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Review Article

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New Therapeutic Compounds and Recent Advancements in Metastasis Cancer Treatment: A Review

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Abstract: Cancer is one of the major diseases with extremely high mortality, accounting for nearly 10 million deaths in 2020. Even though immense research has been done in this domain, a need to develop effective therapeutic strategies still exists. Chemotherapeutic drugs form a crucial part of anti-cancer therapy. The current study summarizes the traditional and recently developed novel therapeutic drugs for advanced and effective cancer treatment with this perspective. Advanced cancer treatments involve photodynamic therapy, targeted therapy, Stem cell therapy, Gene therapy, and hormonal therapy to mitigate Cancer. Photodynamic therapy is a special type of cancer treatment in which a person is injected with a unique light-sensitive drug that stays in the cancer cells for a long time to maintain normal health. Stem cell therapy is advanced for cancer therapy and more effective than other therapies. Stem cells are used to regenerate damaged tissues. About 2000 gene therapy clinical investigations are ongoing in cancer research and therapy. Mostly involved with chemo sensing genes and expression of wild-type tumor suppressor genes. The reported advanced treatments may have more effective and targeted treatments and prevention strategies than conventional treatments. We believe this review will provide the readers with the current state-of-the-art knowledge of anti-cancer drugs and open the horizon for further development of novel anti-cancer therapeutics.

Keywords: Cancer, Metastasis, Phytochemicals, Drugs, Gene Therapy, Stem Cell Therapy.

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1. INTRODUCTION

Cancer affects the skin and tissues that cover internal organs and glands' surface[1-6]. Carcinomas are the most prevalent cancer and often develop as solid tumours[7-11]. The best examples are prostatic carcinoma, colon, lung, and breast cancer[12-17]. Sarcoma is a type of cancer that affects tissues that support structural and connective elements in the muscles, nerves, lymph vessels, body fat, joints, blood vessels, tendons, and cartilage. Blood cancer, mostly known as Leukemia, is a serious type of cancer that begins in our body. Therefore, leukemia begins when normal blood cells mutate and grow uncontrolled manner[18-25]. Traditional cancer treatments include the use of certain chemotherapeutic agents, such as axitinib (Inlyta), which is primarily used to treat kidney cancer, and vandetanib (Caprelsa), which can be used for the treatment of medullary thyroid cancer[26-33] Thalidomide (Synovir) serves as a treatment for multiple myeloma[34] whereas, Bevacizumab (Avastin) is an optional drug used to treat colon, lung cancers, and kidney[35]. Everolimus (Afinitor, Zortress) is primarily used to treat kidney cancer, advanced breast cancer, pancreatic neuroendocrine tumors (PNET), and a unique type of benign tumor of the brain, the subependymal giant cell stellate cell tumor [36] while Ramucirumab (Cyramza) is an excellent advanced treatment for gastric cancer, adenocarcinoma in the junction of gastroesophageal, colon cancer as well as non-small cell lung cancer [37].

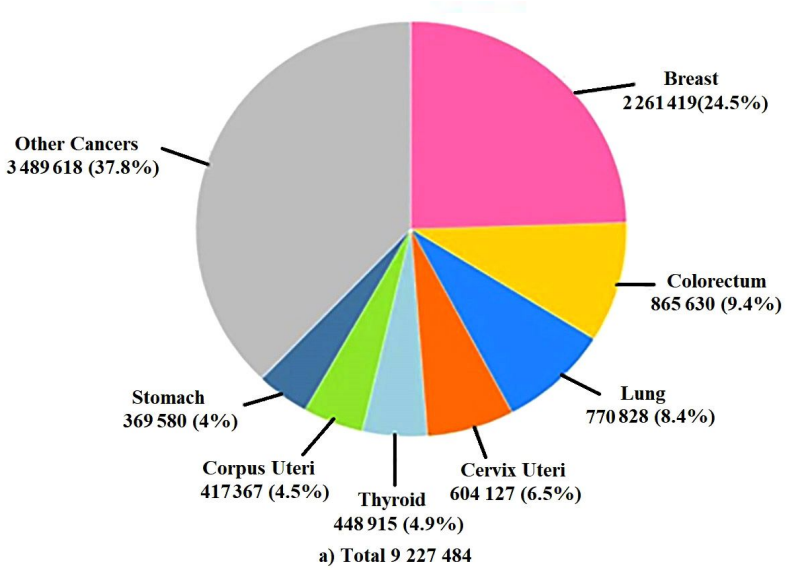

Fig 1: Estimated Number of New Cases in 2020, worldwide, Females, all ages[90]

Figure 1 shows that Cancer is a leading cause of death worldwide, accounting for nearly 10 million deaths in 2020[90]. It is estimated that breast cancer cases are 2 261 419, which means 24.5% of cases in all ages of females across the globe. The colorectum cases were estimated at 865 630, which means 9.4%; lung cancer cases were estimated at 770 828, 8.4%; Cervix uteri cases about 604 127, 6.5%. Thyroid cancer cases about 448 915, which means 4.9%; Corpus Uteri cases about 417 367, which means 4.5%, stomach cancer cases about 369 580, which means 4% and other cancer cases estimated the 3 489 618 means about 38% in all ages of female populations across the world wide.

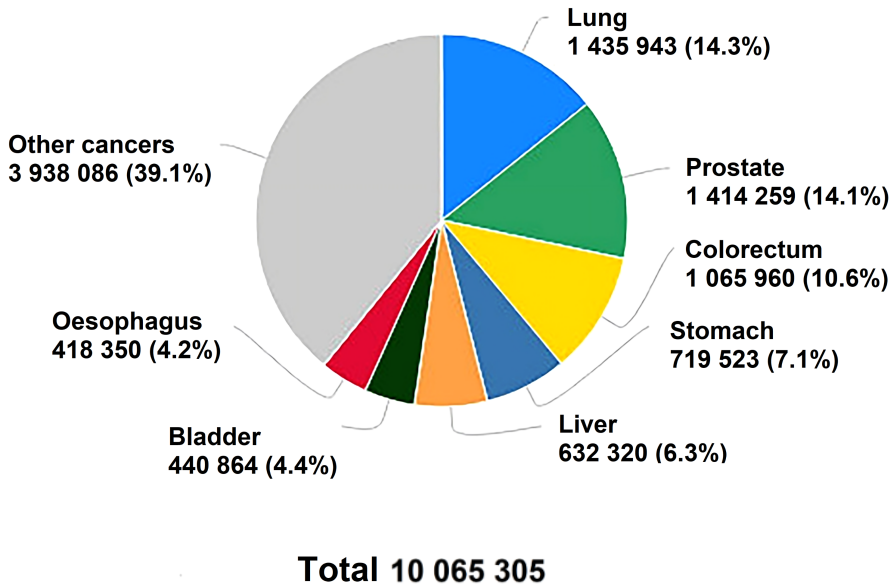

Fig 2: Estimated Number of New Cases in 2020, worldwide, Males, all ages[90]

Figure 2 shows that Cancer is a leading cause of death worldwide, accounting for nearly 10 million deaths in 2020[90]. It is estimated that lung cancer cases are about 14.3% in all ages of males across the globe. Stomach cases were estimated at 7.1%, Liver cancer cases were estimated at 6.3%, bladder cancer cases were about 4.4%, Oesophagus cancer cases were about 4.2%, and other cancer cases were estimated at 39% in all ages of male populations worldwide. Both the above figures thereby indicate that the most affected population with various types of cancers are related to males than females. Advanced treatments for cancer include Photodynamic therapy, a special type of cancer treatment in which a person is injected with a unique light-sensitive drug that stays in the cancer cells for a long time to maintain normal health. The cells somehow convert the drug into an active compound that affects cancer cells. This treatment leads to necrosis of cancer cells and blocks the early growth of cancer cells in the stomach and colon[37]. Another important treatment option includes targeted drug therapy to stop the growth and spread of cancer and thereby inactivate cancer cells. Recent studies reported that Targeted drug therapy worked in many ways to stop the causes that lead to uncontrolled cell growth, inhibit proliferation, and further kill the cancer cells directly [38]. Hormone therapy can be used alone or in the presence of drugs, restricting natural hormone interaction with cells. This help to reduce cancer cell growth [39]. Therefore, it helps to treat cancers caused due to hormones in the case of breast, ovarian, and prostate. Many affected cells from circulating tumor cells (CTCs) release other biomarkers into the bloodstream during cancer. CTC analysis allows taking a liquid biopsy from a patient's blood to predict and monitor treatment response and tumor recurrence. This treatment can be used to treat or eliminate the tumor more accurately. Another major advance in traditional cancer treatment is CAR-T cell therapy[40], the process of remodeling the patient's immune cells to attack cancer, a major success in immunotherapy[41]. The Food and Drug Administration has already approved this treatment for blood cancer, and there are great expectations for treating solid tumors with the help of biological agents. For example, monoclonal antibodies such as Tritely are used against metastatic triple-negative breast cancer. It is now possible to introduce gold nanoparticles into the bloodstream of cancer patients[42]. These nanoparticles accumulate in the tumor, especially because the tumor has leaks of blood vessels. When this region is exposed to near-infrared light, gold nanoparticles present inside the region get heated, resulting in the death of cancer cells [42]. Protein kinase dysregulation is associated with many cancers, and this protein is the target of several anti-cancer drugs. Drugs such as Rozlytrek [43] (entreating) and Tabrecta [44] (lapatinib) treat metastatic non-small cell lung cancer. The advantages and disadvantages of CAR T- Cell therapy are as follows: [40-44]

Advantages of CAR T-cell therapy

- The short treatment time needed about two weeks of inpatient care.
- Patients have a much more rapid recovery than chemotherapy treatment.
- It replaces many types of transplants.
- It is approved for the treatment of patients by the FDA.

Disadvantages of CAR T-cell therapy

- Neurologic toxicity
- Tumor lysis syndrome (TLS)

The study thereby aims to provide the readers with current state-of-the-art knowledge of anti-cancer drugs and open the horizon for further development of novel anti-cancer therapeutics. Thus the study's main objectives are to summarize the cancer types, new drug targets, new therapies, and advanced treatments for cancer. The current study is divided into four sections. The first and second sections discuss the types of cancers and the specific type of tumor markers. Further, the third and four sections deals with new drug targets, novel therapies, and recent advancements in cancer research.

2. CANCER TYPES

2.1 Carcinoma and Sarcoma

Carcinoma develops or forms primarily in the tissue lying on the skin, internal organs, and glands [45]. These cancers usually form by cell aggregations that lead to solid tumors in the body. Carcinoma in squamous cells, which are the structural unit of many organs, just below the outer surface of the skin[46]. Transitional epithelial cancer is cancer-formed transitional epithelium or urothelium, which is found primarily in the bladder, ureter, and part of the lining of the kidney [47]. Sarcoma is a cancer that begins in osteocytes and soft tissues such as fat, muscle, lymph vessels, blood vessels, and fibrous tissue [48]. Osteosarcoma is the most common bone cancer, like leiomyosarcoma, liposarcoma, and malignant fibrous histiocytoma. Leukaemia which is begins in the bone marrow. This type of cancer is where normal red blood cells mutate and turn into uncontrolled white blood cells in the site of bone marrow at an uncontrolled rate [49].

Table 1. Types of Cancer[45-53]

S. No	Cancer Types	Characteristics	Specific Categories
1	Carcinoma	Mainly occurs on the Skin/Tissue	Adenocarcinoma-in Epithelial Cells
		Covering the Internal Organs	Squamous Cell Carcinoma- in Squamous Cells
		Covering the Internal Glands	Transitional Cell Carcinoma-lining around the Uterus/Kidney
2	Sarcoma	Sarcomas-form in Bone and Soft Tissues	Osteosarcoma-Most Common
3	Leukemia	Occurs in Bone Marrow	It consists of mainly 4 types of Leukemia
4	Lymphoma	Mainly occurs in the Lymphocytes (T/B cells)	Hodgkin Lymphoma - Abnormal Lymphocytes from B cells.
			Non-Hodgkin lymphoma is derived from Tcell and Bcells
5	Multiple	Plasma Cells are where it starts.	Myeloma of the plasma cells and Kahler disease

	Myeloma		
6	Melanoma	It starts in the precursor cells of melanocytes.	It forms on the skin & other Pigmented Tissues

2.2 Leukaemia and Lymphoma

Table 1 illustrates the various cancers categorized according to the harm it causes such as acute myelogenous leukemia, acute lymphocytic leukemia, chronic myelogenous leukemia, and chronic lymphocytic leukemia [49]. Lymphoma begins primarily in lymphocytes (T cells or B cells) and functions as white blood cells that fight the disease. Therefore, this type of cancer occurs when abnormal lymphocytes suddenly form in lymph nodes and vessels [50]. For example, People with Hodgkin lymphoma have aberrant lymphocytes. This Hodgkin's broad category of malignancies has lymphocytes as its primary development site. Cancer can develop from B or T cells and spread quickly or slowly [51].

2.3 Multiple myeloma and Melanoma

It is a type of cancer that starts in plasma cells, an additional type of immune cells that further spreads to the bone marrow that then accumulates only the plasma cells with abnormal growth known as myeloma cells, forming tumors throughout the body[52]. Melanoma is a cancer that begins in cells that become melanocytes, a special cell synthesizing melanin[53].

2.4 Specific Type of Tumour Markers

Alpha-fetoprotein (AFP), a protein present in germ cell cancer and liver, assists in diagnosing liver cancer and thereby monitors its response to germ cell tumor treatment [54]. To treat multiple myeloma, chronic lymphocytic leukemia, and certain lymphomas, beta-2-microglobulin (B2M) aids in prognosis determination whereas Human chorionic gonadotropin beta (beta-hCG) helps to assess the prognostic stage and treatment of choriocarcinoma, germ cell tumors, bladder cancer, and kidney or uterine cancers [55].

Table 2. Specific Type of Tumour Markers[54-58]

S.NO	The specific type of Tumour Markers	Associated with a specific type of Cancer	Application
1	Alpha-fetoprotein (AFP)	Germ cell tumors and liver cirrhosis	The determination as well as treat tumors
2	Beta-2-microglobulin (B2M)	Leukemia and multiple myeloma are both chronic diseases.	Determine Prognosis and treatment
3	Human chorionic gonadotropin beta (Beta-hCG)	Germ cell and choriocarcinoma tumors	Assess stage, Prognosis and allow treatment
4	Bladder Tumor Antigen (BTA)	Bladder/Kidney/Ureter Cancer	Cytology & cystoscopy
5	BCR-ABL fusion gene (Philadelphia chromosome)	Chronic Myeloid Leukemia, Acute Lymphoblastic & Myelogenous Leukemia	Confirm diagnosis, Treatment and monitor disease status
6	CD117	Acute myeloid leukemia, mast cell disease, mucosal melanoma, and gastrointestinal stromal tumor	Diagnosis and to help determine treatment
7	CA-125	Ovarian Cancer	Diagnosis & Assessment of Treatment
8	CD30	Classic Hodgkin Lymphoma & B-cell T-cell Lymphomas	Determine Treatment
9	CD33	Acute Myeloid Leukemia	Precise Treatment

Table 2 illustrates the specific types of tumor markers. For example, the BCR-ABL fusion gene on Philadelphia chromosome, which is primarily involved in acute lymphoblastic leukemia, chronic and myelogenous leukaemia[56], and acute myelogenous leukemia, confirms the diagnosis, predicts the response to targeted therapies, which is also a condition that helps determine treatment and monitors the disease. CD117 is useful in diagnosing and treating gastrointestinal stromal tumors, mucosal melanoma, acute myeloid leukemia, and mastocytosis[57]. CD30 primarily helps determine treatments for classic Hodgkin lymphoma, B-cell, and T-cell lymphoma [58].

2.5 Conventional Chemotherapy Drugs

Axitinib (Inlyta) is primarily used to treat kidney cancer[59]. Medullary thyroid carcinoma is treated with vedettetanib (Caprelsa). Multiple myeloma patients can receive therapy with thalidomide (Sinovir)[60]. Treatment options for colon, kidney, and lung cancer involve the use of bevacizumab (Avastin)[61]. Everolimus (Afinitor, Zortress) is generally used to treat pancreatic neuroendocrine tumors (PNET)[62], advanced breast cancer, kidney cancer, and the uncommon benign brain tumor subependymal giant cell astrocytoma. One of the good therapy options for advanced gastric cancer is ramucirumab (Cyramza). The gastroesophageal junction's adenocarcinoma [63] cancer mainly occurs where the esophagus and stomach meet as well as include non-small cell lung cancer and colon cancer. Consequently, the treatment of advanced soft tissue sarcoma and kidney carcinoma is advised for the use of pazopanib (Votrient).

Table 3. Common Inhibitors of Cancer: Conventional Chemotherapy Drugs[59-63]

S. No	Conventional Chemotherapy Drugs	Targeting of Specific Types of Cancer
1	Axitinib (Inlyta)	Kidney Cancer
2	Vandetanib (Caprelsa)	Medullary Thyroid Cancer
3	Thalidomide (Synovir &Thalomid)	treating multiple sclerosis Myeloma
4	Bevacizumab (Avastin)	lung, kidney, and colorectal cancers
5	Everolimus (Afinitor & Zortress)	Pancreatic neuroendocrine tumors, advanced breast cancer, and kidney cancer
6	Ramucirumab (Cyramza)	Advanced Stomach Cancer & Non-small cell Lung Cancers.
7	Pazopanib (Votrient)	Options for treating advanced soft tissue sarcoma and kidney cancer

Table 3 illustrates the common inhibitors used in the treatment of cancers. Treatment options for colon, kidney, and lung cancer mainly involve the use of bevacizumab. Everolimus was generally used to treat pancreatic neuroendocrine tumors, advanced breast cancer, kidney cancer, and the uncommon benign brain tumor and subependymal giant cell astrocytoma. One of the good therapy options for advanced gastric cancer is ramucirumab which is mainly used to treat the gastroesophageal junction's adenocarcinoma, a[63]cancer that mainly occurs where the esophagus and stomach meet and also includes non-small cell lung cancer and colon cancer as well [61,62].

2.6 Novel Drugs Applicable for Cancer

2.6.1 Revlimid

A highly successful drug used in treating multiple myeloma to promote an immune response that slows tumor growth[64]. It is also used to treat the growth of myelodysplastic organs. Celgene is one of the best anti-cancer drugs to treat brain tumors [65].

2.6.2 Herceptin

A monoclonal antibody developed by Roche used primarily as a treatment for breast cancer, that is administered by intravascular injection, which mainly acts by stopping the growth of HER2 receptors on the surface of cancer cells [66]. Roche boasts a high survival rate and thereby provides patients with better access to this life-saving medicine.

2.6.3 Rituxan

Acts primarily as Roche monoclonal antibody that binds to B cells [67] and causes cell death (apoptosis). This reduces the usage of oxygen and nutrients to the tumor cells and thereby reduces the vasculogenic property of the cells. It thus treats various types of blood cancers, including non-Hodgkin's lymphoma and some leukaemia's[68].

Table 4. Common Inhibitors of Cancer: Novel drug applicable for Cancer[64-71]

S.No	Name of the Novel Drug	Mode of Application of Specific Drug	Manufacturing Company	Success Rate of the Drug
1	Revlimid	Slows down the tumor growth.	Celgene	Treatment of Brain Cancer
2	Herceptin	Stop the Growth of HER2 Receptors on Cancer Cells	Roche	High survival rate
3	Rituxan	Death of Cells (Apoptosis) by attaching B-cells	Roche	Various types of Blood Cancers
4	Zytiga	Block the Cytochrome p17 Enzyme	Johnson & Johnson	Treat Prostate Cancer
5	Ibrance	Block the Oestrogen	Pfizer	In combination with Hormone Therapy

Table 4 illustrates the most common Inhibitors of Cancer.
A novel drug applicable for Prostate Cancer is Zytiga which was Manufactured by Johnson & Johnson that blocks the enzyme cytochrome p17 and is used to treat prostate cancer whereas Ibrance, manufactured by Pfizer, blocks the action of estrogenic (female hormone), which stimulates tumor growth. This helps slow the progression of the disease in a way. The drug has thus been approved for advanced and secondary breast cancer cases and is given with hormone therapy [69,70].

2.7 Common Phytochemicals Used for Treating Cancer

Carotenoids like lutein, zeaxanthin, lycopene, and beta-carotene contain certain enzymes that bind to certain receptors present in cancer cells, thereby somehow blocking their further spread inside the body [72]. Apricots, sweet potatoes, winter squash, stewed tomatoes, broccoli, carrots, and leafy greens are rich sources of carotenoids and must be included in the diet regularly. Flavonoids, composed of anthocyanins, quercetin, and catechins, inhibit tumor growth by binding to specific B-cell receptors on the cell surface, causing cell death [73]. Citrus fruits such as apples, onions, soybeans, coffee, tea, lemons, and oranges that contain high amounts of flavonoids must be taken regularly. By inhibiting the development of tumors and lowering the synthesis of hormones linked to cancer, indole, and glucosinolates help lower the chance of developing cancer. They can be found in brussels sprouts, broccoli, collard greens, kale, and other vegetables [74]. Isoflavones prevent the development of tumors, which prevents the release of hormones that cause cancer [75].

Table 5. Common Phytochemicals Used for Treating Cancer [72-77]

S. No	Phytochemicals Useful for Specific Cancer	Mechanism of Action	Natural Source
1	Carotenoids	Certain Enzymes attach to Specific Receptors on Cancer Cells	Broccoli, Carrots, Tomatoes, Leafy Greens,
2	Flavonoids	Inhibit the Tumor Growth	Apples, Onions, Soybeans, Coffee, Citrus Fruits
3	Indoles and Glucosinolates	Prevent the Tumor Growth	Broccoli, Cabbage, Kale, Brussels-Sprouts.
4	Isoflavones	Inhibit the Tumor Growth	Soybean and other Soy Products
5	Polyphenols	Inhibit the Proliferation of Cancer Cells	Green tea, grapes, wine, berries
6	Alkaloids	Possess Anticancer Effects	Capsicum, Green Chilli, Turmeric

Table 5 represents the common phytochemicals used for treating cancer. Soybeans and other soy products also contain Isoflavones. Polyphenols such as ellagic acid and resveratrol inhibit multiple transcription factors and up-regulate p53, caspase, and Bax, but down-regulate surviving cyclin and Bcl-2. It acts on cancer cells and thereby causes necrosis of cancer cells [76]. They are usually present in green tea, berries, wine, grapes, apples, citrus fruits, peanuts, and whole grains. Polyphenols affect cancer growth of cells which along with some other transcription factors are found in green tea, grapes, wine, and berries. Table 5 lists the most common phytochemicals used to treat cancer [77].

2.8 New Drug Targets and Novel Therapeutic Agents

The genome and proteome sequences have made it easier to study the genetic mutants that lead to cancer at the molecular level. Structural cancer biology has been extensively used to study molecular mutagenesis but requires the identification of new therapeutic targets in cancer treatment.

Table 6. Overview of New Drug Targets for Cancer and The Novel Therapeutic Agents in the Treatment of Cancer[88,89]

S.No	New drug target	Novel therapeutic agent	Cancer type
1	Neutrophilic Tyrosine Receptor Kinase Gene	Latrcitinib, Entrecitinib	Ovarian
2	Anaplastic Lymphoma Kinase Gene	Certinib, Lorlatinib	Adenocarcinoma
3	Epithelial Growth Factor Receptor Gene	Erlotinib, Gesitinib	Non-Small-Cell Lung Cancer
4	Tubulin	BMS-XRP9885, BMS-XRP625	Brain cancer
5	Lectins	Irinotecan	Ovarian
6	Human Epidermal Growth Factor Receptor 2	Trastuzumabdruxtecan	Metastases Breast Cancer

Table 6 summarizes new drug targets of cancerous cells and their corresponding novel molecules. Enormous studies have been designed and developed to treat cancer cells with less damage to the host cells. However, novel therapeutic molecules are also required to treat cancer cells effectively to cope with the new targets of cancerous cells. Many studies recently proposed novel specific molecules as therapeutic agents that inhibit cancer cell growth, spread, and mitigation of abnormal cell progression[88,89].

2.9 Recent Advancements in Cancer Treatment

2.9.1 Freezing and Radiofrequency Ablation

Freezing involves inserting a thin rod-shaped needle (or freezing probe) into the skin and thereby pointing it at the region of the cancerous tumor [78]. Here, the gas is pumped to the cryoprobe to freeze the tissue. The tissue is then thawed for temperature control. The freeze-thaw process is repeated several times to kill cancer cells [79]. However, in radiofrequency ablation, a fine needle is inserted through an incision in the skin or cancerous tissue. In this technique, high-frequency energy waves first pass through the needle, heating the surrounding tissue and thus killing the nearby cells along with the cancer cells [80].

2.9.2 Hormone Therapy and Hyperthermia

Hormone therapy stops or blocks the body's natural hormones, primarily through surgery and medication. This surgery removes the organ synthesizing hormones, the ovaries, or tests [81]. These medicines are given as injections or tablets. Therefore, Hormone therapy is widely used to treat cancers caused due to hormones, such as prostate, breast, and ovarian cancer [82]. It thus uses heat energy to damage and kills cancer cells without affecting normal cells. Heat is then applied through an extracorporeal machine or a needle probe placed on the tumor [83]. It can also treat small areas of tissue tumors, organs, and limbs.

2.9.3 Photodynamic Therapy and Immune Therapy

Photodynamic therapy injects certain types of light-sensitive medications into the cells [84]. Compared to healthy cells, cancer cells are more resistant to this type of treatment. The medication is then transformed into a chemical that kills cancer cells by exposing them to light from a laser or other light source by medical professionals [85]. This treatment is used to attack tumors and precancerous growth, which thereby shrinks tumors that block the stomach, colon, or esophagus, as well as lymphatic vessels after surgery to reduce swelling and prevent the spread of tumor cells in the body. An approach of treating cancer relies on the immune

system's capacity to defend against infection that it causes (foreign reactions of the immune system). In the body or the lab, it employs the compounds that boost immunity, which makes the immune system more aggressively combat cancer[86].

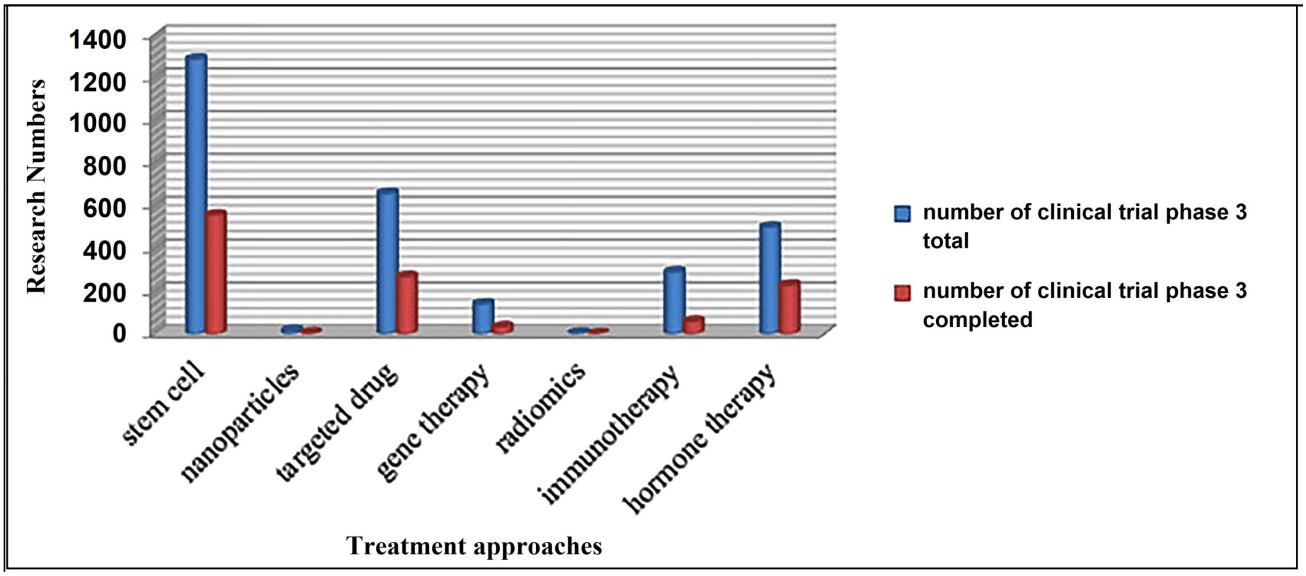

Fig 3: Present scenario of clinical trials on recent advancements in cancer therapy[88].

Figure 3 represents the Present scenario of clinical trials on recent advancements in cancer therapy. Freezing involves inserting a thin rod-shaped needle (or freezing probe) into the skin and pointing it at the cancerous tumor. In the case of radiofrequency ablation, a fine needle is inserted through an incision in the skin or cancerous tissue. Hormone therapy stops or blocks the body's natural hormones, primarily using surgery and medication. Photodynamic therapy injects certain types of light-sensitive medications where compared to healthy cells, cancer cells are more resistant to this type of treatment. Targeted therapy prevents metastasis and extensive growth. This thereby invalidates the cancer cells and prevents them from acting on and spreading to specific targets (molecules) in the surrounding cells.

2.10 Targeted Therapy and Stem Cell Therapy

Targeted therapy prevents metastasis and extensive growth. This invalidates the cancer cells and prevents them from acting on and spreading to specific targets (molecules) in the cancer cells. Therefore, targeted drug therapy works in a variety of ways that finally halt the process which causes extensive growth and metastasis of cancer cells, thereby leading them to die of natural causes or killing them directly[87]. These cells are undifferentiated and can be present in the Bone marrow. Stem cell therapy is an advanced form of cancer therapy and is more effective than other therapies. Stem cells are used to regenerate damaged tissues, but this therapy is currently under investigation [88].

Table 7. Recent Advancements in Cancer Treatment and Summary of Gene Therapies [78-88]

S.No	Recent Advancements	Efficiency of Treatment	Application
1	Cryoablation	Thin Needle (or Cryoprobe) inserted through the Skin towards the Cancer Tumor.	Kill the Cancer Cells with Cold
2	Radiofrequency ablation	High-Frequency Energy Waves	Kill the Cancer Cells by Heating through Electrical Energy
3	Hormonal Therapy	Drugs used to halt or manipulate of Body's Natural Hormones	Treatment of Cancers by Hormones
4	Hyperthermia	Kill the Cancer Cells by Heating	Treatment of Tumor
5	Photodynamic Therapy	The drug is directed toward Cancerous Cells in the Presence of Light	Destroy the Tumors and Precancerous Growth
6	Immunotherapy	Enhance the Body's ability to Fight Infection	Slow down the Growth of Cancer Cells
7	Targeted Drug Therapy	Drugs to Prevent the Proliferation of Cancer Cells	In necrosis, the Cancer Cells Directly
8	Advanced Stem Cell Therapy	Stem cells are used to regenerate damaged tissues.	Bone Cancers
9	Types of Various target agents	Monoclonal antibodies, small molecule inhibitors, Ablation cancer therapy	Cryoablation therapies are recently proposed for effective cancer treatment
10	New Gene Therapy	Around 2000 gene therapy clinical investigations are presently ongoing on cancer therapy	chemosensing genes and expression of wild-type tumor suppressor genes.

11	Oncolytic virotherapy (OV)	Naturally occurring or genetically modified viruses	Tumor immunotherapy
12	Gendicine	Non-replicative adenoviral vector	Neck and head squamous cell carcinoma
13	Rexin-G	Replication-incompetent retroviral vector	Metastatic cancers
14	Kymriah	CAR T cell-based gene	Relapsed B-cell acute lymphoblastic leukemia
15	Zalmoxis	Allogeneic hematopoietic stem cell transplantation (allo-HSCT)	Hematopoietic malignancies

Table 7 shows the recent advancements in cancer treatment and a summary of gene therapies. In cryoablation, a thin needle (or cryoprobe) is inserted through the skin towards the cancer tumor that kills the cancer cells due to cold. In radiofrequency ablation, high-frequency energy waves kill cancer cells by heating through electrical energy. Whereas, in hormonal therapy, drugs are used to halt or manipulate the body's natural hormones in treating cancers by hormones. Although, in photodynamic therapy, the drug is directed toward cancerous cells in the presence of light to destroy the tumors and precancerous growth, it is still under research to be used on a wide scale [84,85] while in targeted drug therapy, specific drugs are used to prevent the proliferation of cancer cells, particularly with the application of the necrosis of the cancer cells directly [87].

2.11 Current Clinical Trials

The most frequently used clinical trial databases, such as www.clinicalTrials.gov, mainly focus on cancer therapies. The database covers stem cell therapy, targeted therapy, advanced immunotherapy, and recently incorporated gene therapy and related data.

Table 8. Comparison of advantages and disadvantageous of new cancer therapies[88].

S.No	Treatment	Advantages	Disadvantages
1	Ablation therapy	Precise treatment	Needs skilled operator
2	Stem cell therapy	Safe and effective	Treatment not durable
3	Gene therapy	Targeted silencing of oncogenes and safety (RNAi)	Setup of doses and suitable conditions for controlled release (RNAi)
4	Targeted therapy	High specificity	Long-term side effects in question

Table 8 illustrates the comparison of the advantages and disadvantages of cancer-related therapies. In the case of current clinical trials, ablation therapy is used as a precise treatment but had the disadvantage of a need for a skilled operator. Stem cell therapy is thereby safe and more effective than ablation therapy, but the treatment is not durable. However, in Gene therapy, targeted silencing of oncogenes and safety (RNAi) is an advantage but the Setup of doses and suitable conditions for controlled release (RNAi). The Targeted therapy is thus highly specific towards cancer cells but there are still chances of Long-term side effects[88].

Table 9. Advanced therapy approaches and delivery systems[88,89].

S.No	Types of therapy	Delivery system	Example
1	Stem cell therapy	Nanoparticles	Hyaluronic acid (HA), Polyvinyl alcohol
2	Immune therapy	Nanoparticles, Scaffolds, Hydrogels	Antigen-TLR agonist fusion vaccines, Porous 3D scaffolds, Anti-PD-1 mAbs
3	Gene therapy	Viral gene delivery, non-viral gene delivery	Polysaccharides, Polyethylemine (PEI), Lipids, Naked DNA
4	Natural antioxidants	Nano delivery systems	Solid nanocrystals, Nanoemulsion, Nanoliposomes

Table 9 illustrates the Recent studies that reported advanced cancer treatments and their complementary approach to delivery systems with suitable examples.

Stem cell therapy is used by nanoparticles such as Hyaluronic acid (HA), Polyvinyl alcohol in cancer treatment. Several studies also suggested immunotherapy through nanoparticles, scaffolds, and hydrogels as delivery systems, such as Antigen-TLR agonist fusion vaccines, Porous 3D scaffolds, and Anti-PD-1 mAbs, respectively. Gene therapy can be done through Viral and non-viral gene delivery, including Polysaccharides, Polyethylene (PEI), Lipid, and Naked DNA molecules, respectively. Natural therapy using natural antioxidants nano delivery systems with the help of Solid nanocrystals, Nanoemulsion, and Nanoliposomes, respectively[88,89].

3. CONCLUSION

Recently, it is reported that novel therapeutic drugs in the treatment of cancer cells are Revlimid, Herceptin, Rituxan, and Vibrance. The most common phytochemicals reported in the treatment of cancer cells are Carotenoids, Flavonoids, Isoflavones, Indoles, and Glucosinolates. Conventional cancer treatment involves certain chemotherapy drugs, which may have side effects. Advanced treatments for cancer involve the use of photodynamic therapy, targeted therapy, and

hormonal therapy in the mitigation of malignant metastasis. The outcome of cancer research is crucial to improve the prevention, detection, and treatment of these cancers and ensure that survivors live longer better-quality lives. Research has helped us to accumulate extensive knowledge about the biological processes that are mainly involved in cancer onset, growth, and spread in the body. The reported advanced treatments may have more effective and targeted treatments and prevention strategies than conventional treatments.

4. AUTHORS CONTRIBUTION STATEMENT

Jana Debarati conceived of the presented idea and wrote the types of cancer and the recent advancements in cancer therapy. Hari Sai Ram developed the theory and performed the write-up, particularly for the inhibitors and phytochemicals involved in cancer treatment. Koteswara Reddy supervised the execution of the project. Hyacinthe Tuyubahe verified the references and the methods involved in cancer therapy. Ganesh and Gopi Krishna contributed the final version of the review paper. All authors discussed the structure of the review paper and contributed to the final manuscript.

5. CONFLICT OF INTEREST

Conflict of interest declared none.

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