

A review on neoplastic diseases and their treatment

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ABSTRACT

Cancer is a significant health concern and a complicated genetic illness that is still the biggest cause of mortality globally, mainly induced by carcinogens. People may be exposed to carcinogens via the environment, water, food, chemicals, and sunshine. The body produces a lot of abnormal white blood cells when someone has leukemia. Numerous cancer medications have been created as a result of increased understanding of the molecular process behind the development of cancer. For present cancer treatments to be more effective, new tactics and chemo-preventive drugs are required. The author of this paper typically goes into detail on a variety of cancer-related diseases that affect both children and adults. This review article discusses the primary adverse effects of first-line medications as well as the medications used in anti-neoplastic drug treatment.

Keywords: Cancer, Neoplasia, Carcinomas, Drug, Anti-neoplastic medications, Disease

The most dreaded kind of neoplasia is cancer [1]. Neoplastic medications either eradicate carcinomas or interfere with the development of cancer cells [2]. More than 277 distinct forms of cancer diseases are included in the term "cancer" in its broadest definition. It is a diverse set of illnesses that may begin in almost any organ or tissue of the human body when aberrant cells proliferate uncontrollably, cross their unique limits to infect other bodily components, or spread to distant organs. Following that, the metastasizing process starts, which results in cancer mortality. Neoplasm and malignant tumor are sometimes thought of as the two common terms for cancer.

Different cancer stages have been found by researchers, suggesting that a number of gene alterations are involved in the aetiology of cancer. The aberrant cell proliferation caused by certain gene mutations. A crucial role in the acceleration of cell proliferation is played by genetic diseases brought on by heredity or hereditary factors. The top cause of death in the world is cancer. As a result, cancer is a significant issue that has an impact on the health of all human communities. At the tissue level, there is a range of diseases, which makes a precise diagnosis and effective

therapy very difficult to achieve [3,4]. The lung, bronchial, and prostate cancer forms that affect men most often are found there, accordingly. The breast, uterine corpus, and thyroid are, correspondingly, the areas of the female body where cancer is most common. According to these statistics, the most common cancers in men and women, respectively, are breast and prostate cancers [5]. Blood cancers, brain tumors, and lymph node cancers, in that order, account for the largest proportion of cancer cases in children [6, 7].

Additionally, other uncommon or severe forms of cancer, such as Ewing's sarcoma, Rhabdomyosarcoma, Retinoblastoma, and Nephroblastoma, are also observed in patients. The development of cancer is caused by a succession of gene changes that alter how cells operate. Evidently, chemical substances have a part in the development of cancerous cells and gene alterations. Additionally, smoking contains a number of chemical substances known to cause cancer and result in lung disease [8]. It's interesting to note that environmental chemicals with carcinogenic tendencies affect cells' cytoplasm and nuclei directly or indirectly, causing genetic diseases and gene alterations [9,10,11].

Table 1: Agent associated with cancer along with their treatment

Agent	Associated cancers	Mechanism	First line drug
Tobacco (<i>Nicotiana tobaccam</i>)	Lung, neck, kidney, head, and pancreas	DNA Damage due to procarcinogens	Platinum compounds
Aflatoxigastn B1	Heapatic carcinomas	DNA Damage	Atezolizumab and Bevacizumab
Nitrosaime	Gastric and esophageal cancer	DNA damage	Platinum compounds
Asbestoes	Mesothelioma	Inflammasome activation that leads to local inflammation	Pemetrexed disodium, Ipilimumab, Nivolumab
Alkylating chemotherapy agent	Acute myeloid leukemia	DNA damage	Fludarabine
UV light	Melanoma	DNA damage	Aldesleukin, Binimetinib, Encorafenib, Cobimetinib, Aldesleukin, Vemurafenib
Helicobacter pylori	Gastric adenocarcinoma	DNA damage	Melphalan, docetaxel, capecitabine
Schistosomiasis	Bladder carcinoma	DNA damage	Gemcitabine

Table 2: Symptoms of cancer

SYMPTOMS	DESCRIPTION
Abnormal bumps	Bumps that are cancerous are typically large, hard, painless to the touch and appear spontaneously. The mass will grow in size steadily over the weeks and months. Cancerous lumps that can be felt from outside of body can appear in the breast, testicle, or neck, but also in the arms and legs.
Pyrexia	Some blood cancers, like lymphoma, cause a fever for days or even weeks.
Unintentional weight loss	Almost half of people who have cancer lose weight. It's often one of the signs that they notice first.
Breast changes	Skin changes include puckering, dimpling, a rash, or redness of the skin of the breast. Some people have a rash or redness of the nipple and the surrounding skin. The skin might look like orange peel or the texture might feel different. This can be caused by other breast conditions.
Hoarseness	Cough is one sign of pulmonary carcinoma, and hoarseness may mean cancer of larynx or thyroid gland.
Appetite alterations	Loss of appetite is a common problem for people with metastatic breast cancer. It can be caused by breast cancer treatment or by the cancer itself. Stress, depression, nausea, constipation, and changes in sense of taste or smell can also affect your appetite.
Groin	If inguinal lymph nodes become cancerous, they can then spread cancer to the pelvic lymph nodes they flow into. In the early stages of cancer, inguinal lymph nodes cannot be felt by hand. If large lymph nodes or a lump in groin are detected, this could be an indication of a more advanced stage of cancer.
Dermal alterations	Merkel cell carcinoma is a rare, aggressive skin cancer. It appears as a painless, flesh-colored or bluish-red nodule growing on your skin. Skin cancer develops primarily on areas of sun-exposed skin, including the scalp, face, lips, ears, neck, chest, arms and hands, and on the legs in women.
Neurological problems	The neurologic syndromes associated with breast cancer include cerebellar degeneration, sensorimotor neuropathy, retinopathy, stiff-persons syndrome, encephalitis, and opsoclonus–myoclonus.
Pain	Bone cancer often hurts from the beginning. Some brain tumours cause headaches that last for days and don't get better with treatment. Pain can also be a late sign of cancer; therefore, it is very necessary to consult a doctor for any explained pain.
Anemia	This is when your body doesn't have enough red blood cells, which are made in your bone marrow. Cancers like leukaemia, lymphoma, and multiple myeloma can damage your marrow. Tumours that spread there from other places might crowd out regular red blood cells.
Belly pain	In most cases, you feel gassy, crampy, and bloated because of something minor. Talk to your doctor if you have these types of symptoms and they don't go away.

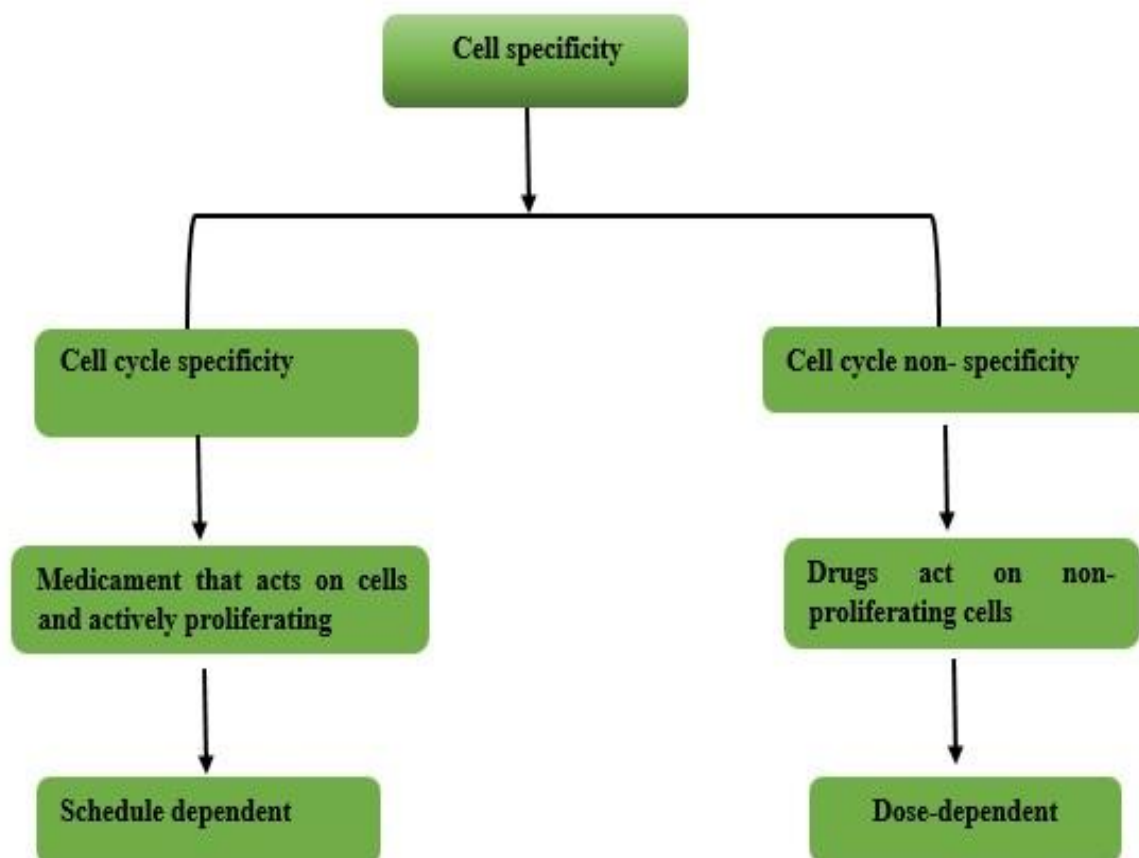


Figure 1 - Anti-neoplastic drugs for several carcinomas [12]

When a tumor forms, carcinomas are transported to different bodily parts through the circulation or lymphatic system. There is a process called metastasis. The first location of spread is lymph nodes. Lung, liver, colon, neck, brain, dermis, and other key organs of the human body are often affected by spread via the circulation. Cancer can campaign many symptoms, but these symptoms, are most often caused by illness, injury, benign tumor, or other modification. Details of major carcinogens and associated cancers are given in table 1 [1,2].

Drug of choice for several kind of cancer with their respective mechanism of action, biological class of drug and major adverse effect. Common Cancer Types are bladder carcinoma, lung cancer, melanoma [13], non-Hodgkin lymphoma, liver [14], and pancreatic cancer [15], prostate, thyroid, and breast cancer.

Toxic Effect of Neoplastic Agent

Anti-neoplastic drug therapy has a variety of long-term or chronic side effects that have been seen in individuals in addition to acute or short-term effects. These include hearing loss, cancer, bone marrow damage, lung and heart damage,

infertility (both temporary and permanent), effects on reproduction and the growing baby in pregnant women, liver and kidney damage, and damage to the lungs and heart.

Table 3: Description of cell specific drugs

Drugs	Phase	Cell Cycle Specific Drugs	Cell Cycle Non-Specific Drug
Etoposide	G1	+	-
Platinum Compounds		-	+
Antimetabolite	S	+	-
Alkylating Agent		-	+
Paclitaxel		+	-
Topoisomerase Inhibitor	G2	+	-
Vinca Alkaloids	M	+	-
Anthracyclins	G2	-	+
Mitomycins C	M	-	+
Taxenes		+	-

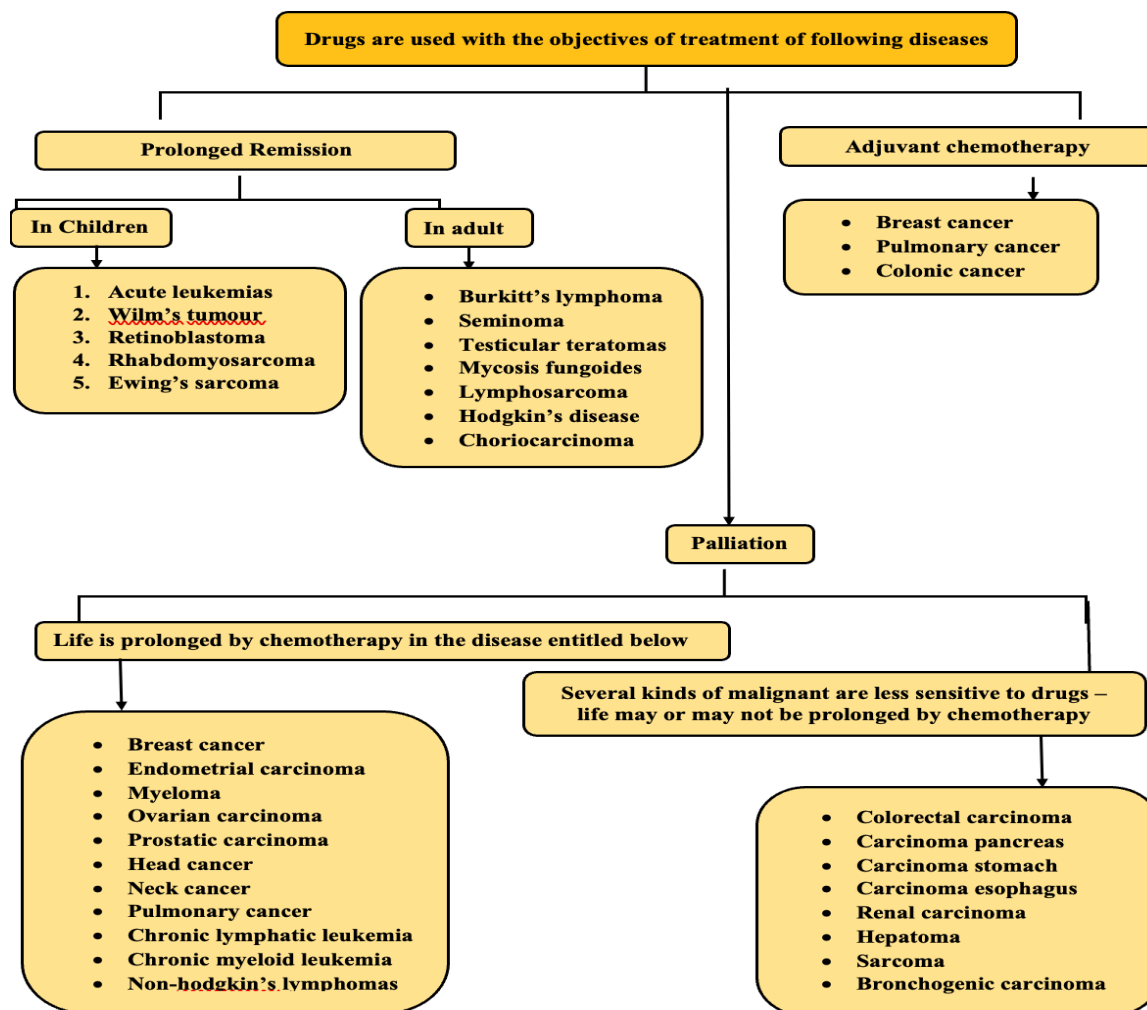


Table 4: Drugs use in the therapeutics of cancer

Disorder	Drug	Class	Mechanism	Ref.
Non-Hodgkin's lymphomas	Cyclophosphamide	Nitrogen mustard	cross linking pairing of DNA strand	[17]
	Doxorubicin	Anti-tumor antibiotic	DNA intercalation and inhibition of RNA and synthesis of protein, and it is nonspecific cell cycle phase	[18]
Wilm's tumor	Dactinomycin			
Colorectal carcinoma	Irinotecan	Comptohecin	Inhibit the resealing of DNA fragments by binding to the topoisomerase I and DNA cleavage	[19]
	5-Fluorouracil	Pyrimidine antagonist	Inhibit thymidylate synthetase that results in failure of DNA synthesis due to non-availability of thymidylate	[20]
Rhabdomyosarcoma	Oncovin	Vinca alkaloids	Mitotic inhibitors and bind to β -tubulin and prevent the polymerization	[21]
	Cyclophosphamide	Nitrogen mustard	cross linking pairing of DNA strand	[17]
	Dactinomycin	Anti-tumor antibiotic	DNA intercalation and inhibition of RNA and synthesis of protein	[18]
Ewing's sarcoma	Doxorubicin			
Hodgkin's disease	Doxorubicin			

	Brentuximab vedotin	Antibody drug conjugates (CD30-directed)	Selectively targets tumor cells expressing the CD30 antigen	[23]			
	Gemcitabine	Pyrimidine antagonist	Inhibit DNA synthesis				
Retinoblastoma	Etoposide	Topoisomerase II inhibitors	React with topoisomerase II and arrest the G2 phase cause DNA cleavage				
	Vincristine	Vinca alkaloids	Mitotic inhibitors and bind to β -tubulin and prevent the polymerization	[21]			
Carcinoma pancreas	Carboplatin	Platinum coordination complex	It hydrolyzed intracellularly to produce a highly reactive moiety which cause cross linking of DNA at the site N ⁷ of guanine residue, and it can react with -SH group of nuclear protein	[23,24]			
	Oxaliplatin						
Bronchogenic carcinoma	Cisplatin	Platinum coordination complex	Mitotic inhibitors and bind to β -tubulin and prevent the polymerization	[21]			
	Carboplatin						
	Vinorelbine						
	Pemetrexed				Folate antagonist	Primary target the enzyme	[24]
	Etoposide				Topoisomerase-2 inhibitor	React with topoisomerase II and arrest the G2 phase cause DNA cleavage	
	Gemcitabine				Pyrimidine antagonist	Inhibit DNA synthesis	[25]
	Docetaxel				Taxanes	Bind to β -tubulin and enhance its polymerization to form excess of tubules	[21]
Taxol	[21,23]						
Endometrial carcinoma	Carboplatin	Platinum coordination complex	It hydrolyzed intracellularly to produce a highly reactive moiety which cause cross linking of DNA at the site N ⁷ of guanine residue	[26,27]			
	Adriamycin	Anti-tumor antibiotic	DNA intercalation and inhibition of RNA and synthesis of protein, and it is nonspecific cell cycle phase	[18]			
	Liposomal doxorubicin						
Testicular teratomas	Bleomycin	Anti-tumor antibiotic	Formation of complex chelate with Fe ²⁺ and produce superoxide ions and intercalate between DNA strand cause chain scission and inhibit repair				
Extragonadal germ cell tumors							
Chronic lymphatic leukemia	Fludarabine	Purine analogues of anti-metabolites	Inhibit DNA polymerase and ribonucleotide reductase interfere with DNA repair and incorporated to form dysfunctional DNA	[28]			
	Cladribine						
Chronic myeloid leukemia	Imatinib	Tyrosine protein kinase inhibitors	Inhibit 'BCR-ABL' tyrosine kinase	[29]			
Burkitt's lymphoma	Rituximab	CD20 Target monoclonal antibodies	Bind with CD20 β -cell antigen expressed on the surface of β -lymphocyte and β -cell lymphoma	[22]			
Mycosis fungoides	Vorinostat	Histone deacetylase inhibitors	Inhibit the enzymatic activity of HDAC1, HDAC2, HDAC3, HDAC6				
	Romidepsin						

Renal carcinoma	Everolimus	mTOR inhibitor	Bind with high affinity to the FK506BP-12, there by forming a drug complex that abolish the stimulation of mTOR that simultaneously reduces the activity of effectors downstream	[30]
	Bevacizumab	Anti-angiogenic agents	Inhibiting the binding of VEGF to its cell surface receptors	[18]
	Axitinib	Tyrosine kinase inhibitor	Inhibit receptor tyrosine kinase including VEGFR-1, VEGFR-2, VEGFR-3 at therapeutic plasma concentrations	[26]
Metastatic kidney cancer	Pembrolizumab	Monoclonal antibody	Bind to the PD-1, preventing PD-L1, PD-L2 from inhibiting the action of T-cells, restoring a patient's tumor specific T-cell response	[18]
	Nivolumab	Monoclonal antibody		

Table 5 - Toxic effect of drugs

DRUG	TOXICITY
Anthracycline	Toxic effect in Cardio region
Cytarabine	Toxic effect in Neurological region such as Cerebral Ataxia
Taxanes and their respective derivatives	Peripheral neuropathy, fluid retention
Cyclophosphamide [25]	Alopecia and haemorrhagic cystitis
Vinca Alkaloids	Peripheral neuropathy
6-Mercaptopurine, 6-Thioguanine	Bone marrow suppression and toxic effect seen in liver
Capecitabine, 5-FU, Fludarabine	Hand and foot syndrome, toxic effect in neurological region, myeloid suppression
Platinum compounds [23]	Ototoxicity, nephrotoxicity, emesis, neuropathy
Methotrexate	In low dose toxicity seen in blood such as megaloblastic anemia and in high dose toxicity seen in hepatic region, obstructive nephropathy
Busulphan, Bleomycin	Pulmonary fibrosis

CONCLUSION

Diverse research has been conducted in the pharmaceutical sector with regard to carcinogens. A methodical analysis of effective anticancer medications might provide insightful information about patterns in the development of anticancer medications, which could aid in the systematic discovery of novel anticancer medications. The authors of this study draw the conclusion that nephroblastoma, neuroblastoma, Ewing's sarcoma, and rhabdomyosarcoma are among the cancer forms that are treated using anti-carcinogens medications.

However, owing to their molecular makeup, these medications induce a variety of toxicities and side effects when ingested by any method. The mechanism of action and side effects of several medications used in the treatment of cancer are further elaborated upon by the writers in this article.

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