

Breast cancer treatment - the next advances

Loirena Tonarelli looks at how new treatments could help advance the fight against the disease

When a close member of my family was diagnosed with breast cancer, the doctors didn't give us much hope. They said there wasn't anything they could do and that we just had to "wait for the inevitable to happen". Which it did.

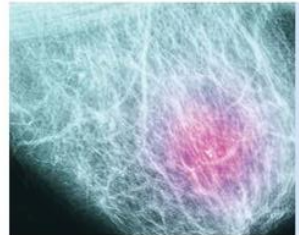
But that was more than 30 years ago. Thankfully, since then treatment and survival rates have improved considerably, and breast cancer is now the most common cancer in women. There are at least two reasons for this. Regular screening programmes and advanced diagnostic methods mean breast cancer is more likely to be detected in the early stages, when it's easier to treat successfully. Secondly, new therapies have been developed which are effective at keeping the disease under control, or preventing its recurrence. As a result, patients can now expect to live longer. Recent statistics show that, for example, that of the 49,700 women who are diagnosed with breast cancer in the UK every year, 85% survive at least 10 years.

Established and new options
In most cases, surgery is the first line of treatment for breast cancer, followed by chemotherapy and, in some cases, radiotherapy. These three cancer treatments are often used in combination. Hormone therapy, usually with tamoxifen, to lower the levels of oestrogen in the body and, in turn, reduce the risk of the cancer coming back. Additionally, targeted therapy agents can be considered, which vary depending on the type of breast cancer.

For example, patients with high levels of human epidermal growth factor receptor-2 (HER2) on their breast cancer cells are typically treated with a drug called trastuzumab (Herceptin) either as monotherapy or in combination with chemotherapy. HER2, a protein produced by a cancer-causing gene mutation found in about 25% of breast cancer patients - generally those with the most aggressive form of the disease - stimulates tumour cell growth. Herceptin, a monoclonal antibody, works by binding to HER2, thereby blocking its action.

Herceptin is now an advanced cancer drug, but it takes up to 90 minutes to complete, so Roche are developing an injectable version. This new formulation takes just five minutes to administer and has shown similar efficacy in the Hannah study, a Phase III open-label trial of 596 women with HER2-positive early breast cancer. Roche is expected to submit a marketing application to regulatory authorities in the European Union in 2011 to help extend Roche's market exclusivity for its blockbuster Herceptin, which will otherwise see its patent expire in 2015.

The antibody-drug conjugate approach
Roche is also testing T-DM1 (trastuzumab emtansine), an experimental antibody-drug conjugate enabling the delivery of the cytotoxic drug emtansine to the cancer cells of patients in the advanced stages of the disease. Phase III trial data presented at the European Multidisciplinary Breast Cancer Conference (EMCC) held in Stockholm last September, indicated that patients receiving only a



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lived without cancer growth, compared to exemestane alone (6.9 versus 2.9 months). Ibrahim El Housseiny, country medical director Oncology at Novartis Pharmaceuticals UK, says the results "are very promising". He adds: "The magnitude of benefit seen in these patients, despite their resistance to previous hormonal therapies, demonstrates that everolimus has the potential to be a game-changing treatment option." Submissions to regulatory authorities are planned for the end of this year.

Meanwhile GlaxoSmithKline's dual kinase inhibitor Tyverb (lapatinib), is in Phase III trials in a head-to-head with Herceptin. Like the latter, Tyverb works only in HER2-positive breast cancer patients.

However, GSK has recently halted the Tyverb alone arm of one of these studies (Tyverb), as it is unlikely to make any significant difference to overall survival compared to trastuzumab alone, with non-inferiority to trastuzumab, according to GlaxoSmithKline.

Static market
So will these advances in breast cancer treatment change the market significantly in the near future? "Not necessarily," in fact, according to analysts Daxton Research, the \$102 billion global market is set to remain more or less static over the next ten years. Although the combined sales of new breast cancer agents will account for over 25% of the global market, the latter will increase by only a modest \$0.2 billion by 2019, say the analysts.

He adds: "What patients don't want is that those drugs can't be used, for example, because the government has decided that they are too expensive. This, understandably, affects patients, especially because they are aware of the fact that they could get them if they lived in Europe or in another part of the country."

Roche says: "The fact that we have a highly effective, non-taxane, antiproliferative dynamics inhibitor treatment, Halverson is a first novel chemotherapy agent to show a 2.5-month statistically significant increase in

What patients want

of course a nice issue, particularly in the UK, where NICE often refuses to recommend new cancer treatments.

Patients want their doctor to be able to make the right decision for them, and use drugs they believe are right for their patients, based on what they, and the wider community, have to say. It's all about what available safety and efficacy data."

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The Patients' Perspective

Access to treatment has not been an issue for a long time. It's always been there. The problem is that of two young boys living in Fife, Scotland.

"Following surgery, chemotherapy and radiotherapy, I was given Herceptin. At that time, access to this drug depended on a post-code lottery," meaning that only breast cancer patients in certain catchment areas could get it. But I was one of the lucky ones, and the doctors were able to prescribe it to me. I was given Herceptin for a series of weeks, at hospital to begin with, and then at home. It was a relief to be able to go back to work after 12 weeks.

"Kirk was diagnosed with breast cancer two years ago and has gone through radical breast cancer surgery and reconstruction. She does a huge amount of fundraising and other work to benefit cancer research locally, and is currently raising funds for a calendar for the Maggie's Breast Cancer Centre in Fife.

Kirk is very positive about her experience, and says she has not had any side effects. She has given a lot of information about available treatments from those involved in her care. This has allowed her to make informed decisions, as it always should be in these circumstances.

Information about the potential problems treatments may cause is also important. "My consultant told us about the risks and various side effects you may experience," says Kirk. "It was important to know what you may feel tired, or have pain, was particularly important to me, because I was able to explain all this to my children beforehand."

She thinks, however, that information about experimental drugs is somewhat lacking. "I, for example, am not aware of what is going on in terms of breast cancer drugs under development. And I believe this is true for many other patients."

Acress, Dorothy Roberts, known for playing Dorothy Bennett in the BBC drama Tenko, and Laura Elliott in the ITV series Peak Practice, agrees. She too has breast cancer and believes knowledge is key. "When I was diagnosed, the Macmillan nurses spoke to me about any concern I had; any explanation I wanted to have again. They interface in helping patients who are some times confused about treatments. "In my experience, some women know that Herceptin is a good drug to prevent recurrence, but they don't know that it only works if you have HER2-positive breast cancer, like I do. "They found I had the HER2 gene, which, together with the fact that my tumour was quite well defined, meant I was a good candidate for the drug."

"It was explained to me very thoroughly the difference that the treatment would have made. Specifically, that it would have helped prevent the tumour from coming back. And, so far, it's been successful."

Because Roberts had chemotherapy before, the blood vessels in her hands were in a bad state, so she wasn't given Herceptin with saline, as she was used to. "I don't think that is known as a port-a-cath (or port). The chest, which goes into a main vessel and can be left in place, weeks, months or even years in some cases."

Every three weeks, when Roberts went for her treatment, the oncology team would simply put a needle through the skin into the port, and deliver the drug.

Roberts: "It made me able to be completely mobile and keep working as usual."



Dr Carlo Palmieri, Cancer Research UK Chairman Scientist

overall survival in patients with advanced breast cancer, but it was rejected by NICE in July last year because it was found not cost effective.

England's Cancer Drugs Fund
The Cancer Drugs Fund (CDF) was launched in England in April 2011 to help cancer patients receive drugs which have been either rejected by NICE, or are still awaiting appraisal.

In November, Breast Cancer Campaign looked at the fund's success in helping more women gain access to breast cancer treatments. It found that just over half of the total of at least 150 women had applications for drugs not routinely available on the NHS approved between April and June 2011.

Drugs accessed through the Fund to treat breast cancer include GSK's Tyverb (lapatinib), Roche's Avastin (bevacizumab) and AstraZeneca's Faslodex (fulvestrant).

Tyverb was the breast cancer drug most consistently accessed across SHAs. Avastin is available to all breast cancer patients that 98% of all breast cancer applications were successful. However, as Palmieri points out that the CDF has not eliminated regional variations in access.

"There are three main agents patients can access through the fund [Tyverb, Avastin, Faslodex]. Some parts of England have all three, access to some of the drugs on the CDF really depends on which part of England you live in."

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