Breast cancer

Breast cancer is the collective term for all the cancers that originate in breast tissue. Most of these begin in the glandular tissue, though the most common of all breast cancers starts in the ducts. Breakthrough Breast Cancer is a UK charity that aims to ensure every person affected by breast cancer gets the best treatment, information and support. This article reviews its research work.

website **breakthrough.org.uk**

Breast cancer is the most commonly diagnosed cancer in women under 35 years—nearly 1,500 women aged 35-39 years are diagnosed annually. It is the second biggest cause of death from cancer for women in the UK, with lung cancer being the biggest. The biggest risk factor after gender, is age with 80% of breast cancer cases occurring in women over the age of 50 years. More women than ever in the UK are surviving breast cancer thanks to better awareness, better screening and better treatments.

Research

Breast cancer takes many forms. We have researched diagnosis, treatment and ways to prevent all types of the disease. Some of this research is very specific, focusing on the unique characteristics of a particular form of breast cancer. However, much of our work will benefit all people with the disease. Since we opened the UK's first dedicated breast cancer research facility, we have enjoyed many successes. As well as the dedicated Breakthrough Breast Cancer Research Centre in London, we have established a network of research units across the UK. Some of our research is listed below.

Hormone sensitive breast cancer

Hormone sensitive cancers have large numbers of hormone receptors and are often referred to as "hormone-receptor positive". This means that female hormones fuel their growth. Around 75% of breast cancers are hormone-sensitive.

Tamoxifen and aromatase inhibitors are highly effective treatments for hormone sensitive breast cancer and have helped save thousands of lives. However, not all hormone sensitive breast cancers respond to treatment in the same way. For this reason, every patient needs a tailor-made treatment programme.

Breakthrough is leading an investigation into ways to identify which women will respond most effectively to tamoxifen and which to the alternative anastrozole. This will help us develop treatments specific to each patient's tumour type and ensure women are treated most effectively.

Some women can become resistant to anti-hormone therapy. To counter this, we are using a new technology called RNA Interference to study resistant cancer cells. This will look for chemicals that will re-sensitise cells to tamoxifen, for development into potential new treatments.

Another Breakthrough study has shown for the first time that a single drug can simultaneously attack hormone sensitive cancer cells in two different ways. This discovery could lead to further two-in-one treatments —potentially reducing the number of drugs women with hormone-positive breast cancer will need to take in the future.

HER2-positive breast cancer

When a cancer is HER2-positive it means the tumour has high levels of the HER2 receptor protein, which helps it grow. Herceptin, a drug designed to target HER2, has proved beneficial for many patients with this form of breast cancer. Some 25% of breast cancers are HER2-positive. They tend to grow quickly and are more likely to return after treatment.

We are working to develop a new, accurate and

sensitive test to predict whether a patient will benefit from Herceptin treatment. This test could also be useful for predicting whether future targeted treatments will benefit individual patients. Herceptin doesn't work for all HER2-positive breast cancer patients, however, and resistance can develop to the treatment.

We are also reseaching for the differences between responsive and resistant tumours. This will help scientists develop new, more accurate ways to treat patients with HER2-positive breast cancer. Dr Jorge Reis-Filho, who leads the Molecular Pathology Laboratory at the Breakthrough Research Centre, has identified several genes that help HER2-positive breast cancers grow and spread. Potentially, new drugs could be developed to target these genes. These genes will also tell us why some HER2 positive tumours resist treatment—information that could help us in future to design new treatments or to re-sensitise tumours to existing treatments.

Triple negative breast cancer

Around 15–20% of breast cancers do not have hormone receptors or HER2 receptors. These are termed triple-negative. They tend to be more aggressive than other forms of breast cancer. They can also be difficult to treat because, lacking receptors, the tumours do not respond to targeted therapies such as Herceptin or to hormone treatments such as tamoxifen. Triple-negative breast cancers occur more frequently in younger women and those of African ethnicity than other breast cancers.

This year we opened a research unit at Kings College London dedicated to improving the treatment of triple-negative breast cancer and its close relation, basal-like breast cancer. By discovering more about these types of tumour, and the faulty molecules that cause their growth, we hope to develop treatments that target cancer cells and leave healthy cells unharmed.

In 2008, along with Cancer Research UK, we launched a clinical trial, which aims to improve treatments for triple-negative breast cancers that spread to other parts of the body. The trial will compare two forms of chemotherapy: carboplatin, not normally used to treat breast cancer, and docetaxel, the standard treatment. If successful, the trial could lead to carboplatin becoming part of a new tailored treatment for this disease.

Breakthrough's Professor Clare Isacke has discovered that some triple-negative breast cancers over-produce a molecule called Endo180, which may encourage the disease to spread to other parts of the body. She is now looking to see if Endo180 can be used as a target for new treatments to prevent this spread, thus improving the chances of successful treatment.

Hereditary breast cancer

Hereditary breast cancer—accounting for around 5% of breast cancer cases—is linked to inherited faulty genes and often affects younger people. BRCA1 and BRCA2 are the most common genes associated with this form of the disease, currently there are no specific treatments for hereditary breast cancer. We have discovered that cells with faulty BRCA genes are particularly sensitive to a class of chemicals called PARP inhibitors. These are now being trialled in the clinic. Led by Breakthrough's Dr Andrew Tutt and KuDOS, part of AstraZeneca, this is the world's first clinical trial of a targeted treatment for hereditary breast cancer. Initial results suggest the drug could benefit many people. Dr Tutt is also leading a clinical trial of a form of chemotherapy using carboplatin. The trial aims to determine if carboplatin is more effective than docetaxel, the standard chemotherapy treatment, for hereditary breast cancer that has spread to other parts of the body.

In 2008, Professor Ashworth made an important discovery about how BRCA-related breast cancers become resistant to drugs. With this knowledge, we hope to counter resistance to certain treatments in the future. There are many genes that play a role in inherited forms of breast cancer, not just BRCA1 and BRCA2 genes. Inheriting a faulty version of one or more of these genes may moderately increase the risk of breast cancer. Although some of these genes have been found, scientists believe there are still many more to be identified.

Conclusion

Breakthrough supports a programme of cutting-edge biological research to reach our vision of "a future free from the fear of breast cancer." Through our research, we will increase our understanding of breast cancer, leading to improvements in diagnosis, treatment, quality of life and prevention of the disease.