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A review of Anticancer therapies and recent advancements in Anticancer treatment

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ABSTRACT: Nowadays, Cancer is the leading cause of death globally. As per the recent statistics by WHO, cancer incidence is increasing steadily worldwide, especially in developed countries. Despite the development of a variety of therapeutic approaches to prevent or manage this disease, there is also a need for additional effective solutions. Extended life span is directly correlated with a dramatic increase in deadly malignancies. Recently, pharmaceutical companies have invested significantly in researching and developing new cancer therapeutics. Even though progress has been made in this research, many obstacles exist that need to be overcome, especially in clinical trials, because the results are disappointing, preventing further development progress. To develop more effective treatment strategies, it is necessary to understand the pathophysiology of the disease properly. After overcoming so many obstacles, it is noteworthy that many significant advances have been made in cancer treatment due to the development of specialized medications, which seem to give better results than traditional therapies in recent years. This article aims to focus on the recent advancement in the developments of antineoplastic agents not only from a traditional point of view but also the recent therapeutics to combat this deadliest disease.

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INTRODUCTION:

Historically, the Greek term karkinos has been used to denote Cancer, characterized by the uncontrolled growth and division of abnormal cells [1]. Cancer is still a significant cause of concern and death in our modern world despite scientific and cultural progress. Age and lifestyle factors increase the risk of developing cancer [2]. The number of people diagnosed with Cancer in the United States in 2012 was 1,638,910, increasing yearly [3]. There were 14.1 million new cancer cases recorded yearly, including 165,000 new cases in children younger than 15. Lung, prostate, colorectal, and stomach cancers are the most common male malignancies and breast cancer in females [4]. According to the prediction

by WHO, 26 million new cancer cases will be diagnosed, and 17 million deaths will occur worldwide by 2030 [5]. As per the study, two-thirds of all malignancies are curable due to advances in cancer research, which has brought up new opportunities in treating Cancer. Over the last decade, new understandings of oncogenes, tumor suppressor genes, cancer cell metastasis, angiogenesis, and immunology have led to improved cancer therapy approaches [6].

As the treatment of Cancer is concerned, Chemotherapy is one of the age-old treatments in combating Cancer. There are several routes in which anticancer medicines can be administered, like intravenous, oral, topical, or others [7]. However, heavy metals used to treat Cancer are cytotoxic due to impeding cellular proliferation and affecting the extracellular growth signals received by cancer cells [8]. Mutations in Cancer are a global health and healthcare concern. However, the discovery of new drugs, chemicals, routes of administration, mechanisms of action, and configurations have

helped progress cancer prevention and treatment. Synthetic and natural anticancer treatments are more effective against cancer cell lines [9]. Despite their toxicity, Chemotherapy, radiation, and immunotherapy are still the mainstream of cancer treatment worldwide. There is a hope that organic molecules and their derivatives, found mainly in plants and animals, may be used to cure Cancer [10]. The main advantage of these medicinal compounds is having low toxicity value compared to synthetic chemicals. Due to this, extensive research is going on these biological remedies, which seem to be a substantial hope in treating cancer [11].

OLD ANTICANCER THERAPIES:

Surgery, radiation, and hormonal therapy are old anticancer therapies but are most effective.

Surgery:

Surgery is one of the most effective cancer therapies due to its ability to remove diseased cells and tissues permanently; hence, the success rate is very high [12]. The introduction of radiation therapy and Chemotherapy in the 1940s made surgery treatment more cautious as they helped treat localized primary and regional lymphatic tumours, making them indispensable cancer therapies [13]. Although the success rate of Surgery is higher than radiation therapy and Chemotherapy, they have their advantages. So, Surgery and combined treatment have helped diminish death and illness rates for solid tumours in the last 40 years [14].

Radiation Therapy:

Nowadays, 45 % of newly diagnosed cancer patients are treated with Radiation Therapy (RT). RT has been demonstrated to be successful in treating 40% of malignancies compared to a 30% success rate in surgery treatment in colorectal/liver metastases at the preliminary stage [15]. Similarly, RT has a cost-effectiveness ratio of 5 % more in industrialized nations' cancer control expenditures than other treatments. Preoperative radiation is exclusively utilized for rectal and oesophageal carcinomas, and RT is often used with Surgery and other treatments [16].

Hormone Therapy:

In order to halt or reduce the progression of hormone-secreting tumours, Hormone Therapy(HT) is utilized to interfere with hormonal signalling pathways. Persons who cannot undergo Surgery or radiation treatment for Cancer may benefit from hormone therapy, which has been shown to lessen cancer symptoms and may prevent or delay recurrence [17]. Depending on the type of Cancer, metastatic potential, growth rate, hormone dependence, and co-morbidities, hormone treatment is often used to treat hormone-dependent prostate and breast cancers [18].

Chemotherapy:

Chemotherapy is the use of drugs to kill cancer cells. There are many different chemotherapy drugs that can be used alone or in combination. Chemotherapy can be given through oral, topical or injectables directly into the tumour site as targeted therapy [19].

NEW ANTICANCER THERAPIES:

Targeted Therapies:

Targeted or molecularly targeted therapy uses drugs to limit cancer cell growth. This targeted therapy is more successful and safer than non-targeted chemotherapies since it does not damage healthy tissues. Targeted therapies aim to target cancer cells with fewer adverse effects. Cancer vaccines, monoclonal antibodies, ADCs, and SMDs are common in target therapies [20].

SMDs (Small Molecular Drugs):

The FDA has approved several small molecular drugs (SMDs) to treat various types of cancers and related disorders.

Kinase Inhibitors(KIs):

Kinase inhibitors, which prevent protein kinases from acting, are chemicals used to treat Cancer and other

disorders. These drugs have a lower molecular mass (under 1000 kDa) and may be taken internally or as injectables [21]. The mode of action of these kinase inhibitors is that they inhibit the kinase to stop acting, which results in the blockage of phosphorylation in amino acids that can be spitted or classified [22]. High doses of kinase inhibitors have been shown to prevent kinases, essential for protein stability, from binding with the Hsp90-Cdc37 chaperone system in cells. Erlotinib, lapatinib, and sorafenib are typical kinase inhibitors used in cancer treatment. Erlotinib is used to treat non-small cell lung cancer, lapatinib is used to treat HER2-positive breast cancer, and sorafenib is used to treat kidney cancer [23].

Proteasome Inhibitors (PIs):

Theseare another type of SMD, which are more effective in treating transformed cells than healthy tissues. Due to their efficacy in treating individuals with multiple myeloma, several PIs have been utilized alone or in combination with other drugs [24].

Cyclin-dependent Kinase (CDK) Inhibitors:

Scientists have developed cyclin-dependent kinase (CDK) inhibitors to address the growing need for more targeted anticancer medicines. To selectively inhibit cyclin-dependent kinases 4 and 6, palbociclib is an oral experimental drug that has received FDA approval [25]. Similar kinases, CDK 4 and CDK 6, help tumour cells move through the G1 and S phases of the cell cycle. Human trials are underway for several CDK inhibitors, including fascaplysin, ryanodine, purvalanol A, and more broad-spectrum CDK inhibitors like flavopiridol and olomoucine [26].

These compounds are not as selective as therapeutic monoclonal antibodies since they may inhibit many sites simultaneously. Combining molecular-targeted drugs with conventional cytotoxic Chemotherapy or MoAbs has enhanced patient outcomes in clinical studies [27].

Monoclonal Antibodies (MoAbs):

Due to their epitope-specific interactions, mobs are a promising cancer therapeutic option because they can target specific antigens like hematopoietic differentiation antigens, extracellular matrix antigens, glycoproteins, growth and differentiation molecules, angiogenic inhibitors, glycolipids, and carbohydrates [28]. These MoAbs can recognize cancer cells due to their unique properties and notify the immune system. These include medications such as ofatumumab (HuMax-CD20), rituximab (Mabthera), alemtuzumab (MabCampath), ibalizumab (IgG2), Cetuximab (IgG1), etc. The CD20 protein is located on the surface of B cells in the human immune system, and ofatumumab is a monoclonal antibody (MoAb) that selectively targets this protein [29]. Panitumumab and Cetuximab treat non-Hodgkin's lymphoma by blocking the epidermal growth factor receptor (EGFR), whereas Rituximab and alemtuzumab block CD20. However, tumour cells may be more susceptible to elimination after apoptosis produced by MoAbs and immune system activation [30].

The US FDA has approved thousands of MoAbs, and many more are undergoing clinical studies. Despite the benefits of these treatments, patients still experience flu-like symptoms, severe allergic responses, organ damage, and other side effects [31]. Also, MoAbs have an average affinity, lower than polyclonal antibodies, and may lose reactivity with mildly altered antigens. Researchers recently discovered a novel monoclonal antibody that may successfully enter cancer cells, a primary target for these vital anticancer treatments [32].

ADCs (Antibody Drug Conjugates):

Antibody-drug conjugates (ADCs) are antibodies that possess other molecules, such as toxins from plants/animals and chemotherapeutic or radioactive compounds. MoAbs work because of the lethal action of toxins expressed within the cancer cell [33]. The procedure is more difficult since the linker attached to the MoAb must be stable for exhibit action. The drug release may be improved if the MoAb is preferentially attached to the target and is taken up by the cell. The ADC's high toxicity makes it particularly effective against the target of interest [34].

The CD20-targeting ADCs 90Y-ibritumomab tiuxetan and 131I-tositumomab, both of which have FDA approval, are used to transport radioactive yttrium-90 to B-cells of non-Hodgkin lymphomas. Tumours with an overabundance of guanylyl cyclase C (GCC) are particularly vulnerable to the investigational ADC MLN0264 [35]. There are many reasons to be optimistic about ADCs as a cancer treatment, but there are also some concerns, such as the fact that it is necessary first to ascertain whether or not the target antigen is expressed in the tumour. Toxicity may occur if the ADC's drug load is released too soon, and damage can arise from non-specific binding to healthy tissues and heterogeneous solid tumours. This weakness highlights the need for cancer vaccine research [36].

OTHER TARGETED THERAPIES:

Anti-HER2 Targeted Therapy:

Trastuzumab, a therapeutic monoclonal antibody targeting the ErbB2 extracellular domain, has received regulatory clearance for its potential to inhibit breast cancer cell growth and xenograft development. It has been well-tolerated and has improved median survival in metastatic breast cancer patients expressing ErbB2 [37]. Trastuzumab's response rates correlated with initial tumor ErbB-2 expression, and after a series of studies, it was recommended as the primary treatment for HER-2 positive breast cancer, either alone or in conjunction with Chemotherapy, for metastatic and adjuvant cases. Lapatinib, an alternate treatment for growth factor receptor signaling, was approved for HER-2-positive metastatic breast cancer after trastuzumab failed to do so [38]. Lapatinib inhibits intracellular tyrosine-kinase activity to block EGFR and HER-2 receptor ATP-binding in trastuzumab-resistant individuals. Lapatinib has been proven to enhance progression-free survival rates by adding to its chemotherapy treatment. Trastuzumab and lapatinib have shown promising results in targeting cancer cells and improving survival rates in breast cancer patients [39].

Anti-EGFR (Epidermal Growth Factor Receptor) Targeted Therapy:

Chemotherapy targets the ErbB receptor family member EGFR (ERBB), with Cetuximab approved by the FDA in 2003. It targets EGFR's extracellular domain and is used in colorectal-positive and colon cancers. Panitumumab, a human IgG2 antibody, is effective as a monotherapy for metastatic colorectal cancer resistant to chemotherapy [40].

Gefitinib and Erlotinib, tiny EGFR tyrosine kinase inhibitors, have minimal anticancer effectiveness data. Gefitinib has partial remissions in 10-15% of NSCLC patients but does not improve therapeutic effectiveness. Lung cancer patients' response to therapy is linked to EGFR gene mutations or in-frame deletions [41].

Cetuximab works better without triggering K-ras mutations in colorectal cancers with EGFR overexpression but no mutations. Panitumumab gives similar results as Cetuximab. In malignant glioma, EGFR ectodomain deletions powerfully predict gefitinib sensitivity [42]. In NSCLC, the T790M mutation causes gefitinib resistance. Cetuximab and curative radiation can cure oropharynx and larynx squamous cell carcinoma well, with Cetuximab plus radiation improving locoregional control and survival rates [43].

Imatinib-Mesylate (Glivec):

The FDA approved imatinib Mesylate (Glivec), a drug that Novartis researchers discovered as a targeted drug for cancer treatment. Imatinib targets BCR-ABL, a kinase crucial to chronic myeloid leukemia (CML), a hematopoietic stem cell disease with clonal proliferation. The drug has induced complete hematological and cytogenetic remission in 90% of CML patients [44]. The FDA approved STI571 after successful phase I trials, but its gene-specific treatment needs dose optimization. STI571 induces brief remissions in CML's acute leukemia phase and rapidly produces drug-resistant cells [45].

De novo and relapse-related STI571 resistance are the most common, with reactivation being the most common mechanism. STI571 has shown 60 % response rates in phase 3 GIST studies but may be less sensitive to other tumors that produce c-kit tyrosine kinase [46]. Early intervention is essential to duplicate STI571's success across cancer types, and finding patients with clinical trial objectives is equally important. Molecular endpoint analysis reagents may help identify therapeutic candidates [47].

Immunotherapy (Cancer Treatment vaccines):

Cancer vaccines, also known as biological response modifiers, are immunotherapies that target cancer cells to eliminate the illness or prevent its spread. It is possible to establish either a particular or non-specific immune response against tumour cells [48]. With the help of a potent cancer vaccine, the immune system may be trained to fight the tumour almost entirely. The presentation of tumour antigens to immune cells triggers the production of CD4 (helper T cells) and CD8 (cytotoxic T cells). In contrast to CD4 T cells, which are indirectly stimulated by dendritic cells and macrophages to produce messengers that promote the activity of CD8 (killer) T cells, CD8 T cells destroy tumour cells directly when activated [49].

Cancer vaccines for various forms of Cancer, including renal cell carcinoma, melanoma, colon, breast, prostate, and blood (haematological) cancer, have shown promising outcomes in early clinical investigations. The first dendritic cell vaccine for the treatment of prostate cancer, sipuleucel-T (APC8015, Provenge), has been approved by the FDA. Other cancer vaccines include those based on antigens, DNA, or vectors [50].

It is widely recognized that embryonic stem cells may be used to produce antitumor immunity against ovarian cancer efficiently. Using entire cells results in fewer Cancer cell-specific antigens being recognized for vaccine production because of the lower proportion of molecules associated with the cell surface and the higher number of inner molecules. The, enriching cell surface material may boost the efficacy of cancer vaccines [51].

RECENT TARGET THERAPIES:

Epigenomic Targets:

The FDA has approved drugs like 5-azacytidine and 5-aza-2'-deoxycytidine for myelodysplastic syndrome, focusing on DNA-demethylating compounds. HDAC inhibitors, which block sirtuins, are potential epigenetic cancer medicines but may have unwanted side effects. The FDA has shown good tolerance in phase I clinical studies, making them a promising class of drugs [52].

Targeting the Non-Tumor Cell: Antiangiogenic Strategies:

Angiogenesis is crucial in physiological and pathological circumstances, with cancer cells requiring oxygen and nutrients from angiogenic vasculature. Anti-angiogenesis was proposed as a cancer therapy in 1971, with pro-angiogenic cytokines like VEGF and anti-angiogenic cytokines like angiostatin and thrombospondin. Bevacizumab, a VEGF-A antibody and PTK787 inhibitor, was approved by the FDA in 2004 for metastasized colorectal cancer [53]. Clinical studies are currently testing VEGF inhibitors like bevacizumab, with SU11248 and Bay 43-9006 being the most sophisticated alternatives. Bevacizumab has reduced cancer development without affecting survival [54].

Individual tumours' neo-angiogenic rate primarily controls the drug's effectiveness, but a predictive biomarker is yet unknown. Antiangiogenic therapy goes beyond drugs, with angiogenesis inhibitors like thalidomide, IFN-, and IL-12 showing anti-angiogenic action beyond their therapeutic uses [55]. Metronomic chemotherapy treatment may have advantages, such as delayed mutation-dependent pathways, longer chemotherapeutic combinations, and safer than the maximum tolerated dose (MTD regimens) [56].

Virotherapy:

Cancer treatment has progressed with targeted medications, such as viral vectors and suicide gene therapy, Gene-directed enzyme prodrug therapy (GDEPT) etc. Virotherapy employs oncolytic viruses to replicate inside tumour cells selectively and has shown promise in treating Cancer. However, cancer cell proliferation is hindered by the lack of disease progression targets and targeted therapies' low ability to deactivate oncogenes [57]. Viruses like DNA and RNA viruses can create oncolytic herpes viruses and tumour-specific influenza viruses. Clinical trials are ongoing, with Seneca Valley Virus, Measles, Newcastle Disease Virus (NDV), Herpes Simplex Virus, Vaccinia Virus, and Adenovirus being under clinical attention [58].

The immune system and tumour stroma also hinder virotherapy, with modern oncolytic targeting the stromal barrier. A comprehensive gene-virotherapy method with powerful immunological and stromal-targeting capabilities is needed to produce successful viral-based cancer treatments [59].

PLANT-BASEDCHEMICALS USED FOR ANTICANCER TREATMENTS:

Polyphenols:

Dietary polyphenols, including green tea catechins, curcumin, resveratrol, and genistein, have been shown to prevent Cancer by eliminating carcinogenic substances, altering cancer cell signalling, and inducing apoptosis and cell cycle arrest. Recent *In vitro* research has revealed that dietary polyphenols affect cancer cell growth enzymes MAPK and PI3K, making them a potential anticancer therapy target. Studies have shown that quercetin, luteolin, genistein, apigenin, and resveratrol may induce apoptosis in cancer cells, making them anticancer [60]. Smoking lowered the incidence of stomach cancer by 16 % and oesophagal Cancer by 31 %, while drinking green tea was associated with an 81 % reduction in both cancers among alcoholics. The risk of developing breast cancer may be reduced by 37% in women under 50 who drink green tea regularly. No adverse effects have been reported with green tea for reducing prostate cancer [61].

Saponins:

Saponins are secondary metabolites with a sugar moiety glycosidically bonded to a hydrophobic aglycone, which is found in plants like Yucca, Christmas rose, horse chestnuts, asparagus fern, daisies, chickpeas, soybeans, and alfalfa. These chemicals have cardioprotective, immunostimulatory, and anticancer biological actions that may enhance health [62]. Sapogenol, a potent aglycone, has been shown to decrease cell growth and inhibit cancer cell growth by binding cholesterol. Other saponins, such as Naringin, rutin, baicalin, and soybean

glycosides, have also been found to be anticancer activity. Saponins from various plants, such as *Agave schottii*, *Yucca schidigera*, and Quillaja, have been tested for their anti-proliferative efficacy [63].

Vinca Alkaloids:

Vinca alkaloids, including vinblastine, vincristine, vindesine, and vinorelbine, have been combined with Chemotherapy to treat solid tumours. Vinflunine, a novel Vinca alkaloid, inhibits microtubule development, cell division, and cell death [64]. The European Medicines Agency approved vinflunine for advanced or metastatic urothelial transitional cell carcinoma in adults in September 2009. Vinflunine and capecitabine have shown significant antitumor activity in metastatic breast cancer (MBC) patients resistant to anthracyclines and taxanes, with few side effects. Further clinical studies are needed to validate this combination [65].

Miscellaneous Phytochemical Agents:

The anticancer efficacy of synthetic analogues of the natural lignin nordihydroguaiaretic acid, found in *Larrea divaricata* Cav. or *Corillea tridentate*, has been investigated. Essential oils derived from *Anemopsis californica* roots containing thymol, piperine, and methyl eugenol have been reported to slow the growth of human endometrial cancer cell line AN3CA and cervical cancer cell line HeLa [66].

Terameprocol, derived from nordihydroguaiaretic acid, is now undergoing a phase I/II clinical trial for cancer treatment. Iridoids found in valerian root and rhizome was experimented with to inhibit cell migration. Lipids derived from *Ammopiptanthus mongolicus* suppress liver tumours. The ethyl acetate portion of *Calligonum comosum* (*Polygonaceae*) has anticancer properties. Cancer cell lines are more sensitive to the cytotoxicity of terrequinone A and terrefuranose from rhizosphere fungus than normal fibroblast cells [67].

The resinous exudates of *Conmmiphora opobalsamum* exhibit substantial lethal effects on human cancer cell lines, while extracts of *Pituranthos tortuous* have been proven to decrease proliferation and apoptosis. Extracts of *Varthemia iphionoides* stymied the proliferation of leukaemia cells. The human prostate cell lines DU145, LNCaP, and PC-3 were inhibited by the polyphenols and sterols in virgin argan oil in a dose-dependent manner. There may be hope for curing metastatic diseases using extracts from the Teucrium polium plant, which has been found to suppress cell growth and induce cell cycle arrest [68].

USE OF METALS IN CANCER THERAPY:

Platinum-Based Analogs in Cancer Therapy:

Platinum compounds, such as cisplatin, are essential anticancer drugs for treating various cancers. These chemicals disrupt DNA replication and transcription, causing cancer cells to die. Cisplatin's ability to generate covalent cross-links with DNA makes it cytotoxic, hindering DNA replication and transcription [69]. Despite its potential, platinum compounds have been synthesized and tested as chemotherapeutic drugs, but only some have reached clinical trials. Innovative platinum-based coordination complexes with oral administration have been sought to improve the solubility and bioavailability of clinically authorized platinum drugs. Akt2 and Akt3 isoforms ensure cancer cells resist cisplatin, while PDK1 and PDK2 regulate them [70].

Gold:

Gold (I) complexes decrease mitochondrial activity and protein synthesis to cross-link DNA, unlike cisplatin, which interacts with DNA to fight Cancer. Gold's coordination chemistry and high oxidation state affect its properties. Auranofin exhibits significant biological targets for anti-inflammatory and anticancer actions, reducing DNA, RNA, and protein production. Gold (III) complexes suppress cancer development and have a higher anticancer impact, with fewer side effects than Gold (I) [71].

Copper:

Copper is essential for energy metabolism, respiration, and DNA synthesis in enzymes and proteins. Copper compounds aid oxidation-reduction processes by generating free radicals with molecular oxygen. They induce DNA double-strand breaks and base oxidation through reactive oxygen species (ROS)[72]. Copper complexes, which form with ligands, are anticancer and cause cellular toxicity by causing unbound copper ions to produce reactive oxygen species (ROS). The reduction of Cu(II) to Cu(I) can occur in the presence of superoxide or reducing agents, causing hydroxyl radicals (OH•) to form, causing oxidative damage to cells [73].

RECENT DRUGS AND CHEMICALS USED FOR CANCER TREATMENTS:

The drugs that are recently used for anticancer therapy include the following, Dostarlimab (Jemperli) is an immunotherapy drug that stops cancer cells from multiplying by attacking a protein called PD-1. This programmed death-1 (PD-1) protein prevents the

immune system from identifying and destroying cancer cells. Dostarlimab has shown potential in treating a variety of malignancies, including endometrial, rectal, and uveal melanoma [74].

Oral tyrosine kinase inhibitor trametinib (Gavreto) slows cell division by decreasing BRAF protein activity. The BRAF gene is often mutated in malignant melanoma and other tumours. In patients whose BRAF-mutated melanoma has progressed after earlier treatment, pralsetcinib may be helpful [75].

Third, the tyrosine kinase inhibitor gefitinib (Iressa) blocks the activity of the EGFR protein. Mutations in the EGFR gene have been linked to lung cancer. Gefitinib shows promise for patients whose EGFR-mutated lung cancer has progressed after earlier treatment [76].

The tyrosine kinase inhibitor afatinib may block the EGFR and HER2 proteins' signal transmission capacity (Gilotrif). Mutations in EGFR and HER2 are often seen in lung cancer. Afatinib shows promise for patients whose EGFR-mutated lung cancer has progressed after earlier treatment [77].

MAP kinase (MEK) inhibitors like trametinib (brand name: Mekinist) block the protein from performing its typical tasks. MEK is a protein with a role in the signal transduction pathway, including the MAPK family of proteins. Trametinib is an option for patients whose BRAF-mutated melanoma has progressed after earlier treatment [78].

The tyrosine kinase inhibitor Xospata (gilteritinib) prevents the IDH2 gene from functioning. Treatment with gilteritinib has been demonstrated to slow the development of cancers caused by mutations in this gene, which is common in myeloid leukaemia [79].

The PD-L1 protein is recognized by the monoclonal antibody emapalumab-lzsg (Gamifant). This raises the possibility that the immune system will identify and eliminate cancer cells [80].

Inhibiting the CTLA-4 protein is the mechanism of action of the immunotherapy drug ipilimumab (Yervoy) [81].

The targeted therapy drug glasdegib (Dovato) blocks the protein IDH1, often mutated in cancer cells, from functioning normally [82].

Antibiotic gatifloxacin (Zyflodex) is a fluoroquinolone that is effective against bacteria. The antimicrotubule medicine eribulin (Halaven) is very effective against acral lentiginous melanoma because it stops the formation of microtubules. Microtubules are essential for cell division; interfering with their creation might kill cancer cells. The use of eribulin to treat advanced breast cancer has been approved by the Food and Drug Administration [83].

The checkpoint inhibitor tremelimumab (Imjudo) blocks PD-1 protein in T cells. Inhibiting this protein makes T cells more selective, killing out cancer cells rather than healthy ones. Tremelimumab has been approved for use in the treatment of melanoma [84].

Atezolizumab (Tecentriq) is a checkpoint inhibitor suppressing PD-L1 expression in cancer cells. Inhibiting this protein makes it easier for the immune system to recognize and eliminate cancer cells that might otherwise evade attack [85]. Atezolizumab is approved for treating many types of Cancer, including lung, bladder, head and neck [86].

Proteasome inhibitors like bortezomib (Velcade) prevent the proteasome from doing its regular job. Since the proteasome is an enzyme vital to cell survival, inhibiting its function may be able to eliminate cancer cells. Bortezomib may now be used in the treatment of both mantle cell lymphoma and multiple myeloma [87].

In other words, carfilzomib (Kyprolis) prevents the proteasome from completing its work. Carfilzomib is like bortezomib but more muscular and with a longer half-life. Carfilzomib's shorter dose intervals compared to bortezomib may improve patients' quality of life [88].

Enhertu (Trastuzumab deruxtecan-nxki) is a targeted therapy that consists of a monoclonal antibody and a chemotherapeutic drug. The HER2 antibody targets a protein present in many different types of cancer cells. Chemotherapy causes rapid cell death in cancerous tissue. In 2019, Enhertu was approved by the FDA to treat HER2-positive breast cancer [89].

RANK ligand interacts with the fusion protein luspatercept (Rebif), which promotes bone marrow cell growth. The blood cancer drug Luspatercept is used to treat myelofibrosis. The FDA finally green-lighted it this year [90].

Abraxane (nab-paclitaxel) is a chemotherapy drug that messes with cancer cells' DNA. Many types of Cancer are treated with it, including breast, pancreatic, and non-small cell lung cancers [91].

Ado-trastuzumab emtansine (T-DM1) is a targeted therapy medication combining monoclonal trastuzumab with the chemotherapeutic drug DM1. Trastuzumab treats breast cancer, and the HER2 protein is a popular therapy target. The potent chemotherapeutic drug DM1 is secreted by cancer cells that contain HER2. T-DM1 is used to treat breast cancers that are HER2 positive [92].

Pembrolizumab (Keytruda) is an immune checkpoint inhibitor that blocks the PD-1 protein. Cancer cells are aided in their attempts to evade the immune system by the PD-1 protein. Pembrolizumab helps the immune system combat cancer. Pembrolizumab is effective against a wide variety of cancers, including melanoma, lung cancer, and head and neck cancer [93].

Nivolumab (Opdivo) is another drug that acts as an immune checkpoint inhibitor by blocking the PD-1 protein. Nivolumab is effective against various cancers, including melanoma, lung, and kidney [94].

Acalabrutinib (Calquence), an inhibitor of Bruton's tyrosine kinase (BTK), is used to treat chronic lymphocytic leukaemia (CLL) and mantle cell lymphoma (MCL). Interacting with the BTK protein reduces the number of B cells to survive [95].

Adcetris (Brentuximab vedotin) is a monoclonal antibody-drug combination (ADC) used to treat Hodgkin lymphoma and systemic anaplastic large cell lymphoma (ALCL). It achieves its purpose by binding to a protein on the surface of cancer cells called CD30 and releasing its payload of chemotherapeutic drugs [96].

Research has revealed that the fusion protein luspatercept (Rebif) may boost erythrocyte (red blood cell) production. Anaemia caused by malignancies such as myelodysplastic syndromes (MDS) and chronic lymphocytic leukaemia (CLL) has been proven to respond well to this treatment [97].

Polatuzumab vedotin-piiq (Polivy) is a chemotherapy drug and antibody treatment administered together that inhibits CD79b. Cancer cell CD79b antibody interaction induces intracellular drug release, leading to cell death. The Food and Drug Administration (FDA) has approved polatuzumab vedotin-piiq for the treatment of patients with relapsed or unresponsive diffuse large B-cell lymphoma (DLBCL) [98].

The immunotherapy drug durvalumab (Imfinzi) blocks the PD-1 checkpoint protein. Cancer cells are aided in their attempts to evade the immune system by the PD-1 protein. As a PD-1 inhibitor, durvalumab stimulates the immune system to attack cancer cells [99].

Tremelimumab is another immunotherapy drug that blocks cancer cell proliferation by targeting the PD-1 checkpoint protein (Imjudo). Tremelimumab is combined with durvalumab and platinum-based compounds to treat metastatic cell lung cancer [100].

Enfortumab vedotin (Padcev), or monomethyl auristatin E (MMAE), is a monoclonal antibody that acts as a cytotoxic agent. Enfortumab vedotin binds to the Nectin-4 receptor, which is expressed in several types of cancer cells. Enfortumab vedotin binds to Nectin-4 and then delivers the cancer-killing agent MMAE to the tumour cells [101].

Lapatinib (Tykerb) is a targeted therapy medication that blocks the HER2 receptor. The overexpression of HER2 characterizes breast cancer. By inhibiting the HER2 receptor, lapatinib prevents cancer cells from dividing and spreading [102].

The targeted medication Lunvoq (moxetumomab pasudotox-tdfk) works by attacking the CD19 antigen. B lymphocytes have a protein called CD19 on their surface. Lunvoq may treat follicular lymphoma that has returned or is resistant to other treatments [103].

Targeted medication Adcetris (brentuximab vedotin) is a monoclonal antibody containing a toxin. The antibody binds to a protein called CD30 that is found on the surface of certain types of cancer cells. When the poison is allowed to enter the cancer cells, they perish [104].

The targeted drug olaparib (Lynparza) prevents the DNA damage repair enzyme PARP from doing its job. This drug treats patients with the BRCA mutation of ovarian or breast Cancer [105].

The targeted trametinib (Mekinist) blocks cellular signalling by decreasing MEK1/2 protein activity. This drug treats advanced melanoma and colorectal cancer [106].

Kadcyla (trastuzumab deruxtecan) is a monoclonal antibody with a DNA-damaging chemical attached as a payload specifically targeting HER2. Kadcyla may be used to treat HER2-positive breast cancer [107].

Idecabtagene violence is a chimeric antigen receptor (CAR) T-cell therapy used to treat multiple myeloma. CAR T-cells are gene-edited T cells already trained to seek out and kill cancer cells [108].

Targeted therapy with tivozanib, a VEGF receptor inhibitor, is another milestone of cancer therapy. Tumour angiogenesis is facilitated by the protein vascular endothelial growth factor (VEGF). Tivozanib can inhibit tumour growth by inhibiting vascular endothelial growth factor (VEGF), a protein essential for survival [109].

The targeted therapy of Entrectinib inhibits the MET receptor. Cancers of the lung and other organs often include mutations in the MET protein. Entrectinibmay reducetumour development by blocking MET protein [110].

Idecabctagene violence, a chimeric antigen receptor (CAR) T-cell therapy, uses a patient's T cells that have

been genetically modified to seek out and buy using tivozanib and other tyrosine kinase inhibitors. It can potentially treat patients with advanced renal cell carcinoma [111].

The targeted drug Entrectinib attacks the mutant MET proteins present in several malignancies. Multiple types of Cancer, including lung, colon, and uterine malignancies, have been demonstrated to be susceptible to its effects [112].

Combination therapy with BRAF and MEK protein inhibitors like sorafenib and binimetinib has been effective in many cancers. Since these proteins are often changed in melanoma, targeting both may be helpful by combining the two drugs mentioned above to block the formation and spread of cancer cells [113].

Bevacizumab (Avastin) is a monoclonal antibody that prevents new blood vessels from forming. VEGF, a protein that promotes the formation of new blood vessels, is essential for tumour growth. Tumour regression may be aided with bevacizumab, a VEGF inhibitor [114].

Encorafenib (Braftovi) is a small-molecule pharmacologic inhibitor of the BRAF gene. The BRAF gene is often mutated in malignant melanoma and other tumours. Encorafenib, a medication used to treat Cancer, works by blocking BRAF [115].

The monoclonal antibody ipilimumab (Yervoy) has been created to target the cytotoxic T-lymphocyte-associated protein 4 (CTLA-4). CTLA-4 is a protein that helps to dampen the immune system. Ipilimumab inhibits CTLA-4 to help the immune system recognize and destroy cancer cells [116].

Cetuximab (Erbitux) is a monoclonal antibody that blocks the effects of the epidermal growth factor receptor (EGFR) protein. EGFR is a protein that promotes the growth of numerous cancer cells. One mechanism through which Cetuximab fights Cancer is via blocking EGFR signalling [117].

The small-molecule drug encorafenib (Braftovi) inhibits the activity of the BRAF protein. Mutations in the BRAF gene account for around 50 % of all melanomas. Melanoma cell growth may be suppressed by the BRAF inhibitor encorafenib [118].

Cancer patients with high levels of the HER2 protein in their bodies may benefit from taking the small molecule drug tucatinib (Tukysa) [119].Multiple forms of Cancer overexpress the HER2 protein. Tucatinib, targets HER2 and helps to kill cancer cells [120].

Similarly, Fotibinostat (Tivozanib) can be used for advanced endometrial cancer therapy [121].

Treatment of advanced bladder cancer with enfortumab vedotin-ejfv (Padcev) can be possible noa- a-days [122].

Pralsetinib (Gavreto) is used for MET exon 14 skipping in advanced solid tumours [123]. More drugs have been developed in recent years for the treatment of Cancer, including Pembrolizumab (Keytruda), Encorafenib (Braftovi), Ramucirumab (Cyramza), Tepotinib (Tepmetko), Cabozantinib (Cabometyx), etc. [124].

An alternative technique for treating Cancer involves the development of nanoparticle-based drug delivery systems [125]. Liposomal and lipid-based formulations have gained significant popularity as sustained drug delivery systems [126]. Marqibo, also known as Talon, is a liposomal formulation of doxorubicin indicated for treating acute lymphoblastic leukaemia (ALL) in patients [127]. Myocet, a liposome-encapsulated formulation of doxorubicin, is employed in treating breast cancer patients [128]. These represent a limited subset of the numerous medications that have received approval from the FDA and fall within this classification [129]. Examining treatment techniques that integrate multiple therapy models currently in use has also been conducted [130].

CONCLUSION:

Recent innovations in cancer treatment have led to the evolution of many novel approaches to treating Cancer. These innovations have been achieved through an enhanced understanding of the biological foundations of Cancer. However, some of the antiquated therapies retain their utility with certain drawbacks. While Surgery and radiation have demonstrated efficacy, they are limited in their ability to address Cancer confined to a single area.

Chemotherapy is a therapeutic intervention that can be employed to manage cancer cells that have metastasized, although it is associated with an enormous number of adverse effects. The treatments above remain relevant in contemporary times and are expected to persist. However, it is imperative to note that alternative treatments may also emerge. Molecular-based or immunological therapies are currently in their nascent phases of advancement. Despite the various adverse effects of this novel cancer treatment, such as acneiform rash, cardiac dysfunction, thrombosis, hypertension, and proteinuria, customized therapeutic approaches

involving immunophenotyping and tumour genomics have demonstrated superior tolerability compared to conventional Chemotherapy. Research has demonstrated that they can enhance the quality of life of individuals with Cancer and decrease their overall survival rate.

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