

Breast Cancer Update

Issue 60 August 2008

European Breast Cancer Conference Reports
Informed Consent - A Consumers View
Young Action on Breast Cancer Report
ANZ BCG Trial Accrual Summary

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Editorial

Dr Jacquie Chirqwin
Medical Oncologist
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Our apologies for the late arrival of this winter edition – now appearing in spring! We do struggle to get the articles in as everybody is always so busy. However, I think it has been worth the wait; there is a comprehensive coverage of the main conference coverage of Breast Cancer globally this year, and this therefore provides, I think, a succinct summary to help keep you abreast of developments in the area.

There is again a listing included of the ANZ Breast Cancer Trials Group trials and in future I plan to develop a list that also includes other sponsored studies, so that it is easy to quickly determine the trials that are available in Victoria.

The topical issue of consent for discussion at multidisciplinary meetings is discussed from the consumer perspective, by Nicola Bruce. There is also a document that has been produced by the National Breast and Ovarian Cancer Centre (NBOCC) and published in the MJA (see key articles listing at the end of the newsletter) which summarises wide discussions that have been held on this subject. Although the document reports a “consensus” on this subject, I am not sure that

the general oncology community is comfortable with this as yet. We would be interested to publish any further comment on this in our next issue.

This Newsletter has previously included re-prints from Wongi Yabber and NBOCC Newsletter; however, these are now referred to via an electronic link to their publications.

As always we are interested to receive ideas for articles and new topics to discuss. For our next edition we will include as always a San Antonio update, and one topic we have highlighted for discussion is the systems available to support the Breast Care Nurse in their work. If you have something to say on this topic, please consider submitting an article. I anticipate that we will also provide an article on the work of the Breast Tumour stream of the ICS in the state, following a meeting planned for the 8 groups to get together in November.

Happy reading!

Jacquie

Contributions Welcome

The Breast Cancer Update welcomes contributions – conference reports, review of an area of interest, reviews of recent journal articles, clinical trial updates.

	Deadline	Issue Date
Mid-year issue	1 June	1 July
Year-end issue	1 November	1 December

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6th European Breast Cancer Conference Summary

EBCC 6: Surgical Summary

Miss Jane O'Brien, Surgeon, Peter MacCallum Cancer Centre

The biennial European Breast Cancer Conference attracts a greater surgical presence than the other international breast meetings and this was reinforced by the timely reminder by one of the speakers that "any survival benefit of adjuvant therapy is only measured in addition to that already conferred by surgery!"

SCREENING & RISK MANAGEMENT

The European Group for Breast Cancer Screening holds a one day meeting prior to the main conference. The clinical results of digital mammography were reviewed. Seven studies comparing screen-film mammography (SF) and full-field digital mammography (FFDM) have been done, with conflicting results, but overall demonstrate a slightly superior diagnostic performance for FFDM. Management of women at increased risk was discussed. The high cost of intensive surveillance of mutation carriers was highlighted. A group of Dutch researchers (Kamm et al) estimated that the screening of such women costs 315 euros per woman per year with the cost to detect one breast cancer 13,168 euros. Christiane Kuhl, the renowned German MRI expert made the very relevant comment that even if the screening method is not available on a population wide scale, and even if it is not cost effective for a society, it may still be medically effective or life saving for an individual.

A Dutch study by Kaas of 251 BRCA mutation carriers who had undergone bilateral prophylactic mastectomy reported the risk of subsequent breast cancer in these women to be reduced to less than 1%, (5% is the previous figure usually quoted) and as such questioned the need for continued surveillance following prophylactic mastectomy.

PREOPERATIVE STAGING & SURGERY:

Two separate papers looked at the impact of preoperative MRI on breast conserving surgery. A retrospective Spanish study of 249 women with breast cancer identified additional malignant lesions in 18 (8%) on MRI, changing the surgical approach in 32 patients (13%). This was felt to be beneficial in 22 (9%), non beneficial in 6 (2.4%) and uncertain in 4 (1.6%). Six patients were felt to have had a "non beneficial" mastectomy. This outcome was met, not surprisingly, with some consternation by the audience

and overall the tone at the meeting was encouragingly one of caution with respect to the over-interpretation of preoperative MRI and the performance of radical surgery based only on MRI findings.

Another retrospective study (Dutch) looked at margin status in breast conserving surgery and found that the addition of preoperative MRI may lead to a lower rate of incomplete excision of invasive ductal carcinoma (6.5% versus 2%).

A half day seminar was devoted to the subject of "oncoplastic" breast surgery, a fast growing speciality area in Europe, occupying the common ground between surgical oncology and plastic and reconstructive breast surgery. Surgical techniques were described, aimed at resolving the conflict between the resection of as much volume as necessary to achieve clear margins and the wish to obtain a good cosmetic result.

Partial reconstructive techniques using tissue displacement (rearrangement) or replacement to correct wide local excision defects were outlined, as were procedures to correct asymmetry to the contralateral breast.

TREATMENT:

Roger Blamey from Nottingham presented the latest updated results from the BASO 11 trial which now has a median follow up of 122 months and a ten year breast cancer specific survival of 98.5%. This trial compared radiotherapy versus no radiotherapy and/or tamoxifen versus no tamoxifen following breast conservation surgery in patients with excellent prognosis tumours (less than 2cm, node negative, grade 1 or special type). Wide local excision alone resulted in a local recurrence rate of 1.7% per annum, +radiotherapy 0.5%, and +tamoxifen 0.5%. The combination of both adjuvant therapies (+radiotherapy and +tamoxifen) led to the lowest annual local recurrence rate of 0.1%.

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EBCC 6: Chemotherapy Review

Dr Mitchell Chipman, Medical Oncologist, Mercy Private Hospital

The EBCC meeting was held in Berlin in early April this year. The conference centre is slightly out of town, an easy subway ride away from most hotels. It was well attended and although placed in between San Antonio and ASCO had better content than might have otherwise been expected but many of the same speakers repeating similar messages to the previous meetings.

One of the main topics of discussion was the adjuvant use of adriamycin. As we all know Steve Jones published his TC versus AC data now nearly three years ago and there is now longer term follow up data out to about 84 months. The overall survival difference is 5% favouring TC. Denis Slamon clearly believes that there are a sub-set of HER-2 over-expressing patients who particularly benefit from Adriamycin - those who also co-amplify topoisomerase IIa. As we all know about a third of these patients (or 8% of all comers) co-over-express and it is these patients who are thought to be particularly sensitive to Adriamycin. Consequently the benefit of adriamycin chemotherapy is much greater in these patients than maybe expected as this effect is diluted when they are included in a larger number of patients. Dr Slamon believes that if accurate testing for HER-2 and topoisomerase IIa genes were available that 4 courses of AC would be adequate treatment for most low or moderate risk breast cancers – without the need for a year of herceptin. The toxicity of anthracyclines was reviewed particularly the cardiac toxicity and leukaemia of which we are all aware. There was no new data in this regard.

Suffice to say this is contentious. If a patient is referred to Denis Slavin he would do topoisomerase IIa testing and if positive and also over-expressing the HER-2 gene would favour AC without any herceptin in the low to intermediate risk patient.

Given Steve Jones' data looking at AC versus TC it's hard not to be considering TC up front as the patient population included was all comers really. We medical oncologists really need to put some pressure on Canberra to have the regulations reflect the literature. TC needs to be self funded in most cases as the rules currently read.

When reviewing state of the art adjuvant chemotherapy the NEAT study demonstrated that there is a significantly better disease free survival with the use of epirubicin and CMF rather than CMF alone.

Similarly the ECTO study looking at adriamycin followed by docetaxel followed by CMF versus adriamycin followed by CMF showed a significantly better disease free survival as did the BIG 2-98 study looking at a similar question.

The BCIRG-001 study in node positive patients was again reviewed. The question is does the substitution of taxotere for 5FU in the TAC versus FAC regimen prolong or increase disease free or overall survival and the answer is that it does both. This may confirm the role of taxanes in higher risk adjuvant patients but does not tell us whether the drugs should be given together or sequentially. The toxicity of the TAC regimen is considerable and survival figures looking at TC or AC followed by docetaxel are also good. One must also remember more recent work looking at the sequencing and timing of docetaxel and taxol and the weekly taxol regimen looking at 12 weeks after 4 AC won, at least in terms of disease free survival, over the three weekly regimens of either taxane or the weekly taxotere. With further regard to taxanes the TACT trial randomised over 4,000 early breast cancer patients to either FEC and CMF or FEC and docetaxel and so far there is no advantage to the taxane arm - but follow up is too short.

Neo-adjuvant chemotherapy was discussed and no firm conclusions were made. There is some work being done by European groups combining epirubicin, cyclophosphamide and herceptin co-administration prior to surgery claiming good clinical & pathological response rates, but with only short term follow up for cardiac toxicity. Definitely a watch this space clinical trial context area in my view with the potential of cardiac damage as yet to appear..

Gene expression profiling received some attention. The MINDACT, the TAILORx and the TACCT trial are all examining the micro-array assays available for "prediction of relapse" & a possible role influencing the prescribing of chemotherapy. There is no firm information on this topic and we are limited by the single New England article looking at oncotype Dx assessment in a small number of breast cancers.

So there was not a lot of definitive discussion but certainly some food for thought. I for one would be glad to see adjuvant anthracyclines go. I continue to believe that they are toxic and nasty drugs. Having used some TC I'm interested to find I also agree with the published information suggesting that its less toxic than AC



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EBCC 6: Debate: This house believes that 'Adjuvantonline!' is standard of care in decision making

Dr Geraldine Goss, Medical Oncologist, Box Hill / Monash

The development of the Adjuvant! Program provides a *quantitative* analysis of risk of relapse and death from breast cancer and benefits of adjuvant therapy.

There are 56954 registered users of Adjuvant!, of whom 53% are outside the US, and its use has been endorsed by NCCN guidelines. At EBCC the topic 'This house believes that 'Adjuvant! online' was debated.

The case for:

The Adjuvant! Program offers evidence based information on prognosis, magnitude of benefit from treatment and its toxicity, accounting also for the effect of competing morbidity and age. Adjuvant! makes *prognostic* projections based on the tumor size, the number of involved nodes, the histologic grade, and estrogen receptor status. These estimates are mainly based on an analysis of breast cancer related *mortality* of untreated patients at 10 years of follow-up from the United States SEER tumour registry of. Estimates of *recurrence* are calculated by Adjuvant!

The sources of *efficacy* estimates used in Adjuvant! are the Overview meta-analyses of randomized adjuvant chemotherapy and hormonal therapy trials for breast cancer and Phase III clinical trial information. These estimates are used to determine how much benefit (in terms of proportional risk reductions) a patient may expect to obtain *on average* from a given adjuvant hormonal therapy or chemotherapy. Because these estimates of recurrence are indirect Adjuvant! recommends that its projections for *mortality* be used, as they are more directly and cleanly calculated.

Since clinical information may be interpreted in different ways, Adjuvant allows the user to override estimates by using the Prognostic factor impact calculator, which will modify the basic 10 year estimate of mortality. To use a prognostic factor the user must know the relative risk conferred by the prognostic factor and the prevalence of the factor. For example, the prognostic impact of Her2 in node negative patients can be added, conferring an approximate ~1.5 independent relative risk. The opportunity also arises to incorporate prognostic information from gene based predictive assays. Information about the toxicity of adjuvant therapy can be found in the extensive help files. It is critical to consider toxicity, as clinical trials generally exclude

patients with significant health problems or poor performance status. In this group toxicity (including mortality) may be higher than for the average patient included in the trials and may offset any benefit.

One criticism of Adjuvant is that new trials may be slow in being added, such as those regarding the use of trastuzumab in Her2 positive early breast cancer. Early reporting of results makes it difficult to accurately predict the 10 year benefit from a particular treatment. Indeed the results of trials with < 5 years of follow-up can appear overly optimistic since in general adjuvant chemotherapy is most effective against the most rapidly growing tumors destined for early recurrence. Analyses of trials at 2 years of follow-up are often dramatically more optimistic than trials at 5 years. As data mature the information offered in Adjuvant! Is updated.

The case against

The opening argument focused on the shortcomings of Adjuvant as a tool applicable in all situations, since population based data set fails to account for individual tumour biology. The average benefit calculated by Adjuvant! may not apply to individual patient. In particular, ER positive breast cancer is biologically and clinically heterogeneous. The definition of endocrine responsiveness by Adjuvant! is an all-or-nothing, however responsiveness to endocrine therapy differs according to quantitative levels of ER expression. The improved benefit of second and third generation chemotherapy regimens may be over or underestimated depending on tumour biology. Some risk factors such as Her2 or vascular invasion are not included by Adjuvant!

Adjuvant! may overestimate the benefit of chemotherapy given that recurrence rates include events such as contralateral breast cancer, meaning that the significance of relapse as cause of death may be overestimated. The benefit of chemotherapy may also be overestimated among premenopausal women with ER positive breast cancer, where the role of ovarian function suppression is not considered.

In contrast, data on individual tumour biology may be obtained by genetic profiling of individual tumours. *OncotypeDX* is a diagnostic assay that quantifies the likelihood of distant disease recurrence and also assesses the benefit from chemotherapy. The assay

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analyzes the expression of a panel of 21 genes. Of these 16 are cancer related genes and 5 genes were selected to allow standardization of the assay). The results are provided as a Recurrence Score (0-100), which can be translated into the probability of distant relapse (essentially metastatic disease) at 10 years of follow-up. Patients are divided into low, intermediate, and high risk groups. No benefit of chemotherapy in patients with a low score, however patients with high scores benefited from chemotherapy in addition to tamoxifen. Thus this assay may determine the most appropriate treatment strategy for an individual patient.

Adjuvant!'s estimates of "risk of recurrence" are usually higher than those of the *OncotypeDX* test. This is because the *OncotypeDX* recurrence estimates is for distant recurrence only (risk of metastatic disease) while the recurrence estimate given by Adjuvant! is for all causes of recurrence (local, regional, contralateral breast cancer, and distant recurrence). Because the risk of distant recurrence is tied closely with risk of breast cancer death, the most appropriate comparisons are between the risk of breast cancer *mortality* as estimated by Adjuvant! and the risk of *distant recurrence* as given by the *OncotypeDX* test.

Currently, the TAILOR-X (Trial Assigning Individualized Options for Treatment (Rx)), study is examining the role of chemotherapy among 10,000 women with node negative, ER positive breast cancer. This is designed to examine the usefulness of chemotherapy in addition to endocrine therapy, especially for women with an intermediate risk of recurrence.

The population used to validate the *Oncotype DX* assay had node negative disease and were treated with tamoxifen, however recently the *Oncotype DX* assay was shown to be both prognostic and predictive of chemotherapy benefit (CAF) in a cohort of post-menopausal women with node positive, HR-positive breast cancer from the SWOG 8814 study. The test is only useful in ER positive disease, and its role is less clear where aromatase inhibitors are used.

A second genomic based prognostic test is the *MammaPrint*®, a 70 gene signature which can predict the 10-year survival for an individual patient. *MammaPrint*® also identifies those untreated individuals who have a poor tumor signature and a high risk for metastasis if untreated. However, no clinical trials have assessed the utility of adjuvant therapy in high risk versus low-risk individuals. This means that the *MammaPrint* is *prognostic* but not *predictive*. The 70-gene signature will be prospectively tested in the MINDACT (Microarray In Node negative Disease may Avoid ChemoTherapy) study of 6000 women with node-negative early-stage breast cancer, to assess whether it can better identify those who can safely be spared adjuvant chemotherapy.

Should 'Adjuvant! Online' be the standard of care in decision making? Ultimately results from molecular profiling may be incorporated into Adjuvant! However, they are not useful in ER negative disease, and there is limited information regarding their applicability in node positive disease. Although not intended to replace clinical judgment, the Adjuvant! Program is the most broadly applicable model, and currently the most useful available aid to clinical decision making.



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EBCC 6: Radiation Oncology Perspective

Dr Michael Chao, Radiation Oncologist, Radiation Oncology Victoria

The 6th EBCC was well worth the trip to Berlin just to hear the preliminary results of the EBCTCG for cycle 5 (trials started before 2000, with follow up to 2005/6).

For patients who choose breast conserving surgery (BCS) the addition of radiotherapy (RT) in patients with N+/N? disease led to a 25.1% absolute improvement in local control at 5 years, 7.8% absolute reduction in breast cancer deaths at 15 years and a 7.7% absolute improvement in OS at 15 years. In patients with N- disease, the addition of RT led to a 14.4% absolute improvement in local control at 5 years, 3.1% absolute reduction in breast cancer deaths at 15 years and a 3.3% absolute improvement in OS at 15 years. We all knew the effect of RT on local control but it demonstrated for the first time the importance of RT in improving survival in N+/N? disease as well as many groups of women with N- disease, albeit after 15 years. Only older women (>60 years) with well differentiated tumours where the absolute improvement in local control is <10% may have very little to gain from RT.

In the post mastectomy setting, the absolute improvement in local control at 5 years is 2.8% for pN0, 15.7% for pN1-3 and 22.3% for pN4+. The absolute reduction in breast cancer deaths at 15 years is -0.6% for pN0, 7.6% for pN1-3 and 6.9% for pN4+. The absolute improvement in OS at 15 years is 5.3% for pN1-3 and 6.2% for pN4+, while those with pN0 suffered a 3.9% absolute reduction in OS. Tumour differentiation was also found to be an independent prognostic factor in patients with pN+ disease. However, even in patients with pN1-3 with well

differentiated tumours, the 5 year gain in local control was still >10%. In summary, post mastectomy RT reduced 15 year breast cancer mortality and improved 15 year OS for both pN1-3 and pN4+ disease. Breast cancer mortality was not improved in pN0 disease and OS is compromised, at least in these older studies.

Non breast cancer mortality is higher in patients who had RT with a 2.2% absolute reduction in OS at 20 years. The effect was significant for age groups <50 years, 50-59 years and 60-69 years, except those >70 years. The absolute loss was 0.7% for <50 years, 1.7% for 50-59 years and greatest for 60-69 years at 3% at 15 years. Not surprisingly heart disease was the greatest culprit with a marked excess seen in RT patients. However, if the mean cardiac dose was kept below 5Gy, the impact of RT on heart disease was not seen.

In summary, while the impact of RT on local control has always been well recognised in patients who undergo BCS, we have now shown an improvement in OS. While N- patients may avoid RT by opting for a mastectomy, those with N+/N? will still benefit from further adjuvant RT despite more aggressive surgery. This review has also demonstrated the impact of RT on patients with pN1-3 disease with improvement in local control and OS. However patients with pN0 disease may actually be harmed from the addition of RT. The use of modern RT techniques may reduce the hazard of RT, thus improving breast cancer mortality and OS.

Informed consent for women whose cases are to be discussed at breast cancer care multidisciplinary team meetings

Dr Nicola Bruce, Breast Cancer Action Group

The Breast Cancer Action Group (BCAG) was asked by the Victorian Cooperative Oncology Group (VCOG) to seek feedback on what women think about a need for an 'informed consent' process prior to their breast cancer case being discussed at Multidisciplinary Team Meetings (MDMs). According to the NH&MRC informed consent should be based on the general principle that:

...patients are entitled to make their own decisions about medical treatments or procedures and should be given adequate information on which to base those decisions (NH&MRC, 2004 p.9).

Apparently following a case heard in the NSW Privacy Tribunal (*KJ v Wentworth Area Health Service* 3 May 2004) clinicians are concerned about women being fully informed about the MDM process to ensure they understand clearly beforehand how their case is to be discussed and by whom. At issue is how informed consent takes place and whether it happens in ways that women are sufficiently informed about how their cases are discussed. The Tribunal finding:

... agreed with the Privacy Commissioner's submissions that the type of personal information at issue is relevant in determining whether an agency has taken such steps as are reasonable in the circumstances to make an individual aware of the matters in section 10 (para. 36). The Tribunal was not satisfied in this case that the Area Health Service took such steps as were reasonably necessary to make KJ aware of the intended recipients of the information (2004).

A recent study from Sydney by Choy, Chiu, Butow, Young and Spillane (2007) proposed that a multidisciplinary care approach 'is the accepted best model of management of breast cancer patients'. Explained by the study is how multidisciplinary care commonly includes the discussion of individual cases at MDMs. The problem is how to communicate the MDM process to women in ways that ensures they fully comprehend what is to occur. Of note is how this time is particularly stressful for women many who are at the beginning of their breast cancer journey. It is

essential therefore for explanations of MDMs to account for any difficulty women may have in understanding the complexity of their care or any future implications for them.

At stake is the protection for treating clinicians from the legal ramifications if a woman does not understand the process. The core of the issue however is how women can be informed about a meeting that discusses details of their personal information and their breast cancer, so they can understand how this may affect their care and the advice they receive, including the value of this multidisciplinary approach.

Clinicians ask whether they should continue as before with verbal explanations of MDMs or is more needed. Perhaps there should be written explanations, a consent form to sign or a combination of the above? To find out women's views, this topic was introduced in an issue of the BCAG newsletter as well as taken up in conversations with individuals and support groups.

From the feedback received it appears that women are puzzled about the need to understand information concerning MDMs in particular, rather than ensuring all information is understood in a way that achieves comprehensive 'informed care' throughout their pathway. One woman said:

I think that women should be given both comprehensive oral and written information. Women have different preferences regarding the presentation of information and it needs to be given in a variety of ways in order to suit various needs. I know that women are often given only verbal explanations and would prefer to read some material ... but that this has not been provided to them.

A woman who recently had her case discussed by an MDM commented that at the time she was in shock and didn't really understand much of what was being said to her. 'All I was interested in, was knowing that I was having the best possible care and could trust the people I was talking to' she said. For her this meant having a breast care nurse explain each step of the way. She wanted something to take home and read

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later but not too much or it became overwhelming. She wanted a phone number for the questions that worry her between appointments. Another woman said bluntly:

Look this is a 'no brainer'. Of course I want to understand my choices – but I can't be the one to take responsibility for what these choices are. I'm not the expert. What I need is to be able to understand what it will mean for me, for my family...but having a team of experts is great for your confidence that you're having the best possible care.

Women say they want to understand, but not just about MDMs. This suggests that the provision of sufficient information to establish 'informed consent' for case discussion at MDMs should be considered in more holistic terms. Such a view would deliver all information in ways that women understand and can make sense of at each stage of their care. If it is necessary for legal reasons that women give formal permission for their case to be discussed, information should be delivered that ensures this consent is informed. It makes even better sense if such information continues to be given in an 'informed' manner throughout a woman's care.

Ian Roos (2007) from Cancer Voices Victoria argues that information should be given so that whoever is in receipt has the option to say 'no'. Indeed he proposes that 'If I have sufficient information to say no, then I can make an informed decision to say yes.' This idea is supported in the literature. Articles such as one to be found at: <http://www.ama-assn.org/ama/pub/category/print/4608.html> argue that ensuring 'informed consent' is much more than telling a patient what to do. It opens with:

Informed consent is more than simply getting a patient to sign a written consent form. It is a process of communication between a patient and physician that results in the patient's authorization or agreement to undergo a specific medical intervention (American Medical Association, 2008).

In 2002 the BMJ published an article entitled 'Informed consent: lessons from Australia'. It starts with the statement:

Courts in Australia and England have begun applying a tougher standard to the information that doctors should give

their patients—that of what a reasonable patient might expect rather than that of what a reasonable body of doctors might think (Skene & Smallwood, 2002).

More recently Joy Mendel (2007) offered alternative ways of providing informed consent based on new models of shared decision making using broader frameworks of delivering information. It is a way of informed decisions being made which includes the input of the clinician with their 'patient', family and community. Other literature from the National Breast and Ovarian Cancer Centre (2007) and the Australian Health Consumer (Carey-Hazell, 2006) highlight the problem and propose informed consent is considered with some importance.

We at BCAG propose that all information should be provided within a considered and evidenced framework. A 'Cancer Patient Information Framework' has recently been produced by the Southern Metropolitan Integrated Cancer Services or SMICS (2008). It makes interesting reading. Suggested is an effective communication strategy that takes account of other languages, visual delivery of information, hearing and cognitive impairment and literacy needs. It proposes that information needs to be delivered in ways that considers the individual and their circumstances. This may mean providing information using a variety of styles of delivery including verbal and visual, an interpreter when required, plus someone who is available for patients to ask follow up questions.

The timing of such complex information provision prior to a woman's case being discussed at a multidisciplinary meeting is not ideal as it occurs shortly after diagnosis. However, if every attempt is made to ensure that women have access to sufficient information in a variety of ways, in a supportive manner that takes account of 'who' they are and that they can say 'no' if they so wish, then surely this becomes informed consent.

The challenge is to consider ways that ensures informed consent about multidisciplinary discussions addresses legal and medical concerns but most importantly provides women with ways to understand and make sense of information that provides benefits for the whole of their care.

References:

American Medical Association. (2008). Informed Consent. Retrieved June 20th 2008, <http://www.ama-assn.org/ama/pub/category/print/4608.html>



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Carey-Hazell, K. (2006). Improving patient information and decision making. *The Australian Health Consumer*, Number One 2005-2006, 21-22.

Choy, E. T., Chiu, E., Butow, P., Young, J., & Spillane, A. (2007). A pilot study to evaluate the impact of involving breast cancer patients in the multidisciplinary discussion of their disease and treatment plan. *The Breast*, 16(178-189).

KJ v Wentworth Area Health Service Privacy and Personal Information Protection Act 1998 (3 May 2004.)
http://www.lawlink.nsw.gov.au/lawlink/privacynsw/ll_pnsw.nsf/pages/PNSW_07_cnadt84

Mendel, J. (2007). The patient, the doctor and the family as aspects of community: New models for informed consent. *Monash Bioethics Review*, 26(1-2), 68-78.

National Breast and Ovarian Cancer Centre. (2007). Multidisciplinary care: what are the medicolegal implications? *National Breast Cancer Centre Update*.

NH&MRC. (2004). *General Guidelines for Medical Practitioners on Providing Information to Patients*. Canberra: Commonwealth of Australia,
<http://www.nhmrc.gov.au/publications/synopses/files/e57.pdf>

Roos, I. (2007). *Can I say No? - The issue of consent*. Paper presented at the National Research Ethics Conference, Melbourne.

Skene, L., & Smallwood, R. (2002). Informed consent: lessons from Australia. *BMJ*, 324(January), 39-41.

Young Action on Breast Cancer

Mary Macheras-Magias, YABC Chairperson

The 1st National Conference for young women with breast cancer – **Up Close and Personal** took place in Melbourne October last year. This was the first time that young women from around Australia had the opportunity to come together to a Conference designed specifically around the issues affecting them. This was a Conference organised by young women for young women.

Up Close and Personal 2 was made possible by the determined commitment, passion and energy of Young Action on Breast Cancer (YABC) organising committee: A small group of young volunteers, who through their vision inspired others to join them in making this event possible.

The Conference aims were to inform; connect; and advocate. These aims were successfully delivered through the wide range of quality speakers who presented during the plenary and workshop sessions; the performances that brought to life issues that touch young women; the amazing hypothetical session that included a panel of experts who so generously shared their knowledge on topics relevant to young women; the amazing energy of the women who attended; the evening celebration that allowed women to have a good time in the company of their peers; and finally the discourse and breadth of ideas shared in the final summation.

Recommendations that were put forward during this session included:

- Better communication and awareness from GPs in diagnosing younger women is needed. Women

should not be dismissed when presenting with symptoms simply because of their younger age.

- Although information dissemination has improved there still appears to be discrepancy in information that is provided to young woman. It was recommended that **all** young women (pre-menopausal) should be informed about fertility options before treatment.
- Financial guidelines and assistance:
 - o Free mammograms and ultra sounds
 - o Better financial support
- Improving resources:
 - o Links to specialists
 - o Information for women with children
 - o Accessing support groups
 - o Support groups for partners; carers
 - o Breast Care Nurses for all women
 - o Advanced Young Women's Group
 - o Peer support program that helps connect women
 - o Develop medical databases
- Linking YABC nationally
- Rotating the Conference around Australia to improve accessibility for other young women
- Increasing awareness around young women's issues

Transcripts, presentations and photos from the Conference are available on www.yabc2007conference.org

YABC thank the women who attended and helped make this such a wonderful and vital event and to our amazing speakers. Thank you to our major sponsors: BCNA; Think Pink Foundation; NAB; and Edgar Trust Foundation.



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ASCO Summary May-June 2008

Dr Mitchell Chipman, Medical Oncologist, Mercy Private Hospital

ASCO this year was held at McCormack Place in South Chicago. For those who haven't attended there before - it is a giant conference centre and despite ASCO's large number of registrants only about two thirds of the available space is used.

In general the discussion of systemic breast cancer treatment is more and more directed toward a target. Targeted and non-targeted treatment strategies are evolving, for instance, even for the management of triple negative breast cancer. Edith Perez discussed triple negative breast cancer and further divided it into ductal, basal-like or non basal-like as well as some other rarer forms. Each of these triple negative characterisations is thought to carry a different prognosis from that of a standard infiltrating ductal carcinoma. Dr Perez summarised some characteristic features of triple negative breast cancer. They often present as an interval cancer, there is a weak relationship between tumour size and nodal status and there is a rapid risk in recurrence following diagnosis. The peak risk of recurrence is 1 to 3 years. The death rate is high in the first 5 years and there is an increased risk of brain metastases. After relapse there is a rapid progression from distant recurrence to death. It was noted that BRCA1 carriers mostly develop triple negative tumours. As there are no readily defined targets rational targeted therapy is not yet possible. Research is to be devoted to identify additional biologically rational targets to lead to new therapeutic agents & better patient outcomes.

Hymen Muss discussed breast cancer in the elderly. There are a large number of patients who may be under treated on the basis of age. Rather, life expectancy and risk of relapse should be the primary determinants for extra treatment. He commented that it was important to tailor endocrine therapy and preferred an AI over tamoxifen. He further stated that those women who have triple negative tumours should benefit from the same intensive therapy normally prescribed for younger women providing

they can tolerate it. Finally he stated that trastuzumab must be considered in the elderly who are HER-2 positive.

Regarding genomics the inter-group program PACCT-1 and the "Trial of Assigning Individualised Options for tTreatment" or TAILORx will evaluate the use of the onco-type Dx recurrence score in assigning patients to a treatment group and will include older patients.

Michael Gnant from Austria discussed the ABCSG-12 trial which looked at pre-menopausal women with endocrine responsive breast cancer. About 1800 women were randomized to goserelin and tamoxifen or anastrozole then further randomized to zoledronic acid or no zoledronic acid. These women were followed up for a median of 60 months and there was no significant survival or disease free survival difference between goserelin and tamoxifen or anastrozole but there was a trend to prolonged disease free survival favouring zoledronic acid. Whilst promising, this trial only involved 1800 patients and involved node negative and node positive women so it's interesting but not conclusive – that statistics could easily be called into question.

Dr Miles discussed the AVADO study which was a phase III study of bevacizumab together with docetaxel or placebo & docetaxel. Previously untreated patients with locally recurrent or metastatic breast cancer were eligible. Two different doses of bevacizumab were used and significantly improved progression free survival and response rate compared with docetaxel alone. The patients needed to be HER-2 negative and the therapy was given every 3 weeks. The benefits were significant in that the response rate of docetaxel alone was about 44% and went up to 63% with docetaxel and the higher dose of bevacizumab. Grade III toxic events were higher in the dual combination arm. Food for thought indeed.

ANZ BCTG Clinical Trials

Pending Activation / Open for Patient Entry

ANZ 02P2 : IBIS-II

An international multi-centre trial of anastrozole vs placebo in postmenopausal women at increased risk of breast cancer and tamoxifen vs anastrozole in postmenopausal women with hormone sensitive DCIS.

ANZ 0501 : LATER - Later adjuvant Aromatase inhibitor Therapy for postmenopausal women with Endocrine Responsive tumour

A randomised double-blind trial in postmenopausal women who have completed 5 years of adjuvant endocrine therapy for early, hormone sensitive breast cancer more than one year previous, and who are disease-free at study entry.

ANZ 0502 : Neoadjuvant Gemcitabine

A phase II trial evaluating the efficacy and safety of epirubicin and cyclophosphamide (EC) followed by docetaxel with gemcitabine (DG) (+ trastuzumab if HER2-positive) as neoadjuvant chemotherapy for women with large operable or locally advanced breast carcinoma.

ANZ 0702 / BIG 2-06 : ALTTO - Adjuvant Lapatinib and/or Trastuzumab Treatment Optimisation Study

A randomised, multi-centre, open-label, phase III study of adjuvant lapatinib, trastuzumab, their sequence and their combination in patients with HER2/ErbB2 positive primary breast cancer.

IBCSG 22-00 : Maintenance Chemotherapy

Low dose cytotoxics as anti-angiogenesis treatment following adjuvant induction chemotherapy for patients with ER-Negative and PgR negative breast cancer.

IBCSG 23-01 : Sentinel Lymph Node Biopsy (Micrometastases)

A randomised trial of axillary dissection versus no axillary dissection for patients with clinically node negative breast cancer and micrometastases in the sentinel node.

IBCSG 24-02 / BIG 2-02 : SOFT - Suppression of Ovarian Function Trial

A phase III trial evaluating the role of ovarian function suppression and the role of exemestane as adjuvant therapies for premenopausal women with endocrine responsive breast cancer.

IBCSG 27-02/BIG 1-02/NSABP B-37 : Chemotherapy for Radically Resected Loco-regional Relapse

A randomised clinical trial of adjuvant chemotherapy for radically resected loco-regional relapse of breast cancer.

IBCSG 34-05 / SWOG S0230 : POEMS - Prevention Of Early Menopause Study

Phase III trial of LHRH analogue administration during chemotherapy to reduce ovarian failure following chemotherapy in early stage, hormonal receptor-negative breast cancer.

IBCSG 35-07 / BIG 1-07 : SOLE - Study Of Letrozole Extension

A Phase III trial evaluating the role of continuous letrozole versus intermittent letrozole following 4 to 6 years or prior adjuvant endocrine therapy for postmenopausal women with hormone receptor-positive, node-positive early stage breast cancer.

Australian New Zealand Breast Cancer Trials Group: Trial Accrual Summary

Total accrual to trials currently open to patient accrual: to 31 May 2008

Trial	Victoria	ANZ BCTG	International	Total	Target Accrual
ANZ 02P2 / IBIS II Prevention	19	234	1861	2095	6000
ANZ 02P2 / IBIS II (DCIS)	16	66	1460	1526	4000
ANZ 02P2 / IBIS II Bone Substudy	0	80	763	843	1000
ANZ 02P2 / IBIS II (Totals)	35	300	3321	3621	10000
ANZ 0501 (LATER)	0	20	0	20	2500
ANZ 0502 (NeoGem)	22	40	0	40	147
IBCSG 22-00	19	54	664	718	900
IBCSG 23-01	6	19	619	638	1960
IBCSG 24-02 / BIG 2-02 (SOFT)	34	147	1625	1772	3000
IBCSG 27-02 / BIG 1-02	1	2	128	130	1750
IBCSG 34-05 / SWOG S0230 (POEMS)	12	25	95	120	416
ANZ 0702 / BIG 2-06 / N063D /EGF103708 (ALTTO)	1	8	1387	1395	8000
BIG 1-98 Cognitive Function Substudy	6	43	92	135	196
ANZ 0701 Co-SOFT	2	3	0	3	357
ANZ 0601 / CIRG / TORI 010	5	14	244	258	273
TOTAL	143	675	8175	8850	29499

For further information please contact: Dianne Lindsay
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Newsletter Link

NBOCC: Have released new pamphlets and publications that can be viewed via the link below

<http://www.nbocc.org.au/>

WONGI YABBER: You can view the latest Wongi Yabber newsletter (Volume 15, Issue 3, August 2008) via the link below:

<http://www.cancer.org.au/Healthprofessionals/AustCancerNetwork/WongiYabber.htm>



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Key Published Articles

Title

Author & Journal

P27 and Skp2 immunoreactivity and its clinical significance with endocrine and chemo-endocrine treatments in node-negative early breast cancer

A. Ravaoli1, F. Monti, M. M. Regan et al
Annals of Oncology, 13 February 2008, 19: 660–668, 200

Can liability rules keep pace with best practice?
The case of multidisciplinary cancer care

David M Studdert
The Medical Journal of Australia 2008; 188 (7): 380-381

Medicolegal implications of a multidisciplinary approach to cancer care: consensus recommendations from a national workshop

A Evans, H Zorbas, M Keaney, et al
The Medical Journal of Australia 2008; 188 (7): 401-404

National Breast Cancer Audit: the use of multidisciplinary care teams by breast surgeons in Australia and New Zealand

C J Marsh, M Boulton, J X Wang, et al
The Medical Journal of Australia 2008; 188 (7): 385-388

The difficult decision-making process for using or not using adjuvant chemotherapy in premenopausal endocrine-responsive breast cancer patients

Del Mastro
Annals of Oncology 19: (7); 1213–1215, 2008.

Premenopausal endocrine-responsive early breast cancer: who receives chemotherapy?

Regan et al
Annals of Oncology 19: (7); 1231–1241, 2008

The Cancer Council Victoria

The Cancer Council Victoria was set up by an Act of Parliament in 1936. To find out more about the Cancer Council visit www.cancervic.org.au/introduction.

Victorian Cooperative Oncology Group

The Victorian Cooperative Oncology Group (VCOG) established in 1976, provides advice to the Cancer Council, on all clinical aspects of cancer control, in particular clinical research, screening diagnosis, treatment, palliative medicine, cancer genetics and professional education. The strategic role of the VCOG is to have a 'parliament' of clinical cancer specialists with a view to promoting a range of cooperative measures to optimise cancer treatment in Victoria. The VCOG consists of a primary committee, 8 cancer-site and 5 task-specific advisory committees and 5 trial research sub-committees. These committees bring together in regular meetings approximately 400 key specialist health care professionals and scientists, representing the various treatment disciplines and Centres in Victoria. The VCOG has established valuable linkages between public and private health care professionals, institutions and governments.

