

Current advances in cancer treatment: A comprehensive review of therapeutic strategies and emerging innovations

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Abstract

Cancer stands as a pressing global health crisis, claiming one in every six lives across the world. The treatment of cancer has evolved into a remarkably intricate endeavour. In recent years, there have been significant advancements in the field of cancer treatment, alongside the longstanding methods of surgery, chemotherapy, and radiotherapy. In the realm of oncology, there has been a surge of innovative treatments, encompassing stem cell therapy, targeted therapy, ablation therapy, nanoparticles, natural antioxidants, radionics, chemo dynamic therapy, sonodynamic therapy, and ferroptosis-based therapy. Contemporary oncology is predominantly dedicated to the progression of cancer nanomedicines, with notable promise found in stem cell therapy, offering the potential to rejuvenate and mend afflicted tissues at both primary and metastatic cancer sites. Nanoparticles have ushered in new avenues for both diagnosis and treatment. Targeted therapy presents a groundbreaking strategy that hinders the proliferation and dissemination of particular cancer cells, while minimizing harm to healthy ones. Ablation therapy, characterized by its minimally invasive nature, enables the elimination of cancer using methods like controlled burning or freezing, eliminating the necessity for open surgery. In the ongoing pursuit of improved cancer therapies, numerous innovative technologies are currently undergoing clinical trials, and some have already gained approval. This review provides a comprehensive update on the recent advancements and breakthroughs in the realm of cancer treatment.

Keywords: Cancer; Antioxidants; Radionics; Chemotherapy; Nanoparticles.

1. Introduction

Cancer is characterized by the unregulated growth and rapid proliferation of cells, often accompanied by the potential for metastasis. [1] A neoplasm or tumour represents an accumulation of cells that have undergone unchecked expansion, which may manifest as a lump or mass, or even disperse throughout the body. [2-4] Cancer can be attributed to a multitude of external influences such as tobacco use, exposure to chemicals, radiation, and infectious agents, in addition to certain internal factors like genetic mutations, hormonal imbalances, immune-related conditions, and spontaneous mutations. The root cause of cancer is manifold, intricate, and not entirely elucidated. Numerous elements are recognized to elevate the likelihood of cancer, encompassing dietary choices, specific infections, sedentary lifestyles, obesity, and exposure to environmental pollutants.[5] These factors may collaborate in initiating or advancing the process of carcinogenesis within the human body, thereby establishing cancer as a prominent cause of mortality.

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Cancer is a highly intricate series of disease states that advance gradually, resulting in a broad loss of control over cell growth. For many decades, the available treatments for cancer patients were limited to individual approaches like surgery, radiation therapy, or chemotherapy. Our comprehension of the mechanisms involved in cancer therapy and how they might be successfully targeted, however, has significantly improved. [6-7] As a result of these developments, highly successful combinatorial techniques have been created, combining various targeted medicines with "traditional" chemotherapeutics like taxanes along with platinum compounds to provide a synergistic impact. In the quest to enhance survival rates and extend the lifespan of individuals with metastatic cancer, novel approaches, including drugs, biological agents, and immune-mediated treatments, are being explored. [8-9] These groundbreaking methods represent a paradigm shift in the treatment of neoplastic cancer, with their effectiveness hinging on the distinctive characteristics and pathways of various tumor types. Among these modalities, chemotherapy stands out as a highly effective and widely employed treatment, whether used in isolation or in conjunction with radiotherapy. Chemotherapy drugs primarily exert their impact by inducing genotoxicity, generating reactive oxygen species that significantly impair tumor cells. [10-13] Furthermore, hormonal treatments are a prevalent strategy for managing cancer malignancies, acting as cytostatic agents that hinder tumor progression by constraining hormonal growth factors through the modulation of the hypothalamic–pituitary–gonadal axis (HPGA), hormone receptor blockade, and suppression of adrenal steroid synthesis. This narrative review offers a thorough examination of state-of-the-art and pioneering cancer treatments, providing insights into emerging strategies under research that seek to address the constraints of traditional therapies. It also explores various avenues in cancer diagnosis and treatment, providing an assessment of their current use in clinical settings and emphasizing their potential as inventive anti-cancer solutions. [14-16]

2. Innovative methods and protocols for treating cancer

Within the realm of cancer treatment, drug resistance and delivery systems present the most significant challenges in achieving a cure and alleviating symptoms. Nonetheless, there are currently numerous approved treatment strategies and drugs available. [17] The effectiveness of conventional cancer treatments is often hindered by the unique pathology of tumors and the abnormal structure of tumor blood vessels.

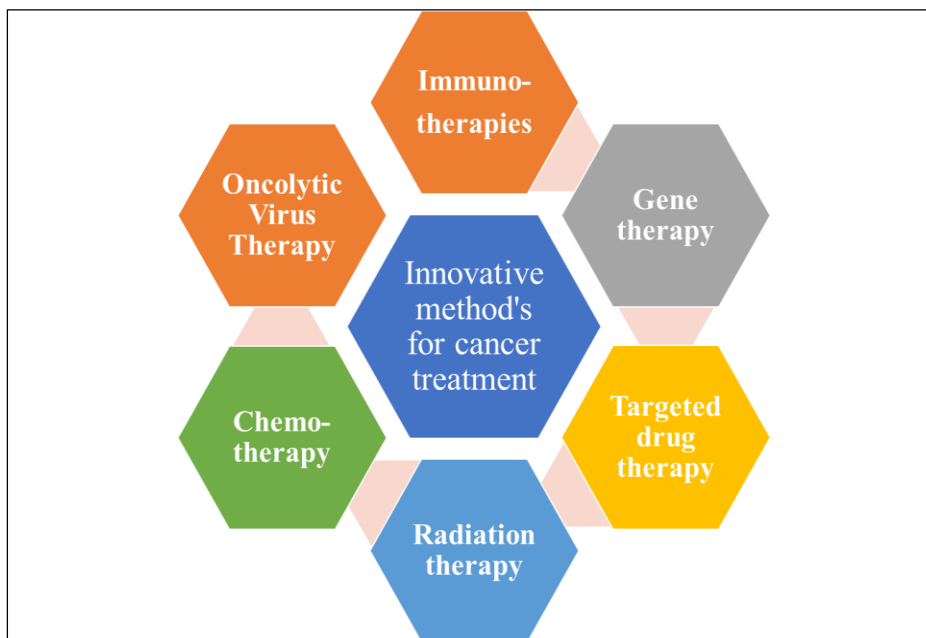


Figure 1 Innovative methods for treating cancer

In the following discussion, we will explore advanced and innovative cancer therapy approaches, examining both their advantages and the challenges they bring.[18]

- Immunotherapies
- Stem cells therapy
- Gene therapy
- Pluripotent stem cells
- Adult stem cells

- Targeted drug therapy
- Hyperthermia
- Radiation therapy/Radiotherapy
- Photodynamic Therapy
- Chemotherapy
- Hormone / Hormonal / Endocrine therapy
- Oncolytic Virus Therapy

2.1. Immunotherapies

Immunotherapy is a treatment method that harnesses your body's own immune system to combat cancer. This approach involves various types of immunotherapies tailored to specific cancer types. Cancer immunotherapy encompasses a range of techniques that utilize the patient's immune system to disrupt or eliminate cancer cells. The majority of these techniques focus on modifying or engineering T-cells, an essential kind of white blood cell in charge of warding off illnesses and infections. A variety of strategies are used by cancer cells to avoid T-cell recognition and eradication.[19] The goal of immunotherapy research is to strengthen the immune system so it can fight off these evasion tactics. It is significant to remember that these therapies are designed for specific patient groups. They may require the presence of particular genes to be effective, and patients might need to be in relatively good health to withstand the treatment. Additionally, the success of a treatment may be limited to specific cancer types due to the different ways the disease attacks healthy cells. It is worth noting that these treatments can carry severe side effects, which will be elaborated upon below. Furthermore, they can be expensive, especially when they involve personalized or genetically engineered treatments.

Immunotherapies are given in different ways, include:

- Oral: Pills or capsules.
- Intravenous (i.v): Directly into a vein.
- Intravesical: Directly into the bladder.
- Topical: A cream applied externally to the skin's surface in the initial stages of skin cancer.[20-23]

2.1.1. Types of Immunotherapies

Checkpoint Inhibitors

These medications are employed to enhance the immune system's capabilities for combating cancer. Rather than directly targeting tumor cells, they function by disrupting cancer cells' ability to evade immune system assaults. They essentially remove the inhibitory mechanisms that prevent T cells, a type of white blood cell integral to the immune system, from effectively engaging in the fight against cancer.

Adoptive Cell Transfer

In this procedure, T cells' natural ability to combat cancer is enhanced, and these cells are extracted from the tumor. Subsequently, the T cells are cultivated in significant quantities within a laboratory environment, a process that typically takes 2 to 8 weeks to complete.

Monoclonal Antibodies

These are synthetic proteins crafted in a laboratory with the capacity to bind to particular markers on cancer cells. They are also known as therapeutic antibodies. These antibodies tag cancer cells, facilitating their recognition and elimination by the immune system.[23-26].

2.2. Stem cells therapy

Stem cells, found in the bone marrow (BM), are undifferentiated cells capable of maturing into various types of body cells.[27] The utilization of stem cells is among the treatment alternatives for cancer, deemed both secure and efficient. Stem cell application remains in the experimental phase of clinical trials, with ongoing investigations into their potential for regenerating damaged tissues, such as the use of mesenchymal stem cells (MSCs) derived from sources like BM, fat tissues, and connective tissues. [28-30]

2.3. Gene therapy

Gene therapy involves inserting a healthy version of a defective gene into the genetic structure to treat a particular disorder. The inaugural application dates back to 1990, when a retroviral vector was harnessed to transport the adenosine deaminase (ADA) gene into T cells of patients suffering from severe combined immunodeficiency (SCID). [31-32] Presently, there are approximately 2,900 ongoing clinical trials in the realm of gene therapy, with two-thirds of them dedicated to cancer-related research. Various strategies, including the expression of proapoptotic and chemosensitizing genes, the expression of intact tumor-suppressor genes, the induction of genes capable of eliciting specific anti-tumor immune responses, and the targeted silencing of oncogenes, are being assessed for cancer gene therapy.[33-35]

The delivery of the Thymidine kinase (TK) gene has proven to be efficacious in activating the expression of the prodrug ganciclovir, leading to specific cytotoxic effects. Recently, clinical evaluation has been conducted on vectors carrying the p53 tumor suppressor gene. ONYX-015, when administered alone or in combination with chemotherapy, yielded a remarkable response rate in non-small cell lung cancer (NSCLC) patients. Furthermore, Gendicine, a recombinant adenovirus carrying the wild-type p53 gene, resulted in complete disease regression in head and neck squamous cell cancer when combined with radiotherapy, achieving a similar level of success.[36]

Gene therapy has encountered several challenges, such as the need to select the appropriate conditions and the optimal delivery method. Recognized limitations of this therapy include genome integration, reduced effectiveness in specific patient subsets, and susceptibility to immune system neutralization. In both basic research and medical applications, RNA interference (RNAi) has emerged as an efficient technology for achieving targeted gene silencing. The RNA-induced silencing complex (RISC) facilitates this process by cleaving messenger RNA (mRNA) and interfering with protein synthesis. Tailored small interfering RNAs (siRNAs) have the capacity to obstruct specific targets linked to processes like cell proliferation and metastatic invasion. Consequently, they have the potential to influence the intricate molecular mechanisms that trigger the formation of tumors. This approach relies on siRNA-mediated gene silencing of antiapoptotic proteins, transcription factors (e.g., the c-myc gene), or cancer-related mutated genes (e.g., K-RAS).[37-39]

2.4. Pluripotent stem cells

Embryonic stem cells (ESCs), derived from the uniform inner mass of an embryo, demonstrate remarkable flexibility in their ability to give rise to various cell types, with the exception of placental cells. A significant milestone in the field of cell biology was reached in 2006 with the discovery of Yamanaka factors, which enabled the creation of induced pluripotent stem cells (iPSCs) from somatic cells in culture.[40] This breakthrough circumvented ethical concerns associated with embryo destruction, as iPSCs and ESCs share equivalent characteristics.

Hematopoietic embryonic stem cells (hESCs) and iPSCs are presently being employed in the generation of effector T cells and natural killer (NK) cells, as well as in the preparation of anti-tumor vaccines.[41]

2.5. Adult stem cells

In tumor therapy, various groups of adult stem cells (ASCs) are frequently employed, including hematopoietic stem cells (HSCs), mesenchymal stem cells (MSCs), and neural stem cells (NSCs). HSCs, situated within the bone marrow, have the capability to produce all mature blood cells within the body. Presently, the only Food and Drug Administration (FDA) approved application is the infusion of cord blood-derived HSCs for the treatment of multiple myeloma and leukemia. [42] MSCs are distributed throughout numerous tissues and organs, fulfilling crucial roles in tissue repair and regeneration by differentiating into cell types such as adipocytes, chondrocytes etc. MSCs possess distinctive biological characteristics and are often utilized in conjunction with other approaches in the treatment of tumors. NSCs exhibit self-renewal capabilities and can generate new neurons and glial cells, making them valuable in the treatment of various types of tumors, including primary and metastatic type of breast cancer.[43]

2.6. Targeted drug therapy

Targeted cancer therapies, often referred to interchangeably as "molecularly targeted drugs," "molecularly targeted therapies," or "precision medicines," operate by disrupting the growth molecules responsible for inhibiting the development and metastasis of cancer. An atypical tumor's tumor microenvironment (TM) is crucial in determining tumor initiation and progression, consisting of various components like endothelial cells, pericytes, smooth muscle cells, fibroblasts, various inflammatory cells, dendritic cells, and cancer stem cells (CSCs). In this intricate setting, cells that form tissue maintenance (TM-forming cells) actively interact with cancerous cells via various signaling mechanisms and pathways. [44] promoting sustained cellular proliferation. Consequently, there is a significant focus on researching TM

conditions to develop effective targeting strategies for cancer therapy. Certain targeted therapies are often categorized as apoptosis-inducing drugs, as they specifically target components within the cell that regulate the survival or demise of cells. Examples of such agents include serine/threonine kinases, such as protein kinase B (PKB/Akt), which promotes cell survival. Inhibitors targeting this protein are currently in the preclinical phase. These substances effectively impede the formation of new blood vessels by tumors, thereby depriving them of the necessary blood supply for growth.

Furthermore, these agents hinder tumor progression by curtailing the blood supply to the tumor through the inhibition of angiogenic factors like vascular endothelial growth factor (VEGF) or its receptors. Research has demonstrated that the survival of patients with advanced colorectal carcinoma was extended by several months through the use of Avastin (bevacizumab) in combination with 5-fluorouracil-based chemotherapy. [45-46]

2.7. Hyperthermia

The concept of employing heat as a cancer treatment has been in existence for some time, although initial efforts yielded varying outcomes. Presently, advanced tools enable more precise heat delivery, and hyperthermia is under investigation as a potential therapeutic approach for numerous cancer types.

2.8. Radiation therapy/Radiotherapy

Radiotherapy technology in the United Kingdom has undergone significant advancements in the last two decades, thanks to its prioritization for investment and development within NHS England's Cancer Strategy. There has been a consistent evolution of conventional external X-ray radiotherapy. This progress is attributed to the integration of cutting-edge imaging and patient immobilization techniques, as well as enhanced machine flexibility, resulting in radiotherapy becoming a highly precise and efficacious treatment method. For instance, intensity-modulated radiotherapy employs lead "leaves" to precisely shape the radiation beam to conform to the tumor. Stereotactic ablative radiotherapy enables the delivery of radiation beams from multiple positions around the body. Notably, the UK now boasts two Magnetic Resonance Linear Accelerator (MR Linac) machines within NHS hospitals. These machines utilize MRI scanners to account for organ movement during and between treatment sessions. Assessing the clinical role and value of these machines is a pivotal focus of clinical research. [47-48]

In this therapy, high doses of radiation are employed to combat cancer by reducing tumor size, eliminating cancer cells, and impeding the growth of cancer cells through DNA damage. The damaged DNA cannot undergo repair, leading to cell death, which is subsequently removed by the body's natural processes. This treatment regimen typically spans several weeks or months and serves as a preventive measure against cancer recurrence. Radiopharmaceuticals, systemic radiation therapy drugs, are utilized to alleviate bone pain caused by cancer spread. External beam radiation is employed to address issues like pain, loss of bowel and bladder control, and breathing difficulties by reducing tumor size. Systemic radiation refers to a treatment that reaches tissues through the bloodstream throughout the body, typically administered through intravenous infusion or oral ingestion. Radiation therapy is frequently combined with various other cancer treatments, including chemotherapy, surgery, and immunotherapy, to improve treatment outcomes. For instance, it may be employed alongside surgical procedures. [49-50]

2.9. Photodynamic Therapy

Photodynamic therapy, abbreviated as PDT, is a therapeutic approach that utilizes specific drugs known as photosensitizing agents, in conjunction with light, to eradicate cancer cells. These drugs become effective only when they are activated or "switched on" by specific types of light.

2.10. Chemotherapy

Within this treatment modality, chemical substances are employed to combat cancer by inhibiting or decelerating the proliferation of cancer cells, inducing cancer cell death, or overcome the size of tumors that contribute to pain and other complications. However, it is important to note that chemotherapy may yield significant side effects. It can be administered as a standalone treatment or in combination with other cancer therapies, with the specific approach contingent upon the type of cancer.[51]

Example

- Neo-adjuvant chemotherapy- In this tumor, neoadjuvant chemotherapy is employed to reduce its size prior to surgical or radiation therapy.
- Adjuvant chemotherapy- In adjuvant chemotherapy, any remaining cancer cells are eradicated after the initial treatment.

Chemotherapy can be administered by -

- Oral: In the form of pills, liquids, or capsules.
- Intravenous (i.v): Delivered directly into the vein.
- Intramuscular (i.m): Injected into the muscle of the thigh, arm, or hip.
- Intrathecal: Introduced into the space between the layers of tissues covering the spinal cord and brain.
- Intraperitoneal (i.p): Injected into the peritoneal cavity, the region containing organs like the stomach, intestine, and liver.
- Intra-Arterial (i.a): Administered into an artery.
- Topical: Applied in the form of creams on the skin's surface. Mainly chemo is given as IV; a thin needle is placed in vein but it is given through ports or catheters and some time with pump.[52-53]

2.11. Hormone / Hormonal / Endocrine therapy

Hormone therapy is employed to address cancers such as prostate and breast cancer by impeding the growth of cancer cells driven by hormones. In the case of prostate cancer, regular PSA tests are conducted to monitor the therapy's efficacy. If the PSA level remains stable or decreases, it indicates that the therapy is effective. Conversely, an increase in PSA levels suggests that the therapy may not be working as intended. For breast cancer treated with hormone therapy, routine examinations encompass the neck, chest, underarm, and breast areas to ensure the therapy's effectiveness.

Hormone therapy can also be combined with other cancer treatments to enhance its overall impact. [54]

2.12. Oncolytic Virus Therapy

Oncolytic virus therapy harnesses naturally occurring or engineered viruses that have the unique ability to selectively replicate within and destroy cancer cells. While this area of research is still in its early stages, it has demonstrated efficacy primarily in specific cancer types. The most advanced viral therapy to date is talimogene laherparepvec (T-VEC), which involves a modified herpes simplex virus. T-VEC has gained approval from the National Institute for Health and Care Excellence (NICE) for certain melanoma (skin cancer) patients.

This virus operates by rupturing tumor cells, releasing antigens into the surrounding region, thus triggering an immune system response in the patient. In clinical trials, T-VEC has shown promise in enhancing the effectiveness of immune checkpoint inhibitors.[55]

3. Conclusion

Contemporary oncology methodologies primarily center on the advancement of cancer nanomedicines that are both safe and effective. Targeted medical treatments have significantly improved the distribution of newly developed or previously tested chemotherapy agents within the specific tissues requiring treatment. Additionally, various innovative approaches, such as immunotherapy, stem cell therapy, adult stem cell therapy, targeted drug therapy, offer new possibilities for individuals battling cancer. Gene therapy plays a crucial role by directly introducing foreign genes into benign tumors at the treatment site. Stem cells, with their distinct biological properties, hold promise for applications in regenerative medicine, serving as therapeutic carriers, facilitating drug targeting, and even assisting in the generation of immune cells. On the other hand, thermal ablation and magnetic hyperthermia represent promising alternatives to traditional surgical procedures for tumor growth management. Furthermore, advanced techniques like radiomics and various omics approaches provide valuable tools for managing and interpreting vast datasets from cancer patients, ultimately enhancing prognosis and treatment outcomes. Although significant development has been made, the field of oncology is still undergoing transformation, with the prospect of numerous additional inventive and personalized strategies on the horizon.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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