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Efficacy and Safety of Adavosertib in Platinum-Resistant and Recurrent Ovarian Cancer: A Systematic Review and A Meta-Analysis

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ABSTRACT

Introduction: Ovarian cancer is a leading cause of mortality among gynaecological malignancies. According to estimates from the American Cancer Society for 2024, approximately 19,680 women in the United States will be newly diagnosed with ovarian cancer, and about 12,740 women will succumb to the disease. Advanced-stage ovarian cancers frequently develop resistance to treatment, resulting in a poor overall prognosis for this patient population. This article presents a systematic review and meta-analysis examining the efficacy and safety profile of adavosertib in treating platinum-resistant or recurrent ovarian cancers.

Methodology: The research question was framed using the PICO framework before initiating the review. A comprehensive literature search was conducted across PubMed, Google Scholar, Scopus, HINARI, and ScienceDirect databases, covering publications up to August 2023. Inclusion and exclusion criteria were defined, and appropriate tools were utilized to assess the risk of bias in the included studies. Descriptive and summary statistics were employed to characterize the sociodemographic features of the study cohort and the adverse effects associated with adavosertib. A random-effects model meta-analysis was performed to evaluate the association between adavosertib and the overall median survival of patients.

Results: In the meta-analysis using a random-effects model, the pooled estimate for the overall survival of patients given adavosertib is 14.71 months (95% CI: 9.01 to 20.41 months). The estimate is statistically significant ($p < 0.0001$), indicating a positive effect of adavosertib on overall survival. The amount of total heterogeneity (variability between studies) is estimated to be 18.97 (SE = 26.19), with a corresponding tau value of 4.35. The I^2 statistic is 77.36%, indicating a high level of heterogeneity among the studies. The most common adverse effects were nausea (69.3%), anemia (60.3%), diarrhea (56.8%), thrombocytopenia (55.0%), neutropenia (54%), vomiting (52.7%), lymphopenia (35.6%), hypomagnesemia (9.0%), and hypokalemia (5.4%).

Conclusion: The meta-analysis suggests that adavosertib has a significant positive effect on overall survival in ovarian cancer patients, with an estimated pooled median survival of 14.71 months. However, the results should be interpreted cautiously due to the high heterogeneity observed among the studies. The top three most common adverse effects were nausea, anemia, and diarrhea. Larger studies are recommended to provide more comprehensive information on this topic.

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Introduction

Ovarian cancer is a significant cause of mortality among gynaecological malignancies. According to the American Cancer Society's estimates for 2024, about 19,680 women will receive a new diagnosis of ovarian cancer, and about 12,740 women will die from ovarian cancer in the United States [1]. Multiple treatment modalities are available for ovarian cancer, with platinum-based chemotherapy being the most common. Ovarian cancer is mostly of the epithelial type and is treated with platinum derivatives (carboplatin, paclitaxel) as first-line therapy, usually six cycles over about 6 months. Ovarian cancer is classified as platinum-sensitive or platinum-resistant. The time from the treatment's end to the disease's relapse determines platinum resistance and is known as the platinum-free interval [2].

The median survival for platinum-responsive ovarian cancer ranges between 3 months to ten years, with a median of two years. On the other hand, the median survival for platinum-resistant ovarian cancer is nine to twelve months. Ultimately, most advanced ovarian cancers tend to become resistant, and the overall prognosis of this patient population remains poor. There is an urgent need for effective therapies for patients with platinum-resistant ovarian carcinomas. Approximately a quarter of the ovarian carcinomas diagnosed are platinum-sensitive; however, they may recur or acquire resistance over time. While the reasons for relapse and treatment failure are variable and progress in determining the appropriate treatment is slow, adavosertib, an inhibitor of the tyrosine kinase WEE1, hinders it from phosphorylating CDK1. In normal cells or most cancer cells, it leads to activation of the G2 checkpoint of the cell cycle and inhibits damaged cells from undergoing mitosis. Trials are underway to determine the efficacy of adavosertib in patients with platinum-resistant ovarian cancer, and so far, it has shown promising anti-tumor efficacy. In this article, we will discuss in detail the efficacy and safety profile of adavosertib in platinum-resistant or recurrent ovarian cancers [3-6].

Aims and Methodology

This systematic review derived information only from published literature; hence, no ethical committee approval was required. The PICO framework for the research question was defined before beginning the review. Participants with any type of ovarian cancer diagnosed by histopathology and resistant to first-line therapy were included. Recurrent ovarian cancer after first-line treatment completion or resistant cancers were being trailed with multiple alternative drug therapies, adavosertib being one of them. Adavosertib, which is usually combined with other drugs for the treatment of resistant or recurrent ovarian cancer, was the intervention. Our primary outcome was the overall survival of participants with recurrent or resistant ovarian cancer after treatment with adavosertib. Our secondary outcomes were progression-free survival, side effects of medication, and subjective and objective response rates.

A literature search was conducted on PubMed, Google Scholar, Scopus, HINARI, and ScienceDirect databases for papers published from any date to August 22, 2022. All articles were exported from the citation manager (Zotero) to a Microsoft Excel sheet. Three reviewers screened the papers independently in two steps - title and abstract screening followed by full-text screening. Randomized control trials, non-randomized control trials, cohort studies, and case-control studies were included, while papers not in the English language were excluded. Additional papers were searched through citations before the completion of the review. All reviewers were blinded to each other's screening process, and screened results were compared after the process. The fourth reviewer reviewed the disputed articles independently to reach a conclusion in case of any disagreement.

Data was extracted from the selected papers under the following subheadings: study design and year of publication, study population with its demographics (number of patients, gender, nationality, age, comorbidities), overall survival and progression-free survival, side effects, quality of life, and response rate. Risk of bias (quality) assessment was done using the ROBINS I tool for randomized trials and the Newcastle Ottawa scale for non-randomized studies. We used Jamovi software and MS Excel for data collection, analysis, and data synthesis. Descriptive and summary statistics were used to describe the study cohort's socio-demographic parameters, with continuous variables presented as mean standard deviation or median as appropriate. Categorical variables were presented as percentages or ratios [7,8].

Intervention(S), Exposure(S)

Ovarian cancer is mostly of the epithelial type and is treated with platinum derivatives (carboplatin, paclitaxel) as first-line therapy, usually six cycles over about 6 months.

Results

We initially identified 272 papers on the relevant topic from various journals. Of these, 82 were duplicates and were eliminated. Following the title and abstract screening, we were left with 190 articles. Of these, 21 papers were noted after the full-text screening, and the remaining were excluded from the study. From these, we finalized and included 6 papers in our study after a thorough evaluation. Figure 1 shows the study selection process as per PRISMA guidelines [9].

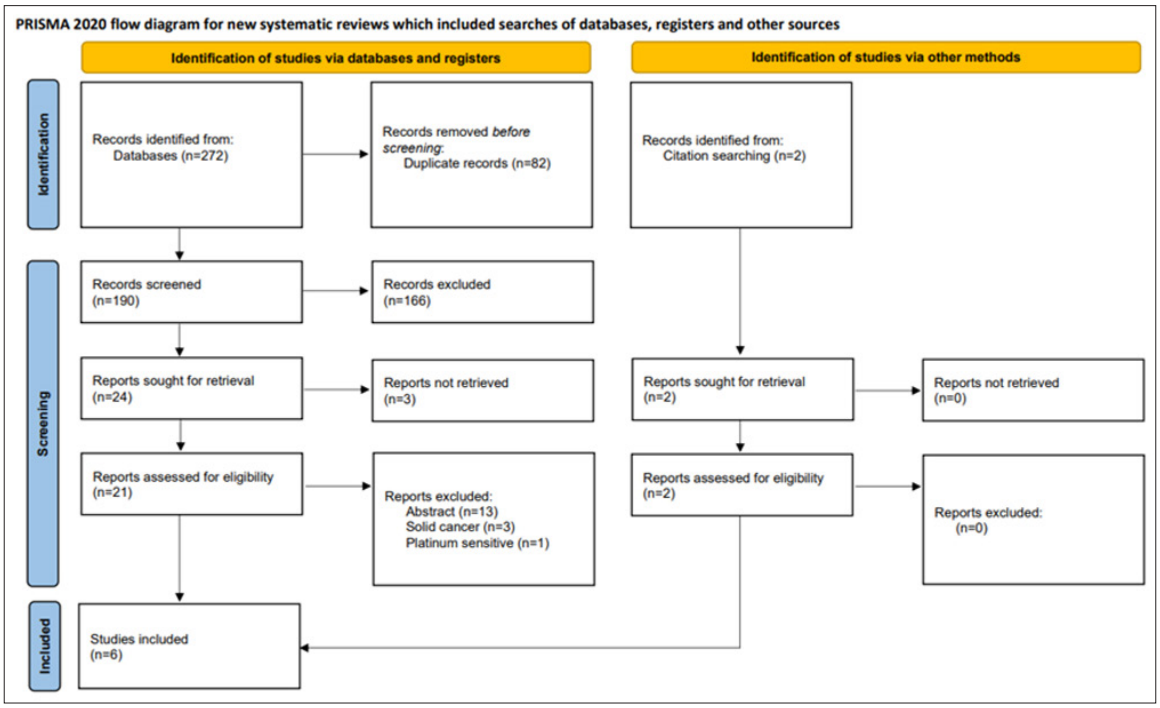

Figure 1: Study Selection Process

Table 1: Study Characteristics

FIRST AUTHOR	TITLE	INCLUSION CRITERIA	STUDY DESIGN	YEAR OF PUBLICATION	LOCATION (COUNTRY)
Lheureux S [10]	Adavosertib plus gemcitabine for platinum-resistant or platinum-refractory recurrent ovarian cancer: a double-blind, randomized, placebo-controlled, phase 2 trial	Platinum-resistant/ recurrent ovarian cancer	Phase II RCT	2021	USA, Canada
Leijen S [11]	Phase II Study of WEE1 Inhibitor AZD1775 Plus Carboplatin in Patients with TP53-Mutated Ovarian Cancer Refractory or Resistant to First-Line Therapy Within 3 Months	Platinum-resistant/ recurrent ovarian cancer	Phase II RCT	2016	Netherlands
Takebe N [12]	Safety, anti-tumor activity, and biomarker analysis in a phase 1 trial of the once-daily Wee1 inhibitor adavosertib (AZD1775) in patients with advanced solid tumors	Failed standard therapy ovarian/solid tumor	Phase I non-randomized CT	2021	USA

Do K [13]	Phase I Study of Single-Agent AZD1775 (MK-1775), a Wee1 Kinase Inhibitor, in Patients with Refractory Solid Tumors	Failed standard therapy ovarian/solid tumor	Phase I non-randomized CT	2015	USA
Moore KN [14]	Adavosertib with Chemotherapy in Patients with Primary Platinum-Resistant Ovarian, Fallopian Tube, or Peritoneal Cancer: An Open-Label, Four-Arm, Phase II Study	Platinum-resistant/ recurrent ovarian cancer	Phase II	2022	USA, Canada, Netherlands
Madariaga A [15]	Patient self-reporting of tolerability using PRO-CTCAE in a randomized double-blind, placebo-controlled phase II trial comparing gemcitabine in combination with adavosertib or placebo in patients with platinum-resistant or refractory epithelial ovarian cancer	Platinum-resistant/ recurrent ovarian cancer	Phase II RCT	2022	Canada, USA, Spain

Table 2: Patient Characteristics

FIRST AUTHOR	NUMBER OF PARTICIPANTS	ACTUAL NUMBER OF INCLUDED PARTICIPANTS	MEDIAN AGE (IN YEARS), RANGE	RACE	STAGES OF CANCER	MUTATIONS	HISTOLOGICAL SUBTYPES	TUMOR LOCATION
Lheureux S [10]	124	Only 86 were eligible in the adavosertib plus gemcitabine group	62 (Range 54–67)	American Indian or Alaska Native, Asian, Black or African American, White, Unknown	99 with high-grade serous ovarian cancer. 25 with non-high-grade serous ovarian cancer.	TP53, BRCA1 and BRCA2	Serous	Epithelial ovaries (104), Fallopian tube (4), Primary peritoneum (11)
Leijen S [11]	24	21 for outcome evaluation of efficacy, 23 for toxicity	58 (Range 25-74)	--	IIB (1), IIIA (1), IIIC (12), IVA (9)	22 TP53, 2 BRCA1	Serous (16), clear cell (3), mucinous (2), mixed epithelial (1), unknown (1)	Ovaries
Takebe N [12]	42	10: Ovarian cancer	64 (Range 26-83)	No race specific	--	BRCA1 and TP53	Epithelial ovarian cancer	Ovaries, endometrium
Do K [13]	25	5: Ovarian cancer	52 (Range 22-78)	--	--	BRCA1/2	Papillary serous	Ovarian
Moore KN [14]	94	Adavosertib + Gemcitabine = 9, Adavosertib + Paclitaxel = 38, Adavosertib + Carboplatin = 35, Adavosertib + pegylated Doxorubicin = 12	60 (Range 34-85)	Caucasians 77.7%	III/IV	BRCA1 = 6.6%, BRCA2 = 3.9%	Epithelial serous 90%	Ovarian, fallopian tube, peritoneal
Madariaga A [15]	61	Gemcitabine + Adavosertib = 28	62 (Range 48-75)	White, Asian, black, native American	High grade	--	Serous	Ovarian, fallopian tube, peritoneal

Table 3: Previous Therapy

FIRST AUTHOR	ANY PREVIOUS CHEMOTHERAPY	NUMBER OF PREVIOUS (FIRST LINE) CHEMOTHERAPY CYCLES RECEIVED	RESULT OF PREVIOUS CHEMOTHERAPY (REFRACTORY/ RECURRENT)	ANY SURGERY	ANY RADIOTHERAPY
Lheureux S [10]	Platinum-based	Median 3 cycles	Primary platinum refractory: 6, Recurrent refractory: 55	Adavosertib plus Gemcitabine group: 57	Adavosertib plus Gemcitabine group: 8
Leijen S [11]	Platinum plus paclitaxel	3 patients with less than 6 cycles, 20 patients with 6 or more	9 - Primary Refractory to first-line therapy, 14 - Resistant (within 3 months) to first-line therapy	All patients underwent either primary or interval debulking surgery	--
Takebe N [12]	Standard first-line therapy (PARP inhibitors)	Median 5 cycles	Refractory	--	--
Do K [13]	Standard first-line therapy	--	Refractory first line	--	--
Moore KN [14]	Platinum-based	More than 4 cycles	Platinum resistance	Yes in 88 (93.6%)	--
Madariaga A [15]	Platinum-based	Median 5 cycles	Refractory to platinum	--	--

Table 4: Effectiveness of Adavosertib Therapy

STUDY	ESTIMATE	SD	CI-LOWER	CI-UPPER
Lheureux S, et al [10]	11.40	2.12	8.2	16.5
Leijen S, et al [11]	12.60	3.78	4.9	19.7
Moore KN, et al [14]	19.20	1.74	12.4	19.2
Pooled *	15.67	1.27	NA	NA

* Two of the five studies were excluded for calculation as they were safety studies or because data was unavailable.

Table 5: Comparison of Overall Survival

AUTHOR	MEAN OVERALL SURVIVAL IN MONTHS (CI)
Lheureux S, et al [10]	11.4 (8.2–16.5)
Leijen S, et al [11]	12.6 (4.9 to 19.7)
Moore KN, et al [14]	19.2 (90% CI 12.4-19.2)
Our study (Pooled data) *	14.71 (9.01, 20.41)

* Two of the five studies were excluded for calculation as they were safety studies or because data was unavailable.

Meta-Analysis Results

In the meta-analysis using a random-effects model, the pooled estimate for the overall survival of patients given Adavosertib is 14.71 months (95% CI: 9.01 to 20.41 months). The estimate is statistically significant ($p < 0.0001$), indicating a positive effect of Adavosertib on overall survival. The total heterogeneity (variability between studies) is estimated to be 18.97 (SE = 26.19), with a corresponding tau value (square root of tau^2) of 4.35. The I^2 statistic, representing the proportion of total variability due to heterogeneity, is 77.36%. This indicates a high level of heterogeneity among the studies. The meta-analysis suggests that Adavosertib has a significant positive effect on overall survival in ovarian cancer patients, with an estimated pooled median survival of 14.71 months. However, the high heterogeneity observed among the studies was a limitation.

Adavosertib Treatment for Ovarian Cancer: Effectiveness and Side Effects

Table 6: Comparison of Overall Effectiveness

FIRST AUTHOR	DURATION/NUMBER OF CYCLES OF SECOND-LINE CHEMOTHERAPY	MEDIAN OVERALL SURVIVAL	MEDIAN PROGRESSION-FREE SURVIVAL	MEDIAN RESPONSE RATE
Lheureux S [10]	Cycle: 28-day. Duration: Until disease progression or unacceptable toxicity.	11.4 months (95% CI 8.2–16.5)	4.6 months (95% CI 3.6–6.4)	14 (23%)
Leijen S [11]	Each cycle: 21 days. Number of cycles: Until disease progression (minimum of two cycles). Carboplatin IV resulted in a target platinum area under the curve (AUC) of 5 mg/mL/min in a 30-minute infusion. AZD1775 225 mg orally twice a day for 2.5 days in 21-day cycles.	12.6 months (95% CI 4.9 to 19.7 months)	5.3 months (95% CI, 2.3 to 9.0 months)	5% showed a complete response. 38% had a partial response. The disease was stable in 33%. Progression was noted in 24%. Overall Response rate = 43% (95% CI, 22% to 66%)
Takebe N [12]	On days 1-5 and 8-12 of each 21-day cycle, with a median number of 4 cycles	--	--	Once-daily = 14%, Twice-daily = 8%
Do K [13]	21-day cycle, twice per day for 2.5 days per week for two weeks	--	--	--
Moore KN [14]	1-day cycle for carboplatin-based combination and 28-day cycle for other drugs	Arm A = 16 months, Arm B = not calculable, Arm C = 14 months, Arm D = 6.2 months, Overall = 19.2 months	Arm A = 1.7 months, Arm B = 5.5 months, Arm C = 16.2 months, Arm D = 2.7 months, Overall = 5.5 months	Complete response = 3.2%, Partial response = 28.7%
Madariaga A [15]	28-day cycle	--	--	--

Table 7: Side Effects with Adavosertib

FIRST AUTHOR	BONE MARROW TOXICITIES [anemia, neutropenia, thrombocytopenia, etc., all grades (number and percentage)]	GI TOXICITIES [nausea, vomiting, diarrhea, etc., all grades (number and percentage)]	ELECTROLYTE ABNORMALITIES
Lheureux S [10]	• Anemia: Any grade: 54 (89%); Grade ≥3: 19 (31%) • Decreased white blood cell count: Any grade: 54 (89%); Grade ≥3: 33 (54%) • Thrombocytopenia: Any grade: 52 (85%), Grade ≥3: 19 (31%) • Neutropenia: Any grade: 50 (82%); Grade ≥3: 38 (62%) • Decreased lymphocyte count: Any grade: 47 (77%); Grade ≥3: 21 (34%)	• Nausea: Any grade: 49 (80%); Grade ≥3: 2 (3%) • Abdominal pain: Any grade: 45 (74%); Grade ≥3: 5 (8%) • Constipation: Any grade: 43 (70%); Grade ≥3: 0 • Diarrhea: Any grade: 38 (62%); Grade ≥3: 4 (7%) • Vomiting: Any grade: 36 (59%); Grade ≥3: 1 (2%) • Anorexia: Any grade: 32 (52%); Grade ≥3: 0 • Dyspepsia: Any grade: 19 (31%); Grade ≥3: 0 • Abdominal distension: Any grade: 12 (20%); Grade ≥3: 0 • Bloating: Any grade: 12 (20%); Grade ≥3: 0	--

Leijen S [11]	• Thrombocytopenia in 16 pts (70%): Grade 1 = 2 pts (9%), Grade 2 = 3 pts (13%), Grade 4 = 11 pts (48%) • Neutropenia in 10 pts (43%): Grade 2 = 1 pt (4%), Grade 3 = 4 pts (17%), Grade 4 = 5 pts (22%) • Anemia in 14 pts (61%): Grade 2 = 12 pts (52%), Grade 3 = 2 pts (9%)	• Nausea in 18 pts (78%): Grade 1 = 14 pts (61%), Grade 2 = 3 pts (13%), Grade 3 = 1 pt (4%) • Diarrhea in 16 pts (70%): Grade 1 = 9 pts (39%), Grade 2 = 6 pts (26%), Grade 3 = 1 pt (4%) • Vomiting in 11 pts (48%): Grade 1 = 8 pts (35%), Grade 2 = 3 pts (13%) • Pyrosis (heartburn) in 4 pts (17%): Grade 1 = 2 pts (9%), Grade 2 = 2 pts (9%)	--
Takebe N [12]	In this category, lymphopenia (71%) is the most common. • Anemia: Grade 1-2 = 47%, Grade 3 = 21% • Leukopenia: Grade 1-2 = 29%, Grade 3 = 12%, Grade 4 = 10% • Lymphopenia: Grade 1-2 = 43%, Grade 3 = 29% • Neutropenia: Grade 1-2 = 12%, Grade 3 = 10%, Grade 4 = 12% • Thrombocytopenia: Grade 1-2 = 31%, Grade 3 = 12%, Grade 4 = 2%	Among gastrointestinal symptoms, Nausea (81%) is the most common. • Diarrhea: Grade 1-2 = 60%, Grade 3 = 5% • Anorexia: Grade 1-2 = 40% • Nausea: Grade 1-2 = 74%, Grade 3 = 7% • Vomiting: Grade 1-2 = 57%, Grade 3 = 12%	• Hyponatremia: Grade 1-2 = 19%, Grade 3 = 2% • Hypokalemia: Grade 1-2 = 12%, Grade 3 = 2% • Hypophosphatemia: Grade 1-2 = 24%, Grade 3 = 14% • Hypocalcaemia: Grade 1-2 = 7%, Grade 3 = 2% • Hypomagnesemia: Grade 1-2 = 17%, Grade 3 = 2%
Do K [13]	• Lymphopenia: 64% • leukopenia: 60% • Anemia: 52% • Thrombocytopenia: 48% • Neutropenia: 40%	• Nausea: 72% • Vomiting: 72% • Diarrhea: 68% • Abdominal pain: 20% • Bloating: 16%	--
Moore KN [14]	• Arm A: Neutropenia = 88.9%, Anemia = 33.3%, Thrombocytopenia = 33.3%, Leukopenia = 22.2% • Arm B: Neutropenia = 65.8%, Anemia = 63.2%, Thrombocytopenia = 39.5%, Leukopenia = 34.2% • Arm C: Neutropenia = 54%, Anemia = 65%, Thrombocytopenia = 77%, Leukopenia = 14% • Arm D: Neutropenia = 25%, Anemia = 41.6%, Thrombocytopenia = 8%, Leukopenia = 16.67% • Overall: Anemia = 58.5%, Neutropenia = 58.5%, Thrombocytopenia = 48.9%, Leukopenia = 23.4%	• Arm A: Nausea = 55.6%, Vomiting = 44.4%, Diarrhea = 33.3% • Arm B: Nausea = 60.5%, Vomiting = 50%, Diarrhea = 81.6% • Arm C: Nausea = 82.8%, Vomiting = 48.57%, Diarrhea = 62.85% • Arm D: Nausea = 66.7%, Vomiting = 41.67%, Diarrhea = 50% • Overall: Nausea = 69.1%, Diarrhea = 66%, Vomiting = 47.9%	• Arm A: Hypomagnesemia = 11.1%, Hypokalemia = 11.1% • Arm B: Hypomagnesemia = 21%, Hypokalemia = 10.5% • Arm C: Hypomagnesemia = 25.71%, Hypokalemia = 14.2% • Arm D: Hypomagnesemia = 0%, Hypokalemia = 8% • Overall: Hypomagnesemia = 19.1%, Hypokalemia = 11.7%
Madariaga A [15]	--	Dysphagia is significantly higher in the treatment group (35%) than in placebo-controlled (5%). Abdominal pain and nausea are noted in 92.95% of the treatment group vs 89% in placebo, and 85% vs 73% for bloating, 50% vs 47% for vomiting respectively.	--

The most common adverse effects observed with adavosertib are bone marrow toxicities including anemia, decreased white blood cell count, thrombocytopenia, neutropenia, and decreased lymphocyte count. Among haematological side effects, lymphopenia is the most common. Gastrointestinal side effects include nausea, vomiting, diarrhea, and bloating, with nausea being the most common gastrointestinal adverse effect. Other side effects include electrolyte abnormalities such as hyponatremia, hypokalemia, hypophosphatemia, hypocalcaemia, and hypomagnesemia [10-15].

Discussion

Globally, the incidence and mortality rates are higher. In 2018, there were approximately 295,414 new cases of ovarian cancer worldwide, accounting for 3.4% of all cancer cases in women. The global mortality for ovarian cancer in 2018 was 184,799 deaths, which represented 4.4% of all cancer-related mortality among women. By 2050, the number of women diagnosed with ovarian cancer worldwide is expected to rise over 55% to 503,448, with annual deaths projected to increase to 350,956, an increase of almost 70% from 2022 [16,17].

The ovarian surface epithelium is the cause of approximately 90% of ovarian malignancies, which are categorized into distinct subtypes: high-grade serous, low-grade serous, mucinous, endometrioid, clear-cell, and transitional cell carcinomas. Each subtype is associated with unique molecular alterations and pathways. High-grade serous carcinoma (HGSC), which accounts for 70–80% of ovarian cancers, typically originates from surface epithelial inclusion glands or the fallopian tube epithelium. It is characterized by mutations in the p53 gene and dysfunction of BRCA1 and BRCA2. Low-grade serous carcinoma (LGSC) represents about 5% of ovarian cancers and arises through an

adenoma-borderline tumor-carcinoma sequence. LGSC is driven by mutations in KRAS and BRAF, leading to activation of the RAS-RAF signalling pathway. Mucinous carcinoma, comprising approximately 3–4% of ovarian cancers, also develops through an adenoma-borderline tumor-carcinoma sequence and is frequently associated with KRAS mutations, present in about 50% of cases. Endometrioid carcinoma, which represents about 10% of ovarian cancers, often originates from endometriosis. Its low-grade forms are commonly associated with mutations in CTNNB1, encoding beta-catenin, and PTEN. Clear cell carcinomas, believed to originate from ovarian endometriosis, are characterized by mutations in the TGFβR2 gene and overexpression of HNF-1β. These molecular insights into ovarian cancer subtypes facilitate the development of targeted diagnostic and therapeutic approaches [18-23].

Adavosertib is a selective small-molecule inhibitor of the tyrosine kinase WEE1, with potential antineoplastic and sensitizing properties. WEE1 is a tyrosine kinase that inactivates the cyclin-dependent kinase 1 (CDK1, also known as CDC2) by phosphorylating it at tyrosine 15, thereby inhibiting the CDC2/cyclin B complex. By inhibiting WEE1 activity, adavosertib prevents the phosphorylation of CDC2, disrupting the G2 DNA damage checkpoint. Adavosertib, with combination therapy, has demonstrated promising anti-tumor activity, especially in platinum-resistant ovarian cancer. Combination therapy with adavosertib showed better progression-free survival (PFS), overall survival, and objective response rates (ORR). Adverse events included gastrointestinal issues, hematologic toxicities, electrolyte abnormalities, and fatigue, with no treatment-related deaths reported. The most common gastrointestinal side effect was nausea, while other noted effects included vomiting, diarrhea, and bloating. Hematologic toxicities primarily included neutropenia, anemia, and thrombocytopenia, with bone marrow toxicity being the leading cause of dose modifications. Electrolyte abnormalities observed were hyponatremia, hypokalemia, hypophosphatemia, hypocalcaemia, and hypomagnesemia [24-26].

Conclusion

Current treatment regimens for recurrent platinum-resistant ovarian cancer typically include cytotoxic agents such as cyclophosphamide, topotecan, and paclitaxel, alongside targeted therapies like bevacizumab. However, emerging evidence suggests that the combination of adavosertib, particularly with gemcitabine, offers superior overall survival (OS) outcomes and a longer progression-free interval compared to conventional chemotherapy. Our meta-analysis revealed that adavosertib has a significant positive impact on overall survival in ovarian cancer patients, with a pooled median survival estimate of 14.71 months. Nonetheless, these findings should be interpreted with caution due to the high heterogeneity observed among the included studies. Adavosertib has demonstrated good tolerability and a favourable safety profile, with the most reported adverse effects being nausea, anemia, and diarrhea. Reviewers emphasize the need for large-scale, robust studies to further elucidate the efficacy and safety of adavosertib in this patient population and provide more definitive conclusions.

Acknowledgments: -NA-

Declarations

Ethics Consideration: Not applicable, since this is a review article.

Consent To Participate and Publication: Not required, since this is a review article.

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Data Availability: All data generated or analyzed during this study are included in this published article.

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