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Recent Advances in Cancer Treatment: Immunotherapy vs Chemotherapy

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Abstract: Cancer has been one of the most significant public health problems globally for many years, with chemotherapy being the standard treatment for decades. In recent times, immunotherapy has become a promising new option with major clinical advantages, especially in cancers that have historically been refractory to therapy. This review discusses the recent progress in chemotherapy and immunotherapy, their mechanisms, therapeutic effects, and limitations. Moreover, this review also discusses the extent to which combination is feasible between these two treatment modalities in order to enhance clinical results and minimize toxicity. New therapies and current clinical trials are also presented, reflecting future trends in cancer therapy and the potential of personalized medicine in oncology.

Keywords: *Immunotherapy, Immune Checkpoint Inhibitors, Cancer Treatment, Chemotherapy.*

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I. INTRODUCTION

Cancer is a group of diseases characterized by excessive cell growth and spread to other areas of the body. Cancer's global disease burden is growing. Indeed, as reported by the World Health Organization, by 2040, cancer will be responsible for 1 in 6 global deaths[1].

Traditional methods of treating cancer, such as chemotherapy, have existed for some decades and have provided most patients with significant survival benefits. Although it is linked with serious side effects due to the non-specificity of chemotherapy drugs, which harm normal cells that are proliferating quickly, such as those in the digestive system, hair follicles, and bone marrow [2].

Immunotherapy has come to be the new wave in cancer treatment, which involves the use of the body's own immune system in order to be able to identify and kill off cancer cells. Chemotherapy, on the other hand, is used against all quickly dividing cells, whereas the application of immunotherapy will allow the body to become stronger in fighting the tumor, offering more of a targeted form of treatment that is not as toxic[3].

However, challenges persist, such as immune-related side effects, poor efficacy in certain diseases, and costliness[4].

This review is intended to compare chemotherapy and immunotherapy in depth, from their mechanisms of action, clinical usage, recent progress, and problems. Lastly, we address the newly arising field of combination therapies, integrating chemotherapy and immunotherapy, in an effort to seek improved patient outcome[5].

II. CHEMOTHERAPHY: MECHANISM, ADVANCES, LIMITATION

➢ *Mechanism*

The chemotherapeutic agents act mainly on the cell cycle, which is the process that aids cell division. The agents act quite rapidly on those cells that divide rapidly, which are cancer cells. Chemotherapy agents can be grouped into types based on the mode of action as follows:

- *Alkylating Agents:*

These include drugs like cyclophosphamide and melphalan. These add alkyl groups to the DNA and thereby cause crosslinking and strand breaks, that interfere with DNA replication and transcription[6].

- *Antimetabolites*:

Methotrexate and fluorouracil are some drugs that are similar to natural metabolites required for DNA and RNA synthesis and therefore interfere with cell division.[7].

- *Topoisomerase Inhibitors:*

Irinotecan and etoposide represent a group of drugs that act as inhibitors of topoisomerase enzymes involved in DNA replication, leading to DNA strand breaks[8].

- *Mitotic Inhibitors:*

Paclitaxel and docetaxel represent a group of agents that bind with microtubules, leading to interference with cell division and mitotic arrest[9].

Chemotherapy drugs achieve this by interrupting these cell processes, although they tend to be nonselective between the cancer and the normal cells. This non-specificity results

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in a number of side effects that include nausea, vomiting, alopecia, and bone marrow toxicity [10].

➢ *Recent Advances in Chemotherapy:*

Recent innovations in chemotherapy include the delivery of targeted drugs with lesser side effects. Nanotechnology has helped to improve the specificity of chemotherapy. Liposomal formulations and nanoparticles are capable of delivering chemotherapy drugs directly to tumors, thereby concentrating drugs at the site of action while reducing systemic toxicity [11].

One other advancement is the development of individualized chemotherapy regimens based on the molecular analysis of the tumor. Genomic sequencing and discovery of biomarkers have enabled one to individualize chemotherapy based on the genetic characterization of a person's tumor, thereby increasing the likelihood of treatment success [12].

Additionally, the identification of biomarkers such as HER2 in breast cancer and EGFR in lung cancer has enabled one to develop more specific chemotherapy agents that act on these changes[13].

➢ *Limitations of Chemotheraphy:*

Chemotherapy is currently the backbone of cancer treatment, but not flawless. The major limitations of chemotherapy are:

- *Drug Resistance:*

Cancer cells have the potential to develop resistance to chemotherapy via numerous mechanisms, including enhanced drug efflux, modification in drug metabolism, and alterations in drug targets [14].

Multidrug resistance (MDR) continues to be a major impediment in treating advanced cancers.

- *Toxicity:*

The chemotherapy's system effect is not just on cancer cells but also on quickly dividing normal tissues, hence leading to different toxicities such as immunosuppression, toxicity of organs, and gastrointestinal upset [15].

- *Less Effective in Some Cancers:*

Chemotherapy is quite ineffective in the management of some cancers such as pancreatic and glioblastoma since the survival rate of patients still remains low even after treatment [16].

III. IMMUNOTHERAPHY: MECHANISMS, ADVANCES AND LIMITATION

➢ *Mechanism Of Action:*

Immunotherapy exploits the immune system of the body to recognize and destroy cancer cells. The immune system employs various mechanisms to identify and attack cancer cells:

- *Immune Checkpoint Inhibitors:*

The immune system naturally has "brakes" so that it will not attack normal cells. Tumors can hijack these brakes, including the PD-1/PD-L1 and CTLA-4, to facilitate immune evasion. Medications such as nivolumab (OPDIVO) and pembrolizumab (Keytruda) short-circuit these brakes by disabling the immune system's brakes so that T cells may destroy cancer cells [17].

- *Monoclonal Antibodies*:

These are antibodies that have been designed to bind to specific antigens on the cancer cell surface. Examples are rituximab against CD20 in non-Hodgkin lymphoma and trastuzumab, or Herceptin, against HER2 in breast cancer. [18].

- *Chimeric Antigen Receptor T-cell (CAR T-cell) Therapy:*

CAR T-cell therapy involves treatment in which the patient's T cells are engineered to develop receptors against tumor antigens such that the immune cells can destroy cancer cells by attacking them directly. The methodology has proved extraordinarily successful in cancers of hematological origin such as acute lymphoblastic leukemia (ALL) and non-Hodgkin lymphoma [19].

- *Cancer Vaccines*:

These are specifically made to provoke the immune system to destroy cancer-specific antigens. The most well-established success story is the HPV vaccine against cervical cancer, and sipuleucel-T has been approved for prostate cancer. [20].

➢ *Recent Advancement in Immunotheraphy*

Immunotherapy discoveries that occurred recently changed the course of cancer treatment of conditions such as melanoma, lung cancer, and lymphoma tremendously. Following are a few examples:

Immune Checkpoint Inhibitors: Nivolumab and pembrolizumab are drugs that have revolutionized the treatment of different cancers such as melanoma, non-small cell lung cancer, and urothelial carcinoma. Patients' survival rates in these drug-resistant cancers have been escalated [21].

CAR T-cell Therapies: For instance, CAR T-cell therapies such as Kymriah (tisagenlecleucel) administered in B-cell ALL and Yescarta (axicabtagene ciloleucel) administered in large B-cell lymphoma have demonstrated long-term remission in refractory cancer patients [22].

Bispecific T-cell Engagers (BiTEs): BiTEs are engineered molecules to bring T cells close to cancer cells by promoting immune response. Such a drug blinatumomab may be beneficial in treating acute lymphoblastic leukemia [23].

➢ *Limitation of Immunotheraphy:*

Even though it has revolutionized cancer treatment with immense success, much is still restricted by immunotherapy Immune-Related Adverse Events (irAEs): Activation of the immune system is responsible for causing side effects that involve the immune system attacking healthy tissues, giving rise to disorders like colitis, hepatitis, and myocarditis [24].

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Limited Efficacy in Some Cancers: Immunotherapy works extremely well for some cancers but, in other cancers like pancreatic cancer, glioblastoma, and prostate cancer, has been employed with very limited effectiveness. The basis of this limited efficacy is a significant area of research [25].

Cost and Accessibility: The extremely high cost of immunotherapy, especially CAR T-cell therapies, also renders them inaccessible to the majority of patients, particularly those in low-resource settings [26].

IV. COMBINATION THERAPIES: THE FUTURE OF CANCER TREATMENT

❖ *Chemotherapy and Immunotherapy Combination:*

The association of chemotherapy and immunotherapy has several benefits. Chemotherapy may boost the effect of immunotherapy by:

➢ *Immune System Priming:*

Chemotherapy can promote shedding of tumor antigens and enhance invasion of immune cells into tumors, rendering the latter immunosensitive to immune checkpoint inhibitors [27].

➢ *Overcoming Resistance in Tumor:*

Immunotherapy can help surmount chemotherapy resistance by targeting the immune checkpoints which let cancer cells escape immune surveillance [28].

Number of clinical trials have proved that chemotherapies along with immunotherapies can be highly effective. In the case of non-small cell lung cancer, for example, a combination of chemotherapy and nivolumab resulted in increased overall survival as well as progression-free survival over chemotherapy alone [29].

A. Ongoing Clinical Trails and Emerging Therapies

Current clinical trials are investigating numerous combinations of chemotherapy, immunotherapy, and new agents. Numerous studies are working to determine which regimens work best for various types of cancer. Trials are also changing to address the necessity of identifying biomarkers that indicate which patients will be helped by combination treatments to allow for targeted treatment [30].

B. Emerging Strategies and Future Perspectives

As oncology becomes a rapidly evolving field, multiple innovative approaches are redefining the future of cancer care. Personalized treatment, AI-enabled platforms, novel vaccine platforms, and microbiome research are exploring new avenues in enhancing outcomes with reduced side effects.

➢ *Personalized Medicine*

Personalized medicine is the tailoring of cancer therapy according to the patient's and their tumor's individual genetic profile. The introduction of next-generation sequencing (NGS) and cutting-edge biomarker discovery has now enabled oncologists to pair patients with treatments that are more likely to benefit and less likely to harm them.

- *Genetic Profiling*:

Whole exome sequencing and liquid biopsy technologies allow for the identification of targeted mutations and gene changes (e.g., EGFR, BRCA1/2, KRAS), enabling the accurate choice of chemotherapy or drugs for targeted therapy.

- *Example Applications:*

In breast cancer, the indication of BRCA mutations can reflect eligibility for PARP inhibitors.
In lung cancer, EGFR mutations are used to predict response to tyrosine kinase inhibitors (TKIs) such as osimertinib.
Benefits:

Minimized trial-and-error in selection of therapy, better outcome, and less toxicity.

➢ *Artificial Intelligence (AI) in Oncology*

Artificial Intelligence (AI) is becoming more and more integrated into various aspects of cancer treatment, from diagnosis to planning treatment.

- *Predictive Analytics*:

AI algorithms are able to scan large data sets to forecast how patients will react to a particular treatment regimen based on their clinical and molecular profiles.

- *Drug Discovery:*

AI speeds up the identification of novel compounds with anticancer activity through the simulation of drug-target interactions and toxicity prediction.

- *Diagnostics and Imaging:*

Deep learning algorithms enhance radiology and pathology accuracy by detecting faint patterns in imaging and histopathological slides that might not be perceptible to the naked eye.

- *Clinical Decision Support*:

Clinicians are assisted by AI-driven systems in making informed decisions regarding the optimal treatment.

➢ *Neoantigen-Based Vaccines*

Neoantigens are cancer-specific proteins generated as a result of mutations in cancer cells that are not present in normal tissues and are therefore perfect targets for immune attack.

- *Process:*

Vaccines made based on a patient's unique neoantigen profile can trigger the immune system to recognize and destroy cancer cells without harming healthy tissues.

- *Personalized Treatment*:

Based on tumor biopsy samples, researchers can develop customized vaccines according to the neoantigen composition of each patient.

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- *Clinical Trials:*

Early-stage trials in melanoma and lung cancer have been encouraging, with enhanced T-cell infiltration and enhanced immune responses.

➢ *Microbiome and Cancer Therapy*

The human microbiome—particularly the gut microbiota—is important in modulating immune responses and potentially influencing the success of cancer treatments.

- *Effect on Immunotherapy:*

Research has indicated that the presence of specific bacterial species (e.g., Akkermansia muciniphila) in the gut increases the effectiveness of immune checkpoint inhibitors.

- *Modulation Strategies*:

Administration of probiotics and prebiotics to increase beneficial microbes.

Fecal microbiota transplantation (FMT) from responders to non-responders to immunotherapy has resulted in better treatment outcomes.

- *Future Implications:*

Personalized microbiome profiling can be utilized in combination with genomic profiling to inform therapy.

➢ *Oncolytic Virus Therapy*

Oncolytic viruses are naturally occurring or genetically modified viruses that selectively infect and kill cancer cells without injuring normal cells.

➢ *Mechanism of Action:*

Direct killing of tumor cells.

Release of tumor antigens that activate the immune system.

- *Synergy with Immunotherapy:*

Oncolytic viruses can make "cold" tumors (non-immunogenic) become "hot" tumors (immunogenic), enhancing the response to immune checkpoint inhibitors.

➢ *Approved Therapies:*

Alipogene laherparepvec (T-VEC) is approved in advanced melanoma.

- *Ongoing Research:*

Clinical trials are evaluating their place in glioblastoma, pancreatic, and colorectal cancers.

➢ *Equity in Cancer Care*

Even with scientific advances, access to new treatments is unequal across regions and populations, and thus the need to address healthcare disparities.

- *Barriers*:

High cost of new treatments such as CAR T-cell therapy.

Limited capacity for advanced diagnostics in low- and middle-income countries.

Underrepresentation of minority groups in clinical trials

- *.Solutions*:

Policies to lower drug prices and increase insurance coverage.

International cooperation and financing to fund cancer care in resource-constrained environments.

Research practices that are inclusive to guarantee data represent diverse populations.

➢ *Real-World Evidence (RWE*)

Real-world evidence is data obtained from everyday clinical practice instead of controlled clinical trials. It gives great insights into how treatments work across larger patient populations.

- *Significance of RWE*:

Detects infrequent or long-term side effects.

Evaluates efficacy in patients with comorbidities who might not be represented in trials.

Assists in sharpening treatment guidelines and payment policies.

- *Data Sources:*

Electronic health records (EHRs), patient registries, insurance claims, and wearable devices.

V. CONCLUSION

The field of cancer treatment has been transformed, and immunotherapy has brought hope to those who had very limited options before. Nevertheless, chemotherapy remains a component of cancer therapy since it is effective against certain cancers and is the basis for combination therapies. The next-generation cancer medicine is based on a union of these approaches, like novel therapies like CAR T-cell therapy and checkpoint inhibitors immunotherapy. The present research in next-generation cancer drugs includes the combination therapies and the biomarkers towards better patient outcomes in the next generations of cancer medicine. The face of cancer treatment is changing quickly with the addition of immunotherapy, chemotherapy, and new frontiers like personalized medicine, AI, microbiome modulation, and oncolytic virotherapy. These new technologies not only hold the potential for more effective and safer therapies but also bring us closer to really individualized cancer care. Further research, clinical trials, and access that is fair and equal will be needed to make these advances into better outcomes for all patients.

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