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CANCER AND ANTICANCER DRUGS: A REVIEW

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ABSTRACT

The development of chemotherapy using conventional anticancer drugs the aim of this review is to evaluate the extent of anticancer drugs and anticancer plant sources using encology. This discovery of novel anticancer drugs of critical for pharmaceutical research and development and patient treatment Systematic investigation of efficient anticancer drugs could provide valuable insights into trends into the discovery of anticancer drugs which may contribute to systematic discovery of new anticancer drugs.

INTRODUCTION

Cancer is a disease characterized by uncontrolled multiplication and spread abnormal forms of the body's own cells. The branch of medicine concerned with the study, diagnosis, treatment and prevention of cancer of Oncology. Cancer may affect people at all ages, even fetuses, but the risk of most varieties increase with ages. All cancer begin in cells, the body's basic unit of life.

Determining what causes cancer is complex. Many things are known to increase the risk of cancer, including tobacco use, certain infections, radiation and lack of physical activity, obesity, and environmental pollutants. These can directly damage genes or combine with existing genetic faults within cells to cause the disease. Approximately five to ten percent of cancers are entirely hereditary.

The Body is made up of many types of cells. These cells grow and divide in a controlled way to produce more cells as they are required to keep the body healthy. When cells become old or damaged, they die and are replaced with new cells. However, Sometimes this orderly process goes wrong. The genetic material (DNA) of a cell can become damaged, producing mutations that affect normal cell growth and division. Cancer can be detected in a number of ways, including the presence of certain signs and symptoms, screening tests, or medical imaging. Once a possible cancer is usually treated with chemotherapy, radiation therapy and surgery. The chances of surviving the disease vary greatly by the type and location of the cancer and the extent of disease at the start of treatment. While cancer can affect people of all ages, and a few types of cancer are more common in children, the risk of developing cancer generally increases with age. In 2007, cancer caused about 13% of all human deaths worldwide (7.9 Million). Rates are rising as more people live to an old age and as mass lifestyle changes occur in the developing world. (1)

Classification of Leukemia:

1. **Acute Leukemia** is characterized by a rapid increase in the number of immature blood cells. Crowding due to such cells makes the bone Marrow unable to produce healthy blood cells. Immediate treatment is required in acute leukemia due to the rapid progression and accumulation of the malignant cells, which then spill over into the bloodstream and spread to other organs of the body. Acute forms of leukemia are the most common forms of leukemia in children.

2. **Chronic leukemia** is characterized by the excessive buildup of relatively mature, but still abnormal, white blood cells. Typically taking month or years to progress, the cells are produced at a much higher rate than normal, resulting in many abnormal white blood cells. Whereas acute leukemia must be treated immediately, chronic forms are sometimes monitored for some time before treatment to ensure maximum effectiveness of therapy.
3. **Acute lymphoblastic leukemia (ALL)** is the most common type of leukemia in young in young children. This disease also affects adults, especially those age 65 and older. Standard treatments involve chemotherapy and radiotherapy. The survival rates vary by age 85% in children and 50% in adults. Subtypes include precursor B acute lymphoblastic leukemia, precursor T acute lymphoblastic leukemia, Burkitt leukemia, and acute phenotypic leukemia.
4. **Chronic Lymphocytic Leukemia (CLL)** most often affects adults over the ages of 55. It sometimes occurs in younger adults, but it almost never affects children. Two-thirds of affected people are men. The five-year survival rate is 75% it is incurable, but there are many effective treatments. One subtype is B-cell pro-lymphocytic leukemia, a more aggressive disease. (1)

Sign and Symptoms of Leukemia

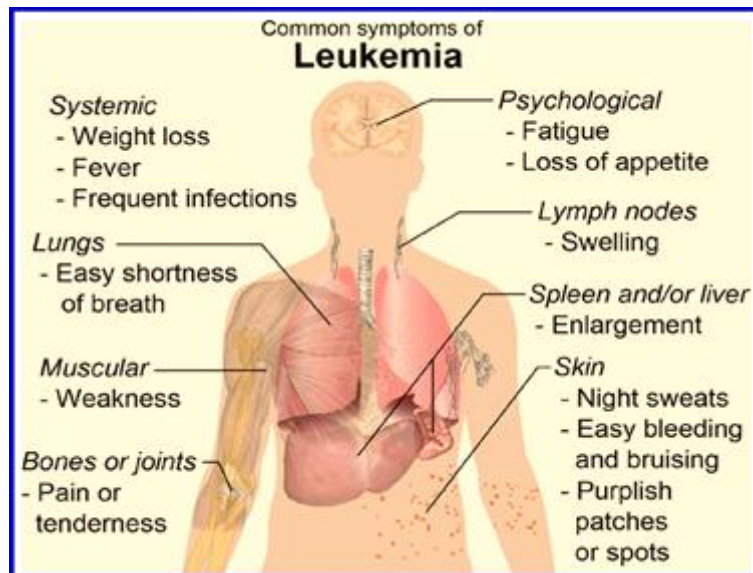


Fig. 1: Sign and Symptoms of Leukemia

Carcinoma

Carcinoma is the medical term for the most common type of cancer occurring in humans. Put simply, a carcinoma is a cancer that begins in a tissue that lines the inner or outer surface of the body, and that generally arises from cells originating in the endodermal or ectodermal germ layer during embryogenesis. More specifically, a carcinoma is a tumor tissue derived from putative epithelial cells whose genome has become altered or damaged to such an extent that the cells become transformed, and begin to exhibit abnormal malignant properties.

Pathogenesis of cancer:

Cancer occurs when a single progenitor cell accumulates mutations and other changes in the DNA, histones, and other biochemical compounds that make up the cell's biochemical components, the biochemical reactions that occur within the cell, and the biological interactions of that cell with other cells. Certain combinations of mutations in the given progenitor cell ultimately result in that cell (also called a cancer stem cell) displaying a number of abnormal, malignant cellular properties that, when taken together, are considered characteristic of cancer, including:

The ability to continue to divide perpetually, producing an exponentially (or near-exponentially) increasing number of new malignant cancerous “daughter cell” (uncontrolled mitosis);

The ability to penetrate normal body surfaces and barriers, and to bore into or through nearby body structures and tissues (local invasiveness);

The ability to spread to other sites within the body (metastasize) by penetrating or entering into the lymphatic vessels (regional metastasis) and / or the blood vessels (distant metastasis).

If this process of continuous growth, local invasion, and regional and distant metastasis is not halted via a combination of stimulation of immunological defenses and medical treatment interventions, the end result is that the host suffers a continuously increasing burden of tumor cells throughout the body. Eventually, the tumor burden increasingly interferes with normal biochemical functions carried out by the host's organs, death ultimately ensues.

Malignant neoplasms are exceptionally heterogeneous entities, reflecting the wide variety, intensity, and potency of various carcinogenic promoters. To date, no simple and comprehensive method for classifying them has yet been devised and accepted within the

scientific community. Traditionally, however, malignancies have generally been classified into various taxa using a combination of criteria, including:

- 1) **Adenocarcinoma:** (adeno=gland) Refers to a carcinoma featuring microscopic glandular related tissue cytology, tissue architecture, and / or gland related molecular products, e.g.mucin.
- 2) **Squamous cell carcinoma:** Refers to a carcinoma with observable features and characteristics indicative of squamous differentiation (intercellular bridges, keratinization, and squamous pearls).
- 3) **Aden squamous carcinoma:** Refers to a mixed tumor containing both adenocarcinoma and squamous cell carcinoma, wherein each of these cell types comprise at least 10% of the tumor volume. (1)

Histological types and variants of carcinoma:

1. **Anaplastic carcinoma:** Refers to a heterogeneous group of high-grade carcinomas that feature cells lacking distinct histological or cytological evidence of any of the more specifically differentiated neoplasm. The tumors are referred to as Anaplastic or Undifferentiated carcinomas.
2. **Large cell carcinomas:** Composed of large, monotonous rounded or overtly polygonal shaped cells with abundant cytoplasm.
3. **Small cell carcinoma:** Cells are usually round and are less than approximately 3 times the diameter of a resting lymphocyte and little evident cytoplasm. Occasionally, small cell malignancies may themselves have significant components of slightly polygonal and / or spindle shaped cells. (1)

Frequent organ sites of carcinoma

1. **Lung:** Carcinoma comprises > 98% of all lung cancers.
2. **Breast:** Nearly all breast cancers are ductal carcinoma.
3. **Prostate:** The most common form of carcinoma of the prostate is adenocarcinoma.
4. **Colon and rectum:** Nearly all malignancies of the colon and rectum are either adenocarcinoma lethal. (2)

Cancer – treatments of choice:

Introduction to cancer chemotherapy:

Chemotherapy: Chemotherapy is a kind of treatment that uses drugs to attack cancer cells. It is called a “systemic treatment” since the drug, entering through the blood stream, travels

throughout the body and kills cancer cells at their sites. Chemotherapy, often shortened to just “chemo” The drugs may rarely be intended to have a local effect, but in most cases, the intention is to destroy cancer cells wherever they may exist in the body.

Chemotherapeutic drugs are chemically designed to target cells that are dividing and growing rapidly. Once they reach the cancer cells, they act to retard their growth, eventually resulting in their destruction.

Chemotherapy may be given at home, in a clinic or in a hospital. The frequency of chemotherapy can be daily, weekly, monthly or an on-off schedule depending on the type of drug, the body’s response and the type of cancer. The chemotherapy is decided on the basis of the type of cancer. The dosage is calculated on the basis of the patient’s body weight and the drug’s toxicity.

The chemotherapy is concerned with the whole body.

Chemotherapy is used to treat:

Early-stage invasive breast cancer to get rid of any cancer cells that may be left behind after surgery and to reduce the risk of the cancer coming back.

Advanced-stage breast cancer to destroy or damage the cancer cells as much as possible.

In some cases, chemotherapy is given before surgery to shrink the cancer.

At present more than 50 anticancer drugs have been discovered. They are used in several ways:

Monotherapy or only one drug

Combination chemotherapy or a group of drugs which work together

Combined modality or chemotherapy along with other treatment such as surgery and radiotherapy

The drugs are delivered to the affected cells in the following forms:

Oral (tablet form, by mouth)

Intravenous or Intramuscular (injected by needle into a vein or muscle)

Intrathecal chemotherapy (injected through a needle in the back)

Working of Chemotherapy:

1. Chemotherapy medicines prevent cancer cells from growing and spreading by destroying the cells or stopping them from dividing.
2. Cancer cells tend to grow and divide very quickly with no order or control. Because they’re growing so fast, sometimes cancer cells break away from the original tumor

and travel to other places in the body. Chemotherapy weakens and destroys cancer cells at the original tumor site AND throughout the body.

3. Most normal cells grow and divide in a precise, orderly way. Still, some normal cells do divide quickly, including cells in hair follicles, nails the mouth, digestive tract, and bone marrow (bone marrow makes blood cells). Chemotherapy also can unintentionally harm these other types of/ rapidly dividing cells, possibly causing chemotherapy side effects.
4. When treating early breast cancer, it's fairly common for chemotherapy to be given after surgery, as soon as you recover. Doctors call this "adjuvant" chemotherapy because it's given in addition to surgery, which is considered the primary treatment.
5. In some cases, chemotherapy is given before surgery to shrink the cancer so that less tissue has to be removed. When chemotherapy is given before surgery, It's called "Neoadjuvant" chemotherapy.
6. In many cases, chemotherapy medicines are given in combination, which means you get two or three different medicines at the same time. These combinations are known as chemotherapy regimens. In early-stage breast cancer, standard chemotherapy regimens lower the risk of the cancer coming back. In advanced breast cancer, chemotherapy regimens make cancer responds differently to chemotherapy.(Ref.No.1)

Side effects of chemotherapy:

Since chemotherapy also affects normal actively dividing cells such as those in the bone marrow, the gastrointestinal tract, the reproductive system and in the hair follicles, most patients experience some degree of side effects, which may include any or all of the following:

1. **Nausea and Vomiting:** This is a common side effect of chemotherapy. It can be controlled with anti-sickness drugs (anti-emetics).
2. **Fatigue:** chemotherapy affects different people in different ways. Some find they can lead fairly normal lives during treatment, but many find they become tired and have to take things more slowly. Just do as much as you can and be careful not to over-strain. Taking short naps may help.

3. **Hair loss:** This is the least harmful side effect, yet can be the hardest to bear. The use of a cold compress around the scalp when taking chemotherapy helps stop hair loss to some extent. Hair will grow back surprisingly quickly once treatment is over.
4. **Susceptibility to infections:** When the drugs act on cancer cells, they also destroy normal cells including white blood cells, which fight infections. When white blood cells are in short supply, the body's immune system is weakened making you susceptible to infections. Any fever should be reported to the doctor. (Ref.No.1)

Facts about cancer:

Approximately 14 million new cases and 8.2 million cancer related deaths in 2012.

The number of new cases is expected to rise by about 70% over the next 2 decades.

Among men, the 5 most common sites of cancer diagnosed in 2012 were lung, prostate and stomach cancer.

Cancer deaths are due to the 5 leading behavioral and dietary risks: high body mass index, low fruit and vegetable intake, lack of physical activity, tobacco use, alcohol use.

Tobacco use is the most important risk factor for cancer causing around 20% of global cancer deaths and around 70% of global lung cancer deaths.

Cancer causing viral infections such as HBV and HPV are responsible for up to 20% of cancer deaths in low and middle income countries.

More than 60% of world's total new annual cases occur in Africa, Asia and Central and South America. These regions account for 70% of the world's cancer deaths.

It is expected that annual cancer cases will rise from 14 million in 2012 to 22 within the next 2 decades. (3)

Sign and symptoms:

You should know some signs and symptoms of cancer but remember, having any of these does not mean that you have cancer many other things cause these sign and symptoms, too.

1. Fever
2. Pain
3. Skin Changes
4. Recent Change in a wart or mole or any new skin change
5. Nagging cough
6. Breathlessness

7. Mouth or tongue ulcer
8. Sores they do not heal. (2)

FDA approved anticancer drugs

NUBEQA Darolutamide Tablets

The molecular weight is 398.85 and the molecular formula is $C_{19}H_{19}Cl N_6O_2$. The Structural formula is:

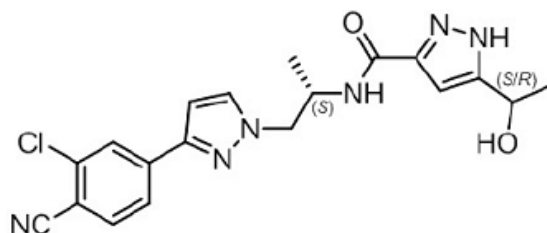


Fig. 2: Structure of Darolutamide

FDA Approved: Yes (First approve jully 30,2019)

Brand name :Nubeqa

Generic name :darolutamide

Dosage form : Tablets

Company : Bayer Healthcare Pharmaceuticals Inc.

Treatment for : Prostate Cancer

Nubeqa (darolutamide) is an androgen receptor inhibitor (ARi) indicated for the treatment of non-metastatic castration resistant prostate cancer (nmCRPC)

Turalio (Pexidartinib)

FDA Approved: Yes (First approved August 2, 2019)

Brand name: Turalio

Generic name: Pexidartinib

Dosage form: Capsules

Company: Daiichi Sankyo

Treatment for: Tenosynovial giant cell Tumor. It is kinase inhibitor indicated for the treatment of symptomatic tenosynovial giant cell tumor (TGCT) adults.

Hepatotoxicity: Turalio can cause serious and potentially fatal liver injury (see warnings and precautions) Turalio is available only through a restricted program called the turalio risk evaluation and mitigation strategy (rems) program (see warnings and precautions) (4)

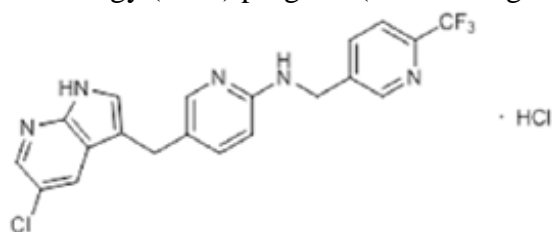


Fig. 3: Structure of Pexidartinib

CONCLUSION:

In this study we provided a comprehensive data source including anticancer drug. Cancer is the abnormal growth of cell in our bodies that can lead to death. For treatment of cancer there are very synthetic compounds are present but they have many adverse effects as compare to medicinal plant. That have anticancer activity sum medicinal plant like turmeric, Vinca, Taxus, Neem, Aloe vera, Broccoli etc. Hve chemical constituent as curcumin, Vincristine, Vinblastine, and also new FDA approval Drug in Anticancer also have sum anticancer drug Neubeqa (darolutamide), Turalio(Pexidartinib), Kanjinti, in compound have their in important role on treatment and prevention of cancer.

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