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REVIEW ARTICLE **OPEN ACCESS**

Current Advancements in Cancer Treatment – A Review

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ABSTRACT
Cancer is a disease of altered signaling and metabolism, causing uncontrolled division and survival of transformed cells. A host of molecules, factors, and conditions have been designated as underlying causes for the inception and progression of the disease. Cancer is a disease that results from the uncontrolled proliferation and growth of cells. Cancer is a disease that can be difficult to treat. However, new advances in the treatment of cancer can help people battle and even overcome this. It is important to be aware of the latest advances in treatment. Due to early detection methods, there is a decrease in death rates in many types of cancer. However, among the causes of death worldwide, cancer still ranks second after cardiovascular diseases. Therefore, cancer research has focused mainly on developing more effective treatments to reduce deaths from cancer. With a better understanding of the molecular mechanisms in cancer cells, advances in cancer treatment have evolved and changed. The main priority of research is to develop treatment modalities with the highest response rate and less side effects. In this context, immunotherapies have started a new era in cancer treatments. In this review, an overview of the future of next-generation treatment methods is presented by including the most preferred immunotherapy methods. Several new technologies are currently under research in clinical trials, and some of them have already been approved. Much progress has been made, but many others are likely to come soon, producing more and more ad hoc personalized therapies. Further development and refinement of drug delivery systems are essential for improving therapeutic outcomes. This review presented an update on recent advances and breakthroughs in cancer therapies.
Keywords: *Cancer, gene therapy, monoclonal antibodies, antimetabolites.*

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INTRODUCTION

Cancer, a multifaceted for disguised in various forms, casts a lengthy shadow on human health. It is a kaleidoscope of cancers, each resulting from a unique dance of genetic mutations and environmental circumstances. This assessment is not a dive into the dark, but rather a spotlight on the most recent advances in this complicated conflict. We set out on a journey to unravel the complicated network of cancer's DNA. Observe how seemingly innocuous cells succumb to the seduction song of mutations, transforming into dangerous malignancies. We have arrived at the zenith of precision medicine, when focused medicines, like microscopic darts, target specific weaknesses in these rogue cells. In the valleys of immunotherapy, we see the body's own immune system being activated and trained, turning it into a powerful army against the invader. Cancer's chameleon nature, its capacity to wear many different masks and adjust to treatment, requires constant vigilance. We must recognize the limits of our current arsenal even as we celebrate our small successes. In this review, we bridge the gap between research and clinical practice. We shift through the massive amount of data, finding promising trends and identifying critical eddies, setting the stage for future progress. The battle against cancer may be difficult, but in the pursuit of understanding, lies the ultimate reward: one day to emerge from the maze, the enigma unmasked, the enemy defeated (1,2).

Incidence and prevalence of different types of cancer

Cancer is a leading cause of death worldwide, accounting for nearly 10 million deaths in 2020, or nearly one in six deaths. The most common cancers are breast, lung, rectum, and prostate cancers. Around one third of deaths from cancer are due to tobacco use, high body mass index, alcohol consumption, low fruit and vegetable intake, and lack of physical activity. Cancer causing infections, such as human papillomavirus

(HPV) and hepatitis, are responsible for approximately 30% of cancer cases in low and lower-middle-income countries. Many cancers can be cured if detected early and treated effectively.
Estimated number of new cases in 2020, world, both sexes, all ages. The number of incident cases of cancer in India for the year 2022 was found to be 14,61,427. The incidence of cancer cases is estimated to increase by 12.8% in 2025 as compared to 2022. According to the Global Cancer Observatory (GLOBOCAN) estimates there were 19.3 million incidence cancer cases worldwide for the year 2020. India ranked 3rd after China and US of America. GLOBOCON predicted that cancer cases in India would increases to 2.8 million in 2040 from 2020. In India the incidence of cancer cases is likely to increase from 1.46 million in 2022 to 1.57 million in 2025.

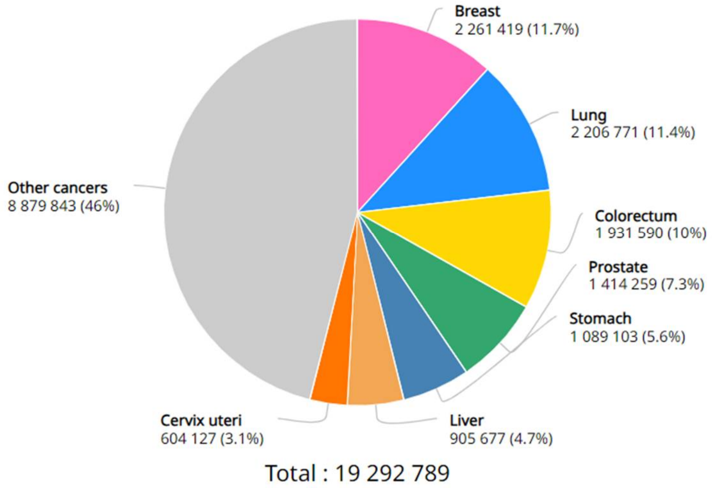

Figure 1: Cancer cases in the World

Cancer is a major public health problem worldwide and is the second leading cause of death in the United States. The corona virus disease 2019 (COVID-19) pandemic caused delays in the diagnosis and treatment of cancer because of health care setting closures, disruptions in employment and health insurance, and fear of COVID-19 exposure. Although the impact was largest during the COVID-19 peak in mid-2020, the provision of health care has not fully rebounded. In this article, we provide the estimated numbers of new cancer cases and deaths in 2023 in the United States. Breast, lung and bronchus, prostate, and colorectal cancers account for almost 50% of new cancer cases in the United States. Lung and bronchus, colorectal, pancreatic, and breast cancers are responsible for nearly 50% of all deaths. In 2023, roughly 2.0 million people will be diagnosed with cancer in the United States. An estimated 297,790 women and 2,800 men will be diagnosed with breast cancer, which makes it the most common cancer diagnosis. Prostate cancer is the leading cancer diagnosis among men and the second most common diagnosis overall with 288,300 expected cases. Lung cancer and bronchus cancer is the third most common cancer diagnosis with an estimated 238,340 new cases.

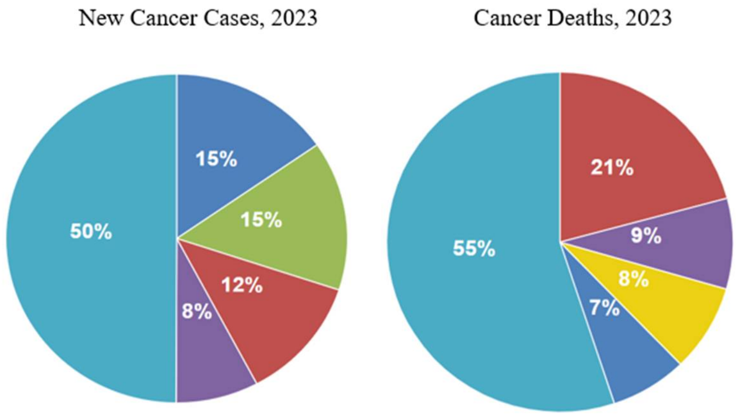

Figure 2: Cancer cases and deaths in United States

Table 1: Cancer cases and deaths in United States

Cancer type	New cases, 2023	% Of new cases	No. of deaths 2023	% Of no. deaths
Breast cancer	300,590	15	43,700	07
Prostate cancer	288,300	15	34,700	06
Lung and bronchus	238,340	12	127,070	21
Colon and rectum	153,020	08	52,550	09
Others	978,060	59	335,950	55

The number of cancer cases in the country is projected to go up from 14.6 lakh in 2022 to 15.7 lakh in 2025, according to the Indian Council of Medical Research-National Cancer Registry Program (ICMR-NCRP), the government informed Parliament on March 14. Under the initiative, those aged above 30 years are targeted for screening for three common cancers - oral, breast and cervical. Screening for these common cancers. The number of cancer cases in the country is projected to go up from 14.6 lakh in 2022 to 15.7 lakh in 2025, according to the Indian Council of Medical Research-National Cancer Registry Programmer (ICMR-NCRP) (3-6).

Table 2: The most common cancer sites in United States

S. No.	Cancer Type	Male	Female
1	Breast cancer	2800	297,790
2	Prostate cancer	288,300	0
3	Lung& bronchus	117,550	120,790
4	Colorectal	81,860	71,160
5	Melanoma of the skin	58,120	39,490
6	Urinary bladder	62.420	19,870
7	Non-Hodgkin lymphoma	44,880	35,670
8	Kidney and renal pelvis	52,360	29,440
9	Uterus	0	66,200
10	Leukaemia	35,670	23,940
11	Pancreas	33.130	30,920
12	Thyroid	12,540	31,180
13	Stomach	15,930	10,570
14	Bone and joint	2,160	1,810
15	Oesophagus	17,030	4,530
16	Larynx	9,900	2,480
17	Ovary	0	19,710
18	Testis	9,190	0
19	Small intestine	6,580	5,490
20	Oral cavity and pharynx	39,290	15,250

Methods used for diagnosing and screening of cancer

Cancer is a disease in which one observes there is an uncontrollable growth of cells in a body and these develop into tumours as they can be both malignant and benign type of tumours and they encroach on the nearby tissues. It Is capable of wreaking havoc on millions of lives worldwide and has a compelling effect on the society. It is a second leading cause of death all over the world. The best hope one can have for curing a cancer frequently comes by diagnosing it at its earliest stages. However, the crucial thing to remember is that not all the diagnostic methods present an accurate result and that many cases may also go undiagnosed. As previously said, early diagnosis can have a better chance at curing cancer but point to be noted here is that early cancer detection cannot be accomplished by using a single diagnostic method. There are countless methods to diagnose various forms of cancer by performing them with one another to detect cancer in a body. Diagnostic testing entails numerous methods to determine the right type of tumour its location, stage, and the extension of it in the nearby tissues. Understanding the pathophysiology of oncology will help us more by educating on the cancer instances and their effects. It will also make the process of detecting cancer easier and more effective. Enhancing the quality of the pathophysiology of cancer is of immense importance, Given that the number of individuals receiving cancer diagnoses is steadily rising and that these diagnoses are made through pathologic analysis of tissue samples, diagnosis is crucial. The cancer incidence from 28 Population-Based Cancer Registries (PBCRs) for the years 2012–2016 was reported in the National Cancer Registry Programme Report 2020. This served as the foundation for estimating the incidence of cancer in India.The country's States and regions were assigned to PBCRs in order to better understand the epidemiology of cancer. The majority of research on the effectiveness of oncologic diagnosis focuses mostly on patient safety. The range of diagnostic mistakes in oncologic pathology is 1–15%, contingent on multiple circumstances. There are no major consequences resulting from these diagnostic errors although there will be repeated various diagnostic procedures which delays the detection of cancers. The pathology diagnosis serves as the basis for nearly all primary and many recurring cancer diagnoses. Here are some major diagnostic methods that are used to detect cancer. The diagnostic methods that are mentioned above are performed while taking appropriate measures and a working diagnostic could consist of several potential diagnoses or just one [Raman spectroscopy which has caught quite an attention] (6-9).

Medical history and physical examination

Generally, while examining doctor may ask about the patient's medical history, including any symptoms or previously diagnosed illnesses their age and any occurrence of any type of cancer in the genetic line of the patient. They also examine any physical changes that have been occurring in the patient's body as in changes in the skin colour changes in the BMI and may observe any organ enlargements on specific parts of your body or any occurrence of visible lumps that could be cancerous (1,10).

Laboratory imaging tests

A diagnostic imaging procedure enables medical professionals to view what is happening inside your body. Patient's body is led to be be exposed to energy patterns such as x rays, radioactive particles or magnetic fields and it develops an image of the body tissues according to these energy patterns. The images obtained show how your inside organs appear and work so that doctors can spot any changes that could be caused by illnesses like cancer. X Rays uses small amount of radiation to get an inside view of the body and detect tumours in the bone and other organs, MRI scans which uses magnetic field waves to project a detailed view of the body and helps in identifying tumours in the soft tissues and spinal cord brain etc. and another scan which is CT scan (computed tomography). Several X-ray images are combined in a CT scan to produce detailed cross-sectional images of the body. There are many other numerous imaging tests which are used widely like PET scan which employ a little amount of radioactive material to find regions of the body with higher metabolic activity and endoscopy which is a complex procedure which utilizes a thin flexible tube to which a camera is fixed and introduced into the body through the oesophagus and view the digestive tract and detect any tumours present in such hollow organs. Another popular type of scan that makes use of high frequency sound waves to provide images of the body's organs is the ultrasound (11-13).

Laboratory and blood tests

Laboratory tests as in biopsies, medical research has progressed in identifying numerous novel biopsy techniques. Biopsy is performed by removing a sample of tissue from your body and examined for the existence of tumour cells. Other biopsy methods as in anoscope, bronchoscopy etc. Lumbar puncture, procedure which widely used to detect tumours in brain and spinal cord by obtaining a sample of your cerebrospinal fluid. Blood tests are the most common tests that are simple to analyse and produce faster, more reliable findings. Blood tests that are frequently used: CBC's (complete blood count) this helps in measuring number of blood components, platelet count and if any abnormalities are found that can indicate presence of leukaemia tumour_markers are the specific kind of chemical substances which in response to cancer, cancer cells either create these markers or they get released into the blood stream. There are certain markers for a particular cancer like-LDH (lactate dehydrogenase) used for lymphoma, AFP (alpha-fetoprotein) used for liver cancer, and many others like PSA, CEA, CA-125, Beta hcG. Cell free DNA (cfDNA) and ctDNA: The bloodstream contains DNA fragments called cfDNA and ctDNA. They may have tumor-specific genetic changes or mutations in cancer patients. These changes can be found by liquid biopsy testing, which help with cancer diagnosis, monitoring, and treatment formulation (14).

Genetic testing

Typically, any modifications to DNA fragments are regarded as gene mutations, which tend to raise the chance of developing cancer. Both inherited genes and exposure to radioactive radiation have the potential to cause DNA abnormalities. CHEK2 is an example for inherited gene mutation which causes colorectal cancer.

Advanced genome testing

In this procedure cells which are cancerous are extracted out from a biopsy tissue sample and these cells are subjected to DNA sequencing in the lab to detect any characteristics which are identical to the mutations. In Genetic Testing the DNA from a little sample of your saliva or a hair follicle is used in genetic testing to look for any gene changes. One of the major breakthroughs in the medical research is Raman spectroscopy which is an individual diagnostic method which produces an accurate result without any conjugation with other diagnostic procedures. It is also non-expensive and can even be performed *in vivo*.

In this method RS projects the whole biochemical composition data of a sample in the form of a fingerprint and it entails minute details of the composition and any changes in it, can be easily detected during an onset of a disease.

Cancer biomarkers

A Cancer Biomarker is a trait and is characteristic that can be quantified to indicate cancer risk, cancer occurrence or patient prognosis. These traits maybe imaging based, cellular, molecular, or physiological in nature. miRNAs which are blood circulating can be used as potent cancer biomarkers that are helpful for Diagnosing cancer. These miRNAs can act as tumour suppressors or oncogenes and they are regarded as a molecular tool for non-invasive cancer diagnosis and prognosis since altered expression of these molecules has been linked to the incidence of numerous cancer illnesses, they act by attaching to the complementary promoter sequence and they can enhance the degradation of mRNA, prevent the access to it or stimulate the production of a gene. These small molecules regulate the protein coding genes in humans and any kind of observance of abnormality in the miRNAs expression has a significant influence on many different cellular processes that control human cancers, including cell division (metastasis), apoptosis (cell death) (2,15,16).

Screening tests

Screening tests are the type of testing which meant to find tumours early on, before any symptoms of cancer manifest. The use of screening tests has several downsides, including bleeding and tears in the colon lining. Additionally, some results may indicate the presence of cancer when there is not any, while other results may indicate the absence of cancer when there is a cancer risk.

Types of screening tests:

The Cervical cancer screening (HPV testing) and Pap smear screening, these two risks of cervical cancer in females, these tests are used to detect cervical cancer, in pap smear small number of cells are collected from the cervix of the patient and tested in the lab for any changes or indications of cancer. The purpose of HPV testing is to identify the presence of the human papilloma virus, which increases. It is done concurrently with the pap smear. Breast cancer is identified through mammography screening. This screening test has been shown to lower the death rate among female breast cancer patients. Low dose computed tomography (LDCT) lung screening is used to identify and prevent fatalities from lung cancer, which primarily affects heavy smokers. MCED, multi cancer early detection test. It is a liquid biopsy screening technique, a single test method used to identify 50 types of tumour cells. It compares a blood sample to the DNA and protein profiles of cancer cells in the lab, and if there is a match, the result is positive for cancer. Currently, for over 70% cancers screening tests are not yet found and this may lead to increase the risk of cancer and death rate. In such cases MCED test is found to be very useful. MCED tests is not yet FDA approved screening test but though some researchers are developing these tests and are hopeful for an approval from FDA. It was determined that 14,61,427 incident cases of cancer would occur in India in 2022. In India, around one in nine individuals will face cancer at some point in their lives. The most common cancers in men and women, respectively, were lung and breast cancers. According to the Global Cancer Observatory (GLOBOCAN) estimation, people in India affected by oral cancer are of highest range in statistics compared to the other cancer types like cervical cancer which is next in line to oral cancer, then lung cancer exhibiting similar range to cervical cancer and the least in the chart is Breast cancer of which 1 in every 8 women is getting effected by it. Cancer screening in India typically costs between Rs. 5999 and Rs. 30,000. However, costs may range amongst hospitals in various cities. The most effective screening recommendations differ from cancer to malignancy, for several different malignant and benign tumours, further screening procedures are still being investigated and developed (17,18).

Treatment options for cancer

Cancer is a prevailing disease which is currently does not have any effective treatment to prevent and cure the cancer but there are some advances that will help to treat cancer and there are some researches going using new age technology to prevent the cancer. Below given are the detail description of the current treatments and new research going to treat cancer.

Chemotherapy:

Chemotherapy plays a significant role in treatment of cancer. It involves several chemotherapeutic agents which are classified into number of classes based on how they work, which includes antimetabolites, topoisomerase inhibitors, alkylating agents, mitotic spindle inhibitors. The main aim of chemotherapeutic agents is to impair the DNA and supress cellular mechanism of tumour cells. The main target of alkylating agents is DNA base guanine. They cause alkylation of guanine resulting in mislaid DNA base which inhibits separation of strands during synthesis of genetic material carrier. Antimetabolites suppress few enzymes involved in synthesis of DNA or RNA like DNA polymerase, dihydrofolate reductase and ribonucleotide reductase which hinders the DNA formation. Antimetabolites include pyrimidine antagonist (gemcitabine), purine antagonist (fludarabine), and ribonucleotide reductase inhibitor (hydroxy urea). The DNA formation can be impaired by Topoisomerase-1 inhibitor (topotecan) and topoisomerase-2 inhibitor (etoposide) which antagonises topoisomerase and inhibit DNA replication. Mitotic spindle inhibitors show their action by retarding microtubules of mitotic spindles during telophase of cell cycle which promotes apoptosis. Mitotic spindle inhibitors include vinca alkaloids (vinblastine, vincristine) and taxanes (docetaxel), enzymes such as L-asparaginase, disturb regular metabolism of cell by breaking down amino acid L-asparagine. By inhibition of rapid cell growth and protein synthesis, DNA synthesis and cell division is hindered. This action is shown by antibiotic, bleomycin. The challenges of chemotherapy include MDR (multi drug resistance). The neoplastic cells are developing resistance to chemotherapeutics. The resistance is created by inhibiting apoptosis, reduced DNA strand breaking, increased production of interleukins, reduced activity of tumour supressing gene, increased production of enzymes which cause gene magnification, increased activity of carcinogens which results in increased tumour cells amplification and their activity. MDR can be overcome by using combination therapies like multi specific inhibitors, by which sensitivity of tumour cells to drugs can be increased which increases effectiveness of chemotherapy in cancer treatment (19).

Immunotherapy:

Immunotherapy modifies immune system to fight against tumour cells in various locations. Tumours can be recognised and eliminated by immune cells. Immune cells participate in tumour monitoring and elimination by stimulating and utilising body's own tumour-specific immune response to defeat tumour escape. Cell immunotherapy has high rate of success in blood cancer, but the efficacy for solid tumour is not as good as anticipated because of variations inside solid tumours and exterior microenvironment. Adoptive Cellular Immunotherapy (ACI)- By using immunological effector cells that have been genetically engineered, malignant cells can be attacked. ACI is classified as two types- specific ACI and non-specific ACI. Immune cells of non-specific ACI ineffective in targeting in cancer cells and is employed in supplementary treatment. Immune cells of non-specific ACI includes natural killer cells, dendritic cells and macrophage activated cells. Specific ACI includes CD8+T cells and CD4+T cells. Specific ACI has high precision, less drug resistance, and minimal adverse reactions. Specific ACI can be used in severe cases (20,21).

Chimeric antigen receptor T-cell (CAR-T) immunotherapy:

Chimeric antigen receptor T-cell immunotherapy, or CAR-T, is an effective kind of adoptive cell treatment. To accomplish tumour-specific death, it primarily yields the patient's body T cells by leukocyte reduction techniques, genetically modifies them into surface CAR-T cells, and then conveys them to the patient's tumour. For malignancies expressing CD19 proteins, such as B-cell acute leukaemia and large B-cell lymphoma, the treatment offers a great recovery. NK Cell Therapy-NK cells are lethal endogenous immune cells which rapidly react to tumour development. The stimulation of NK cells is controlled and enhanced by activated cytokines like IL-2, IL-5 and antibody dependent cell-mediated cytotoxicity which enables NK cells to identify and eradicate tumour cells with an antibody coating. Cancer cells possess means of blocking NK cells to evade the immune system by increasing the levels of HLA-G and soluble activated NKG2D ligand, making it difficult for NK cells to attach to NKG2D ligand on tumours and allowing constant activation of NK cells close to tumours, which decreases degree of identification of tumour cells. The anti-tumour effect of NK cells can be accomplished by blocking NK cells inhibitory signalling pathway and activating NK cells activation pathway, that enables NK cells to travel tumour point and boosts anti-tumour effect and lowers adverse reaction (9,21).

Immune checkpoint inhibitors (ICIs):

The surface of T-cells has immune checkpoint which prevent overactivation of T-cells. During normal conditions inhibitory checkpoint protein avoid autoimmune disease. When confronted with a tumour, inhibitory checkpoint will block T-cells, limiting system's capacity to recognise and eradicate tumours. Employing ICIs allow stimulation of T-cells immunological response and restores immune system anti-cancer effect. Major ICIs are PD-1 ICI use to treat breast cancer and malignant melanoma and PD-L1 ICI use to treat Merkel cell carcinoma. The major drawback of immunotherapy is it is highly expensive, and usage of ICIs can result in autoimmune disorders (22).

Chemoimmunotherapy-immunotherapy in combination with chemotherapy:

Immunotherapy in combination with chemotherapy has shown high-rate success in phase- 3 clinical trials for several benign tumours such as lung cancer, oesophageal cancer, breast cancer and pancreatic cancer. Chemoimmunotherapy mechanism include lymphopenia, reduction in regulatory T-cells and increase in proliferation of effector T-cells, Anti-angiogenesis, reduction in targeted myeloid immunosuppressive cells and immunogenetic tumour cell death.

Tumour debulking:

Immune reactions are blocked by immunosuppressive agents which are produced by tumour cells. Debulking of cancer cells (combination of surgery and immunotherapy or chemotherapy) enhances anti-tumour effect. By debulking only few tumour cells are left, which becomes easy for immune system to attack them and escape from immune system changes are reduced. Intensive chemotherapy may result in chemotherapy driven immunodepression (23).

Radiotherapy:

The use of radiotherapy is practically achieved by radiation-dose fractionation which identifies variations in features of tumours cells and normal tissues. With significant advancements in computer-aided, 3D treatment planning systems with high-accuracy technology that track organ mobility throughout distribution. These delivery enhancements have been coordinated with imaging improvements that support intensity-modulated radiation therapy (IMRT) strategies. IMRT allows for the targeting of specific doses to tumours and minimising dose and toxicity to nearby normal tissue. Fractionated radiotherapy consists of 5Rs-namely repair, redistribution/reassortment, repopulation, and reoxygenation and radiosensitivity. Typical daily low-dose fractions of around 2 Gy, administered five times per week, can produce results that are frequently better than radiation administered in less individual high doses. Biologically targeted agents radio sensitizes the tumours and produce cytotoxic effects, radiotherapy may be required to produce a substantial cell death. The cancer cells microenvironment can be changed by radiotherapy, supporting its use in combination therapies by activating body's immune system or enhance medication absorption. The potential of intensity-modulated radiation therapy (IMRT)and heavy-ion charged-particle therapy (CPT) to deliver radiation dosage more accurately to cancer locations will help localise and magnify any drug-radiotherapy synergy. The main target for radiotherapy is DNA repair pathway. Ionization radiation act as cytotoxic agent by causing irreparable lesions. Minor DNA damage can usually be fixed, but extensive lesions that occur within one to two loops of the strand are more difficult and result in DNA double-strand breaks (DSBs) that are fatal to cells. Poly (ADP-ribose) polymerase-1 (PARP-1) focusing on DNA repair. The primary idea behind the use of PARP inhibitors is that they prevent single strand break (SSB) repair, enhancing the quantity and complexity of lesions. Radiation treatment has a potential target on chromatin structure. Research shows that the chromatin design places significant restrictions on DNA damage and repair and that the chromatin arrangement varies when DSBs develop. Ionization radiations generate reactive oxygen radicals which condenses chromatin cause DNA damage and cell death (21,24).

Application of artificial intelligence in radiotherapy:

The radiotherapy (RT) is an intricate process that involves multiple time-consuming processes that affect the effectiveness of the treatment. By automating and streamlining procedures, artificial intelligence (AI) has been suggested as a technique to improve the standardisation, speed, and quality of these phases, ultimately resulting in more precise and safe radiation distribution.

Automatic segmentation and treatment planning were found to be the most often used AI aided applications, followed by synthetic computed tomography (SCT) generation, according to a recent assessment on the clinical usage of AI in radiotherapy. It also indicated a need for integrating AI into medical practise. Steps for integrating the latest innovations into clinical practise: commissioning the AI-based application, clinical implementation, daily use of the AI model and model- and case-specific quality assurance.

Application of radiosensitizers in radiotherapy:

Chemicals or pharmacological substances known as radiosensitizers can increase the lethal impact on cancer cells by destruction of DNA and generating free radicals. Radiosensitizers often have less impact on healthy cells. Radiosensitizers mode of action is mainly by DNA damage. They cause inhibition of intracellular thiols or other naturally occurring radioprotective agents, radiolysis of the radiosensitizer results in the formation of cytotoxic substances, reduce DNA repair, thymine analogues that can be incorporated into genetic material, produce electrophilic activity oxygen radicals that cause DNA damage.

Based on structure radiosensitizers are classified into-1-small molecules which include oxygen, oxygen mimics (nitrobenzene) and active components such curcumin. 2-Macromolecules which include proteins and peptides such antibodies like cetuximab, microRNA, short interfering RNA and oligonucleotides. 3-Nano materials which include noble nano particles like gold, silver and platinum and heavy nano particles like tantalum, tungsten, and bismuth.

Surgery:

Surgery is one of the main techniques in cancer treatment. For variety of solid malignancies, surgery is a common treatment approach. Although developments in resection methods, remnant tumour cells may be found in the resection areas or in the circulatory system after surgery, which will raise the chance of cancer metastasizing and returning. The rapidly emerging areas of both regional and systemic controlled drug delivery systems, using several dosage form and devices, such as implantable wafers, parentals/sprayable hydrogels and micro/nanoparticles are used to reoccurrence of tumours. Post operation a potential method to prevent regional and distal tumour reappearance in the resected area is by using implants for controlled drug delivery system. Surgery followed by chemotherapy or radiotherapy would be effective in preventing the reoccurrence of cancer (25).

Applications of metal nano particles in cancer treatment:

A particle with size range between 1 and 100 nm is referred to as a nanoparticle (NP). Their small size has large surface area which prolongs $t_{1/2}$ of polar drugs and proteins, increased solubility of polar drugs, and their capacity to regulate and localise drug release at tumour cells, NP-based drug delivery systems are more effective than standard drug delivery methods. Advances in early identification, testing, prognostics, and treatment approach are all driven by nanotechnology's capacity to identify a broad spectrum of molecular signals and biomarkers immediately. Metal nano particles have anticancer effect. They effect cancer cells by active or passive targeting of tumour, they damage the blood vessels of tumours and effect the receptors on tumours which enhance the tumour activity, cancer cells are harmed by gene silencing, drug delivery through nano particles results in increased t1/2 of drugs and delivered to desired location and NO are used in radiotherapy to target only tumours cells, leaving the normal cells unharmed. Various nano particles utilized in cancer treatment, noble metal-based nanoparticles-gold nanoparticles, silver nanoparticles, platinum nanoparticles and palladium nano particles and non-noble metal-based nanoparticles-magnetic nanoparticles, zinc oxide nanoparticles, copper nanoparticles, titanium nano particles and magnesium nano particles. Usage of nanoparticles is limited because they cause oxidative stress which results in toxicity, inflammation, and organ failure (26).

Hormone therapy:

Hormones are chemicals produced by the body that target specific sites in the body. Certain malignancies rely on hormones to proliferate. Hormone therapy locates and regulates hormones throughout the body. To locate and target the hormones, the medications used in hormone treatment move across the body. This distinguishes it from therapies that just target a particular part. Hormone therapy or endocrine therapy reduce or prevent the development of malignancies or reduce the signs and symptoms of tumour by halting the hormone's synthesis in the body, prevent the hormone from adhering to malignant cells, modify the hormone to prevent it from functioning normally. The main indication for hormone therapy is the treatment of specific types of prostates and breast cancer that develop in response to sex hormones. In breast cancer estrogen and progesterone bind to protein receptors, which causes breast cancer cells to proliferate. Endocrine therapy refers to treatments that prevent these hormones from binding to these receptors. To lower the chance of recurring cancer, hormone treatment is frequently given as adjuvant therapy following surgery. Drugs used in hormone therapy include Aromatase inhibitors such as anastrozole and letrozole, Selective estrogen receptor modulators (SERMs), such as tamoxifen and raloxifene and estrogen receptor antagonists, such as fulvestrant and toremifene. In prostate cancer androgens (testosterone and dihydrotestosterone) increase the proliferation of tumour cells. Hormone therapy lowers body's levels of androgens to prevent proliferation of prostate cancer cells. Drugs used in treatment of prostate cancer are anti-androgens such as apalutamide, enzalutamide, bicalutamide and flutamide, CYP17 inhibitors such as abiraterone and ketoconazole (27).

Biosimilar drugs:

A drug that closely resembles a biologic drug in terms of its structure as well as its operation is known as a biosimilar drug. Biologicals are a broad category of pharmaceuticals that include human blood and plasma-derived products, immunological modulators, growth factors, vaccinations, and monoclonal antibodies. In cancer treatment, biologics function in a variety of ways. They aid in boosting the body's immune system in identifying and eliminating cancerous cells, strike specific proteins on or within tumour cells to inhibit their development and assist the body in producing more blood cells to replenish those destroyed by prior cancer therapies. This indicates that the biologic and the biosimilar are regarded as equally safe and effective. FDA has officially authorized the use of biosimilars. Biosimilars for the biologic medicine-bevacizumab (Avastin) are Mvasi, Zirabev, Alymsys, Vegzelma and Avzivi. Biosimilars for the biologic medicine-rituximab (Rituxan) are Truxima and Ruxience. Biosimilars for the biologic medicine-pegfilgrastim (Neulasta) are Fulphila, Udenyca, Ziextenzo, Nyvepria, Fylnetra.

Angiogenesis inhibitor:

The process of forming new blood vessels is known as angiogenesis. Certain cancerous cells are highly adept in growing new arteries and veins, which boosts the tumour's circulation and promotes its fast growth. By delivering impulses and chemicals to surrounding tissue and triggering growth factors, malignant cells initiate the angiogenesis process, which enables the tumour to produce new blood vessels. Vascular endothelial growth factor (VEGF) is one such chemical.

To hinder the growth process of blood vessels scientists created medications known as angiogenesis inhibitors, sometimes referred to as anti-angiogenic treatment. These medications seek out and attach to VEGF molecules, preventing them from binding to and activating receptors of blood vessel endothelial cells. This is the mechanism of action of bevacizumab (Avastin®). Malignancies of the lung, kidney, breast, colon, and rectum are treated with it. Further angiogenesis blockers function by preventing signals from VEGF receptors from reaching blood vessel cells, which is a separate aspect of the process. The term "tyrosine kinase inhibitor" (TKI) refers to these medications. An instance of a tyrosine kinase inhibitor is sunitinib (Sutent®).In this way angiogenesis inhibitors decrease blood circulation to the tumours resulting in their degeneration. Angiogenesis inhibitors do not eliminate the cancer cells completely; hence these drugs are used in combination with chemotherapeutics (28).

New approaches for cancer treatment

Stem cell therapy

In the bone marrow (BM), stem cells are undifferentiated cells with the capacity to develop into any kind of tissue or organ. Stem cell therapy is a cancer therapy method that is effective and has less side effects. The stem cells are used to restore the damaged tissue. Pluripotent stem cells are used in production of anti-cancer vaccines. Adult stem cells present in bone marrow like hematopoietic stem cells and neural stem cells can produce all kinds of blood cells. This method is used to treat blood cancer.

Ablation cancer therapy

When surgery is not an option for tiny malignancies smaller than 3 cm in size, ablation is a therapy method that destroys tumours without eliminating them.

Thermal ablation:

This method destroys tumour tissue by applying intense heat or cold. The body gradually eliminates the tissue once it has been killed in its place.

Cryoablation:

Cryoablation destroys tumours cells by freezing it to fatal levels, followed by liquid formation. Most of the tumours in initial stages are treated by this method.

Gene therapy

To treat a disease condition, gene therapy involves inserting a healthy copy of a damaged gene into the genome. Cancer gene therapy approaches include targeted inactivation of cancer-causing genes, expression of proapoptotic and chemo sensitizing genes, expression of wild-type tumour suppressor genes, expression of genes which trigger certain anticancer immune responses, and activation of tumour suppressor genes (21,29,30).

CONCLUSION

In conclusion, Significant progress has been made in the diverse field of cancer research, leading to a more profound comprehension of the complex systems that control the onset and advancement of the disease. Innovative diagnostic and treatment techniques have been made possible by the combined efforts of scientists, physicians, and researchers, who have uncovered the intricate workings of genetic abnormalities and deciphered the intricate interactions between the immune system and the tumour microenvironment. While the field of precision medicine has made significant strides toward personalized therapy, there are still unresolved issues that require the scientific community to push the frontiers of understanding. Because cancer is inherently heterogeneous and may evolve to escape treatment efforts, it is imperative that interdisciplinary methods and continuous collaboration are employed. The application of cutting-edge technology like immunotherapy, genomics, and artificial intelligence promises to transform paradigms in cancer treatment and diagnostics as we negotiate its changing terrain. Moreover, the secret to enhancing patient outcomes and reducing the burden of this terrible illness is to prioritize early identification, customized medication, and targeted therapeutics. It is critical to recognize the holistic effects of cancer on patients, families, and society at large in the pursuit of a full understanding of the disease. A comprehensive approach to cancer care goes beyond the lab and clinic; it also includes public awareness campaigns, supportive care systems development, and handling the psychological elements of cancer. To put it in simple terms, the fight against cancer is a lifelong undertaking that requires constant commitment, teamwork, and creativity. As we consider the progress that has been accomplished thus far, the hope that cancer may one day not only be treated but also defeated inspires us all to work together to advance research, enhance patient care, and eventually change the perception of this powerful enemy.

REFERENCES

1. Siegel, Rebecca L et al. (2023). Cancer statistics. Ca Cancer J Clin. 73(1):17-48.
2. Crowley E, Di Nicolantonio F, Loupakis F, Bardelli A. (2013). Liquid biopsy: monitoring cancer-genetics in the blood. Nat Rev Clin Oncol. 10(8):472–484.
3. Ganesh K, Massagué J. (2021). Targeting metastatic cancer. Nat Med. 27:34–44.
4. Ishihara S, Otani K, Yasuda K, Nishikawa T, Tanaka J, Tanaka T, et al. (2015). Recent advances in robotic surgery for rectal cancer. Int J Clin Oncol. 20(4):633–640.

5. Okazaki T, Honjo T. (2007). PD-1 and PD-1 ligands: from discovery to clinical application. Int Immunol. 19(7):813–824.
6. Stephanie Byrne, Terry Boyle, Muktar Ahmed, Sang Hong Lee, Beben Benyamin, Elina Hyppönen. (2023). Lifestyle, genetic risk and incidence of cancer: a prospective cohort study of 13 cancer types. International Journal of Epidemiology. 52(3):817–826.
7. Naji A, Eitoku M, Favier B, et al. (2019). Biological functions of mesenchymal stem cells and clinical implications. Cell Mol Life Sci. 76(17):3323–3348.
8. Chhikara BS, Parang K. (2023). Global Cancer Statistics 2022: the trends projection analysis. Chemical Biology Letters. 10(1):451.
9. Ames BN, Gold LS, Willett WC. (1995). The causes and prevention of cancer. Proceedings of the National Academy of Sciences. 92(12):5258–5265.
10. Lewandowska, Anna Maria, et al. (2018). Environmental risk factors for cancer-review paper. Annals of Agricultural and Environmental Medicine. 26(1):1-7.
11. Wu, S., Zhu, W., Thompson, P., & Hannun, Y. A. (2018). Evaluating intrinsic and non-intrinsic cancer risk factors. Nature communications. 9(1):3490.
12. Zur Hausen, Harald. (2009). The search for infectious causes of human cancers: where and why. Virology. 392(1):1-10.
13. Mareel, M.; Leroy, A. (2003). Clinical, Cellular, and Molecular Aspects of Cancer Invasion. Physiological Reviews. 83(2):337–376.
14. Kalluri R. (2016). The biology and function of exosomes in cancer. J Clin Invest. 126(4):1208–1215.
15. Sung H, Ferlay J, Siegel RL, et al. (2021). Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 71:209–249.
16. Carter P. (2001). Improving the efficacy of antibody-based cancer therapies. Nat Rev Cancer. 1(2):118–129.
17. Fujii M, Shimokawa M, Date S, Takano AI, Matano M, Nanki K, et al. (2016). A colorectal tumor organoid library demonstrates progressive loss of niche factor requirements during tumorigenesis. Cell Stem Cell. 18(6):827–838.
18. Bu H, He D, He X, Wang K. (2019). Exosomes: Isolation, analysis, and applications in cancer detection and therapy. Chem Bio Chem. 20(4):451–461.
19. Valter K, Chen L, Kruspig B, et al. (2017). Contrasting effects of glutamine deprivation on apoptosis induced by conventionally used anticancer drugs. Biochim Biophys Acta Mol Cell Res; 1864(3):498–506.
20. Hoeben A, Joosten EAJ, van den Beuken-van Everdingen MHJ. (2021). Personalized Medicine: Recent Progress in Cancer Therapy. Cancers (Basel). 13:242.
21. Ando K, Hu Q, Kasagi Y, Oki E, Mori M. (2021). Recent developments in cancer research: Expectations for a new remedy. Ann Gastroenterol Surg. 5(4):419–426.
22. Pardoll DM. The blockade of immune checkpoints in cancer immunotherapy. *Nat Rev Cancer*. 2012;12(4):252–64.
23. Helmink BA, Khan MAW, Hermann A, Gopalakrishnan V, Wargo JA. (2019). The microbiome, cancer, and cancer therapy. *Nat Med*. 25(3):377–88.
24. Subhan MA, Torchilin VP. (2020). siRNA based drug design, quality, delivery and clinical translation. *Nanomedicine*; 29: 102239.
25. Korpan NN. (2007). A history of cryosurgery: its development and future. *J Am Coll Surg*; 204(2): 314–324.
26. Tanner JE. (2005). Designing antibodies for oncology. *Cancer Metastasis Rev*; 24(4): 585–598.
27. Crowley E, Di Nicolantonio F, Loupakis F, Bardelli A. (2013). Liquid biopsy: monitoring cancer-genetics in the blood. *Nat Rev Clin Oncol*. 10(8): 472–84.
28. Kalluri R. (2016). The biology and function of exosomes in cancer. *J Clin Invest*. 126(4): 1208–15.
29. Sato T, Clevers H. (2015). SnapShot: growing organoids from stem cells. *Cell*. 161(7): 1700–e1.
30. Moloudizargari M, Asghari MH, Abdollahi M. (2018). Modifying exosome release in cancer therapy: How can it help? *Pharmacol Res*. 134:246–256.

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