

**CANCER HITS, BODY PAYS & THERAPY SAYS: SILVER BULLET****Dr. Kishor Dholwani, Kushal Nandi, Tanistha Mumtaz Chatterjee, Arpita Biswas and Dr. Dhrubo Jyoti Sen\***Department Of Pharmaceutical Chemistry, School Of Pharmacy, Techno India University, Salt Lake City, Sector-V,  
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**ABSTRACT**

Cancer can be treated by surgery, chemotherapy, radiation therapy, hormonal therapy, targeted therapy (including immunotherapy such as monoclonal antibody therapy) and synthetic lethality. The choice of therapy depends upon the location and grade of the tumour and the stage of the disease, as well as the general state of the patient (performance status). Cancer genome sequencing helps in determining which cancer the patient exactly has for determining the best therapy for the cancer. A number of experimental cancer treatments are also under development. Under current estimates, two in five people will have cancer at some point in their lifetime.

Complete removal of the cancer without damage to the rest of the body (that is, achieving cure with near-zero adverse effects) is the ideal, if rarely achieved, goal of treatment and is often the goal in practice. Sometimes this can be accomplished by surgery, but the propensity of cancers to invade adjacent tissue or to spread to distant sites by microscopic metastasis often limits its effectiveness; and chemotherapy and radiotherapy can have a negative effect on normal cells. Therefore, cure with nonnegligible adverse effects may be accepted as a practical goal in some cases; and besides curative intent, practical goals of therapy can also include (1) suppressing the cancer to a subclinical state and maintaining that state for years of good quality of life (that is, treating the cancer as a chronic disease), and (2) palliative care without curative intent (for advanced-stage metastatic cancers).

Because "cancer" refers to a class of diseases, it is unlikely that there will ever be a single "cure for cancer" any more than there will be a single treatment for all infectious diseases. Angiogenesis inhibitors were once thought to have potential as a "silver bullet" treatment applicable to many types of cancer, but this has not been the case in practice.

**KEYWORDS:** Synthetic lethality, Mutation, Radiotherapy, Chemotherapy, Hormone therapy, Targeted therapy, Monoclonal antibody, Angiogenesis Inhibitor, Immunotherapy, Hospice, Exosomes.

**INTRODUCTION**

The treatment of cancer has undergone evolutionary changes as understanding of the underlying biological processes has increased. Tumour removal surgeries have been documented in ancient Egypt, hormone therapy and radiation therapy were developed in the late 19<sup>th</sup> century. Chemotherapy, immunotherapy and newer targeted therapies are products of the 20<sup>th</sup> century. As new information about the biology of cancer emerges, treatments will be developed and modified to increase effectiveness, precision, survivability, and quality of life.

**Synthetic Lethality:** Synthetic lethality arises when a combination of deficiencies in the expression of two or more genes leads to cell death, whereas a deficiency in only one of these genes does not. The deficiencies can arise through mutations, epigenetic alterations or inhibitors of one or both of the genes. Cancer cells are

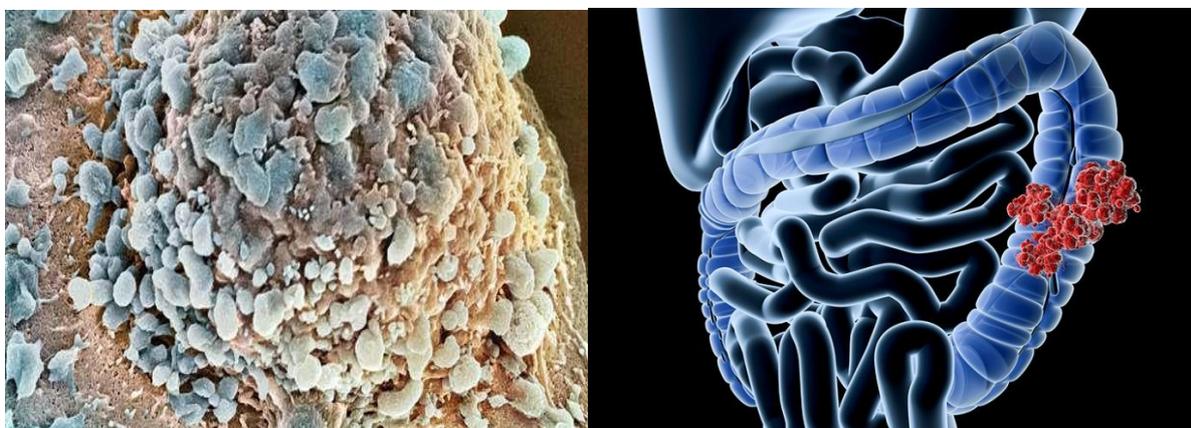
frequently deficient in a DNA repair gene. This DNA repair defect either may be due to mutation or, often, epigenetic silencing. If this DNA repair defect is in one of seven DNA repair pathways, and a compensating DNA repair pathway is inhibited, then the tumour cells may be killed by synthetic lethality. Non-tumourous cells, with the initial pathway intact, can survive.<sup>[1]</sup>



**Figure-1: Ovarian cancer.**

**Ovarian cancer:** Mutations in DNA repair genes *BRCA1* or *BRCA2* (active in homologous recombination repair) are synthetically lethal with inhibition of DNA repair gene *PARP1* (active in the base excision repair and in the microhomology-mediated end joining pathways of DNA repair). Ovarian cancers have a mutational defect in *BRCA1* in about 18% of patients (13% germline mutations and 5% somatic mutations). Olaparib, a PARP inhibitor, was approved in 2014 by the US FDA for use in BRCA-associated ovarian cancer that had previously been treated with chemotherapy. The FDA, in 2016, also approved the PARP inhibitor rucaparib to treat women with advanced ovarian cancer who have already been treated with at least two chemotherapies and have a *BRCA1* or *BRCA2* gene mutation.

**Colon cancer:** In colon cancer, epigenetic defects in the *WRN* gene appear to be synthetically lethal with inactivation of *TOP1*. In particular, irinotecan inactivation of *TOP1* was synthetically lethal with deficient expression of the DNA repair *WRN* gene in patients with colon cancer. In a 2006 study, 45 patients had colonic tumours with hypermethylated *WRN* gene promoters (silenced *WRN* expression), and 43 patients had tumours with unmethylated *WRN* gene promoters, so that *WRN* protein expression was high. Irinotecan was more strongly beneficial for patients with hypermethylated *WRN* promoters (39.4 months survival) than for those with unmethylated *WRN* promoters (20.7 months survival). The *WRN* gene promoter is hypermethylated in about 38% of colorectal cancers.



**Figure-2: Colon cancer.**

There are five different stages of colon cancer, and these five stages all have treatment:

- Stage 0, is where the patient is required to undergo surgery to remove the polyp (American Cancer Society). Stage 1, depending on the location of the cancer in the colon and lymph nodes, the patient undergoes surgery just like Stage 0.
- Stage 2 patients undergo removing nearby lymph nodes, but depending on what the doctor says, the patient might have to undergo chemotherapy after surgery (if the cancer is at higher risk of coming back).
- Stage 3, is where the cancer has spread all throughout the lymph nodes but not yet to other organs or body parts. When getting to this stage, Surgery is conducted on the colon and lymph nodes, then the doctor orders Chemotherapy (FOLFOX or CapeOx) to treat the colon cancer in the location needed (American Cancer Society). The last a patient can get is Stage 4.

- Stage 4 patients only undergo surgery if it is for the prevention of the cancer, along with pain relief. If the pain continues with these two options, the doctor might recommend radiation therapy. The main treatment strategy is chemotherapy due to how aggressive the cancer becomes in this stage, not only to the colon but to the lymph nodes.<sup>[2]</sup>

### Treatment

**Surgery:** In theory, non-hematological cancers can be cured if entirely removed by surgery, but this is not always possible. When the cancer has metastasized to other sites in the body prior to surgery, complete surgical excision is usually impossible. In the Halstedian model of cancer progression, tumours grow locally, then spread to the lymph nodes, then to the rest of the body. This has given rise to the popularity of local-only treatments such as surgery for small cancers. Even small localized tumours are increasingly recognized as possessing metastatic potential.

Examples of surgical procedures for cancer include mastectomy for breast cancer, prostatectomy for prostate cancer, and lung cancer surgery for non-small cell lung cancer. The goal of the surgery can be either the removal of only the tumour, or the entire organ. A single cancer cell is invisible to the naked eye but can regrow into a new tumour, a process called recurrence. For this reason, the pathologist will examine the surgical specimen to determine if a margin of healthy tissue is present, thus decreasing the chance that microscopic cancer cells are left in the patient.

In addition to removal of the primary tumour, surgery is often necessary for staging, e.g. determining the extent of the disease and whether it has metastasized to regional lymph nodes. Staging is a major determinant of prognosis and of the need for adjuvant therapy. Occasionally, surgery is necessary to control symptoms, such as spinal cord compression or bowel obstruction. This is referred to as palliative treatment.<sup>[3]</sup>

Surgery may be performed before or after other forms of treatment. Treatment before surgery is often described as neoadjuvant. In breast cancer, the survival rate of patients who receive neoadjuvant chemotherapy are no different to those who are treated following surgery. Giving chemotherapy earlier allows oncologists to evaluate the effectiveness of the therapy, and may make removal of the tumour easier. However, the survival advantages of neoadjuvant treatment in lung cancer are less clear.

### Treatment Approaches by The Medium of Therapies:

There are many different approaches for treating cancer, depending on the type of cancer, how advanced it is, what types of treatment are available, and what the goals of treatment are.

Many procedures and drugs are available to treat cancer, with many more being studied. Some are "local" treatments like surgery and radiation therapy, which are used to treat a specific tumour or area of the body.

### The various methods of therapies are being briefly discussed:

**1. Radiation Therapy:** Radiation therapy or radiotherapy, often abbreviated RT, RTx, or XRT, is a therapy using ionizing radiation, generally as part of cancer treatment to control or kill malignant cells.

Radiation therapy is commonly applied to the cancerous tumour because of its ability to control cell growth. Ionizing radiation works by damaging the DNA of cancerous tissue leading to cellular death. To spare normal tissues (such as skin or organs which radiation must pass through to treat the tumour), shaped radiation beams are aimed from several angles of exposure to intersect at the tumour, providing a much larger absorbed dose there than in the surrounding healthy tissue. Besides the tumour itself, the radiation fields may also include the draining lymph nodes if they are clinically or radiologically involved with the tumour, or if there is thought to be a risk of subclinical malignant spread. It is necessary to include a margin of normal tissue around the tumour to allow for uncertainties in daily set-up and internal tumour motion. These uncertainties can be caused by internal movement (for example, respiration and bladder filling) and movement of external skin marks relative to the tumour position.<sup>[4]</sup>

Basically, tumours can be broadly classified into the following types:

- radiosensitive tumours
- tumours of limited sensitivity
- radioresistant tumours



**Figure-3: Radiotherapy.**

**Medical use:** It is important to distinguish the radiosensitivity of a particular tumour, which to some extent is a laboratory measure, from the radiation "curability" of a cancer in actual clinical practice. For example, leukemias are not generally curable with radiation therapy, because they are disseminated through the body. Lymphoma may be radically curable if it is localised to one area of the body. Similarly, many of the common, moderately radioresponsive tumours are routinely treated with curative doses of radiation therapy if they are at an early stage. For example, non-melanoma skin cancer, head and neck cancer, breast cancer, non-small cell lung cancer, cervical cancer, anal cancer, and prostate cancer. Metastatic cancers are generally incurable with radiation therapy because it is not possible to treat the whole body. Before treatment, a CT scan is often performed to identify the tumour and surrounding normal structures. The patient receives small skin marks to guide the placement of treatment fields. Patient positioning is crucial at this stage as the patient will have to be placed in an identical position during each treatment. Many patient positioning devices have been developed for this purpose, including masks and cushions which can be moulded to the patient. third technique is to enhance the radio sensitivity of the cancer by giving certain drugs during a course of radiation

therapy. Examples of radio sensitizing drugs include Cisplatin, Nimorazole, and Cetuximab.

**Side effects associated with radio therapy:** Side effects are dose- dependent; for example, higher doses of head and neck radiation can be associated with cardiovascular complications, thyroid dysfunction, and pituitary axis dysfunction. Modern radiation therapy aims to reduce side effects to a minimum and to help the patient understand and deal with side effects that are unavoidable. The main side effects reported are fatigue and skin irritation, like a mild to moderate sun burn. The fatigue often sets in during the middle of a course of treatment and can last for weeks after treatment ends. The irritated skin will heal, but may not be as elastic as it was before.

**2. Chemotherapy:** Chemotherapy (often abbreviated to chemo and sometimes CTX or CTx) is a type of cancer treatment that uses one or more anti-cancer drugs (chemotherapeutic agents) as part of a standardized chemotherapy regimen. Chemotherapy may be given with a curative intent (which almost always involves combinations of drugs), or it may aim to prolong life or to reduce symptoms.<sup>[5]</sup>



**Figure-4: Chemotherapy.**

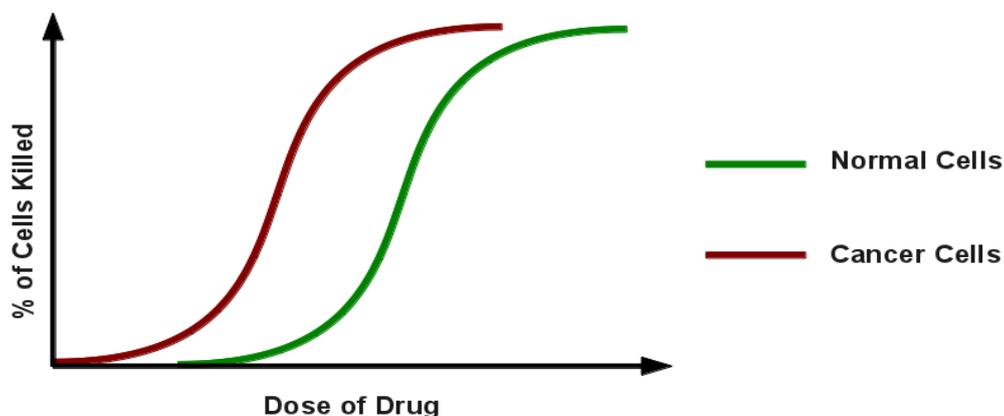
**Table-1: Drugs for neoplastic disease.**

Cancer type	Drugs	Acronym
Breast cancer	Cyclophosphamide, methotrexate, 5-fluorouracil, vinorelbine	CMF
	Doxorubicin, cyclophosphamide	AC
Hodgkin's lymphoma	Docetaxel, doxorubicin, cyclophosphamide	TAC
	Doxorubicin, bleomycin, vinblastine, dacarbazine	ABVD
	Mustine, vincristine, procarbazine, prednisolone	MOPP
Non-Hodgkin's lymphoma	Cyclophosphamide, doxorubicin, vincristine, prednisolone	CHOP
Germ cell tumour	Bleomycin, etoposide, cisplatin	BEP
Stomach cancer	Epirubicin, cisplatin, 5-fluorouracil	ECF
	Epirubicin, cisplatin, capecitabine	ECX
Bladder cancer	Methotrexate, vincristine, doxorubicin, cisplatin	MVAC
Lung cancer	Cyclophosphamide, doxorubicin, vincristine, vinorelbine	CAV
Colorectal cancer	5-fluorouracil, folinic acid, oxaliplatin	FOLFOX

Various techniques were employed in administration of chemotherapy. Neoadjuvant chemotherapy is given prior to a local treatment such as surgery, and is designed to shrink the primary tumour. It is also given for cancers with a high risk of micro metastatic disease. Adjuvant chemotherapy is given after a local treatment (radiotherapy or surgery). It can be used when there is little evidence of cancer present, but there is risk of

recurrence. It is also useful in killing any cancerous cells that have spread to other parts of the body. Maintenance chemotherapy is a repeated low-dose treatment to prolong remission.

**DOSAGE:** Standard method of determining chemotherapy dosage is based on calculated body surface area (BSA).

**Figure-5: Neoplasm graphics.**

Dose response relationship of cell killing by chemotherapeutic drugs on normal and cancer cells. At high doses the percentage of normal and cancer cells killed is very similar. For this reason, doses are chosen where anti-tumour activity exceeds normal cell death.

**Adverse effects:** Chemotherapeutic techniques have a range of side-effects that depend on the type of medications used. The most common medications affect mainly the fast-dividing cells of the body, such as blood cells and the cells lining the mouth, stomach, and

intestines. chemotherapeutic regimens can cause depression of the immune system, often by paralysing the bone marrow and leading to a decrease of white blood cells, red blood cells, and platelets. Anemia and thrombocytopenia may require blood transfusion. Neutropenia (a decrease of the neutrophil granulocyte count below  $0.5 \times 10^9$ /litre) can be improved with synthetic G-CSF (granulocyte-colony-stimulating factor, e.g., filgrastim, lenograstim. Hair loss (alopecia) can be caused by chemotherapy that kills rapidly dividing cells; other medications may cause hair to thin. These are most

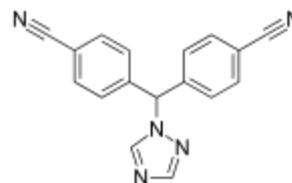
often temporary effects: hair usually starts to regrow a few weeks after the last treatment, but sometimes with a change in color, texture, thickness or style. Sometimes hair has a tendency to curl after regrowth, resulting in "chemo curls." Severe hair loss occurs most often with drugs such as doxorubicin, daunorubicin, paclitaxel, docetaxel, cyclophosphamide, ifosfamide and etoposide. Permanent thinning or hair loss can result from some standard chemotherapy regimens.<sup>[6]</sup>

**Limitations:** Chemotherapy does not always work, and even when it is useful, it may not completely destroy the cancer. People frequently fail to understand its limitations. In one study of people who had been newly diagnosed with incurable, stage 4 cancer, more than two-thirds of people with lung cancer and more than four-fifths of people with colorectal cancer still believed that chemotherapy was likely to cure their cancer. Here are a few possible causes of resistance in cancer, one of which is the presence of small pumps on the surface of cancer cells that actively move chemotherapy from inside the cell to the outside. Cancer cells produce high amounts of these pumps, known as p-glycoprotein, in order to protect themselves from chemotherapeutics. Medications to inhibit the function of p-glycoprotein are undergoing investigation, but due to toxicities and interactions with anti-cancer drugs their development has been difficult. Another mechanism of resistance is gene amplification, a process in which multiple copies of a gene are produced by cancer cells. This overcomes the effect of drugs that reduce the expression of genes involved in replication. With more copies of the gene, the drug can not prevent all expression of the gene and therefore the cell can restore its proliferative ability. Cancer cells can also cause defects in the cellular pathways of apoptosis (programmed cell death).<sup>[7]</sup>

**HORMONAL THERAPY:** Hormonal therapy in oncology is hormone therapy for cancer and is one of the major modalities of medical oncology (pharmacotherapy for cancer), others being cytotoxic chemotherapy and targeted therapy (biotherapeutics). It involves the manipulation of the endocrine system through exogenous or external administration of specific hormones, particularly steroid hormones, or drugs which inhibit the production or activity of such hormones (hormone antagonists). Because steroid hormones are powerful drivers of gene expression in certain cancer cells, changing the levels or activity of certain hormones can cause certain cancers to cease growing, or even undergo cell death.

**Aromatase inhibitors:** Aromatase inhibitors are an important class of drugs used for the treatment of breast cancer in postmenopausal women. At menopause, estrogen production in the ovaries ceases, but other tissues continue to produce estrogen through the action of the enzyme aromatase on androgens produced by the adrenal glands. When the action of aromatase is blocked, estrogen levels in post-menopausal women can drop to

extremely low levels, causing growth arrest and/or apoptosis of hormone-responsive cancer cells.<sup>[8]</sup>



**Letrozole:** Letrozole and anastrozole are aromatase inhibitors which have been shown to be superior to tamoxifen for the first-line treatment of breast cancer in postmenopausal women.

**Androgens:** Fluoxymesterone, an anabolic steroid (testosterone-like) medication, is occasionally used for the treatment of advanced breast cancer.

**Progestogens:** Progestins (progesterone-like drugs) such as megestrol acetate and medroxyprogesterone acetate have been used for the treatment of hormone-responsive, advanced breast cancer, endometrial cancer, and prostate cancer. Progestins are also used in the treatment of endometrial hyperplasia, a precursor to endometrial adenocarcinoma. The exact mechanism of action of these hormones is unclear, and may involve both direct effect on the tumour cells.

**Estrogens:** The estrogen diethylstilbestrol (DES) is occasionally used to treat prostate cancer through suppression of testosterone production. It was previously used in the treatment of breast cancer, but has been replaced by more effective and less toxic agents. Estrace is an estrogen which was also formerly used for antiandrogen therapy of prostate cancer.

**TARGETED THERAPY:** Targeted cancer therapies are expected to be more effective than older forms of treatments and less harmful to normal cells. Many targeted therapies are examples of immunotherapy (using immune mechanisms for therapeutic goals) developed by the field of cancer immunology. Thus, as immunomodulators, they are one type of biological response modifiers.

Targeted therapy or molecularly targeted therapy is one of the major modalities of medical treatment (pharmacotherapy) for cancer, others being hormonal therapy and cytotoxic chemotherapy. As a form of molecular medicine, targeted therapy blocks the growth of cancer cells by interfering with specific targeted molecules needed for carcinogenesis and tumour growth. There are targeted therapies for lung cancer, colorectal cancer, head and neck cancer, breast cancer, multiple myeloma, lymphoma, prostate cancer, melanoma and other cancers.<sup>[9]</sup>

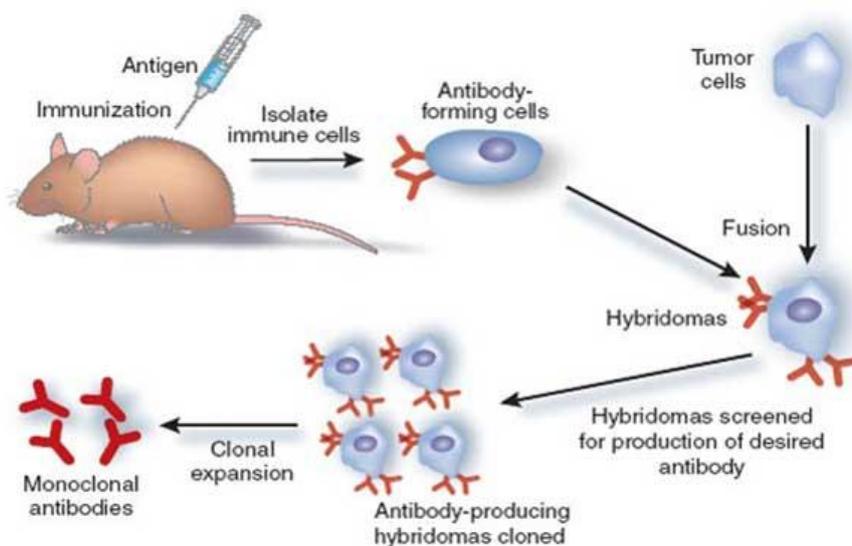
Biomarkers are usually required to aid the selection of patients who will likely respond to a given targeted therapy.

**Types:** The main categories of targeted therapy are currently small molecules and monoclonal antibodies.

**SMALL MOLECULES:** Many are tyrosine-kinase inhibitors. **Imatinib** (Gleevec, also known as STI-571) is approved for chronic myelogenous leukemia, gastrointestinal stromal tumour and some other types of cancer. Early clinical trials indicate that imatinib may be effective in treatment of dermatofibrosarcoma protuberans. **Gefitinib** (Iressa, also known as ZD1839), targets the epidermal growth factor receptor (EGFR) tyrosine kinase and is approved in the U.S. for non-small cell lung cancer. **Erlotinib** (marketed as Tarceva). Erlotinib inhibits epidermal growth factor receptor, and works through a similar mechanism as gefitinib. Erlotinib has been shown to increase survival in metastatic non-small cell lung cancer when used as second line therapy. Because of this finding, erlotinib has replaced gefitinib in this setting. **Sorafenib** (Nexavar), **Sunitinib** (Sutent), **Dasatinib** (Sprycel), **Lapatinib** (Tykerb), **Nilotinib** (Tasigna), **Bortezomib** (Velcade) is

an apoptosis-inducing proteasome inhibitor drug that causes cancer cells to undergo cell death by interfering with proteins. It is approved in the U.S. to treat multiple myeloma that has not responded to other treatments. **Monoclonal antibody therapy** is a form of immunotherapy that uses monoclonal antibodies (mAb) to bind monospecifically to certain cells or proteins. The objective is that this treatment will stimulate the patient's immune system to attack those cells. Some examples of licensed monoclonal antibodies include:

- **Pembrolizumab** (Keytruda) binds to PD-1 proteins found on T cells. Pembrolizumab blocks PD-1 and help the immune system kill cancer cells. It is used to treat melanoma, Hodgkin's lymphoma, non-small cell lung carcinoma and several other types of cancer.
- **Trastuzumab** targets the Her2/neu (also known as ErbB2) receptor expressed in some types of breast cancer
- **Rituximab** targets CD20 found on B cells. It is used in non-Hodgkin lymphoma.
- **Trastuzumab** targets the Her2/neu (also known as ErbB2) receptor expressed in some types of breast cancer



**Figure-6: Monoclonal antibody.**

**Angiogenesis Inhibitor:** An angiogenesis inhibitor is a substance that inhibits the growth of new blood vessels (angiogenesis). Some angiogenesis inhibitors are endogenous and a normal part of the body's control and others are obtained exogenously through pharmaceutical drugs or diet. Angiogenesis inhibitors were once thought to have potential as a "silver bullet" treatment applicable to many types of cancer, but the limitations of anti-angiogenic therapy have been shown in practice. Nonetheless, inhibitors are used to effectively treat cancer, macular degeneration in the eye, and other diseases that involve a proliferation of blood vessels.<sup>[10]</sup>

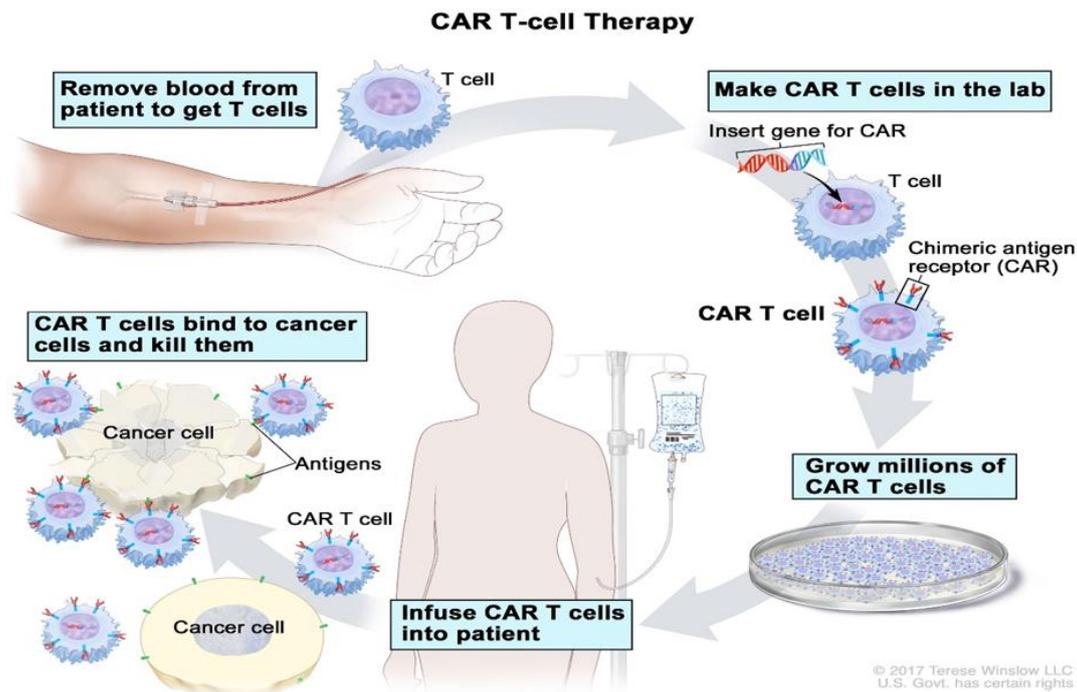
#### How do they work?

Angiogenesis inhibitors are unique cancer-fighting agents because they block the growth of blood vessels that support tumour growth rather than blocking the growth of tumour cells themselves. Angiogenesis inhibitors interfere in several ways with various steps in blood vessel growth. Some are monoclonal antibodies that specifically recognize and bind to VEGF. When VEGF is attached to these drugs, it is unable to activate the VEGF receptor. Other angiogenesis inhibitors bind to VEGF and/or its receptor as well as to other receptors on the surface of endothelial cells or to other proteins in the downstream signaling pathways, blocking their activities.

Some angiogenesis inhibitors are immunomodulatory drugs—agents that stimulate or suppress the immune system—that also have antiangiogenic properties. In some cancers, angiogenesis inhibitors appear to be most effective when combined with additional therapies. Approved angiogenesis inhibitors include: **Axitinib** (Inlyta®), **Bevacizumab** (Avastin®), **Cabozantinib** (Cometriq®), **Everolimus** (Afinitor®), **Lenalidomide** (Revlimid®), **Lenvatinib mesylate** (Lenvima®), **Pazopanib** (Votrient®), **Ramucirumab** (Cyramza®), **Regorafenib** (Stivarga®), **Sorafenib** (Nexavar®), **Sunitinib** (Sutent®), **Thalidomide** (Synovir, Thalomid®), **Vandetanib** (Caprelsa®), Ziv-aflibercept (Zaltrap®)

**Side effects:** It can include haemorrhage, clots in the arteries (with resultant stroke or heart attack), hypertension, impaired wound healing, reversible posterior leukoencephalopathy syndrome (a brain disorder), and protein in the urine. Gastrointestinal perforation and fistulas also appear to be rare side effects of some angiogenesis inhibitors.<sup>[11]</sup>

**Cancer immunotherapy:** It (sometimes called immunoncology) is the artificial stimulation of the immune system to treat cancer, improving on the immune system's natural ability to fight the disease. It is an application of the fundamental research of cancer immunology and a growing subspecialty of oncology. Cancer immunotherapy exploits the fact that cancer cells often have tumour antigens, molecules on their surface that can be detected by the antibody proteins of the immune system, binding to them. The tumour antigens are often proteins or other macromolecules (e.g., carbohydrates). Normal antibodies bind to external pathogens, but the modified immunotherapy antibodies bind to the tumour antigens marking and identifying the cancer cells for the immune system to inhibit or kill. **Tisagenlecleucel** (Kymriah), a chimeric antigen receptor (CAR-T) therapy, was approved by FDA in 2017 to treat acute lymphoblastic leukemia (ALL). This treatment removes CD19 positive cells (B-cells) from the body (including the diseased cells, but also normal antibody producing cells). **Axicabtagene ciloleucel** (Yescarta) is another CAR-T therapeutic, approved in 2017 for treatment of diffuse large B-cell lymphoma (DLBCL).



**Figure-7: Immunotherapy.**

#### What drugs are used for immunotherapy?

General Immunotherapies. This can help your immune system return to normal activity after chemotherapy. Other drugs including imiquimod (Zyclara), lenalidomide (Revlimid), pomalidomide (Pomalyst), and thalidomide (Thalomid) kick-start immune system reactions and are used to treat some cancers. Immunotherapy is not appropriate for all patients and all types of cancer. At this time, hematologists/oncologists at Penn Medicine use immunotherapy to treat the

following: Breast cancer. Hematologic (blood) cancers, including multiple myeloma and lymphoma.

Immunotherapy is a standard treatment for some types of cancer, for example melanoma that has spread. And it is in trials for other types of cancer. Immunotherapy uses our immune system to fight cancer. It works by helping the immune system recognise and attack cancer cells.<sup>[12]</sup>

**Side Effects Associated with Immunotherapy:** The most common side effects found are the following pain, swelling, soreness, redness, itchiness, rash.

**Symptom control & Palliative care:** Although the control of the symptoms of cancer is not typically thought of as a treatment directed at the cancer, it is an important determinant of the quality of life of cancer patients, and plays an important role in the decision whether the patient is able to undergo other treatments. Although doctors generally have the therapeutic skills to reduce pain, chemotherapy-induced nausea and vomiting, diarrhea, hemorrhage and other common problems in cancer patients, the multidisciplinary specialty of palliative care has arisen specifically in response to the symptom control needs of this group of patients. Pain medication, such as morphine and oxycodone, and antiemetics, drugs to suppress nausea and vomiting, are very commonly used in patients with cancer-related symptoms. Improved antiemetics such as ondansetron and analogues, as well as aprepitant have made aggressive treatments much more feasible in cancer patients. Cancer pain can be associated with continuing tissue damage due to the disease process or the treatment (i.e. surgery, radiation, chemotherapy). Although there is always a role for environmental factors and affective disturbances in the genesis of pain behaviors, these are not usually the predominant etiologic factors in patients with cancer pain. Some patients with severe pain associated with cancer are nearing the end of their lives, but in all cases palliative therapies should be used to control the pain. Issues such as social stigma of using opioids, work and functional status, and health care consumption can be concerns and may need to be addressed in order for the person to feel comfortable taking the medications required to control his or her symptoms. The typical strategy for cancer pain management is to get the patient as comfortable as possible using the least amount of medications possible but opioids, surgery, and physical measures are often required. Historically, doctors were reluctant to prescribe narcotics to terminal cancer patients due to addiction and respiratory function suppression. The palliative care movement, a more recent offshoot of the hospice movement, has engendered more widespread support for preemptive pain treatment for cancer patients. The World Health Organization also noted uncontrolled cancer pain as a worldwide problem and established a "ladder" as a guideline for how practitioners should treat pain in patients who have cancer. Cancer-related fatigue is a very common problem for cancer patients, and has only recently become important enough for oncologists to suggest treatment, even though it plays a significant role in many patients' quality of life.<sup>[13]</sup>

**Hospice in cancer:** Hospice is a group that provides care at the home of a person that has an advanced illness with a likely prognosis of less than 6 months. As most treatments for cancer involve significant unpleasant side

effects, a patient with little realistic hope of a cure or prolonged life may choose to seek comfort care only, forgoing more radical therapies in exchange for a prolonged period of normal living. This is an especially important aspect of care for those patients whose disease is not a good candidate for other forms of treatment. In these patients, the risks related to the chemotherapy may actually be higher than the chance of responding to the treatment, making further attempts to cure the disease impossible. Of note, patients on hospice can sometimes still get treatments such as radiation therapy if it is being used to treat symptoms, not as an attempt to cure the cancer.

**Research:** Clinical trials, also called research studies, test new treatments in people with cancer. The goal of this research is to find better ways to treat cancer and help cancer patients. Clinical trials test many types of treatment such as new drugs, new approaches to surgery or radiation therapy, new combinations of treatments, or new methods such as gene therapy. In addition to tumour angiogenesis, other processes related to tumour progression such as evasion of the immune system and tumour-induced neurogenesis are targets for the development of new therapies. A clinical trial is one of the final stages of a long and careful cancer research process. The search for new treatments begins in the laboratory, where scientists first develop and test new ideas. If an approach seems promising, the next step may be testing a treatment in animals to see how it affects cancer in a living being and whether it has harmful effects. Of course, treatments that work well in the lab or in animals do not always work well in people. Studies are done with cancer patients to find out whether promising treatments are safe and effective. Patients who take part may be helped personally by the treatment they receive. They get up-to-date care from cancer experts, and they receive either a new treatment being tested or the best available standard treatment for their cancer. At the same time, new treatments also may have unknown risks, but if a new treatment proves effective or more effective than standard treatment, study patients who receive it may be among the first to benefit. There is no guarantee that a new treatment being tested or a standard treatment will produce good results. In children with cancer, a survey of trials found that those enrolled in trials were on average not more likely to do better or worse than those on standard treatment; this confirms that success or failure of an experimental treatment cannot be predicted.<sup>[14]</sup>

**Exosome research:** Exosomes are lipid-covered microvesicles shed by solid tumours into bodily fluids, such as blood and urine. Current research is being done attempting to use exosomes as a detection and monitoring method for a variety of cancers. The hope is to be able to detect cancer with a high sensitivity and specificity via detection of specific exosomes in the blood or urine. The same process can also be used to more accurately monitor a patient's treatment progress.

Enzyme linked lectin specific assay or ELLSA has been proven to directly detect melanoma derived exosomes from fluid samples. Previously, exosomes had been measured by total protein content in purified samples and by indirect immunomodulatory effects. ELLSA directly measures exosome particles in complex solutions, and has already been found capable of detecting exosomes from other sources, including ovarian cancer and tuberculosis-infected macrophages. Exosomes, secreted by tumours, are also believed to be responsible for triggering programmed cell death (apoptosis) of immune cells; interrupting T-cell signaling required to mount an immune response; inhibiting the production of anti-cancer cytokines, and has implications in the spread of metastasis and allowing for angiogenesis. Studies are currently being done with "Lectin affinity plasmapheresis" (LAP), LAP is a blood filtration method which selectively targets the tumour-based exosomes and removes them from the bloodstream. It is believed that decreasing the tumour-secreted exosomes in a patient's bloodstream will slow down progression of the cancer while at the same time increasing the patient's own immune response.

**Complementary & alternative:** Complementary and alternative medicine (CAM) treatments are the diverse group of medical and health care systems, practices, and products that are not part of conventional medicine and have not been shown to be effective. "Complementary medicine" refers to methods and substances used along with conventional medicine, while "alternative medicine" refers to compounds used instead of conventional medicine. CAM use is common among people with cancer; a 2000 study found that 69% of cancer patients had used at least one CAM therapy as part of their cancer treatment. Most complementary and alternative medicines for cancer have not been rigorously studied or tested. Some alternative treatments which have been investigated and shown to be ineffective continue to be marketed and promoted.<sup>[15]</sup>

#### Special circumstances

**In pregnancy:** The incidence of concurrent cancer during pregnancy has risen due to the increasing age of pregnant mothers and due to the incidental discovery of maternal tumours during prenatal ultrasound examinations. Cancer treatment needs to be selected to do least harm to both the woman and her embryo/fetus. In some cases a therapeutic abortion may be recommended. Radiation therapy is out of the question, and chemotherapy always poses the risk of miscarriage and congenital malformations. Little is known about the effects of medications on the child. Even if a drug has been tested as not crossing the placenta to reach the child, some cancer forms can harm the placenta and make the drug pass over it anyway. Some forms of skin cancer may even metastasize to the child's body. Diagnosis is also made more difficult, since computed tomography is infeasible because of its high radiation dose. Still, magnetic resonance imaging works normally.

However, contrast media cannot be used, since they cross the placenta. As a consequence of the difficulties to properly diagnose and treat cancer during pregnancy, the alternative methods are either to perform a Cesarean section when the child is viable in order to begin a more aggressive cancer treatment, or, if the cancer is malignant enough that the mother is unlikely to be able to wait that long, to perform an abortion in order to treat the cancer.

**In utero:** Fetal tumours are sometimes diagnosed while still in utero. Teratoma is the most common type of fetal tumour, and usually is benign. In some cases, these are surgically treated while the fetus is still in the uterus.<sup>[16]</sup>

**Racial and social disparities:** Cancer is a significant issue that is affecting the world. Specifically, in the U.S, it is expected for there to be 1,735,350 new cases of cancer, and 609,640 deaths by the end of 2018. Adequate treatment can prevent many cancer deaths but there are racial and social disparities in treatments which has a significant factor in high death rates. Minorities are more likely to suffer from inadequate treatment while white patients are more likely to receive efficient treatments in a timely manner. Having satisfactory treatment in timely manner can increase the patient's likelihood of survival. It has been shown that chances of survival are significantly greater for white patients than for African American patients. The annual average mortality of patients with colorectal cancer between 1992 and 2000 was 27 and 18.5 per 100,000 white patients and 35.4 and 25.3 per 100,000 black patients. In a journal that analyzed multiple studies testing racial disparities when treating colorectal cancer found contradicting findings. The Veterans administration and an adjuvant trial found that there was no evidence to support racial differences in treating colorectal cancer. However, two studies suggested that African American patients received less satisfactory and poor-quality treatment compared to white patients. One of these studies specifically was provided by the Center for Intramural Research. They found that black patients were 41% less likely to receive colorectal treatment and were more likely to be hospitalized in a teaching hospital with less certified physicians compared to white patients. Furthermore, black patients were more likely to be diagnosed with oncologic sequelae, which is a severity of the illness in result of poorly treated cancer. Lastly, for every 1,000 patients in the hospital, there were 137.4 black patient deaths and 95.6 white patient deaths. In a breast cancer journal article analyzed the disparities of breast cancer treatments in the Appalachian Mountains. African American women were found to be 3 times more likely to die compared to Asians and two times more likely to die compared to white women. According to this study, African American women are at a survival disadvantage compared to other races. Black women are also more likely to receive less successful treatment than white women by not receiving surgery or therapy. Furthermore, The National Cancer Institute panel, identified breast

cancer treatments, given to black women, as inappropriate and not adequate compared to the treatment given to white women. From these studies, researchers have noted that there are definite disparities in the treatment of cancer, specifically who have access to the best treatment and can receive it in a timely manner. This eventually leads to disparities between who is dying from cancer and who is more likely to survive. The cause of these disparities is generally that African Americans have less medical care coverage, insurance and access cancer centers than other races. For an example, black patients with breast cancer and colorectal cancer were shown to be more likely to have medicaid or no insurance compared to other races. The location of the health care facility also plays a role in why African Americans receive less treatment in comparison to other races. However, some studies say that African Americans don't trust doctors and don't always seek the help they need and this explains why there are less African Americans receiving treatment. Others suggest that African Americans seek even more treatment than whites and that it is simply a lack of the resources available to them. In this case, analyzing these studies will identify the treatment disparities and look to prevent them by discovering potential causes of these disparities.

## CONCLUSION

There are many types of cancer treatment. The types of treatment that you have will depend on the type of cancer you have and how advanced it is. Some people with cancer will have only one treatment. But most people have a combination of treatments, such as surgery with chemotherapy and/or radiation therapy. You may also have immunotherapy, targeted therapy, or hormone therapy. Clinical trials might also be an option for you. Clinical trials are research studies that involve people. Understanding what they are and how they work can help you decide if taking part in a trial is a good option for you. When you need treatment for cancer, you have a lot to learn and think about. It is normal to feel overwhelmed and confused. But, talking with your doctor and learning all you can about all your treatment options, including clinical trials, can help you make a decision you feel good about. Treatment of cancer may include surgery, chemotherapy and radiation therapy. There are various types of cancer:

**Breast cancer:** Its treatment depends on the stage of cancer. It may consist of chemotherapy, radiation, hormone therapy and surgery. **Prostate cancer:** Some types of prostate cancer grow slowly. In some of these cases, monitoring is recommended. Other types are aggressive and require radiation, surgery, hormone therapy, chemotherapy or other treatments. **Basal cell cancer:** Treatments include prescription creams or surgery to remove the cancer. In some cases, radiation therapy may be required. **Skin cancer (melanoma):** Treatment may involve surgery, radiation, medication or in some cases, chemotherapy. **Colon cancer:** Colorectal cancer treatment depends on the size, location and how

far the cancer has spread. Common treatments include surgery to remove the cancer, chemotherapy and radiation therapy.

**Lung cancer:** Treatments vary but may include surgery, chemotherapy, radiation therapy, targeted drug therapy and immunotherapy. **Leukemia:** Treatment is highly variable. For slow-growing leukaemias, treatment may include monitoring. For aggressive leukaemias, treatment includes chemotherapy that's sometimes followed by radiation and stem-cell transplant. **Lymphoma:** Treatment may involve chemotherapy, medication, radiation therapy and rarely stem-cell transplant. The FDA has approved a form of gene therapy called CAR T-cell therapy. It uses some of your own immune cells, called T cells, to treat your cancer. Doctors take the cells out of your blood and change them by adding new genes so they can better find and kill cancer cells.

The goal of cancer treatment is to achieve a cure for your cancer, allowing you to live a normal life span. This may or may not be possible, depending on your specific situation. If a cure isn't possible, your treatments may be used to shrink your cancer or slow the growth of your cancer to allow you to live symptom free for as long as possible.

### Cancer treatments may be used as:

**Primary treatment:** The goal of a primary treatment is to completely remove the cancer from your body or kill all the cancer cells. Any cancer treatment can be used as a primary treatment, but the most common primary cancer treatment for the most common types of cancer is surgery. If your cancer is particularly sensitive to radiation therapy or chemotherapy, you may receive one of those therapies as your primary treatment.

**Adjuvant treatment:** The goal of adjuvant therapy is to kill any cancer cells that may remain after primary treatment in order to reduce the chance that the cancer will recur. Any cancer treatment can be used as an adjuvant therapy. Common adjuvant therapies include chemotherapy, radiation therapy and hormone therapy. Neoadjuvant therapy is similar, but treatments are used before the primary treatment in order to make the primary treatment easier or more effective.

**Palliative treatment:** Palliative treatments may help relieve side effects of treatment or signs and symptoms caused by cancer itself. Surgery, radiation, chemotherapy and hormone therapy can all be used to relieve symptoms. Other medications may relieve symptoms such as pain and shortness of breath. Palliative treatment can be used at the same time as other treatments intended to cure your cancer.

Many cancer treatments are available. Your treatment options will depend on several factors, such as the type and stage of your cancer, your general health, and your preferences. Together you and your doctor can weigh the

benefits and risks of each cancer treatment to determine which is best for you.

**Cancer treatment options include:**

**Surgery:** The goal of surgery is to remove the cancer or as much of the cancer as possible.

**Chemotherapy:** Chemotherapy uses drugs to kill cancer cells.

**Radiation therapy:** Radiation therapy uses high-powered energy beams, such as X-rays or protons, to kill cancer cells.

Radiation treatment can come from a machine outside your body (external beam radiation), or it can be placed inside your body (brachytherapy).

**Bone marrow transplant:** Your bone marrow is the material inside your bones that makes blood cells from blood stem cells. A bone marrow transplant, also known as a stem cell transplant, can use your own bone marrow stem cells or those from a donor. A bone marrow transplant allows your doctor to use higher doses of chemotherapy to treat your cancer. It may also be used to replace diseased bone marrow.

**Immunotherapy:** Immunotherapy, also known as biological therapy, uses your body's immune system to fight cancer. Cancer can survive unchecked in your body because your immune system doesn't recognize it as an intruder. Immunotherapy can help your immune system "see" the cancer and attack it.

**Hormone therapy:** Some types of cancer are fueled by your body's hormones. Examples include breast cancer and prostate cancer. Removing those hormones from the body or blocking their effects may cause the cancer cells to stop growing.

**Targeted drug therapy:** Targeted drug treatment focuses on specific abnormalities within cancer cells that allow them to survive.

**Cryoablation:** This treatment kills cancer cells with cold. During cryoablation, a thin, wand like needle (cryoprobe) is inserted through your skin and directly into the cancerous tumor. A gas is pumped into the cryoprobe in order to freeze the tissue. Then the tissue is allowed to thaw. The freezing and thawing process is repeated several times during the same treatment session in order to kill the cancer cells.

**Radiofrequency ablation:** This treatment uses electrical energy to heat cancer cells, causing them to die. During radiofrequency ablation, a doctor guides a thin needle through the skin or through an incision and into the cancer tissue. High-frequency energy passes through the needle and causes the surrounding tissue to heat up, killing the nearby cells.

**Clinical trials:** Clinical trials are studies to investigate new ways of treating cancer. Thousands of cancer clinical trials are underway.

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