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Scientific research

University of Babylon

College of pharmacy

Study of side effects associated with Biotherapy (Herceptin) in Breast Cancer-Patients in Al Hilla city, Iraq

Research project

Submitted to the Council College of Pharmacy, university of Babylon in partial fulfillment of the requirements for degree of Bachelor's in microbiology

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

{ يَرْفَعِ اللَّهُ الَّذِينَ آمَنُوا مِنكُمْ وَالَّذِينَ أُوتُوا الْعِلْمَ دَرَجَاتٍ }

صدق الله العلي العظيم

إهداء

إلهي لايطيب الليل إلا بشكرك ولا يطيب النهار إلا بطاعتك
ولاتطيب اللحظات الا بذكرك .. ولا تطيب الآخرة إلا بعفوك...

ولا تطيب الجنة إلا برؤيتك ...

إلى من بلغ الرسالة وأدى الأمانة . ونصح الأمة .. إلى نبي الرحمة ونور العالمين

سيدنا محمد صلى الله عليه واله وسلم

لمن يكدح أطراف أصابعه ليمنحنا لحظة من السعادة لمن حصد الأشواك من طريقي ليمهد لي طريق المعرفة إلى القلب الكبير ... والدي العزيز.

لمن شرب الكأس فارغه ليعطيني قطرة من الحب لمن غذاني الحب والحنان إلى رمز الحب وبلسم الشفاء إلى القلب الأبيض أمي العزيزة.

إلى إخواني وأخواتي الذين ساعدوني ودعموني ووفروا لي الملاذ الآمن في أوقات الشدائد.

وللقلوب الطاهرة والطيبة والنفوس البريئة أصدقائي مساندتي في حياتي

شكر وتقدير

بِسۡمِ ٱللَّهِ ٱلرَّحۡمَٰنِ ٱلرَّحِيمِ، والحمد لله رب العالمين الذي وفقنا وأعاننا على انهاء هذا البحث والخروج به بهذه الصورة المتكاملة، فبالأمس القريب بدأنا مسيرتنا التعليمية ونحن نتحسس الطريق برهبة وارتباك، فرأينا أن (الصيدلة) هدفا سامياً وحبا وغاية تستحق السير لأجلها وأن بحثنا يحمل في طياته طموح شباب

يحلمون بصناعة مستقبل جميل يليق ببلدهم.

وانطلاقاً من مبدأ انه لا يشكر الله من لا يشكر الناس، فإننا نتوجه بالشكر الجزيل

للاستاذ المعلم الدكتورة القديرة " أ.د امل طالب السعدي "

التي رافقتنا في مسيرتنا لأنجاز هذا البحث وكان لها بصمة واضحة من خلال توجيهاتها البناءة والدعم الأكاديمي

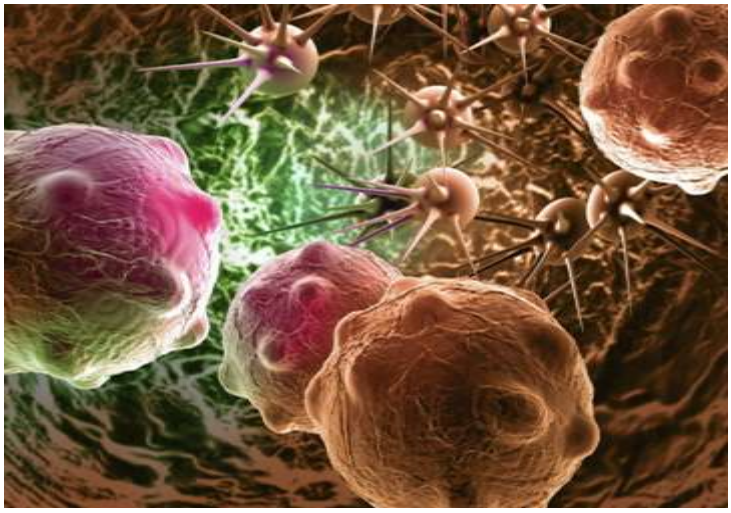
وكذلك الشكر موصول الى الاساتذة اعضاء لجنة المناقشة القديرين الذين تفضلوا بقراءة هذا البحث.

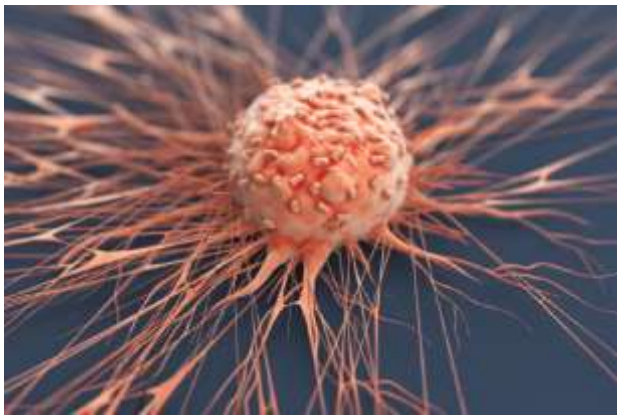
Introduction

What is cancer ?

Cancer is the name commonly used for what your doctor would call a malignant tumor . In everyday English , that means " harmful growth " . A cancer is a harmful growth of tissue somewhere in the human body . If this harmful growth is allowed to keep growing , it will eventually interfere with the physiological functions of the body's vital organs causing death .[1]

Benign tumors do not spread into, or invade, nearby tissues. When removed, benign tumors usually don’t grow back, whereas cancerous tumors sometimes do. Benign tumors can sometimes be quite large, however. Some can cause serious symptoms or be life threatening, such as benign tumors in the brain.[2]





Cancers are a group of diseases associated with abnormal growth of cells . Without any check the disease may keep on progressing ultimately leading to premature death . They can arise anywhere in the body and can affect people from all age groups , socio - economic strata and race Cancer is the leading cause of morbidity and mortality in the world . According to data by International Agency for Research on Cancer, there were 141 lakh new cancer cases , 82 lakh cancer deaths and 326 lakh people living with cancer in 2012 worldwide . In our own country , about 4.7 lakh new cases of cancer are detected annually . Cancer is responsible for death of about 3.5 lakh people annually in India itself . Lung cancer is the most common cause of death from cancer worldwide , estimated to

be responsible for nearly one in five deaths (15.9 lakhs deaths . 19.4 % of the total) . Amongst women , breast cancer is the commonest cause of death and is responsible for 5.2 lakh deaths annually .

These figures are just numerical representation of the vast damage caused by cancer worldwide . One might want to assume that with recent rapid developments in medical sciences , the incidence and prevalence of cancer may be coming down . Sadly that isn't so . According to WHO , within next two decades annual incidence of cancer may increase up to 220lakhs . With increase in adoption of modern lifestyle with unhealthy habits like lack of physical activity , decreased intake of fruit and vegetables , increasing use of tobacco , fast food , alcohol , etc. the incidence of cancer is expected to further increase .[3]

Cancer is a disease which may recur or persist throughout the lifetime of the cancer patient . Some cancer patients are never completely free of the disease . Other cancer patients may be free of the disease after treatment or may be in remission and then the cancer may recur . When patients are and may receive various types of treatment . The term cancer management refers to all the diagnostic procedures that go into the discovery of the patient's cancer , the treatment received , and the continuing follow - up of the patient after release from the hospital . Before cancer or any other disease can be properly treated , it must be diagnosed . Abnormal symptoms lead in remission , they may have cancer cells in their bodies but the cells are in a state which does not interfere with the functions of the body . Still other patients may never have a recurrence . In any case , the patient should be followed throughout life . The disease of cancer has to be viewed as a biological continuum , that is , an uninterrupted , ordered sequence of biological events . During his or her lifetime a cancer patient may make many visits to the hospital a person to seek medical attention . The physician's job is to identify diagnose the disease process which is causing these symptoms . The term diagnosis means identification of the nature of the disease and its manifestations . In making a diagnosis of cancer , the physician may employ a variety of diagnostic techniques

At one time , medical practitioners believed that when a treated cancer had not reappeared within five years , it was an indication that the patient was cured . We now know that a malignancy can reappear 10 , 15 , or even 20 years after treatment .[1]

TYPES OF CANCERS

According to conventional allopathic medicine there are over 150 types of cancers that can be categorized as follows : [4]

1) Lung , breast , prostate , skin , stomach , and colon cancers are called carcinomas and are characterized by solid tumors
2) Sarcomas are cancers that form in the bone and the soft tissues surrounding organs . They are solids and are the most rare and deadly forms of malignant tumors .
3) Leukemia forms in the blood and the bone marrow . These are non - solid tumors and are characterized by abnormal production of white blood cells .
4) Lymphomas are cancers of the lymph nodes . They are divided into two categories , Hodgkin's and Non - Hodgkin's .
5) Myelomas are rare tumors that form in the antibodies producing plasma cells in various tissues .

Carcinoma

Carcinoma refers to a malignant neoplasm of epithelial origin or cancer of the internal or external lining of the body. Carcinomas, malignancies of epithelial tissue, account for 80 to 90 percent of all cancer cases. Epithelial tissue is found throughout the body. It is present in the skin, as well as the covering and lining of organs and internal passageways, such as the gastrointestinal tract.

Carcinomas are divided into two major subtypes: adenocarcinoma, which develops in an organ or gland, and squamous cell carcinoma, which originates in the squamous epithelium.

Adenocarcinomas generally occur in mucus membranes and are first seen as a thickened plaque-like white mucosa. They often spread easily through the soft tissue where they occur. Squamous cell carcinomas occur in many areas of the body. Most carcinomas affect organs or glands capable of secretion, such as the breasts, which produce milk, or the lungs, which secrete mucus, or colon or prostate or bladder.

Sarcoma

Sarcoma refers to cancer that originates in supportive and connective tissues such as bones, tendons, cartilage, muscle, and fat. Generally occurring in young adults, the most common sarcoma often develops as a painful mass on the bone. Sarcoma tumors usually resemble the tissue in which they grow.

Examples of sarcomas are:

a) Osteosarcoma or osteogenic sarcoma (bone)
b) Chondrosarcoma (cartilage)

c) Leiomyosarcoma (smooth muscle)
d) Rhabdomyosarcoma (skeletal muscle)
e) Mesothelial sarcoma or mesothelioma (membranous lining of body cavities)
f) Fibrosarcoma (fibrous tissue)
g) Angiosarcoma or hemangioendothelioma (blood vessels)
h) Liposarcoma (adipose tissue)
i) Glioma or astrocytoma (neurogenic connective tissue found in the brain)
j) Myxosarcoma (primitive embryonic connective tissue)
k) Mesenchymous or mixed mesodermal tumor (mixed connective tissue types)

Myeloma

Myeloma is cancer that originates in the plasma cells of bone marrow. The plasma cells produce some of the proteins found in blood.

Leukemia

Leukemias ("liquid cancers" or "blood cancers") are cancers of the bone marrow (the site of blood cell production). The word leukemia means "white blood" in Greek. The disease is often associated with the overproduction of immature white blood cells. These immature white blood cells do not perform as well as they should, therefore the patient is often prone to infection. Leukemia also affects red blood cells and can cause poor blood clotting and fatigue due to anemia. Examples of leukemia include:

Myelogenous or granulocytic leukemia (malignancy of the myeloid and granulocytic white blood cell series)

Lymphatic, lymphocytic, or lymphoblastic leukemia (malignancy of the lymphoid and lymphocytic blood cell series)

Polycythemia vera or erythremia (malignancy of various blood cell products, but with red cells predominating)

Lymphoma

Lymphomas develop in the glands or nodes of the lymphatic system, a network of vessels, nodes, and organs (specifically the spleen, tonsils, and thymus) that purify bodily fluids and produce infection-fighting white blood cells, or lymphocytes. Unlike the leukemias which are sometimes called "liquid cancers," lymphomas are "solid cancers." Lymphomas may also occur in specific organs such as the stomach, breast or brain. These lymphomas are referred to as extranodal lymphomas. The lymphomas are subclassified

into two categories: Hodgkin lymphoma and Non-Hodgkin lymphoma. The presence of Reed-Sternberg cells in Hodgkin lymphoma diagnostically distinguishes Hodgkin lymphoma from Non-Hodgkin lymphoma.

Mixed Types

The type components may be within one category or from different categories. Some examples are:

a) adenosquamous carcinoma
b) mixed mesodermal tumor
c) carcinosarcoma
d) teratocarcinoma

BREAST CANCER [27]

Breast cancer is a malignancy originating from breast tissue. Disease confined to a localized breast lesion is referred to as early, primary, localized, or curable. Disease detected clinically or radiologically in sites distant from the breast is referred to as advanced or metastatic breast cancer (MBC), which is usually incurable.

EPIDEMIOLOGY

Two variables most strongly associated with occurrence of breast cancer are gender and age. Additional risk factors include endocrine factors (eg, early menarche, nulliparity, late age at first birth, and hormone replacement therapy), genetic factors (eg, personal and family history, mutations of tumor suppresser genes [BRCA1 and BRCA2]), and environmental and lifestyle factors (eg, radiation exposure, weight, height, and alcohol use).

Breast cancer cells often spread undetected by contiguity, lymph channels, and through the blood early in the course of the disease, resulting in metastatic disease after local therapy. The most common metastatic sites are lymph nodes, skin, bone, liver, lungs, and brain.

CLINICAL PRESENTATION

A painless, palpable lump is the initial sign of breast cancer in most women. The typical malignant mass is solitary, unilateral, solid, hard, irregular, and nonmobile . Nipple

changes are less commonly seen. More advanced cases present with prominent skin edema, redness, warmth, and induration.

Symptoms of MBC depend on the site of metastases but may include bone pain, difficulty breathing, abdominal pain or enlargement, jaundice, and mental status changes.

Many women first detect some breast abnormalities themselves, but it is increasingly common for breast cancer to be detected during routine screening mammography in asymptomatic women.

DIAGNOSIS

1. Initial workup should include a careful history, physical examination of the breast, three-dimensional mammography, and, possibly, other breast imaging techniques, such as ultrasound and magnetic resonance imaging (MRI).
2. Breast biopsy is indicated for a mammographic abnormality that suggests malignancy or for a palpable mass on physical examination.

STAGING

Stage (anatomical extent of disease) is based on primary tumor extent and size (T1_4), presence and extent of lymph node involvement (N1_3), and Carcinoma in situ or disease that has not invaded the basement membrane presence or absence of distant metastases (M0_1).

Early breast cancer

Stage 0: Carcinoma in situ or disease that has not invaded the basement membrane

Stage I: Small primary invasive tumor without lymph node involvement

Stage II: Involvement of regional lymph nodes

Locally advanced breast cancer

Stage III: Usually a large tumor with extensive nodal involvement in which the node or tumor is fixed to the chest wall

Advanced or metastatic breast cancer

Stage IV: Metastases in organs distant from the primary tumor

TREATMENT OF CANCER

The most important aim of cancer treatment is to achieve cure and secondly to palliate (life prolongation and relief of sufferings) where cure is not possible due to advanced disease. Nowadays, 30% of all cancers are routinely cured. Treatment should achieve cure whenever possible and that the quality of life is acceptable. The relief of symptoms may follow on from curative treatment, but where cure is not possible the speedy relief of symptoms becomes important.

There are traditionally three primary approaches to treating cancer: surgery, radiation and pharmacological therapy (including chemotherapy, targeted therapy, hormone therapy and immunotherapy). Some patients receive all three treatment modalities, while others receive one or two types. Costs to the patient vary depending on the type and extent of the treatment.

Surgical oncology is emerging as a specialist discipline; recent advances include more precise identification of the tumour margin, leading to reduced local recurrence.

New technology has facilitated minimal invasive surgery, laparoscopy and fibreoptic endoscopy .The greatly elevated cancer risk in individuals with familial cancer syndromes increasingly raises the prospect of preventive surgery, e.g. mastectomy in carriers of BRCA1/2 mutations and colectomy in patients with familial adenomatosis coli.

Surgical management is underpinned by recognition of the whole patient, and not merely focused on tumour excision.[6]

Radiotherapy is fundamental to the optimal management of cancer patients; its efficacy is affected by technical (the nature and delivery of the beam) and biological factors (tumour susceptibility modulated by hypoxia and drugs).

Provision of radiotherapy services is central to national cancer control strategies, requiring long-term planning and appropriate assessment of health care resources. Without recourse to sophisticated technology, effective radiotherapy for many cancers can be comprehensively provided at moderate cost.[6]

Pharmacological therapy:

Chemotherapy is basically used to control the disseminated subclinical disease and also, for elementary lesion treatment; moreover, this method could be followed by other modalities . For preventing drug resistance, different drug classes and modes of action are used in chemotherapy. The purpose of cytotoxic chemotherapy is to eradicate tumor cells

while sparing normal tissue, the sensitivity of tumors varies by histology and class of drugs with high cure rates in tumors that are highly sensitive to the drug administrate. [7]

Hormone therapy is used to treat cancers that are fueled by hormones, such as breast, prostate, and ovarian cancers. It uses surgery, or drugs to stop or block the body's natural hormones. This helps slow the growth of cancer cells. The surgery involves removing organs that make hormones: the ovaries or testes. The drugs are given by injection or as pills.[8]

Targeted therapy involves testing various types of cancer for genetic biomarkers that can predict the response to chemotherapeutic agents that attack the biomarkers directly or indirectly. In the past decade, the U.S. Food and Drug Administration (FDA) has approved approximately 40 new targeted therapies for 12 different cancers.[9,10,11]

Types of Targeted Therapy

Targeted therapies can be divided into four general categories:

1. monoclonal antibodies
2. small molecule inhibitors
3. antibody-drug conjugates
4. immunotherapy

Monoclonal antibodies are identical immunoglobulins that bind a specific antigen. Targeted oncology monoclonal anti- bodies are most commonly used to target an antigen on a cancer cell, leading to downregulation of oncogene signaling, or to flag tumor cells for destruction by the immune system. The anti-human epidermal growth factor receptor 2 (HER2) monoclonal antibodies trastuzumab (Herceptin) and pertuzumab (Perjeta) have drastically improved outcomes for HER2-positive breast cancer, which accounts for 15% to 25% of patients with breast cancer." All patients with breast cancer should undergo testing for HER2 overexpression. Trastuzumab binds to HER2 on tumor cells, leading to internalization and down- regulation of HER2, which is a pro- growth stimulator.[12,13]

Small molecule inhibitors impede a vast number of targets to slow or kill tumor cells. The majority target protein kinases that are highly active progrowth signaling initiators present in all cells and are exploited by many cancers. Examples of protein kinases targeted by small molecule inhibitors include the EGFR, anaplastic lymphoma kinase, and HER2. These protein kinases are also expressed across healthy tissues, so small molecule inhibitors also have systemic effects.[9]

Antibody-drug conjugates use a monoclonal antibody bound to a cytotoxic chemotherapy molecule by a peptide linker. This allows cytotoxic therapy to be delivered directly to, and cleaved inside, a tumor cell. When tumor cells undergo apoptosis, cytotoxic chemotherapy is released, killing additional nearby tumor cells. Normal host cells in the vicinity of the tumor may also be killed; this is called the bystander effect. Additionally, amounts of the cytotoxic agent can be released prematurely into the systemic circulation. Thus, antibody-drug conjugates can still r in systemic adverse effects such as fatigue, nausea, peripheral neuropathy, and thrombocytopenia.[14]

Immunotherapy is a broad term that includes monoclonal antibodies against cytotoxic T-lymphocyte-associated protein 4 (CTLA-4), programmed cell death protein 1 (Pl or programmed cell death ligand 1 (PD-L1), which capable of activating the adaptive immune system against tumor cells. These immunotherapy molecules inhibit negative immune regulation and, therefore, enhance antitumor immune responses.[15]

Results &discussion

The essential role of HER2 in the HER signaling network led to the development of anti-HER2 monoclonal antibodies (MAbs) for cancer therapy. In particular, the humanized MAb trastuzumab (Herceptin) has antitumor activity against HER2-overexpressing human breast tumor cells and is widely used for the treatment of women with HER2 overexpressing breast cancers. Trastuzumab induces HER2 receptor downmodulation and, as a result, inhibits critical signalling pathways (i.e. ras-Raf-MAPK and PI3K/Akt) and blocks cell cycle progression by inducing the formation of p27/Cdk2 complexes. Herceptin is believed to block intracellular signaling pathways. By attenuating the signal transduction downstream, Herceptin may promote apoptosis and arrest cell proliferation.[19,20,21]

THE HISTORY OF TREATMENT:

In 1986, Alex Ullrich, a scientist working for the biomedical company Genentech, discovered a protein that was created by the HER2 gene. HER2 is considered an oncogene that causes cancer to develop and grow. The HER2 gene belongs to a family of genes that stimulates cell growth. In 1998, it was discovered that the HER2 gene and protein were associated with adverse breast cancer outcomes. It was at this time that measuring HER2 entered the world of clinical medicine. Doctors began measuring HER2 protein levels in breast tumors and using this information to determine a prognosis and whether a patient required chemotherapy. The HER2 gene was considered active, or what doctors call overexpressed, in approximately 20-25% of breast cancers

For about a decade, HER2 was measured solely to predict prognoses. Then, in the early to mid-1990s, an antibody (called a monoclonal antibody) was developed that blocked the tumor-stimulating effects of the HER2 gene. The drug was called Herceptin (trastuzumab) and was developed by the company Genentech. Initially, as in other drug therapies, Herceptin was used to treat patients with metastatic disease. However, as the drug rang up successes in the metastatic setting, attention turned to using the drug in the adjuvant setting (given after surgery in curable breast cancer). As in the metastatic setting, adjuvant Herceptin found similar success. Finally, and much more recently, Herceptin markedly improved tumor shrinkage when given before surgery (neoadjuvant therapy)If there was one hero in the HER2-Herceptin story, it was Dr. Dennis Slamon, the current chairman of medical oncology at UCLA. It was through the efforts of Dr. Slamon that Genentech funded research leading to the development of Herceptin It is now 2020, and despite all of the advances of the last decade, we have just arrived at the beginning. There are now at least six drugs that inhibit the HER2 gene. There are also chemotherapy drugs that have been chemically attached to Herceptin, along with similar targeted drugs that we should see in clinical use in the very near future.[2]

The method of work included a visit to tumor centers in the city of Hilla in the province of Babylon from 6 december to 30 april, Under the direct supervision of the research supervisor, Dr. Amal Talib. On his first visit to the oncology center, the director of the center at Imam Al-Sadiq Hospital, Dr. Muhammad, gave an orientation lecture on cancer and the drugs used for treatment .The lecture included

how to properly deal with patients, taking into account their psychological aspects. where a tour was made for cancer patients who were taking Herceptin treatment and we discussed the patient about the side effects of the disease where They suffer from it, and an electronic questionnaire was also made and published in order to reach a larger number of cancer patients who take targeted therapy. Cooperation was made with the director of the tumor center, as well as with the medical staff in the tumor center in order to facilitate the research task

Aim of study

In the current study, the primary objective was to estimate the most common side effects in cancer patients undergoing Biotherapy (Herceptin) in Babylon Governorate, Iraq. A secondary objective was to evaluate possible relationships of side effects with the patient's age and gender.

Results and Discussion

"Herceptin" has been used since 1998 until now to treat more than 230,000 patients around the world suffering from metastatic breast cancer who have high levels of HER2 protein, and "Herceptin" is the only approved treatment for The treatment of HER2-positive breast cancer In addition, it provides patients with the best chance of surviving the disease.

Trastuzumab, a monoclonal antibody, was included in the World Health Organization's List of Essential Medicines in 2015 as a primary treatment for about 20% of breast cancers. It has shown high efficacy in the treatment of breast cancer at an early stage and, in some cases, in more advanced cases of the disease.[23]

Herceptin is used as an adjuvant drug for HER2-overexpressing breast cancer to prevent recurrence. It is also used to treat patients with metastatic breast cancer, adenocarcinoma of the stomach, or gastroesophageal junction cancer that overexpress HER2. The drug is used to treat HER2-positive breast cancer and to stop the growth of the cancer Herceptin is used together with other cancer medications when used to treat stomach cancer. Herceptin is only licensed for use in adults. Herceptin is an anti-cancer drug that targets the HER2 gene. Binds to HER2 receptors (docking stations) on cancer cells, preventing them from growing. To reduce the risk of breast cancer recurring from earlier stages of

HER2-positive breast cancer, either as part of a chemotherapy protocol or alone after an anthracycline-containing chemotherapy regimen (recurrence).[24]

SIDE EFFECTS:

1) Insomnia.
2) cough
3) rash
4) fluid retention
5) Headache
6) diarrhea
7) nausea
8) Urinary Tract
9) hot flashes
10) Back, joint or abdominal pain
11) fever
12) Chills
13) Depression
14) anemia
15) exhaustion
16) dizziness;
17) Low levels of platelets
18) fever
19) Sores that take longer than usual to heal
20) blood clot
21) swelling
22) loss of strength
23) shortness of breath
24) pain in chest
25) muscle cramps
26) Acute renal failure
27) numbness
28) tingling
29) allergy

This information is provided by Breastcancer.org.

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Cancer cells grow in an uncontrolled fashion. Herceptin works on the surface of the cancer cell by blocking the chemical signals that can stimulate this uncontrolled growth. Genes are like instruction manuals that tell each cell of your body how to grow, what kind of cell to become, and how to behave. Genes do this by ordering the cell to make special proteins that cause a certain activity — such as cell growth, rest, or repair. Some cancer cells have abnormalities in genes that tell the cell how much and how fast to grow. Sometimes the cancer cells have too many copies of these genes with abnormalities. When there are too many copies of these genes, doctors refer to it as "overexpression." With some forms of gene overexpression, cancer cells will make too many of the proteins that control cell growth and division, causing the cancer to grow and spread. Some breast cancer cells make too many copies of (overexpress) a particular gene known as HER2. The HER2 gene makes a protein known as a HER2 receptor. HER2 receptors are like ears, or antennae, on the surface of all cells. These HER2 receptors receive signals that stimulate the cell to grow and multiply. But breast cancer cells with too many HER2

receptors can pick up too many growth signals. This causes them to start growing and multiplying too much and too fast. Breast cancer cells that overexpress the HER2 gene are said to be HER2-positive. Herceptin works by attaching itself to the HER2 receptors on the surface of breast cancer cells and blocking them from receiving growth signals. By blocking the signals, Herceptin can slow or stop the growth of the breast cancer. Herceptin is an example of an immune targeted therapy. In addition to blocking HER2 receptors, Herceptin can also help fight breast cancer by alerting the immune system to destroy cancer cells onto which it is attached.

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Is Herceptin right for you?
Herceptin is used to treat breast cancers that are HER2-positive. There are several tests used to find out if breast cancer is HER2-positive. Two of the most common tests are: IHC (ImmunoHistoChemistry) The IHC test uses a chemical dye to stain the HER2 proteins. The IHC gives a score of 0 to 3+ that measures the amount of HER2 proteins on the surface of cells in a breast cancer tissue sample. If the score is 0 to 1+, it's considered HER2-negative. If the score is 2+, it's considered borderline. A score of 3+ is considered HER2-positive. If the IHC test results are borderline, it's likely that a FISH test will be done on a sample of the cancer tissue to determine if the cancer is HER2-positive. FISH (Fluorescence In Situ Hybridization) The FISH test uses special labels that attach to the HER2 proteins. The special labels have chemicals added to them so they change color and glow in the dark when they attach to the HER2 proteins. This test is the most accurate, but it is more expensive and takes longer to return results. This is why an IHC test is usually the first test done to see if a cancer is HER2-positive. With the FISH test, you get a score of either positive or negative (some hospitals call a negative test result "zero"). Learn more about HER2 status.

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What to expect when taking Herceptin
Herceptin can only be given by intravenous (IV) infusion, which means it is delivered directly into your bloodstream through an IV or a port. The first dose of Herceptin takes about 90 minutes. After that, it only takes about 30 minutes to get other doses of Herceptin. Your Herceptin treatment schedule will depend on whether you are receiving

it with other medicines. You can talk to your doctor about your treatment schedule options. If you've been diagnosed with early-stage HER2-positive breast cancer, you'll likely receive Herceptin together with a chemotherapy regimen. You will receive it for a specific amount of time. If you've been diagnosed with metastatic HER2-positive breast cancer, you will keep being treated with Herceptin as long as you are getting benefits from the medicine and aren't having troubling side effects. It's important to know that women who are pregnant or planning to get pregnant should not take Herceptin. Herceptin can harm the developing fetus. If there is any chance you can become pregnant, you must use effective birth control while you're taking Herceptin and for at least 7 months after your last dose. Also, women who are breastfeeding or plan to breastfeed shouldn't take Herceptin. Together, you and your doctor will decide if you should take Herceptin or breastfeed.

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Herceptin side effects
Like almost all medicines, Herceptin can cause side effects, some of them severe. The most common side effects of Herceptin are: headache diarrhea nausea chills fever heart problems infection insomnia cough rash If you are receiving Herceptin with chemotherapy, you may also experience chemotherapy side effects . Herceptin also may cause serious side effects, including: Heart problems Herceptin may cause serious heart problems, including some that don't have symptoms, such as reduced heart function, and some that do have symptoms, such as congestive heart failure. Symptoms to watch for include swelling of the ankles or legs, shortness of breath, cough, or weight gain of more than 5 pounds in less than 24 hours. Contact your doctor immediately if you have any of these symptoms. Your risk of heart problems is higher if you are receiving Herceptin in combination with anthracycline chemotherapy. Before starting Herceptin therapy, you should have an echocardiogram or a MUGA (multigated blood-pool imaging) scan to check how well your heart is functioning. An echocardiogram uses sound waves to take detailed pictures of the heart as it pumps blood. For this quick test, you lie still for a few minutes while a device that gives off sound waves is briefly placed on your ribs, over your heart. There is no radiation exposure with this test. A MUGA scan takes about an hour. In this test, a tiny amount of radioactive material is injected into a vein in your arm. This material temporarily hooks onto your red blood cells. You lie still while a special camera that can detect the radioactive material takes pictures of the blood flow through

your heart as it beats. Your doctor will continue to monitor your heart function while you are receiving Herceptin, as well as after you complete treatment. Lung problems
Herceptin may cause inflammation of the lungs, which can be life-threatening. Symptoms include trouble breathing, cough, tiredness, and fluid in the lungs.

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Donate to support free resources and programming for people affected by breast cancer.

Herceptin biosimilars
Herceptin is a monoclonal antibody, "biologic" drug. This means that it is made from living organisms, in this case a protein from a mouse cell. A monoclonal antibody is a type of protein made in the lab that can bind to substances in the body, including cancer cells. Each monoclonal antibody is made so that it binds only to one substance. Herceptin binds to the HER2 receptor proteins in cancer cells. Because they are made from living organisms, biologic drugs are much more complex to make than conventional drugs that are made from a mixture of chemicals. The chemical structure of conventional drugs can be easily identified and duplicated, which is why there are so many generic drugs on the market. A biosimilar is a new type of biologic drug. A biosimilar is almost identical to a biologic drug that is already approved by the FDA (or similar organizations in other countries). It can help to think of a biosimilar as a generic version of a biologic drug, though that comparison isn't completely accurate.

This information is provided by Breastcancer.org.
Donate to support free resources and programming for people affected by breast cancer.

Conclusions

Although Herceptin is one of the important preventive treatment for breast cancer approved worldwide, which has recorded very high cure rates, it is associated with a set of side effects that cannot be overlooked and that may be affected by the age of the patient.

REFERENCES:

1. Louisiana Regional Medical Program under the direction of C.Dennis Fink, Ph.D., Program Director, HumRRO and Robert F. Ryan, M.D., Technical Advisor, Tulane University.
2. U.S. Department of Health and Human Services ,National Institutes of Health ,National Cancer Institute USA.gov
3. "Tata Memorial Centre - About Us" www.actrec.gov.in. Retrieved 18 January 2021
4. Beating Cancer with Natural Medicine 2003 by Michael I am. All rights reserved. ISBN: 1-4107-3244-4 (e-book)
5. Farhad Islami, MD, PhD, Surveillance and Health Services Research Program, American Cancer Society Ahmedin Jemal, DVM, PhD, Surveillance and Health Services Research Program, American Cancer Society
6. Porter A, Aref A, Chodounsky Z, Elzawawy A, Manatrakul N, Ngoma T, Orton C, Van't Hooft E, Sikora K (1999) A global strategy for radiotherapy: a WHO consulta- tion. Clin Oncol (R Coll Radiol), 11: 368-370. Price P, Sikora K, eds (2000) Treatment of Cancer, 4th Edition, London, Chapman and Hall.
7. Greenhalgh TA, Symonds RP. Principles of chemo- therapy and radiotherapy. Obstet Gynaecol Reprod Med 2014; 24: 259-65
8. Doroshow JH. Approach to the patient with cancer. In: Goldman L, Schafer AI, eds. Goldman-Cecil Medicine. 26th ed. Philadelphia, PA: Elsevier; 2020:chap 169.
9. Prasad V, Gale RP The ASCO Post. What precisely is precision oncology-and will it work? January 25, 2017. AccessedMarch1,2020.https://www.ascopost.com/issues/january-25-2017/what-precisely-is- precision-oncology-and-will-it-work/
10.. Hyman I Collins FS, Varmus H. A new initiative on precision medicine. N Engl J Med. 2015;372(9):793-795.

11. U.S. Food and Drug Administration. 2010 notifications. Updated February 13, 2018. Accessed December 18, 2019. https://www.fda.gov/drugs/resources-information-approved-drugs/2010-notifications
12. Slamon DJ. Godolphin W. Jones LA, et al. Studies of the HER-2/neu proto-oncogene in human breast and ovarian cancer. Science. 1989; 244(4905) 707-71
13. Wolff AC. Hammond MEH, Allison KH, et al. Human epidermal growth factor receptor 2 testing in breast cancer. American Society of Clinical Oncology/College of American Pathologists clinical practice guideline focused update. J Clin Oncol 2018:36(20):2105-2122

14. Thomas A, Teicher BA, Hassan R Antibody-drug conjugates for cancer therapy Lancet Oncol. 2016 175) 254-262
15. Haslam A, Prasad V. Estimation of the percentage of US patients with cancer who are eligible for and respond to checkpoint inhibitor immu- 41. Drilon A notherapy drugs. JAMA Netw Open. 2019,2(5):e192535 42
16. Herbst RS. Review of epidermal growth factor receptor biology. Int J Radiat Oncol Biol Phys 2004;59 (2 suppl)
17. Herceptin [package insert]. South San Francisco, California; Genentech I; 2006
18. book by Robert Bazel" Herceptin
19. Antibody-Drug Conjugates-A Tutorial Review. (https://pubmed.ncbi.nlm.nih.gov/34063364/) Baah S, et al. Molecules
20. Targeted therapeutic options and future perspectives for HER2-positive breast cancer. (https://pubmed.ncbi.nlm.nih.gov/31637013/) Wang J, et al. Signal Transduct Target Ther. 2019. PMID: 31637013 Free PMC article
21. ERBB1- and ERBB2-Positive Medullary Thyroid Carcinoma: A Case Report. (https://pubmed.ncbi.nlm.nih.gov/29642647/) Minuto M, et al.
22. 1Slamon DJ, Neven P, Chia S, et al. Overall survival with ribociclib plus fulvestrant in advanced breast cancer. N Engl J Med. Published online December 11, 2019. doi:
23. Oncology Nursing Clinical Reference - Shirley E. Otto 2004
24. Mosby's Canadian Nursing Drug ,Linda Skidmore-Roth, Faith Richardson 2020.
25. Biology in Context for Cambridge International AS & A Level,Glen Toole, Susan Toole 2015
26. Tarascon Pharmacopoeia 2017,FAAEM ,FACMT, FACEP, Editor in Chief, Richard J. Hamilton 2016
27. Breast Cancer, authored by Bonnie Lin Boster, Neelam K. Patel, and Laura Boehnke