

**San Antonio Breast Cancer Symposium (SABCS) on an Alamo Scholarship
Report by Libby Burgess, Chair of BCAC**

SABCS is a key annual research meeting on the breast cancer calendar at which the latest breast cancer research results are presented to an audience of around 9,000 oncologists, researchers and patient advocates. In December 2007, I attended the 30th SABCS and associated Patient Advocate sessions, made possible by an advocate scholarship from the Alamo Breast Cancer Foundation (ABCF). ABCF invites leading breast cancer researchers to summarise key presentations for the advocates at nightly Mentor Sessions during the Conference, enabling delegates to meet and ask questions of the experts.

Thirty-five scholars attended the Conference. Twenty nine were women from around the USA and Canada, all of whom had completed the Project LEAD® science training course developed by the National Breast Cancer Coalition. This training is designed to arm breast cancer activists with the knowledge needed to influence research and public policy on breast cancer. The six international attendees were from the UK, Germany, Nigeria, Namibia, Australia and (of course) New Zealand.

I have learned a lot about the science of breast cancer through my involvement with BCAC and our struggle to improve NZ women's access to effective medicines. This prepared me well for the SABCS which ranks as the most intense and information-rich conference I have ever attended! Poster sessions ran from 7 to 9am each day and participants were lured by the promise of an excellent buffet breakfast. A plenary lecture was delivered from 9 to 9.30am, followed by research papers until lunch at noon. Advocates attended training lunches each day. A further plenary was delivered at 1pm, and papers were presented until 5 or 5.30pm, followed by a further 2 hour poster session. Advocates attended a Mentor Session from 5.30 to 7.30pm each evening, followed by a hosted dinner. The jet-lagged among us (and probably the locals as well!) then fell into bed exhausted until the rude awakening of the early morning alarm signalled another day in the lecture hall was about to begin.

Each advocate was assigned a "Hot Topic", an area of information requiring a report to be written and submitted within a month of the Conference. My topic was *The use of genomics in breast cancer sub-type identification, prognostic prediction and treatment optimisation*. This topic involves the study of breast cancer genes, their mutations and expression patterns. Genomics is a relatively new branch of science enabling researchers to identify and understand different types of breast cancer driven by different biological mechanisms. This knowledge provides the basis upon which researchers develop treatments that specifically target and shut

down the processes involved in each of these breast cancer “sub-types” providing a more individualised and generally less toxic, more effective response to each patient’s cancer. In the not too distant future we will know enough and have a diverse enough arsenal of targeted medicines to enable oncologists to treat breast cancer much more successfully and with fewer side-effects. Our challenge in NZ will be to transform our country’s system for accessing pharmaceuticals so we keep up with the rest of the world in fighting this (and every other) disease.

Some key findings presented at SABCS:

- A new test revealing gene expression profiles of 21 genes (OncotypeDX™) in individual patients has been validated as a means of defining groups of patients likely to benefit from anthracycline (AC) chemotherapy and those unlikely to benefit. The test predicts likely recurrence in those with post-menopausal, node-positive, ER+ breast cancer. This emerging data is likely to reassure some patients that they will benefit from standard AC chemo and allow others to avoid being given unnecessary treatment along with all the associated toxic effects.
- Another new test (Mammaprint®) links a 70 gene expression profile with a likely outcome in patients with only 1 to 3 positive lymph nodes, and will provide a further new tool in helping patients to choose the best treatment option. After 8 years follow-up, the group identified by this test as having a low-risk profile had a survival rate of 98%, while the group predicted to be high risk had a 64% survival rate.
- The ATLAS trial is comparing the use of tamoxifen for 5 years vs 10 years in preventing recurrence of ER+ breast cancer. Preliminary results are showing trends towards reduced recurrence and mortality in those treated for longer. This international study has recruited 11,500 participants from 400 hospitals around the world. The results suggest that current recommendations to restrict the use of tamoxifen to 5 years were based on a relatively small dataset and may have been premature.
- Nine year follow-up data was presented from the ATAC trial comparing 5 years of tamoxifen with 5 years of the aromatase inhibitor (AI) anastrozole (Arimidex) in post-menopausal women with invasive breast cancer. Those treated with anastrozole had an absolute advantage of 4.8% in time to recurrence and a 2.4% advantage in distant recurrence. Interestingly, the anastrozole group also had a 1.7% advantage in new occurrences of cancer in the other breast, suggesting anastrozole may be a more effective preventative agent than tamoxifen. During the treatment period of this study, the incidence of fractures was nearly 30% higher in the anastrozole-treated patients, but fracture rates after the completion of treatment were virtually identical in both groups.

- New drugs available for those patients with low bone density receiving aromatase inhibitors (AIs) to prevent the recurrence of oestrogen receptor positive (ER+) breast cancer, are providing positive results in clinical trials. The third generation bisphosphonate, zoledronic acid, reduces the chance of bone fractures allowing AIs to be used in vulnerable patients. Clinical trial data was also presented on a new treatment, the monoclonal antibody denosumab. This agent, when injected 6-monthly in patients receiving an AI, resulted in 5.5% better spinal bone mineral density at 6 months and a 7.6% advantage at 24 months, and similar benefits in hip and wrist bones, with no negative side-effects observed, although longer-term effects cannot yet be ruled out.
- HER2 gene amplification occurs in 20 to 25% of breast cancer patients, and in about a third of HER2 positive cancers a further gene, TOPO IIa, is also amplified. Targeted therapies trastuzumab (Herceptin) and lapatinib (Tykerb) are effective treatments for HER2 positive cancers, but data suggests that AC chemotherapy is only strongly effective against those that additionally have the TOPO IIa amplification.
- Pertuzumab (Omnitarg) is a monoclonal antibody that targets different elements of the HER2 signalling pathway from trastuzumab. Researchers are testing combinations of agents with the aim of completely shutting down HER2 over-expression. A small study in which patients with advanced breast cancer were given a combination of pertuzumab and trastuzumab, showed the combined treatment was active and well-tolerated, although some adverse effects were noted. Further studies of safety and efficacy are planned.
- A new radiation therapy technique termed MIGA improves the dose to the breast cancer tumour bed while minimising damage to normal tissue. Similarly, another delivery technique, IMRT, reduces side-effects of whole breast irradiation.
- Twelve years of follow-up data have shown that radiation delivered in fewer and stronger doses (AHWBI) can still achieve the same reductions in recurrence and gains in overall survival that standard techniques deliver. The reduction in overall treatment time and numbers of clinic visits make this technique more convenient for some patients.
- Novel biological markers have been identified that can accurately predict the likelihood of ductal carcinoma in situ (DCIS) progressing to produce future tumours. DCIS lesions with basal-like molecular characteristics (similar to the “basal” type of invasive cancer) are associated with a greatly increased risk of developing tumours. This represents another breakthrough, enabling oncologists to better predict prognosis and advise their patients on the best treatment strategy depending on their particular

- cancer sub-type, thus avoiding unnecessary treatment and providing more aggressive options where they are needed.
- Researchers have noted that body mass index (BMI), caloric intake, birth weight, adolescent growth spurt and exercise are all prognostic or predictive factors in breast cancer. Interestingly they are also all related to regulation of the insulin/insulin growth factor (IGF) system. The IGF-I receptor also has some similarities to the HER2 receptor. Insulin/IGF appears to have functions beyond its well-known energy regulation activity, as it also targets epithelial cells. Breast cancer cells can have insulin and IGF receptors and these observations suggest the possibility of adding novel approaches to personalised breast cancer treatment, based not on tumour characteristics but on patient metabolism.
 - Results from the Women's Intervention Nutrition Study (WINS), presented at SABCS 2006, showed that early breast cancer patients with a high dietary fat intake (greater than 20% of calories), who reduce their fat intake sufficiently to result in weight loss had reduced recurrence and increased survival. The benefits were seen mostly in hormone receptor negative patients. This year, results were presented from the Women's Healthy Eating and Living (WHEL) study involving 3088 women who had been treated for early breast cancer. The study looked at the influence on prognosis of a low fat diet very high in vegetables, fruits and fibre. After 7.6 years of follow-up there were no differences in recurrence or survival between those with the healthy diet and those who had not changed their diet.
 - Studies of breast cancer in mice showed strong benefits of combining a new form of the taxane, paclitaxel (Taxol) with bevacizumab (Avastin). Nab-paclitaxel (Abraxane) is a nanoparticle (a tiny particle less than 100 millionths of a millimetre in size) coated in the blood-soluble protein albumin. This coating reduces the toxic side effects of paclitaxel, and targets it better to tumour cells thus reducing the dose required. Bevacizumab is a monoclonal antibody that prevents the formation of blood supply to tumours. Mice used in the study had breast cancer tumours as well as metastases in the lymphatic system and lungs. When used singly, the two treatments had limited effect, but when combined they acted synergistically to completely eradicate the breast tumours as well as the metastases. These results suggest a promising combination for use in future human clinical trials.
 - Pharmacogenetics is the study of genetic variation that leads to different responsiveness to drugs. The safety and efficacy of drugs may be affected by a single nucleotide polymorphism (SNP), i.e. a minor variation in genetic coding in an area of DNA that codes for a drug target, transporter or drug metabolising enzyme. Researchers presented results suggesting that variations in the gene encoding the 2D6

- liver protein, can result in variant forms of 2D6 that alter the conversion of tamoxifen into its most active metabolite, endoxifen. The researchers noted that patients with forms of the 2D6 gene resulting in high blood levels of endoxifen would be most likely to benefit from tamoxifen, but observed that these patients tended to suffer greater side effects and were therefore more likely to cease treatment.
- A novel technique for breast reconstruction following partial mastectomy is showing positive results after 12 months' follow-up in a small clinical trial. The ground-breaking approach, termed "Cell Enhanced Reconstruction" uses fat and stem cells harvested from the patient's abdomen, hips or trunk. Cells of the desired type are then separated, purified, concentrated and mixed outside the body, then injected back into the breast in the area depleted by the removal of the tumour. Adipose (fatty) tissue is a rich source of stem cells, and these are needed to promote the formation of a new blood supply to the area and to keep the re-injected fat cells alive.

SABCS was fascinating and as you can see, there is an incredible amount of research under way. Every element of data presented came from the many thousands of women worldwide who participate in clinical trials. Many of the researchers at SABCS gratefully acknowledged the priceless contribution of these women whose willingness to take part in trials is advancing medical science and knowledge, benefiting those who follow.

The results summarised above represent only a tiny fraction of the information presented in 82 oral presentations and 770 posters displayed. There is a huge international effort under way to understand and effectively treat breast cancer, and to move from the "one size fits all" approach to tailoring treatments to match the specific biological characteristics of each patient's disease. I left SABCS with a strong feeling of optimism that research will lead to effective treatments and cures for the various forms of breast cancer in the not too distant future.

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