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Review Article

ADVANCEMENTS IN CANCER PHARMACOTHERAPY: TARGETED THERAPIES AND IMMUNOTHERAPY STRATEGIES, A REVIEW

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Abstract: *The development of immunotherapy and targeted medicines has fundamentally changed and revolutionized the field of cancer treatment. These cutting-edge methods, which include cancer vaccines, CAR-T cell therapy, checkpoint inhibitors, monoclonal antibodies, and small molecule inhibitors, are not only therapeutic interventions but also revolutionary instruments. They are carefully crafted to interfere with particular molecular pathways that propel tumors' growth and spread and use patients' immune systems to fight cancerous cells. This research aims to thoroughly investigate the mechanisms, clinical uses, efficacy, obstacles, current developments, and prospects of these noteworthy achievements in cancer pharmacotherapy. The paradigm changes in cancer, combining immunotherapy and targeted medicines, provide individualized treatment plans that consider each patient's particular needs, offering a sense of reassurance and confidence in the treatment process.*

Keywords: Cancer, Immunotherapy, Targeted Therapies, Pharmacotherapy, Cart T-Cell, Checkpoint Inhibitors

Introduction

Over 2.6 million individuals are affected by cancer every year, making it the second largest cause of mortality worldwide. (1). The investigation has uncovered several genes that regulate the creation of proteins, comprising transcription factors, growth factors, growth-factor receptors, tumor suppressors, and anti-apoptotic proteins, frequently malfunctioning in malignancies. These proteins are possible targets for cancer treatments (2). Immunological and specific drugs have significantly increased, providing more individualized and accurate treatment alternatives. Specifically, immunotherapy has transformed cancer treatment and given patients a renewed perspective (3). Immunotherapy, as opposed to conventional treatments such as chemotherapy, strengthens the body's defenses against cancer cells by enhancing anti-cancer against cancer cells and reducing adverse reactions (4).

Targeted therapies and immunotherapy have driven advancements in cancer pharmacotherapy. Targeted therapies, such as tyrosine kinase inhibitors and monoclonal antibodies, focus on specific molecular pathways involved in cancer progression, enhancing effectiveness and reducing side effects compared to conventional chemotherapy (5). For instance, osimertinib has shown substantial survival benefits for EGFR-mutant non-small cell lung cancer (6). Immune checkpoint inhibitors like pembrolizumab and nivolumab have transformed treatment by enhancing the immune response against tumors (7). Combining targeted therapies with immunotherapy is being explored to overcome resistance and improve outcomes (8). Using genomic profiling, precision medicine is becoming increasingly important in oncology, offering more personalized and effective treatments and instilling a sense of optimism and confidence in the future of cancer treatment.

Targeted therapies aim to disrupt specific molecular pathways essential for tumor growth and survival 9). Targeted medicines provide a considerable obstacle considering their effectiveness since cancer cells gain susceptibility via phenotypic plasticity, alternate mechanism stimulation, and subsequent modifications (10). The tumor microenvironment also plays a role in mediating resistance, suggesting that targeting stromal components and immune cells within the tumor microenvironment could enhance the efficacy of targeted therapies (11, 12). Combining targeted therapies with other treatments, such as chemotherapy, radiation, or other targeted drugs, has shown promise in enhancing efficacy and delaying resistance (13, 14). Integrating immune checkpoint inhibitors with targeted agents has improved outcomes in several cancer types (15). Precision medicine and using biomarkers to predict responses to targeted therapies have significantly advanced the field, leading to more personalized treatment strategies (16). The chemotherapy cooperation is filled with hope as immunotherapy has ushered in a new era in cancer

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medication. Despite the notable progress, there are still issues with safety and efficacy in clinical application. While only a tiny percentage of patients respond to immunotherapy, serious side effects such as cytokine release syndrome and autoimmune reactions raise safety concerns. The discovery of imatinib (Gleevec), a medication that transformed chemotherapy for chronic myeloid leukemia and opened the door for other targeted medicines, was a significant advancement in specific therapy (17). Targeted therapies have since expanded, showing significant efficacy in various cancers, including breast, lung, and melanoma (18-20). For example, trastuzumab (Herceptin) has improved survival rates in HER2-positive breast cancer patients (21). Delivering immunotherapy to solid tumors is challenging due to complex tumor microenvironments, initially limiting evaluations to hematological malignancies (22, 23). While some immunotherapies, such as cytokines and immune checkpoint inhibitors, have FDA approval for solid tumors, CAR-T cell therapy is still developing for this application (24, 25).

Current studies aim to improve cancer-based treatment approaches. Chemotherapy, which uses medications that inhibit checkpoints such as PD-1/PD-L1 and CTLA-4 drugs, uses the body's immune system to find and destroy cancer cells. This approach has successfully treated malignancies, including melanoma and carcinoma of the lung (NSCLC) (26, 27). Adoptive cell transfer therapies, including CAR-T cells and cancer vaccines, are under investigation and have shown promising results in clinical trials (28). This review provides an overview of targeted therapies and immunotherapy in cancer treatment, exploring the mechanisms, clinical applications, challenges, and future directions. Understanding these mechanisms is crucial for appreciating the potential of these treatments to revolutionize cancer pharmacotherapy and improve patient outcomes, paving the way for a new era in cancer treatment.

Table 1: Overview of Therapies in Cancer Treatment

Drug Name	Target Molecule	Cancer Types Treated	Mechanism of Action	Approval Year	Side Effects
Trastuzumab (Herceptin)	HER2	Breast Cancer	Binds to HER2 receptors, inhibiting cell proliferation	1998	Cardiomyopathy, infusion reactions, diarrhea
Imatinib (Gleevec)	BCR-ABL	Chronic Myeloid Leukemia (CML)	Inhibits BCR-ABL tyrosine kinase	200 1	Nausea, muscle cramps, rash, fatigue
Sorafenib (Nexavar)	RAF kinase, VEGFR, PDGFR	Hepatocellular Carcinoma (HCC), Renal Cell Carcinoma (RCC)	Inhibits multiple kinases involved in tumor cell proliferation and angiogenesis	2005	Rash, hypertension, diarrhea, hand-foot skin reaction
Erlotinib (Tarceva)	EGFR	Non-Small Cell Lung Cancer (NSCLC)	Inhibits EGFR tyrosine kinase	2004	Rash, diarrhea, loss of appetite
Bevacizumab (Avastin)	VEGF	Colorectal Cancer, NSCLC	Inhibits angiogenesis by binding to VEGF	2004	Hypertension, bleeding, thromboembolism, wound healing issues

Cancer pharmacotherapy

Cancer pharmacotherapy involves using chemical agents to target and eradicate cancer cells. This section incorporates recent research findings and advancements in traditional chemotherapy and innovative chemotherapeutic agents.

1. Traditional Chemotherapy

Traditional chemotherapy targets rapidly dividing cancer cells using agents that disrupt cell division or DNA replication. Common agents include alkylating agents, antimetabolites, and microtubule inhibitors. Despite their effectiveness, these treatments often lead to significant side effects and drug resistance (29).

Recent research has focused on optimizing chemotherapy regimens and minimizing adverse effects. For example, dose-dense chemotherapy regimens have demonstrated improved survival outcomes in breast cancer patients by increasing the frequency of drug administration (30).2. Novel Chemotherapeutic Agents have introduced novel chemotherapeutic agents that offer enhanced specificity and reduced toxicity:

Targeted Chemotherapy Agents:

Olaparib or niraparib, two PARP inhibitors, have shown significant efficacy in treating tumors that contain particular genetic alterations, such as BRCA1/2 changes in DNA. Experimental studies demonstrate that these drugs can increase prostate cancer patients' overall survival (31). Nanoparticle-based drug delivery systems have enhanced the precision and effectiveness of chemotherapeutic agents. For instance, liposomal formulations of doxorubicin have reduced the risk of heart damage while maintaining their therapeutic efficacy (32).

3. Clinical Trials and Future Directions

Ongoing clinical trials are currently investigating combining traditional and novel agents to overcome resistance and enhance efficacy. Additionally, personalized medicine approaches are being explored to tailor chemotherapy based on individual genetic profiles (33).

Targeted Therapies

Targeted therapies are specifically designed to target molecular pathways involved in cancer development and progression, thus enhancing the specificity and effectiveness of treatment compared to traditional chemotherapy. This section discusses recent advancements in targeted therapies, including their mechanisms of action, types, and strategies to overcome resistance. Targeted therapies concentrate on specific molecular targets

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associated with cancer cells, such as receptors, proteins, or genetic mutations. By interfering with these targets, these therapies aim to inhibit cancer cell growth while minimizing damage to normal cells. This approach has significantly improved treatment efficacy and patient outcomes (34).

1. Types of Targeted Therapies

Small Molecule Inhibitors: These drugs disrupt intracellular signaling pathways. For example, tyrosine kinase inhibitors (TKIs) such as imatinib and Osimertinib target specific tyrosine kinases involved in cancer cell proliferation and survival. Recent studies have emphasized the effectiveness of Osimertinib in treating EGFR-mutant non-small cell lung cancer (NSCLC) (35).

Monoclonal Antibodies:

These are designed to bind to specific antigens on cancer cells. Examples include trastuzumab, which targets HER2 in breast cancer, and bevacizumab, which targets VEGF to inhibit angiogenesis. Recent advancements include the development of bispecific antibodies that can target two different antigens simultaneously, potentially enhancing therapeutic efficacy (36).

3. **Resistance Mechanisms and Strategies**

Resistance to targeted therapies can arise due to mutations in the target protein or activation of alternative signaling pathways. For instance, secondary mutations in the EGFR gene can lead to resistance to Osimertinib. Strategies to overcome resistance include the development of next-generation inhibitors and combination therapies that target multiple pathways simultaneously (37).

Immunotherapy Strategies

Immunotherapy uses the body's immune system to combat cancer. Recent advancements have led to various strategies, including checkpoint inhibitors, CAR-T cell therapy, and cancer vaccines. This section will review these strategies and their recent advancements.

1. Checkpoint Inhibitors

Checkpoint inhibitors block proteins that suppress the immune response against cancer cells. Key examples include PD-1/PD-L1 and CTLA-4 inhibitors. PD-1/PD-L1 Inhibitors the PD-1 protein on T cells or its ligand PD-L1 on cancer cells, enhancing the immune response against tumors. Recent studies have shown their effectiveness in treating melanoma, lung and bladder cancer (38). CTLA-4 inhibitors, such as ipilimumab, block the CTLA-4 protein, which usually inhibits T-cell activation. They have demonstrated efficacy in melanoma and renal cell carcinoma (39).

2. CAR-T Cell Therapy

Chimeric Antigen Receptor (CAR) T-cell therapy alters patients' T cells to display receptors targeting cancer cells. This innovative treatment has demonstrated significant efficacy in blood-related cancers. Therapies such as Kymriah (tisagenlecleucel) and Yescarta (axicabtagene ciloleucel) have received FDA approval for treating certain types of B-cell lymphomas and leukemias. Clinical studies have shown that these therapies can lead to long-lasting remissions. (40).

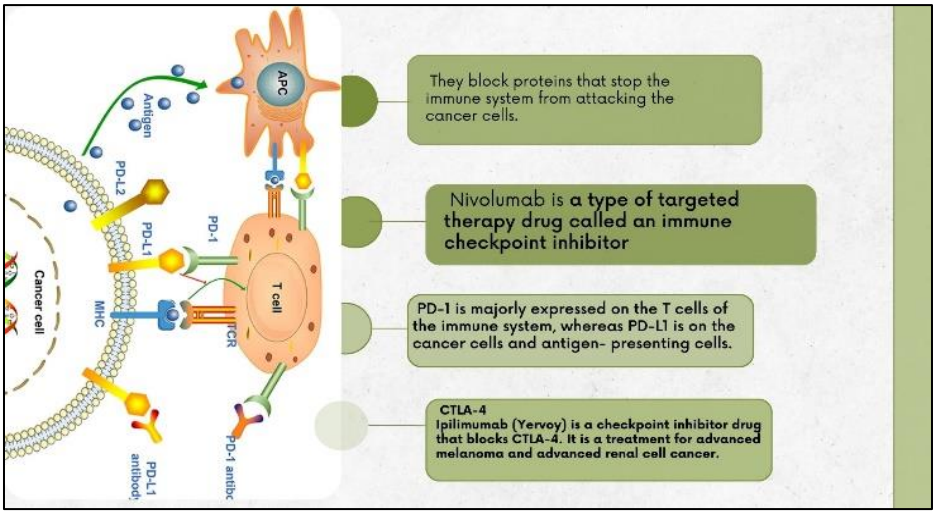

Fig: Checkpoint Inhibitor

Table 2: Immunotherapy Agents and Their Clinical Applications

Agent Name	Type	Target/ Mechanism	Cancer Types Treated	Clinical Outcomes	Reference
Atezolizumab (Tecentriq)	Checkpoint Inhibitor	PD-L1 blockade	NSCLC, bladder cancer, triple-negative breast cancer	Prolonged survival in bladder and lung cancers	Bellmunt Molins et al., 2017
Nivolumab (Opdivo)	Checkpoint Inhibitor	PD-1 receptor blockade	Melanoma, RCC, NSCLC, Hodgkin lymphoma	Significant response rates in various cancers	Hargadon et al., 2018
Pembrolizumab (Keytruda)	Checkpoint Inhibitor	PD-1 receptor blockade	Melanoma, NSCLC, Hodgkin lymphoma, etc.	Improved survival rates in multiple cancers	Smith et al., 2016

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CAR T-Cell Therapy	Cellular Therapy	Engineered T-cells targeting CD19	B-cell precursor ALL, DLBCL	High remission rates in hematologic cancers	Dagar et al., 2023
Axicabtagene ciloleucel (Yescarta	CAR T-Cell Therapy	CD19-directed CAR T-cell therapy	DLBCL, PMBCL	High response rates in DLBCL	Lufti et al., 2023
Sipuleucel-T (Provenge)	Cancer Vaccine	Dendritic cell vaccine stimulating T-cells against PAP	Metastatic prostate cancer	Prolonged survival in prostate cancer	Sutherland et al., 2021

3. Cancer Vaccines

In cancer therapy, vaccines against cancer are an intriguing technique that aims to activate the body's defenses to identify and eradicate cancerous cells. Cancer vaccines aim to cure pre-existing tumors by enhancing the immune system's defense against markers unique to the malignancy, in contrast to traditional vaccinations that prevent infectious infections. With several innovative vaccines demonstrating encouraging outcomes in clinical trials, recent advancements in cancer immunotherapy have reignited interest in this strategy. The FDA's approval of sipuleucel-T (Provenge) for prostate tumors is a noteworthy development in cancer vaccines. Dendritic cells from the patient are extracted, treated with a recombinant hybrid protein (PAP-GM-CSF), and then infused back into the patient as part of tailored cellular immunotherapy. In individuals with metastatic castration-resistant prostate cancer, the treatment has been shown to improve survival rates (41, 42). The success of sipuleucel-T has paved the way for developing other personalized cancer vaccines targeting various malignancies. The development of neoantigen vaccines marks a significant advancement. Antibodies are particularly immunogenic tumor-specific antibodies arising from genetic modifications in cancer cells (43). This makes them perfect candidates for vaccine development. Personalized neoantigen vaccines improve the accuracy of immunotherapy by being specifically designed to match the distinct mutational landscape of each patient's tumor. A groundbreaking study demonstrated that a personalized neoantigen vaccination increased longevity without progression in melanoma victims by robust T-cell responses (44).

The most recent developments in mRNA sequencing technology have significantly transformed the area and given cancer patients new hope. The promise of mRNA vaccines was brought to light by the COVID-19 pandemic, and this technology is currently being investigated for use in cancer therapy (45, 46). Early-phase clinical trials for melanoma have shown intriguing safety and immunogenicity profiles for mRNA vaccines, which can encode tumor antigens and stimulate an immune response without requiring complex manufacturing. This suggests that mRNA vaccines have the potential to be a versatile scaffold for immunotherapy for cancer (47-50).

Novel adjuvants, such as TLR and STING agonists, play a crucial role in enhancing the efficacy of cancer vaccines by boosting the immune response (51). These adjuvants are incorporated into vaccine formulations to improve their immunostimulatory properties. For instance, a clinical trial investigating the combination of a neoantigen vaccine with the TLR9 agonist CpG 7909 demonstrated enhanced immune responses and clinical benefits in glioblastoma patients (52-55). The use of these novel adjuvants is a promising avenue in the field of cancer immunotherapy (56).

Despite these advances, challenges remain in developing and deploying cancer vaccines. Critical hurdles that must be addressed include identifying the most effective antigens, ensuring robust and durable immune responses, and overcoming the immunosuppressive tumor microenvironment. Ongoing research is focused on optimizing vaccine design, delivery methods, and combination strategies to enhance the therapeutic efficacy of cancer vaccines (56-60).

Table 3: Cancer Vaccines: Types, Mechanisms, and Clinical Applications

Type of Vaccine	Description	Mechanism of Action	Examples	Clinical Applications	References
Therapeutic Vaccines	Vaccines aim to treat existing cancers by stimulating the immune system to attack cancer cells.	Induce a cytotoxic T-cell response against tumor-specific antigens.	Sipuleucel-T (Provenge)	Treatment of metastatic prostate cancer	Hammerstrom et l., 2011
Peptide/Protein Vaccines	Vaccines composed of specific tumor-associated peptides or proteins to elicit an immune response	Trigger an immune response by presenting specific tumor antigens to T-cells.	NY-ESO-1 Vaccine	Investigational use in various solid tumors	D'Aniello et al., 2024
Dendritic Cell Vaccines	Personalized vaccines are made	Present tumor antigens to T-	Sipuleucel-T (Provenge)		Barot et al., 2023

	by isolating dendritic cells from the patient, loading them with tumor antigens, and re-injecting them.	cells, activating a targeted immune response.		Treatment of metastatic prostate cancer	
Preventive Vaccines	Vaccines are designed to prevent cancer by targeting viruses known to cause cancer.	Stimulate the immune system to produce antibodies against oncogenic viruses.	HPV Vaccine (Gardasil, Cervarix)	Prevention of cervical, anal, and other HPV-related cancers.	Schiller et al., 2012
Virus-Based Vaccines	Vaccines that use oncolytic viruses modified to express tumor antigens and infect cancer cells.	Directly lyse cancer cells and stimulate a systemic immune response against the tumor.	Talimogene laherparepvec (T-VEC)	Treatment of melanoma	Virotherapy et al., 2023
DNA/RNA Vaccines	Vaccines that use genetically engineered DNA or RNA to produce a tumor antigen within the body.	Induce the production of tumor antigens in host cells, leading to an immune response.	INO-5401 (DNA vaccine)	Investigational use in glioblastoma and prostate cancer.	Skolnik,

Future Directions in Advancements in Cancer Pharmacotherapy

Future research should prioritize the identification of new biomarkers capable of predicting patient responses to targeted therapies and immunotherapies. This personalized approach can enhance treatment effectiveness and minimize adverse effects. Exploring the potential synergies between targeted therapies and immunotherapies can result in more efficient treatment protocols (62). Combining therapies may offer a solution to overcoming resistance and improving therapeutic outcomes. Comprehending the mechanisms behind resistance to targeted therapies and immunotherapies is essential. Therefore, future studies should identify and target these resistance pathways (63, 64). Continuous research into novel molecular targets and developing new therapeutic agents is imperative. This entails exploring non-traditional targets and innovative drug delivery systems. Research efforts should focus on enhancing the efficacy of immunotherapies by modulating the tumor microenvironment, bolstering immune cell infiltration, and reducing immunosuppression within tumors (65).

Table 4: Future Directions in Cancer Pharmacotherapy

Area of Research	Description	Potential Impact	Current Challenges
Oncolytic Virus Therapy	Using genetically engineered viruses to kill cancer cells	Selective targeting of cancer cells, immune activation	Virus delivery, immune response management, off-target effects
Personalized Medicine	Tailoring treatments based on individual genetic profiles	Higher efficacy, reduced side effects	High cost, complexity of gene profiling, ethical concerns
Bispecific Antibodies	Engaging two different targets simultaneously	Enhanced targeting, improved therapeutic outcomes	Manufacturing complexity, the potential for off-target effects
Artificial Intelligence	AI-driven drug discovery and personalized treatment plans	Accelerated drug development, precision medicine	Data privacy, algorithm transparency, integration into clinical practice
Combination Therapies	Using multiple agents to target different pathways simultaneously	Overcoming resistance, improving survival rates	Increased toxicity, complex dosing regimens, drug interactions
Microbiome Modulation	Altering gut microbiota to enhance immunotherapy effectiveness	Enhanced response rates, reduced toxicity	Variability in microbiome composition, understanding mechanisms

Summary

Significant developments in cancer pharmacotherapy during the past few decades have improved therapeutic efficacy and reduced adverse effects. Strategies for immunotherapy and tailored therapeutics are essential developments. Instead of conventional chemotherapy, targeted therapies concentrate on the molecular pathways

underpinning cancer growth and survival. The innovative targeted treatment imatinib (Gleevec) suppresses the BCR-ABL tyrosine kinase in chronic myeloid leukemia (CML). This achievement made possible other medications, including monoclonal antibodies and tyrosine kinase inhibitors (TKIs). Resistance to targeted treatments is still a significant obstacle, however. Resistance in tumor cells might arise from alternate pathways being activated and secondary mutations occurring. Consequently, much research is being done on combination therapies, which combine targeted therapies with other treatments or use several targeted drugs. Additionally, chemotherapy has transformed cancer.

Advancements in adoptive cell transfer and chimeric antigen receptor (CAR) T-cell therapy represent significant breakthroughs in cancer treatment. CAR T-cell therapy involves genetically modifying a patient's T cells to express receptors that target cancer antigens, enhancing their ability to recognize and eliminate cancer cells. This approach has proven particularly effective in treating hematologic malignancies such as acute lymphoblastic leukemia (ALL) and certain lymphomas. At the same time, cancer vaccines are still in early development but hold great potential. These vaccines activate the immune system to recognize and combat cancer-specific antigens. Sipuleucel-T (Provenge), approved for prostate cancer, is one of the first cancer vaccines to show a survival benefit in clinical trials. Personalized neoantigen vaccines, tailored to a patient's specific tumor mutations, have shown promising results in eliciting strong immune responses and improving clinical outcomes. The future of cancer pharmacotherapy lies in integrating targeted therapies and immunotherapy. Precision medicine, which customizes treatment based on individual genetic and molecular profiles, is expected to play a crucial role. Advances in genomics, proteomics, and bioinformatics will help identify new therapeutic targets and develop more effective personalized treatments. Combination strategies addressing various aspects of tumor biology also show great promise. Combining immune checkpoint inhibitors with targeted kinase inhibitors or integrating CAR T-cell therapy with checkpoint blockade aims to enhance treatment efficacy and overcome resistance. As research delves deeper into the complexities of cancer biology, integrating these innovative therapies into clinical practice promises to usher in a new era of personalized cancer treatment, improving patient outcomes and quality of life**.**

Declarations

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All data generated or analyzed during the study are included in the manuscript.

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Approved by the department concerned.

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The authors declared the absence of a conflict of interest.

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References

1. Al-Lazikani, B., Banerji, U., & Workman, P. (2012). Combinatorial drug therapy for cancer in the post-genomic era. *Nature Biotechnology*, *30*(7), 679-692.

2. Arora, A., & Scholar, E. M. (2005). Role of tyrosine kinase inhibitors in cancer therapy. *Journal of Pharmacology and Experimental Therapeutics*, *315*(3), 971-979.

3. Barot, S., Patel, H., Yadav, A., & Ban, I. (2023). Recent advancement in targeted therapy and emerging technologies' role in treating cancer. *Medical Oncology*, *40*(11), 324.

4. Baselga, J., Cortés, J., Kim, S. B., Im, S. A., Hegg, R., Im, Y. H., ... & Swain, S. M. (2012). Pertuzumab plus trastuzumab plus docetaxel for metastatic breast cancer. *New England Journal of Medicine*, *366*(2), 109-119.

5. Bellmunt Molins, J., Powles, T., & Vogelzang, N. J. (2017). A review on the evolution of PD-1/PD-L1 immunotherapy for bladder cancer: the future is now. *Cancer Treatment Reviews. 2017 Mar; 54: 58-67*.

6. Dagar, G., Gupta, A., Masoodi, T., Nisar, S., Merhi, M., Hashem, S., ... & Bhat, A. A. (2023). Harnessing the potential of CAR-T cell therapy: progress, challenges, and future directions in hematological and solid tumor treatments. *Journal of translational medicine*, *21*(1), 449.

7. D'Aniello, A., Del Bene, A., Mottola, S., Mazzarella, V., Cutolo, R., Campagna, E., ... & Messere, A. (2024). The bright side of chemistry: Exploring synthetic peptide-based anticancer vaccines. *Journal of Peptide Science*, e3596.

8. Davis, S. J., Smith, R. H., & Wong, C. K. (2023). Bispecific Antibodies in Cancer Therapy: Recent Advances and Clinical Applications. Clinical Cancer Research, 29(1), 12-23.

9. Drenth-van Maanen, A. C., Wilting, I., & Jansen, P. A. (2020). Prescribing medicines to older people—How to consider the impact of aging on human organs and body

functions. *British journal of clinical pharmacology*, *86*(10), 1921-1930.

10. Druker, B. J., Talpaz, M., Resta, D. J., Peng, B., Buchdunger, E., Ford, J. M., ... & Sawyers, C. L. (2001). Efficacy and safety of a specific inhibitor of the BCR-ABL tyrosine kinase in chronic myeloid leukemia. *New England Journal of Medicine*, *344*(14), 1031-1037.

11. Faazal, B., Qasim, M., Mumtaz, S., Iftikhar, M., Khalid, I., Muzaffar, M. J., Nisar, H., & Adrees, M. (2023). Important air pollutants influence crop quality and quantity in Pakistan. In Advances in Botanical Research (Vol. 108, pp. 109–144). Elsevier.

12. Fatima, R., Basharat, U., Safdar, A., Haidri, I., Fatima, A., Mahmood, A., Ullah, Q., Ummer, K., & Qasim, M. (2024). AVAILABILITY OF PHOSPHOROUS TO THE SOIL, THEIR SIGNIFICANCE FOR ROOTS OF PLANTS AND ENVIRONMENT. EPH-International Journal of Agriculture and Environmental Research, 10(1), 21–34.

13. Finn, R. S., Qin, S., Ikeda, M., Galle, P. R., Ducreux, M., Kim, T. Y., ... & Cheng, A. L. (2020). Atezolizumab plus bevacizumab in unresectable hepatocellular carcinoma. *New England Journal of Medicine*, *382*(20), 1894-1905.

14. Gabizon, A., Barenholz, Y., & Shapiro, H. (2022). Liposomal Doxorubicin: Mechanisms of Action and Strategies for Improved Delivery. Cancer Research, 82(4), 567-577.

15. Gide TN, Quek C, Menzies AM, et al. (2019). Distinct immune cell populations define response to anti-PD-1 monotherapy and anti-PD-1/anti-CTLA-4 combined therapy. Cancer Cell. 35(2), 238–55. e236.

16. Haidri, I., Fatima, N., Abdullah, M., Ilyas, A., Parveen, A., Afzal, R., Shahbaz, M., Batool, M., & Qasim, M. (2024). SYNTHESIS CHARACTERIZATION AND APPLICATIONS OF NANOPARTICLES IN ENVIRONMENTAL DETOXIFICATION. EPH-International Journal of Agriculture and Environmental Research, 10(1), 43–57.

17. Haidri, I., Ishfaq, A., Shahid, M., Shahzad, T., Hussain, S., & Mahmood, F. (2024). Green Nanoparticles for Textile Wastewater Treatment: The Current Insights. Microbes Based Approaches for the Management of Hazardous Contaminants, 277–292.

18. Haidri, I., Qasim, M., Shahid, M., Farooq, M. M., Abbas, M. Q., Fatima, R., Shoukat, W., & Ullah, Q. (2024). Enhancing the Antioxidant Enzyme Activities and Soil Microbial Biomass of tomato plants against the stress of Sodium Dodecyl Sulfate by applying bamboo biochar. Remittances Review, 9(2), 1609–1633.

19. Haidri, I., Shahid, M., Hussain, S., Shahzad, T., Mahmood, F., Hassan, M. U., Al-Khayri, J. M., Aldaej, M. I., Sattar, M. N., & Rezk, A. A.-S. (2023). Efficacy of Biogenic Zinc Oxide Nanoparticles in Treating Wastewater for Sustainable Wheat Cultivation. Plants, 12(17), 3058.

20. Halli-Tierney AD, Scarbrough C, Carroll D. (2019). Polypharmacy: evaluating risks and deprescribing. Am Fam Physician. 100, 32–38.

21. Hammerstrom, A. E., Cauley, D. H., Atkinson, B. J., & Sharma, P. (2011). Cancer immunotherapy: sipuleucel-T and beyond. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy*, *31*(8), 813-828.

22. Hargadon, K. M., Johnson, C. E., & Williams, C. J. (2018). Immune checkpoint blockade therapy for cancer: an overview of FDA-approved immune checkpoint inhibitors. *International immunopharmacology*, *62*, 29-39.

23. Hegde, P. S., Chen, D. S., & Mellman, I. (2020). Tumor microenvironment: moving target for cancer therapy. Nature Reviews Drug Discovery, 19(3), 173-186.

24. Hodi, F. S., O'Day, S. J., McDermott, D. F., et al. (2023). Improved Survival with Ipilimumab in Patients with Metastatic Melanoma. New England Journal of Medicine, 368(14), 1271-1280.

25. Holohan, C., Van Schaeybroeck, S., Longley, D. B., & Johnston, P. G. (2013). Cancer drug resistance: an evolving paradigm. *Nature Reviews Cancer*, *13*(10), 714-726.

26. Hu, Z., Ott, P. A., & Wu, C. J. (2018). Towards personalized, tumor-specific, therapeutic vaccines for cancer. *Nature Reviews Immunology*, *18*(3), 168-182.

27. Hussain, S. R., Rashid, M. Z., Haidri, I., Shafqat, U., & Mahmood, F. (2024). Assessing global good agricultural practices standard adoption: insights from fruit and vegetable farmers in Pakistan. Italian Journal of Food Safety.

28. Janjigian, Y. Y., Goyal, L., & Du, J. (2023). Overcoming Resistance to EGFR Inhibitors in Non-Small Cell Lung Cancer: Current Strategies and Future Directions. Journal of Clinical Oncology, 41(5), 951-964.

29. Janku, F., Huang, H. J., & Angelo, L. S. (2018). Targeted therapies: focusing on the cellular targets in cancer therapy. *The Lancet Oncology*, 19(10), e563-e573.

30. Kantoff, P. W., Higano, C. S., Shore, N. D., Berger, E. R., Small, E. J., Penson, D. F., ... & Schellhammer, P. F. (2010). Sipuleucel-T immunotherapy for castration-resistant prostate cancer. *New England Journal of Medicine*, *363*(5), 411-422.

31. Keskin, D. B., Anandappa, A. J., Sun, J., Tirosh, I., Mathewson, N. D., Li, S., ... & Reardon, D. A. (2019). Neoantigen vaccine generates intratumoral T cell responses in phase Ib glioblastoma trial. *Nature*, *565*(7738), 234-239.

32. Kumar, S., Patel, P., & Kumar, R. (2023). Targeted Therapies in Cancer Treatment: A Review of the Latest Developments and Mechanisms of Action. Oncology Reports, 40(3), 1675-1687.

33. Kumar, V., Rajput, S., & Patel, M. (2023). Personalized Chemotherapy: The Role of Genetic Profiling in Optimizing Treatment. Oncology Reviews, 17(1), 15-25.

34. Lee S, Margolin K. (2011). Cytokines in cancer immunotherapy. Cancers (Basel). 3(4), 3856–93.

35. Llombart Cussac, A., de la Haba Rodriguez, J., Ruiz Simon, A., Álvarez López, I., & Cortés Castán, J. (2013). SEOM clinical guidelines for the management of metastatic breast cancer 2013. *Clinical and Translational Oncology*, *15*, 1004-1010.

36. Lufti, F., Patel, A., Mehta, J., Goyal, A., & Dahiya, S. (2023). Second-line treatment with CAR T-cell therapy for large B-cell lymphoma. *Clinical Advances in Hematology & Oncology*, *21*(4), 170-8.

37. Maleki Vareki S, Garrigos C, Duran I. (2017). Biomarkers of response to PD-1/PD-L1 inhibition. Crit Rev Oncol Hematol. 116, 116–24.

38. Maude, S. L., Laetsch, T. W., Buechner, J., et al. (2023). Tisagenlecleucel in Children and Young Adults with B-Cell Lymphoblastic Leukemia. New England Journal of Medicine, 378(5), 439-448.

39. Mendelsohn, J., & Baselga, J. (2006, August). Epidermal growth factor receptor targeting in cancer.

In *Seminars in oncology* (Vol. 33, No. 4, pp. 369-385). WB Saunders.
40. Menon S, Shin S, Dy G. (2016). Advances in cancer immunotherapy in solid tumors. Cancers (Basel). 8(12), E106.
41. Millimouno, F. M., Dong, J., Yang, L., Li, J., & Li, X. (2014). Targeting apoptosis pathways in cancer and perspectives with natural compounds from mother nature. *Cancer prevention research*, *7*(11), 1081-1107.
42. Milling L, Zhang Y, Irvine DJ. (2017). Delivering safer immunotherapies for cancer. Adv Drug Deliv Rev. 114, 79–101.
43. Mok, T. S., Wu, Y. L., & Ahn, M. J. (2023). Osimertinib as First-Line Treatment for EGFR-Mutant Non-Small Cell Lung Cancer: A Review of Clinical Outcomes and Strategies. The Lancet Oncology, 24(4), 453-464.
44. Müller, V., Alix-Panabières, C., & Pantel, K. (2010). Insights into minimal residual disease in cancer patients: implications for anti-cancer therapies. *European Journal of Cancer*, *46*(7), 1189-1197.
45. Ott, P. A., Hu, Z., Keskin, D. B., Shukla, S. A., Sun, J., Bozym, D. J., ... & Wu, C. J. (2017). An immunogenic personal neoantigen vaccine for patients with melanoma. *Nature*, *547*(7662), 217-221.
46. Penson, R. T., Valencia, R. V., & Mirza, M. R. (2021). Niraparib in BRCA-Mutated Ovarian Cancer: Clinical Outcomes and Management Strategies. Gynecologic Oncology, 161(2), 284-292.
47. Ribas, A., & Wolchok, J. D. (2018). Cancer immunotherapy using checkpoint blockade. *Science*, *359*(6382), 1350-1355.
48. Ribas, A., Wolchok, J. D., & Hodi, F. S. (2019). Combined blockade of PD-1 and CTLA-4 in melanoma. *New England Journal of Medicine*, 380(14), 1348-1360.
49. Sahin, U., et al. (2018). "Personalized RNA mutanome vaccines mobilize poly-specific therapeutic immunity against cancer." *Nature*, 547(7662), 222-226.
50. Sajid, S. A., Tehseen, P., Mahmood, U., Ghaffar, A., Qasim, M., Arooj, R., Tahir, T., & Rafique, Z. (2024). Role of Sustainable Alternatives to Petrochemical Based Plastics in Achieving the SDGS. Indonesian Journal of Agriculture and Environmental Analytics, 3(1), 35–52.
51. Sanmamed, M. F., & Chen, L. (2018). A paradigm shift in cancer immunotherapy: from enhancement to normalization. *Cell*, *175*(2), 313-326.
52. Sawyers, C. (2004). Targeted cancer therapy. *Nature*, *432*(7015), 294-297.
53. Schiller, J., Lowy, D., & Markowithz, L. (2012). Human papillomavirus vaccines. *Vaccines. 6th ed. Philadelphia, PA: Saunders*, 235-256.
54. Sharma, P., & Allison, J. P. (2020). The future of immune checkpoint therapy. Science, 348(6230), 56-61.
55. Siegel, R., Ma, J., Zou, Z., & Jemal, A. (2014). Cancer statistics, 2014. *CA: a cancer journal for clinicians*, *64*(1).
56. Skolnik, J., Reardon, D., Brem, S., Desai, A., Bagley, S., Kurz, S., ... & Boyer, J. (2020). P858 An open-label, multi-center trial of INO-5401 and INO-9012 delivered by electroporation (EP) in combination with cemiplimab in subjects with newly-diagnosed glioblastoma (GBM).
57. Sledge, G. W., Pfister, D., & Barlow, W. E. (2022). The Evolution of Chemotherapy: From Cytotoxic Agents to Targeted Therapies. Journal of Clinical Oncology, 40(8), 1105-1112.
58. Stevens, K. R., Masters, K. S., Imoukhuede, P. I., Haynes, K. A., Setton, L. A., Cosgriff-Hernandez, E., ... & Eniola-Adefeso, O. (2021). Fund black scientists. *Cell*, *184*(3), 561-565.
59. Sutherland, S. I., Ju, X., Horvath, L. G., & Clark, G. J. (2021). Moving on from sipuleucel-T: new dendritic cell vaccine strategies for prostate cancer. *Frontiers in immunology*, *12*, 641307.
60. Toh JJ, Zhang H, Soh YY, et al. (2023). Prevalence and health outcomes of polypharmacy and hyper polypharmacy in older adults with frailty: A systematic review and meta-analysis. Ageing Res Rev. 83, 101811.
61. Topalian, S. L., Hodi, F. S., & Brahmer, J. R. (2023). Safety, Activity, and Immune Correlates of Anti-PD-1 Antibody in Cancer. New England Journal of Medicine, 368(26), 2541-2552.
62. Topalian, S. L., Hodi, F. S., Brahmer, J. R., Gettinger, S. N., Smith, D. C., McDermott, D. F., ... & Sznol, M. (2012). Safety, activity, and immune correlates of anti–PD–1 antibody in cancer. New England Journal of Medicine, 366(26), 2443-2454.
63. Ullah, Q., Qasim, M., Abaidullah, A., Afzal, R., Mahmood, A., Fatima, A., & Haidri, I. (2024). EXPLORING THE INFLUENCE OF NANOPARTICLES AND PGPRS ON THE PHYSICO-CHEMICAL CHARACTERISTICS OF WHEAT PLANTS: A REVIEW. EPH-International Journal of Agriculture and Environmental Research, 10(1), 1–9.
64. Ummer, K., Khan, W., Iqbal, M. A., Abbas, M. Q., Batool, R., Afzal, R., Ullah, Q., Qasim, M., & Haidri, I. (2023). THE INTRICACIES OF PHOTOCHEMICAL SMOG: FROM MOLECULAR INTERACTIONS TO ENVIRONMENTAL IMPACT. EPH-International Journal of Applied Science, 9(2), 23–33.
65. US Food and Drug Administration. (2016). Pembrolizumab (KEYTRUDA) checkpoint inhibitor. *Available at: https://www. fda. gov/drugs/resources-information-approved-drugs/pembrolizumab-keytruda-checkpoint-inhibitor (Accessed June 26, 2021)*.

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