

Clinical Trails and Bioavailability Research

Review Article

Molecular Genetic Markers of Ovarian Cancer

BON L.I.^{1*}, MAKSIMOVICH N.YE.¹, DREMZA I.K.¹, VARABYOU H.Y.¹, KHARYK A.A.¹, MISIK V.A.¹, KIPEN K.M.¹

¹T.A Grodno State Medical University, 80, Gorkogo St., 230009, Grodno, Republic of Belarus.

***Corresponding Author:** Bon L.I., T.A Grodno State Medical University, 80, Gorkogo St., 230009, Grodno, Republic of Belarus.

Received Date: 15 April 2026; **Accepted Date:** 05 May 2026; **Published Date:** 09 May 2026

Copyright: © 2026 BON L.I., this is an open-access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Abstract

Ovarian cancer (OC) is a collective term for a group of diseases that differ in their morphological and molecular characteristics and represent one of the leading causes of death among patients with gynecological malignancies. The insufficient accuracy of standard diagnostic methods necessitates the search for new, more convenient, and precise techniques. This article reviews recently discovered ovarian cancer biomarkers, the theoretical foundations for their application, and their clinical significance. The need for further research into novel markers and the integration of existing ones into clinical practice is highlighted.

Keywords: Ovarian cancer, Biomarker, Diagnostics.

Introduction

To date, ovarian cancer remains one of the primary causes of mortality among patients with cancers of the reproductive system [52]. It is currently well-established that OC is an umbrella term for several diseases characterized by distinct morphological and molecular profiles [53]. According to the classification of ovarian tumors by origin, they are divided into epithelial, mesenchymal, sex cord-stromal, germ cell tumors, tumor-like lesions, and other tumors not categorized elsewhere. The predominant type is epithelial ovarian cancer, which accounts for approximately 90% of cases [52]. Epithelial cancer, in turn, is subdivided into several morphological categories: serous carcinomas, mucinous carcinomas, endometrioid carcinomas, clear cell carcinomas, transitional cell Brenner tumors, as well as mixed and undifferentiated types [54].

Due to differences in morphology, etiology, molecular biology, the requirement for targeted chemotherapy, and, consequently, treatment prognosis and survival rates, it is essential to differentiate between all cancer types. A number of biomolecules have been identified as criteria for differential diagnosis, such as FOXL2 for adult-type granulosa cell tumors [55], DICER1 for Sertoli–Leydig cell tumors [56], CTNNB1 for microcystic stromal tumors [57], and SMARCA4 for small cell carcinoma of the ovary, hypercalcemic type [58]. However,

this information remains insufficient for the comprehensive diagnosis of all cancer types, creating a clear need for further development in this field.

MicroRNAs

MicroRNAs (miRNAs) are short RNA molecules that regulate gene expression and participate in various biological processes. Their biogenesis involves the transcription of pri-miRNA and its subsequent cleavage into pre-miRNA. The mature form is produced in the cytoplasm following the cleavage of pre-miRNA and functions through complementary binding to mRNA, leading to its degradation or translational inhibition. Dysregulation of miRNAs is associated with the development of various human diseases, including ovarian cancer [1]. Aberrant miRNA expression in this malignancy possesses significant diagnostic and prognostic potential [2]. Currently, over 2,500 miRNAs have been identified that are capable of influencing gene expression within signaling pathways [3–5].

The let-7 and miR-200 families exhibit alterations in ovarian cancer, with the let-7 family potentially being significant for chemotherapy selection [5, 6]. A decrease in the expression of miRNA processing enzymes correlates with tumor stage

progression and adverse outcomes. Both the let-7 and miR-200 families frequently demonstrate changes in ovarian cancer [6].

Chemoresistance in ovarian cancer is linked to the aberrant expression of several miRNAs, including let-7e, miR-30c, miR-125b, miR-130a, miR-335, miR-340, miR-381, and miR-520f, among others [7]. Circulating miRNAs in blood and urine are promising diagnostic markers, as they correlate with histotypes, treatment resistance, and prognosis [8]. Specifically, miR-21, miR-200a, and miR-200c hold diagnostic and prognostic value, while let-7f and miR-141 are associated with shorter progression-free survival. Furthermore, miR-193a acts as a tumor suppressor [9]. In a study by Yokoi et al., an eight-miRNA panel was able to distinguish early-stage ovarian cancer from benign tumors with a sensitivity of 86% and a specificity of 83% [10].

BRCA1 and BRCA2

These genes belong to the category of genes encoding enzymes involved in DNA repair systems. Although alternative pathways for repairing double-strand breaks exist, clinically significant mutations in the BRCA1 and BRCA2 genes lead to genomic instability. This instability arises from the accumulation of genetic damage, which facilitates the malignant transformation of cells [11–13]. The probability of mutations in the BRCA1 gene is four times higher than in the BRCA2 gene [14]. Hereditary forms of ovarian cancer account for 10% to 15% of the total number of cases [15]. The lifetime risk of developing ovarian cancer in the presence of pathogenic BRCA1 mutations is estimated to be between 20% and 50%, whereas for BRCA2 mutations, this figure is approximately 10% to 20%. According to research findings, the mean age at diagnosis for ovarian carcinoma is lower in BRCA1 mutation carriers compared to BRCA2 mutation carriers [16–17]. In terms of histological characteristics, high-grade serous ovarian carcinoma is the predominant subtype among carriers of both BRCA1 and BRCA2 mutations [18]. In a cohort screening conducted by Stavropoulou et al. involving 592 patients with sporadic ovarian cancer, 27 individuals (4.6% of the total sample) were identified as carriers of the most common BRCA1 mutations [16]. A study by De Leeneer et al. involving 193 cases of sporadic breast and ovarian cancer showed that among seven women with concurrent breast and ovarian cancer, three (42.9%) were carriers of BRCA1/2 mutations [17]. In Poland, an evaluation of 148 consecutive ovarian cancer patients identified BRCA1/2 mutations in 21 women, representing 13.9% of the total cases [20]. In the Russian Federation, the prevalence of BRCA1/2 mutations among 74 patients was higher, with the carrier frequency reaching 19% [21]. In a study conducted by Pohlreich [see note below], among patients with a burdened family history of ovarian cancer, 13 out of 40 subjects (33%) were BRCA1/2 mutation carriers. In the group of patients without a burdened

family history, mutations were identified in 23 out of 283 individuals (8%) [22].

B7-H4 (VTCN1)

The B7-H4 protein, encoded by the VTCN1 gene (V-set domain containing T-cell activation inhibitor 1), is a transmembrane protein localized on the cell surface. Differential expression analysis of the VTCN1 gene conducted by Lysanne D. A. N. de Muynck et al. revealed high log2 fold change (Log2FC) values. For primary tumors, this value was 8.56, while for metastases, it was 6.53. In healthy tissues, including the ovaries, omentum, peritoneum, and lymph nodes, VTCN1 RNA expression was virtually absent, with transcripts per million (TPM) levels below 0.5. Immunohistochemical (IHC) analysis confirmed B7-H4 protein overexpression in 86% of the examined tumor samples (74 out of 86).

Furthermore, an analysis of expression stability demonstrated that high B7-H4 levels were maintained in both primary tumors and their corresponding omental, peritoneal, and lymph node metastases, indicating the stability of this marker during disease progression ($p > 0.05$). Notably, expression remained high in specimens obtained both after primary cytoreductive surgery and following neoadjuvant chemotherapy, suggesting that the marker is resistant to the effects of the administered treatment [23].

HE4

The HE4 protein, encoded by the WFDC2 gene, is a glycoprotein belonging to the class of serine protease inhibitors. This protein serves as a potential biomarker for ovarian cancer and can be detected in blood and urine samples using enzyme-linked immunosorbent assay (ELISA). HE4 overexpression is characteristic of specific histological subtypes of ovarian tumors, with an occurrence frequency of 100% in endometrioid carcinomas and 93% in serous carcinomas. In combination with other prognostic factors, HE4 can serve as an additional predictor of mortality in ovarian cancer, particularly in the serous histotype [24].

According to the results of a meta-analysis conducted by Nalini et al., which included 38 studies involving a total of 14,745 participants, serum HE4 demonstrated significant diagnostic value as an ovarian cancer biomarker. The marker's performance indicators were characterized by acceptable sensitivity (0.79) and clinically significant specificity (0.92) [25]. In a study by Barr et al. involving 1,229 symptomatic women, the combination of CA125 and HE4, along with the ROMA (Risk of Ovarian Malignancy Algorithm) algorithm, were evaluated for ovarian cancer diagnosis. The ROMA algorithm showed the best performance (AUC = 0.96). In women under 50 years of age, the combination of CA125 and HE4 demonstrated higher sensitivity and specificity, whereas the ROMA algorithm was more effective in the older age group. Individually, HE4 possessed higher sensitivity but lower specificity

compared to CA125 [26].

A study by Chudecka-Głaz et al. evaluated the prognostic significance of HE4 during first-line chemotherapy in ovarian cancer patients. It was established that HE4 levels predict platinum sensitivity and are associated with progression-free survival (PFS), overall survival (OS), and surgical outcomes. HE4 demonstrated potential as a valuable biomarker for assessing treatment efficacy and prognosis [27]. In another study by Chudecka-Głaz et al. involving 188 ovarian cancer patients, elevated HE4 levels at diagnosis, after cytoreduction, and during first-line chemotherapy were associated with a high risk of recurrence. Increased HE4 levels were also observed in cases of large residual tumors following primary surgery and in platinum-resistant patients. At the time of the second recurrence, significantly higher HE4 levels were detected in patients with residual lesions exceeding 10 mm [28].

CA-125

CA125 is a glycoprotein encoded by the *MUC16* gene located on chromosome 19 [29]. In a study by Ahmad et al., the highest CA125 levels were observed in the serous ovarian cancer subtype and stage II, followed by stages III, I, and IV [30]. Cooper et al. confirmed that elevated preoperative CA125 values are associated with serous histology, advanced stages (III–IV), high-grade malignancy, and the presence of ascites [31]. Measuring CA125 is most informative in postmenopausal women, where it demonstrates higher sensitivity, specificity, and predictive value [32]. However, Antovska et al. concluded that CA125 has limited efficacy as a standalone test [33]. Yang et al. found that while CA125 alone identifies more than half of early-stage ovarian cancer cases, its combination with HE4 Ag-AAb complexes increased the detection rate to 81% [34]. Consequently, Kim et al. recommended using CA125 in combination with HE4 and the ROMA algorithm to improve diagnostic accuracy [35]. Furthermore, Sorensen and Mosgaard established that the serum CA125/CEA ratio can be utilized for the preoperative differential diagnosis of ovarian masses. Their results showed that with a CA125/CEA index above 25, the probability of a malignant ovarian tumor reaches 82% [36].

Andersen et al. revealed that the combination of CA125 and a symptom index identified cancer in 89.3% of women, including 80.6% of those with early-stage disease and 95.1% of those with advanced forms [37]. CA125 is widely used for monitoring ovarian cancer and assessing treatment response [38–40]. Potenza et al. showed that the normalization of CA125 by the fourth cycle of chemotherapy indicates a positive response to treatment [41]. Akhavan et al. also demonstrated the prognostic value of CA125 decline dynamics following neoadjuvant chemotherapy [42]. An analysis by Rodriguez et al., involving 103 patients with stage III–IV disease, established that a preoperative level of ≤ 1000 U/mL is

associated with a high probability of complete cytoreduction [43].

In a study by Piatek et al., it was found that a 5 U/mL increase in CA125 levels at 3 and 6 months post-treatment is associated with a significant reduction in 5-year survival. Additionally, a preoperative CA125 level exceeding 535 U/mL indicates the presence of lymph node metastases [44]. Chiang et al. found that patients with low CA125 levels (<35 U/mL) have a higher likelihood of successful interval debulking surgery and longer progression-free survival compared to patients with levels >100 U/mL [45]. Chan et al. demonstrated that elevated CA125 levels before the initiation of chemotherapy are independently associated with lower recurrence-free survival (HR = 2.13, 95% CI: 1.23–3.69; $p = 0.007$) and overall survival (HR = 1.99, 95% CI: 1.10–3.59; $p = 0.022$) [46]. Baseline CA125 levels prior to maintenance chemotherapy correlate with the risk of recurrence, and its rise serves as an early marker of clinical relapse [44, 47–49]. Paik et al., in a study of 99 patients with recurrent epithelial ovarian cancer, established that rising CA125 levels are associated with an increased probability of extrapelvic and multiple recurrences [50]. Finally, Wilder et al. showed that a gradual increase in CA125 levels within the normal range over a period of 1–3 months is associated with an elevated risk of ovarian cancer recurrence [51].

RAD51

RAD51 is one of the key proteins involved in DNA repair via the double-strand break (DSB) pathway. It catalyzes the re-synthesis of the damaged genomic region. Numerous studies have reported RAD51 overexpression in various types of cancer [59]. This may indicate a compensatory repair mechanism for damaged DNA in tumor cells, suggesting that dysregulation of this protein's expression could lead to an increased mutational burden [52]. For RAD51 to function correctly, two additional protein complexes are required: BCDX2 (comprising RAD51B, RAD51C, RAD51D, and XRCC2) and CX3 (comprising RAD51C and XRCC3). These two complexes act at different stages of DNA repair: BCDX2 is responsible for the recruitment and stabilization of RAD51 at damage sites, whereas the CX3 complex acts following RAD51 recruitment [60]. The BRCA1–PALB2–BRCA2 complex exhibits mediator activity, loading the RAD51 protein onto single-stranded DNA (ssDNA) regions coated with replication protein A (RPA), thereby recruiting RAD51 to the repair site [61, 62].

Research into RAD51C gene mutations has shown that variants associated with a partial or complete loss of RAD51C functionality are linked to an increased risk of ovarian cancer (OC) [52]. According to meta-analytical data, mutations such as c.706-2A>G, c.577C>T (p.Arg193Ter), c.224dupA (p.Tyr75Terfs), and c.955C>T (p.Arg319Ter) are associated with OC [63]. In another study, the variant c.790G>A (p.Gly-

264Ser) was interpreted as a moderate-penetrance risk allele [64]. Investigations within the Finnish population have revealed that the c.93delG and c.837+1G>A mutations (in BRCA1/BRCA2-negative cases) confer a higher risk for familial or sporadic OC, a lower risk for familial breast cancer (BC) combined with OC, and no association with BC-only populations. In the same study, the c.790G>A (p.Gly264Ser) mutation did not reach statistical significance, although a trend toward an increased risk of OC was observed [65]. Similarly to RAD51C, mutations in its paralog RAD51D are also associated with ovarian cancer. The majority of these mutations (approximately 80%) consist of nonsense mutations or frameshifts, with the most frequent being c.694C>T (p.Arg232Ter), c.270_271dupTA (p.Lys91Ilefs), c.556C>T (p.Arg186Ter), and c.748delC (p.His250Thrfs). Statistically, these mutations are associated with a high risk of developing OC, with the exception of p.Lys91Ilefs, which is considered a moderate-risk variant in Caucasian populations [66].

The MMR System

The DNA Mismatch Repair (MMR) system is a complex consisting of seven core proteins—MLH1, MLH3, MSH2, MSH3, MSH6, PMS1, and PMS2—essential for the detection and correction of DNA replication errors. The MMR complex functions through the interaction of several heterodimers: MSH2–MSH6 (MutS α), MSH2–MSH3 (MutS β), MLH1–PMS2 (MutL α), MLH1–PMS1 (MutL β), and MLH1–MLH3 (MutL γ) [67–70]. Alterations or epigenetic inactivation of MMR genes are associated with microsatellite instability (MSI). MSI is considered both a risk factor for the development of malignancies and a predictor of a positive response to immunotherapy, due to the high burden of aberrant antigens that render the tumor immunogenic [71, 72]. Some studies have established that MMR deficiency (dMMR) occurs more frequently in non-serous ovarian cancer (OC), specifically in endometrioid and clear cell carcinomas [73]. Mutations in the MLH1 and MSH2 genes are most commonly observed in patients diagnosed with early-onset non-serous OC [74]. Furthermore, in vitro studies have linked MMR deficiency to resistance to platinum-based chemotherapy [67]. The expression of MLH1 and MSH2 proteins, assessed by staining intensity, varied depending on the histopathological subtype and disease stage; these proteins exhibited more intense staining in serous OC compared to non-serous subtypes [75].

Conclusion

In this study, key molecular and genetic markers determining the biological behavior of ovarian cancer were analyzed. It has been established that conventional diagnostic methods possess insufficient specificity during the early stages of the disease.

The analysis of current data confirms that the implementa-

tion of molecular profiling—specifically the determination of BRCA1 and BRCA2 mutation status—has radically transformed patient management strategies. The identification of germline and somatic mutations in these genes, as well as the assessment of Homologous Recombination Deficiency (HRD), are now mandatory diagnostic steps that allow for the prediction of response to PARP inhibitors and platinum-based agents.

Thus, a shift from histological classification to the molecular-genetic stratification of ovarian tumors is a prerequisite for improving patient survival rates. Integrating genetic panels into routine clinical practice will not only optimize therapeutic approaches but also enable the identification of risk groups among healthy women for timely preventive interventions.

References

1. MacFarlane, Leigh-Ann, and Paul R Murphy. "MicroRNA: biogenesis, function and role in cancer." *Current genomics* 11, no. 7 (2010): 537-561.
2. Aboutalebi, Hamideh, Afsane Bahrami, Atena Soleimani, Nikoo Saeedi, Farzad Rahmani, Majid Khazaei, Hamid Fiuji et al. "The diagnostic, prognostic and therapeutic potential of circulating microRNAs in ovarian cancer." *The international journal of biochemistry & cell biology* 124 (2020): 105765.
3. Bartel, David P. "MicroRNAs: target recognition and regulatory functions." *cell* 136, no. 2 (2009): 215-233.
4. Pritchard, Colin C., Heather H. Cheng, and Muneesh Tewari. "MicroRNA profiling: approaches and considerations." *Nature Reviews Genetics* 13, no. 5 (2012): 358-369.
5. Prahm, Kira Philipsen, Guy Wayne Novotny, Claus Høgdall, and Estrid Høgdall. "Current status on micro RNA s as biomarkers for ovarian cancer." *Apmis* 124, no. 5 (2016): 337-355.
6. Singh, Alka, Sameer Gupta, and Manisha Sachan. "Epigenetic biomarkers in the management of ovarian cancer: current perspectives." *Frontiers in cell and developmental biology* 7 (2019): 182.
7. Llauradó, Marta, Blanca Majem, Tatiana Altadill, Lucia Lanau, Josep Castellví, Jose Luis Sánchez-Iglesias, Silvia Cabrera et al. "MicroRNAs as prognostic markers in ovarian cancer." *Molecular and Cellular Endocrinology* 390, no. 1-2 (2014): 73-84.
8. Katz, Betina, Claes G. Tropé, Reuven Reich, and Ben Davidson. "MicroRNAs in ovarian cancer." *Human pathology* 46, no. 9 (2015): 1245-1256.
9. Aboutalebi, Hamideh, Afsane Bahrami, Atena Soleimani, Nikoo Saeedi, Farzad Rahmani, Majid Khazaei, Hamid Fiuji et al. "The diagnostic, prognostic and therapeutic potential of circulating microRNAs in ovarian cancer." *The international journal of biochemistry & cell biology* 124 (2020): 105765.
10. Yokoi, Akira, Yusuke Yoshioka, Akihiro Hirakawa, Yusuke Yamamoto, Mitsuya Ishikawa, Shun-ichi Ikeda, Tomoyasu Kato et al. "A combination of circulating miRNAs for the early detection of ovarian cancer." *Oncotarget* 8, no. 52 (2017): 89811.

11. Khanson, K. P., and E. N. Imianitov. "Molekuliarnaia genetika raka iaichnikov." *Prakticheskaia Onkologija* 1, no. 4 (2000): 3-6.
12. Khokhlova, S. V., V. A. Gorbunova, L. N. Lyubchenko, and E. N. Imyanitov. "BRCA-associated ovarian cancer (the experience of the Chemotherapy Department in NN Blokhin Russian Cancer Research Center of the Ministry of Health of Russia)." *Journal of Modern Oncology* 18, no. 1 (2016): 37-44.
13. Lu, Hsiao-Mei, Shuwei Li, Mary Helen Black, Shela Lee, Robert Hoiness, Sitao Wu, Wenbo Mu et al. "Association of breast and ovarian cancers with predisposition genes identified by large-scale sequencing." *JAMA oncology* 5, no. 1 (2019): 51-57.
14. Parkin, D. Max, Freddie Bray, J. Ferlay, and Paola Pisani. "Global cancer statistics, 2002." *CA: a cancer journal for clinicians* 55, no. 2 (2005): 74-108.
15. Carroll, June C., Carol Cremin, Judith Allanson, Sean M. Blaine, Heather Dorman, Clare A. Gibbons, Jeremy Grimshaw et al. "Hereditary breast and ovarian cancers." *Canadian Family Physician* 54, no. 12 (2008): 1691-1692.
16. Stavropoulou, Alexandra V., Florentia Fostira, Maroulis Pertsis, Marianthi Tsiitlaidou, Gerassimos E. Voutsinas, Olga Triantafyllidou, Aristotelis Bamias et al. "Prevalence of BRCA1 mutations in familial and sporadic greek ovarian cancer cases." *PloS one* 8, no. 3 (2013): e58182.
17. De Jong, M. M., I. M. Nolte, G. J. Te Meerman, W. T. A. Van der Graaf, J. C. Oosterwijk, J. H. Kleibeuker, M. Schaapveld, and E. G. E. De Vries. "Genes other than BRCA1 and BRCA2 involved in breast cancer susceptibility." *Journal of medical genetics* 39, no. 4 (2002): 225-242.
18. Shaw, P. A., J. R. McLaughlin, R. P. Zweemer, S. A. Narod, H. Risch, R. H. M. Verheijen, A. Ryan, F. H. Menko, P. Kenemans, and I. J. Jacobs. "Histopathologic features of genetically determined ovarian cancer." *International Journal of Gynecological Pathology* 21, no. 4 (2002): 407-411.
19. De Leeneer, Kim, Ilse Coene, Brecht Crombez, Justine Simkens, Rudy Van den Broecke, Alain Bols, Barbara Stragier et al. "Prevalence of BRCA1/2 mutations in sporadic breast/ovarian cancer patients and identification of a novel de novo BRCA1 mutation in a patient diagnosed with late onset breast and ovarian cancer: implications for genetic testing." *Breast cancer research and treatment* 132, no. 1 (2012): 87-95.
20. Brozek, Izabela, Karolina Ochman, Jarosław Debniak, Lucyna Morzuch, Magdalena Ratajska, Magdalena Stepnowska, Maciej Stukan, Janusz Emerich, and Janusz Limon. "High frequency of BRCA1/2 germline mutations in consecutive ovarian cancer patients in Poland." *Gynecologic oncology* 108, no. 2 (2008): 433-437.
21. Smirnova, T. Yu, N. I. Pospekhova, L. N. Lyubchenko, S. A. Tjulandin, R. F. Gar'kavtseva, E. K. Ginter, and A. V. Karpukhin. "High incidence of mutations in BRCA1 and BRCA2 genes in ovarian cancer." *Bulletin of Experimental Biology and Medicine* 144, no. 1 (2007): 83-85.
22. Pohlreich, Petr, Michal Zikan, Jana Stribrna, Zdenek Kleibl, Marketa Janatova, Jaroslav Kotlas, Jana Zidovska et al. "High proportion of recurrent germline mutations in the BRCA1 gene in breast and ovarian cancer patients from the Prague area." *Breast cancer research* 7, no. 5 (2005): R728.
23. Iysanne D. a. N. de Muynck, Peter J. K. Kuppen, Eva M. de Ronde, Tom B. Kuipers, Hailiang Meic, Tjalling Bosse, Alexander I. Vahrmeijer, Katja N. Gaarenstroom, Inge t. a. Peters. "Evaluating a data-driven approach to biomarker discovery for tumor-targeted imaging in epithelial ovarian cancer." Taylor & Francis Group 2026;2-12
24. Furrer, Daniela, Jean Grégoire, Stéphane Turcotte, Marie Plante, Dimcho Bachvarov, Dominique Trudel, Bernard Têtu, Pierre Douville, and Isabelle Bairati. "Performance of preoperative plasma tumor markers HE4 and CA125 in predicting ovarian cancer mortality in women with epithelial ovarian cancer." *PLoS One* 14, no. 6 (2019): e0218621.
25. Nalini, Neelam, Amit Kumar, Saumya Sharma, Bijeta Singh, Aditya V. Singh, Jay Prakash, and Shreshtha Singh. "The diagnostic accuracy of serum and urine human epididymis protein 4 (HE4) in ovarian cancer in 15,394 subjects: an updated meta-analysis." *Cureus* 14, no. 10 (2022).
26. Barr, Chloe E., Garth Funston, David Jeevan, Sudha Sundar, Luke TA Mounce, and Emma J. Crosbie. "The performance of HE4 alone and in combination with CA125 for the detection of ovarian cancer in an enriched primary care population." *Cancers* 14, no. 9 (2022): 2124.
27. Chudecka-Głaz, Anita, Aneta Cymbaluk-Płoska, Małgorzata Węzowska, and Janusz Menkiszak. "Could HE4 level measurements during first-line chemotherapy predict response to treatment among ovarian cancer patients?." *PloS one* 13, no. 3 (2018): e0194270.
28. Chudecka-Głaz, Anita, Aleksandra Strojna, Kaja Michalczyk, Sylwia Wieder-Huszlá, Krzysztof Safranow, Edyta Skwirczyńska, and Anna Jurczak. "Evaluation of he4 use in the diagnosis of ovarian cancer: first and second recurrence, and an analysis of HE4 concentration during second-and third-line chemotherapy." *Diagnostics* 13, no. 3 (2023): 452.
29. Badgwell, Donna, and Robert C. Bast Jr. "Early detection of ovarian cancer." *Disease markers* 23, no. 5-6 (2007): 397-410.
30. Ahmad, Bashir, Seema Nawaz, Sajid Ali, Shumaila Bashir, Nourin Mahmood, and Bushra Gul. "Level and evaluation of tumor marker CA-125 in ovarian cancer patients in Khyber Pakhtunkhwa, Pakistan." *Asian Pacific Journal of Cancer Prevention* 16, no. 1 (2015): 185-189.
31. Cooper, Brian C., Anil K. Sood, Charles S. Davis, Justine M. Ritchie, Joel I. Sorosky, Barrie Anderson, and Richard E. Buller. "Preoperative CA 125 levels: an independent prognostic factor for epithelial ovarian cancer." *Obstetrics & Gynecology* 100, no. 1 (2002): 59-64.

32. Grzybowski, Wojciech, Jarosław Beta, Anna Fritz, Andrzej Durczyński, Mariusz Bidziński, Marek Grabiec, and Artur Jakimiuk. "Predictive value of CA 125 in detection of ovarian cancer in pre-and postmenopausal patients." *Ginekologia polska* 81, no. 7 (2010).
33. Antovska, S. V., N. Bashevska, and Natasha Aleksioska. "Predictive values of the ultrasound parameters, CA-125 and risk of malignancy index in patients with ovarian cancer." *Klin Onkol* 24, no. 6 (2011): 435-42.
34. Yang, Wei, Lei, Zhen Lu, Jing Guo, Bryan M. Fellman, Jing Ning, Karen H. Lu, Usha Menon et al. "Human epididymis protein 4 antigen, autoantibody complexes complement cancer antigen 125 for detecting early, stage ovarian cancer." *Cancer* 126, no. 4 (2020): 725-736.
35. Kim, Boyeon, Yongjung Park, Banseok Kim, Hyo Jun Ahn, Kyung, A. Lee, Jae Eun Chung, and Sang Won Han. "Diagnostic performance of CA 125, HE 4, and risk of ovarian malignancy algorithm for ovarian cancer." *Journal of clinical laboratory analysis* 33, no. 1 (2019): e22624.
36. Sørensen, Sofie Sølvsten, and Berit Jul Mosgaard. "Combination of cancer antigen 125 and carcinoembryonic antigen can improve ovarian cancer diagnosis." *Dan Med Bull* 58, no. 11 (2011): A4331.
37. Andersen, M. Robyn, Barbara A. Goff, Kimberly A. Lowe, Nathalie Scholler, Lindsay Bergan, Charles W. Drescher, Pamela Paley, and Nicole Urban. "Combining a symptoms index with CA 125 to improve detection of ovarian cancer." *Cancer: Interdisciplinary International Journal of the American Cancer Society* 113, no. 3 (2008): 484-489.
38. Ferraro, Simona, Cristina Robbiano, Nicoletta Tosca, Andrea Panzeri, Anna Maria Paganoni, and Mauro Panteghini. "Serum human epididymis protein 4 vs. carbohydrate antigen 125 in ovarian cancer follow-up." *Clinical Biochemistry* 60 (2018): 84-90.
39. Wilboux, M., E. Hénin, A. Oza, O. Colombar, E. Pujade-Lauraine, G. Freyer, M. Tod, and B. You. "Prediction of tumour response induced by chemotherapy using modelling of CA-125 kinetics in recurrent ovarian cancer patients." *British journal of cancer* 110, no. 6 (2014): 1517-1524.
40. Tuxen, Malgorzata K., G. Sölétormos, and P. Dombernowsky. "Serum tumor marker CA 125 for monitoring ovarian cancer during follow-up." *Scandinavian journal of clinical and laboratory investigation* 62, no. 3 (2002): 177-188.
41. Potenza, Enrico, Giulia Parpinel, Maria E. Laudani, Chiara Macchi, Luca Fuso, and Paolo Zola. "Prognostic and predictive value of combined HE-4 and CA-125 biomarkers during chemotherapy in patients with epithelial ovarian cancer." *The International journal of biological markers* 35, no. 4 (2020): 20-27.
42. Akhavan, Setareh, Yalda Jefrideh, Azamosadat Mousavi, Mitra Modares-Gilani, and Shahrzad Sheikh-Hasani. "Does a Decrease in CA-125 in Advanced Ovarian Cancer Following Neoadjuvant Chemotherapy Predict the Clinical Outcome of Patients? A Cross-sectional Study." *International Journal of Women's Health & Reproduction Sciences* 10, no. 3 (2022).
43. Rodriguez, Noah, J. Alejandro Rauh-Hain, Melina Shoni, Ross S. Berkowitz, Michael G. Muto, Colleen Feltmate, John O. Schorge, Marcela G. Del Carmen, Ursula A. Matulonis, and Neil S. Horowitz. "Changes in serum CA-125 can predict optimal cytoreduction to no gross residual disease in patients with advanced stage ovarian cancer treated with neoadjuvant chemotherapy." *Gynecologic oncology* 125, no. 2 (2012): 362-366.
44. Piatek, Szymon, Grzegorz Panek, Zbigniew Lewandowski, Mariusz Bidziński, Dominika Piatek, Przemysław Kosinski, and Mirosław Wielgos. "Rising serum CA-125 levels within the normal range is strongly associated recurrence risk and survival of ovarian cancer." *Journal of ovarian research* 13, no. 1 (2020): 102.
45. Chiang, An Jen, Jiabin Chen, Yu-Che Chung, Huan-Jung Huang, Wen Shiung Liou, and Chung Chang. "A longitudinal analysis with CA-125 to predict overall survival in patients with ovarian cancer." *Journal of Gynecologic Oncology* 25, no. 1 (2014): 51-57.
46. Chan, John K., Chunqiao Tian, Joshua P. Kesterson, Ken Y. Lin, Kathleen Darcy, Michael T. Richardson, Daniel S. Kapp et al. "Preoperative and pre-chemotherapy CA-125 levels in high-risk early-stage ovarian cancer—An NRG/GOG study." *Gynecologic oncology* 181 (2024): 54-59.
47. Markman, Maurie, P. Y. Liu, Mace L. Rothenberg, Bradley J. Monk, Mark Brady, and David S. Alberts. "Pretreatment CA-125 and risk of relapse in advanced ovarian cancer." *Journal of clinical oncology* 24, no. 9 (2006): 1454-1458.
48. Wang, Fang, Yanfen Ye, Xia Xu, Xuehui Zhou, Jinhua Wang, and Xiaoxiang Chen. "CA-125—indicated asymptomatic relapse confers survival benefit to ovarian cancer patients who underwent secondary cytoreduction surgery." *Journal of ovarian research* 6, no. 1 (2013): 14.
49. Tuxen, M. K., G. Sölétormos, and P. Dombernowsky. "Serum tumour marker CA 125 in monitoring of ovarian cancer during first-line chemotherapy." *British journal of cancer* 84, no. 10 (2001): 1301-1307.
50. Paik, E. Sun, Tae-Joong Kim, Yoo-Young Lee, Chel Hun Choi, Jeong-Won Lee, Byoung-Gie Kim, and Duk-Soo Bae. "Comparison of survival outcomes after recurrence detected by cancer antigen 125 elevation versus imaging study in epithelial ovarian cancer." *Journal of Gynecologic Oncology* 27, no. 5 (2016).
51. Wilder, James L., Edward Pavlik, John M. Straughn, Tyler Kirby, Robert V. Higgins, Paul D. DePriest, Frederick R. Ueland, Richard J. Kryscio, Ronald J. Whitley, and John Van Nagell. "Clinical implications of a rising serum CA-125 within the normal range in patients with epithelial ovarian cancer: a preliminary investigation." *Gynecologic oncology* 89, no. 2 (2003): 233-235.
52. Kalfa, Margarita A., Ilya O. Golovkin, Artem E. Lazarev, Lena P. Golubinskaya, Olga Yu Gritskovich, and Evgenia Yu Zyablitskaya. "Molecular genetic markers of ovarian cancer tumor cells and their microenvironment, study methods, and clinical value: a review." *Journal of Modern Oncology* 25, no. 3 (2023): 308-312.

53. Gorodnova T.V., Sokolenko A.P., Kotiv Kh.B., Ivantsov A.O., Nekrasova E.A., Ibragimov Z.N., Berlev I.V., Imyanitov E.N. Acquired Platinum Resistance of BRCA1-associated Ovarian Cancer after Neoadjuvant Chemotherapy. Title. 2022;21(5):87-91. (In Russ.) <https://doi.org/10.31550/1727-2378-2022-21-5-87-91>
54. Kurman RJ. WHO Classification of tumours of female reproductive organs. Lyon: International Agency for Research on Cancer, 2014
55. Leung, Dilys TH, Peter J. Fuller, and Simon Chu. "Impact of FOXL2 mutations on signaling in ovarian granulosa cell tumors." *The international journal of biochemistry & cell biology* 72 (2016): 51-54.
56. Heravi-Moussavi, Alireza, Michael S. Anglesio, S-W. Grace Cheng, Janine Senz, Winnie Yang, Leah Prentice, Anthony P. Fejes et al. "Recurrent somatic DICER1 mutations in non-epithelial ovarian cancers." *New England Journal of Medicine* 366, no. 3 (2012): 234-242.
57. Maeda, Daichi, Junji Shibahara, Takahiko Sakuma, Masanori Isobe, Shinichi Teshima, Masaya Mori, Katsutoshi Oda et al. "β-catenin (CTNNB1) S33C mutation in ovarian microcystic stromal tumors." *The American journal of surgical pathology* 35, no. 10 (2011): 1429-1440.
58. Jelinic, Petar, Jennifer J. Mueller, Narciso Olvera, Fanny Dao, Sasinya N. Scott, Ronak Shah, JianJiong Gao et al. "Recurrent SMARCA4 mutations in small cell carcinoma of the ovary." *Nature genetics* 46, no. 5 (2014): 424-426.
59. Lu, Hsiao-Mei, Shuwei Li, Mary Helen Black, Shela Lee, Robert Hoiness, Sitao Wu, Wenbo Mu et al. "Association of breast and ovarian cancers with predisposition genes identified by large-scale sequencing." *JAMA oncology* 5, no. 1 (2019): 51-57.
60. Chun, Jarin, Erika S. Buechelmaier, and Simon N. Powell. "Rad51 paralog complexes BCDX2 and CX3 act at different stages in the BRCA1-BRCA2-dependent homologous recombination pathway." *Molecular and cellular biology* 33, no. 2 (2013): 387-395.
61. Prakash, Rohit, Yu Zhang, Weiran Feng, and Maria Jasin. "Homologous recombination and human health: the roles of BRCA1, BRCA2, and associated proteins." *Cold Spring Harbor perspectives in biology* 7, no. 4 (2015): a016600.
62. Sullivan, Meghan R., and Kara A. Bernstein. "RAD-ical new insights into RAD51 regulation." *Genes* 9, no. 12 (2018): 629.
63. Suszynska, Malwina, Magdalena Ratajska, and Piotr Kozłowski. "BRIP1, RAD51C, and RAD51D mutations are associated with high susceptibility to ovarian cancer: Mutation prevalence and precise risk estimates based on a pooled analysis of ~30,000 cases." *Journal of ovarian research* 13, no. 1 (2020): 50.
64. Thompson, Ella R., Samantha E. Boyle, Julie Johnson, Georgina L. Ryland, Sarah Sawyer, David YH Choong, Georgia Chenevix-Trench et al. "Analysis of RAD51C germline mutations in high, risk breast and ovarian cancer families and ovarian cancer patients." *Human mutation* 33, no. 1 (2012): 95-99.
65. Peltari, Liisa M., Tuomas Heikkinen, Deborah Thompson, Anne Kallioniemi, Johanna Schleutker, Kaija Holli, Carl Blomqvist, Kristiina Aittomäki, Ralf Bützow, and Heli Nevanlinna. "RAD51C is a susceptibility gene for ovarian cancer." *Human molecular genetics* 20, no. 16 (2011): 3278-3288.
66. Yao, Hongwen, Ning Li, and Hua Yuan. "Clinical characteristics and survival analysis of Chinese ovarian cancer patients with RAD51D germline mutations." *BMC cancer* 22, no. 1 (2022): 1337.
67. Groothuizen, Flora S., and Titia K. Sixma. "The conserved molecular machinery in DNA mismatch repair enzyme structures." *DNA repair* 38 (2016): 14-23.
68. Amaral, Silva, Gleyson Kleber do, Manoela Domingues Martins, Hélder Antônio Rebelo Pontes, Eduardo Rodrigues Fregiani, Marcio Ajudarte Lopes, Felipe Paiva Fonseca, and Pablo Agustin Vargas. "Mismatch repair system proteins in oral benign and malignant lesions." *Journal of Oral Pathology & Medicine* 46, no. 4 (2017): 241-245.
69. Gupta, Dipika, and Christopher D. Heinen. "The mismatch repair-dependent DNA damage response: Mechanisms and implications." *DNA repair* 78 (2019): 60-69.
70. Erie, Dorothy A., and Keith R. Wenginger. "Single molecule studies of DNA mismatch repair." *DNA repair* 20 (2014): 71-81.
71. Ciona, Maria, Luca Giovanni Locatello, Luca Novelli, and Orreste Gallo. "The mismatch repair system (MMR) in head and neck carcinogenesis and its role in modulating the response to immunotherapy: a critical review." *Cancers* 12, no. 10 (2020): 3006.
72. Loeb, Lawrence A. "A mutator phenotype in cancer." *Cancer research* 61, no. 8 (2001): 3230-3239.
73. Rambau, Peter F., Máire A. Duggan, Prafull Ghatage, Khadija Warfa, Helen Steed, Renee Perrier, Linda E. Kelemen, and Martin Köbel. "Significant frequency of MSH2/MSH6 abnormality in ovarian endometrioid carcinoma supports histotype, specific Lynch syndrome screening in ovarian carcinomas." *Histopathology* 69, no. 2 (2016): 288-297.
74. Helder-Woolderink, Jorien M., E. A. Blok, Hans FA Vasen, H. Hollema, M. J. Mourits, and G. H. De Bock. "Ovarian cancer in Lynch syndrome; a systematic review." *European Journal of Cancer* 55 (2016): 65-73.
75. Samimi, Goli, Daniel Fink, Nissi M. Varki, Amreen Husain, William J. Hoskins, David S. Alberts, and Stephen B. Howell. "Analysis of MLH1 and MSH2 expression in ovarian cancer before and after platinum drug-based chemotherapy." *Clinical cancer research* 6, no. 4 (2000): 1415-1421.