



Lecture 18: Treating Breast Cancer





Risk factors for breast cancer



Direct factors

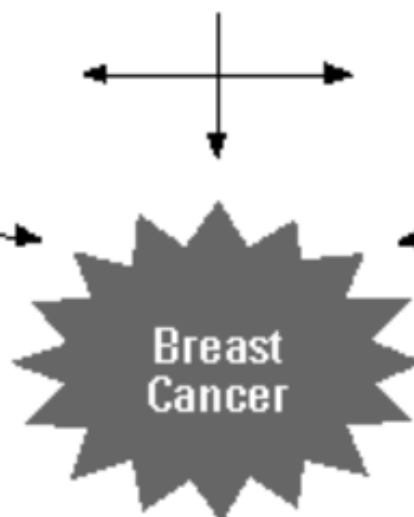
- ✦ Radiation, especially during puberty
- ✦ Inherited mutations

Contributing factors

- ✦ Lack of exercise
- ✦ Excess of alcohol
- ✦ Deficiencies of vitamin D, fiber, melatonin??
- ✦ Harmful xenohormones (some plastics, fuels, pesticides)
- ✦ Increased insulin-like growth factor

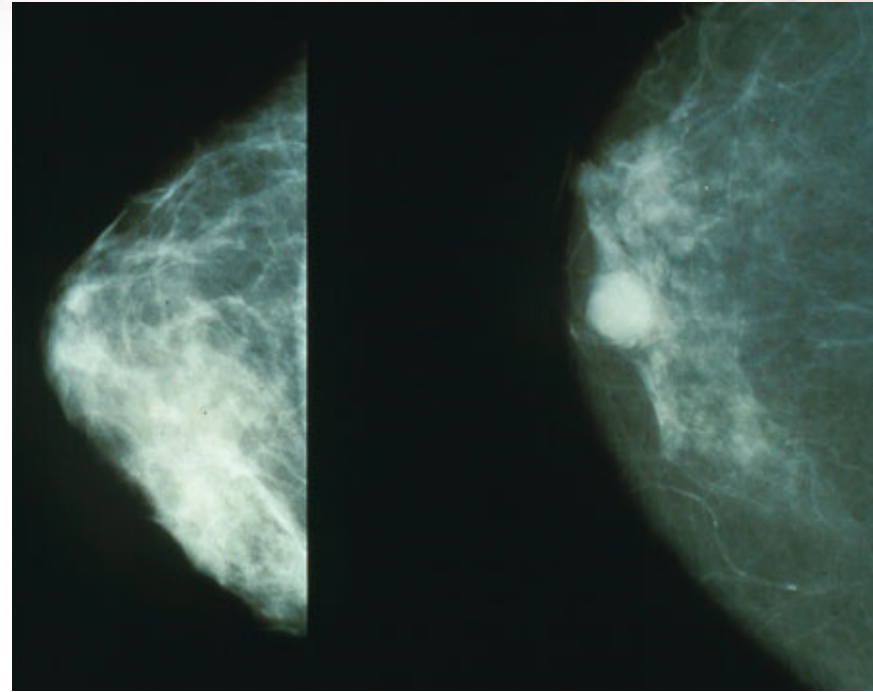
Vulnerability factors

- ✦ Early menses
- ✦ Late menopause
- ✦ No pregnancy or lactation

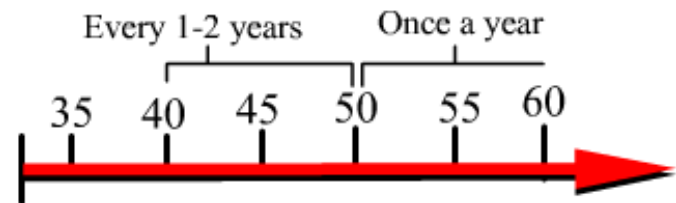




Mammography



Most doctors recommend that a woman have her first mammogram at the age of 40. They should be continued once a year or once every two years until the age of 49. After age 50, she should have a mammogram every year.



Mammography Conflicting Recommendations



Differing mammogram guidelines

In 2009, the U.S. Preventive Services Task Force (USPSTF) — a group of health experts that reviews published research and makes recommendations about preventive health care — issued revised mammogram guidelines.

Those guidelines include the following:

- Screening mammograms should be done every two years beginning at age 50 for women at average risk of breast cancer.
- Screening mammograms before age 50 should not be done routinely and should be based on a woman's values regarding the risks and benefits of mammography.
- Doctors should not teach women to do breast self-exams.
- There is insufficient evidence that mammogram screening is effective for women age 75 and older, so specific recommendations for this age group were not included.

These guidelines differ from those of the American Cancer Society (ACS).

The ACS mammogram guidelines call for yearly mammogram screening beginning at age 40 for women at average risk of breast cancer. Meantime, the ACS says the breast self-exam is optional in breast cancer screening.

According to the USPSTF, women who have screening mammograms die of breast cancer less frequently than do women who don't get mammograms. However, the USPSTF says the benefits of screening mammograms don't outweigh the harms for women ages 40 to 49. Potential harms may include false-positive results that lead to unneeded breast biopsies and accompanying anxiety and distress.

At Mayo Clinic, a three-tiered approach is used:

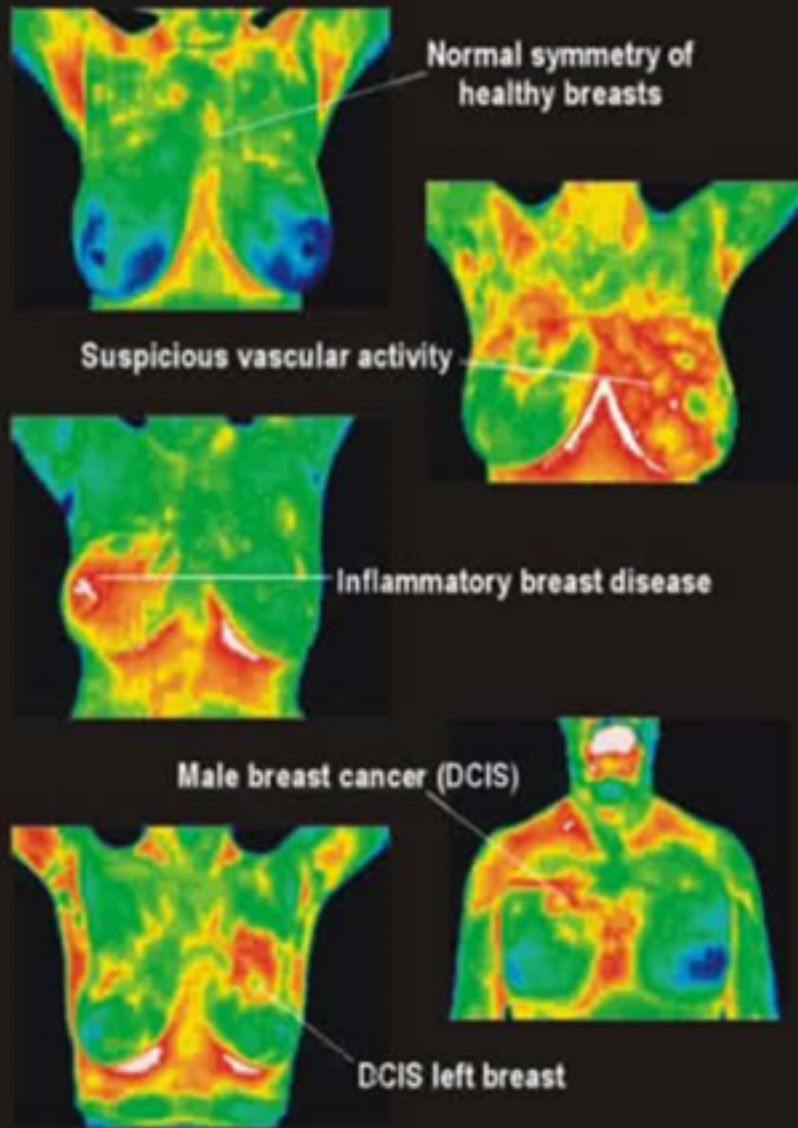
- Breast health awareness, which includes a woman becoming familiar with her breasts in order to identify breast abnormalities or changes, and to inform her doctor of any changes that may need further evaluation
- Clinical breast exam performed by a health care provider and recommended annually beginning at age 40
- Screening mammography beginning at age 40

Screening mammograms can detect breast abnormalities early in women in their 40s. Findings from a large study in Sweden of more than 1 million women in their 40s who received screening mammograms showed a decrease in breast cancer deaths by 29 percent. And it's important to remember that most women who get breast cancer have no family history or other known risk factors for the disease.

Screening mammography is not a perfect exam. But it is the best available tool to detect cancer early, which can lead to better options and possibly less aggressive treatments.

If you're concerned about screening mammograms, talk to your doctor and learn what's right for you based on your individual risks. It's important that the two of you work together to develop a screening plan.

Digital Infrared Thermal Imaging - **Thermography**



- ❑ Not widely used, but could be more effective than mammography
- ❑ Measures temperature increase due to increased blood flow and metabolism at site of tumor.
- ❑ Uses a heat sensitive camera, which works much like a night vision camera to record thermal changes in the breast tissue.
- ❑ **UNPROVEN ACCURACY**



The FDA's own [consumer information recommends](#) that

“ despite widely publicized claims to the contrary, thermography should not be used in place of mammography for breast cancer screening or diagnosis.

The FDA notes that it has previously issued warning letters to practitioners making misleading claims, including well-known [anti-vaccinationist and quackery promoter Joe Mercola](#). (The link to the letter is no longer good, but you can find out more about the case on [Quackwatch](#) and in the [Chicago Tribune](#).)



FDA warns doctor: Stop touting camera as disease screening tool

On popular website, thermography device is promoted for early detection of breast cancer, lupus, arthritis and more

April 25, 2011 | By Trine Tsouderos, Tribune reporter



f Recommend

167

Tweet

2

Share

1327

+1

0

On Dr. Joseph Mercola's popular website, women are warned against getting mammograms to screen for breast cancer.

Instead, the Chicago-area physician touts thermograms — digital images of skin surface temperatures — as an early detection tool for a wide range of conditions from cancer to back pain, from lupus to arthritis.



Dr. Joseph Mercola's website says, "If you're female, please ..."

Ads By Google

The FDA, in its warning letter to Meditherm, ordered the company to stop making broad claims about its cameras, pointing to a Web page that lists "76 specific conditions for which you say your device can be used ... for example, lower motor neuron disease, neoplasias (melanoma, squamous cell, basal) and nutritional disease (alcoholism, diabetes)."

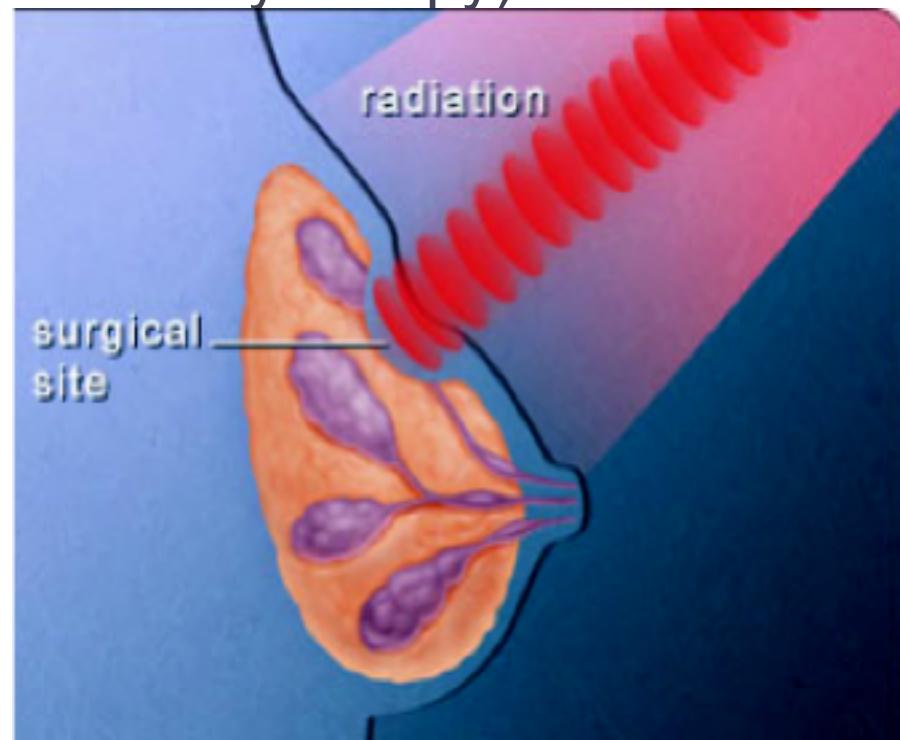
Breast Cancer Treatment Options



- Treatment options dependent on stage of cancer
- **Local or regional tumor:** treated with surgery, radiation or chemotherapy
- **Systemic treatments** are directed to the whole body or "system" for metastasized cancers

Radiation Therapy/ Brachytherapy

- ❑ Use of high-energy radiation to kill cancer cells and shrink tumors
- ❑ External-beam radiation therapy-destroy cells, either directly or by interfering with cell reproduction using high-energy X-rays
- ❑ Radioactive material placed in body in the area near cancer cells (internal radiation therapy, implant radiation, or brachytherapy).

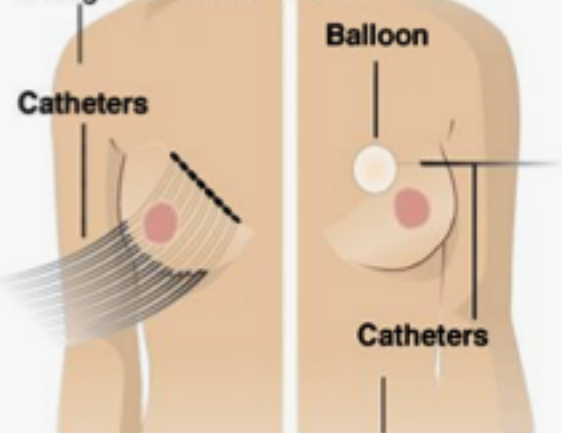


Zeroing in on breast cancer

Women with early-stage breast cancer who have only the tumor removed, not the whole breast, usually receive about six weeks of radiation to destroy any stray cancer cells. Doctors are studying whether shorter treatments, usually about five days, would work as well.

Two Brachytherapy methods:

In one method, a machine runs a radioactive seed down catheters which are threaded through the affected breast



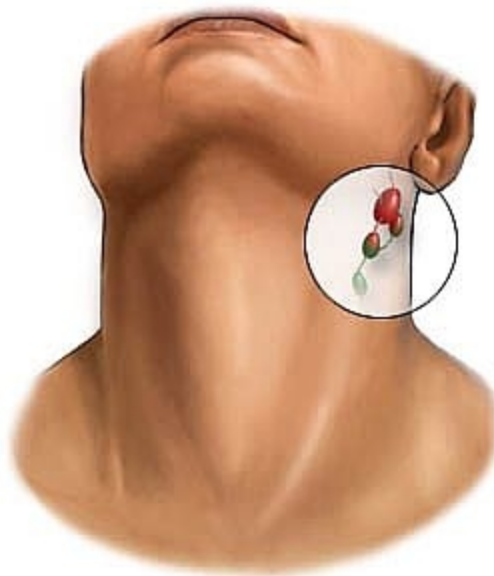
In another method, a balloon fits into the space where a tumor was removed and a radioactive source enters through a catheter



Sentinel Lymph Node Biopsy

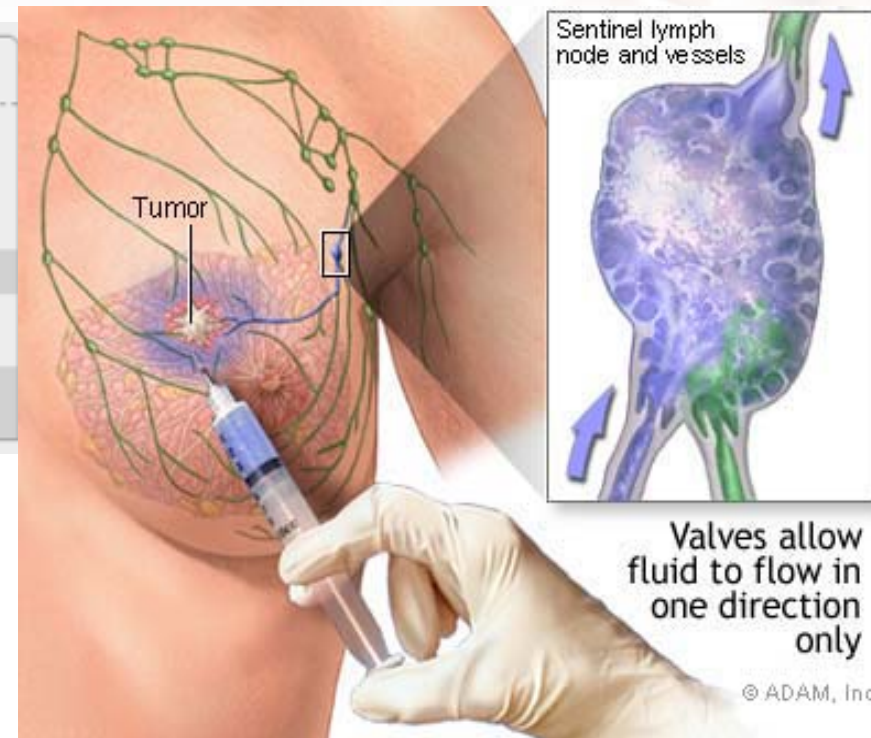
How Lymph Node Status Influences Survival

Lymph Node Status	Chances of Surviving 5 Years	Chances of Surviving 10 Years	Chances of Surviving 10 Years Without Recurrence
No cancer in any node	Better than 90%	Better than 80%	Better than 70%
Cancer in one to three nodes	About 60 to 70%	About 40 to 50%	About 25 to 40%
Cancer in four or more nodes	About 40 to 50%	About 25 to 40%	About 15 to 35%



Swollen lymph node

Normal lymph node



Significantly reduces lymphedema (swelling)

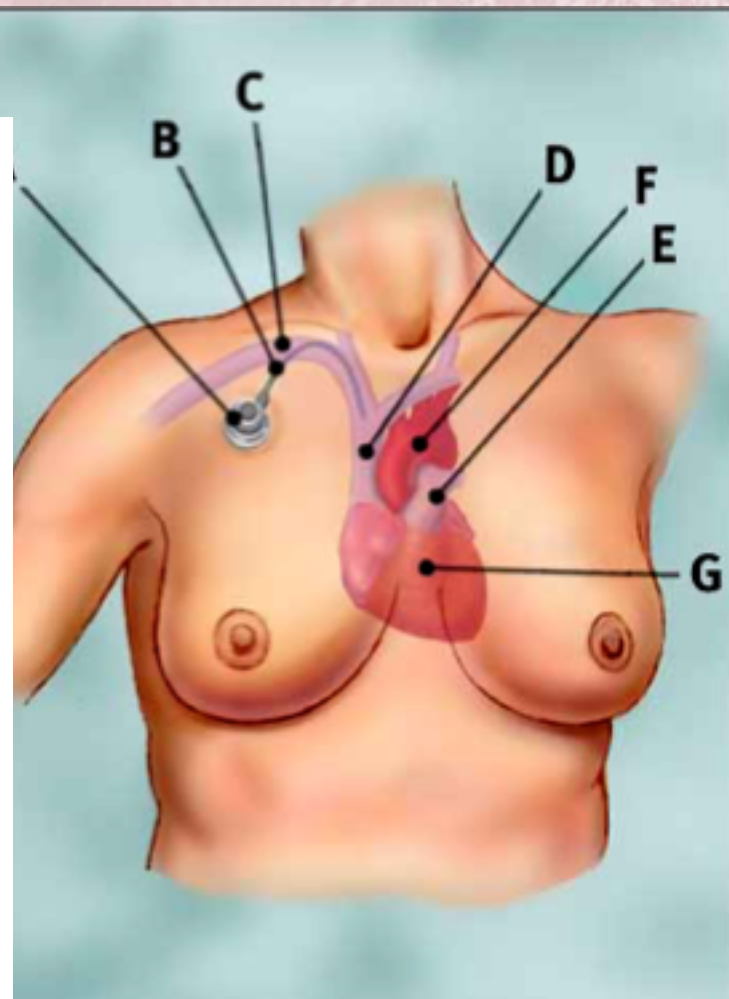


Chemotherapy



Expert Quote

"No patient walks in and says, 'I want chemotherapy.' Why on earth would anyone want it? But they leave with the understanding that chemotherapy has advantages, and that the majority of patients who have breast cancer will benefit from some form of adjuvant therapy—whether it's chemotherapy, anti-estrogen therapy, or both." —Lisa Weissmann, M.D.



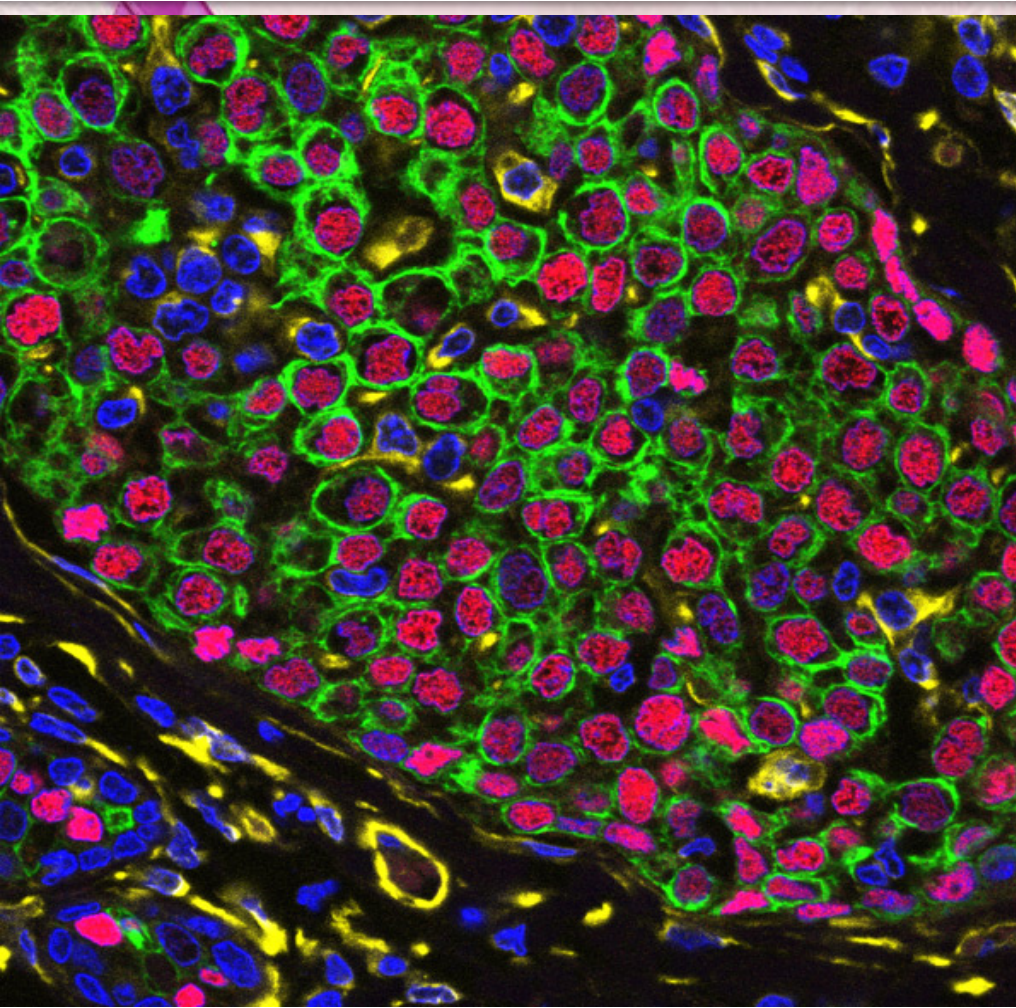
A port
B catheter [tubing]
C subclavian vein
D superior Vena cava
E pulmonary vein
F aorta
G heart

**ADJUVANT
THERAPY**

**NEOADJUVANT
THERAPY**

- Adjuvant therapy for breast cancer is any treatment given after primary therapy to increase the chance of long-term survival. Neoadjuvant therapy is treatment given before primary therapy.
- Adjuvant therapy for breast cancer can include chemotherapy, hormonal therapy, the targeted drug trastuzumab (Herceptin®), radiation therapy, or a combination of treatments.

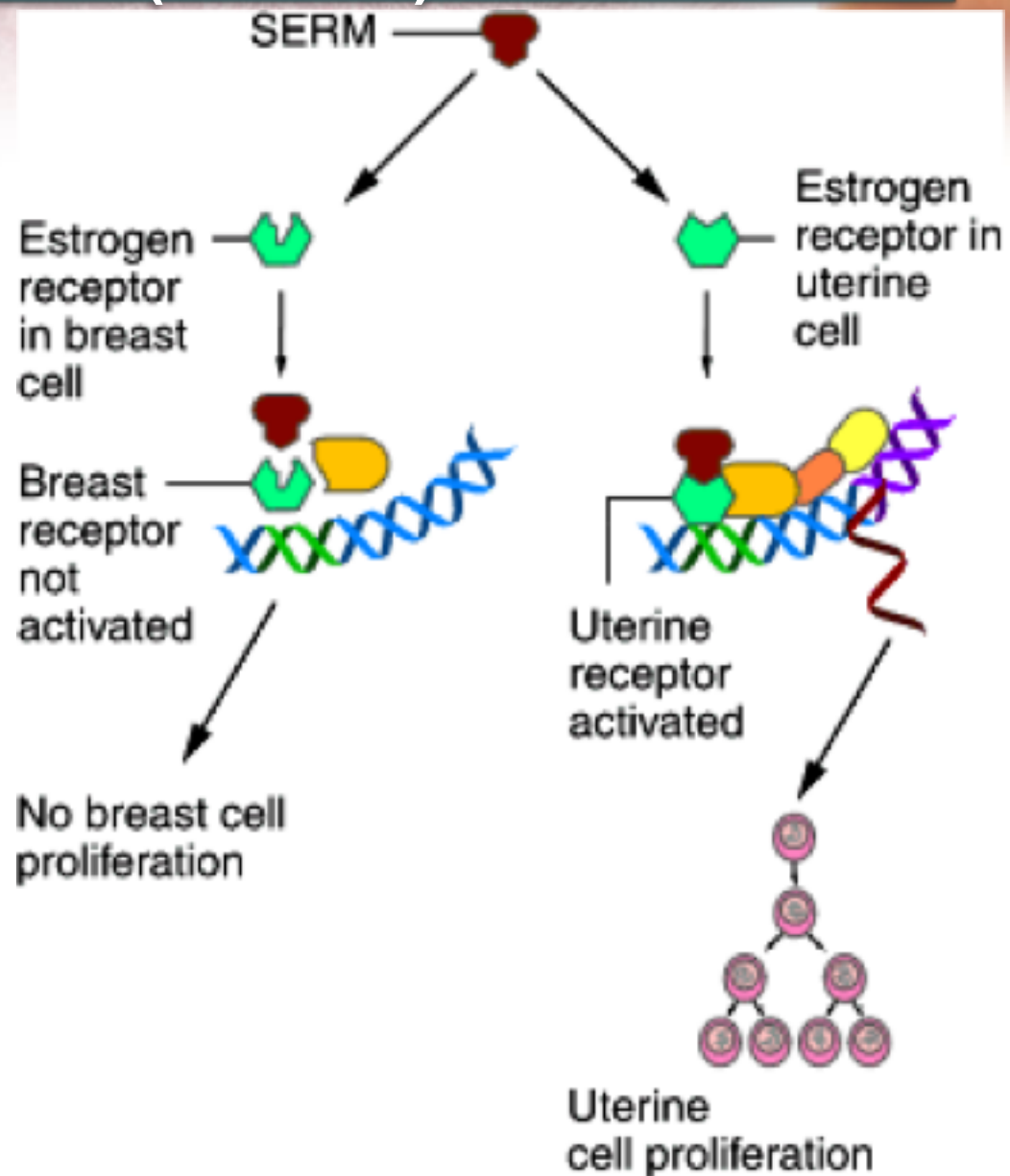
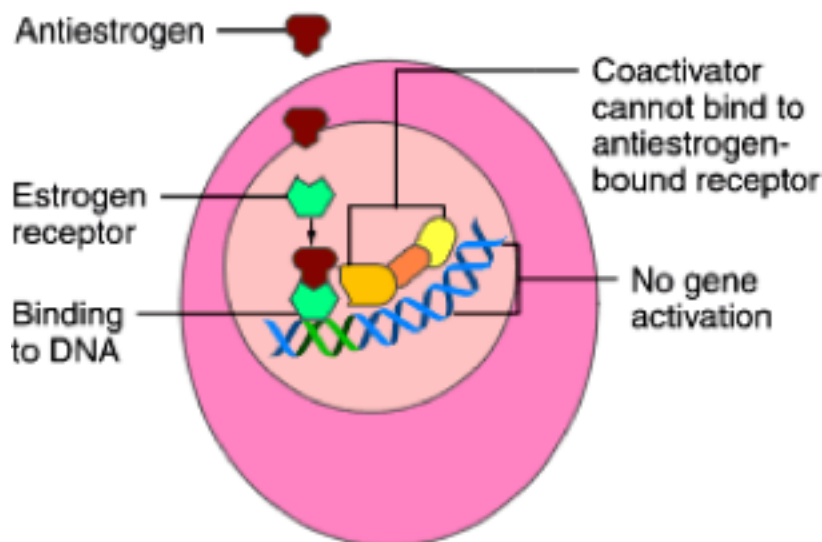
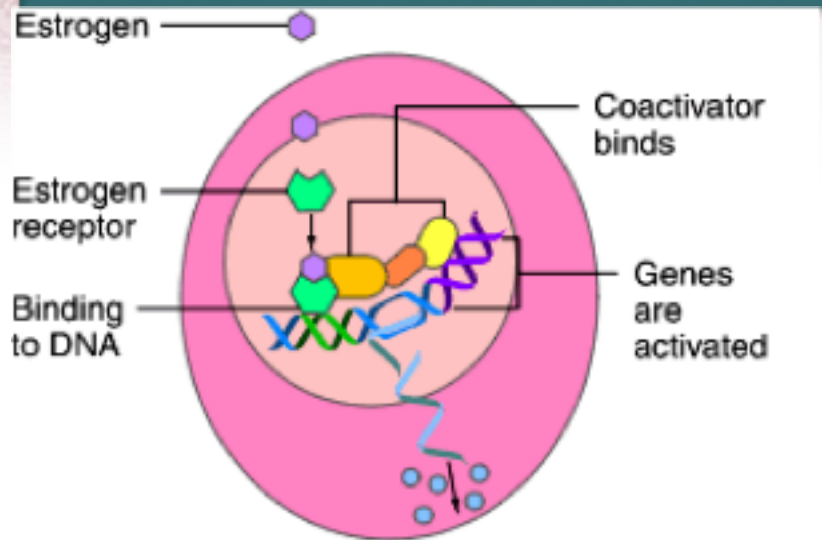
What Percentage of Breast Cancers have Hormone Receptors?



Multiple immunofluorescence labeling of fixed sections of breast cancer. A breast cancer positive for estrogen receptor (ER). An area of ductal carcinoma shows high-resolution four-color immunolabeling after in situ staining for cytokeratin 8/18 (green), ER (red) and vimentin (yellow). Nuclei were counterstained with DAPI (blue).

- ❑ ~75% of breast cancers are estrogen-receptor-positive ("ER-positive" or "ER+").
- ❑ ~65% of ER-positive breast cancers are also progesterone-receptor-positive ("PR-positive" or "PR+").
- ❑ Approximately 25% of breast cancer patients have tumors that are HER2+.

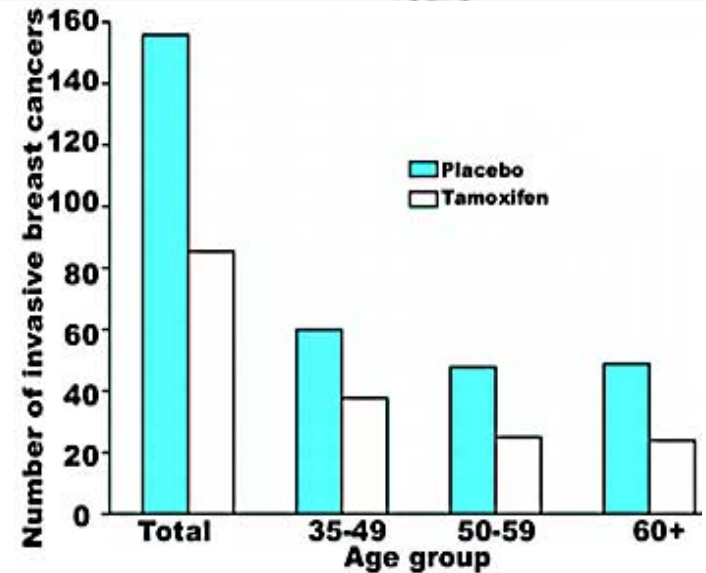
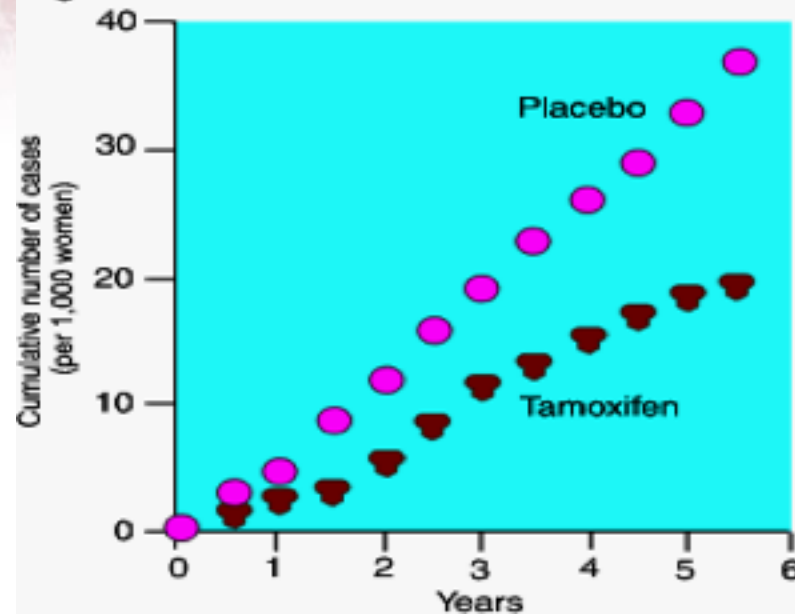
Anti-Estrogens/Selective Estrogen Receptor Modulators (SERMs)



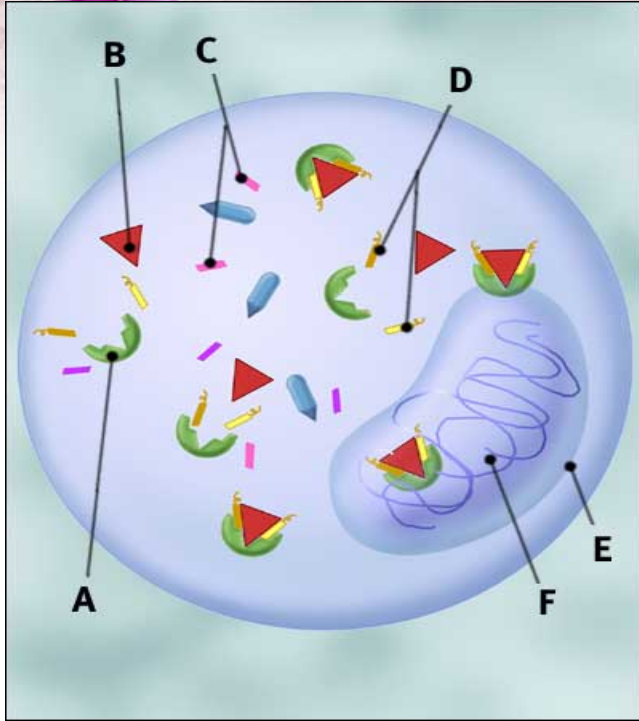
Tamoxifen Helps Prevent Breast Cancer

- ❑ Tamoxifen is a *selective estrogen receptor modulator*, or SERM
- ❑ 1992 NCI study involving ~13,000 healthy women at high risk for breast cancer based on their family or medical history.
- ❑ Half were given tamoxifen, while other half were given a placebo.
- ❑ After 5 years, group receiving tamoxifen had a lower rate of breast cancer.

Invasive breast cancer rates in women at high risk



How Tamoxifen Works & Who Gets it

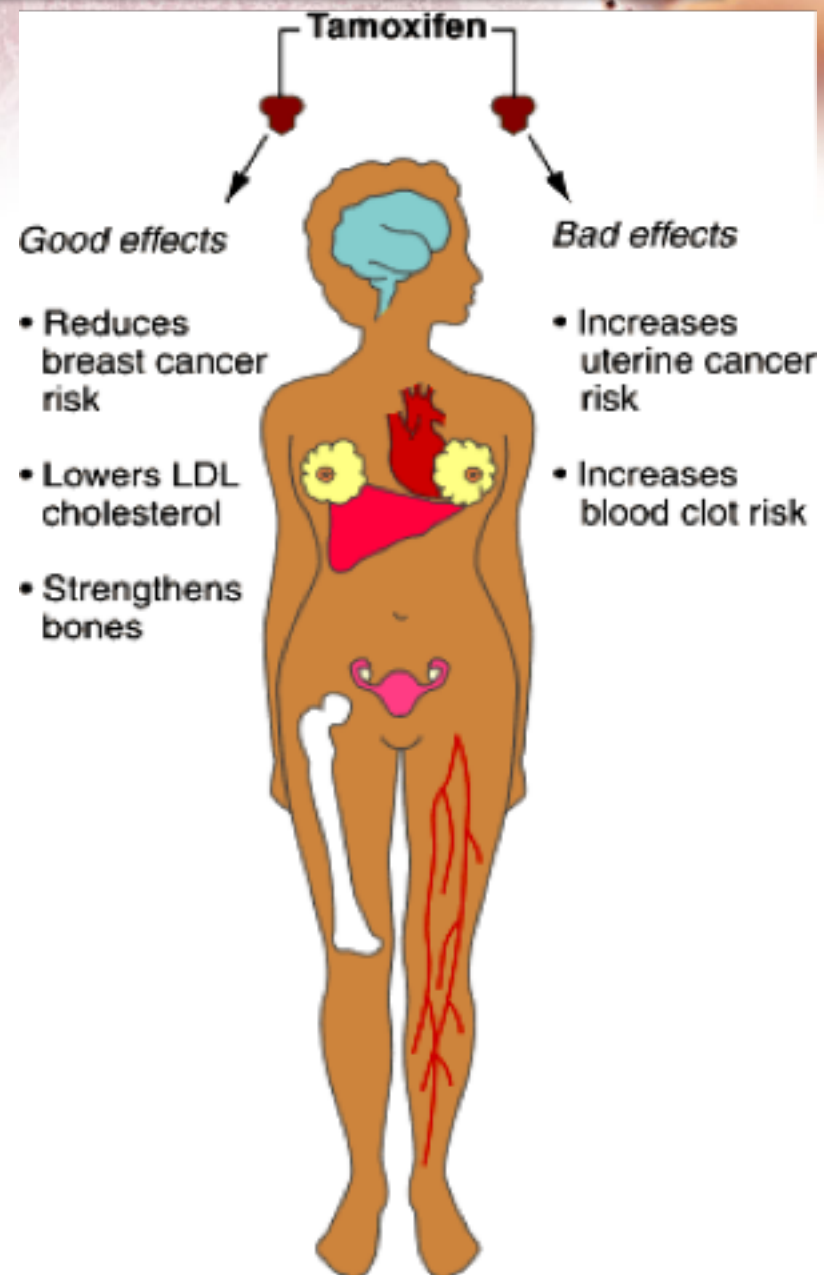
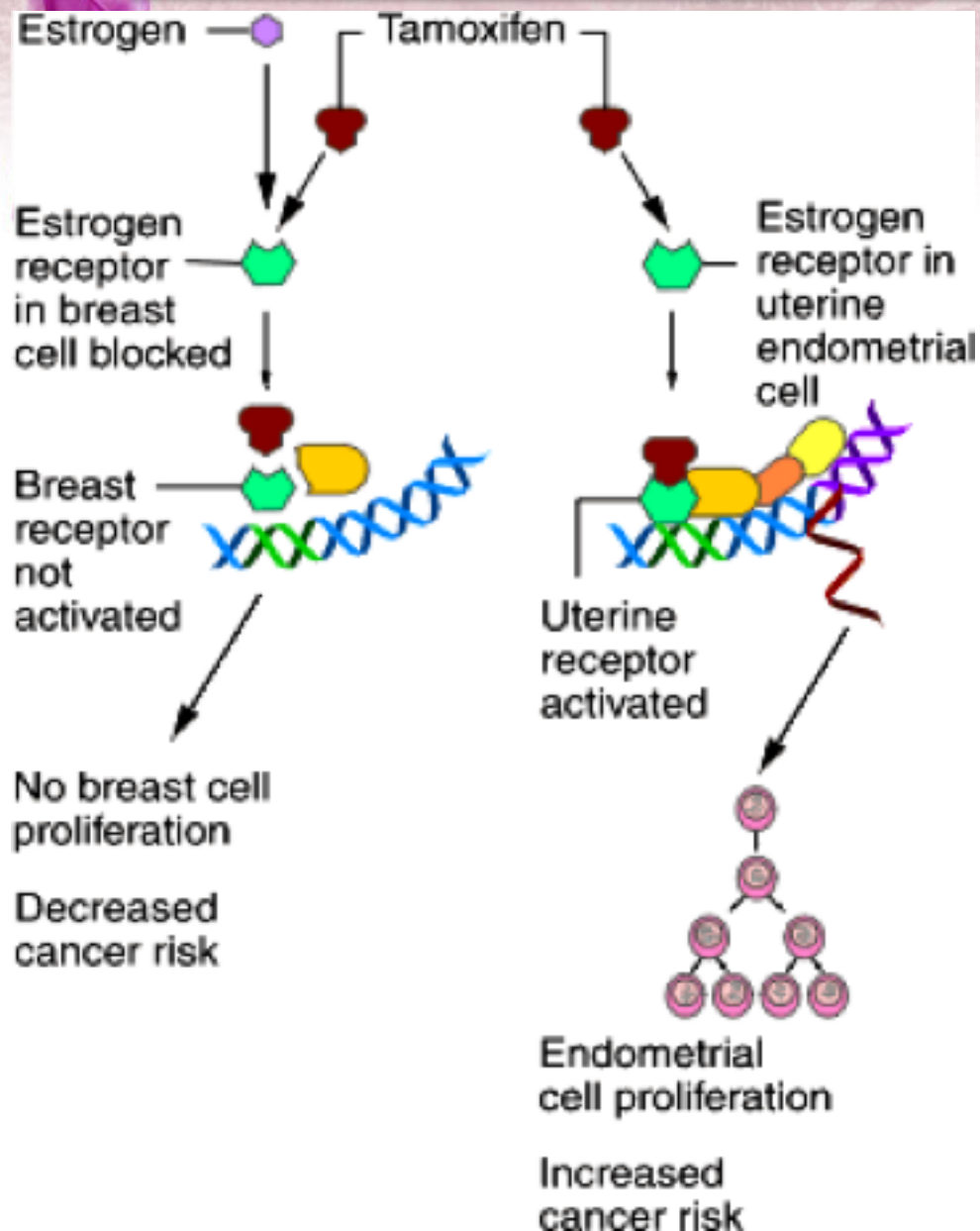


Cell with estrogen receptors blocked by tamoxifen and helper proteins.

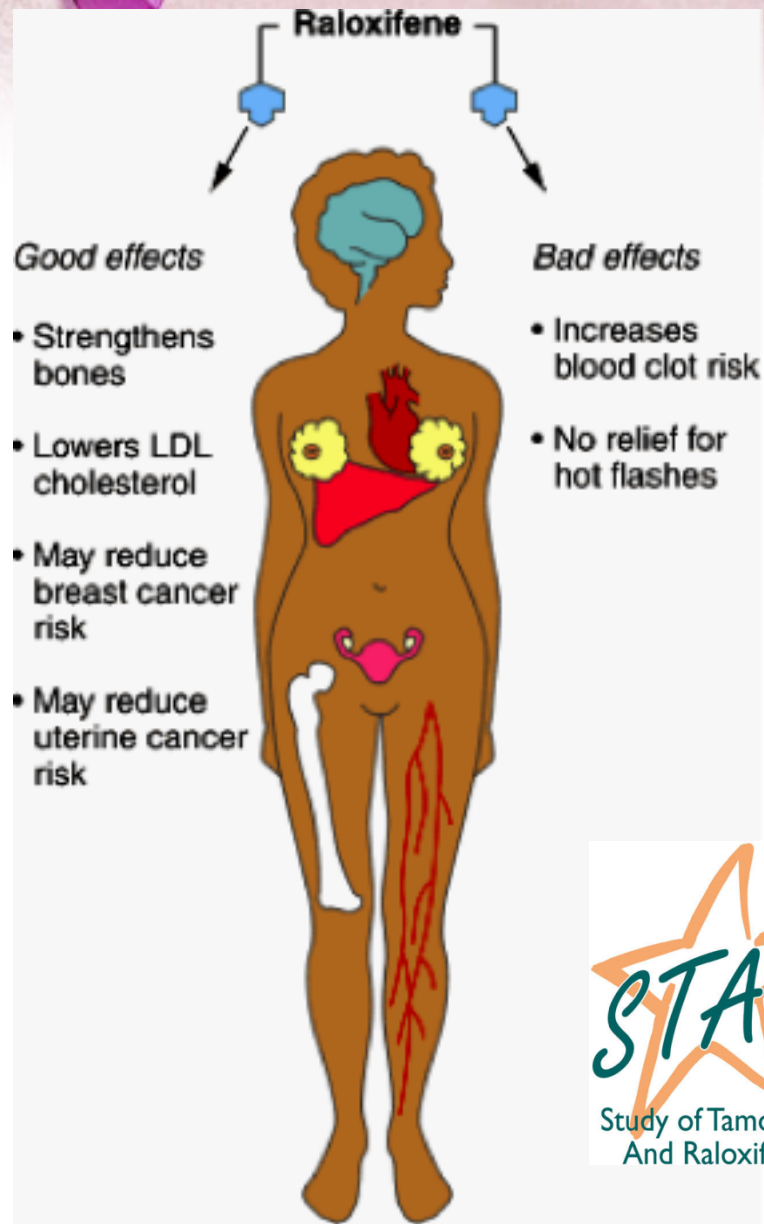
- A** Estrogen receptor
- B** Tamoxifen
- C** Estrogen helper proteins
- D** Tamoxifen helper proteins
- E** Nucleus
- F** DNA genetic material

- ❑ Tamoxifen is the oldest of all the SERMs (Selective Estrogen Receptor Modulators)
- ❑ Prescribed for women with hormone-receptor-positive breast cancer before and after menopause.
- ❑ Reduces the risk of breast cancer for women who:
 - are at high risk of breast cancer but have no personal history of the disease, or
 - have non-invasive, hormone-receptor-positive breast cancer, or DCIS (ductal carcinoma in situ), or
 - have hormone-receptor-positive invasive breast cancer at any stage

Side Effects of Tamoxifen



Raloxifene and Breast Cancer Treatment



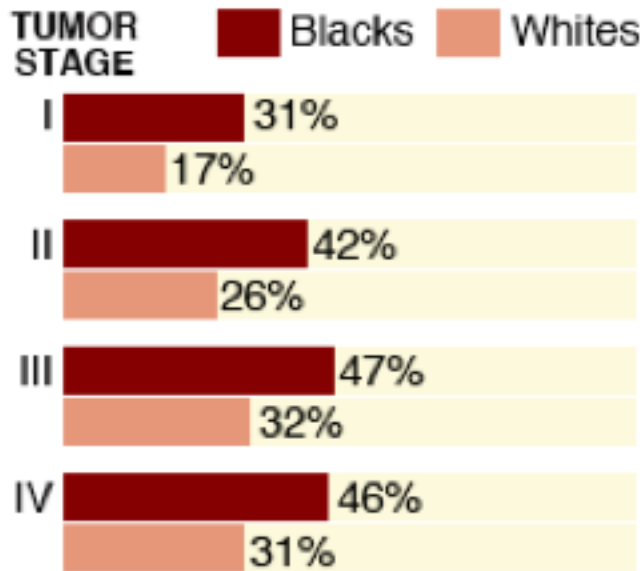
- ❑ Raloxifene is another anti-estrogen SERM medication.
- ❑ Approved by the FDA in 1997 for preventing osteoporosis in postmenopausal women
- ❑ Reduces risk of breast cancer without stimulation of uterine cell division exhibited by tamoxifen.
- ❑ NCI sponsored STAR (Study of Tamoxifen and Raloxifene), was begun in 1999 and followed more than 20,000 women for a period of 5 to 10 years.

Hormone Receptors Make A Difference

Cancer and race

Black women have more breast cancers that are estrogen receptor-negative, or resistant to hormone treatments, than white women do, a study found.

Proportion of cases ER-negative



SOURCE: University of Michigan

AP

- ❑ Estrogen and progesterone receptors, allow the tumors to take in the hormones
- ❑ If a woman's tumor is positive for hormone receptors, it improves her chance of surviving
- ❑ After 5 years, 91% of women with hormone receptor +ve tumors are alive, compared with 80–81% of women whose tumors test -ve
- ❑ Tumors that do not contain hormone receptors are more likely to be able to spread to other parts of the body.
- ❑ There are better treatments to reduce recurrence of receptor-positive tumors.



50,000 WOMEN ARE DIAGNOSED WITH BREAST CANCER EVERY YEAR

♀ = 1,000



15 - 20% OF THESE CASES ARE TRIPLE NEGATIVE



Triple negative breast cancer is more common in women who develop breast cancer under 40, and in black women.

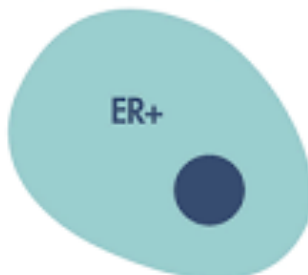


Triple negative breast cancers are defined by what they **don't have**:

HER2
PROTEIN



HORMONE
SENSITIVITY



TRIPLE
NEGATIVE



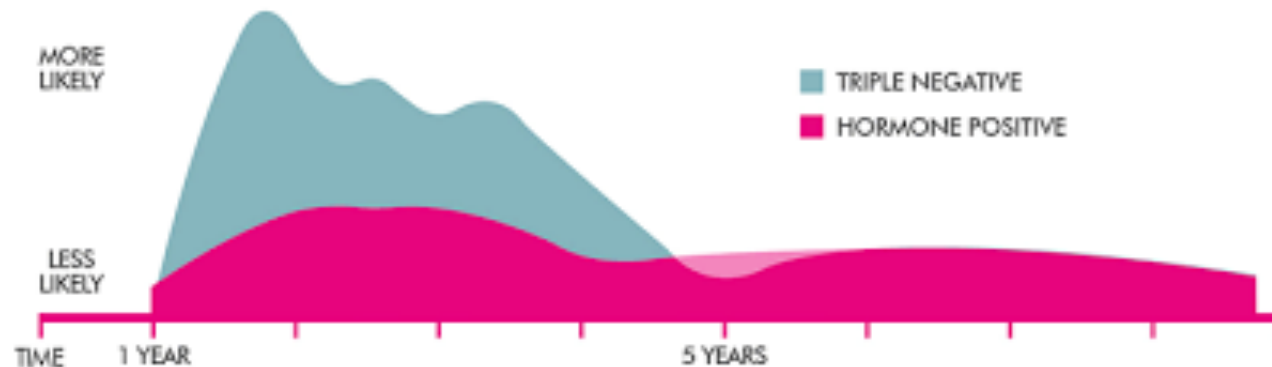
Cancers that test **negative** for progesterone receptors, estrogen receptors and a protein called HER2 are known as **triple negative**. Lacking any of these receptors, triple negative tumours do not respond well to targeted therapies such as Herceptin, or hormone treatments such as tamoxifen.



Triple Negative Breast Cancer: TNBC



Triple negative tumours are usually treated with some combination of surgery, chemotherapy and radiation therapy. But the outcomes for triple negative breast cancers are worse than for other breast cancers...



...and triple negative tumours are more likely to recur after treatment in the first five years after diagnosis than hormone positive tumours.



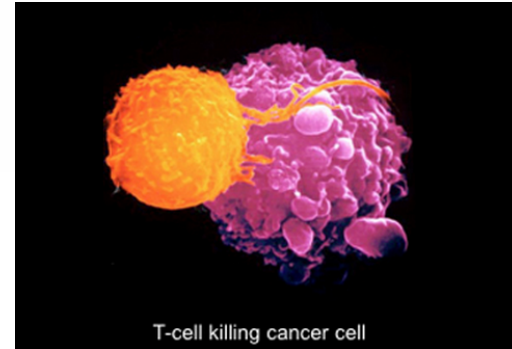
Immunotherapies Opdivo Keytruda anti PDL abs

No ordinary patient: Carter's Stage IV melanoma and how it will be treated



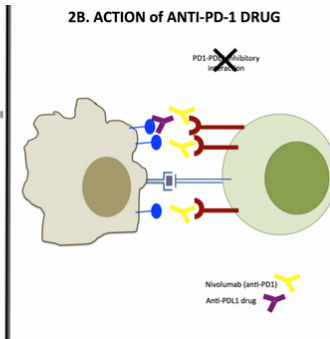
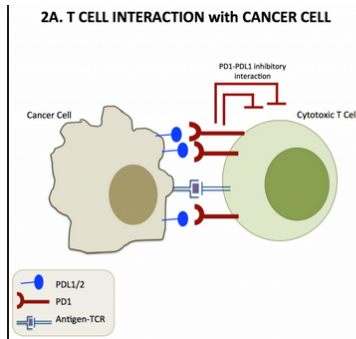
By Jen Christensen, CNN

Updated 8:33 AM ET, Fri August 21, 2015 | Video Source: CNN



Anti PD-1 Mechanism of action

- PD-1 is expressed on antigen-stimulated T cells and induces downstream signaling that inhibits T-cell proliferation, cytokine release, and cytotoxicity.
- Many tumors, including melanoma, suppress cytotoxic T-cell activity by expressing PD-1 ligand (PD-L1) on the cell surface.
- Anti-PD-1 and PD-L1 antibodies can reverse this T-cell suppression and induce long-lasting antitumor responses in patients with advanced solid tumors, including advanced melanoma.



NICE rejects **Opdivo** for lung cancer once again

PMLIVE - May 12, 2016

Opdivo was launched in the UK last August and is already being made available to some patients via the Early Access to Medicines Scheme ...

NICE deems Bristol-Myers' **Opdivo** too pricey for lung cancer

FiercePharma - May 12, 2016

[View all](#)

 Patient Information >

A humanized monoclonal immunoglobulin (Ig) G4 antibody directed against human cell surface receptor PD-1 (programmed death-1 or programmed cell death-1) with potential immune checkpoint inhibitory and antineoplastic activities. Upon administration, pembrolizumab binds to PD-1, an inhibitory signaling receptor expressed on the surface of activated T cells, and blocks the binding to and activation of PD-1 by its ligands, which results in the activation of T-cell-mediated immune responses against tumor cells. The ligands for PD-1 include programmed cell death ligand 1 (PD-L1), overexpressed on certain cancer cells, and programmed cell death ligand 2 (PD-L2), which is primarily expressed on APCs. Activated PD-1 negatively regulates T-cell activation and plays a key role in in tumor evasion from host immunity. Check for [active clinical trials](#) using this agent. ([NCI Thesaurus](#))

Roche wins first immunotherapy approval for triple-negative breast cancer

Abraxane chemo drug inhibits mitosis
Taxol natural product

AUTHOR

Ned Pagliarulo

@NedPagliarulo

PUBLISHED

March 8, 2019

SHARE IT

in POST

f SHARE

🐦 TWEET

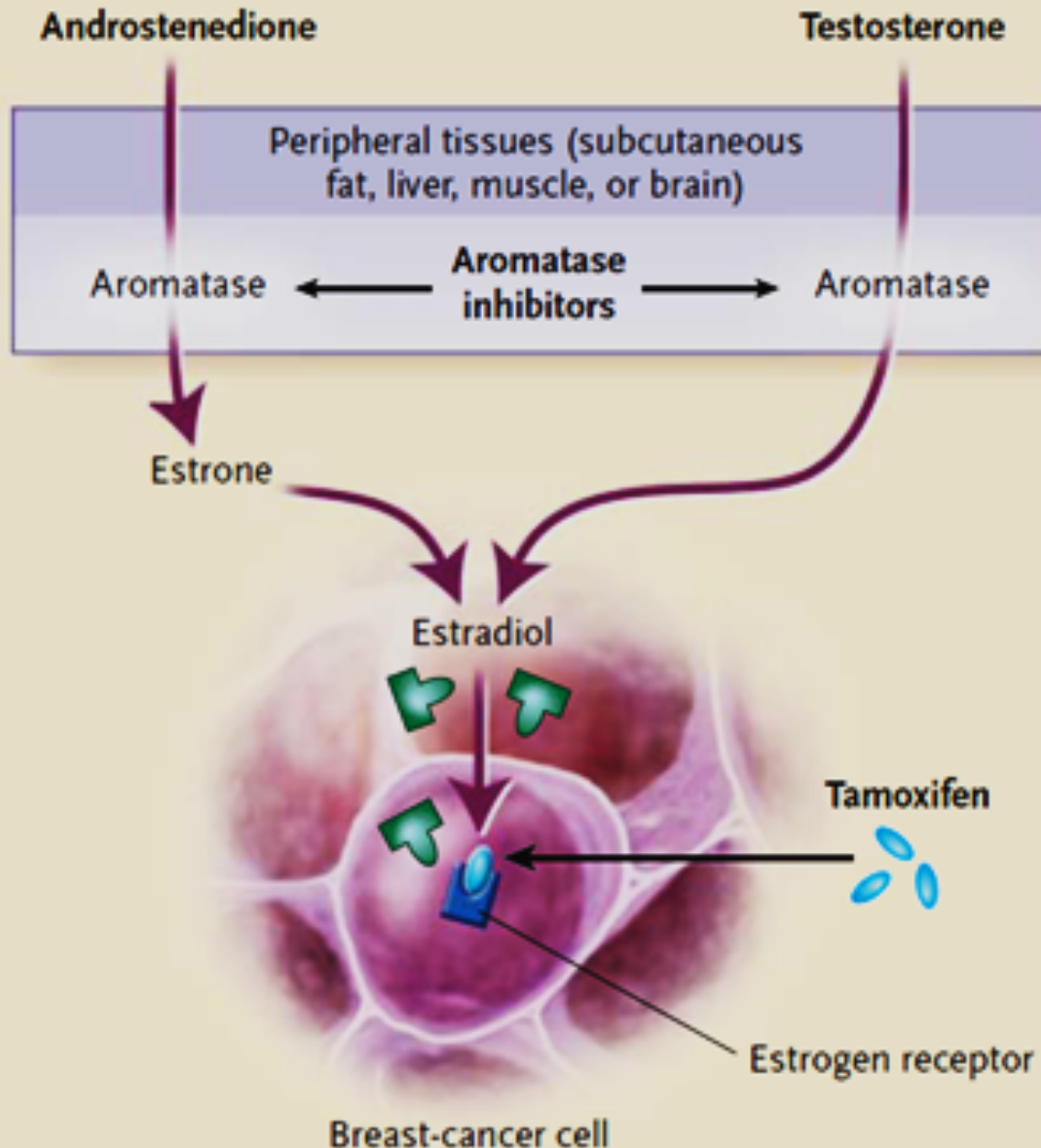
Dive Brief:

Tecentriq = Atezolizumab anti PD-L1 antibody

- The Food and Drug Administration on Friday approved the first immunotherapy regimen to target a hard-to-treat type of metastatic breast cancer, granting an accelerated OK to a combination of Roche's Tecentriq and an older chemotherapy called Abraxane.
- Patients with so-called triple-negative breast cancer and whose tumors express a biomarker known as PD-L1 are eligible to receive the Tecentriq regimen under the label cleared by the FDA. The FDA's approval, however, is contingent on further study to confirm the benefit Roche observed in the Phase 3 study supporting its application.
- In that trial, called IMpassion 130, treatment with Tecentriq and Abraxane extended progression-free survival by a little over two months versus Abraxane alone in previously untreated patients. Data on survival, however, were not yet analyzable.



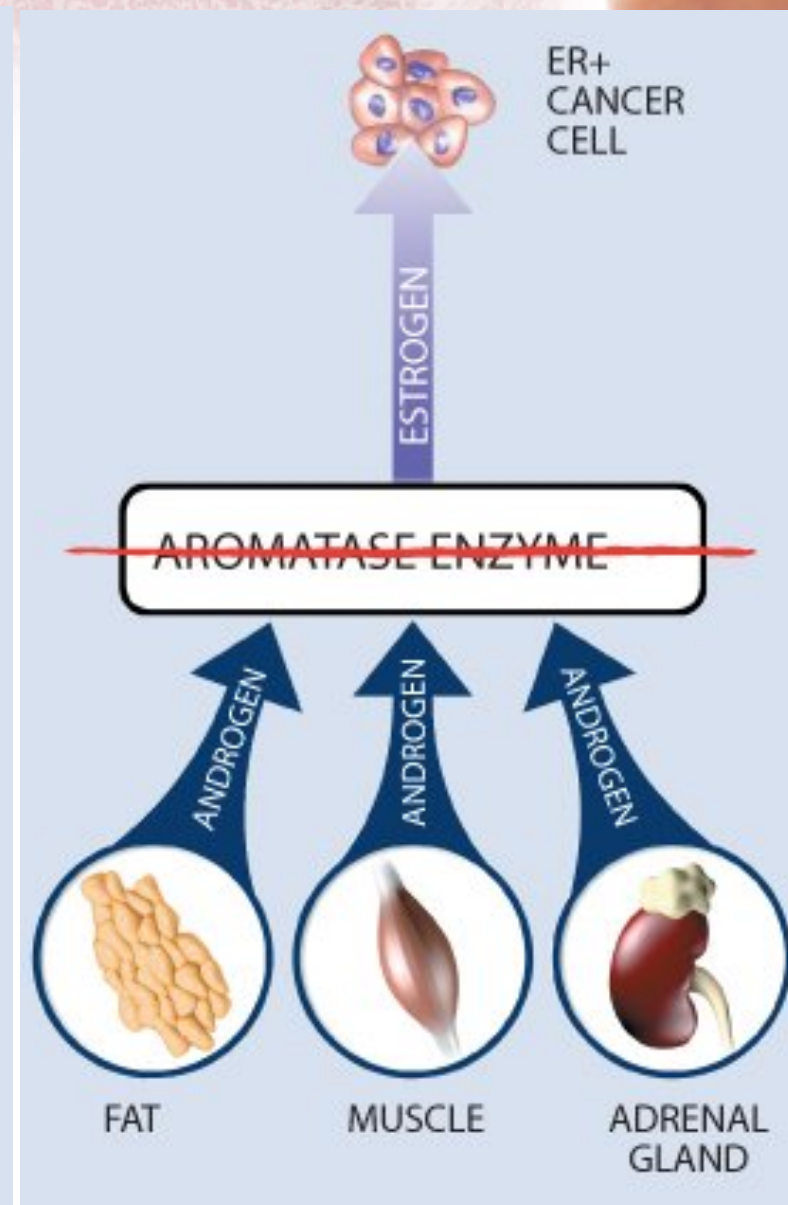
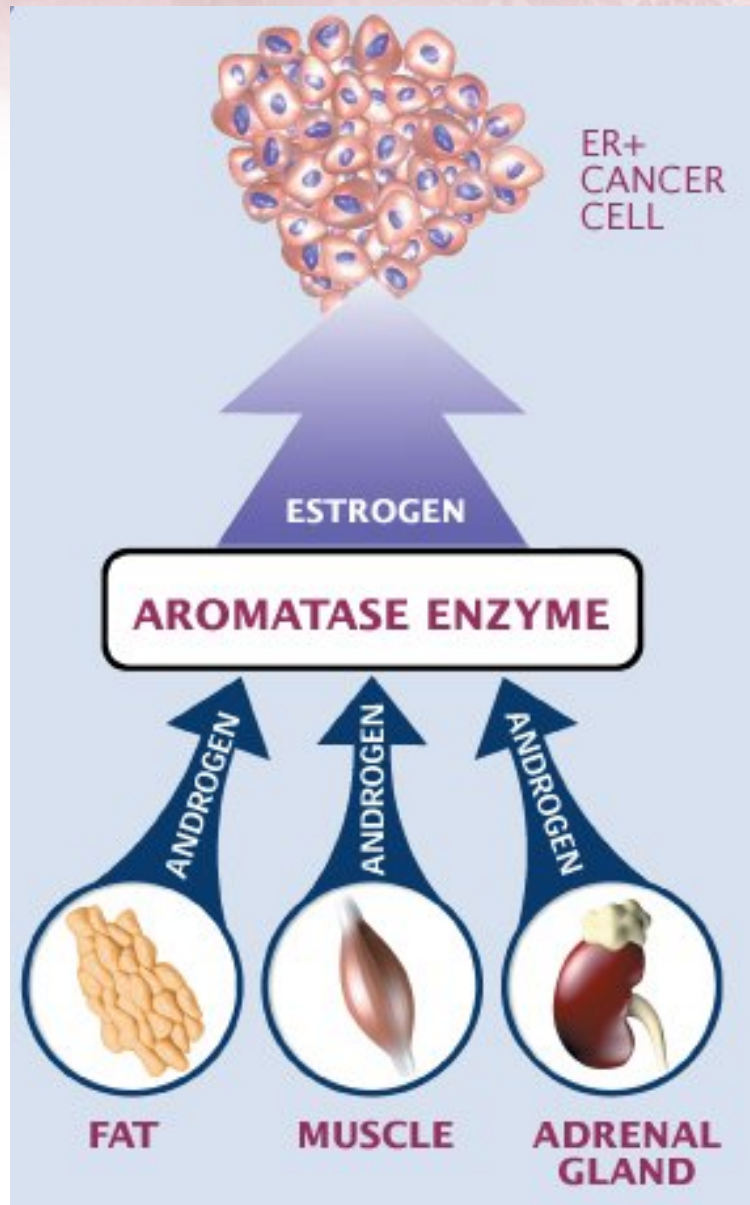
Mechanism of Aromatase Inhibitors and Tamoxifen in Breast Cancer Treatment



Aromatase Inhibitors Supersede Tamoxifen in some Breast Cancers

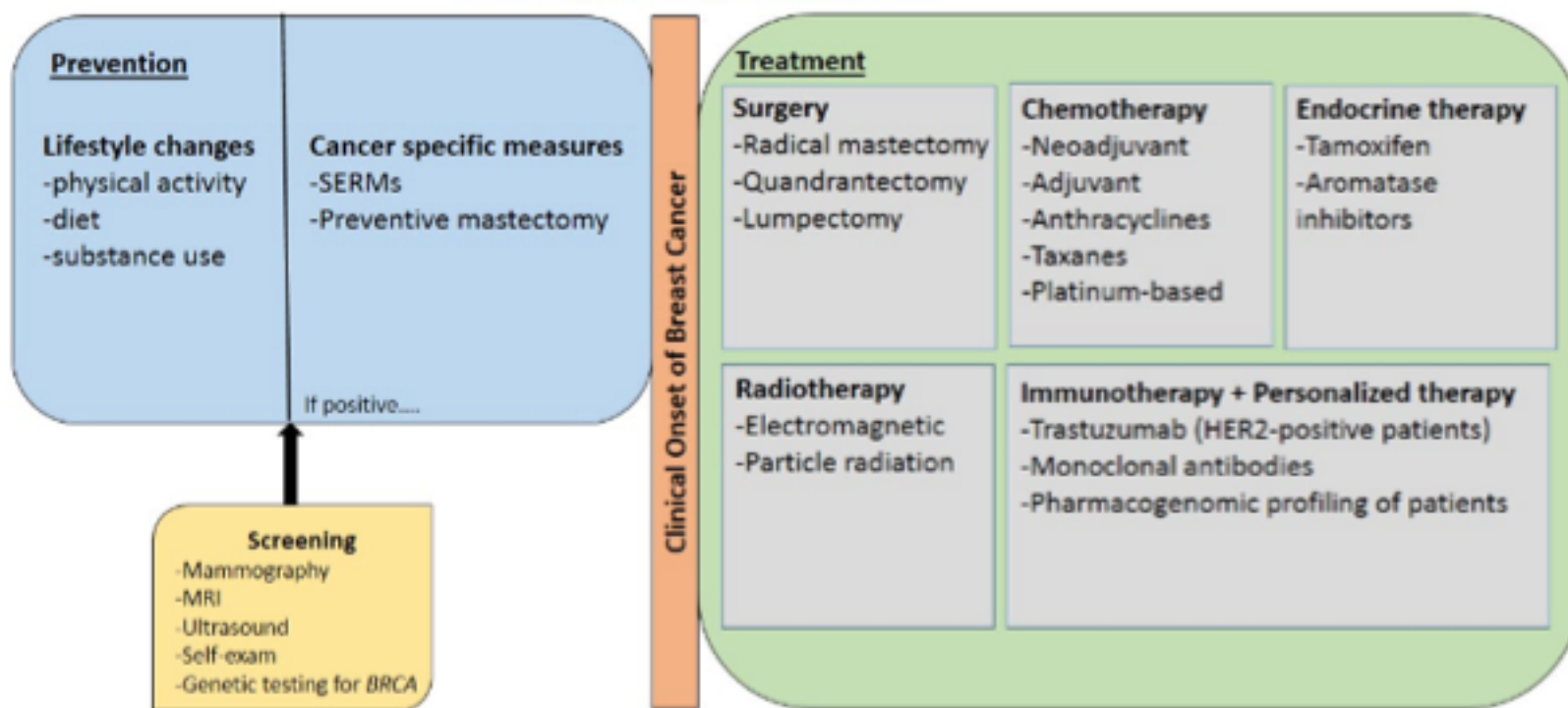


How Aromatase Inhibitors Like Femara® (letrozole)





Breast Cancer Management Overview





Pinkwashing



182,460 – the number of new cases of breast cancer diagnosed in 2008.

41,000 – the number of women who will die from the disease this year.

25¢ - the amount one company is donating to breast cancer research for each \$4.95 pink pen it sells.

If all the products that slap pink ribbons on their label actually donated a portion of their total proceeds to fighting breast cancer, this disease may have gone the way of the dinosaur by now.



Before you toss another pink product on it into your shopping cart this October, look at the label to see how much of what you're spending will actually go to women battling breast cancer or towards finding a cure.

A Public Service Announcement by Tigerlily Communications