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Checkpoint inhibitors: Revolutionizing cancer treatment strategies.

Rexa Colonis*

Pathological Anatomy Service, Hospital de Santa Maria, CHULN, Lisbon, Portugal

Correspondence to: Rexa Colonis, Pathological Anatomy Service, Hospital de Santa Maria, CHULN, Lisbon, Portugal, E-mail: rexac@zju.edu.cn

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Introduction

Cancer remains one of the most challenging diseases to treat, largely due to its capacity to evade immune surveillance. However, the advent of immune checkpoint inhibitors (ICIs) has transformed the oncology landscape, offering new therapeutic options across a spectrum of malignancies. By targeting regulatory pathways that restrain immune activation, these drugs restore the ability of T cells to recognize and eliminate tumor cells. This article explores the mechanisms, clinical successes, limitations, and future directions of checkpoint inhibitors in cancer treatment [1, 2].

Checkpoint inhibitors are now being assessed in: An aggressive subtype lacking hormonal receptors but rich in immune infiltration. Colorectal cancers with MSI show strong responses; other types are being investigated. Typically immunologically cold tumors that require strategies to increase T-cell recruitment. Immune checkpoints are critical modulators of the immune system, designed to prevent overactivation that could damage normal tissues. Tumors exploit these pathways to suppress immune responses and promote survival. Two of the most studied checkpoints are: PD-1 (Programmed Death-1): Expressed on T cells, it interacts with PD-L1/PD-L2 on tumor or stromal cells to inhibit T-cell activation [3, 4].

CTLA-4 (Cytotoxic T-Lymphocyte-Associated Antigen 4): Competes with CD28 to bind B7 ligands, preventing co-stimulatory signals needed for full T-cell activation. Blocking these inhibitory pathways allows T cells to mount a robust anti-tumor response. Checkpoint inhibitors have demonstrated remarkable success in treating several cancer types: Melanoma: The approval of ipilimumab (anti-CTLA-4) marked a milestone, followed by pembrolizumab and nivolumab (anti-PD-1), which improved survival rates significantly [5, 6].

Non-Small Cell Lung Cancer (NSCLC): PD-1 inhibitors, often used in combination with chemotherapy, have become frontline treatments. Renal Cell Carcinoma, Hodgkin Lymphoma, Head and Neck Cancer: All have shown responsiveness to ICIs, expanding their applicability. Restoring T-cell effector functions in the tumor microenvironment. Promoting clonal expansion of tumor-specific lymphocytes. Enhancing cytokine production and tumor infiltration by immune cells. Interestingly, ICIs don't directly target cancer cells but modulate the host immune response a fundamentally different approach than chemotherapy or targeted therapy. Predicting who will benefit from checkpoint blockade is an ongoing challenge. Several biomarkers are under study: High levels on tumor cells correlate with better response but are not definitive [7, 8].

The field is rapidly evolving, with innovations including: TIM-3, LAG-3, TIGIT, and VISTA offer additional inhibitory nodes. Multi-parametric algorithms integrating genomic, proteomic, and immune data may improve patient selection. Tailored delivery systems could enhance checkpoint inhibition while reducing toxicity. Higher mutation load may produce more neoantigens, increasing immunogenicity. Tumors with deficient mismatch repair show heightened responses to PD-1 inhibitors. Despite their promise, checkpoint inhibitors have drawbacks: Inflammation of skin, colon, lungs, and endocrine organs may occur due to loss of immune tolerance. Many patients show no initial response or relapse

after an initial benefit. Resistance may arise due to immune exclusion, loss of antigen presentation, or compensatory immune checkpoints [9, 10].

Conclusion

Checkpoint inhibitors have redefined how we approach cancer therapy, transitioning from tumor-centric to immune-centric models. Their success has ushered in a new era of immuno-oncology, but challenges remain in optimizing efficacy, minimizing toxicity, and expanding accessibility. As we refine strategies and deepen our understanding of tumor-immune dynamics, checkpoint blockade will continue to evolve—likely as part of personalized, combination approaches in precision medicine.

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