

Treating breast cancer usually involves one or more drugs, surgery, and sometimes radiation. Though there are numerous new breast cancer therapies currently in development, many of the drugs used today have been on the market for decades.

Although Susan G. Komen for the Cure did not fund the development of these drugs, because they were developed prior to our founding or at a time when our research investment focused on the basic biology of breast cancer, Komen has funded research to improve the use of these treatments and better understand how they work. Much of the research has centered on:

- understanding which breast cancers will respond to a particular therapy (markers of sensitivity),
- predicting which might develop resistance to the drug (markers of resistance),
- developing better treatments by combining these older drugs with new therapies, and
- finding ways to reduce side effects (toxicity).

The following sections provide a brief background on HER2-targeted therapies, seven common chemotherapies and two hormonal agents and specifics on some of the Komen funded research. The chart below shows the general areas of research on each breast cancer drug. These studies are part of Komen's sustained commitment to breast cancer research with the goal of saving lives and reducing suffering from the disease.

CHEMOTHERAPIES

Adriamycin (doxorubicin) was discovered in 1969 by Farmitalia Research Laboratories in Italy. Komen-funded research on doxorubicin includes methods for preventing toxicity from treatment with doxorubicin and a clinical study on the cardiac effects of the drug.

Cytoxan (cyclophosphamide) was developed and tested in the 1950s. Komen funding has supported laboratory studies using cyclophosphamide with new drugs for possible breast cancer treatments, including triple negative disease (TNBC), and to test its potential to suppress metastasis.

Focus of Komen-funded research	Adriamycin	Cytoxan	Fluorouracil	Methotrexate	Taxol	Taxotere	Xeloda	Femara	Tamoxifen
Sensitivity: identifying markers and/or restoring sensitivity	●	●	●	●	●	●		●	●
Resistance: identifying markers and/or overcoming resistance	●	●	●	●	●	●	●	●	●
Toxicity: identifying markers of toxicities and/or strategies for overcoming toxicities	●	●		●	●	●		●	●
Combination therapy: preclinical studies with new drugs or other therapies (e.g., radiation)			●		●	●		●	
Clinical trials: Dosing schedules							●		
Biomarkers							●		
Predictive/prognostic tests	●	●	●		●				

The Susan G. Komen for the Cure® promise is to save lives and end breast cancer forever.

Fluorouracil (5FU) was developed in the 1950s by Hoffman-La Roche. With Komen funding, researchers have done preclinical studies to look at 5FU in combination with new drugs for treatment of specific types of breast cancer and metastatic breast cancer.

Methotrexate, one of the original chemotherapeutic drugs, was developed in 1947 for the treatment of leukemias. Komen-funded research on methotrexate has included strategies for preventing cardiac toxicity.

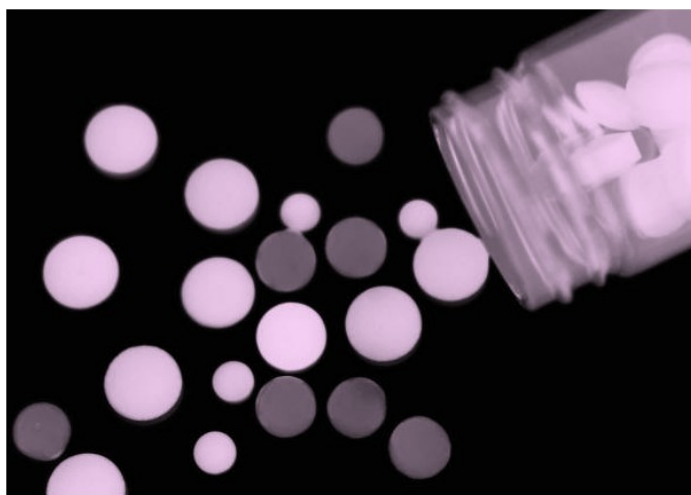
Taxotere (docetaxel) was developed in 1986 by Rhone-Poulenc (now Sanofi-Aventis). Komen has supported research on the drug, including pharmacogenetics and markers of sensitivity and approaches to restore sensitivity to or overcome resistance to docetaxel.

Taxol (paclitaxel) was discovered in the mid-1960s by the NCI's Cancer Chemotherapy National Service Center. In addition to topics shown in the table, Komen funding has supported studies into the mechanism of action of paclitaxel and pre-clinical development of methods to deliver paclitaxel directly to cancer cells, which include paclitaxel bound to antibodies and nanoparticle-based delivery methods.

Xeloda (capecitabine) is an oral chemotherapy that was first approved in 1998 for metastatic breast cancer. The body converts capecitabine into 5FU, a chemotherapy that was developed in the 1950s (see below). Komen has supported several research projects on this drug including a study for HER2+ metastatic breast cancer that is using a HER2-targeted vaccine with the drugs lapatinib and capecitabine.

HORMONAL THERAPIES

Tamoxifen is a selective estrogen receptor modulator (SERM) that was first synthesized in 1966 by the pharmaceutical company now called Astra-Zeneca, and it was first used against breast cancer in 1971. [Dr. V. Craig Jordan](#), a [Komen Scholar](#), was the first one to show that tamoxifen could be used to treat breast cancer and later demonstrated that it could also prevent breast cancer. Komen has funded Dr. Jordan and other investigators to study



tamoxifen, which was the first targeted therapy for breast cancer. These studies have looked into improved prevention strategies by combining tamoxifen with other agents. Komen-funded researchers have studied the effects of tamoxifen on cognitive functioning as well as the mechanism underlying the drug's harmful effects on the uterus. Yet another project has studied the mechanism by which tamoxifen reduces efficacy of other chemotherapies.

Femara (letrozole) is a non-steroidal, reversible aromatase inhibitor (AI) that was developed by Ciba-Geigy (now Novartis AG) in the 1980s. It was approved for the treatment of advanced breast cancer in Europe in 1996, and in the US in 1997. With Komen funding, researchers have looked for ways to differentiate who will respond to letrozole over tamoxifen, or vice versa. They are also conducting preclinical studies of letrozole in combination with a new category of drugs (called HDAC-inhibitors) for treating ER-negative breast cancer and/or preventing metastasis.

HER2-TARGETED THERAPIES

Herceptin (trastuzumab), developed by Genentech, was approved for the treatment of metastatic HER2-positive breast cancer in 1998. Though Komen did not fund the development of trastuzumab, we have invested more than \$41* million in research on HER2-positive disease and the drugs for treating this type of breast cancer. For more information about these grants, see [Research Fast Facts: HER2-Positive Breast Cancer](#) (available on [komen.org](#)).

*Through FY2010