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The Exploration of Immunotherapy Methods for Endometrial Cancer

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Abstract Immunotherapy holds significant importance and broad prospects in the treatment of endometrial cancer. Traditional treatment methods have limited efficacy for advanced or recurrent patients, while immunotherapy can activate the patient's own immune system to attack tumor cells, offering more precise and effective treatment outcomes. Personalized immunotherapy can select the most suitable treatment plan based on the patient's immune and tumor characteristics, improving therapeutic effects and reducing side effects. Immunotherapy demonstrates enduring treatment effects, prolonging patient survival and enhancing quality of life. Combined with other treatment modalities, immunotherapy forms a comprehensive therapeutic strategy, augmenting treatment efficacy. Future research and innovation will further drive the application of immunotherapy in the treatment of endometrial cancer. The purpose of this research is to provide a comprehensive understanding of the disease, analyze the efficacy and safety of existing methods, and explore future research directions and challenges. Through the presentation and analysis of these contents, valuable information and references can be provided to the public, promoting research and application of immunotherapy for endometrial cancer and advancing medical progress and treatment innovation.

Keywords Immunotherapy; Endometrial cancer; Personalized treatment; Persistent effects; Comprehensive therapy

Endometrial cancer is one of the most common gynecological malignancies in women, mainly occurring in endometrial tissue. Although early endometrial cancer usually has a good prognosis, the treatment of advanced or recurrent endometrial cancer remains a challenge. At present, the main treatment methods for endometrial cancer include surgical resection, radiotherapy, and chemotherapy. However, these traditional treatment methods have some limitations and side effects. Surgery is effective for early cases, but the treatment effect for advanced or recurrent endometrial cancer is limited. Although radiotherapy and chemotherapy can control disease progression, they are often accompanied by severe toxic side effects and the development of drug resistance.

Finding more effective treatment methods is one of the focuses of current research on endometrial cancer. In this context, immunotherapy is considered a promising option. By regulating the function of the immune system, immunotherapy can provide better treatment outcomes and survival rates for patients with endometrial cancer. In summary, the importance and potential of immunotherapy in cancer treatment have been widely recognized. Immunotherapy provides a new treatment approach and possibility for the treatment challenge of endometrial cancer. This research will explore immunotherapy strategies for endometrial cancer, including immune checkpoint inhibitors, tumor vaccines, and CAR-T cell therapy, and discuss their progress and challenges in clinical application and efficacy evaluation.

Endometrial cancer is currently one of the main health issues for women, posing a huge burden on both patients and the medical community. Although traditional cancer treatment methods such as surgery, radiotherapy, and chemotherapy have achieved certain results to some extent, there are still many challenges and limitations. In recent years, immunotherapy, as an emerging treatment method, has attracted widespread attention and research, and its importance and potential in cancer treatment have been highly recognized. This research discusses the progress of immunotherapy for endometrial cancer, including different treatment methods such as immune checkpoint inhibitors, immune cell therapies, vaccines, and immune modifiers. The aim is to convey to readers the

latest achievements and progress of immunotherapy in endometrial cancer, identify future research directions and priorities, and explore how to further improve the efficacy and safety of immunotherapy, And how to address the promotion and popularization of immunotherapy in endometrial cancer.

1 Immunotherapy's Fundamental Principles

1.1 Functionality and mechanisms of the immune system

The immune system is a complex defense mechanism within the human body, aimed at protecting the body from pathogens and other abnormal cells. It orchestrates immune responses through the interaction of various cells and molecules. Innate immunity is a nonspecific defense reaction and acts as the body's primary defense against pathogens. It prevents the invasion and spread of pathogens through mechanical barriers (like skin and mucosa) and nonspecific immune cells (such as neutrophils and macrophages). While this immune response is rapid, its disadvantage lies in its lack of specificity, unable to mount precise responses against different pathogens (Bolivar et al., 2018).

Adaptive immunity is a highly specific immune response based on lymphocytes (T cells and B cells) activity. It develops in early life through exposure to pathogens or vaccination. When pathogens invade the body, their antigenic components are captured by antigen-presenting cells and presented to T cells. T cells bind to the presented antigen, activating other immune cells like B cells. Activated B cells differentiate into plasma cells, producing antibodies to neutralize pathogens or aid in their clearance (MacKintosh and Crosbie, 2018).

1.2 Classification and mechanisms of immunotherapy

Immunotherapy activates or enhances the immune system's responses to combat diseases. Passive immunotherapy uses exogenous antibodies to neutralize pathogens or activate immune cells., while active immunotherapy involves methods like vaccines, cellular immunotherapy, and immune checkpoint inhibitors to activate the patient's immune system. These immunotherapeutic methods have shown significant clinical success and play vital roles in treating various diseases. However, immunotherapy still faces some challenges such as uncertain treatment efficacy and immune-related adverse reactions persist, requiring further research and improvement. Vaccines, containing pathogen antigens or related components, simulate infection to trigger an immune response. They activate the immune cells and antibody production in the body, providing protection against specific pathogens. Vaccines have broad applications, including preventing infectious diseases and certain cancers (Crosbie et al., 2022).

Cellular immunotherapy utilizes the patient's own immune cells to target tumor cells. This method includes CAR-T cell therapy and tumor-associated antigen (TAA)-specific T cell therapy. CAR-T cell therapy modifies a patient's T cells to express specific antigen receptors (CARs) that identify and eliminate tumor cells. TAA-specific T cell therapy utilizes the patient's own T cells, amplified and activated to recognize and attack tumor cells. Immune checkpoint inhibitors constitute a class of drugs that boost immune cell attacks on tumor cells by inhibiting negative regulatory signals in the immune system. These inhibitors primarily target immune checkpoint molecules like PD-1, PD-L1, and CTLA-4, restoring immune cell activity to effectively recognize and eliminate tumor cells (Cao et al., 2021).

1.3 Mechanisms of immune checkpoint inhibitors

Immune checkpoint inhibitors are a class of drugs that enhance a patient's immune system's ability to attack tumor cells by inhibiting the function of immune checkpoint molecules. These molecules are proteins that negatively regulate the activity of the immune system. Their function is to prevent excessive activation of immune cells, protecting normal cells from immune attacks. Tumor cells can exploit immune checkpoint molecules to evade immune system attacks, thereby promoting tumor growth and spread. The mechanism of action of immune checkpoint inhibitors involves blocking the binding between immune checkpoint molecules and their ligands, releasing the immune system's inhibition and restoring immune cells' ability to kill tumor cells.

The most common immune checkpoint inhibitors are anti-CTLA-4 antibodies and anti-PD-1/PD-L1 antibodies. CTLA-4 is a molecule that negatively regulates during T cell activation, suppressing T cell activity. Anti-CTLA-4 antibodies can block the binding of CTLA-4 to its ligand, enhancing T cells' ability to attack tumor cells. PD-1 is a molecule expressed on activated T cells' surfaces, and its ligand PD-L1 is often expressed on tumor cell surfaces. The binding of PD-1 to PD-L1 inhibits T cell activity. Anti-PD-1 and anti-PD-L1 antibodies can block the binding between PD-1 and PD-L1, restoring T cell cytotoxicity.

Immune checkpoint inhibitors have shown significant success in treating various cancers. They not only improve patient survival rates but also provide enduring treatment effects. However, immune checkpoint inhibitors also have side effects such as immune-related toxicities, including skin inflammation, colitis, and hepatitis. Therefore, close monitoring and management of patients' immune-related side effects are necessary when using immune checkpoint inhibitors. The fundamental principle of immunotherapy is to modulate and enhance the functionality of a patient's immune system to recognize, attack, and eliminate tumor cells. Immune checkpoint inhibitors represent an important immunotherapy method by blocking the function of immune checkpoint molecules to bolster the immune system's ability to target tumor cells. Nevertheless, immunotherapy still faces challenges, including immune resistance and immune-related toxicities. Further research and clinical practice are essential to enhance the efficacy and safety of immunotherapy (Figure 1).

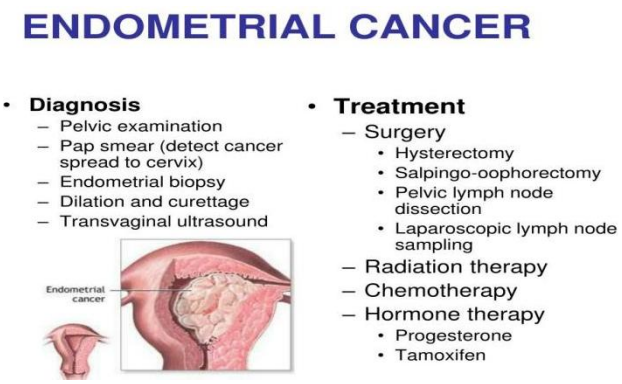

Figure 1 Diagnosis and method of endometrial cancer

2 Uterine Endometrial Cancer Immunotherapy Strategies

2.1 Clinical application of PD-1/PD-L1 inhibitors

PD-1/PD-L1 inhibitors are a class of drugs targeting immune checkpoint molecules. By interrupting the interaction between programmed cell death protein 1 (PD-1) and programmed death-ligand 1 (PD-L1), these drugs enhance the immune cells' ability to attack tumor cells. In clinical studies, PD-1/PD-L1 inhibitors have shown significant efficacy in various tumor types, including uterine endometrial cancer. Currently, PD-1/PD-L1 inhibitors have made important strides in clinical research on uterine endometrial cancer. One of the extensively studied PD-1/PD-L1 inhibitors is Pembrolizumab. Pembrolizumab is a high-affinity humanized monoclonal antibody that selectively binds and blocks the interaction between PD-1 and PD-L1. In the treatment of uterine endometrial cancer, Pembrolizumab has demonstrated clear efficacy in several clinical trials (Huvila et al., 2021).

A clinical trial named KEYNOTE-028 investigated Pembrolizumab's application in patients with advanced or metastatic uterine endometrial cancer. The results indicated that approximately 20% to 30% of patients treated with Pembrolizumab experienced either partial or complete tumor regression. Furthermore, the study found that PD-L1-positive patients exhibited longer survival periods following Pembrolizumab treatment. Apart from Pembrolizumab, other PD-1/PD-L1 inhibitors such as Nivolumab and Atezolizumab have been under study in clinical trials for uterine endometrial cancer. Nivolumab is a PD-1 inhibitor, and Atezolizumab is a PD-L1 inhibitor. Early study outcomes suggest similar efficacy of these inhibitors in treating uterine endometrial cancer. However, further research is needed to determine the optimal usage and dosage of these drugs.

Despite showing potential in the treatment of uterine endometrial cancer, PD-1/PD-L1 inhibitors still face challenges and limitations. Not all patients respond favorably to PD-1/PD-L1 inhibitor therapy. Further research is required to identify which patients are most sensitive to these drugs. Long-term safety and tolerability of PD-1/PD-L1 inhibitors still need more observation and study. The widespread use of PD-1/PD-L1 inhibitors faces economic constraints due to their high drug costs. PD-1/PD-L1 inhibitors are a class of drugs with potential efficacy for uterine endometrial cancer treatment. Pembrolizumab has shown significant therapeutic effects in clinical trials for uterine endometrial cancer, and other PD-1/PD-L1 inhibitors are also under investigation. However, more research is still needed to determine the optimal application of PD-1/PD-L1 inhibitors in uterine endometrial cancer treatment. Addressing the challenges and limitations they face will provide more effective treatment options and improve the prognosis for uterine endometrial cancer patients (Zhao et al., 2023).

2.2 Clinical research on CTLA-4 inhibitors

CTLA-4 inhibitors are a type of immunotherapeutic medication that enhances the body's anti-tumor immune response by blocking the Cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) pathway. In clinical studies, CTLA-4 inhibitors have shown potential therapeutic effects in various types of cancers, including melanoma and non-small cell lung cancer. Currently, one of the most extensively studied drugs among CTLA-4 inhibitors is Ipilimumab. Ipilimumab was the first immunotherapeutic drug approved by the FDA for treating malignant melanoma. It enhances the immune system's attack capabilities by blocking CTLA-4's inhibition of tumor-specific T cells. In the treatment of malignant melanoma, Ipilimumab has been shown to increase patients' survival periods.

Apart from melanoma, CTLA-4 inhibitors have made significant progress in clinical studies for other cancer types. For instance, in the treatment of non-small cell lung cancer, combined immune therapy utilizing CTLA-4 inhibitors alongside PD-1 inhibitors has demonstrated promising efficacy. Additionally, CTLA-4 inhibitors have been studied in other cancer types such as renal cell carcinoma, colorectal cancer, and gastric cancer. However, the application of CTLA-4 inhibitors faces challenges and limitations. The therapeutic effects of CTLA-4 inhibitors may come with severe immune-related adverse events, including autoimmune reactions and intestinal inflammation. These adverse events need to be identified and handled in a timely manner to reduce the risk of adverse reactions in patients.

CTLA-4 inhibitors may exhibit lower response rates in certain patients, necessitating further research to identify those most sensitive to this class of drugs. Long-term safety and tolerability of CTLA-4 inhibitors still require more observation and study. CTLA-4 inhibitors are a class of immunotherapeutic drugs with potential efficacy for the treatment of various types of tumors. While Ipilimumab has shown remarkable success in the treatment of malignant melanoma, and combination immune therapies have shown some efficacy, further research is needed to determine the optimal application of CTLA-4 inhibitors in different cancer types and address the challenges and limitations they face, in order to provide more effective treatment options and improve the prognosis of tumor patients (Figure 2).

2.3 Application of tumor vaccines

2.3.1 Progress in antigen-specific vaccines

Antigen-specific vaccines are designed to activate the immune system using tumor-specific antigens. These antigens can be tumor-associated antigens (TAA) or tumor-specific antigens (TSA). Currently, numerous studies are exploring the potential of antigen-specific vaccines. A common strategy involves using tumor antigen proteins to stimulate the immune system. These proteins can be specific antigens expressed by tumor cells or synthetic recombinant proteins. Injected into patients, these proteins activate antigen-presenting cells, initiating an immune response. Clinical trials have demonstrated the potential efficacy of antigen-specific vaccines in certain cancers like melanoma and prostate cancer. Another strategy for antigen-specific vaccines is to prepare vaccines using tumor cells or components of tumor cells. These vaccines are called whole cell vaccines.

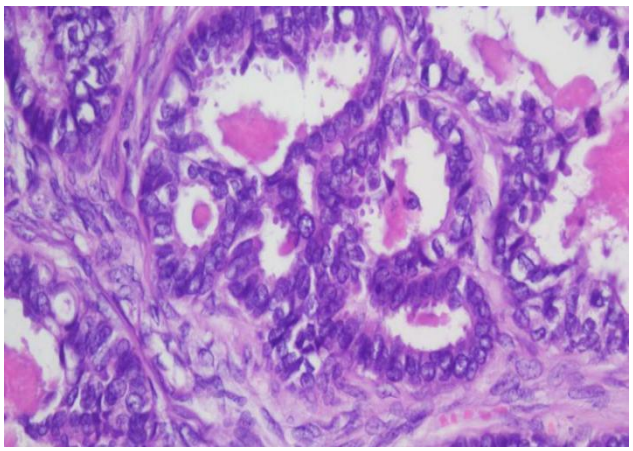

Figure 2 Morphology of the cancer cells under the microscope

Whole-cell vaccines can include entire tumor cells, parts of tumor cells, or genetically modified tumor cells. These vaccines can activate the immune system to generate an immune response against tumor cells. Clinical trials have shown that whole cell vaccines have certain therapeutic effects in various types of tumors. Despite the potential shown by antigen-specific vaccines in cancer treatment, challenges persist. Identifying and selecting appropriate tumor antigens remains critical. Variations in antigen expression levels among different tumor types and patients require further research to determine optimal vaccine targets. Antigen-specific vaccines may exhibit lower immune responses in some patients. Researchers need to further understand immune escape mechanisms and develop new strategies to enhance vaccine effectiveness. Large scale production and cost issues also need to be addressed in order to widely apply antigen specific vaccines in clinical practice.

2.3.2 Potential of DNA and RNA vaccines

DNA vaccines involve injecting DNA containing specific antigen-coding sequences into patients. Once taken up by cells, the DNA is transcribed and translated into antigen proteins, activating the immune system. DNA vaccines' advantages lie in their ability to trigger T cell and B cell immune responses with relatively lower side effects. Numerous clinical trials have shown the potential efficacy of DNA vaccines in various cancers, including prostate cancer, breast cancer, and lung cancer. In contrast, RNA vaccines involve injecting RNA containing specific antigen-coding sequences into patients. RNA vaccines can directly translate into antigen proteins, activating the immune system. RNA vaccine's advantages include their efficiency, flexibility, and rapid preparation and modification. In recent years, RNA vaccines have gained significant attention, especially with the tremendous success in developing COVID-19 vaccines. In cancer treatment, RNA vaccines have shown potential in clinical trials for cancers like melanoma and breast cancer.

DNA vaccines and RNA vaccines are a new type of cancer vaccine with the potential to become innovative methods for cancer treatment. Their principle involves injecting DNA or RNA sequences containing specific antigens into patients to activate the immune system via transfection mechanisms. Tumor vaccines present a potential immunotherapeutic approach to combat tumor cells by activating the immune system. Antigen-specific vaccines, DNA vaccines, and RNA vaccines have shown potential, yet further research and optimization are needed to enhance their efficacy and scope of application. The development of these tumor vaccines presents new opportunities for cancer treatment, offering more effective and personalized therapeutic options for patients.

Despite the potential demonstrated by DNA and RNA vaccines in cancer treatment, further research is needed to address challenges. Further understanding and optimization of vaccine delivery and expression efficiency to enhance the intensity and persistence of immune responses are crucial. Additionally, research and optimization of immune adjuvants are necessary to enhance vaccine immunogenicity. Researchers also need to tackle large-scale production and cost issues to ensure widespread clinical application of these vaccines.

2.4 CAR-T cell therapy

2.4.1 Basic principles of CAR-T cell therapy

CAR-T cell therapy is an exciting form of immunotherapy based on modifying a patient's own T cells to enhance their anti-tumor capabilities. The cornerstone of this treatment lies in Chimeric Antigen Receptors (CARs), enabling T cells to identify and attack tumor cells. CARs consist of an external antigen recognition domain and internal signal transduction domains. The external domain typically uses the variable regions of monoclonal antibodies to recognize specific antigens on tumor cells. The internal signal transduction domain contains molecules necessary for T cell activation and proliferation, like the CD3 chain. When CAR-T cells bind to antigens on tumor cells, the internal signal transduction domain activates the T cells, initiating an immune response and destroying the tumor cells.

The advantage of CAR-T cell therapy lies in its highly personalized nature. CAR-T cells are extracted from a patient's own T cells and modified, thereby possessing better compatibility and safety. Additionally, CAR-T cells can recognize and attack specific antigens on tumor cells, evading escape mechanisms observed in traditional treatment methods. This highlights the potential of CAR-T cell therapy in treating tumors that are resistant to or difficult to manage with traditional approaches. Despite significant progress in cancer treatment, challenges persist in CAR-T cell therapy. The preparation process is relatively complex, involving genetic modification and ex vivo expansion, resulting in higher costs. Additionally, CAR-T cell therapy can lead to severe adverse reactions like cytokine release syndrome and neurotoxicity, requiring vigilant monitoring and management.

Further research and validation are necessary to determine the long-term efficacy and tolerance of CAR-T cell therapy in cancer treatment. At present, clinical trials have been conducted to evaluate the efficacy and safety of CAR-T cell therapy in different tumor types, and further improve the design and application of CAR-T cells. The future holds promise for CAR-T cell therapy to play a more significant role in cancer treatment. With advancements in technology, the preparation process for CAR-T cells is expected to become more streamlined and efficient, reducing costs and increasing production efficiency. Moreover, the efficacy and safety of CAR-T cell therapy are anticipated to undergo further improvement and optimization. As an emerging cancer treatment modality, CAR-T cell therapy holds immense potential. By enhancing a patient's own T cells' ability to combat tumors, CAR-T cell therapy overcomes limitations seen in traditional treatments and plays a crucial role in treating challenging cancers. Despite facing some challenges such as complex preparation processes and potential adverse reactions, with further research and improvement, CAR-T cell therapy is expected to become one of the important means of cancer treatment.

2.4.2 Prospects of CAR-T cell therapy in endometrial cancer treatment

Endometrial cancer stands as one of the most prevalent malignant tumors in the female reproductive system. Current treatments include surgical resection, radiation, and chemotherapy. However, for advanced or recurrent endometrial cancer patients, the efficacy of traditional treatment methods is limited. In such cases, CAR-T cell therapy might offer a promising therapeutic option. The individualized nature of CAR-T cell therapy presents significant advantages in endometrial cancer treatment. By modifying a patient's own T cells to recognize and attack tumor cells, CAR-T cell therapy can be customized based on patient characteristics and specific surface antigens of the tumor, thereby improving treatment specificity and effectiveness. This individualized treatment strategy holds promise for achieving better therapeutic outcomes in endometrial cancer patients and reducing reliance on traditional treatment methods.

The efficacy of CAR-T cell therapy has been established in immunotherapy for other tumor types, providing theoretical support for its application in endometrial cancer treatment. The advantage of CAR-T cell therapy lies in its ability to attack specific antigens on tumor cells, avoiding escape mechanisms observed in traditional treatment methods. This potential positions CAR-T cell therapy to be highly effective in treating tumors that are resistant to conventional therapies or challenging to manage. In the treatment of endometrial cancer, CAR-T cell therapy can target specific antigens like HER2 and EGFR on tumor cells, enhancing therapeutic outcomes.

CAR-T cell therapy also shows promise in treating recurrent endometrial cancer. Patients with recurrent endometrial cancer often have low tolerance to traditional treatment methods, whereas CAR-T cell therapy, by modifying a patient's own T cells, enhances their ability to attack tumor cells, effectively controlling disease progression. Furthermore, due to the personalized nature of CAR-T cell therapy, the most suitable CAR design can be selected based on the tumor characteristics of patients with recurrent endometrial cancer, thereby improving treatment specificity and effectiveness.

Despite the potential benefits, CAR-T cell therapy in endometrial cancer treatment faces challenges. The heterogeneity of endometrial cancer poses a challenge in selecting appropriate specific antigens. Thus, finding more specific and widely expressed antigens will be a crucial research direction for CAR-T cell therapy in endometrial cancer treatment. Safety concerns surrounding CAR-T cell therapy in endometrial cancer treatment also require further research and resolution. CAR-T cell therapy may lead to serious adverse reactions like cytokine release syndrome and neurotoxicity, necessitating close monitoring and management. Despite facing challenges, the prospects of CAR-T cell therapy in the treatment of endometrial cancer are still promising. With the in-depth research and continuous improvement of CAR-T cell therapy technology, it is expected that CAR-T cell therapy will be widely used in the treatment of endometrial cancer (Loukovaara et al., 2022; Yang et al., 2023).

3 Clinical Application and Efficacy Evaluation of Immunotherapy

3.1 Application of immunotherapy in first-line treatment of endometrial cancer

Immunotherapy, as a novel treatment approach, holds vast potential in the first-line treatment of endometrial cancer. First-line treatment refers to the therapy administered upon the initial diagnosis of endometrial cancer, aimed at improving patient survival rates and treatment outcomes. Currently, immunotherapy's application in the first-line treatment of endometrial cancer primarily involves immune checkpoint inhibitors and vaccine therapy. Immune checkpoint inhibitors work by suppressing inhibitory signaling molecules on the surface of tumor cells, activating the body's immune system to attack and eliminate tumor cells. Vaccine therapy, on the other hand, introduces tumor-related antigens to stimulate the body's immune response to suppress tumor growth.

Studies indicate that immune checkpoint inhibitors have shown significant efficacy in the first-line treatment among certain endometrial cancer patients. For instance, the PD-1 inhibitor Pembrolizumab has been confirmed to significantly prolong progression-free survival and improve overall survival in first-line treatment. Additionally, some vaccine therapies have demonstrated certain therapeutic potential, such as cell-based vaccines and gene-engineered vaccines. As a first-line treatment option, epidemic treatment has certain advantages. Immunotherapy has lower toxicity compared to traditional chemotherapy and radiation therapy, potentially enhancing patients' quality of life. By activating the body's immune system, immunotherapy aims to boost patients' immune responses, potentially fostering anti-tumor immune effects, overcoming tumor resistance, and improving treatment durability (Zhang and Mao, 2023).

It should be pointed out that the application of immunotherapy in the first-line treatment of endometrial cancer is still in the exploratory stage. Currently, there's a lack of sufficient clinical trial data to fully support its precise efficacy in first-line treatment. Additionally, individual differences and the response rates to immunotherapy are factors that need consideration. Therefore, clinical practitioners need to assess the pros and cons of treatment regimens and tailor personalized treatment plans based on each patient's specific circumstances. In conclusion, immunotherapy holds potential application prospects in the first-line treatment of endometrial cancer. As further research and clinical practice advance, gaining a more comprehensive understanding of the efficacy of immunotherapy in first-line treatment aims to offer more effective treatment options for patients (Figure 3).

3.2 Application of immunotherapy in recurrent or metastatic endometrial cancer

Recurrent or metastatic endometrial cancer refers to the reoccurrence or spread of the primary lesion after surgical treatment or its extension to other sites. Conventional treatment methods often show limited effectiveness in such

scenarios, making the search for new treatment approaches particularly crucial. Immunotherapy, as a novel therapeutic strategy, is being extensively researched and applied in the treatment of recurrent or metastatic endometrial cancer. One primary method of immunotherapy involves immune checkpoint inhibitors. These medications work by blocking inhibitory signaling molecules on tumor cells' surfaces, such as PD-1 or PD-L1, activating the body's immune system and enhancing its ability to attack tumors. Research indicates that immune checkpoint inhibitors show certain efficacy in the treatment of recurrent or metastatic endometrial cancer.

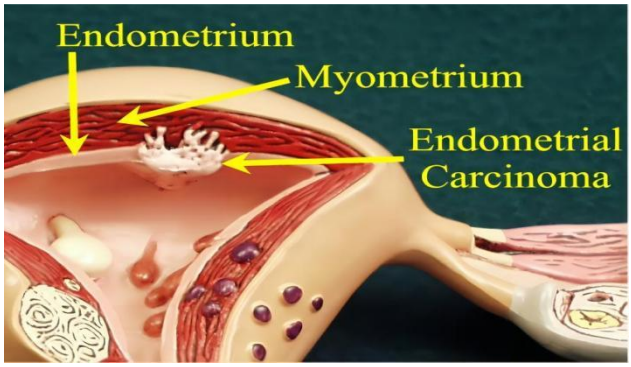

Figure 3 May form the site of cancer

Clinical trials have demonstrated considerable efficacy of the PD-1 inhibitor Pembrolizumab in patients with recurrent or metastatic endometrial cancer. One study reported an overall response rate of approximately 30% in patients treated with Pembrolizumab. Additionally, another clinical trial indicated that the PD-L1 inhibitor Avelumab exhibits some therapeutic potential in recurrent or metastatic endometrial cancer. Besides immune checkpoint inhibitors, other immunotherapy strategies are under investigation for the treatment of recurrent or metastatic endometrial cancer. Immune cell therapy is a treatment method that modifies the patient's own immune cells and then injects them into the body. For instance, CAR-T cell therapy modifies a patient's T cells to recognize and attack tumor cells, subsequently reintroducing them into the patient's body. Recent studies suggest that CAR-T cell therapy demonstrates certain therapeutic potential in recurrent or metastatic endometrial cancer.

Despite showing certain efficacy in the treatment of recurrent or metastatic endometrial cancer, immunotherapy faces challenges and limitations. Immunotherapy response rates are limited, and there might be variations in immune responses among different patients. Hence, when selecting immunotherapy regimens, considering individual patient characteristics and immune status is crucial. Immunotherapy may trigger immune-related adverse effects like inflammatory reactions and autoimmune diseases. Therefore, close monitoring and management of immunotherapy-related adverse events are essential. Immunotherapy, as a novel treatment strategy, demonstrates certain efficacy in the treatment of recurrent or metastatic endometrial cancer. Immune checkpoint inhibitors and immunocellular therapy are the primary immunotherapy methods presently. However, further research is needed to determine the optimal application methods and patient selection criteria for immunotherapy in recurrent or metastatic endometrial cancer. Advancements in scientific technology and a deeper understanding of immunotherapy mechanisms aim to enhance its efficacy and offer better treatment choices for patients.

3.3 Evaluation metrics and methods for immunotherapy efficacy assessment

Survival duration is a crucial indicator for assessing treatment effects. Common survival durations include progression-free survival (PFS) and overall survival (OS). PFS refers to the time patients survive without disease progression, while OS measures the time from treatment initiation to death. By comparing the survival periods of immunotherapy and control groups, the efficacy of immunotherapy can be evaluated. Complete response rate (CR) and partial response rate (PR) are vital indicators for assessing tumor treatment effects. CR signifies the disappearance or undetectability of tumors, while PR indicates tumor shrinkage but not complete disappearance. The response rate of immunotherapy can be determined by measuring changes in tumor volume or lesion size.

Clinical trials are a key method for evaluating the efficacy of immunotherapy. Randomized grouping and double-blind designs allow comparison of treatment effects between immunotherapy and control groups. Clinical trials provide high-quality evidence to assess immunotherapy efficacy. Case-control studies retrospectively compare treatment effects in patients receiving immunotherapy and those who did not, offering preliminary evidence supporting the effectiveness of immunotherapy. Follow-up observations involve long-term monitoring of patient efficacy. Regular check-ups and follow-ups allow for the evaluation of long-term efficacy and survival duration of immunotherapy in practical clinical settings.

Imaging assessments are crucial in evaluating tumor treatment effects. Common imaging techniques include CT scans, MRI, and PET-CT scans. Comparing changes in lesion size, number, and metabolic activity before and after treatment assesses the efficacy of immunotherapy. It's essential to note that different evaluation metrics and methods have their pros, cons, and applicability. Therefore, comprehensive consideration of multiple indicators and methods is necessary for a more accurate assessment of immunotherapy efficacy. Moreover, specific evaluation strategies may be required for different tumor types and immunotherapy methods, emphasizing the need for tailored evaluation strategies based on specific circumstances. Selecting appropriate evaluation strategies according to specific circumstances enables a more accurate assessment of immunotherapy efficacy. Continuous advancements in immunotherapy research may introduce more effective evaluation metrics and methods, offering greater choices for evaluating immunotherapy efficacy (Connor and Rose, 2018).

4 Challenges and Future Prospects of Immunotherapy

4.1 Mechanisms of immune tolerance and resistance

Immunotherapy has made significant breakthroughs in the field of cancer treatment; however, challenges of immune tolerance and resistance persist. Immune tolerance refers to how tumor cells evade attacks from the immune system, while resistance signifies tumor cells developing resistance to immunotherapeutic drugs. Tumor cells can achieve immune tolerance through various mechanisms, altering antigen expression to reduce recognition opportunities by immune cells. For instance, tumor cells might decrease expression of tumor-associated antigens or inhibit immune cell recognition by altering expression pathways. Tumor cells can modify immune cell functions, suppressing their activity or inducing immune cell tolerance. These mechanisms enable tumor cells to evade immune system attacks, limiting the effectiveness of immunotherapy.

Resistance poses another challenge for immunotherapy. Tumor cells can gain resistance to immunotherapeutic drugs through multiple mechanisms. They might diminish the effects of immunotherapy drugs by mutations or alterations in gene expression, affecting aspects like antigen presentation, immune cell recognition, or immune cell activity. Tumor cells can also generate resistance by altering the tumor microenvironment, where immune suppression factors or immune evasion mechanisms disrupt immune cell functions, weakening the efficacy of immunotherapy. Further research and understanding are needed regarding the mechanisms of immune tolerance and resistance.

A deeper understanding of these mechanisms could lead to the development of new strategies to overcome immune tolerance and resistance, thereby enhancing the effectiveness of immunotherapy. One approach involves enhancing treatment efficacy by combining immunotherapeutic drugs. Different types of immunotherapeutic drugs might attack tumor cells through distinct mechanisms, reducing the risk of resistance. For example, immune checkpoint inhibitors relieve immune cell suppression, while CAR-T cell therapy modifies a patient's T cells to attack tumor cells. The combined application of these different immunotherapeutic drugs can enhance the effectiveness of immunotherapy on multiple fronts.

Another strategy involves personalized immunotherapy to address immune tolerance and resistance. Personalized immunotherapy relies on individual patient differences, analyzing their immune and tumor characteristics to select the most suitable treatment. For instance, genetic sequencing and proteomics analysis can determine a patient's tumor mutation burden and immune evasion mechanisms, guiding treatment selection. Personalized

immunotherapy maximizes treatment efficacy and reduces the occurrence of immune tolerance and resistance. Additionally, advancements in basic research offer new opportunities to overcome immune tolerance and resistance. Researchers are exploring new treatment targets and strategies to enhance the effectiveness of immunotherapy, such as developing new immune cell engineering technologies like CRISPR-Cas9 gene editing to modify immune cell functions and characteristics.

4.2 Combination of immunotherapy with other treatment modalities

Immunotherapy, as an emerging treatment modality, has shown significant success in cancer treatment. However, to further improve its efficacy, immunotherapy often needs to be combined with other treatment modalities. This combined application can synergize in different ways, enhancing overall treatment effectiveness. The combined application of immunotherapy with other treatment modalities is a critical strategy to improve tumor treatment effectiveness. Synergistic effects from different treatment modalities can enhance tumor control and cure rates. However, combined applications require precise understanding of treatment sequences and timings, consideration of patient characteristics and treatment indications, and effective treatment evaluation and monitoring. Exploring further the combined application of immunotherapy with other treatment modalities in future research and clinical practice will aid in developing more effective tumor treatment strategies.

A common combination of immunotherapy and other treatment methods is the combination with chemotherapy drugs. Chemotherapy drugs reduce tumor burden by killing tumor cells and may increase tumor cell immunogenicity. Immunotherapy can further enhance the effects of chemotherapy by activating the immune system to attack tumor cells. Additionally, chemotherapy drugs might reduce immune cell suppression, improving the effectiveness of immunotherapy. Hence, the combined application of immunotherapy and chemotherapy can enhance treatment effectiveness on multiple levels. Radiation therapy is another common treatment modality combined with immunotherapy. It can directly kill tumor cells, reduce tumor burden, and potentially increase tumor cell immunogenicity. Immunotherapy can further activate the immune system to attack tumor cells, improving the effectiveness of radiation therapy. Additionally, radiation therapy can enhance the effectiveness of immunotherapy by altering the tumor microenvironment, releasing a range of antigens that activate immune cell attack capabilities. Thus, the combined application of immunotherapy and radiation therapy can enhance treatment effectiveness through various pathways.

Targeted therapy can also be combined with immunotherapy. Targeted therapy kills tumor cells by inhibiting specific tumor signaling pathways, potentially affecting tumor cell immune evasion mechanisms. Immunotherapy can further activate the immune system to attack tumor cells, enhancing the effectiveness of targeted therapy. Additionally, targeted therapy might reduce immune cell suppression, further improving the effectiveness of immunotherapy. Therefore, the combined application of immunotherapy and targeted therapy can enhance treatment effectiveness on multiple levels. Besides the mentioned common combined application methods, immunotherapy can also be combined with other treatment modalities such as hyperthermia, cryotherapy, or laser therapy. These treatment modalities can alter tumor cell immunogenicity, enhancing the effectiveness of immunotherapy. Simultaneously, immunotherapy can strengthen the effectiveness of these treatment modalities by activating the immune system. Through combined application, synergistic enhancement of treatment effectiveness can be achieved, improving tumor control and cure rates.

4.3 Prospects and challenges of personalized immunotherapy

Personalized immunotherapy is a treatment strategy based on individual patient differences, aiming to provide tailored treatment plans for specific patients. As research and development in tumor immunotherapy continue, the prospects for personalized immunotherapy in cancer treatment are becoming increasingly broad. However, personalized immunotherapy also faces challenges that need to be overcome to realize its potential. Personalized immunotherapy can better meet patient needs. Each patient's immune system and tumor characteristics are unique, so personalized immunotherapy can design treatment plans based on individual differences of patients, providing more precise and effective treatment. Analyzing a patient's genetic variations and immune features can predict

their response and tolerance to treatment, enabling the adjustment of treatment plans to reduce unnecessary side effects. Personalized immunotherapy can increase treatment success rates by targeting specific immune and tumor features, enhancing treatment specificity and effectiveness. It can select suitable immunotherapy methods for patients, such as immune checkpoint inhibitors or CAR-T cell therapy, thereby improving treatment success rates.

Personalized immunotherapy faces challenges: it requires extensive genomic and immunological data support. The design of personalized immunotherapy requires a comprehensive analysis of the patient's genome, epigenome, and immunohistochemical characteristics. However, currently the cost of obtaining this data is high and requires complex laboratory equipment and technology. Therefore, how to acquire and analyze these data on a large scale in clinical practice remains one of the challenges for personalized immunotherapy. The design and implementation of personalized immunotherapy require multidisciplinary collaboration. Personalized immunotherapy necessitates collaboration among immunologists, oncologists, genomic scientists, and other disciplines to ensure treatment accuracy and effectiveness. However, currently, cooperation and communication between different disciplines still face certain difficulties. Thus, establishing mechanisms and platforms for multidisciplinary collaboration to promote communication and cooperation among various fields is an important task for the development of personalized immunotherapy.

Personalized immunotherapy faces challenges in manufacturing and production. For example, CAR-T cell therapy involves collecting T cells from a patient's body, genetically modifying them, and reintroducing them into the patient's body. This process includes cell preparation, quality control, and clinical application, requiring highly specialized technical support. Therefore, establishing an efficient and reliable CAR-T cell preparation and production system remains one of the challenges for personalized immunotherapy. Personalized immunotherapy also needs to address ethical and legal issues. It involves sensitive issues such as a patient's personal privacy and genetic information, thus requiring the establishment of relevant ethical guidelines and regulations to govern treatment implementation and data usage. At the same time, the high cost of individualized immunotherapy is also a concern, and ensuring the accessibility and fairness of individualized immunotherapy is one of the urgent problems to be solved in the development of individualized immunotherapy (Wang and Fu, 2023).

5 Current Status and Progress

In the immunotherapy of endometrial cancer, early clinical trials have shown certain efficacy. For instance, the use of PD-1 antibody drugs in advanced endometrial cancer patients resulted in tumor shrinkage and prolonged survival. Furthermore, research indicates that combining immune checkpoint inhibitors with chemotherapy can enhance treatment effectiveness. Apart from immune checkpoint inhibitors, CAR-T cell therapy is also considered a promising approach for immunotherapy in endometrial cancer. CAR-T cell therapy is a personalized treatment method that enhances the immune system's ability to attack tumor cells by collecting a patient's T cells, genetically modifying them, and reinfusing them into the patient's body. Currently, CAR-T cell therapy has shown promising results in other tumors such as leukemia and lymphoma (Gao et al., 2023).

Immunotherapy holds important significance and vast prospects in the treatment of endometrial cancer. Traditional treatment methods like surgery and chemotherapy can control the disease to some extent, but their efficacy remains limited for advanced or recurrent patients. Immunotherapy, as a new treatment strategy, activates a patient's own immune system to attack tumor cells, offering more precise and effective treatment. Immunotherapy can overcome the limitations of traditional treatments. The development of endometrial cancer is closely related to immune evasion mechanisms, where tumor cells evade immune surveillance by suppressing immune cell activity. Immunotherapy restores immune cell recognition and attack capabilities against tumor cells by activating the immune system, compensating for the shortcomings of traditional treatments. Immunotherapy not only directly destroys tumor cells but also triggers immune memory effects, establishing lasting immune defense against tumor cells.

With further understanding of endometrial cancer's immune characteristics and the development of technology, there's potential to optimize immunotherapy plans and apply them to a broader patient population. The development of personalized immunotherapy will offer unique treatment plans for each patient, improving treatment success rates and survival period. Immunotherapy also holds the promise of integrating with other treatment methods, forming a multidisciplinary comprehensive treatment strategy. The combined use of immunotherapy with chemotherapy, radiation therapy, or targeted therapy can leverage the advantages of various treatment methods, enhancing treatment effectiveness. The application of this comprehensive treatment strategy will yield better treatment outcomes and offer patients more treatment choices. The future holds expectations for further breakthroughs in immunotherapy for the treatment of endometrial cancer. With ongoing scientific and technological advancements and deeper research into endometrial cancer's immune characteristics and mechanisms, more effective and personalized immunotherapy plans can be developed. Through continuous efforts and innovation, immunotherapy will become an integral part of endometrial cancer treatment, improving patient survival and quality of life.

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