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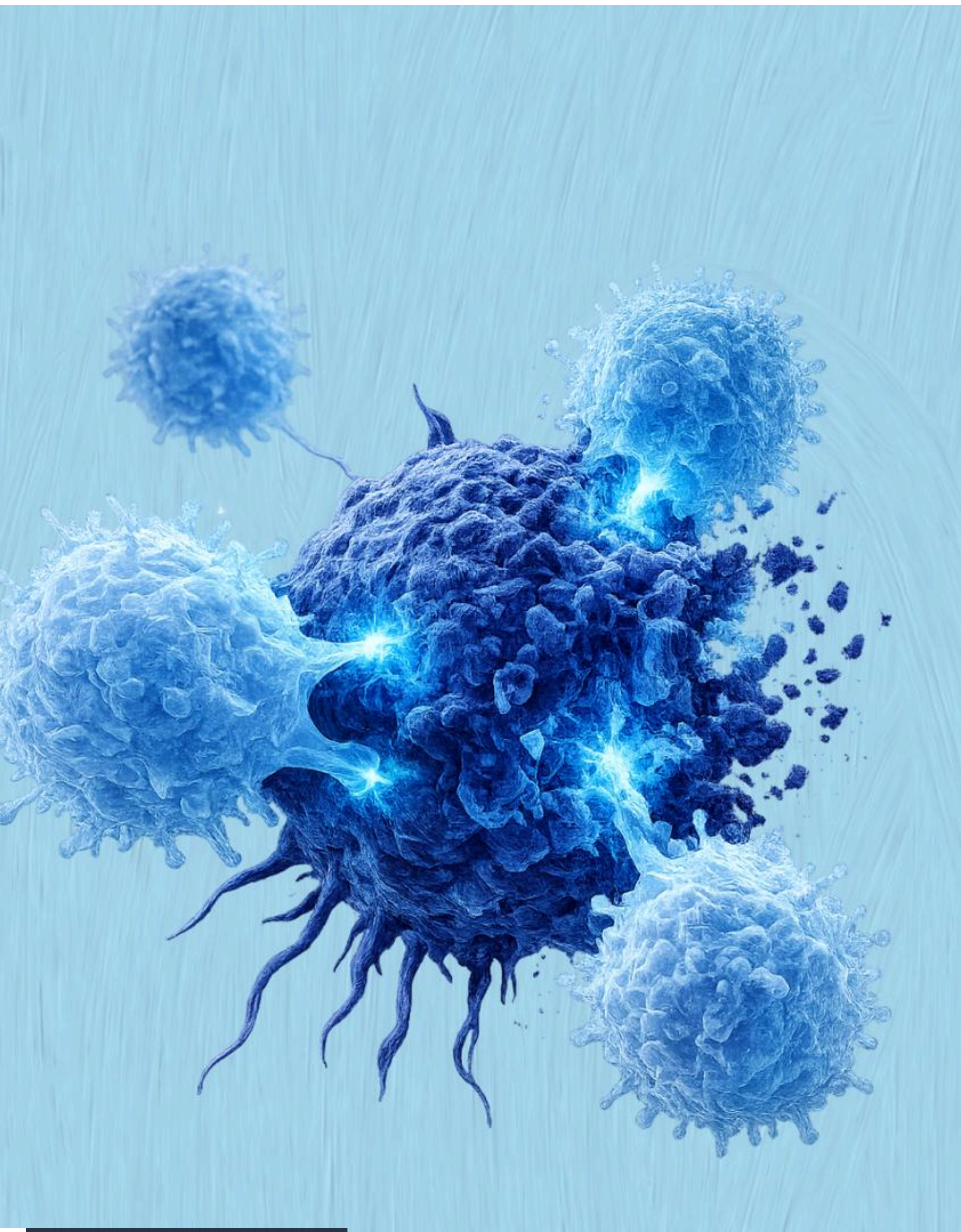
Immunotherapy and Thyroid Cancer

Aline Abilmona

Edited By: Maria Abi Fadel



Introduction

One of the most common endocrine malignancies is thyroid cancer, which is the most frequent type with significantly high rates of incidence. There are many types of treatments that can target thyroid cancers, such as surgery, thyroid hormone suppression, or radioactive iodine therapy (Haugen et al., 2016). Some patients may become resistant to treatments, leading to the development of metastatic forms of the cancer. The spectrum of aggression of these cancers varies, whereby some forms show resistance against the therapeutic attempts.

Immunotherapy is a new therapeutic technique introduced in oncology. Such a technique is based on strengthening the immune system to recognize and fight the tumor cells.
This technique provides hope for cancer patients without destroying their healthy cells. Accordingly, this paper explores the impact of immunotherapy on the suppression of thyroid cancer, along with the mechanisms, clinical applications, and future attempts that could be integrated to enhance the effectiveness of the immunotherapeutic techniques applied.

Overview of Thyroid Cancer

Thyroid cancer originates from the mutated forms of the follicular and parafollicular cells of the thyroid gland. It's divided into differentiated thyroid cancers, including papillary and follicular, medullary thyroid carcinoma, and anaplastic thyroid carcinoma. Differentiated thyroid cancers are usually the most common ones. As for the medullary thyroid carcinoma, it arises from parafollicular C cells, where it could be inherited or sporadic. Anaplastic thyroid carcinoma is rare but highly aggressive. However, this type is highly resistant to the therapy.

Differentiated thyroid cancers can be effectively treated by the standard treatments, such as surgery and radioactive iodine therapy. However, in some cases, iodine can't be absorbed by the tumor cells. This is mainly due to some gene mutations, like BRAF mutations, that alter the capacity of the cells to recognize iodine and take it up. In such cases, standard treatments would be substituted by systemic ones such as immunotherapy.

Principles of Immunotherapy

Immunotherapy works on strengthening the immune system. However, tumor cells develop an escape mechanism by which they exploit immune checkpoint pathways. Eventually, the immune responses won't recognize these cells. This favors the formation of an immunosuppressive microenvironment. Immunotherapeutic strategies seek to overcome these mechanisms (Pardoll 2012)

Immune checkpoint inhibitors, cancer vaccines, adoptive cell therapy, and cytokine-based treatments are different procedures under which immunotherapy is applied. Among these, immune checkpoint inhibitors play a pivotal role in fighting thyroid cancer. These agents target inhibitory pathways such as programmed cell death protein 1 (PD-1), its ligand PD-L1, and cytotoxic T-lymphocyte-associated protein 4 (CTLA-4). By blocking these checkpoints, T-cell-mediated antitumor responses are being activated (Pardoll 2012).

Immunotherapy in Thyroid Cancer

Thyroid tumors, particularly aggressive and poorly differentiated types, have been found to express immune checkpoint molecules such as PD-L1. This discovery has provided a strong rationale for the use of immune checkpoint inhibitors in thyroid cancer.

Clinical trials investigating the effects of the drugs pembrolizumab and nivolumab have shown promising results, especially in patients with advanced stages of thyroid cancer. Although the spectrum of the response rates varies significantly, it remains generally lower compared to other malignancies like melanoma or lung cancer. Despite that, some patients revealed a positive experience with effective responses.

Studies have shown that anaplastic thyroid carcinomas are limited by immunotherapeutic procedures, knowing that these carcinomas are the most aggressive form. Binding targeted therapies with immune checkpoint inhibitors was successful in decreasing the aggressiveness of this type of cancer and increasing the survival rates of the patients (Iyer et al., 2018). Ongoing research is also exploring biomarkers that can predict response to immunotherapy, such as PD-L1 expression, tumor mutational burden, and immune cell infiltration.

Challenges and Limitations

Despite its potential, immunotherapy in thyroid cancer can be limited somewhat. The response to the treatment varies depending on the patient, and the immune-related adverse effects can be

severe, affecting organs such as the skin, gastrointestinal tract, and endocrine glands. Additionally, the optimal timing, combination of therapeutic strategies, and patient selection criteria remain vague (Postow, Sidlow, & Hellmann, 2018). Resistance complicates the treatment's effectiveness. One resistant mechanism includes "hiding" the tumor-specific antigens and tumor-associated antigens in order to escape the immune attack. Another mechanism involves downregulating the cytolytic response by inactivating the chemokines that attract the natural killer cells. These NK cells get introduced to the tumor cells through recognizing MHC class-I molecules on the surface of these cells. A process known as "comoflauge" involves reducing the expression of the MHC class-I molecules, which eventually reduces the recognition. This reaction is followed by another one known as "sabotage" that involves disrupting anti-tumor immunity. As such, this renders the effectiveness of immunotherapeutic approaches.

Future Perspectives

The future of immunotherapy in thyroid cancer depends on combination approaches and personalized medicine. Combining immunotherapy with targeted therapies, chemotherapy, or radiation may improve response rates and overcome resistance. For instance, monoclonal antibodies, which are targeted therapy tools, can guide the chemotherapeutic drug to the site of the tumor, thus decreasing the devastating effects of chemotherapy and enhancing the effectiveness of the treatment. Advances in genomic and immunologic profiling may allow clinicians to identify patients most likely to benefit from immunotherapy.

Ongoing clinical trials and translational research continue to expand knowledge in this field, raising optimism that immunotherapy will become an integral component of thyroid cancer treatment, particularly for aggressive and refractory cases.

Conclusion

Immunotherapy represents a promising therapeutic approach that provides hope for thyroid cancer patients regardless of the stage of advancement of the cancer. While traditional therapies remain effective for most cases, immunotherapeutic approaches offer new possibilities that the standard techniques can't provide. Despite the effectiveness of immunotherapy, further research is being conducted to investigate all the limitations that hinder the treatment of thyroid cancer. With further advancements, immunotherapy has the potential to significantly improve outcomes and quality of life for patients facing this complex disease through facilitating the healing process and spreading the hope of an attainable remission.

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