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Short Communication

A panoramic view of the strategies for epithelial ovarian cancer: a review of current challenges

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ABSTRACT

Epithelial ovarian cancer (EOC) remains a formidable challenge in the field of gynecological oncology, accounting for a significant proportion of cancer-related deaths among women worldwide. Despite advances in surgical techniques and chemotherapeutic regimens, the prognosis for patients with advanced-stage disease continues to be dismal, underscoring the urgent need for novel and more effective treatment strategies. This editorial review examines intriguing therapeutic modalities that have the potential to improve treatment outcomes as well as overcome the current difficulties in managing EOC. It presents a brief but comprehensive examination of current research literature about epithelial ovarian cancer, challenges, disease recurrence, molecular complexity, and emerging therapeutic modalities. The importance of gene- and stem-cell therapy in pursuing effective ovarian cancer treatments still holds the platform. While traditional chemotherapy remains crucial for advanced cases, surgical interventions remain pivotal for early-stage patients. Treatment options include innovative DNA polymerase (alpha/delta/epsilon) inhibitors, personalized treatments, and immunotherapies toward advanced cases for quality survival. The challenges posed by epithelial ovarian cancer and late diagnosis necessitate a continuous quest for improved therapeutic options. Emerging approaches such as gene and stem cell therapies show promise in reshaping treatment paradigms. Further exploring localized treatment modalities presents avenues for enhancing improved patient payoff.

Keywords: Epithelial ovarian cancer, Immunotherapy, Vascular endothelial growth factor, DNA polymerase inhibitor, Combinatorial approach

INTRODUCTION

Current challenges

The clinical epidemiology of epithelial ovarian cancer (EOC) marks it as the eighth leading cause of cancer-related mortality in females. EOC presents advanced-stage diagnosis (70-80%). Hence, a poor long-term (>10 years) survival rate worldwide, underscoring the understanding and updating of innovative treatment approaches, appears to be the need for an hour.[1] Despite significant progress in surgical and chemotherapeutic techniques, patients with advanced-stage EOC present a five-year survival rate of 45%.[2] This editorial review addresses the ongoing challenges in managing EOC. It specifically investigates small molecule drugs and lines of treatments. The editorial offers the potential of these compounds for transformative treatment, leading to better patient outcomes.

Late diagnosis and advanced disease stage

One of the primary obstacles in the effective management of EOC is the insidious nature of its early symptoms, often leading to delayed diagnosis at an advanced stage when the disease has already metastasized. The lack of specific and reliable screening methods further exacerbates this challenge, resulting in most patients presenting with a diagnostic blunder. This late presentation significantly

limits the effectiveness of conventional treatment approaches and contributes to poor overall survival rates.

Chemoresistance and disease recurrence

Despite the initial response to standard chemotherapy regimens, the development of chemoresistance remains a significant hurdle in the long-term management of EOC. Recurrence rates are high, and a substantial proportion of patients experience disease progression, ultimately leading to treatment failure. The mechanisms underlying chemoresistance are multifaceted, involving complex molecular pathways and favorable tumor microenvironmental that promote the survival and proliferation of resistant cancer cells.

Tumor heterogeneity and molecular complexity

EOC is a heterogeneous disease, encompassing various stratifications: high-grade (70%) and low-grade serous (3%), endometrioid and clear cell (12%), mucinous carcinoma (3%).[3] Histological subtypes with distinct molecular profiles; p53 normal/abnormal/wild type (p53abn/wt); MAPK mutations (MAPKmut); deficient mismatch (MMRd); deficient homologous repair (HRDdef); BRCA1-associated tandem duplications/deletions (BRCA1 dup/del); mutated POLE (POLEmut); fold-back inversions (FBI); tandem duplications (TenD); napsin A (NAPSA), and clinical behaviors.[4] This heterogeneity poses a significant challenge in developing targeted therapies that can effectively address the diverse molecular landscapes of EOC tumors. Additionally, the intricate interplay between genetic and epigenetic alterations, as well as the dynamic nature of tumor evolution, further complicates the development of personalized treatment strategies.

Limited targeted therapies and treatment options

While targeted therapies have revolutionized the treatment landscape for certain cancers, their impact on EOC has been relatively limited. The complex biology of EOC, coupled with the lack of actionable molecular targets, has hindered the development of effective targeted agents. Consequently, the treatment options for EOC patients, particularly those with recurrent or chemoresistant disease, remain relatively limited, underscoring the urgent need for novel therapeutic approaches.

EMERGING THERAPIES

PARP inhibitors and synthetic lethality

Poly (ADP-ribose) polymerase (PARP) inhibitors have emerged as a promising class of drugs in treating EOC, particularly in patients with germline or somatic BRCA mutations. These inhibitors exploit the concept of synthetic lethality by targeting DNA repair deficiencies in cancer cells, rendering them more susceptible to cell death. PARP inhibitors have demonstrated significant clinical benefits in maintenance and treatment settings, leading to their approval for specific indications in EOC.[5]

Hitching up the immune system

Immunotherapy represents a paradigm shift in cancer treatment, harnessing the body's immune system to recognize and eliminate cancer cells.[6] Mutated, damaged, or structurally perturbed DNA is reported to be immunogenic and is a potential target for understanding the efficacy of immunotherapies.[7,8] In the context of EOC, immune checkpoint inhibitors, such as anti-PD-1 and anti-PD-L1 antibodies, have shown promising results in clinical trials, particularly in combination with other therapies (Figure 1). Additionally, novel immunotherapeutic approaches, including adoptive cell therapies and cancer vaccines, are being actively investigated, with the potential to enhance the immune system's ability to target and eradicate EOC cells.

Antiangiogenic agents targeting tumor vasculature

Angiogenesis, the formation of new blood vessels, plays a crucial role in tumor growth, invasion, and metastasis. Antiangiogenic agents, such as bevacizumab, a monoclonal antibody targeting vascular endothelial growth factor (VEGF), have shown promising results in combination with chemotherapy for treating advanced EOC. By targeting the tumor vasculature and disrupting the supply of nutrients and oxygen to cancer cells, these agents provide a complementary approach to conventional cytotoxic therapies.

Targeted therapies/precision medicine

Ongoing research focuses on identifying and targeting specific molecular alterations in EOC tumors, such as mutations in KRAS, PIK3CA, and other driver genes.[9] Developing targeted therapies tailored to these molecular aberrations holds the potential for more personalized and effective treatment strategies. Additionally, integrating genomic profiling and molecular biomarkers may facilitate the identification of patient subgroups most likely to benefit from specific targeted therapies, paving the way for precision medicine approaches in EOC.

Novel drug delivery systems and formulations

Innovative drug delivery systems and formulations are being explored to enhance the efficacy and minimize the toxicity of existing therapeutic agents. For example, nanoparticle-based drug delivery platforms have shown promise in improving the pharmacokinetic and biodistribution profiles of chemotherapeutic agents, potentially increasing their accumulation in tumor tissues while reducing systemic toxicity. Additionally, intraperitoneal chemotherapy administration has gained attention as a strategy to maximize local drug exposure while minimizing systemic side effects.

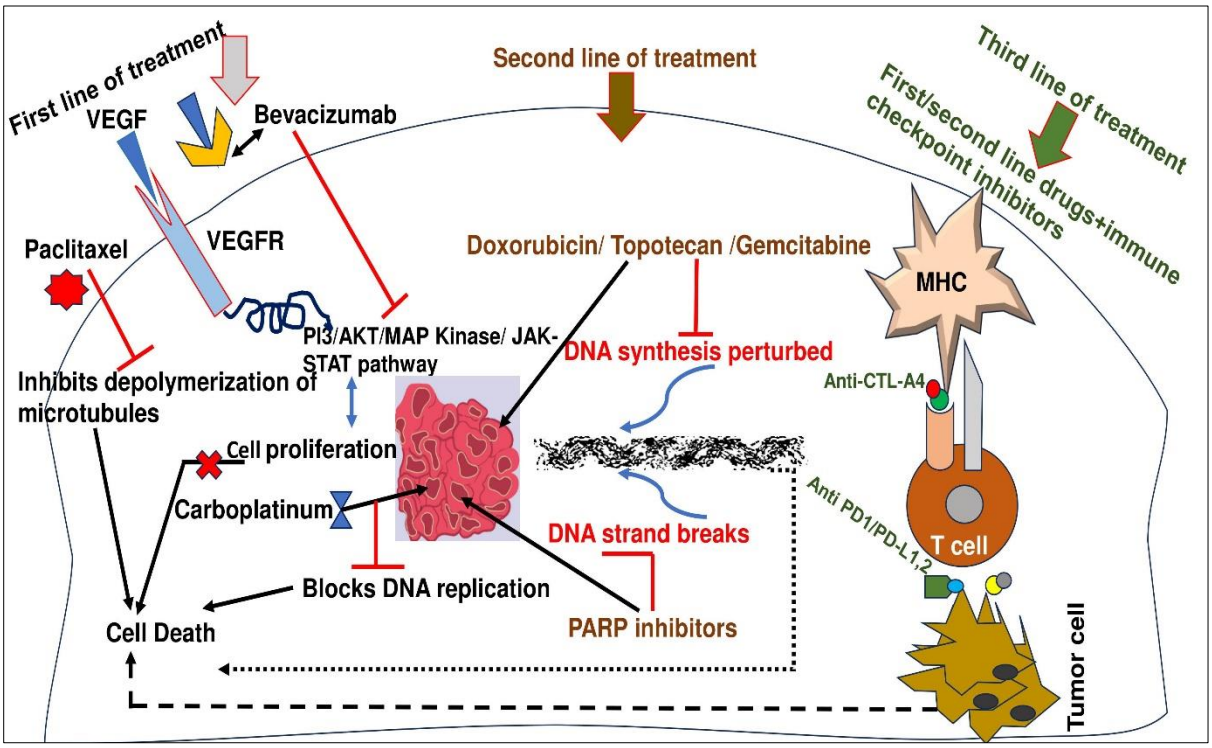

Figure 1: This figure represents the treatment modalities for epithelial ovarian cancer.

Combinatorial approaches and rational drug combinations

Given the complexity and heterogeneity of EOC, combinatorial approaches involving the strategic combination of different therapeutic modalities are being actively investigated. Rational drug combinations, such as the combination of PARP inhibitors with chemotherapy, immunotherapy, or targeted agents, may offer synergistic effects and potentially overcome resistance mechanisms.[10] These combinatorial strategies aim to simultaneously target multiple pathways and vulnerabilities in EOC cells, thereby maximizing therapeutic efficacy.

CONCLUSION

Despite the substantial challenges posed by epithelial ovarian cancer, the field is witnessing an unprecedented surge in innovative therapeutic strategies and emerging technologies. The development of PARP inhibitors, immunotherapies, antiangiogenic agents, and targeted therapies has ushered in a new era of hope for patients with this devastating disease. However, continued research efforts and clinical trials are paramount to elucidate the underlying mechanisms of EOC further and refine these emerging therapies.

Collaboration among researchers, clinicians, and pharmaceutical companies is crucial to accelerate the translation of these promising approaches into clinical practice. Additionally, integrating precision medicine principles and leveraging genomic profiling and molecular biomarkers can personalize treatment strategies and improve outcomes for EOC patients.

While the road ahead is arduous, the scientific community's unwavering dedication and the rapid pace of technological advancements offer a glimmer of hope for enhanced treatment strategies and improved survival rates for women afflicted with epithelial ovarian cancer.

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