

Immunotherapy in Vulvar Cancer: Advances and Future Perspectives

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DESCRIPTION

Vulvar cancer, although relatively rare compared to other gynecological malignancies, poses significant challenges in terms of treatment options and outcomes. Immunotherapy, a revolutionary approach in cancer treatment, has shown promising results in various cancer types, including vulvar cancer. This article explores the role of immunotherapy in vulvar cancer, highlighting recent advances, current challenges, and future perspectives.

Understanding vulvar cancer

Vulvar cancer is a malignant tumor that originates in the tissues of the vulva, the external female genitalia. It can arise from different cell types, including squamous cells, melanocytes, and glandular cells. Squamous Cell Carcinoma (SCC) is the most common histological subtype, accounting for approximately 90% of all vulvar cancer cases. Risk factors for vulvar cancer include age, Human Papillomavirus (HPV) infection, smoking, chronic vulvar inflammation, and immunosuppression.

Conventional treatment modalities

The management of vulvar cancer typically involves a multidisciplinary approach, including surgery, radiation therapy, and chemotherapy. Surgery remains the primary treatment modality for localized disease, with options ranging from wide local excision to radical vulvectomy with lymph node dissection. Radiation therapy may be used as adjuvant therapy or primary treatment for unresectable tumors or patients who are not surgical candidates. Chemotherapy, often in combination with radiation therapy, is employed in advanced or metastatic disease settings.

Challenges in vulvar cancer treatment

Despite advances in treatment modalities, vulvar cancer poses several challenges, including high rates of recurrence, treatment-related morbidity, and limited systemic therapy options for advanced disease. Additionally, the heterogeneity of vulvar

cancer and the presence of immune evasion mechanisms within the tumor microenvironment contribute to treatment resistance and disease progression.

Role of immunotherapy

Immunotherapy has emerged as a promising treatment strategy for various cancer types by harnessing the body's immune system to recognize and eliminate cancer cells. Immune checkpoint inhibitors, which block inhibitory pathways that dampen immune responses, have shown remarkable efficacy in restoring anti-tumor immunity and improving clinical outcomes in several malignancies, including melanoma, lung cancer, and bladder cancer.

Advances in immunotherapy for vulvar cancer

While the role of immunotherapy in vulvar cancer is still evolving, several studies have investigated its potential efficacy in this disease setting. Key advances in immunotherapy for vulvar cancer include

Immune checkpoint inhibitors: Clinical trials evaluating immune checkpoint inhibitors, such as pembrolizumab and nivolumab, have shown promising results in patients with advanced or metastatic vulvar cancer. These agents target Programmed Cell Death Protein 1 (PD-1) or its ligand (PD-L1), restoring T-cell-mediated antitumor immune responses and leading to durable responses in a subset of patients.

Combination therapies: Combinations of immune checkpoint inhibitors with other systemic therapies, such as chemotherapy or targeted agents, are being explored to enhance treatment efficacy and overcome resistance mechanisms. Preclinical studies have demonstrated synergistic effects of immune checkpoint blockade with chemotherapy or radiation therapy in stimulating antitumor immune responses and improving tumor control.

Biomarker-driven approaches: Biomarkers, including PD-L1 expression, Tumor Mutational Burden (TMB), and immune cell infiltration, are being investigated as predictive markers of response to immunotherapy in vulvar cancer. Identifying patients

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who are most likely to benefit from immunotherapy can optimize treatment selection and improve clinical outcomes.

Neoadjuvant and adjuvant immunotherapy: Neoadjuvant or adjuvant immunotherapy may offer additional benefits in the management of locally advanced or high-risk vulvar cancer. By priming the immune system before surgery or consolidating treatment after surgery, immunotherapy has the potential to reduce tumor burden, eradicate micrometastases, and improve long-term survival outcomes.

Future perspectives

The future of immunotherapy in vulvar cancer holds great promise, with ongoing research efforts focused on identifying novel therapeutic targets, optimizing treatment combinations, and overcoming resistance mechanisms. Key areas of future investigation include

Novel immune checkpoints: Targeting additional immune checkpoints or co-stimulatory molecules implicated in T-cell activation and regulation may expand the repertoire of immunotherapeutic targets in vulvar cancer. Preclinical studies are exploring the therapeutic potential of antibodies targeting alternative immune checkpoints, such as Lymphocyte Activation Gene-3 (LAG-3), T-cell immunoglobulin and mucin domain-containing protein 3 (TIM-3), and T-cell immunoglobulin and ITIM domain (TIGIT).

Personalized immunotherapy: Precision medicine approaches, including genomic profiling and tumor immune profiling, are facilitating the identification of patient-specific vulnerabilities and immune evasion mechanisms in vulvar cancer. By tailoring immunotherapy based on individual tumor characteristics and immune profiles, personalized treatment strategies can optimize therapeutic outcomes and minimize treatment-related toxicities.

Combination immunotherapy: Combinations of immune checkpoint inhibitors with other immunomodulatory agents, such as cytokines, oncolytic viruses, cancer vaccines, and

adoptive cell therapies, are being investigated to enhance immune responses and overcome resistance mechanisms in vulvar cancer. Clinical trials evaluating novel combination regimens are underway to explore synergistic effects and improve treatment efficacy.

Immunotherapy in early-stage disease: The role of immunotherapy in the neoadjuvant or adjuvant setting for early-stage vulvar cancer is an area of active investigation. Clinical trials are evaluating the efficacy of immune checkpoint inhibitors alone or in combination with standard therapies to reduce the risk of recurrence and improve long-term survival outcomes in patients with high-risk or locally advanced disease.

Immunotherapy resistance mechanisms: Understanding the mechanisms of primary and acquired resistance to immunotherapy in vulvar cancer is critical for developing strategies to overcome treatment resistance and improve patient outcomes. Preclinical studies are investigating immune escape mechanisms, tumor microenvironment dynamics, and host-tumor interactions to identify novel therapeutic targets and combination strategies.

CONCLUSION

Immunotherapy represents a promising treatment approach for vulvar cancer, offering the potential for durable responses and improved survival outcomes in patients with advanced or metastatic disease. While significant progress has been made in understanding the role of immunotherapy in vulvar cancer, several challenges remain, including identifying predictive biomarkers, optimizing treatment combinations, and overcoming resistance mechanisms. Future research efforts focused on personalized immunotherapy, novel combination regimens, and overcoming treatment resistance hold promise for advancing the field and improving outcomes for patients with vulvar cancer. By harnessing the power of the immune system to target and eradicate cancer cells, immunotherapy offers hope for a brighter future in the management of this challenging disease.