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A Review of Drugs for Breast Cancer

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CERTIFICATE

This is to certify the review work Report embodied in this thesis entitled "A SPECIFIC MEDICATION OF BREAST CANCER "was compiled by Khushbu patel (Enrollment no:-172614290002)studying at sigma institute of pharmacy(261) for partial fulfilment of B.pharm degree to be awarded by Gujrat Technological University.This review work has been compiled under my supervision and is to my satisfaction.

DECLARATION

We here by certify that we are the sole authors of this review work report andthat neither any part of this review work report nor the whole of the review work report has been submitted for a degree to any other university or institution.

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ABSTRACT:-

Breast cancer is a disease in which cells inside the breast grow out of the control. These are different the kind of breast on which cells in the breast turn into the cancer. Breast cancer is the most frequently diagnosed cancer among the women. In this review focused on different treatment therapy of breast cancer with their pharmacological activity generally we can prevent or reduce breast cancer by following some change in life style that prevent the cancer always keep on weight in check , be physically active , eat fruits and vegetables , avoid alcohol and smoke, breast feed of possible , avoid birth control pills particularly age after 35, avoiding menopausal hormones. Tamoxifen and raloxifen lower the risk of breast cancer in women at high risk of disease. In this we also have discussed there are ways to treat the breast cancer by the different type of surgery like lumpectomy and axillary, mastectomy . radiation therapy following BCT (breast conserving therapy)and RT(radiation therapy) are commonly used to r4duce the breast cancer and also it's produce less side effects . among ,currently available treatment is chemotherapy that is expensive option but, none of them is safe . these are many types chemotherapy used to treat breast cancer include docetaxel(tamotere), paclitaxel(taxol), doxorubicin , epirubicine (ellence

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) , pegylated liposomal doxorubicine , capecitabine , carboplatine , cisplatine , fluorouracil , methotrexate , vinorelbine . overview in this mainly concerned on commone pharmacological actionof drugs , their adverse effect and drugsinteraction . Ultimately women can prevent the breast cancer by changing their life style.

Keywords:- breast cancer, ductal carcinoma in situ(DCIS) , invasive cancer , non-invasive cancer , chemotherapy , radiation therapy , medication for breast cancer.

I. INTRODUCTION:-

Breast cancer is the most common invasive cancer in women and the second leading cause of cancer death in women after lung cancer.

Breast cancer refers to cancers originating from breast tissue, most commonly from the inner lining of milk ducts or the lobules that supply the ducts with milk.

Breast cancer is about 100 times more commone in women than in men, althrough males tend to have poorer outcomes due to delays in diagnosis.

Cancer cells are very similar to cells of the organism from which they origibnated and have similar (but not identical)DNA and RNA.this is the reason why they are not very often detected by the immune system,in particular,if it is weakened[[1]].

Cancer cells are formed from normal cells due to a modification/mutation of DNA and /or RNA. These modifications can occur spontaneously ill Law of thermodynamics-increase of entropy or they may be induced by other factors such as ;nuclear radiation ,electromagnetic radiation ,chemicals in the air,water and food mechanical cell-level injury,free radicals ,ageing of DNA and RNA.,etc. all these can produce mutatios that may start cancer.

Cancer can be called therefore"entropic disease" since it is associated with the increase of entropy of the organism to the point where the organisum cannot correct this itself external intervention is required to allow the organism to return to a stable entropic state[[2]].

Cancer devepols if the immune system is not working properly and /or the amount of cells produced is too great for the immune system to eliminate[[3]].The rate of DNA nad RNA mutations can be too high under some conditions such as; unhealthy emironment (due to radiation, chemiicals,etc.[[4]]). Poor diet [[5]],people with genetic predispositions to mutations[[6]] and people of advanced age {about 80-75}[[7]].

The cell cycle:-In cancerous cells, the process of cell division is disrupted and unregulated, resulting in cell proliferation and tumor growth. The normal cell cycle is presented in figer.

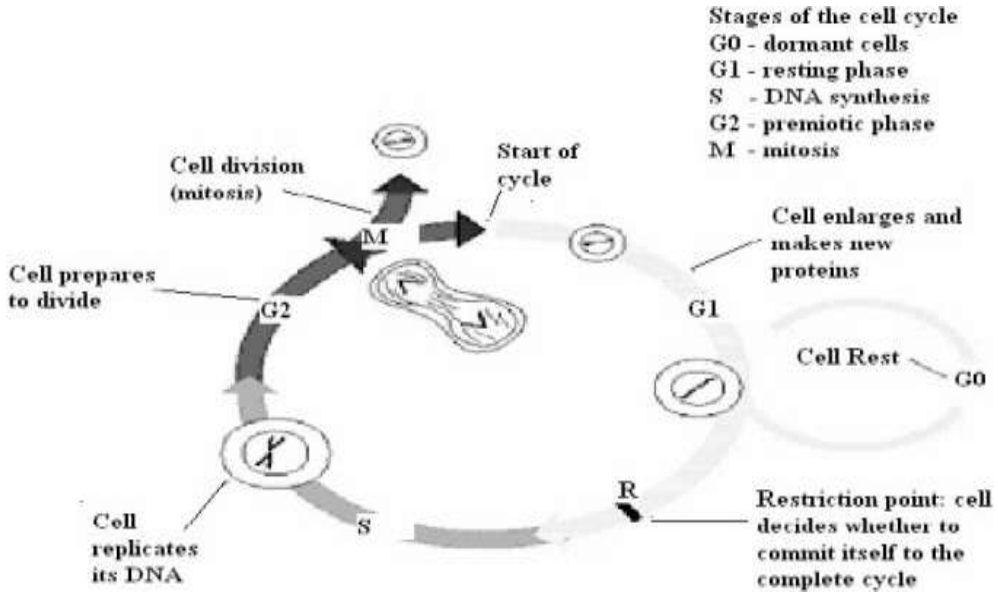

Figure 1(cell cycle)

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BREAST CANCER:

Breast cancer is a disease in which cells in the breast grow out of control .these are different kinds of breast cancer .the kind of breast cancer dependes on which cells in the breast turn into cancer.

The breast cancert is composed of two main types of tissues i.e., glandular tissues and stromal (supporting)tissue . glandur tissues house the milk – producing glands (lobules) and the ducts(the milk passages) while stromal tissues include fatty and fibrous connective tissue of the breast .the breast is also made up of lymphatic tissue-immune system tissue that removes cellular fluids and waste[[8]].

There are several types of tumors that may develop within different areas of the breast. Most tumors are the result of benign (non-cancerous) change within the breast.for,example, fibroystic change is a non-cancerous condition in which women develop cysts (accumulated packets of fluid),fibrosis (formation of scar-like connective tissue),Lumpiness, and areas of thickening , tenderness, or breast pain .

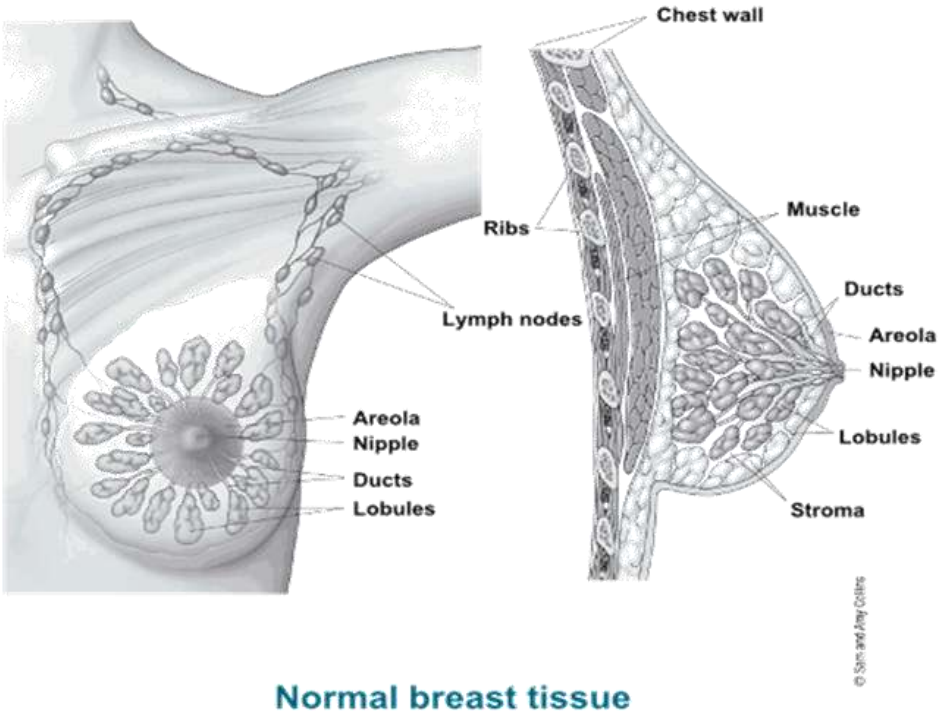

Figure 2(structure of breast)

Mostly ,Breast cancers can start from different parts of the breast.,

- Most breast cancers begin in the ducts that carry milk to the nipple (ductal cancers) [[10]].
- Some start in the gland that make breast milk(lobular cancers)[[10] below]
- There are also other types of breast cancer that are less common like phyllodes tumor and angiosarcoma.
- A small number of cancer start in other tissues in breast .these cancers are called SARCOMAS and LYMPHOMAS and are not really through of as breast cancers.

➢ **History:-**

The most commone cancer in US women and 2nd leading cause of cancer death is breast cancer. In US, breast cancer is rapidly increasing with the age. They are also rising rapidly in several Asian countries(e.g., in japan) which have the lowest incidence rates .these rapid increases may mean that environmental factors are responsible .incidence rates rise greatly with age until the last 40s.US women at highest risk of breast cancer are jewish women, urban women, single women, and women living in the northern US. Women at lowest risk include Mormon and seventh-day Adventist women, Hispanic and Asian women, rural women,women living in the southern US, and married women. Factors that have a relative risk

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greater than 2 are mother and sister with history of breast cancer,especially if diagnoses at an early age,;atypical epithelial cells in nipple aspirate fluid ;nodular densities on the mammogram ;history of cancer in 1 breast ;mother or sister with history of breast cancer; biopsy-confirmed benign proliferative breast disease; hyperplastic epithelial cells without atypia in nipple aspirate fluid ; and radiation to chest in moderate to high doses.

Other types of breast cancer ,like HER2+ breast cancer is the gene cancer. ,and that is mostly shown in women. In California , los angeles,medical researches understand the links between HER2+ and various types of cancer.they found vary high levels of HER2 in about 25% breast cancers that this was associated with a higher risk of recurrence, metastasis , and lower overall survival rates.HER2+ positive breast cancer ,as it came to be known, was identified as a specific subtype of the disease , noted for it`s aggressive behaviour and poor prognosis.[[11]].then ,following a series of clinical trials, the US food and drug administration (FDA) approved the HER2+ specific monoclonal antibody trastuzumab for use in treating patients with metastatic HER2+ breast cancer. But , other types of breast cancer are rapidly growth.

Ovarian hormones appear to stimulate cell division in the breast ,thus elevated levels may be risk factors. Exogenous hormones may lso increase the risk .women are exposed to these exogenous hormones through estrogen replacement therapy, progestin only pills, oral contraceptives , long acting injectable contraceptives, and diethylstilbestrol. Postmenopausal obesity increases the risk while premenopausal obesity decreases the risk . A high fat diet in childhood and adolescence may increase the risk.alcohole drinking may also increase the risk .older, white and nulliparous women are more likely to have estrogen receptore-positive cancers. breast cancer in males tends to share the same risk factors as well as it`s own unique factors. Prevention of postmenopausal obesity is the only established primary prevention effort. Screening is the only secondary prevention means.

- **TYPES OF BREAST CANCER :-**

There are several types of breast cancer, and they are divided into two main categories**: invasive** and **non-invasive**or in situ**.** While invasive cancer has spread from the breast ducts or glands to other parts of the breast[[12]]., Non-invasive cancer has not spread from the original tissue.

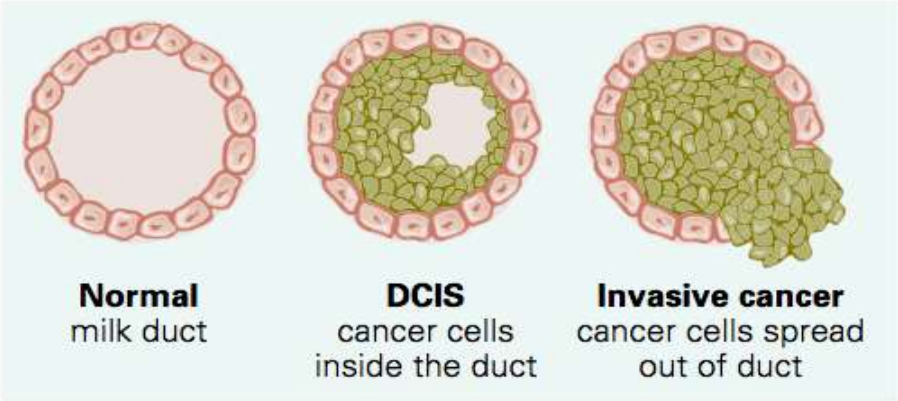

Fig 2: Normal cells lining a milk duct may develop into DCIS; sometimes this will progress to invasive cancer.

Figure 3

There two categories are used to describe the **most common types of breast cancer**, which include.,

i. **Ductal carcinoma in situ:-** Ductual carcinoma in situ (DCLS) is a non-invasive condition. With DCLS, the cancer cells are confined to the ducts in breast and have not invaded the surrounding breast tissue.

ii. **Lobular carcinoma in situ (LCIS):-**lobular carcinoma in situ is cancer that grows in the milk-producing glands of breast .like DCLS ,the cancer cells have not invaded the surrounding tissue.

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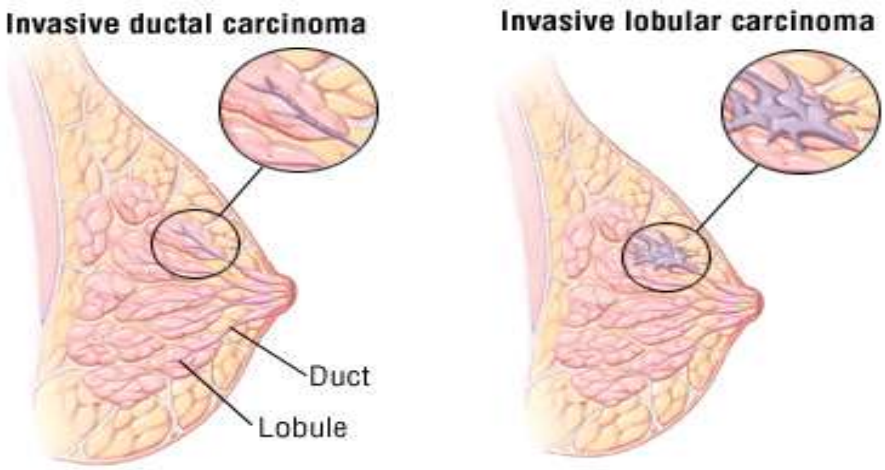

Figure 4

iii. **Invasive ductal carcinoma(IDC) :-**Invasive ductal carcinoma is the most common type of breast cancer. This type of breast cancer begins in your breast`s milk ducts and then invades nearly tissue in the breast . Once the breast cancer has spread to the tissue outside milk ducts, it can begin to spread to other nearly organs and tissue.

iv. **Invasive lobular carcinoma(ILC):**-ILC first devepols in breast`s lobules and has invaded near by tissue .

Less commonly occurring breast cancer type:,

v. **Paget disease of the nipple:**- This type of breast cancer begins in the ducts of the nipple ,but as it grows, it begins to affect the skin and areola of the nipple .

vi. **Angiosarcoma:**- This is cancer that grows on the blood vessels or lymph vessels in the breast.

vii. Medullary carcinoma:-medullary carcinoma is an invasive breast cancver yhat forms a distinct boundary between tumor tissue and normal tissue .

viii. Mutinous carcinoma:- Also called colloid carcinoma, mutation carcinoma is a rare breast cancer forms by the mucus producing cancer cells. Women with mutinous carcinoma generally have a better prognosis than women with more common types of invasive carcinoma.

ix. **Inflamatory breast cancer(IBC):**-IBC is a rare but, aggressive type of breast cancer.

In, IBC condition,cells block the lymph nodes near the breast ,so the lymph vessels in the breast can't properly drain or clean. Instead of creating a tumor ,IBC cause breast to swell, look red and feel very warm.

MAINLY THEY ARE CONTAIN THREE TYPES,

1. **ER+ breast cancer :-**A cancer is called estrogen-receptore positive,if it has receptors for estrogen. this suggests that the cancer cells ,like normal breast cells, may receive signals from estrogen, that could promote their growth.The cancer is progesterone-receptore positive,if it has progesterone receptors.

2. **HER2+ breast cancer:**-HER2+ is a growth-promoting protine on the outside of all breast cells.HER2+ breast cancer is occur, by increase the level of HER2 protein. these cancers trend to be aggressive and fast-growing.

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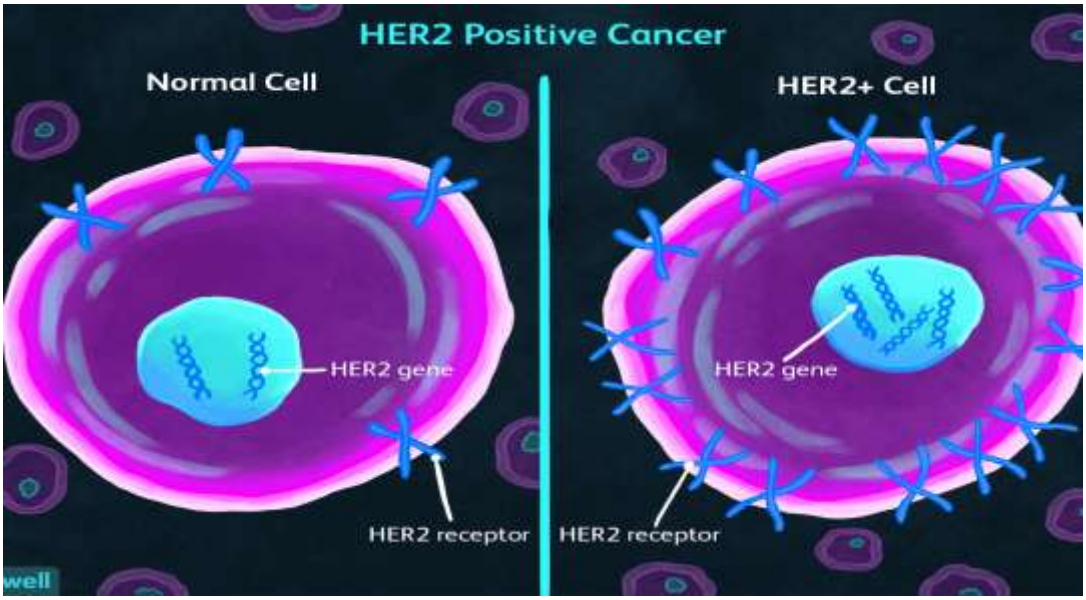

Figure 5

3.**TNBC(Triple negative breast cancer):-**Triple-negative breast cancer is another rare disease type.to be,diagnosed as triple-negative breast cancer, a tumor must have all three of the following characteristics:,

- **It Lacks estrogen receptors**:- these are receptors on the cells that bind, or attach ,to the hormone estrogen.if a tumor has estrogen receptors, estrogen can stimulate the cancer to grow.
- **It Lacks progesterone receptors**:-these receptors are cells that bind to the hormone progesterone. if a tumor has progesterone receptpors, progesterone can stimulate the cancer to grow.
- **It does not have additional HER2 proteins on it`s surface**:-HER2 is a protein that fuels breast cancer growth.

If a tumor meets these three criteria, it's labelled a triple-negative breast cancer. this type of breast cancer has a tendency to grow and spread more quickly than other types of breast cancer.

➢ **Breast cancer stages:-**

Breast cancer can be divided into stages based on how large the tumour or tumors are and how much it has spread .Cancers that are large and/or have invaded nearly tissue or organs are at a higher stage than cancers that are small and/or still contained in the breast.

Breast cancer has five main stages:,

1) **Stage 0 breast cancer:-**stage 0 is DCIS. Cancer cells in DCIS remain confined to the ducts in breast and have not spread into nearly tissue.

2) **Stage 1 breast cancer**

- **Stage 1A:-**the primary tumor is 2 centimeters wide or less and the lymph nodes are not affected.
- **Stage 1B:-**cancer is found in nearly lymph nodes,and either there is no tumor in the breast,or the tumor is smaller than 2cm.

3) **Stage 2 breast cancer**

- **Stage 2A:-**the tumor is smaller than 2cm and has spread to 1-3 nearly lymph nodes, or it's between 2 and 5 cm and has not spread to any lymph nodes.
- **Stage 2B:-**the tumor is between 2 and 5 cm and has spread to 1-3 axillary lymph nodes, or it's larger than 5 am and hasn't spread to any lymph nodes.

4) **Stage 3 breast cancer**

- **Stage 3A :**the cancer has spread to 4-9 axillary lymph nodes or has enlarged the internal mammary lymph nodes, and the primary tunor can be any size.

-Tumors are greater than 5 cm and the cancer has spread to 1-3 axillary lymph nodes or any breastbone nodes .

- **Stage 3B:-**a tumor has invaded the chest wall or skin and may or may not nave invaded up to 9 lymph nodes.
- **Stage 3C:-**cancer is found in 10 or more axillary lymph nodes, lymph nodes near the collarbone, or internal mammary nodes.

5) **Stage 4 breast cancer:-**stage 4 breast cancercan have a tumor of any size, and it's

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cancer cells have spread to nearly and distant lymph nodes as well as distant organs.

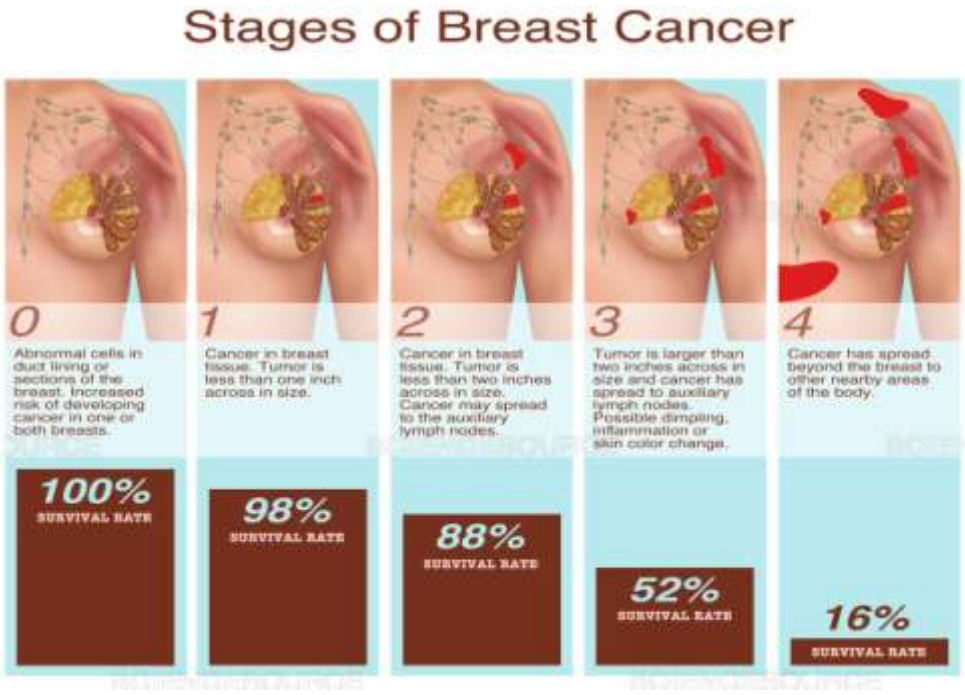

Figure 6(stages of breast cancer)

- **Risk factors for breast cancer:-**

A risk factor is anything that increase a person's chance of developing cancer. although risk factors often influence the development of cancer, most do not directly cause cancer. some people with several risk factors never develop cancer, while others with no known risk factors do.

Most breast cancers are large, sporadic ,meaning they develop from damage to a person's genes, that occurs by chance after they are born.

That are many risk factors that cause the breast cancer such as age, family history, genetics, personal history of breast cancer, certain breast change, race/ethnicity ,being overweight, pregnancy history, breasting history, menstrual history, drinking alcohol, lack of exercise, smoking, environmental factor .

Age:-Age is the most important factor in breast cancer. increasing age and female sex are established risk factors for breast cancer. Sporadic breast cancer is relatively uncommon among women younger than 40 years but, increase significantly thereafter. The effect of age on risk is **illustrated** in the SEER (Surveillance ,epidemiology and end results)data,where the incidence of invasive breast cancer for women younger than 50 years is 44.o per 100,000 as compared with 345 per 100,000 for women ages 50 years or older[[13]].

The total and age-specific incidence for breast cancer is bimodal(two types of behaviour in ,but opposite), with the first peak occurring at about 50 years and the second occurring at about 70 years[[14]]. This bimodal pattern may reflect the influence of age within the different tumor subtypes; poorly differentiated, high-grade disease tend to occur earlier, where as hormone-sensitive ,slower-growing tumors tend to occur with advancing age.

Family history:-family history is the main factor that,produce breast cancer, a family history score based on expected as well as observed breast cancers in a family can give greater risk discrimination on breast cancer incidence than conventional parameters based soley on cases in affected relatives. Our modelling suggests that a yet stronger predictor of risk might be a combination of this score and age at diagnosis in relatives.

Smoking:-smoking causes a number of diseases and is linked to a higher risk of breast cancer in younger, permenopausal women. Research also has shown that there may be link between very heavy second-hand smoke exposure and breast cancer risk in postmenopausal women . somking also can

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increase complications from breast cancer treatment ,including:

- Damage to the lungs from radiation therapy
- Difficulty healing after surgery and breast reconstruction
- Higher risk of blood clots when taking hormonal therapy medicines.

Reproductive factors and steroid hormones :- Late age at first pregnancy,nulliparity, early onset of menses, and late age of menopause have all been consistently associated with an increased risk of breast cancer.[[15],[16],[17],[18],[19]] prolonged exposure to elevated levels of sex hormones has long been postulated as a risk factor for developing breast cancer,explaning the association between breast cancer and reproductive behaviors [[20], [21]].

Women who started menstruating(having oeriods)younger than age 12 have a higher risk of breast cancer later in life .The same is true for women who go through menopause when they are older than 55.over the past 15 years, girls have been starting puberty at younger ages. Breast development has started even earlier than menstrual; periods. This unexpexted shift has been attributed to the obesity epidemic and boad exposure to hormone distruptors, since a rise in hormone triggers the onset of breast cancer development and puberty. The age when women go through menopause, however, has stayed about the same .

The earlier you breast from, the sooner they are ready to interact with hormones inside and outsie your body,as well as with chemicals in products that are hormone distruptors. This longer interaction with hormones and hormone distruptors can increase risk.

A risk factor is anything that increase your chances of getting a disease, such as breast cancer .But having a risk factors ,or even many does not mean that you are sure to get the disease. Certain breast cancer risk factors are related to personal behaviors ,such as diet and exercise. Other life style-related risk factors include decisions about having children and taking medicines that contain hormones.

Drinking alcohol:-Drinking alcohol Is clearly linked to an increased risk of breast cancer.the risk increases With the amount of alcohol consumed .woman who have 1alcoholic drink a day have a Small (about 7 %to 10%) increase in risk compared with non-drinkers, while woman who Have 2 to 3 drinks a day a have about a 20% higher risk than non-drinkers. Alcohol is linked to an increased risk of other types of cancer,to

Estogen:-Both endogenous and exogenous esteogens are associated with the risk of breast Cancer.the endogenous estrogen is usually produced by the ovary inPremenopausal women and ovariectomy can reduce the risk of breast cancer [[22]].the main sources of exogenous estrogen are the oral contraceptives and the hormone replacement therapy (HRT) .the oral contraceptives have been widely used since 1960s and the formulations have Been upgraded to reduce side-effects .however,the or is still higher than 1.5 for African women and Iranian populations[[23], [24]].nevertheless,oral contraceptives do not increase the risk of breast cancer in women who stop to use them for more than 10 years [[25]].HRT in volves the administration of exogenous estrogen or other hormones for the menopausal or postmenopausal women. A number of studies have shown that the use of HRT can increase the breast cancer risk. The million Women study in UK reported a relative risk (RR)of 1.66 between current users of HRT and those who never used it [[26]] .A cohort study of 22,929 women in Asia demonstrated HRs of 1.48 and 1.95 after HRT use for 4 and 8 years, respectively [[27]]. However, the risk of breast cancer has been shown to significantly decrease after two years of stopping HRT [[28]].The recurrence rate is also high among breast cancer survivors who take HRT , and the HR for a new breast tumor is 3.6[[29]]. Since the adverse effects of HRT were published in 2003 based on the women's health initiative randomized controlled trial ,the incidence rate of breast cancer in America has decreased by approximately 7% due to the reduction in the use of HRT[[30]].

LIFESTYLE is the main risk-factor for breast cancer,,

Lifestyle:-Modern lifestyles such as excessive alcohol consumption and too much dietary fat intake can increase the risk of breast cancer. Alcohol consumption can elevate the level of estrogen-related hormones in the blood and trigger the estrogen receptore pathways.A meta-anaysis based on 53 epiderminological studies indicated that an intake of 35-44 grams of alcohol per day can increase the risk of breast Cancer by 32%,with a 7.1% increase in the RR for each additional 10 grams of alcohol per day [[31],[32]]. Modern western diet contains too much fat and excess intake of fat , especially the saturated fat ,is associated with mortality (RR=1.3) and poor

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prognosis inbreast cancer patients[[33]].Although the relationship between smoking and breast cancer risk remain controversial ,mutagens from cigarette smoke have been detected in the breast fluid from non-lactating women. The risk of breast cancer is also elevated in women who both smoke and drink (RR=1.54)[[34]].up to now ,accumulating evidences demonstrate that smoking ,especially at an early age ,has a higher risk on breast cancer occurrence[[35] ,[36]].

- **PREVENTION OF BREAST CANCER:-**

There is no sure way to prevent breast cancer. but there are things you can do that might lower your risk. many risk factors are beyond your control , such as being born female an getting older. But other risk factors can be changed and may lower your risk.

For women who are known to be at increased risk for breast cancer, there are additional steps that might reduce the risk of developing breast cancer.

Naturally ,we can prevent or reduce breast cancer by following some home treatment , and that is very useful for as.

Keep weight in check:-It's easy to tune out because, it gets said so often, but maintaining a healthy weight is an important goal for everyone. Being overweight can increase the risk of many different cancers, including breast canceer, especially after menopause.

Be physically active :- Exercise is as close to a silver bullet for good health as there is , and women who are physically active for at least 30 min a day have a lower risk of breast cancer. Regular exercise is also one of the best way to help keep weight in check.

Eat Fruits &Vegetables- and Avoid Too Much Alcohol:- Ahealty diet can help lower the risk of breast cancer. Try to eat a lot of fruits and vegetables an keep alcohol at moderate levels or lower (a drink a day or under). While moderate drinking can be good for the heart in older adults, even low levels of intake can increase the risk of breast cancer.

Don't smoke:-Smokers and non-smokers a like know how unhealthy smoking is. On top of lowering quality of life and increasing the risk of heart disease, stroke ,and at least 15 cancers – including breast cancer –it also causes smelly breast ,bad teeth, and wrinkles .Now that's motivation to stay smoke-free or work to get smoke –free.

Breastfeed, If possible:- Breastfeeding for a total of one year or more (combined for all children) lowers the risk of breast cancer.it also has great health benefits for the child.

Avoid Birth Control pills, particularly After Age 35 or If Smoke:- Birth control pills have both risks and benefits. The younger a women is, the lower the risks are.While women are taking birth control pills ,they have a slightly increased risk of breast cancer. This risk goes away quickly, through , after stopping the pill. The risk of stroke and heart attack is also increased while on the pill particularly if a women smoke .however, long-term use can also have important benefits, like lowering the risk of overian cancer, colon cancer and uterine cancer-not to mention unwanted pregnancy-so there's also a lot in it 's favour. If you are very concerned about breast cancer, avoiding birth control pills is one option to lower risk.

Avoid Post-Menopausal Hormones:-post-menopausal hormones should not be taken ling term to prevent chronic disease, like osteoporosis and heart disease. Studies show they have a mixed effect on health, increasing the risk of some disease and loweing the risk of others ,and both estrogen only hormones and estrogen-plus-progestin hormones increase the risk of breast cancer. If women do take post-meopausal hormones, it should be for the shortest time possible .the best person to talk to about the risks and benefits of post-menopausal hormones is your doctor.

Tamoxifen and Raloxifene for Women at High Risk:-Although not commonly through of as a ''healthy behaviour ',taking the prescription drugs tamoxifen and raloxifen can significantly lower the risk of breast cancer in women at high risk of the disease.

Approved by the FDA for breast cancer prevention ,these powerful durgs can have side effects, so they are not right for everyone .if you think you are at high risk ,talk to your doctor to see if tamoxifen or raloxifene may be right for you.

Don't forget screening :- Despite some controversy , studies show that breast cancer screening with mammography saves lives. It doesn't help prevent cancer, but it can help find cancer early when it is most treatable. for most women, regular mammograms can begin at age 40, but specific recommendations vary by age and risk.

- If you are age 40-44: you can choose to begin yearly mammograms.it is important to talk to a doctor about the risk and benefits of mammograms at these ages.
- If you are age 45-54: mammograms are recommended every year.

- If you are age 55 or over: mammograms are recommended every other year. You can choose to continue to have them every year.

Clinical breast exams and self-exams are not recommended. But, you should be familiar with your breasts and tell a health care provider right away if you notice any changes in how your breasts look or feel.

➢ **Management of breast cancer:-**

Incancer care , doctors specializing in different areas of cancer treatment-such as surgery, radiation oncology , and medical oncology—work together with radiologists and pathologists to create a patient's overall treatment plan that combines different types of treatments. This is called a **multidisciplinary team**. Cancer care trams include a variety of other health care professionals, such as physician assistants ,nurse practitioners, oncology nurses, social workers, pharmacists, counsellors, nutritionists, and others.

Breast cancer is reduce by surgery radiation therapy, treating cancer with medication,the type of systemic therapies used for breast cancer[include:- chemotherapy, hormonal therapy,targeted therapy,immunotherapy].

I. Surgery:-

Surgery is the branch of medical practice that treats injuries, diseases, and deformities by the physical removal, repair, or readjustment of organs and tissue, often involving cutting into the body.

Surgery is the removal of the tumor and some surrounding healthy tissue during an operation. Surgery is also used to examine the nearby axillary lymph nodes, which are under the arm. A **surgical oncologist** is a doctor who specializes in treating cancer with surgery. Surgery is the oldest type of cancer treatment .And it is still effective for many types of cancer today .

There are many reasons to have surgery;

- To diagnose cancer
- To remove all or some of a cancer
- To find out where the cancer is located
- To find out if the cancer has spread or is affecting the functions of other organs in the body
- To restore the body's appearance or function
- To relieve side effects

They are many types of surgery depending on surgery ,means if you may have surgery in a doctor's office, clinic, surgery Center , or hospital ,you need to more time for heal . Inpatient surgery means that you need to stay in the hospital overnight or longer to recover after the surgery. Outpatient surgery means that you do not need to stay overnight in the hospital before or after surgery.

Types of breast cancer surgery

There are different types of surgery for breast cancer. the type you have depends on:,

- The size of the cancer
- Where the cancer is in your breast
- The size of your breasts
- Your personal wishes and feelings

Lumpectomy/breast conservation and mastectomy are two main types of breast cancer surgery .

Lumpectomy:-

A lumpectomy , also referred to as breast conserving or breast-sparing surgery, removes only the tumor (lump) and a small margin of normal-appearing tissue around the lump (see below) . A lumpectomy can be done for most small tumors. It is usually followed by radiation therapy, designed to kill microscopic cancer hiding in other parts of the breast. For patients with TNBC, chemotherapy is either given before surgery or given after surgery but,before radiation.

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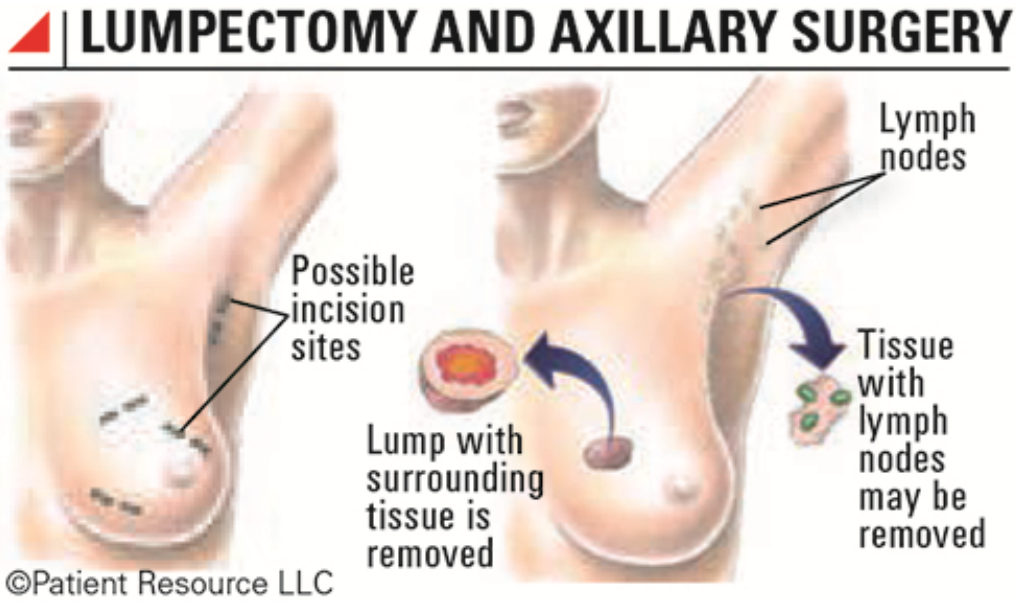

Figure 7:- Lumpectomy and Axillary Surgery

Mastectomy:-

A mastectomy involves removing the entire breast and may be preferred for large tumors, especially when they occur in a smaller breast (see below) . several types of mastectomy exist, including total mastectomy and modified radical mastectomy . total mastectomy surgically removes the entire breast without removing muscle. A modified radical mastectomy is a total mastectomy that is performed along with removing a block of underarm/axillary, lymph node tissue (axillary dissection). Doctor may recommend a mastectomy if you have a large tumor, multiple tumour in the breast or cancer that has spread to the skin . or if you were previously treated with lumpectomy and radiation therapy for a cancer in that same breast.

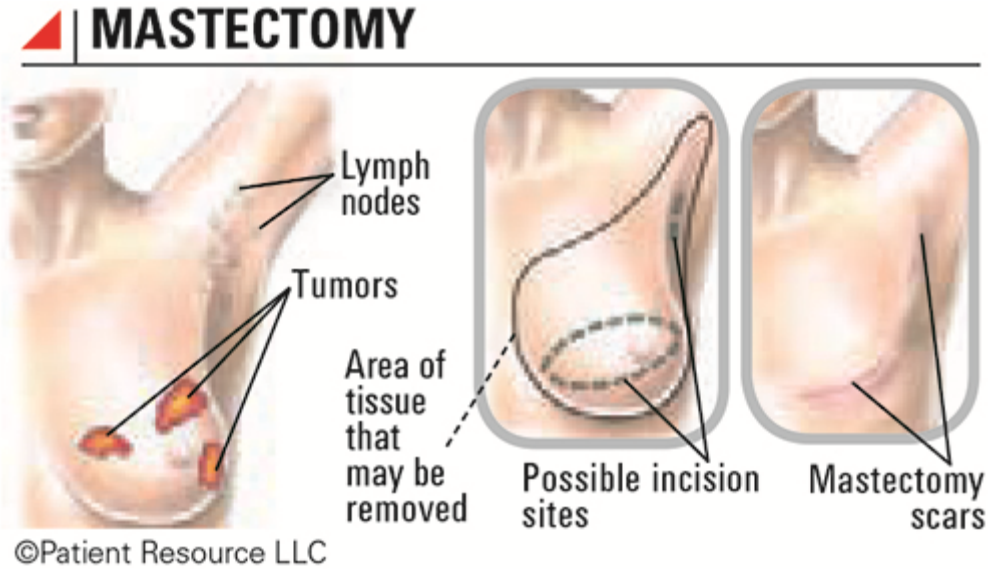

Figure 8:- Mastectomy

Patients with hereditary breast cancer , such as those with BRCA mutations (see Genetic testing), may opt to undergo bilateral mastectomy even if they only have a single small tumors as a strategy for reducing their chances of developing a future second breast cancer. Since ,outcome form breast cancer tends to be determined by the aggressiveness and metastatic risk of a women's first breast cancer (rather than whether she chooses mastectomy versus lumpectomy), patients with

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BRCA mutations may still be candidate for breast –conserving surgery.

Most TNBC,as well as non-TNBC , patient will need to undergo surgery to remove some of the lymph nodes (glands) in the underarm (axillary)region . Information regarding whether or not the breast cancer has spread into these lymph nodes is important prognostically, and can influence other aspects of treatment, such as your chemotherapy and radiation plan.

Some patients will be candidates for a relatively small axillary procedure called a sentinel lymph node biopsy which involves removing only the few most important axillary nodes. Other patients require a more extensive operation to control their disease called an axillary lymph node dissection (see above). The axillary surgery plan ,that is most appropriate for your cancer will be based upon the extent of your disease and your other treatments, including radiation therapy and chemotherapy.

Additional surgical procedures may be an option for people who have BRCA mutations and /or hereditary breast cancer. These women have a higher-than-average risk for developing new cancers in the contralateral (opposite) breast, or in either breast if they have had a lumpectomy.
Prophylactic mastectomy reduces the risk of a new breast cancer but, it does not completely eliminate the risk because microscopic amounts of breast tissue can remain hidden in the skin flaps or in the underarm fatty tissue after a mastectomy. Before ,you decide that ,this prophylactic surgery is right ,you concerned your doctor or it's give the suggestion about it.

II. RADIATION THERAPY:- Radiation therapy uses high levels of radiation to kill cancer cells or keep them from growing dividing or spreading to other body parts . because it targets only the cancer cells, it causes less damage to healthy cells .

BCT(breast-conserving therapy) and RT (radiation therapy)are commonly to reduce the breast cancer . and it's produce less side effects.

In 1980s more breast cancer patients are survive, because of improved technologies. and that time RT is the most popular therapy for breast cancer. But it's estimated that each centigray the heart may be damaging[[37], [38]]. It is estimated that each centigray exposure the heart receives increases the risk of death due to heart disease by 3%[[39]]. The incidence and severity of cardiac morbidity and mortality risk greater for left- sided disease by virtue of humane anatomy [[40] ,[41]],

Types of radiation therapy:-

A. **External beam radiation :-** External beam radiation is most commonly used to treat breast cancer. A machine outside your body aims a beam of radiation on the area affected by the disease.
B. **Brachytherapy:-** Brachytherapy delivers radiation to the cancer through something implanted in your body .
C. **Proton therapy:-** Protone-therapy sends highly targeted radiation just your breast tissue and not into your heart or lungs.

a) External beam radiation:-you all have small marks and stickers placed on your skin along the treatment area to give your medical team a map to follow. Don't try to wash these marks off or retouch them if they fade; the therapist will re-mark them when needed.

When you go for a treatment ,your therapist will escort you into the room and help you get in the right position.Then she will leave and start the treatment.

It is important to hold still and stay relaxed. Cameras and an intercom allow the therapist to see and hear you. Tell her right away if you are concerned about something.

The therapist will be in and out of the room to reposition the machine and your body .The machine won't touch you, and the treatment itself won't hurt.

Side effects of external beam radiation:-
Depending on the dose and type , you may notice these during treatment.

- Hair loss
- Less sweat where you were treated
- Fatigue
- Breast swelling
- Changes in skin sensation

These side effects usually go away gradually within 4 to 6 weeks after yout last treatment. Checking the out side skin after treatment.
Long-term side effects can last beyond a year after treatment . They may include:

- A slight darkening of your skin
- Enlarged pores on your breast
- More sensitive or less sensitive skin
- A change in the size of your breast

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b) **Proton-therapy:-** This is a type of external beam radiation that uses energy from positively charged particals called protons to damage the DNA in cancer cells so, they can no longer divide or grow . you usually get it 4 to 6 weeks after surgery or chemotherapy , and you will get it 5 days a week for several weeks for 30-40 min a day.

c) **Brachytherapy:-** Radiation seeds or pellets as small as grains of rice are placed inside the breast , near the cancer . whetherthis treatment might be right for you will depend on your tumor's size , location and other things.

Brachytherapy can be used alone or with external beam radiation.

Side effects of brachytherapy:

- Most people have reactions like redness, bruising, breast pain
- Less likely , but still possible, problems include: infection, damage to fatty tissue in the breast , weakness and fracture of the ribs in rare cases , fluid collecting in the breast (seroma).

III. Chemotherapy:-

Chemotherapy is the use of drugs to destroy cancer cells, usually by keeping the cancer cells from growing, dividing and making more cells. It may be given before surgery to shrink a large tumour, make surgery easier, and/or reduce the risk of recurrence, called **adjuvant chemotherapy.**

A chemotherapy regimen, or schedule. usually consists of a combination of drugs given in a specific number of cycles over a set period of time .chemotherapy may be given on many different schedules depending on what worked best in clinical trials for that specific type of regimen. It may be given once a week, once every 2 weeks, once every 3 weeks, or even once every 4 weeks.

These are many types of chemotherapy used to treat breast cancer.

Common drugs include: Docetaxel (taxotere), paclitaxel (taxol), Doxorubicin ,epirubicin(ellence) ,pegylated liposomal doxorubicine,capecitabine, carboplatine ,cisplatine, fluorouracil,methotrexate, vinorelbine

- **DOCETAXEL(taxotere)[ ]:-**

Docetaxel is a chemotherapy medication used to treat a number of types of cancer.

Mechanism of action:-The cytotoxic activity of docetaxel is exerted by promoting and stabilising microtubule assembly, while preventing physiological

Microtubule depolymerisation/disassembly in the absence of GTP [[42][43][44]].this leads to a significant decrease In free tubulin, needed for microtubule formation and results in inhabitation of mitotic cell division between metaphase and anaphase , preventing future cancer cell progeny[[45], [42], [46]].

Because microtubules do not disassemble in the presence of docetaxel , they accumulate inside the cell and cause initiation of apoptosis [[46]].apoptosis is also encouraged by the blocking of apoptosis-blocking bcI-2 oncoprotein [[42]]. Both in vitro and in vivo analysis show the anti-neoplastic activity of docetaxel to be effective against a wide range of known cancer cells , cooperate with other anti-neoplastic agents activity , and have greater cytotoxicity than paclitaxel, possibly due to it's more rapid intracellular uptake[[42]].

The main mechanism of therapeutic action of docetaxel is the suppression of microtubule dynamic assembly and fisassembly . rather than microtubule bundling leading to apoptosis, or the blocking of bcI-2[[42], [46]].

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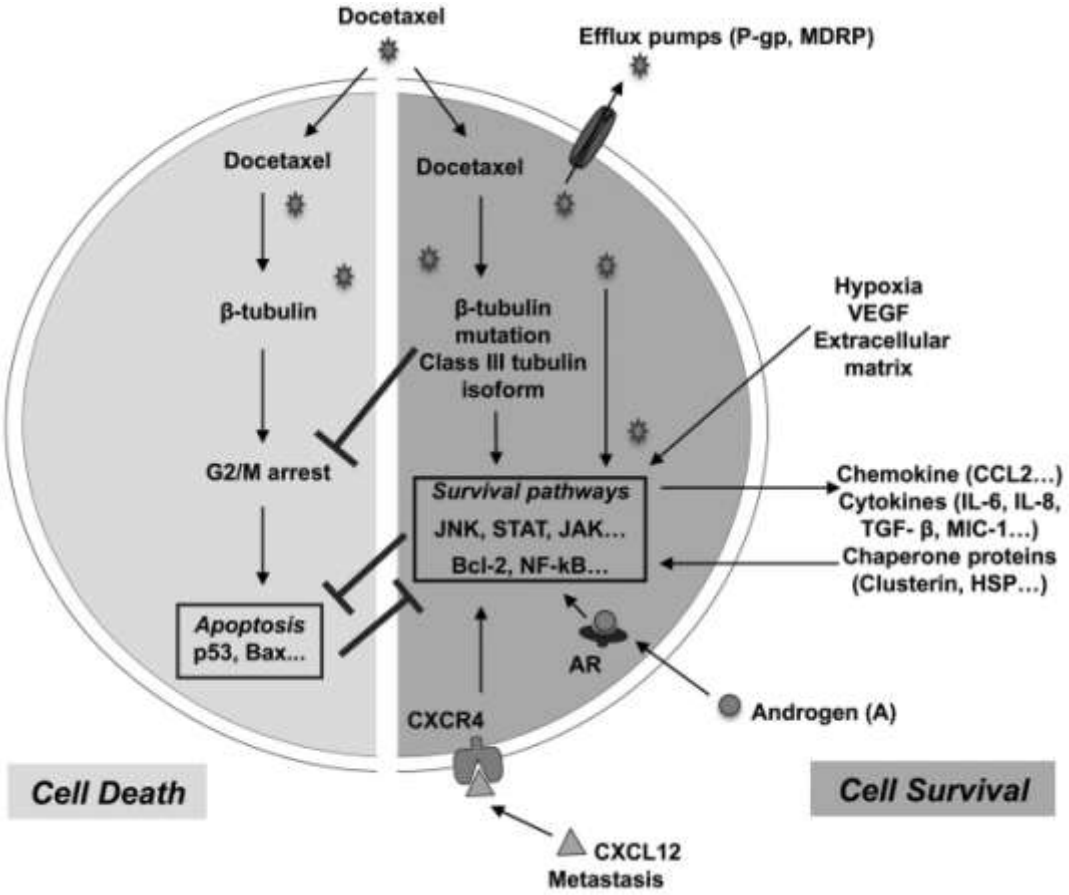

Figure 9:- docetaxel MOA

Drug interactions:- durg interactions may be the result of altered pharmacokinetics or pharmacodynamics due to one of the drugs involved[[47]], cisplatine , dexamethasone , doxorubicin , etoposide , and vinblastine are all potentially co-administered with docetaxel and did not modify docetaxel plasma binding in phase II studies[[48]]. Cisplatine is known to have a complex interaction with some CYPs and has in some events been shown to reduce docetaxel clearance by up to 25%[[47]]. Anticonvulsants induce some metabolic pathways relevant to doctaxel. CYP450 and CYP3A show increased expression in response to the use of anticonvulsants and the metabolism of docetaxel metabolite M4 is processed by these CYPs. A corresponding increase in clearance of M4 by 25% is observed in patients taking phenytoin and phenobarbital , common anticonvulsants[[47]].

Common and/or likely drug-durg combinations and known side effects from drug interactons:,

Table 1: DRUG INTERACTION

Drug interaction with docetaxel	**Adverse effects from interaction**
Cisplatin	Increased risk of delayed neuropathy
Cyclosporine , dalfopristin , erythromycin, intraconazole , ketoconazole , quinuprostin , terfenadine , troeandomycin	Increased risk of docetaxel toxicity including some or all of the following :anaemia,leucopoenia,thrombocytopenia , fever , disrrhoea
Doxorubicin hydrochloride	Cholestatic jaundice and pseudomembranous colitis
Doxorubicin hydrochloride liposome	Increased doxorubicin exposure
Vaccinations for Bacillus of Calmette and Guerin , measles, mumps , poliovirus	Increased risk of infection by live vaccine

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, rotavirus, rubella, smallpox, typhoid, varicella , yellow fever	
Thalidomide	Increased risk of venous thromboembolism

Erythromycin, ketoconazole and cyclosporine are CYP3A4 inhibitors and therefore inhibit the metabolic pathway of docetaxel[ ].when used with anticonvulsants, which induce CYP3A4, an increased dose of docetaxel may be required[[47]].

Pre-treatment with corticosteroids has been used to decrease hypersensitivity reaction and oedema in response to docetaxel and has shown no effect on the pharmacokinetics of docetaxel.[[47]].the efficacy of docetaxel was improved by treatment with oral capecitabine , and after more than 27 months follow up the survival benefit has been confirmed [[50]]. Doxorubicin was combined with docetaxel in one study of 24 patients and resulted in an increased AUC of docetaxel by 50 to 70%, including doxirubicinnmay affect the disposition of docetaxel [[49]].etoposide has also been shown to decrease docetaxel clearance, through patient numbers for this observation have been low [[49]].

Prednisone given with docetaxel led to improved survival , quality of life and pain management in patients with hormone-refractory prostate cancer.

Adverse effect : injection site reactions(pain ,redness or swelling), nausea, vomiting , diarrhea , constipation , loss of appetite , feeling weak or tired, muscle pain.

Uses:-this is used to treat a number of type of cancer. this includes breast cancer ,head and neck cancer ,stomach cancer, prostate cancer and non-small-cell lung cancer. It may be used by itself or along with other chemotherapy medication.

- **DOXORUBICIN :**-doxorubicin belongs to anthracycline and antitumor ,antibiotic.

Doxorubicin is a chemotherapy medication used to treat cancers like breast cancer,bladder cancer, lymphoma and acute lymphocytic leukemia.

MECHANISUM OF ACTION:-

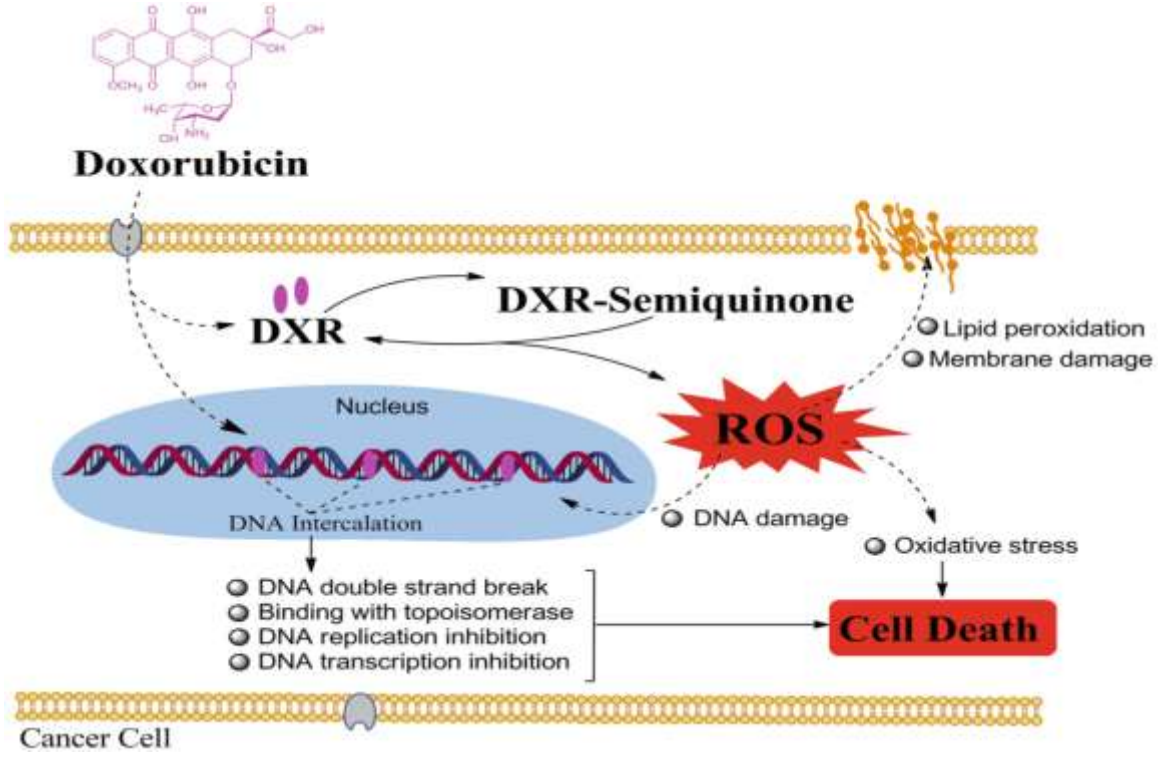

Figure 10 :- DOXORUBICIN

Doxorubicin interacts with DNA by interaction and inhabitation of macromolecule biopsynthesis . Doxorubicin inhibits the progession of the enzyme topoisomerase II, which relaxes supercoils in DNA

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for transcription and then stops the process of replication.

Drug interactions:-Doxorubicin may potentiate the toxicity of other anticancer therapies . doxorubicin + ~~clin~~etidine increase the level of doxorubicin. Doxorubicin may decrease the patients antibody response to vaccines and/or may increase adverse effects of a live virus vaccine due to immunosuppression. This effect may persist from three months to one year.Doxorubice may raise the concentration of blood uric acid, secondary to rapid lysis of neoplastic cells; dosage adjustment of antigout agents (e.g; allopurinol . colchicine, probenecid,sulfinpyrazone) may be necessary to control hyperuricaemia.

Adverse effect:-Neutopenia, anemia , CHF, Alopecia, thrombocytopenia, red urine , hyperuricemia.

Uses:- Doxorubicin is used in combination with other medication to treat certain types of bladder, breast, lung, stomach , and ovarian cancer, Hodgkin's lymphoma and non- Hodgkin's lymphoma .

- **CARBOPLATINE:-**It is a chemotherapy medication.

Mechanism of action:-

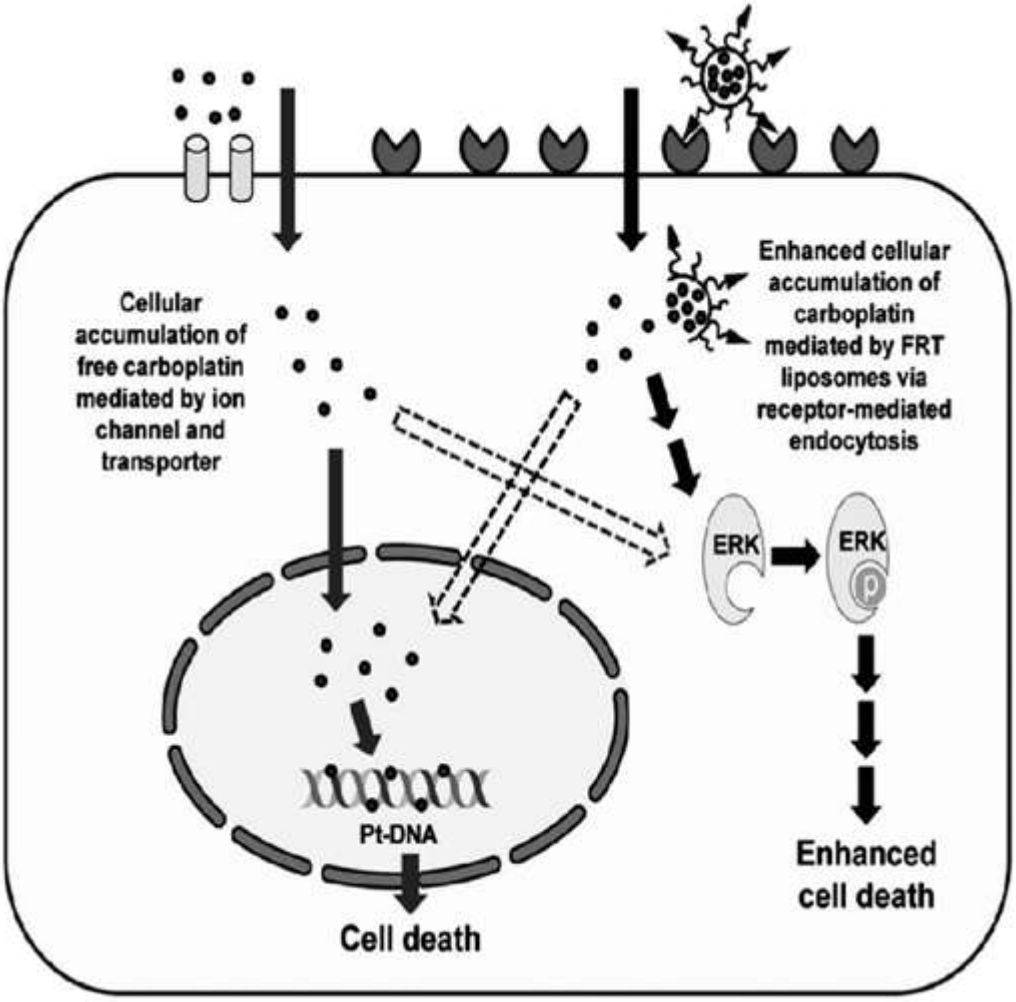

Figure 11:- CARBOPLATINE

Side effects:- Stomach pain , body aches/pain. Diarrhea, constipation , weakness, nausea , and vomiting may occue.

Uses:-it is used to treat ovarian cancer. And also used for other types of cancer, including lung, head, and neck, bladder.

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A patient may receive 1 drug at a time or a combination of different drugs given at the same time. Research has shown that combinations of certain drugs are sometime more effective than single drugs for_ adjuvant_treatment_ASCO (**American society of clinical oncology**). Does not recommend routinely adding platinum chemotherapy (cisplatine or carboplatine) to antracycline (doxorubicin or epiribicin) or taxan (paclitaxel or docetaxel) chemotherapy to treat people with inherited BRCA mutations before or after surgery.

The following drugs or combinations of drugs may be used as adjuvant therapy for early-stage and locally advanced breast cancer:

- AC (doxorubicin, cyclophosphamide)
- EC (epirubicin , cyclophosphamide)
- AC or EC followed by T (paclitaxel or docetaxel or he reverse)
- CAF (cyclophosphamide ,epirubicine and 5-FU)
- CEF(cyclophosphamide, epirubicine and 5-fu)
- CMF(cyclophosphamide , methotrexate, and 5-fu)
- TAC(docetaxel, doxorubicin and cyclosphamide)
- TC(docetaxel and cyclophosphamide)

Therapies that target HER2 receptore may be given with chemotherapy for HER2-positive breast cancer (see''targeted therapy'', below). An example is the antibody tratuzumab. Combination regimens for early-stage HER2-positive breast cancer may include,

- AC-TH(doxorubicin , cyclophosphamide, paclitaxel or docetaxel , trastuzumab)
- AC-THP (doxorubicin, cyclophosphamide, paclitaxel or docetaxel , trastuzumab, pertuzumab)
- TCH(paclitaxel or docetaxel ,carboplatin ,trastuzumab)

The side effects of chemothera;py depend on the individual , the drugs used , whether the chemotherapy has been combined with other drugs ,and schedule and dose used. These side effects can include fatigue , risk of interaction , nausea and vomiting , hair loss, loss of appetite, diarrhea, constipation, numbness and tingling, pain, early menopause, weight gain . these side effects can often be very successfully prevented or managed during treatment with supportive medications, and they usually go away after treatment is finised , for hair loss reduction, talk with your doctor about where they do cold cap techniques. Rarely ,long-term side effects may occur, such as heart damage , permanent nerve damage or secondary cancers such as leukemia or lymphoma.

Many patients feel well during chemotherapy and are actively taking care of their families , working and exercising during treatment , althrough each person's experience can be different. Talk with your health care team about the possible side effects of your specific chemotherapy plan, and seek medication attention immediately if you experience a fever during chemotherapy.

IV. HORMONAL THERAPY:-

Hormonal therapy, also called endocrine therapy ,is an effective treatment for most tumors that test positive for either estrogen or progesterone receptors, this type of tumour uses hormones to fuel, it's growth blocking the hormones can help prevent a cancer recurrence and death from breast cancer when hormonal therapy is used either by itself or after chemotherapy.

Hormonal therapy for breast cancer treatment is different than menopausal hormone therapy (**MHT**).MHT may also be called postmenopausal hormone therapy or hormone replacement therapy (**HRT**). Hormonal therapies used in breast cancer treatment act as " anti-hormone'' or "anti-estrogen ''therapies. They block hormone actions or lower hormone levels in the body. Hormonal therapy may also be called endocrine therapy. The endocrine system in the body makes hormones.

Hormone therapy may be given before surgery to shrink a tumour , make surgery easier, and/or lower the risk of recurrence. This is called **neo-adjuvant hormonal therapy .** when given before surgery , it is typically given for at least 3 to 6 months before surgery and continued after surgery. It may also be given solely after surgery to reduce the risk of recurrence. This is called **adjuvant hormonal therapy**.

Many drugs used for preventing hormones (estrogen or progesterone),

- **Tamoxifen (Nolvadex):-**

Tamoxifen is come under a class of Selective Estrogen Receptor Modulator (SERM). The most important drug worldwide for hormone receptor positive breast cancer.

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Mechanism of action:-

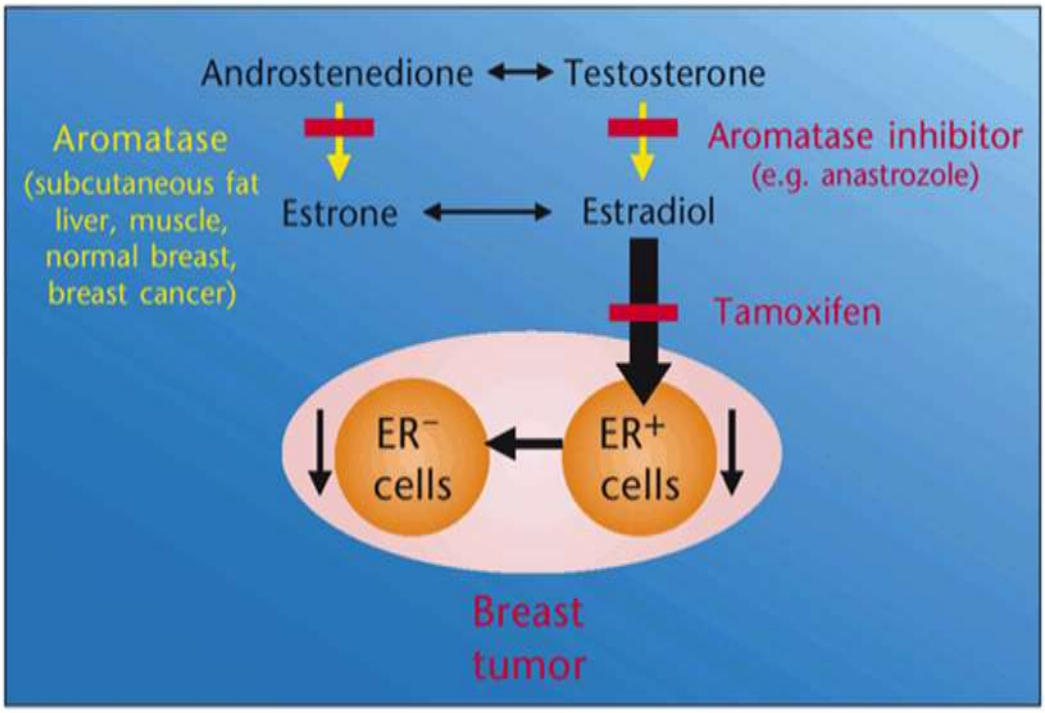

Figure 12:- TAMOXIFEN

tamoxifen completitively inhibite estrogen binding to it's receptore , which is critical for it's activity in breast cancer cell's [[51]]. Tamoxifen leads to a decrease in tumour growth factore alpha and insulin -like growth factore , and an increase in sex hormone binding globulin. The increase in sex hormone binding globulin limits the amount of freely available estradiol . these changes reduce levels of factores that stimulate tumour growth.

Tamoxifen has also been shown to induce apoptosis in estrogen receptore positive cells[[52]].this action is thought to be the result of inhabitation of protein kinase C, which prevents DNA synthesis[[52]]. Alternate theories for the apoptotic effect of tamoxifen comes from the approximately 3 fold increase in intracellular and mitochondrial calcium ion levels after administration or the induction of tumor growth factor beta.

Contraindications:-

Tamodex is contraindication in patients with a hypersensitivity to tamoxifen or any other component of this medication. This medication is contraindicated in pregnancy or breast-feeding women.

Tamoxifen during pregnancy:- tamoxifen has been classified by the US FDA as pregnancy Category D. Tamodex may cause fetal harm when administered to a pregnant women. Women should be advised not to become pregnant while taking tamodex or within 2 months of discontinuing tamoxifen therapy.

Adverse effect:- hot flushes , nausea , vomiting , changes in your period , unusual/changes in vaginal discharge, headache , dizziness or light-headedness , diarrhoea or constipation , unusual hair loss or thinning

Uses:- tamoxifen is effective in the treatment of metastatic breast cancer in women and men.

It is used to treat early breast cancer in women who have already been treated with surgery , radiation , and/or chemotherapy.

Tamoxifen is also indicated to reduce the incidence of breast cancer in women high risk for breast cancer.

- **Anastrozole(Arimidex), Exemestane (aromasin), letrozole (femara):-**

Anasrozole , exemestane , letrozole are aromatase inhibitors drugs. Aromatase inhibitor drugs are used to prevent or stops estrogen production.

Two major classes of aromatase inhibitors have been developed and are currently in clinical use**. Type I** steroidal drugs include formestane and exemestane; they are androgen substance analogues that bindcompetitively but irreversibly to the enzyme and have been marketed as " inactivators''.

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Type II nonsteroidal inhibitors such as anastrozole and letrozole are triazole; they biond reversibly to the enzyme and fit into the substrate binding site, such that azole nitrogens interact with the heme prosthetic group. This type of association provides exquisite potency for and specificity against the aromatase enzyme . these agents represent several generation of development, with each step in the evolution producing an increase in both potency and specificity .the least aromatase inhibitors are drugs of immense potential that will undoubtedly play a major role in the management of postmenopausal women with hormone dependent breast cancer. They also represent tools by which to elucidate the role of both aromatase and estrogen in the development and growth of breast cancer.

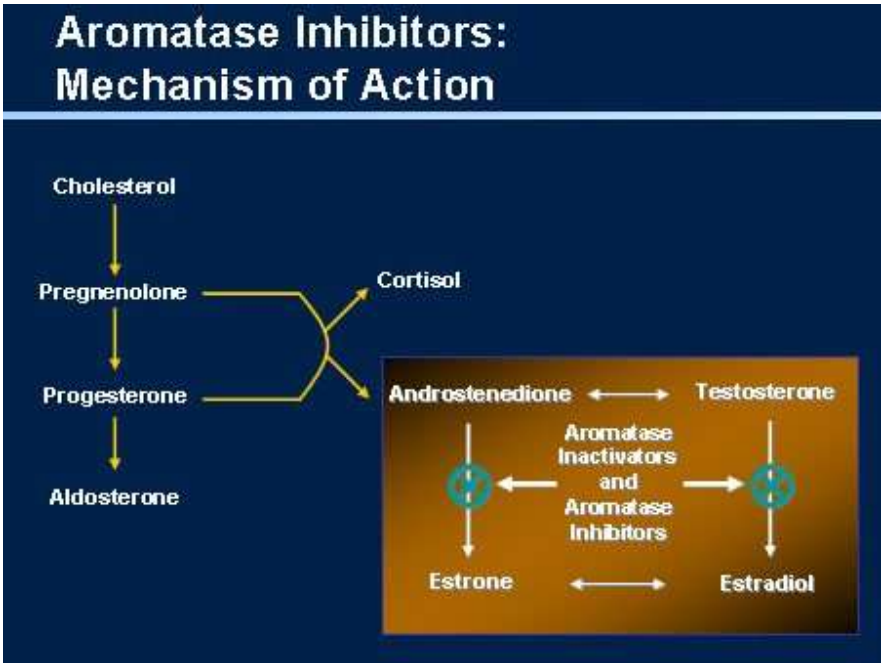

Figure 13:- AROMATASE INHIBITORS MOA

Mechanism of action :-these medication stops estrogen production. They are only used in women , who are already gone through menopause/pregnancy.

Interaction:- the clinica development of aromatase inhibitore has been targetly largely confined to postmenopausal breast cancer patients and strongly guided by pharmacological data. Comparative oestrogen suppression has been helpful in circumstances in which at least one of the comparitors has caused substantially non-maximal aromatase inhibitore . However, the triazole inhibitore, letrozole , and anastrozole , and the steroidal inhibitor , exemestane , all cause≥ 95% inhabitation of comparisons between these drugs therefore require more sensitive approaches such as the direct measurement of enzyme activity by isotopic means . none of these three agents has significant effects on other endocrine pathways at it's clinically applied doses. Pharmacokinetic analyses of the combination of tamoxifen and letrozole have revealed that these drugs interact, resulting in letrozole concentrations approximately 35-40% lower than when letrozole is used alone.

Side effect:-headache , nausea , peripheral eoddema, fatigue , hot flushes, skin reactions

Uses:- these are currently used in breast cancer , endometriosis , induction of ovulation , poor responders.

- **Fulvestrant:-** fulvestrant is a medication used to treat hormone receptor (HR-) positive metastatic breast cancer in postmenopausal women with disease progression as well as HR-positive , HER2-negative advanced breast cancer in combination with palbociclib in women with disease progression after endocrine therapy.

Mechanisum of action:-fulvestrant competitively and reversibly binds to estrogen receptors present in cancer cells and achieves it's anti-estrogen effects through two separate mechanisms. first, fulvestrant binds to the receptors and downregulates them so that esyrogen ios no longer able to bind to these receptors. Second, fulvestrant degrades the estrogemn receptors to which it is

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bound. Both of these mechanism inhibit the growth of tamoxifen-resistant as well as estrogen-sensitive human breast cancer cell lines.

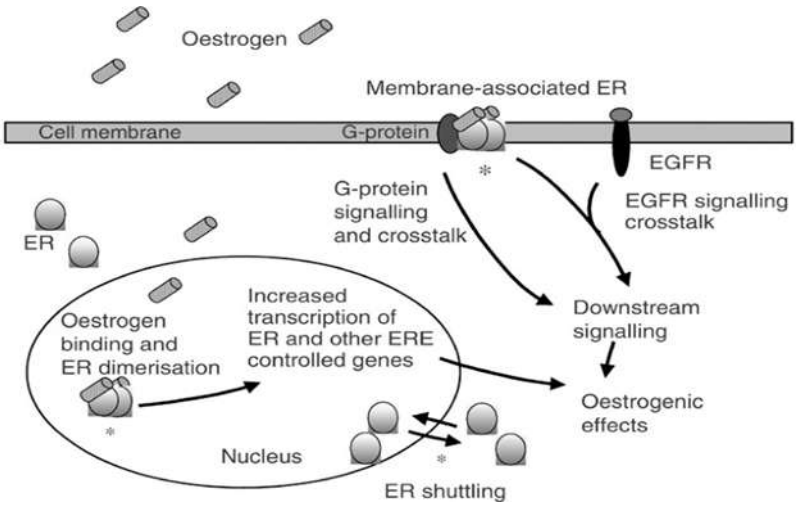

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Figure 14:- FULVESTRANT MOA

Side effects:-headache, nausea, bone pain , joint pain , vomiting , loss of appetite, diarrhea , cough , feeling short of breath;
Uses:-it is used for hormone + breast cancer.

V. Targeted therapy:_

Targeted therapy is a treatment that targets the cancer's specific genes, proteins or the tissue environment that contributes to cancer growth and survival. These treatments are very focused and work differently than chemotherapy. This type of treatment blocks the growth and spread of cancer cells and limits damage to healthy cells.
HER2-targeted therapies were approved to treat HER2-positive breast cancer.

HER2-targeted therapy:-
HER2 + breast cancer is the gene cancer. That is mostly shown in women . researcherssay ,that the HER2+ breast cancer is increase, by increasing HER2(**human epidermal growth factor receptor 2**) in body[[53]]. And this type of breast cancer is rapidly grow up in body[[54]].

HER2-targeted therapies target HER2- positive breast cancers. They are only used to treat HER2-positive breast cancers. They have no role in the treatment of HER2-negative cancers.
Testing for HER2 status:-
The HER2 status of a tumor is determined by testing tissue removed during a biopsy. All newly diagnosed breast cancers are tested for HER2 status.
About 10-20 % of newly diagnosed breast cancers are HER2-positive [[55], [56]]. These breast cancers can be treated with HER2- targeted therapies.
Many antibiotics are used to treat the breast cancer, like trastuzumab , pertuzumab, lapatinib .

- **Trastuzumab (Herceptin):-**trasruzumab is the targeted drug, that bind to HER2 protein—reduces the risk of the cancer coming back. This are given after surgery . It can also be used for early breast cancer.

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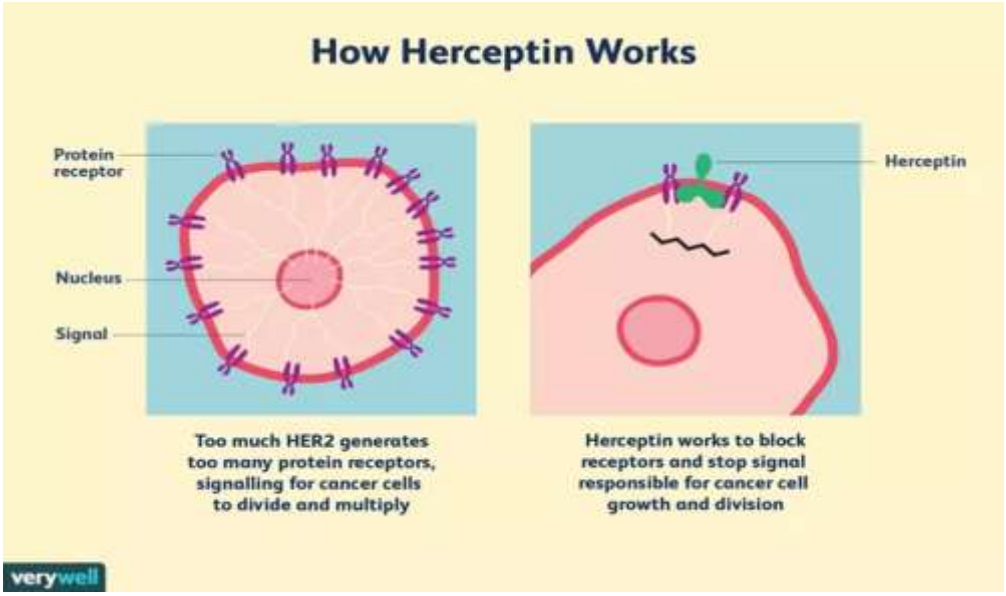

Figure 15

Mechanism of action:-

Trastuzumab binds to the extracellular juxtamembrane domin of HER2 and inhibits the proliferation and survival of HER2-dependent tumors . it is approved by the food and drug administration(FDA) for patients with invasive breast cancers that overexpress.

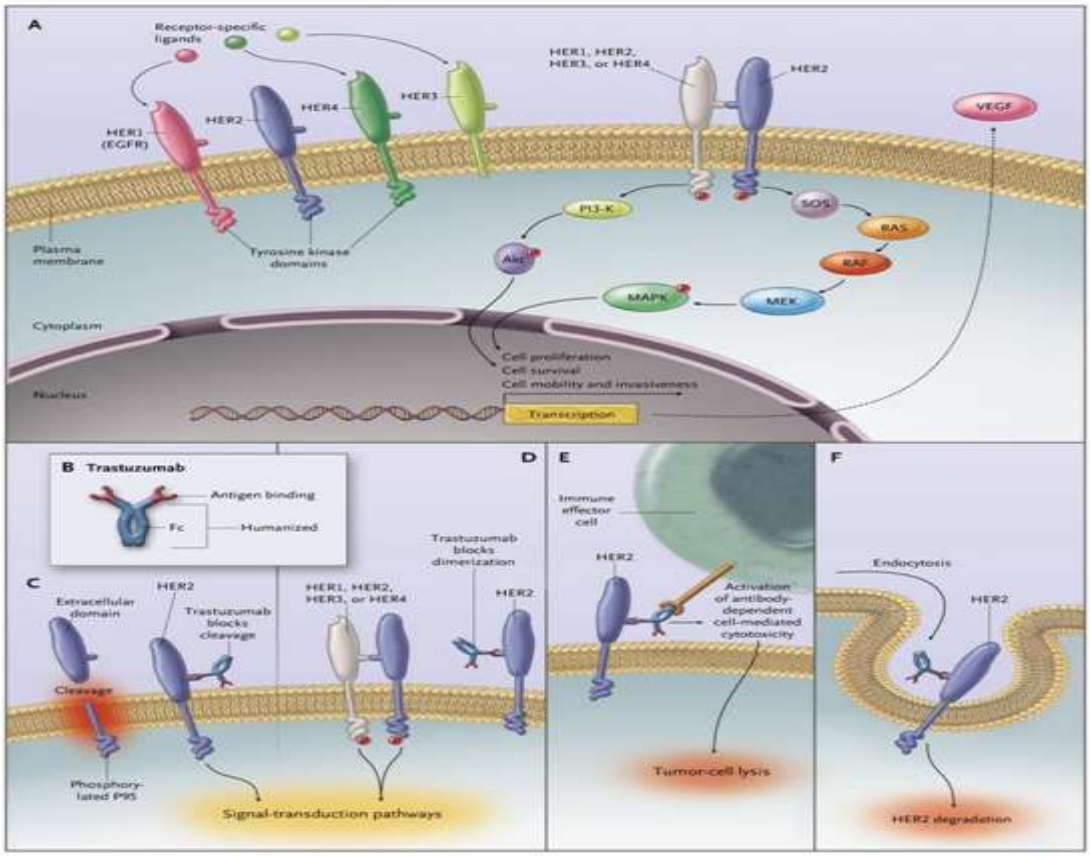

Figure 16

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Side effects:-headache , diarrhea , nausea , chills , fever , heart problems , infection , insomnia, a runny nose , pain in your muscles , joints , chest and tummy , loss of appetite and weight loss.
Uses:-it's used to treat some types of breast cancer , oesophageal cancer and stomach cancer.

- **Ado-trastuzumab:-**

Ado-trastuzumab emtansine is used to treat some womenwith HER2-positive breast cancer who have cancer remaining in their breast or lymph nodes after neoadjuvant(before surgery) chemotherapy.the use of ado-trastuzumab emansine in these women can reduce the risk of breast cancer recurrence or breast cancer death by 50% compared to treatment with trastuzumab[[57]].

Ado-trastuzumab emansine is given by vein (through an iv) every 3 weeks for 14 cycles . treatment with ado-trastuzumab ematansine begins after breast surgery.

Ado-trastuzumab emtansine is under study for use in the neoadjuvant setting[[58]].
Side effects:-possible side effects of ado-trastuzumab emtansine include nausea , fatigue , muscle and joint pain , low platelet count , headache and constipation[[57], [59]].it can also cause liver and heart problems[[59]].

- **Pertuzumab (perjeta):-**

Pertuzumab is an antibody that targets HER2 – positive cancer cells , but in a different way than trastuzumab.

Mechanism of action:-

Pertuzumab binds to subdomain II and prevents dimerization. Pertuzumab also mediates antibody dependent cell mediated cytotoxicity (ADCC).trastuzuman(Herceptin) binds to subdomainIVpreventsdimerization;ADCC.pertuzumab and trastuzumab combination provide a more comprehensive block.

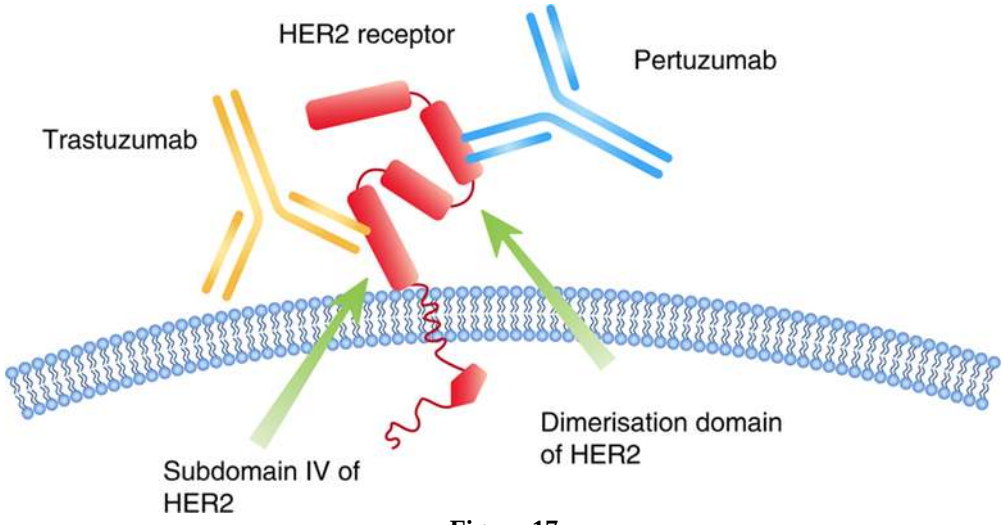

Figure 17

Side effects:- possible side effects of pertuzumab include diarrhea and fatigue. Pertuzumab , may increase the risk of heart problems.

Pertuzumab is given in combination with trastuzumab . trastuzumab can cause congestive heart failure,a serious heart condition .

Neratinib:-Tyrosine – kinase inhibitors, such as neratinib ,are a class of drugs that targeted enzymes important for cell functions (called tyrosine – knase enzymes). These drugs can block tyrosine-kinase enzymes at many points along the HER2 cancer growth pathway.

Mechanism of action:-Neratinib irreversibly binds to the intercellular signalling domain of HER1 , HER2, ,HER3, and epirhelial growth factore receptore , and inhibits phosphorylation and several HER downstream signalling pathways . The results is decreased proliferation and increased cell death.

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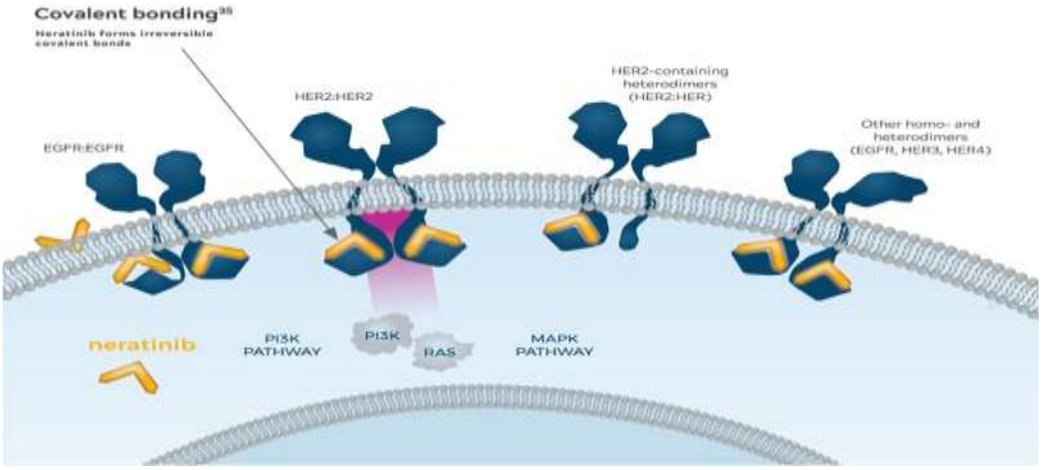

Figure 18

Side effects:-neratinib can cause life-threatening diarrhea in some people and mild to moderate diarrhea in almost everyone. Similarly there is a risk of severe liver damage and many paatients have some level of it ;symtomes of liver damage include fatifue , nausea, vomiting ,righ appre quadeant pain or tenderness, fever , rash , aand high levels of eosinophils.

II. CONCLUSION:-

This conclusion focused on overview of breast cancer prevention , biopsy techniques , and treatment options for breast cancer patients , including surgery , radiation therapy , chemotherapy , targeted therapy treatments. Targeted therapy is a treatment that targets the cancers specific genes , protines or the tissue environment that contributes to cancer growth and survival . These treatments are much focused and work differently than chemotherapy . This type of treatment blocks the growth and spread of cancer cells and limits damage to healthy cells. HER2-targeted therapies were approved to treat HER2-positive breast cancer. Thus review targeted is the evidence supporting the role of adjuvant radiontherapy as the standard of care for breast cancer after breast conserving surgery.

This conclusion reviews typical treatments based on stage I and stage II breast cancers are usually treated with breast-conserving surgery and radiation therapy . Stage III breast cancer typically requires induction chemotherapy to downsize the tumour to facilitate breast conserving surgery . inflammation breast cancer , although considered stage III , is aggressive and requires induction chemotherapy followed by mastectomy , rather than breast conserving surgery , as well as axillary lymph node dissection and chest wall radiation . prognosis is poor in women with recurrent or metastatic (stage IV) breast cancer.

Radiation therapy following breast conserving surgery decreases mortality and recurrence . choice of adjuvant systemic therapy depends on lymph node involvement , hormone receptor status , ERBB2 (formerly HER2 or HER2/neu) overexpression , and patient age and menopausal status. In general . node-positive breast cancer is treated systemically with chemotherapy , endocrine therapy and trastuzumab.

In this review treatment options must balance benefits in the length of life and reduced pain against harms . the conclusion of review targeted on breast cancer prevention and treatment options that can help family, physicians for their patient and especially for the women during and after cancer treatment.

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