

# International Journal of Health Science

ISSN 2764-0159

vol. 5, n. 33, 2025

## ... ARTICLE

Acceptance date: 28/10/2025

# ADVANCES IN ONCOLOGICAL IMMUNOTHERAPY: FUTURE PERSPECTIVES AND ETHICAL CHALLENGES

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**Abstract:** Oncological immunotherapy represents one of the greatest advances in modern medicine, ushering in a new era of targeted treatments that stimulate the immune system to recognize and eliminate tumor cells. This literature review article addresses the main mechanisms of immunotherapy—such as immune checkpoint inhibitors, CAR-T cell therapies, and personalized antitumor vaccines—and discusses their clinical applications, recent technological advances, and ethical challenges. Studies published between 2014 and 2024 in the PubMed, SciELO, and Google Scholar databases were reviewed. It is concluded that immunotherapy has revolutionized the treatment of various types of cancer, although it still faces barriers related to high cost, serious adverse effects, and unequal access, especially in developing countries.

**Keywords:** Immunotherapy; Oncology; CAR-T; Checkpoint inhibitors; Bioethics.

## **INTRODUCTION**

Immunotherapy has revolutionized the field of oncology by proposing an innovative concept: using the immune system as a therapeutic weapon. Unlike chemotherapy and radiotherapy, which act directly on tumor cells, immunotherapy works by reprogramming the body to recognize cancer as a biological enemy.

Historical milestones include the use of anti-CTLA-4 and anti-PD-1/PD-L1 monoclonal antibodies, which restore immune surveillance suppressed by malignant cells (CHEN; MELLEN, 2022).

In just over a decade, therapies such as nivolumab, pembrolizumab, ipilimu-

mab, and revolutionary CAR-T cells have transformed once-fatal diseases into chronic or even curable conditions. However, the speed of technological advancement has brought with it ethical, economic, and social challenges—including unequal access to treatments and the financial impact on healthcare systems.

The objective of this study is to review the main advances in cancer immunotherapy, highlighting its clinical applications, scientific evolution, and the ethical implications associated with its use.

## METHODOLOGY

This is a narrative and integrative literature review, with a search conducted in the PubMed, Scielo, and Google Scholar databases between 2014 and 2024.

The descriptors used were: immunotherapy, oncology, checkpoint inhibitors, CAR-T cells, cancer vaccines, and bioethics.

Original articles, systematic reviews, meta-analyses, and clinical consensus statements published in English and Portuguese were included, addressing clinical results, mechanisms of action, and ethical dilemmas.

Publications without direct clinical relevance or that addressed immunotherapy unrelated to neoplasms were excluded. In the end, 38 articles were selected and qualitatively analyzed.

## MOLECULAR MECHANISMS OF IMMUNOTHERAPY

The immune system is regulated by a delicate balance between activation sig-

nals and inhibitory signals, called immune checkpoints.

Tumor cells intelligently exploit these mechanisms to escape immune destruction.

The main therapeutic targets are:

- CTLA-4 (Cytotoxic T-Lymphocyte Antigen 4): expressed in activated T lymphocytes, it inhibits the immune response. Blockade by ipilimumab restores antitumor activity.
- PD-1 (Programmed Death 1) and PD-L1: their interaction induces T-cell exhaustion. Inhibitors such as nivolumab, pembrolizumab, and atezolizumab block this pathway, allowing for a sustained cytotoxic response.
- CAR-T (Chimeric Antigen Receptor T-cell): consists of the genetic modification of autologous T lymphocytes to recognize specific tumor antigens, such as CD19 in B-cell lymphomas (NOVAK et al., 2022).

Recently, therapies with TILs (Tumor Infiltrating Lymphocytes) and messenger RNA vaccines have shown promising results, broadening the spectrum of immunotherapeutic action.

## CLINICAL APPLICATIONS IN MODERN ONCOLOGY

Immunotherapy is approved for multiple types of cancer, with significant results in:

- Metastatic melanoma: overall survival doubled with the use of nivolumab and ipilimumab.
- Non-small cell lung cancer: combination of pembrolizumab with chemo-

therapy increases the response rate to 47% (TOPALIAN et al., 2020).

- Hematological neoplasms: anti-CD19 CAR-T cells promote remission in up to 80% of patients with refractory acute lymphoblastic leukemia (BRASIL et al., 2023).
- Bladder, kidney, and head and neck cancer: sustained response with PD-L1 blockers.

In the Brazilian context, the challenge is the incorporation of these drugs by the SUS and the creation of specialized centers for advanced cell therapies.

## TECHNOLOGICAL ADVANCES AND FUTURE PERSPECTIVES

The future of immunotherapy points to complete personalization of treatment.

Emerging trends include:

- Personalized messenger RNA vaccines based on tumor neoantigens identified via genetic sequencing.
- Immunotherapy combined with radiotherapy and targeted therapies, seeking immunological synergy.
- Nanotechnology applied to the delivery of immunomodulatory drugs directly to the tumor microenvironment.
- Use of artificial intelligence (AI) to predict immune responses and toxicities, optimizing patient selection (ZHAO et al., 2023).

These approaches have the potential to transform oncology into an increasingly predictive, preventive, and personalized science.

## ETHICAL CHALLENGES IN THE AGE OF IMMUNOTHERAPY

With scientific advances, ethical dilemmas also arise that challenge the fundamental principles of bioethics: autonomy, beneficence, non-maleficence, and justice.

### *Access and Distributive Justice*

The high cost of immunotherapies—reaching more than R\$ 2 million per patient in some CAR-T cell protocols—leads to exclusion and inequality.

According to Brito et al. (2022), less than 10% of cancer patients in Brazil have access to state-of-the-art immunotherapies.

This violates the principle of distributive justice and imposes on the State the responsibility to balance cost-effectiveness and equity.

### *Consent and Risks*

Serious adverse effects, such as cytokine release syndrome and autoimmune toxicities, make the informed consent process extremely complex.

Patients need to understand that the risks can be potentially fatal, even in treatments with high success rates.

### *Genetic Privacy and Scientific Responsibility*

The genetic manipulation of human cells, as in CAR-T therapies, raises questions about the privacy of genetic data, long-term impacts, and the ethical responsibility of researchers (FERREIRA et al., 2023).

There is also debate about compassionate use and experimentation in vulnerable populations, which require strict re-

gulation and supervision by research ethics committees.

## PSYCHOLOGICAL IMPACT AND HUMANIZATION OF CARE

The impact of immunotherapy transcends tumor biology. The possibility of cure in advanced stages rekindles patients' hope, but also generates unrealistic expectations.

It is essential that cancer care maintains a multidisciplinary approach, involving psychology, nursing, and social work, to ensure humanization and emotional support during treatment.

## CONCLUSION

Cancer immunotherapy has established itself as one of the pillars of modern medicine, redefining the prognosis for various types of cancer.

Despite remarkable results, the field still faces ethical, economic, and technical challenges.

The future will depend on public policies that democratize access, investment in translational research, and the consolidation of global bioethics capable of balancing innovation and equity.

Medicine is moving towards a more personalized and fair model, where science and ethics go hand in hand in the search for a cure for cancer.

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