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Review Article

A comprehensive review of mucinous ovarian cancer: insights into epidemiology, risk factors, histological characteristics, and clinical outcomes

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ABSTRACT

Mucinous ovarian cancer (MOC) represents a rare subtype within the spectrum of epithelial ovarian carcinoma (EOC). In contrast to a uniform approach applied to all EOC subtypes, MOC stands out as a distinctive entity. A nuanced understanding of the pathological features and genomic profile of MOC holds the potential for enhancing management strategies and, consequently, prognostic outcomes. The differentiation between primary MOC and metastatic mucinous carcinoma poses a challenge but is imperative for accurate clinical decision-making. Notably, early-stage MOC exhibits a favourable prognosis, while advanced disease is characterized by a less favourable outcome. Surgical intervention assumes a pivotal role both in the early stages and metastatic scenarios. Chemotherapy is typically initiated from stage II MOC onwards, with the conventional gynaecological protocol commonly employed; however, there is also precedent for the application of gastrointestinal (GI) regimens. Given the association of MOC with diverse molecular alterations, the consideration of targeted therapy emerges as a potential therapeutic avenue for this unique disease entity. The main tool used for this literature review was PubMed. MOC stands as a distinct entity within EOC subtypes, distinguished from GI mucinous carcinoma by its unique clinical behavior, pathological features, molecular profile, prognosis, and response to standard treatment. The challenges lie in both the diagnosis and treatment of MOC, emphasizing the complexity and specialized considerations required for managing this particular subtype of OC.

Keywords: MOC, Metastatic mucinous carcinoma, Genomic profile, Surgery, Chemotherapy, Targeted therapy

INTRODUCTION

Ovarian cancer (OC) stands eighth in terms of cancer-related deaths in women and is the seventh most common malignancy globally.[1] With 239,000 new cases annually, the incidence of OC rises with age and peaks in the sixth and seventh decades of life.[2] The group of neoplasms identified as OC is incredibly diverse, encompassing many histological subtypes that exhibit unique clinical manifestations, molecular characteristics, and prognostic consequences.[3] EOC is the most common histological type, accounting for 90% of all malignant EOC. As per Kurman et al type 1 tumours comprise low-grade serous carcinoma, endometrioid carcinoma, clear cell carcinoma, and MOC, while type 2 tumours consist of high-grade serous carcinoma (HGSOC), carcinosarcoma, and undifferentiated carcinoma.[4] Large, solitary cystic neoplasms with a sluggish, indolent growth are typical of type 1 EOCs. In addition to having minimal chromosomal instability, a low frequency of homologous recombination defects, and the potential for actionable mutations, these tumours rarely exhibit TP53 mutations. On the other hand, type 2 EOCs have a poor prognosis and develop quickly and aggressively. High chromosomal instability, homologous recombination abnormalities, and TP53 mutations are common. Type 2 EOCs exhibit a higher incidence of response to chemotherapy than type 1 tumours, although they also experience more recurrences.[4]

While MOC is rare and its frequency has sometimes been incorrectly reported as making up 5-10% of EOC, HGSOC is the most common histological subtype.[5] Nonetheless, a number of research claim that the actual percentage of MOC is somewhere between 1% to 3%.[6] Because of its unique behaviour, molecular profile, responsiveness to chemotherapy, and prognosis in comparison to the more prevalent HGSOC, MOC stands apart from other histotypes of EOC.

MOC emerges as the most prevalent histological subtype in women below the age of 40.[7] Notably, the recognized risk factors commonly associated with high-grade serous OC (HGSC), including nulliparity, early menarche, late menopause, lack of breastfeeding, and BRCA (Breast cancer gene) mutations, do not exhibit correlations with MOC. The sole potential risk factor linked to MOC is tobacco smoking.[8] The majority of HGSCs are typically diagnosed at an advanced stage, in contrast to MOC, which is identified as stage 1 in 80% of cases.[9] The prognosis is more favourable in the early stages but becomes less favourable in advanced stages, especially when compared to HGSC. This difference is primarily attributed to the suboptimal response of MOC to platinum-based chemotherapy.[10,11]

DIAGNOSTIC EVALUATION

Due to the rarity of MOC, it is imperative that patients newly diagnosed with this tumor undergo a thorough evaluation to eliminate the possibility of a GI primary tumor. Two distinct studies conducted by the gynaecologic oncology group revealed that a significant portion of cases initially classified as mucinous ovarian carcinoma were later reclassified as GI primary tumors upon re-evaluation of pathologic specimens, accounting for 55% in the study by Gore et al and 57-63% in the study by Zaino et al.[12,13] While this study lacks specific data on the site of origin, an additional analysis of published literature indicates that colorectal primaries are the most prevalent GI source, followed by gastric, appendiceal, and pancreatic origins.[14] Hence, a meticulous review of specimens by a gynaecologic pathologist is crucial. Additionally, to conclusively rule out a GI primary tumor, patients should undergo colonoscopy and upper GI endoscopy. This comprehensive approach ensures accurate diagnosis and informs appropriate treatment strategies.

Baseline staging for MOC should incorporate computed tomography (CT) scans of the chest, abdomen, and pelvis, consistent with the staging protocol for other OC types. In addition to imaging, assessing tumor markers such as CA125, carcinoembryonic antigen (CEA), and CA19-9 is recommended for both diagnosis and surveillance of mucinous ovarian tumors.[15,19] At baseline, the levels of these tumor markers should be carefully evaluated.

A noteworthy diagnostic indicator is the ratio of CA125 to CEA levels, with a ratio exceeding 25 to 1 potentially suggestive of a gynaecologic primary tumor. It is crucial to note that while this ratio has a positive predictive value of 82%, it is not definitive.[20] Unfortunately, MOC is frequently not identified until after surgery, and consequently, levels of tumor markers may appear normal postoperatively, even if they were elevated at the baseline assessment. This underscores the complexity of MOC diagnosis and emphasizes the importance of a comprehensive approach that integrates imaging and tumor marker assessments for an accurate evaluation of the disease.

PATHOLOGIC FEATURES

Approximately 80% of mucinous carcinomas of the ovary are metastatic, with a substantial 80% of primary tumors being identified at stage I. The most prevalent primary sites that metastasize to the ovary include 45% from the GI tract, 20% from the pancreas, 18% from the cervix and endometrium, and 8% from the breast.[21,22] The diagnosis of primary MOC demands meticulous pathological assessment due to its histological resemblance to other mucinous carcinomas, particularly colorectal carcinoma (CRC). A critical aspect of this diagnostic process involves recognizing the microscopic features and understanding the immunohistochemistry (IHC) profile of MOC. This thorough evaluation is imperative for achieving a definitive diagnosis, facilitating appropriate treatment, and providing an accurate prognosis. MOC typically presents as a heterogeneous tumor, encompassing benign, borderline, and carcinoma components. This heterogeneity suggests a stepwise progression to carcinoma, reflecting distinct stages in the development of the tumor.

The 2014 world health organization classification system distinguishes primary MOC into two subtypes: expansile (confluent) and infiltrative. While data is somewhat limited, recent literature reviews suggest that approximately 50-60% of reported mucinous ovarian tumors may display infiltrative histology.[23]

Expansile tumors are characterized by confluent glandular growth with minimal or no intervening stroma and lack stromal invasion. These tumors typically have low metastatic potential, and in 95% of cases, they remain confined to the ovary. Moreover, less than 5% of patients with stage I disease and the expansile subtype experience recurrence. On the other hand, infiltrative tumors exhibit destructive stromal invasion with haphazard glands and an associated desmoplastic stromal reaction. These tumors are more aggressive, and while 75% are diagnosed at stage I, 15-30% of women with stage I disease will experience recurrence.[24]

Both expansile and infiltrative MOC s commonly show diffuse positive staining for CK7. They may also exhibit positive staining for CK20, PAX-8, and/or estrogen receptor. However, when positive, the staining pattern is focal or patchy, not diffuse. This differs from the staining pattern observed in metastatic colorectal carcinoma, which

typically shows diffuse positive staining for CK20 and negative staining for CK7, Table 1.[27]

Table 1: Summary of IHC expression of MOC and colorectal cancer.

IHC	MOC	Colorectal cancer
CK7	+	-
CK20, CEA, CA19.9, CDX2	+	+

In the differentiation of primary MOC from metastatic disease originating from a GI tumor, tumor size and laterality can be instructive. If the tumor is unilateral and exceeds 10 cm in diameter, the ovary is the primary site in over 80% of cases. Conversely, if the tumor is bilateral and/or smaller than 10 cm in diameter, the primary site is within the GI tract in over 90% of cases.

MOLECULAR PROFILE

Molecular distinctions between MOC and serous sEOC have been identified, suggesting the need to consider these tumors as distinct entities. Studies have revealed an overexpression of the k-ras oncogene and a relative absence of mutations in the tumor suppressor gene p53 in MOC, contrasting with sEOC where the opposite pattern is observed.[25,26] Interestingly, mucinous tumors originating from the GI tract, such as colorectal and pancreatic cancers, also exhibit overexpression of the k-ras oncogene, Table 2.[27,28]

Table 2: Molecular markers expression in MOC, sEOC, colorectal cancer.

Molecular markers	MOC	sEOC	Colorectal
P53	-	+	+
k-ras	+	-	+

Available data support the concept that MOC develops through an adenoma–carcinoma sequence, originating from cystadenomas and mucinous borderline tumors. Adjacent to borderline or invasive mucinous tumors, normal epithelium and sites of transitional epithelium may be observed.[29] Mutations in k-ras are likely early genetic events in the development of mEOC, with an increasing frequency of k-ras mutations demonstrated in benign, borderline, and malignant mucinous tumors. This molecular insight contributes to a deeper understanding of the unique characteristics and progression of MOC.[30]

GENETICS

The preponderance of women with hereditary OC exhibits a germline mutation in either BRCA1 or BRCA2. Around 10% of women diagnosed with invasive EOC will carry a mutation in one of these genes. OCs associated with BRCA1 and BRCA2 mutations typically manifest with predominantly serous pathology and are often diagnosed at an advanced stage. Notably, mEOC is not linked to these mutations, emphasizing that these tumors follow distinct developmental pathways. This underscores the importance of recognizing the diverse genetic underpinnings and histopathological characteristics within the spectrum of OCs.[31]

SURGICAL TREATMENT

The surgical management of primary MOC closely follows the approach employed for other types of EOC. This typically involves a comprehensive procedure, including a total hysterectomy, bilateral salpingo-oophorectomy, omentectomy, and the excision of any visible tumor metastases, with the primary aim of achieving complete gross resection of the disease. It is advisable that surgery for MOC be conducted by gynecologic oncologists whenever possible. Traditionally, staging and debulking procedures were conducted through laparotomy. However, there has been a recent increase in the use of minimally invasive approaches, particularly in patients with isolated pelvic masses. In cases where minimally invasive surgery is employed, caution must be exercised to prevent intra-abdominal rupture and spillage, as this can lead to an elevation in the final disease stage. This highlights the importance of tailoring the surgical approach to the individual characteristics of the patient and the disease for optimal outcomes.

STAGING PROCEDURE

At a minimum, staging for mucinous ovarian carcinoma should encompass essential procedures such as pelvic washings, omentectomy, and peritoneal biopsies. However, the role of lymphadenectomy is less clearly defined in mucinous ovarian carcinoma compared to high-grade serous ovarian carcinoma. The decision to perform lymphadenectomy should be carefully considered, taking into account factors such as the individual characteristics of the patient, the extent of disease, and the overall clinical context. This reflects the nuanced approach required in the management of mucinous ovarian carcinoma, where optimal staging strategies may differ from those employed for other subtypes of OC.

ROLE OF LYMPHADENECTOMY

Recent data has indicated a very low frequency of lymph node metastasis in MOC, ranging from 0% to 2%.[32-35] Consequently, lymphadenectomy was often omitted in patients with grossly normal appearing lymph nodes. However, emerging evidence suggests that while lymph node metastases are rare in expansile MOC, they may be present in up to 30% of patients with the infiltrative subtype.[36] As a result, lymph node evaluation should generally be considered, particularly in patients with infiltrative tumors. Nevertheless, determining the subtype of MOC intra-operatively poses a practical challenge due to its difficulty. Therefore, careful consideration and individualized decision-making are essential when

determining the necessity of lymphadenectomy in the surgical management of MOC. Therefore, lymph-adenectomy should be routinely performed in early-stage disease.

ROLE OF FROZEN SECTION

Frozen section analysis of mucinous ovarian tumors is acknowledged for its difficulty, and research suggests that the final diagnosis (benign vs. borderline vs. invasive mucinous carcinoma) may deviate from the diagnosis based on frozen section evaluation in around 10% of cases.[37] Realistically, understanding the subtype of MOC-whether infiltrative or expansile-becomes particularly valuable when a patient has undergone unilateral oophorectomy, and the decision is being deliberated regarding whether to re-operate for staging purposes. In such cases, knowledge of the specific subtype can aid clinicians in making informed decisions about the necessity and extent of further surgical procedures for accurate staging and optimal patient management.

ROLE OF APPENDICECTOMY

In the past, it was a common practice to recommend routine appendectomy for any patient diagnosed with a borderline or invasive MOC. The rationale behind this approach was to ensure that the appendix was not the actual primary site of the tumor. However, recent data suggests that the likelihood of finding an occult appendiceal primary tumor in a patient with a normal-appearing appendix is relatively low, estimated to be around 1% or less.[38-40]

Therefore, the current recommendation is to routinely evaluate the appendix intra-operatively. Still, an appendicectomy may be omitted if the appendix appears grossly normal, especially if no gross metastatic disease is identified.

FERTILITY PRESERVATION

In primary MOC, as in other types of EOC, fertility preservation with unilateral salpingo-oophorectomy can be contemplated for patients with disease confined to one ovary. This option is particularly suitable for individuals who have a normal-appearing contralateral ovary and express a desire for future fertility. The consideration of fertility preservation in the management of MOC reflects an individualized approach, acknowledging the patient's reproductive goals while ensuring appropriate oncological care. It is crucial for patients to have thorough discussions with their healthcare team to weigh the benefits and potential risks associated with fertility-preserving interventions in the context of their specific disease characteristics and overall health.

In primary MOC, fertility preservation with USO can be considered in stage 1A ,1C1,1C2 who desire future fertility.

ADVANCED MOC

The standard surgical approach for advanced MOC involves the total macroscopic removal of the tumor, aiming for no residual disease (R0). Comparable to advanced serous OC, numerous studies have indicated that achieving optimal debulking, defined as minimal or no remaining visible tumor, is associated with improved survival outcomes for MOC.[41,42] Consequently, the primary objective of surgical treatment for advanced MOC is debulking surgery, with the goal of achieving a macroscopically complete resection. This emphasizes the importance of thorough and precise surgical intervention in the management of advanced MOC, aligning with the principles of optimal debulking for improved patient outcomes.

CHEMOTHERAPY

The current standard of care for managing all EOCs, including MOC, involves surgical staging for early-stage disease and cytoreductive surgery for advanced-stage disease, followed by platinum-based chemotherapy. The most commonly employed chemotherapy regimen for MOC is the combination of carboplatin and paclitaxel, which serves as the standard protocol for all types of EOCs. Notably, landmark clinical trials that have influenced clinical practice in EOCs have typically included a small percentage of MOC patients, ranging from 2.5% to 7%.[43-46] Due to the relatively low prevalence of MOC, there is a lack of dedicated clinical trials specifically focused on this subtype, making it important to consider evidence extrapolated from broader OC studies in the management of MOC.

In early-stage HGSC, adjuvant chemotherapy has demonstrated efficacy in reducing the risk of recurrence. However, the benefit of adjuvant chemotherapy in early-stage MOC is not as clear. Two primary trials investigating adjuvant chemotherapy in early-stage EOC, namely ACTION and ICON-1, included a total of 180 patients with MOC. The results did not reveal a statistically significant reduction in the recurrence rate between the observation arm (without chemotherapy) and the treatment arm (with chemotherapy).[47,48] This suggests that the role and effectiveness of adjuvant chemotherapy in early-stage MOC require further investigation and careful consideration in the context of individual patient characteristics and disease characteristics.

In a retrospective analysis by Nasioudis et al data from 4242 patients sourced from the national cancer data base (NCDB) in the United States were examined to assess the potential benefits of chemotherapy in early-stage MOC. The findings indicated no statistically significant difference in 5-year overall survival (OS) between patients who received chemotherapy and those who did not, specifically in stage 1A, 1B, and 1C. The 5-year OS rates were 86.8% and 89.7% for patients who did or did not receive chemotherapy, respectively. This lack of

significant difference persisted even after stratifying the data by disease sub-stage and tumor grade. The researchers concluded that, given the scarcity of evidence, the decision to offer adjuvant chemotherapy in this setting should be individualized and discussed thoroughly with patients.[49]

MOC has demonstrated lower responsiveness to platinum-based chemotherapy in comparison to other subtypes of EOC. The effectiveness of the standard chemotherapy regimen plays a crucial role in determining overall outcomes, and MOC has been consistently identified as platinum-resistant by several investigators. Response rates to platinum-based chemotherapy in MOC typically range between 12% and 35%, whereas HGSC exhibits response rates of around 70%.[50] This distinction in response underscores the importance of tailoring treatment approaches based on the specific characteristics of MOC to optimize therapeutic outcomes.

Due to the observed biological and molecular similarities between MOC and mucinous colorectal cancer (CRC), alternative GI chemotherapy protocols have been proposed as potential treatment options in addition to the standard gynecology regimen. Table 3 summarizes various GI protocols and their evidence in MOC.

Table 3: Various GI protocols and their evidence in MOC.

Chemotherapy regimen	Response rate
FOLFOX BCCA protocol	
Oxaliplatin 85 mg/m^2, IV over 2 h.	About 30%
Leucovorin 400 mg/m^2, IV over 2 h.	
5-FU 400 mg/m^2, IV push after LV, then 5-FU 2400 mg/m2, IV infusion over 46 h.	
The cycle is repeated every 2 weeks.	
XELOX BCCA protocol	
Day 1: Oxaliplatin 130 mg/m^2, IV.	No data in OC. High response rates were seen in colorectal cancer.[51,52]
Day 1-14: Capecitabine 1000 mg/m^2, orally twice per day.	
The cycle is repeated every 3 weeks.	

One notable study, the gynecology oncology group (GOG) trial 241, was specifically designed to investigate the efficacy of a colorectal chemotherapy regimen in newly diagnosed MOC. This phase III trial randomly assigned patients to receive either carboplatin/paclitaxel or capecitabine/oxaliplatin.[51] A second randomization involved the administration of bevacizumab or placebo to assess the activity of this antiangiogenic agent. Unfortunately, due to slow accrual, the trial was prematurely terminated after recruiting only 50 women. Data from the enrolled patients did not reveal a statistically significant difference in progression-free survival or toxicity profiles between the treatment arms.[52]

Recommendations for administering adjuvant treatment in patients with MOC vary, particularly in stage I disease. Most organizations agree that patients with stage II, III, or IV disease should receive adjuvant treatment, as outcomes for this group tend to be poor. A recent database study supported the use of adjuvant treatment, showing an improvement in overall survival for patients with stages II-IV MOC who received chemotherapy.

For patients with stage I disease, recommendations are mixed. The national comprehensive cancer network (NCCN) suggests that patients with stage IC disease receive adjuvant chemotherapy, while those with stage IA or IB disease do not, irrespective of other histologic findings (Figure 1).[53]

On the other hand, the European society for medical oncology (ESMO) guidelines recommend that treatment decisions for stage I disease be influenced, at least in part, by the histologic subtype. This is because infiltrative tumors tend to behave more aggressively than expansile tumors, influencing the consideration of adjuvant treatment in this subgroup. Individualized decision-making, considering various factors including stage, histologic subtype, and patient characteristics, is crucial for optimizing treatment outcomes in MOC.[54]

The ESMO guidelines (Figure 2) offer specific recommendations for adjuvant chemotherapy in patients with stage I MOC based on different subgroups. The guidelines recommend against adjuvant chemotherapy for patients with stage IA expansile, grade 1-2 tumors. However, for other subgroups of patients with stage I disease, the ESMO guidelines suggest varying considerations: For patients with stage IA infiltrative tumors or stage IB or IC expansile tumors, chemotherapy should be considered and for patients with stage IB or IC infiltrative tumors, chemotherapy is recommended.

These nuanced recommendations reflect the recognition that histologic subtypes and the degree of invasion can influence the behaviour of MOC, guiding decisions regarding the potential benefit of adjuvant chemotherapy in specific patient groups. As always, individualized treatment decisions, taking into account the patient's overall health, preferences, and potential risks and benefits, are crucial for optimizing care. The consideration of neoadjuvant chemotherapy in the management of advanced-stage MOC is a topic that lacks substantial research. Patient selection for neoadjuvant chemotherapy is often based on algorithms developed for other types of OC. However, it's important to note that neoadjuvant chemotherapy for MOC remains understudied. In the three largest trials of neoadjuvant chemotherapy for OC, MOC was diagnosed in no more than 3% of the patients.[55-57] As a result, the safety and efficacy of neoadjuvant chemotherapy with subsequent interval debulking

surgeries in patients specifically with MOC remain unknown. The limited representation of MOC in these trials underscores the need for dedicated research to better understand the potential benefits and risks of neoadjuvant chemotherapy in this particular subtype. Until more evidence becomes available, the approach to neoadjuvant chemotherapy in MOC should be carefully considered on an individual basis, taking into account the specific characteristics of the patient and the disease.

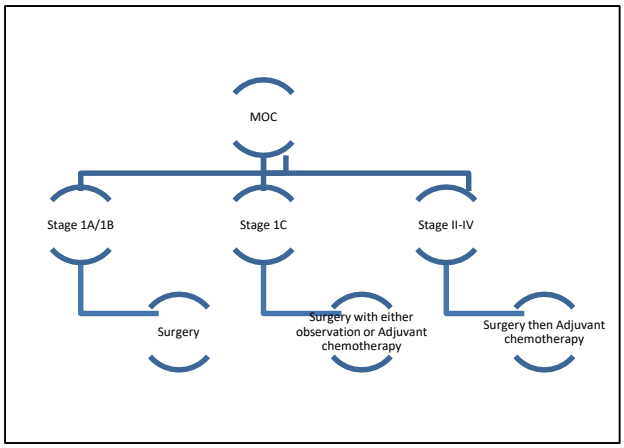

Figure 1: NCCN guideline for management of MOC.

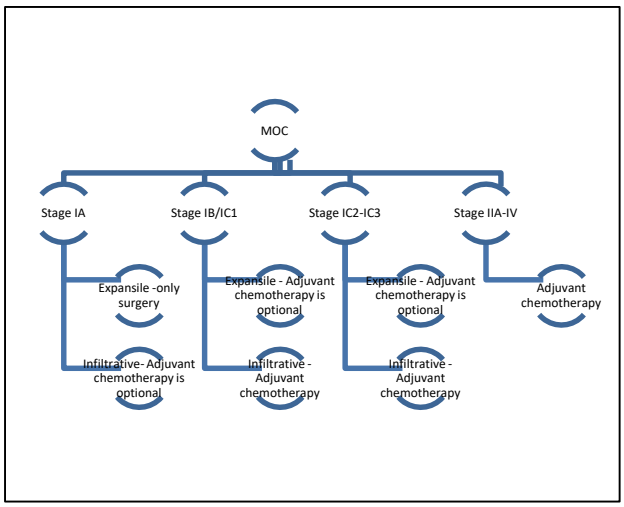

Figure 2: ESMO guidelines for adjuvant chemotherapy option in MOC.

HYPERTHERMIC INTRA-PERITONEAL CHEMOTHERAPY (HIPEC)

Certainly, the potential benefits of HIPEC for patients diagnosed with EOC have become a subject of heightened discussion. A study conducted by van Driel and colleagues in the Netherlands has notably contributed to this. Their research specifically demonstrated advantages in terms of recurrence-free and overall survival associated with the incorporation of HIPEC during interval debulking procedures for patients diagnosed with stage III EOC. This suggests that HIPEC could play a role in enhancing treatment outcomes for individuals at this particular stage of OC.[58]

The application of HIPEC in the context of MOC is an area where data is currently sparse. Notably, the study conducted by van Driel et al, as mentioned earlier, had a limited representation of patients with MOC, with only three out of the total 245 patients falling into this category. Despite the scarcity of data, there persists a considerable level of interest in exploring the potential utility of HIPEC for MOC. This interest stems from the perceived similarity of MOC to GI tumors, particularly in terms of peritoneal carcinomatosis. In the realm of GI tumors, HIPEC is frequently employed as part of treatment strategies. The parallels between MOC and GI tumors have spurred ongoing exploration and discussion regarding the potential role of HIPEC in managing MOC, even in the face of limited empirical evidence.[59]

TREATMENT OF RECURRENT AND PROGRESSIVE DISEASE

The challenges of treating MOC are underscored by the limited availability of data, particularly when it comes to second-line systemic treatments. While there is already a scarcity of information regarding first-line systemic treatments for MOC, the situation is even more pronounced in the context of second-line therapies

The challenges in managing MOC, particularly at the time of recurrence or progression, are reflected in generally poor responses to standard-of-care chemotherapy. For patients who have previously undergone adjuvant treatment with combinations of platinum agents and taxanes, there may be some potential benefit in exploring alternative regimens commonly used in GI cancer. Examples include capecitabine and oxaliplatin or 5-fluorouracil and oxaliplatin.

However, it's crucial to acknowledge that despite attempts with GI cancer regimens, outcomes for MOC remain suboptimal. Even in cases where patients have previously received regimens typical for GI tumors, the prognosis may not substantially improve. This emphasizes the aggressive nature of MOC and the need for alternative approaches. In the absence of well-established standard second-line treatments for MOC, there is a suggestion to consider extrapolating from data on mucinous GI tumors. This involves contemplating second-line GI cancer regimens, especially for patients who maintain good functional status after undergoing multiple lines of treatment. Bevacizumab may also be beneficial for treatment of recurrent or progressive disease

TARGETED THERAPY

The efficacy of PARPIs (poly adenosine diphosphate-ribose polymerase inhibitors) in managing non-mucinous type EOC is a milestone in OC management. It is the first targeted agent to be approved in OC treatment in both the

primary and recurrent settings. PARPIs have no role in the management of MOC as these tumors are not associated with BRCA. The vascular endothelial growth factor (VEGF) inhibitor, bevacizumab, shown to improve PFS and OS in MOC. Cetuximab is epithelial growth factor receptor (EGFR) monoclonal antibody was only able to employ anti-proliferative activity in MOC cell lines, which did not have KRAS mutations.[60] Trastuzumab, a HER2 monoclonal antibody, showed benefits to OS in MOC.[61]

CONCLUSION

MOC stands out as a distinct disease entity within the spectrum of EOC, displaying notable differences from GI mucinous carcinoma. These distinctions are evident across various dimensions, including clinical behaviour, pathological features, molecular profile, prognosis, and response to standard treatment. Remarkably, a substantial proportion of MOC cases, up to 80%, present as early-stage disease, contributing to an excellent prognosis. However, the outlook for advanced-stage disease is considerably poorer compared to HGSC, primarily due to a limited response to platinum-based chemotherapy. Despite these clinical nuances, diagnosing MOC remains challenging for pathologists. Presently, based on available data, the decision to omit routine pelvic and para-aortic lymphadenectomy depends on the tumor's characteristics-grossly confined expansile-type MOC may not necessitate lymphadenectomy, whereas it is recommended for infiltrative types. The role of appendectomy in MOC diagnosis remains uncertain. For young, carefully selected patients, fertility sparing surgery (FSS) is an option following comprehensive counselling. In advanced disease, the success of cytoreductive surgery and the extent of residual disease post-surgery emerge as pivotal factors influencing prognosis. Navigating the complexities of MOC management requires a multidisciplinary approach, considering the unique attributes of this subtype within the broader landscape of OC.

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