The Future of Combination Immunotherapy for Cancer Treatment

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Abstract

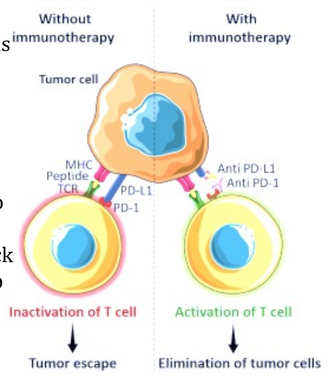
- Cancer cases and deaths in the United States remain a significant public health challenge and combination immunotherapy has emerged as a promising approach to improve clinical outcomes for cancer patients.
- Novel immunotherapy targets, including checkpoint inhibitors, antibody drug conjugates, and bispecific antibodies, are being explored for cancer therapy.
- In recent years, combination immunotherapy has shown promising results in the treatment of several types of cancer, including melanoma, lung cancer, and bladder cancer.
- The role of pharmacists becomes vital to improving patient outcomes by focusing on the administration and management of combination immunotherapy, especially in older cancer patients who may be at risk for drug-drug interactions and unnecessary medication usage.

Objectives

- To understand how monoclonal antibody immunotherapy for cancer works and how it is continually evolving.
- Elucidate the benefits of checkpoint inhibitors in novel oncology treatment.
- Discuss the advantages of combination treatment with checkpoints inhibitors in cancer therapy.

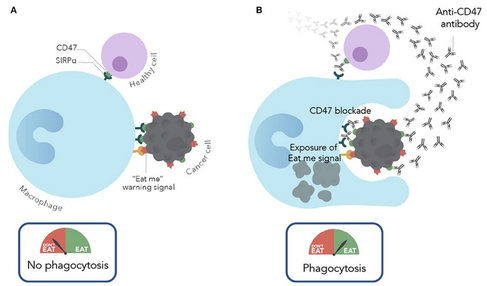
Background

- Immunotherapy can be used alone or in combination with other therapies, such as chemotherapy, radiotherapy, and as an adjuvant therapy to reduce cancer recurrence or spread.
- Monoclonal antibodies (mAbs) are laboratory-made proteins that mimic the body's natural antibodies and are used to target specific proteins on cancer cells.
- Checkpoint inhibitors are drugs that block certain proteins on cancer cells that help them evade the immune system, making cancer cells more visible to the immune system.
- The Nobel Prize in Physiology or Medicine 2018 was awarded for the discovery of cancer treatment of immune checkpoint therapy.
- However, combination immunotherapy can also lead to side effects, as the immune system may attack healthy cells along with cancer cells; hence, careful patient monitoring and management of side effects are important for successful treatment.
- Immune-related adverse events (irAEs) is one of the most common side effects caused by the immune system attacking healthy tissues in the body including a skin rash, colitis, and hepatitis



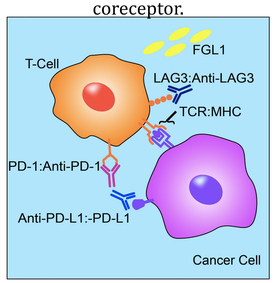
Results

CD 47 is a protein found on the surface of cells and is overexpressed in many types of cancer cells which allows them to evade the immune system and continue growing unchecked.



(A) CD-47 binds to a macrophage to stop the phagocytosis of cancerous cells
(B) Anti-CD47 antibodies present, CD47 proteins are not able to bind to the macrophage, thus allowing the tumor cells to be eaten.

PD-1 is a checkpoint protein on T cells that binds to PD-L1 on cells to prevent an immune attack from T cells
LAG-3 is a receptor that mimics CD4 coreceptor.



PDL1 and LAG3 mechanisms creates a synergistic effect in a patient's immune response to tumors. This shows promising treatment results as shown in clinical trials.

Type of cancer	Drug	Tolerability	Outcomes	Phase
Unresectable hepatocellular carcinoma	Nivolumab + Ipilinumab	Induction doses: grade 3-4 adverse events	Inconclusive	II
HER2+ breast cancer	Trastuzumab emtansine + pembrolizumab	Safe and tolerable	Inconclusive	Ib
Metastatic colorectal cancer	trametinib + durvalumab	Safe and tolerable	Inconclusive	II
Metastatic castration-resistant prostate cancer	Nivolumab + rucapari	Safe and tolerable	Inconclusive	II
Advanced solid tumors	Nivulomab+ Varlilumab	Safe and tolerable	Inconclusive	I/II

Methods

- The current literature review was conducted according to the Preferred Reporting Items for Systemic Reviews and Meta-analysis (PRISMA) statement.
- Initial screening was performed by 3 authors independently. We screened the PubMed, Embase, and Journal of Immunotherapy of Cancer database of literature reviews from inception to March 2023 for meta-analysis or systemic reviews of observational studies in investigating effects of combination therapy compared to monotherapy in the treatment of untreated or advanced cancer. By fully reading the title and abstract, we have eliminated duplicate literature. For the rest of the literatures, we read the full-text to assess the eligibility. In addition, we also manually searched reference by literature for other potential related articles. We searched keywords "combination immunotherapy," "pharmacists' role," "checkpoint inhibitors" and "cancer."

Discussion

- Combining PD-L1 and LAG-3 inhibitors has shown promising results in clinical trials for the treatment of metastatic or unresectable melanoma.
- It is important to note that a a triple combination therapy targeting 41BB, LAG-3, and CXCR2 has shown total tumor regression and 90% overall survival in preclinical models of pancreatic cancer.
- Opdualag, a combination of Nivolumab and Relatimab, has been approved by the FDA for the treatment of unresectable or metastatic melanoma.
- There are ongoing clinical trials for adoptive cell transfer using CAR-T cells and TILs, with promising results seen in the treatment of certain types of cancer.

Conclusion

- The future of cancer therapy is combination checkpoint inhibitors as immunotherapy may be more effective in treating patients with tumor burden over monotherapy treatment.
- Pharmacists' expertise in medication managements, drug interactions, and adverse effects, as well as their ability to communicate with other members of the healthcare team, makes them an essential part of the patient's care team in administering and managing combination immunotherapy for cancer.

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Disclosures

Authors have nothing to disclose concerning possible financial or personal relationships with commercial entities that may have direct or indirect interest in the subject matter of this presentation at the time data was collected.

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