 (breast cancer gene 2). Rather than intentionally causing ovarian cancer, these genes help in typically preventing this fatal disease. To promptly suppress the uncontrolled growth of the cancerous tumor, they instantly restore the damaged DNA. However, in some unfortunate cases, these specific genes did not behave correctly because of specific gene mutation which triggers cancer [12].

III.PATHOPHYSIOLOGY OF OVARIAN CANCER:

International Journal of Pharmaceutical research and Applications
Volume 8, Issue 5, Sep.-Oct. 2023, pp: 1711-1718 www.ijprajournal.com ISSN: 2456-4494

Ovarian cancer was one of the most vulnerable cancers in females. Epithelial ovarian cancer (EOC) accounts for the maximum number of ovarian cancers. Ovarian cancer was heterogeneous. Infectious cancer of the fallopian tube and peritoneal tube were typically considered as one specific entity for treatment purposes in ovarian cancer. Scientifically based on the onset of the typical cell, Epithelial, stromal and germ cell cancer were undoubtedly three possible classifications for ovarian cancer. There correctly was no exact clarification on the cellular origin or the exact etiology of epithelial ovarian cancer, while epithelial ovaria n cancer was complex or multifactorial process development[13]. According to recent studies, High-grade serous carcinomas (HGSC) typically arise in the epithelium of the distal fallopian tube, with serous tubal intraepithelial carcinomas (STICs). The possible outcome of standard subtypes Endometrioid and clear cell carcinoma was adequately reduced by the salpingectomy method. A salpingectomy significantly reduces the adverse impact of ovarian cancer subtype incidences[14].

The most general malignant condition in females was ovarian cancer. Menstruation, hormonal balance, bone metabolism, and fertilization were typically organized by a specific organ appropriately called the ovary. Various investigations on ovarian cancer have undoubtedly provoked us to typically discover various key factors naturally leading to the frequent occurrence of these specified types of infectious diseases. Germ cell tumors, sex-cord stromal tumors, and epithelial tumors were developed in ovarian neoplasm and scientifically studied with tumors of other organs[15].

Ovarian cancer typically refers to a diverse group of malignancies adversely affecting the ovary. Epithelial cells, sex cord-stromal cells, germ cells were three specific cell types that had typically developed ovarian tumors. Ovarian cancer after proper diagnosis was further classified into various specific stages to precisely calculate their fetal rate; these specific stages were namely Stage I, Stage II, Stage III and Stage IV. These specific stages properly inform us about how far the discovered tumor had naturally extended from the ovary to other essential parts of the human body. According to official WHO guidelines, these cancerous tumors were primarily of eight histological subtypes; serous, mucinous, endometrioid, clear cell, transitional cell, squamous cell, mixed epithelial and undifferentiated. Among these eight, three most common were serous, endometrioid, and mucinous; in which serous tumor typically resembles fallopian tube epithelium, endometrioid tumor typically resembles the endometrial gland, and mucinous tumor typically resembles endocervical epithelium[16].

IV. MACROSCOPIC AND MICROSCOPIC FEATURES OF THE OVARY:

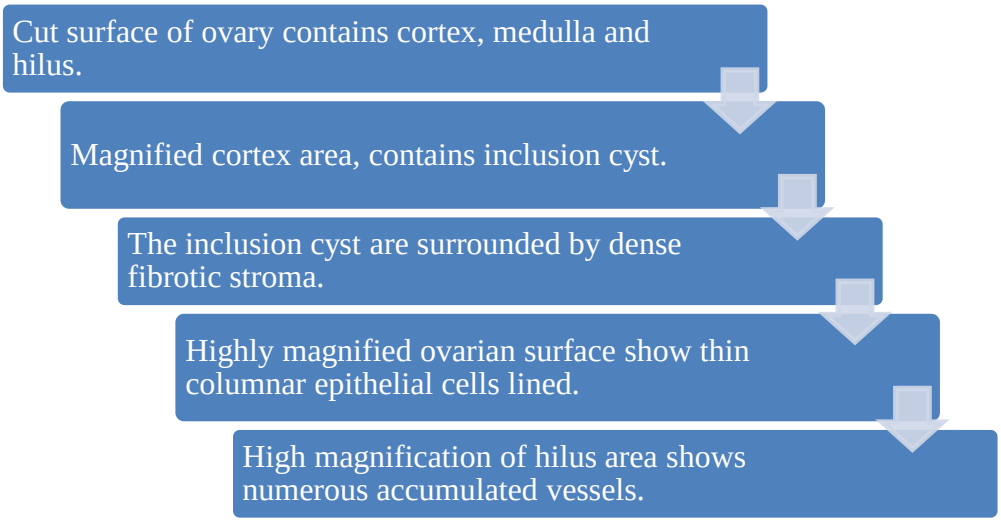

Fig. 2: Flowchart on macroscopic features of ovary

International Journal of Pharmaceutical research and Applications
Volume 8, Issue 5, Sep.-Oct. 2023, pp: 1711-1718 www.ijprajournal.com ISSN: 2456-4494

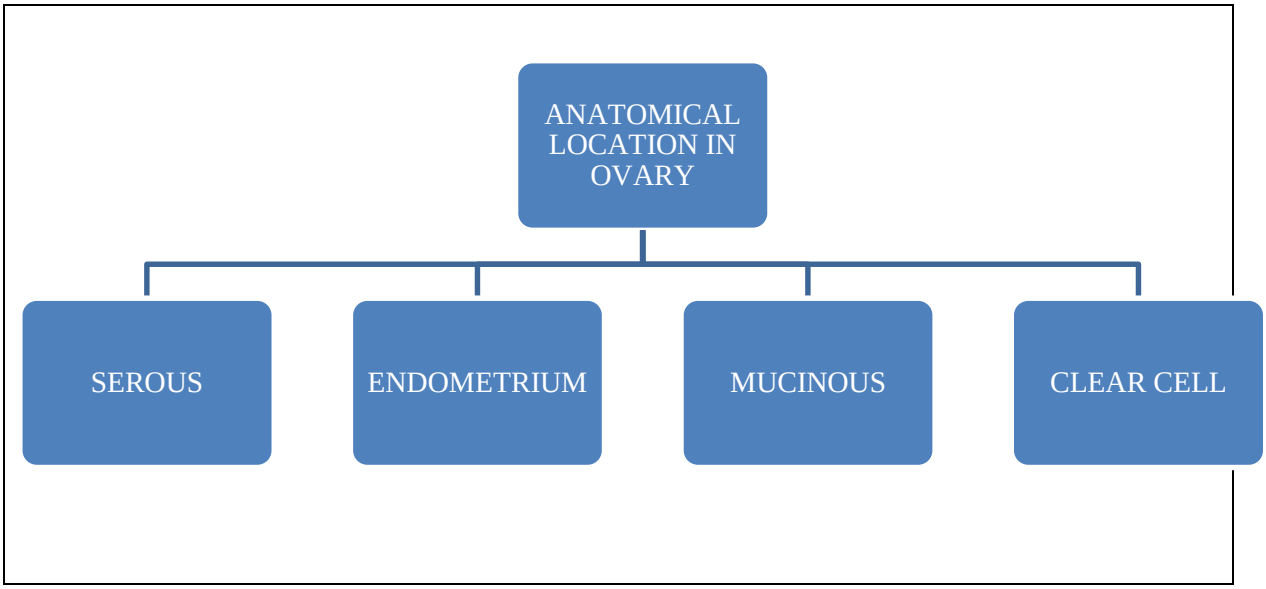

Fig. 3: Flowchart on anatomical locations in the ovary

The above flowchart typically indicates some of the common subtypes of histological tumors that were endometrioid, serous, mucinous, clear cell. There were major differences between these subtypes showing different tumor behavior, clinical outcome, and incidence[17].

Hormones or hormonal therapy was typically used to treat or eliminate ovarian cancer. It was typically an effective treatment of addition, blocking and removal of responsible hormones. Cell action and growth were typically some of the body functions precisely controlled by hormones present in our body.

V. HORMONES USED IN HORMONAL THERAPY:

Luteinizing hormone release hormone (LH RH) agonist which helps in lowering estrogen levels in women who had not reached menopause. LHRH typically includes goserelin (Zoladex), and leuprolide (Lupron, Lupron Depot, Eligard). Anti-estrogen blocks hormones like estrogen from naturally entering the cancer cell. Tamoxifen (Nolvadex, Tamofen) was typically used to treat cancer. Aromatic inhibitors used to block aromatase enzymes which turn other hormones into estrogen. It carefully lowers the level of estrogen. It typically includes; letrozole (Femara) , anastrozole (Arimidex) , exemestane (Aromasin)[18]. Specific drugs involved in the novel therapy typically comprise a possible combination of carboplatin plus paclitaxel as a preferred regime. Cisplatin plus paclitaxel was another combination dosage form with a similar effective response as indicated by carboplatin plus paclitaxel but typically produce a more toxic profile. To reduce the risk of neurotoxicity, a 24-hour infusion of paclitaxel should be properly administered if treatment was typically performed in a possible combination with cisplatin[19].

Chemotherapy agents were cisplatin (Platinol), carboplatin, liposomal doxorubicin (Doxil) and paclitaxel (taxol) was properly utilized in the essential or initial treatment of ovarian cancer[20]. *Antineoplastic agents* inhibit abnormal cell growth and proliferation. These specific agents typically include etoposide, topotecan (Hycamtin), gemcitabine (Gemzar), docetaxel (Taxotere), vinorelbine(Navelbine), ifosfamide, fluorouracil (adrucil), melphalan (Alkeran), altretamine (Hexalen), bevacizumab (Avastin)[21]. *PARP inhibitors* result in the disruption of cellular homeostasis and cell death. These specific inhibitors typically include effective drugs like olaparib (Lynparza), rucaparib (Rubraca), niraparib (Zejula) [22]. *Cytoprotective agents* typically include mesna (Mesnex) which detoxifies the metabolism of ifosfamide and cyclophosphamide, typically given to the patients being treated with ifosfamide and cyclophosphamide[23]. *Antiemetics*

International Journal of Pharmaceutical research and Applications
Volume 8, Issue 5, Sep.-Oct. 2023, pp: 1711-1718 www.ijprajournal.com ISSN: 2456-4494

were constantly used in treating nausea and vomiting associated with chemotherapy. It notably includes ondansetron (Zofran), granisetron (Kytril), palonosetron (Aloxi), dexamethasone (Decadron) [24].

There were some of the visible sign and symptoms of ovarian cancer:

1. Abdominal bloating or swelling
2. Quickly feeling full when eating
3. Weight loss
4. Mild discomfort in the pelvis area
5. Changed bowel habits, like constipation
6. Frequent need to urinate

These above mentioned were typically some of the visible signs or symptoms in ovarian cancer as early-stage rarely display any symptoms, while few symptoms were typically noted at the advanced stage of this infectious disease. Ovarian cancer as the term suggests typically begins from the ovaries. These female reproductive parts were responsible for naturally producing eggs or ova, as well as these ovaries, were also held responsible for naturally producing key hormones like estrogen and progesterone whose increased amount leads to ovarian cancer disease, unfortunately25].

VI. PARP INHIBITORS

Poly (adenosine diphosphate [ADP]-ribose) polymerase (PARP) inhibitors work on repairing damaged DNA as these work in the absence or dysfunction of the specific BRCA gene. These selective inhibitors stay as a very effective tool in properly managing the tumors caused by the dysfunction of the specific BRCA gene. There were various PARP inhibitors like olaparib, niraparib, rucaparib, veliparib, talazoparib, etc[26].

1. OLAPARIB (ASTRA ZENECA)

Olaparib was one of the first treatment dose manufactured or personalized for the specific patients typically suffering from high-grade ovarian cancer. The local activity of these selective inhibitors is typically based on synthetic lethality, where HRD (homologous recombination repair deficiency) makes the tumor cells highly susceptible to selective PARP inhibitors[27].

There were some of the dosage formulations or treatment arms of olaparib for treating ovarian cancer. These were respectively, Olaparib 400mg BID Placebo, Olaparib 400mg BID, etc were typically used [28].

Olaparib work by trapping PARP on DNA and typically preventing the repair of the single-strand break and generating double-strand break that cannot be repaired accurately in tumors typically having a defect in homologous recombination repair, these tumors having specific BRCA1/2 gene mutation. These specific inhibitors lead to a possible accumulation of DNA damage and tumor–cell death[29].

2. RUCAPARIB (CLOVIS)

Rucaparib typically had potent activity against PARP-1, -2, -3. It was universally approved for efficiently handling adult patients with BRCA mutated ovarian cancer and it was additionally used as maintenance therapy in adult patients responding positively to platinum-based chemotherapy[30].Tumors with mutations in the specific BRCA1/2 gene were usually sensitive to selective PARP inhibitors because of their synthetic lethality. Rucaparib had been used in treating BRCA-mutant and BRCA-wild-type epithelial ovarian cancer. Dosage formulations were: Rucaparib 600mg BID, etc[31].

3. NIRAPARIB (TESARO)

Niraparib was the first specific PARP inhibitor typically approved for ovarian cancer patients who did not harbor a germline or somatic mutation in the specific BRCA gene[32].It is an selective and potent inhibitor of the specific PARP-1and PARP-2 inhibitors. A standard dose of about 300mg remains the maximum tolerated dose for about 24hrs of standard time. The antitumor effect was also observed in niraparib[33].

VII. FUTURE DIRECTIONS:

1. New treatment approaches are typically needed. New or modified regimens are being practiced, preferred drugs are typically added or carefully aligned with carboplatin including paclitaxel. New platinum and taxane analogs are being studied for further development[34].
2. MIDGE (minimal immunological defined gene expression) technology is a possible alternative to plasmid in the possible future for improved gene therapy, minimal size, biosafety, and little immune reaction in non-viral ovarian gene therapy[35].
3. New PARP inhibitors are carefully formulated, undoubtedly gaining a more effective response. Various academic studies on these selective inhibitors with several other oncologic diagnoses typically related to specific BRCA1/2 mutations are carried out[36].

International Journal of Pharmaceutical research and Applications
Volume 8, Issue 5, Sep.-Oct. 2023, pp: 1711-1718 www.ijprajournal.com ISSN: 2456-4494

4. Selective PARP inhibitors are extremely effective, but there is a need to work on how to operate them more effectively on advised patients undergoing specific BRCA mutations[37].
5. Selective PARP inhibitors either as a single agent or in possible combination with other agents are under investigation for future use[38].
6. Future research on the possible combination of specific PARP inhibitors with antiangiogenic, cytotoxic, etc to overcome resistance problems and progressively expanding their clinical utility in non-homologous deficient tumors[39].

VIII. DISCUSSION

Genome integrity conservation typically remains the most essential part to be played by selective PARP inhibitors. PARP inhibitors work affectively by their specific mechanism of targeting defective tumors in cancer patients showing enhanced clinical results[40]. Journals have typically shown that medicating with niraparib resulted in the declined risk of mortality when putting side by side with placebo in various clinical tests or treatment processes [41].Fatigue and severe nausea have almost identical rates in every PARP inhibitors while the major difference of hematologic adverse events (AEs) is typically seen in every PARP inhibitors. Specific PARP inhibitors like niraparib lead to increased blood pressure while the use of rucaparib can elevate your cholesterol level[42].The academic researchers are typically working on using bevacizumab with selective PARP inhibitors in possible combinations. This clinical trial will undoubtedly provide lots of limitless possibilities to tailor the standard therapy according to the patient's specific condition. Some clinical professionals believe patients should be typically diagnosed with selective PARP inhibitors as a maintenance therapy to maintain the pressure on the tumor [43].

The various approved PARP inhibitors to be used in treating ovarian cancer do not produce identical therapeutic results when administered by the patient. Specific PARP inhibitors like rucaparib are approved for the selected patients suffering from germ-line or somatic BRCA mutations.While olaparib is typically used as an approved therapy for the maintenance and effective treatment of recurrent ovarian cancer. Clinical trials are examined and performed on combination regimens of PARP inhibitors to get a more advanced drug regimen in the field of ovarian cancer disorder [44.45].

IX. CONCLUSION

In selective PARP inhibitors; rucaparib, olaparib, and niraparib typically remain the effective drugs to be administered or given preference while treating fetal ovarian cancer disorder. Selective PARP inhibitors are one of the most preferred drug regimes when talking about the effective treatment of ovarian cancer. PARP inhibitors work by acting upon the BRCA mutation gene which causes defective DNA repair leading tumor formations. Selective PARP inhibitors are typically targeted drug therapy working directly on the targeted tumors cells and leaving normal cells unaffected. New and more advanced PARP inhibitors are being tested or practiced for future use. PARP inhibitors future is basically based on combination of various different dosage regimens. These drugs are of more potential but there is lack of uncertainties in their proper administration method. There are different effects shown by these drugs for different group of patients. These drugs have a wide future in the treatment of ovarian cancer disease. PARP inhibitors are one of the most essential dosage forms for the upcoming future of ovarian cancer treatment processes.

Abbreviation used

PARP - Poly ADP ribose Polymerase
BRCA - Breast Cancer Gene
WHO - World Health Organization
EOC - Epithelial Ovarian Cancer
OSE - Ovarian Surface Epithelial cell
HGSC - High-Grade Serous Carcinomas
STICs - Serous Tubal Intraepithelial Carcinomas
LHRH - Luteinizing Hormone Release Hormone
HRD - Homologous Recombination Repair Deficiency
MIDGE - Minimal Immunological Defined Gene Expression

REFERENCES

[1]. Franzese, Elisena, Sara Centonze, Anna Diana, Francesca Carlino, Luigi Pio Guerrera, Marilena Di Napoli, Ferdinando De Vita, Sandro Pignata, Fortunato Ciardiello, and Michele Orditura. "PARP inhibitors in ovarian cancer." Cancer treatment reviews 73 (2019): 1-9.
[2]. Cross, J., 2006. MEDLINE, PubMed, PubMed Central, and the NLM. Editors' Bulletin, 2(1), pp.1-5.

International Journal of Pharmaceutical research and Applications
Volume 8, Issue 5, Sep.-Oct. 2023, pp: 1711-1718 www.ijprajournal.com ISSN: 2456-4494

[3]. Papa, A., Caruso, D., Strudel, M., Tomao, S. and Tomao, F., 2016. Update on Poly-ADP-ribose polymerase inhibition for ovarian cancer treatment. Journal of translational medicine, 14(1), p.267.
[4]. Iqbal S, Rattu MA, Neal Shah, Role of PARP Inhibitors in BRCA-Related Malignancies, US Pharm. 2018;9(43),PP-10-16.
[5]. DALTON, W., 2003. Proteasome inhibition: a new pathway in cancer therapy. Cancer Treatment Reviews, 29, pp.1-2.
[6]. Singh, D., 2003. Evidence-based Oncology section – policies and scope. Cancer Treatment Reviews, 29(2), pp.121-122.
[7]. Sakorafas, G., 2003. The management of women at high risk for the development of breast cancer: risk estimation and preventative strategies. Cancer Treatment Reviews, 29(2), pp.79-89.
[8]. CHIONH, F., MITCHELL, G., LINDEMAN, G., FRIEDLANDER, M. and SCOTT, C., 2011. The role of poly adenosine diphosphate ribose polymerase inhibitors in breast and ovarian cancer: Current status and future directions. Asia-Pacific Journal of Clinical Oncology, 7(3), pp.197-211.
[9]. Ahmed, A., Becker, C. and Bast, R., 2011. The origin of ovarian cancer. BJOG: An International Journal of Obstetrics &Gynaecology, 119(2), pp.134-136.
[10]. Zhou, H., 2008. The debut of PMC Biophysics. PMC Biophysics, 1(1).
[11]. Wooster, R. and Weber, B., 2003. Breast and Ovarian Cancer. New England Journal of Medicine, 348(23), pp.2339-2347.
[12]. Verma, S., Dent, S., Paquet, L. and Bitonti, L., 2008. When the BRCA test is negative—Prevention strategies in women who have no detectable mutation (BRCA-) compared to women harboring positive BRCA mutations (BRCA+). Journal of Clinical Oncology, 26(15_suppl), pp.1534-1534.
[13]. Furuya, M., 2012. Ovarian Cancer Stroma: Pathophysiology and the Roles in Cancer Development. Cancers, 4(3), pp.701-724.
[14]. Tone, A.A., Salvador, S., Finlayson, S.J., Tinker, A.V., Kwon, J.S., Lee, C.H., Cohen, T., Ehlen, T., Lee, M., Carey, M.S. and Heywood, M., 2012. The role of the fallopian tube in ovarian cancer. Clin Adv Hematol Oncol, 10(5), pp.296-306.
[15]. Sternberg, W. and Roth, L., 1973. Ovarian stromal tumors containing leydigcells.I. Stromal-leydig cell tumor and non-neoplastic transformation of ovarian stroma to leydig cells. Cancer, 32(4), pp.940-951.
[16]. Pimlott, D. and Mossman, H., 1959. A Macroscopic Ovary-Sectioning Method. The Journal of Wildlife Management, 23(2), p.232.
[17]. Karst, A. and Drapkin, R., 2010. Ovarian Cancer Pathogenesis: A Model in Evolution. Journal of Oncology, 2010, pp.1-13.
[18]. CA: A Cancer Journal for Clinicians, 1957. KINESCOPE 28: HORMONAL AND CHEMICAL TREATMENT OF CANCER. 7(3), pp.95-96.
[19]. Fotopoulou, C. and Herzog, T.J., 2017. Pathophysiology and classification. In Fast Facts: Ovarian Cancer. Karger Publishers.
[20]. Ashraf, T. and Haroon, S., 2013. Gynaecological Malignancies. The Professional Medical Journal, 20(05), pp.752-758.
[21]. Kolesnik, O.O. and Rybin, A.I., 2017. The quality of life of patients with ovarian cancer as an indicator of functional assessing the effectiveness of anticancer therapy. Journal of Education, Health and Sport, 7(5), pp.539-551.
[22]. Ashraf, T., Haroon, S. and Kamal, Z., FREQUENCY OF GYNAECOLOGICAL MALIGNANCIES AT BOLAN MEDICAL COLLEGE COMPLEX HOSPITAL QUETTA. Cell, 92, pp.300-9381378.
[23]. Aust, S. and Pils, D., 2014. Epithelial ovarian cancer-more data, more questions?. Wiener MedizinischeWochenschrift, 164(21-22), pp.479-486.
[24]. Auer, K., Bachmayr-Heyda, A., Aust, S., Sukhbaatar, N., Reiner, A.T., Grimm, C., Horvat, R., Zeillinger, R. and Pils, D., 2015. Peritoneal tumor spread in serous ovarian cancer-epithelial mesenchymal status and outcome. Oncotarget, 6(19), p.17261.
[25]. Babic, A., Cramer, D., Titus, L., Tworoger, S. and Terry, K., 2014. Menstrual pain and epithelial ovarian cancer risk. Cancer Causes & Control, 25(12), pp.1725-1731.
[26]. Plummer, R., 2014. Poly(ADP-ribose)polymerase (PARP) Inhibitors: From Bench to Bedside. Clinical Oncology, 26(5), pp.250-256.

[27]. Ledermann, J.A. and Pujade-Lauraine, E., 2019. Olaparib as maintenance treatment for patients with platinum-sensitive relapsed ovarian cancer. Therapeutic advances in medical oncology, 11, p.1758835919849753.
[28]. Serono, E.M.D. and Kettering, M.S., DATA GENERATION (AND REVIEW CONSIDERATIONS) FOR USE OF A COMPANION DIAGNOSTIC FOR A GROUP OF ONCOLOGY THERAPEUTIC PRODUCTS.
[29]. Moore, K., Colombo, N., Scambia, G., Kim, B.G., Oaknin, A., Friedlander, M., Lisyanskaya, A., Floquet, A., Leary, A., Sonke, G.S. and Gourley, C., 2018. Maintenance olaparib in patients with newly diagnosed advanced ovarian cancer. New England Journal of Medicine, 379(26), pp.2495-2505.
[30]. Jenner, Z.B., Sood, A.K. and Coleman, R.L., 2016. Evaluation of rucaparib and companion diagnostics in the PARP inhibitor landscape for recurrent ovarian cancer therapy. Future Oncology, 12(12), pp.1439-1456.
[31]. Babu, M. and C. J., J., 2017. Rucaparib: a PARP inhibitor for the treatment of advanced ovarian cancer. International Journal of Basic & Clinical Pharmacology, 6(4), p.1018.
[32]. Cancer Discovery, 2016. Niraparib Slows Ovarian Cancer Progression. 6(12), pp.OF2-OF2.
[33]. Franzese, E., Centonze, S., Diana, A., Carlino, F., Guerrera, L.P., Di Napoli, M., De Vita, F., Pignata, S., Ciardiello, F. and Orditura, M., 2019. PARP inhibitors in ovarian cancer. Cancer treatment reviews, 73, pp.1-9.
[34]. Tripathi, M.K., Doxtater, K., Keramatnia, F., Zacheaus, C., Yallapu, M.M., Jaggi, M. and Chauhan, S.C., 2018. Role of lncRNAs in ovarian cancer: defining new biomarkers for therapeutic purposes. Drug discovery today, 23(9), pp.1635-1643.
[35]. Kaur, T., Slavcev, R. and Wettig, S., 2009. Addressing the Challenge: Current and Future Directions in Ovarian Cancer Therapy. Current Gene Therapy, 9(6), pp.434-458.
[36]. Konecny, G. and Kristeleit, R., 2016. PARP inhibitors for BRCA1/2-mutated and sporadic ovarian cancer: current practice and future directions. British Journal of Cancer, 115(10), pp.1157-1173.
[37]. Soupos, N., Laschos, K., Bournakis, E., Kostouros, E. and Aravantinos, G., 2015. OLAPARIB: A promising PARP Inhibitor for the treatment of ovarian cancer. Forum of Clinical Oncology, 6(3), pp.1-7.
[38]. Gien, L.T. and Mackay, H.J., 2010. The emerging role of PARP inhibitors in the treatment of epithelial ovarian cancer. Journal of oncology, 2010.
[39]. Boussios, Karathanasi, Cooke, Neille, Sadauskaite, Moschetta, Zakynthinakis-Kyriakou and Pavlidis, 2019. PARP Inhibitors in Ovarian Cancer: The Route to "Ithaca". Diagnostics, 9(2), p.55.
[40]. Wielgos, M. and Yang, E.S., 2013. Discussion of PARP inhibitors in cancer therapy. Pharmaceutical patent analyst, 2(6), pp.755-766.
[41]. Musella, A., Marchetti, C. and Panici, P., 2016. PARP inhibitors in ovarian cancer treatment: more than a hope. Cancer Breaking News, 4(3), pp.3-5.
[42]. Musella, A., Bardhi, E., Marchetti, C., Vertechy, L., Santangelo, G., Sassu, C., Tomao, F., Rech, F., D'Amelio, R., Monti, M., Palaia, I., Muzii, L. and Benedetti Panici, P., 2018. Rucaparib: An emerging parp inhibitor for treatment of recurrent ovarian cancer. Cancer Treatment Reviews, 66, pp.7-14.
[43]. PharmacoEconomics& Outcomes News, 2017. ICER draft report on PARP inhibitors for ovarian cancer. 783(1), pp.3-3.
[44]. Lee, J. and Gulley, J., 2017. Checkpoint and PARP inhibitors, for whom and when. Oncotarget, 8(56).
[45]. Paradiso, A., Andreopoulou, E., Conte, P., Eniu, A. and Saghatchian, M., 2018. PARP Inhibitors in Breast Cancer: Why, How, and When?.Breast Care, 13(3), pp.216-219.