



Breast Cancer Update

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EBCC MEETING REPORT

ASCO MEETING REPORT

Q&A ON THE INTEGRATED CANCER
SERVICES (ICS)

DR JOHN COLEBATCH FELLOWSHIP

SIR EDWARD DUNLOP FELLOWSHIP

Produced by the Breast Cancer Committee
of the Victorian Cooperative Oncology Group
Centre for Clinical Research in Cancer



BREAST CANCER UPDATE

July 2006

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This newsletter is produced by The Cancer Council Victoria's Breast Cancer Committee and sent to health professionals interested in management of breast cancer(s). The Victorian Cooperative Oncology Group's advisory committees on gastrointestinal, gynaecological, lung, skin and urological cancers also produce twice yearly cancer updates.

If you would like to have your name removed from the distribution list, or if you are interested in receiving any of the other updates please contact Leigh Williams, Ph: (03) 9635 5174.

***** **Last Issue – No. 55 – December 2005** *****

The articles in the Breast Cancer Update have been published to contribute to professional debate and exchange. The opinions expressed are not necessarily those of The Cancer Council Victoria.

Editorial

*Dr Jacquie Chirgwin
Medical Oncologist
Box Hill & Maroondah Hospitals*

I am happily writing this in the sunshine of Nice. So, I will be brief – must get back to the roller blading and the warm Mediterranean Sea with the children...

I would like to again thank everybody who has put the effort into writing some excellent articles for this edition – there is a lot covered, and I am particularly pleased to include an update hot off the press from ASCO, prepared by one of the Advanced Trainees, Kathryn Field. By the time this goes to press there should also be a “Question and Answer” section from the DHS Cancer and Palliative Care on the ICS and future plans.

There are also two short articles on clinical trials that I think deserve support. I have started what I hope will be a continuing ‘Reader’s Comments’ section in future editions. Please contribute comments on topics of interest, trials or other issues that might spark discussion and debate for our next edition due in December.

Thank you again to Susan Fitzpatrick and Leigh Williams for the huge amount of work that goes into producing this newsletter.

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

Contributions should be forwarded to:

The Editor, Breast Cancer Update
C/- Centre for Clinical Research in Cancer
The Cancer Council Victoria
1 Rathdowne Street
CARLTON VIC 3053
Leigh.Williams@cancervic.org.au

Reader's Comments

Comment on the Development of Data Collection in Breast Cancer

Dr Jacquie Chirgwin
Medical Oncologist
Box Hill & Maroondah Hospitals

Many clinicians working in the breast cancer field have been involved with considerable development in the service provision for breast cancer patients, courtesy of the Breast Services Enhancement Program, and the State based Performance Indicator and Standards development projects. The learnings from these activities have been summarized in several publications of the DHS. One of the areas that has clearly been identified as a priority, and was a focus of quite a number of programs was the development of data collection and databases. As a result considerable work towards this has been duplicated across many sites. The progress appears to have been relatively slow and expensive, and is heading towards a higgledy-piggledy collection of different programs that will have no capacity to communicate with other databases across the State, let alone nationally.

It is unbelievable that in 2006 most, if not all centres of breast cancer care in Victoria are unable to provide outcome data for their patients treated for breast cancer. It has also been noted that there are no simple methods or processes in place for identifying patients with advanced breast cancer, making the development of collectible performance indicators for this population of patients impossible. Without these basic resources we cannot make any progress in measurement of treatment outcomes nor in quality improvement programs, either locally, or on a state or national level. It would seem mandatory that this deficiency is rectified urgently.

It would appear that there are a number of disparate organizations that are developing data collection systems for various purposes and at various levels. These include:

- the ACCORD database, collecting information from four Melbourne sites (Clinical Trials Australia hospitals) for research purposes, and linkage with hospital PAS
- HealthSMART state hospital information collection
- National e-health transition authority (nehta) and Health Connect program, a national organization involved in the upgrading of electronic health information collection
- Molecular Medicines Informatics Model (MMIM) funded by the Commonwealth to collect cancer information, so far mainly for colorectal cancer at pilot sites
- The Australian Cancer Grid
- The Victorian Cancer Outcomes Network (VCON) a Ministerial Taskforce and Cancer Council of Victoria initiative to trial and develop systems of statewide collection of NCCI Clinical Cancer Core Dataset, which will link with the Victorian Cancer Registry to provide detailed outcome data.
- DHS Cancer and Palliative Care proposal to develop an information system to support MD team meetings.

There seems to be a significant focus on research and population data collection by these organizations with only a minor focus on clinical data collection, and to date it appears there has been little involvement of clinicians. There is widespread concern amongst clinicians at the lack of clarity of the above list and the various interactions and relationships of these agendas. I would hope that the fact that clinical data collection systems are still in their infancy at most sites, will give us the opportunity to approach this in a unified way. Ideally collection of data for research, population health, (registry information), outcome statistics etc. and local clinical datasets can be coordinated under the one umbrella (preferably national).

I suggest that this is one of the high priority areas that we should be focusing on via the ICS, and in particular, ensuring that each ICS does not approach this alone; it must be a co-ordinated effort. We must learn from the BSEP outcomes,

and prevent the further development of multiple clinical databases that will subsequently be difficult or impossible to integrate into a unified system.

Although this is a costly process, it is surely wiser to spend the funds on this than to spend funds piecemeal on repetitious development of individual systems. I urge that we collectively prioritise this and lobby government to do the same.

Breast Cancer Network Australia Comments sought on New Secondary Breast Cancer Resource

'Secondary breast cancer is confronting, but it is not contagious. After my diagnosis, there appeared to be a wall of silence and I felt a real pressure not to speak of my experience.'

This year, Breast Cancer Network Australia (BCNA) has commenced an exciting new project to help meet the needs of women with secondary breast cancer. In 2004 BCNA launched the *My Journey Kit*, our free information kit for women newly diagnosed with primary breast cancer. Since the launch, almost 14,000 *My Journey Kits* have been distributed, receiving a very positive response from women all over the country.

Based on the *My Journey Kit*, BCNA is now developing a new national information and support resource for women newly diagnosed with secondary breast cancer. The resource will provide women with information based on the experiences of others with secondary breast cancer. It will also direct women to state-based resources and services which other women have found helpful.

The resource is needed because women living with secondary breast cancer report that there is no central place where they can access information and support options. Women have also said it is exhausting and time consuming to search for such information, and they feel alone in doing so. The aim of the resource is to fill that gap and make women's journeys easier and less isolating.

BCNA's Project Manager, Anne-Maree Polimeni, conducted individual interviews with women from Queensland, New South Wales, Victoria and Tasmania, and facilitated two focus groups in Victoria and in Queensland to explore women's experiences, especially when they were newly diagnosed with secondary breast cancer. She found that consistent themes emerged, including the need for:

- women to hear messages of hope and stories of survival
- women to speak to others living with secondaries
- emotional support and to freely discuss worries (with counsellors or in support groups)
- information about how women can contribute to their own health and wellbeing (such as nutrition, relaxation, coping with side effects)
- a good working relationship with health professionals
- information about financial assistance

Women living with secondary breast cancer have said there is a lack of accessible information, including medical information and information about where to get practical, emotional and financial support. They also cite a lack of appropriate, accessible and affordable emotional support options, including individual or group support. There are very few support groups or peer support programs for women with secondary breast cancer in Australia. Using the services of psychologists or psychiatrists can be very costly, and often women are not well enough to attend services that might exist.

We are currently asking women to identify the information, resources, services, and supports that they found useful and not so useful during their experience with secondary breast cancer. A survey to women, distributed through BCNA's database, will enable us to consult with a wider range of women of different ages, locations and situations around Australia so that the final product will result from extensive consultations with a diverse range of women. As with the *My Journey Kit*, we will draft the resource, seek comment from a range of women and breast cancer clinicians, and request endorsement from professional associations to ensure currency, validity and quality.

We expect to launch the resource early 2007. We welcome readers of the VCOG Breast Cancer Update Newsletter to contribute ideas (including research articles, relevant services or resources recommended for women) and support this vital and worthwhile resource for women living with secondary breast cancer. It will be most important for women to receive the resource as soon as possible after diagnosis. As

with the *My Journey Kit* we will be relying on breast cancer clinicians to inform women about the resource.

If you would like to comment on or contribute to this unique resource, please contact Anne Maree Polimeni, Project Manager, Breast Cancer Network Australia, on (03) 9805 2511 or email ampolimeni@bcna.org.au

Readers are invited to contribute comments on any issues of concern or on articles / comments in previous editions. We would like to encourage discussion and debate about issues that affect us all. Please forward all contributions to Leigh Williams at the Cancer Council Victoria – Leigh.Williams@cancervic.org.au

Prevention of Chemotherapy Induced Premature Menopause - IBCSG 34-05

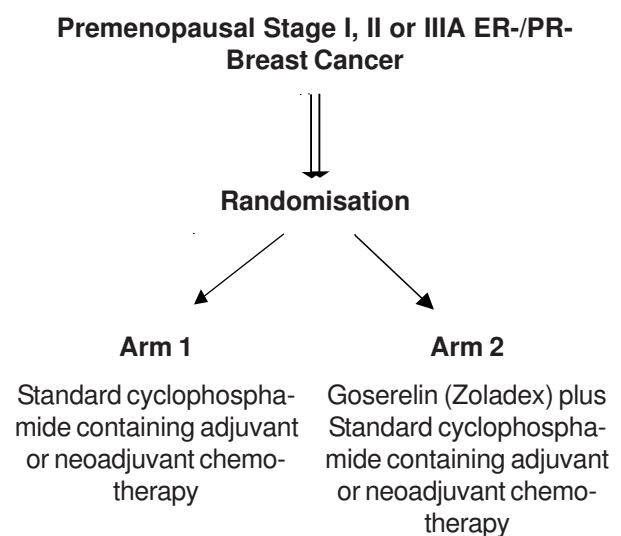
*Assoc Professor Kelly-Anne Phillips
Cancer Council Victoria Dr John Colebatch Clinical Research Fellow
Dept Haematology and Medical Oncology
Peter MacCallum Cancer Centre*

This trial is coordinated by the ANZ BCTG / IBCSG and is now ready for activation at interested centres.

Several non-randomised Phase II studies have suggested that LHRH analogs may be effective in reducing the risk of premature chemotherapy-induced menopause in women receiving chemotherapy. This Phase III randomised study will determine whether this is indeed the case. This is an important study for breast cancer patients, as premature menopause is a common side-effect of chemotherapy, which causes considerable distress and can lead to major long-term health implications yet, in those with hormone receptor negative tumours, it is not thought to have any therapeutic benefit.

The study is a collaboration between the US Southwest Oncology Group (SWOG), the International Breast Cancer Study Group (IBCSG) and the Australian and New Zealand Breast Cancer Trials Group (ANZBCTG). It is currently open in the US and has just opened at the Peter MacCallum Cancer Centre. It is

expected to open at many other sites around Australia and New Zealand in the next few months. Enquires can be directed to Associate Professor Kelly Phillips at the Peter MacCallum (03 9656 1701).



Breast Cancer, Aromatase Inhibitors & Knee Cartilage Study

*Women's Health Program
Monash Department of Medicine
Alfred Hospital*

With the increased use of aromatase inhibitors as adjuvant treatment in women with breast cancer, there is a need to understand why there is a high rate of arthralgia reported by these women

Study Aim

To determine whether the arthralgia associated with aromatase inhibition therapy in these women is linked with greater loss of knee joint articular cartilage volume or an increase in new chondral defects, as assessed by knee joint MRI, than that observed in women not receiving this therapy.

As well, the women will complete the Physical Activity Scale for the Elderly (PASE) and the osteoarthritis questionnaire (WOMAC) to assess joint pain and change in physical activities during treatment with an aromatase inhibitor compared with untreated controls.

Secondary Objectives

To compare menopausal symptoms of women on aromatase inhibition therapy, with untreated controls (assessed by the Menopause Quality of Life questionnaire (MenQOL)).

To determine whether there is a difference in wellbeing between those women on aromatase inhibition therapy and untreated controls (as assessed by the psychological General Wellbeing Index - PGWB).

Eligible Women

- Prior breast cancer surgery
- Commenced on anastrozole or letrozole within previous 10 weeks
- Aged between 40 & 65
- Not treated with tamoxifen for more than 8 weeks in the previous 2 years

- Have one healthy knee, which has not had significant pain or injury
- In the opinion of their physician, are likely to complete this 2 year study

Patient's Participation Entails

- A MRI knee scan at baseline (within 12 weeks of commencing an AI) and after 2 years of therapy. Performed at the Epworth Hospital, at no cost
- At the same time, completion of brief questionnaires

Principal Investigators

Professor Susan Davis

A/Prof Robin Bell

A/Prof Flavia Cicuttini

NHMRC Centre of Clinical Research Excellence for the Study of Women's Health, Department of Medicine, Central & Eastern Clinical School, Monash University.

Patient & Physician Enquiries:

Women's Health Program: (03) 9903 0827

Questions and Answers on the DHS Integrated Cancer Services (ICS)

*Cancer and Palliative Care Section
Department of Human Services Victoria*

Following endorsement of the *Cancer Services Framework for Victoria* in November 2003, five regional and three metropolitan Integrated Cancer Services (ICS) have been established.

The purpose of the ICS is to develop service delivery structures that provide coordinated cancer planning and care provision across specified geographical areas, and to support the delivery of cancer care through the application of agreed best practice frameworks in ten defined tumour streams.

A program of cancer service improvement is being implemented by ICS, funded through the Department of Human Services. Those involved in the breast cancer redevelopment process will be familiar with the concept of funded service improvement initiatives, but for other areas of cancer care, this type of work is quite new.

Progress in establishing new service systems can be challenging and time consuming, and many clinicians are wondering when the results of these initiatives and the funding spent to date will flow on to improvements in care for patients.

Here Elise Davies and the Cancer and Palliative Care Section in the Department of Human Services answer some questions regarding Integrated Cancer Services, and outline plans for the future of cancer care in Victoria.

1. What do you consider to be the most valuable achievements of the first year of the ICS?

In their first year of operation, the main focus for the ICS has been to develop functional relationships between participating health services, to establish representative governance structures and processes for decision-making, to appoint staff to support the work of the ICS, and to map current service provision.

All ICS have appointed a Director (funded on a sessional basis), a Strategic Planner/Program Manager (1 EFT) and project staff (some part time, some full time). In rural regions, a Regional Cancer Nurse Coordinator has been employed (1 EFT).

A comprehensive service mapping process to identify service strengths and gaps has been undertaken. These data have informed the development of a three year Cancer Services Plan for each ICS, which were submitted to DHS in December 2005.

The ICS are establishing local collaborating tumour groups (LCTGs), and have each selected priority tumour streams for their initial focus. This has involved the identification of clinical leaders for each tumour group and a process for the group to advise on and implement the Patient Management Frameworks (championed by the Ministerial Taskforce for Cancer). Tumour groups will provide opportunities for clinical networking, multidisciplinary team development and service development with a tumour specific focus.

2. What have been the major stumbling blocks?

The configuration of some of the ICS has been challenging, with groupings based on geography and population size rather than pre-existing relationships between health services. In some cases, long-standing competition between health services initially constrained the early formation of good relationships. These issues have now been largely overcome, and ICS Executive Groups are beginning to take up their roles in cancer planning and service improvement.

The authority and accountability of the ICS has been a big issue, with emerging tensions between the status of ICS decisions versus the directions of individual health services within ICS. The reasons for this include competing organisational priorities and pressures on health services, and the variable commitment of stakeholders to the development of a new and sustainable system model in cancer. It also relates in part to the lack of clarity about the permanency of funding for ICS, which has now been resolved (see question 4). Strong clinical and managerial leadership, capable of reaching across organisational boundaries is essential if the ICS model is to flourish. The authority and accountability of ICS will be strengthened in the near future through the establishment of a new Victorian Integrated Cancer Services Committee. This high-level group will oversight state-wide ICS activities and directions, and will include health service executive level and senior clinical representation.

3. What do you believe will be achieved during the next 12 months?

The next twelve months will see:

- The establishment of the local collaborating tumour groups (LCTGs) in the priority tumour streams, with translation to other tumour streams. This will initially involve examination of the service mapping data against the patient management frameworks (PMFs), identification of gaps and the prioritisation of service improvement initiatives to be implemented.
- Monitoring implementation of initiatives and outcomes
- Achievement of agreements between health services and health care providers for the provision of the multidisciplinary (MD) approach to cancer care. This will include an increase in MD team formation, MD meetings, development of team protocols and commencement of multidisciplinary team and meeting audit processes.
- Utilising the PMFs, LCTGs will determine agreed optimal referral pathways in priority tumour streams in their ICS, including the communication mechanisms required between the treatment team (including GP) and the patient.

- The development of multidisciplinary psychosocial and supportive care networks to scope the requirements for a coordinated and collaborative supportive care service within the ICS. This may include identification of referral pathways, determination of protocols to ensure appropriate referral and access, supportive care training for cancer teams, implementation of mentoring and supervision programs across the ICS, shared appointments etc.
- Commencement of a statewide quality framework that will support service delivery and improvement via tumour streams.

4. It is clear that the funds provided by the ICS programs are non-recurrent and intended for development work. Many BSEP initiatives (supported by similar non-recurrent project funds) have resulted in innovations that no longer exist due to lack of continued funding, because of no ongoing funding by health services. How do you plan to prevent this from happening with the ICS process?

The ICS acknowledge the need to implement service improvements across the system and patient pathway to achieve coordinated quality care. They have also identified that certain ongoing core service improvement roles are critical to ensuring sustainable change and continuing engagement and commitment of key stakeholders.

The Minister for Health has recently approved a package of recurrent funding for ICS, which includes funding to support:

- ICS leadership and management
- Tumour stream development (including the capacity to fund sessional payments for the lead clinicians in each tumour stream)
- MD care coordination and development
- Initiatives to improve coordination of care.

Funding allocated against these items in 2006–07 is \$1.2 million per metropolitan ICS and \$0.77 million per regional ICS (Total metropolitan ICS=\$3.6 million, total regional ICS = \$3.85 million).

In addition, in 2006–07 the ICS will receive development funds of \$0.25 million (each metro ICS) and \$0.18 million (each regional ICS) to support quality improvement and the development of psychosocial and supportive care models.

DHS will continue to discourage ICS from utilizing their change management funds to plug service delivery gaps (such as core nursing or medical staff), which would yield minimal service development and improvement outcomes. For example, the conversion of the metropolitan ICS funding to WIES would equate to approximately 470 WIES to be distributed across a number of health services. Instead, ICS are being encouraged to utilise their program funds:

- To identify opportunities for service improvement
- To engage health service management in the review and allocation of core inpatient and outpatient funding for cancer services
- To develop evidence for funding requirements to address gaps in services.

5. It appears that much of the involvement of medical staff in the ICS program is expected to be donated. What is being done to redress this situation?

There are considerable time and management pressures on specialist cancer clinicians. This is particularly evident in regional Victoria where there are limited numbers of medical and radiation oncologists and supportive care oncology workforce to meet increasing demand. In addition, in rural and regional Victoria the majority of surgeons are generalists rather than specialists. The capacity of Regional ICS to establish tumour specific LCTGs is limited, and in some regional ICS one clinical reference group has been established to undertake the work of a LCTG across a number of tumour streams. The ICS have clearly indicated a requirement for funds to support tumour stream development, including project staff to implement service improvement initiatives and remuneration for lead clinicians. Following concerns raised by ICS on their capacity to support the ongoing work of the LCTGs, each ICS will receive recurrent funding from 06/07 specifically allocated to address the above issues.

6. What is being done to support the provision of basic care to patients (which is clearly considered to be inadequately funded in many situations) to allow clinicians to participate in projects looking at “adding the icing to the cake”?

Improving the provision of basic care to cancer patients is at the heart of all cancer reforms. The ICS initiatives aim to improve service provision through four key outcome areas: implementing MD care, improving care coordination, addressing psychosocial and supportive care needs and reducing variations in care.

The PMFs, which are guides to consistent care, will enable clinicians across the state to review how they can contribute to ensuring that cancer care and delivery of cancer services are coordinated, multidisciplinary, high quality, accessible and equitable for all Victorians with cancer.

The identification of gaps in service delivery will enable quantification of the need for service redesign and additional resources, including the case for further funding.

7. How is the Victorian Cancer Agency expected to contribute to cancer research in Victoria?

The new Victorian Cancer Agency has been funded to build research capacity and to connect research and clinical services through collaborative cancer research networks.

The key functions of the agency are:

- To build and fund cancer research capacity across Victoria, including the development of a comprehensive translational research program.
- To align cancer research and cancer services, and to connect clinical academic and cancer research organisations through the development of collaborative cancer research networks and clinical trials capacity. The networks will comprise of ICS, research institutes, universities and peak bodies such as the Cancer Council of Victoria.

- To fund and coordinate cancer research development and innovation, including support for new platform technologies and research and development functions such as the Victorian Cancer Research Tissue Bank and the new Australian Cancer Grid.

Establishment of the new Victorian Cancer Agency will commence in 2006–07. The Agency will work closely with ICS to provide a clear alignment between cancer research and cancer services and to foster translational research.

8. Are there plans to provide recurrent funding for MD care and co-ordination of care for health services? Are these to be earmarked for this purpose?

MD care has been a key focus for the ICS and is internationally recognised as best practice for treatment planning and care of cancer patients. The Cancer and Palliative Care Section has developed a MD care toolkit for use by the ICS, and a MD care policy is being developed in consultation with the ICS. Metropolitan ICS have used some of their funding to purchase essential equipment to support MD care development.

From 2006–07 the ICS will be provided with recurrent funds to support MD care development. The Australian Government, through the Australian Better Health Initiative is to introduce an MBS item for multidisciplinary meetings in November this year.

The development of information/data systems to support clinical management of patients including MD care is being progressed through the proposed appointment of a consultant to scope the issues and needs of ICS, for consideration by the Ministerial Taskforce for Cancer.

Recurrent funds have also been made available to the ICS to support care coordination. Care coordination is seen as requiring a whole of system approach that incorporates the system, health service, team and individual health provider and consumer levels, not just the development of care coordination roles. This multifaceted approach recognises the inherent interface of care coordination with other priority areas and strategies including MD care, the

development of routine psychosocial assessment, clinical protocols, referral pathways and information provision. A policy on cancer care coordination is being developed in consultation with the ICS.

9. What is envisaged for the ICS in the future: is this structure to be a continuing agency for cancer care, or like BSEP, a short term body expected to effect change?

Cancer reforms in Victoria are not a short-term strategy. It is recognised that changes as significant as these will take considerable time to establish and embed into practice. The recurrent funding that has been approved supports this premise and it is envisaged that the ICS will remain the infrastructure to enable delivery of the cancer reforms.

Establishment of a Victorian ICS Committee is being proposed. The Committee will provide a mechanism to provide a consistent statewide approach to cancer reform, and strengthen ownership and leadership of the cancer reform process at a local and statewide level. It will also foster decision making and working across organisational boundaries and over time will allow the ICS to develop as the key planning and decision making bodies for cancer services delivery in their geographic regions.

10. Are there any plans to change the mechanisms for funding of cancer care?

A number of options have been proposed about the longer term mechanisms for funding cancer care including possible per capita payments to support best practice and options for ICS fund holding for chemotherapy or other specified treatments. Review of options for funding reform will continue to be progressed in the context of the impact of such changes on the broader health funding system, although no early changes to current policy are anticipated.

However the DHS has been conducting a cost weights review in radiotherapy and chemotherapy. In radiotherapy the cost weights review will inform on requirements for updating the weights to reflect changes in technology and

practice since the model was implemented in 1998. It will also advise on how funding for the Single Machine Unit Radiotherapy services in Ballarat, Bendigo and Traralgon could be mainstreamed. Services will be expected to shadow fund against the new cost-weights in 2006–07, with a view to their implementation in 2007–08.

In chemotherapy, a number of recommendations have been made regarding funding reform. Further consideration of these proposals is required, with any changes to be made to the existing funding for chemotherapy likely to be several years away.

11. What is planned for the provision of appropriate psychosocial care for cancer patients, which is very poorly provided at present?

Assessment of psychosocial and supportive care needs, along with timely referral and access to psychosocial and supportive care services, have been identified as areas of significant concern across the State. The limited number of existing dedicated and skilled personnel necessitates the development of a broader and multifaceted approach that incorporates staff training in assessment of need and the development of referral pathways and protocols – both of which are linked to the implementation of the Patient Management Frameworks (PMFs). Detailed service mapping will enable identification of service provision gaps and areas in need of improvement.

A staged approach to addressing all interlinked factors impacting on the provision of timely and appropriate psychosocial and supportive care will support the development of sustainable and supported service delivery models to meet the needs of patients, carers and health professionals. This will be undertaken at both the state-wide and ICS level.

12. How is the DHS planning to provide appropriate data collection mechanisms? Does the DHS support the development of a statewide (and ideally national) data collection system? What is being done to facilitate a coordinated approach?

The DHS recognises the challenges faced by the ICS regarding the lack of a statewide data collection system and the pressing need to develop such a system for quality improvement, to facilitate multidisciplinary and continuity of care, to better support research and population initiatives and assist clinicians in their management of cancer patients.

The Victorian Cancer Outcomes Network (VCON) is an initiative of the Ministerial Taskforce for Cancer and Cancer Council Victoria to trial and develop systems for the statewide collection of the NCCI Clinical Cancer Core Dataset (CCCD). The system is currently being piloted at RWH and Barwon Health.

Through the Data and Information Workshop and Cancer Service Plans, health services and ICS have identified major cancer data and information issues. It was identified that a system is needed to improve clinician access to patient data to support clinician decision-making and facilitate:

- Information management of MD care, including documentation of MD meetings and recommendations.
- The clinical management of cancer patients
- Timely feedback from data systems to clinicians
- Identification of common practices and treatment pathways
- The provision of data for existing and future research and public health initiatives.

The DHS is working with ICS and the Ministerial Taskforce For Cancer to progress the work required to ensure the development of a state-wide system to address the above issues.

A national approach to data collection, analysis and usage may become possible through the establishment of Cancer Australia.

13th European Cancer Conference (ECCO)

Paris, France, 30 October – 3 November 2005

Dr Geraldine Goss

Medical Oncologist

Box Hill Hospital & Monash Medical Centre

Paris is the most beautiful city and a wonderful place to visit for ECCO 2005. Much of the data presented in Paris had been presented at other forums and was reviewed; briefly, the ARNO/ABCSG study showed that switching from tamoxifen to anastrozole during the 5 years of adjuvant endocrine therapy for hormone-sensitive breast cancer is associated with an improvement in disease-free survival. The first results of BIG1-98 showed a 20% improvement in disease-free survival for letrozole versus tamoxifen. Aromatase inhibitors and tamoxifen have a different safety- and toxicity profile.

The sequence of FEC-100 ×3 followed by docetaxel ×3 was superior when compared to FEC ×6 in the adjuvant setting of high risk breast cancer. In 2005 the St Galen panellists used endocrine responsiveness not only for selection of endocrine therapies but also for chemotherapies. HER2 and vessel invasion were added to nodal status, tumor size, grade and hormone receptors as prognostic/predictive factors.

The addition of bevacizumab, an antiangiogenic drug, to paclitaxel showed an important improvement in response rate and time to disease progression when added to taxol given as first-line chemotherapy for advanced disease. This was on the background of a strikingly disappointing response rate to paclitaxel alone (14%). The most striking improvement in breast cancer therapy has been achieved by the adjuvant use of trastuzumab as shown by the first results of three large randomised studies conducted in patients with HER2 over-expression. Disappointingly, no further updates on these trials were presented since ASCO, with data presented in Paris already published.

The most interesting data presented revolved around the aromatase inhibitors as adjuvant therapy and especially the emerging differences between these drugs.

Adjuvant AI Studies

MA17 randomized 5187 postmenopausal women with early stage breast cancer after 5 years of tamoxifen to 5 years of letrozole (L) or placebo (P). At the first interim analysis, after 30 months median follow-up (range 1.5–61.4 months), disease-free survival (DFS) was superior in the overall study population for L (HR 0.58 with 95%CI 0.45–0.76; $p = 0.00004$). There were 89/2527 deaths among women receiving letrozole and 152/2530 events among women receiving placebo. Events were defined as local or locoregional recurrence, new primary tumour and distant metastases. Dr James Ingle presented an estimate of hazard rates in the future, should the trend continue. This projected estimate implied a greater benefit of letrozole over time if current trends continue. I found this presentation truly astounding; what ever happened to reporting results after they have occurred? Because the trial was stopped early the optimal duration of therapy is left uncertain. However, no further analysis beyond those available at the first interim analysis was presented.

The MA17 study did demonstrate an improved overall survival among women with node positive disease, although the number of events is very small (28/1184 in the letrozole group, 45/1187 in the placebo group). Does this difference of 17 deaths justify treatment of 2371 women? In the node negative group there was no significant difference (19/1298 v 14/1301). At the very least it seems we can reassure patients finishing 5 years of tamoxifen that their prognosis is indeed very good, with a total of only 106 breast cancer deaths among 4970 women.

Paul Goss then presented data looking at hormone receptor expression among 4653 participants in MA17. Almost all patients (97.4%) had estrogen receptor (ER) and/or progesterone receptor (PgR) positive primary tumors. Retrospective exploratory analyses were

conducted to compare time to recurrence in the four receptor sub-groups by ER (\pm) and PgR (\pm) status. ER and PgR positivity was defined as ≥ 10 fmol/mg protein, or positive by ERICA or PgRICA. The benefit of letrozole was most pronounced in women with ER+/PgR+ and ER-/PgR+ tumors. The ER+PgR+ compared with the ER+PgR- group indicated a statistically significant difference in the treatment effect between them ($p = 0.02$) however this was not a pre-planned comparison. Adjustment for nodal status and prior adjuvant chemotherapy did not affect this result. A plan for central measurement and comparison of standard ER and PgR levels is now underway. Refer Table 1 below.

How does this compare with other studies of AIs?

These results are strikingly dissimilar to those of the **ATAC study** of 9366 women randomised to anastrozole, tamoxifen or both. This study also defined events as locoregional recurrence, distant recurrence and new primary cancer which included DCIS. Among the whole group, there was an improvement in disease free survival among women taking anastrozole. The benefit was seen predominantly in those with node negative disease and those who had not received chemotherapy. However, the major and most striking benefit was seen among women with ER+/PR- tumours. This was regardless of nodal status, tumour size/grade or prior chemotherapy. Indeed, had ATAC been confined to women whose tumours were ER+/PR+ then it would have been a negative study; there was a 16% reduction in events with anastrozole in this group, which was not statistically significant. In addition, in the HR+ group, time to distant recurrence is not significantly different between Tamoxifen and anastrozole.

In the **BIG-98** study, 8010 women were randomised to receive primary adjuvant therapy with letrozole or tamoxifen or both in sequence. In the comparison of letrozole and tamoxifen, at a median follow up of 25.8 months, there was an improvement in DFS among women taking letrozole. This was predominantly among women with node positive disease and those who had received chemotherapy. There was no significant difference in DFS for women with node negative disease. In addition, the benefit was significant in ER+/PR+ as well as ER+/PR- tumours.

In the trials of sequencing AIs following tamoxifen,

there were also differences in DFS benefit from AIs over tamoxifen according to pattern of ER/PR expression. In the ARNO trial where participants were randomised to continue tamoxifen or switch to anastrozole the benefit was also much greater in the ER+/PR- group, while in the IES study benefits were similar in ER+/PR+ and ER+/PR- subgroups. Data from the ITA study are not available.

Significance of PR Expression

PR expression has not been established as an independent prognostic factor in breast cancer but is a predictor of reduced responsiveness to tamoxifen in metastatic breast cancer, and PR loss is common with the emergence of tamoxifen resistance (Ravdin 1994). Expression of PR is under the control of oestrogen. One theory suggests that signalling of growth factors from the EGF family interfere with PR gene expression. In a study of 43000 tumors, those expressing ER+/PR- compared with ER+/PR+ are more likely to be >2 cm, have higher numbers of involved lymph nodes and higher S-phase and

Table 1

	n	Letrozole (L) events	Placebo (P) events	HR* L vs P (95%CI)
ER+ PgR+	3809	60 (3%)	117 (6%)	0.50 (0.36–0.68)
ER+ PgR-	636	19 (6%)	17 (5%)	1.19 (0.62–2.29)
ER- PgR+	200	4 (4%)	5 (5%)	0.62 (0.17–2.31)
ER- PgR-	8	–	–	–

more aneuploidy. In tumours with ER+/PR- high levels of EGFR predict for tamoxifen resistance; thus AIs might be expected to be more effective in ER+/PR- tumours. Loss of PR may be a surrogate for high growth factor receptor signalling, which may contribute to PR loss and tamoxifen resistance. However, this does not explain the differences in outcome in the ATAC and BIG/MA17 trials, and it is possible that AIs are not interchangeable in practice. Paul Goss suggested centralised testing of ER/PR for all tumours in ATAC, BIG and MA17; this huge task would likely add to the understanding of the differences if any, between the AIs.

Tamoxifen is associated with increased risk of endometrial hyperplasia, venous thromboembolism and with increase in bone mineral density. It is uncertain, however, if the AIs are interchangeable in clinical practice; emerging data suggest that the distinct molecular structures of the AIs may result in different safety profiles. Long term safety data are of great importance in selection of appropriate adjuvant treatment, especially with respect to bone health, cardio and cerebrovascular effects and cognitive function. Assessment of overall risk/benefit aids in selection of adjuvant hormonal therapy. Additionally, understanding of the interaction of the ER/PR and EGFR in breast cancer may aid in selection of adjuvant treatment most likely to offer greatest benefit to the patient.

5th European Breast Cancer Conference (EBCC)

Nice, France, 21-25 March 2006

*Dr Jacquie Chirgwin
Medical Oncologist
Box Hill & Maroondah Hospitals*

Nice seems to be rather grey and drab in March, but there were many other activities to enjoy, including some outstanding eating, gardens and things European – not to mention the European summary of recent breast cancer research, with their individual “spin” and flavour added. The opportunity to discuss current, developing and imagined trials with European researchers, especially our IBCSG colleagues is always interesting and often entertaining.

There was good representation from Australia, as there always is at these meetings, and I will add little here, as there are excellent summaries included in this edition of Radiation Oncology issues (Karen Taylor) and Surgical topics (David Speakman) for which I thank them. Much of what was presented in Medical Oncology has been presented before – and summarised in previous reports appearing in this newsletter. I will report briefly, however on two topics:

The first is regarding the updated follow up of **MA17** (Letrozole vs Placebo post 5 years of adjuvant Tamoxifen), specifically the outcome

for women initially assigned placebo, but, who, when unblinding occurred in October 2003, were then offered and took Letrozole. Of 2,247 women on placebo who were well without recurrence, 1601 crossed over to Letrozole, at varying time delays. Delayed Letrozole resulted in significant improvement in survival with hazard ratios as follows:

DFS	0.31
DDFS	0.28
OS	0.51
Contralat BC	0.38

Although, with all patients on Letrozole there was an increase in osteoporosis, there was no increase in fractures, nor in cardiovascular disease, although cholesterol levels rose in the first 6 months off Tamoxifen. Results were similar for N-ve and N+ve patients, except that the event rate for N+ve patients was double that in the N-ve cohort (4% vs 2% per annum).

Treatment post 5 years of tamoxifen (or perhaps indeed any agent), is likely therefore to be important, a contention also supported by long-term survival statistics: for patients free of disease at 5 years, the ER-ve cohort has an 85% 20

year survival, whereas for the ER+ve cohort has a 20 year survival of only 60%, indicating a considerable and continuing risk of relapse after 5 years which can potentially be reduced by extended adjuvant treatment.

Various views were also presented at the meeting on the place of adjuvant Tamoxifen, AI's, and the timing of switching. Kent Osborne presented the hypothesis that endocrine adjuvant treatment may in future be tailored by molecular signatures. At present we have to make the best of what data we have available to us, and use receptors as well as risk assessment in making recommendations. He noted that the benefit of switching increases with time.

Secondly, I was most interested to attend a panel session led by Martine Piccart exploring the concept of **Guideline Development in Metastatic Breast Cancer (MBC)**, similar to the St. Gallen Guidelines for adjuvant treatment. A set of 12 statements relating to the "standard" medical and psychosocial care of patients with MBC were presented and discussed. It was agreed the purpose of the guidelines is to improve survival and QOL for patients and to improve the economics of MBC management. It must be shown that these guidelines have practical impact in order to determine that this process is worthwhile. The following is a brief summary of the 12 statements:

1. Management of MBC is complex; therefore all appropriate specialties should be involved in a Multi Disciplinary Team (MDT). Eg. medical, radiation and surgical oncologists, pathologist, palliative care and psychosocial practitioners, nurses etc
2. From the first diagnosis of MBC, patients should be offered appropriate psychosocial, supportive and symptom related interventions as a routine part of their care
3. Following thorough assessment and confirmation of MBC, the potential treatment goals must be specified and discussed. Patients should be invited to participate in all decision making; caregivers should also be included
4. A small but very important subset of MBC patients can achieve CR and long survival. They should be identified, to allow appropriate management decisions. (this item discussed ++ and will be modified to reflect that it may

not be possible to identify these individuals, but it is important to make decisions for "pseudo-cure" treatment in some patients eg. with "oligo-metastatic" disease)

5. Minimal staging workup for MBC includes history, physical examination, complete haematology and biochemistry, imaging of chest, abdomen and bones (?brain, pelvis); thoughtful imaging of target lesion(s)
6. Treatment choices should take into account:
 - Previous treatment
 - Disease free Interval
 - HR status
 - Tumour burden
 - Biological age
 - Menopausal status
 - Co-morbidities
 - Performance status
 - Need for rapid disease/symptom control
 - Socio-economic and psychological factors (list not exhaustive)
7. Hormonal treatment is the preferred treatment option for HR+ve unless there is concern or proof of endocrine resistance. Optimal endocrine treatment for postmenopausal patients is AI (although Tamoxifen remains a viable option) For premenopausal patients, Tamoxifen plus Ovarian suppression/ablation is the treatment of first choice unless Tamoxifen resistant Post AI treatment uncertain Maintenance endocrine treatment after chemotherapy is not established but is reasonable Concomitant chemotherapy and hormone therapy is discouraged
8. Trastuzumab should be offered early to all HER2+ve MBC patients, after failure of endocrine therapy if this is appropriate (this point was discussed ++ as trastuzumab may be beneficial in combination with endocrine treatment up front)

Currently the optimal management of patients progressing on trastuzumab is unknown; there are no clinical data to support trastuzumab after progression; but based on expert opinion it is reasonable to continue with a second chemotherapy regimen, but therapy thereafter is to be generally discouraged.
9. For the majority of patients overall survival outcomes from sequential use of single cytotoxic drugs are equivalent to

combinations. The choice between the two approaches should be taken after consideration of the factors in paragraph 6, with greatest emphasis on the need for rapid and significant response and QOL. Duration of each regimen and number of regimens should be tailored to each individual patient.

10. There are few proven standards of care in MBC management, therefore inclusion in well designed randomized controlled trials is recommended.
11. The medical community must be aware of the problems raised by the cost of MBC treatment and must make balanced decisions with patient factors paramount.
12. Management decisions should be made using regular and formal QOL assessments, as well as clinical assessments.

Much of this may seem obvious, especially in Australia, where the NBCC Clinical Management Guidelines for the care of patients with advanced breast cancer have been available for some years. It does however, provide a concise framework for all aspects of care which can increase the equality and standards of care internationally and which can also provide a framework for regular discussion and update as new data emerge and new treatment paradigms are adopted. It also highlights the issue of MDTs in advanced disease, an area that we are only beginning to develop. It is proposed that the guidelines be reviewed and updated regularly, perhaps at each second yearly EBCC. I think this is a valuable process to support.

5th European Breast Cancer Conference (EBCC) Radiotherapy Update

Nice, France, 21 - 25 March 2006

Dr Karen Taylor

Radiation Oncologist

William Buckland Radiotherapy Centre, Alfred Hospital

Invasive Breast Cancer

Dr Yarnold - Royal Marsden, Sutton

● **Radiotherapy dose and fractionation :**

Dose escalation was initially discussed. Bentzen (IJROBP 2004) described a shallow dose response in breast as approximately 70% of women do not recur without RTX. Four trials (>7000 women) have shown a boost of 10–16Gy, following whole breast RTX, reduces local recurrence (HR 0.59–0.8). Bartelink's trial (NEJM 2001) showed a 16Gy increase in dose halved the local recurrence rate but the absolute number of local recurrences prevented was modest, at a cost of cosmesis (fair/poor cosmesis increased from 14 to 29%). The benefits appear to be age related (but see later) preventing 20 local recurrences/100 women in women under 40 and 4/100 women in the over 40 age group.

He then discussed fractionation changes based on his hypothesis that breast cancer may be as

sensitive to RTX fraction size as dose limiting late effects. If this is true he postulated that modulating fraction size should be as effective as adjusting the number of fractions. He described 4 trials of hypofractionation in 8000 women with 2.67–3.3 Gy/fraction in 13–16 fractions. Whelan's trial from Ontario (JNCI 2002) of 42.5Gy/16 showed equivalent local tumour control to 50Gy/25 (but a low actual number of events n=44) with similar excellent to good cosmesis with short follow up of only 5 years. Dr Yarnold's own Royal Marsden/Gloucester Oncology Centre trial of 50Gy/25 vs 39Gy/13 vs 42.9Gy/13 with 10 years follow up showed similar local control with 42.9 Gy and 50Gy and reduced control with 39Gy. Cosmesis was best with 39Gy and worst with 42.9Gy. Further hypofractionation trials are in progress including UK FAST, looking at 50Gy/25 vs 30Gy/5 fractions vs 28.5Gy/5, all over 5 weeks and IMPORT, looking at a large field to the whole breast, a smaller field to "less than the whole breast" and a third field to the typical boost field.

He concluded with the comments that the morbidity could be increased and is often late occurring and that hypofractionation should remain within the contexts of clinical trials only.

Target volume definition :

He described the benefits gained in localisation of breast tissue with multi-level CT planning, although the tumour bed can still be difficult to identify (helped with the placement of titanium clips). Other advantages are definition of heart lung volumes and the definition of a 3D volume for 3D dosimetry. He noted that the indistinct border between glandular and fatty tissue led to an inter-observer variation in CT volume mostly at the upper and posterolateral borders. Methods for reduction of cardiac irradiation were discussed including elevated arm position, deep inspiratory breath holds, active breathing control, cardiac shielding, conformal RTX & IMRT and compromising on the target volume depending where the primary tumour site was located. A caveat was that due to the position of the left anterior descending coronary artery there may not be a volume effect in the heart.

Dr Fourquet - Institut Curie, Paris

Radiotherapy in early breast cancer: who does not need it? :

Large randomised trials have shown RTX reduces locoregional recurrence with a 66% relative risk reduction and 20-30% absolute risk reduction with a breast preservation rate of 90%. An absolute reduction in mortality has now been shown. The trials also showed that a significant number of women who did not receive RTX did not recur locally. Identifying these women is a challenge as ultimately RTX could then be omitted. He discussed the usual predictors of low risk including older age, free margins, node negative, grade 1, no LVSI, hormone receptor positivity, non-lobular histology, EIC negative and the use of systemic therapy. However recurrence rates increase with increasing longevity of follow up. The common predictors of failure therefore do not adequately select patients for radiotherapy or not. Other markers are required.

Dr Bartelink - Netherlands Cancer Institute, Amsterdam

Radiotherapy in early breast cancer: who needs more? :

The EORTC boost trial was discussed which showed that in women <40 a 16Gy boost was required to reduce the risk of local recurrence

but in women >40 this became less important and could be omitted. However, with longer follow up the results have changed and show that there was a significant effect in all age groups but was greatest in the women <40 (Antonini, in press). He discussed the importance of preventing local recurrence as for every 4 local recurrences prevented there is improvement in one woman's survival (EBCTCG 2005). MRI may be able to detect more cancers than conventional imaging, especially in young women, and could potentially reduce the local recurrence rate. He finished with a comment that microarrays have not been able to predict for local recurrence in a way that they have for metastatic disease.

Dr Arriagada - Villejuif, France

Impact of delaying radiotherapy in early breast cancer :

Tumour doubling time influences whether or not delaying RTX impacts on tumour control probability. A tumour with a doubling time of a few days would be influenced far more than one with a doubling time nearer 50 days. Huang (JCO 2003) reviewed 8 studies looking at a delay of more or less than 8 weeks. Local relapse was higher (RR 1.62) with delays more than 8 weeks. However a study from the UK (Mikeljevic Br J Cancer 2004) showed only after 20 weeks of delay there was increased local recurrence (HR 1.49). He commented that systemic treatment appears to reduce local recurrence by 20-25%, its effects being largely independent to RTX. Sequencing studies have indicated that delays in chemotherapy lead to increased systemic relapse, therefore chemotherapy is given prior to RTX. He concluded that in the absence of effective systemic therapy, RTX delay is important, especially in fast growing tumours. EUSOMA recommend that the delay should not exceed 8 weeks unless chemotherapy was being given, and then should not exceed 6 months.

Dr Wood - Atlanta, USA

Breast conservation – why still a challenge? :

Palpation, mammography and ultrasound should be routinely used but there can still be difficulty in determining the true extent of the tumour. MRI can offer further information and has been shown to alter planned surgery by up to 26% (Czerniecki Am J Onc Rev 2004). Neoadjuvant therapy leads to further challenges in determining

extent of surgery. Extensive DCIS can increase the risk of local relapse but does not contraindicate conservation if completely excised. There are more problems with widespread calcifications and non-calcifying DCIS. He commented that good specimen orientation and marking is essential for optimal review and reporting.

Dr Yarnold - Royal Marsden, Sutton

Partial breast irradiation :

The EBCTCG 2005 review has shown that whole breast radiotherapy (WBRT) affords a 5.4% reduction in breast cancer mortality (5.3% reduction in all cause mortality) but with well recognised adverse effects including breast shrinkage/distortion/hardness/pain, intercostal/pectoral muscle fibrosis, rib fracture, lung fibrosis and cardiac damage. Donovan (Royal Marsden Hospital 2005) showed 30% of women had ongoing breast changes and 10% of women had marked changes, even with 3D planning. Dr Yarnold put forward the case for partial breast radiotherapy (PBRT) as it targets the site of 75% of local relapses and reduces the complications of WBRT. The case against includes a 10% incidence of neoplastic foci >4cm from the primary, even when the primary was 2cm or less in diameter (Holland 1985). At the time of first relapse the management is usually mastectomy and this obviously censors the patient at the time of first relapse (removing the potential of small foci outside the initial quadrant to subsequently become a problem). Very long term follow up data from Fox Chase (2005) now suggests that WBRT reduces ipsilateral new primaries. His final point against PBRT was whether or not it is needed at all in the good prognosis group it is being used in, now that we have more effective endocrine treatment. He went on to describe the 4 large trials comparing PBRT to WBRT (NSABP 39, TARGIT, ELIOT and UK IMPORT). He left us with questions regarding what is the optimal target volume and dose? Is the volume defined by the wall of the excision cavity? He described the paradox of if all that is needed is a 5-8mm wall PBRT treatment then this should be equivalent to re-excision, but pointed out that even in the Milan studies that used quadrantectomy, the group that had quadrantectomy and WBRT had a lower risk of local recurrence.

Dr Overgaard - Aarhus University Hospital, Denmark

Radiotherapy related morbidity :

He discussed the SEER data from Lancet Oncology (2005). He commented that the effects of RTX and anthracyclines on the heart are additive and care should be taken to avoid the heart. Simultaneous RTX and chemotherapy should also be avoided as there is an increased incidence of subcutaneous fibrosis and telangiectasia. The lung cancer incidence also seen in the EBCTCG (2005) is of concern. He commented that hypofractionation could potentially reduce tumour control and at the same time increase cardiac damage due to the low α/β ratio of the heart (1-3Gy). He presented some of Donovan and Yarnold's data from Paris (ECCO 13) that showed homogeneity of dose improves cosmesis, and reminded us of the concept of "double trouble" in areas of inhomogeneity. He finished with a discussion as to whether morbidity could be predicted. He considered that not only was there no correlation between early and late endpoints but that there were different endpoints for different late effects such as telangiectasia and fibrosis.

Dr Jassem - Gdansk, Poland

Management of local relapse in breast cancer :

Local relapse occurs following breast conserving therapy at a rate of ~2%/year and after mastectomy at 1-2%/year. Traditionally chest wall relapse has been said to be a poor prognostic factor but failure analysis from EORTC 10801 shows that relapse after breast conserving surgery can have a similar poor prognosis. The cumulative incidence of relapse is one third local and two thirds distant. Refer Table 1.

Post mastectomy relapse :

Prognosis is determined by volume of relapse (one nodule usually confers a better prognosis than two/more and diffuse relapse a poor prognosis), time to relapse (later is better) and stage at initial presentation (smaller tumours and node negativity are better). Local control after relapse confers a good prognosis. RTX (if not previously given) was discussed. Halverson (IJROBP 1990) suggested treatment of the whole chest wall with 45-50Gy. There is no data on the role of a boost to the involved area. Areas of macroscopic disease should get at least 60Gy. He recommended the SCF should be treated due

Table 1: Management of local relapse in breast cancer - Cumulative incidence of relapse

	Post mastectomy relapse	Post conservation relapse
Location	50–75% in scar	>80% in same quadrant
Method of detection	physical exam	>50% by mammography
Regional involvement	50%	<10%
Distant metastases	10–50%	10–15%
Median time to relapse		
No adjuvant treatment	2–3 years	3–4 years
Adjuvant treatment	2–5 years	5–7 years

to the increased risk of subsequent relapse but that axillary lymph node irradiation was controversial. In women who relapse post reconstruction, the reconstruction does not influence outcome (Chapgar Am J Surg 2004). There is no data on the role of chemotherapy as EORTC 10920 failed to accrue and IBCSG 27-02 is ongoing. Endocrine therapy has been shown to improve outcome in post menopausal women only (Borner JCO 1994). In women who have received previous RTX the options are extensive surgery, limited field RTX, brachtherapy and combined RTX and hyperthermia.

Post breast conservation relapse:

5 year survival is 50–85%. Factors affecting prognosis are time to relapse, histopathology, size and stage, method of detection, skin involvement and original number of lymph nodes involved (if heavily involved initially local relapse tends to be associated with an increased incidence of distant relapse). Salvage mastectomy +/- reconstruction remains the gold standard and >85% of local relapses are able to be managed this way. Subsequent local control is in the order of 70–95%. There is limited data on reconsevation and no phase III trials. Sentinel lymph node biopsy can be helpful and can identify a node in up to 75% of cases. There is no data on the use of chemotherapy or endocrine therapy. It is often difficult to determine whether relapse outside the tumour bed is local recurrence or a new primary. The prognosis tends to be better if it is a new primary with fewer further local relapses and less distant disease.

Dr Perez - Jacksonville, USA

Radiotherapy concurrent with trastuzumab

is well tolerated in the adjuvant treatment of women with HER2-positive breast cancer: cardiac safety data from the NCCTG N9831 study:

Three year data was presented. In this study RTX followed chemotherapy and was commenced at the same time as Herceptin +/- endocrine therapy (within 5 weeks of completing paclitaxel). There was no IMC RTX. 75% of women had RTX (48% left sided). There was no difference at 3 years in cardiac dysfunction between the group that did not have RTX (2.4–4.4%) and those that did (no difference either in the left (1.9–2.5%) and right (1.8–2.3%) sides). There is still ongoing review with regard to cutaneous, pulmonary and haematological toxicity but the comment was that overall it was well tolerated. Update ASCO 2006.

Ductal Carcinoma In Situ

Dr Fourquet - Institut Curie, Paris

DCIS:

Three large multicentre prospective randomised trials (NSABP B-17, EORTC, UKDCIS) involving 2846 women provide evidence that the addition of WBRT (predominantly 50Gy/25) to surgery reduced the rate of ipsilateral breast recurrence by 50–60%, for both invasive and in situ disease. Follow up was 5–11 years. The risk factors for local recurrence were discussed. A young age was the strongest predictor. Others included margin involvement, presence of necrosis, residual mammographic calcifications, absence of calcifications on the original mammogram and

mode of detection. The randomised trials failed to identify subgroups of patients who would not benefit significantly from the addition of WBRT. As in invasive breast cancer the effects of RTX are proportional, the magnitude of the benefit depending on the baseline risk. It was recommended that RTX should not routinely be omitted, even in low risk groups, unless it is within the confines of a prospective study or the woman's choice. A further prospective randomised trial with 8 year follow up is due to be published from Sweden.

Dr Cutili - Reims, France

Optimal management of DCIS :

The opening comment reminded everyone that if DCIS recurs as invasive disease then lymph node metastases are found in 13–20% of cases. Risk factors for local recurrence were again discussed. Age <40 is an independent factor (perhaps due to either insufficient surgical excision or biologically more aggressive disease). DCIS detected clinically is more likely to relapse than that detected mammographically (Cutili). Other factors are narrow margins (van Nuys), higher grade lesions (van Nuys, EORTC) and a low excision volume, especially in young women (Joint Centre). Will dose escalation reduce risk of local recurrence? NSABP B17, EORTC and Swedish trials used 50Gy/25 with no boost. Other studies have used a boost in up to 60% of women (often when margins were doubtful). This is yet to be studied. The results so far from the use of Tamoxifen are conflicting. Aromatase Inhibitors are to be studied. He concluded that:

- (1) Mastectomy should be performed for large/multicentric lesions and for insufficient margins (often in young women) along with a sentinel lymph node biopsy to avoid a second procedure

if invasive disease is found. (2) Only for very low risk DCIS (low/intermediate grade, <2cm, >1cm margin, age>60) one should consider omitting RTX and this should be in the context of a detailed discussion and preferably a trial. A prospective trial from Boston of wide local excision alone in DCIS of low/intermediate grade, mammographic extent ≤ 2.5 cm with final margins after wide excision of ≥ 1 cm closed early because the number of local recurrences met the predetermined stopping rules (Wong et al 24, JCO 2006).

Lobular Carcinoma In Situ

Dr Cutili - Reims, France

Optimal management of LCIS :

There appears to be more aggressive subtypes of LCIS that are more pleomorphic with large nuclei and necrosis or involve >10 individual lobules. The treatment options are breast conservation, mastectomy, conservation + RTX and Tamoxifen (NSABP P1). After excision 10–30% recur locally, ~60% of these recurrences are invasive. A French study was discussed that looked at 292 women with LCIS, with a median age of 49 and median follow up of 9.4 years. Local recurrence was seen in 20% of women following conservation surgery, 2.7% following conservation surgery and RTX and no recurrences seen after mastectomy. He suggested that RTX after conservation surgery for LCIS may reduce the risk of local recurrence in a similar way to DCIS. He referred to his paper and an editorial from last year in EJC. He then suggested a prospective study was required that should analyse LCIS risk factors, identify aggressive subtypes, evaluate the potential benefits of radiotherapy in some subgroups and optimise follow up modalities.

Clinical Practice Guidelines on Familial Aspects of Cancer

This document is being developed with Associate Professor Judy Kirk as Chair. It is a revision of a 1999 document. It will be completed late this year. A question of

publishing a revised Familial Aspects of Bowel Cancer Guide is being discussed as there is significant demand for it.

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5th European Breast Cancer Conference (EBCC) A Surgical Perspective

Nice, France, 21-25 March 2006

*Mr David Speakman
Surgeon
Peter MacCallum Cancer Centre*

Not surprisingly, the surgical content of the program did not contain any major revelations however there were many items of interest to surgeons and this, combined with the delightful and pleasant setting of Nice, made this a worthwhile meeting.

Sessions around **sentinel lymph node biopsy** were principally run by Emil Rutgers from The Netherlands Cancer Institute. There were several points relevant to Australian surgeons. It was reported that to maintain appropriate experience in sentinel lymph node biopsy, the surgeon should be performing at least six or more cases per month. Regarding sentinel lymph node micrometastases (0.2–2.0 mm), European data shows approximately 20% of patients will have an additional positive node in the non-dissected axilla. This has led them to recommend that a patient with micrometastases should proceed to a completion dissection and radiotherapy should be offered as an alternative form of local control if complete dissection is not undertaken.

The issue of isolated tumour cells (ITC) remains unresolved. Again the data showed metastases detected by immunohistochemistry alone associated with a 9% rate of residual disease in the axilla. The conclusion regarding isolated tumour cells was that although this area is still unclear, an observation only policy for the axilla is justifiable as completion dissection will not alter the management plan in most patients. In terms of internal mammary chain nodes, they have been found more commonly with deeper tumours in The Netherlands experience, presumably lying beyond the watershed area between the superficial and deep lymphatics. Internal mammary node retrieval altered the management in 29% of cases however this is mostly seen with the addition of radiation to the internal mammary chain if an IM node was positive. Interestingly, lymphoscintigraphy showed 12% of cases to have a sentinel lymph

node identified outside both the axilla and/or the internal mammary chain.

The European group for **breast cancer screening** met immediately prior to the EBCC. The major discussion was around digital mammography and its imminent arrival in most screening programs along with the issue of over diagnosis of benign type lesions. MRI screening of high risk women was discussed in several sessions but most particularly by Christine Kuhl. She had pooled the results of several of the larger MRI studies and reported the following in a comparison of mammography versus MRI: sensitivity 35% versus 80%, specificity 96% versus 90%, interval cancers 30% versus 5% and a positive predictive value 24% versus 50%. She forcefully concluded that MRI screening of higher risk women should now be mandatory as it was the best method available and was also clearly of the opinion that governments should begin to consider its use as a screening tool for the entire population! Data was also presented regarding the use of MRI in patients with a recent diagnosis of breast cancer. 'Significant lesions' were detected in the ipsilateral breast in 27% of cases by MRI along with occult carcinoma discovered in the contralateral breast in 3–6% of patients.

Ian Ellis, pathologist from Nottingham, presented some interesting work on the **basal phenotype of breast cancer**. The Nottingham group have been working on predicting basal type tumours from the histological profile rather than microarray studies. They appear to be largely grade 3 tumours with a high mitotic count but a lack of tubule formations. Although often ductal NOS in type, both classical and atypical medullary and salivary type tumours predominate. There was a high rate of p53 positivity. They are CK5/6 or CK14 positive but CK18 negative. In many ways, they have similar features or profile to BRCA1 type cases. Indeed in the Nottingham experience,

in patients under 60 with the above type of tumour, 55% were BRCA1 mutation positive.

Peter Boyle from France presented some interesting statistics regarding **weight and breast cancer prognosis**. In a study of 5200 patients with breast cancer sourced from the NHS in the UK, an increased BMI was associated with an increased risk of breast cancer death based on the patient's weight pre-diagnosis. Interrogation of the IBCSG database revealed that overweight women often received inadequate or subtherapeutic doses of chemotherapy when compared to women with normal BMI. The reasons for this were unclear. The benefits of exercise in this regard for breast cancer patients were also highlighted along with some interesting laboratory data showing a significant drop in oestrogen levels in postmenopausal women who exercise regularly.

A further topic of interest to surgeons at this meeting was the **design of new breast cancer trials**. There is certainly a trend away

from long trials involving large numbers of women to the development of smaller *in vivo* trials using biomarkers to assess outcomes. In particular, the use of both chemotherapy and endocrine therapies in a neo-adjuvant setting with tumour assessment pre and post treatment and prior to surgery, will become more frequent and consequently require greater involvement of surgeons both in recruitment and harvesting of specimens to make such trials workable.

The **MINDACT trial** is about to commence and this was discussed extensively at the meeting. This study is using microarray technology for patients with node negative disease to determine their need for chemotherapy, comparing the decision made by genetic profiling to the more conventional parameters used in decision making regarding systemic therapy. As the driving force behind this trial is to identify women who do not require systemic chemotherapy and who can avoid its side effects, this is of considerable interest to all breast clinicians.

42nd American Society of Clinical Oncology (ASCO) Breast Cancer Update

Atlanta, Georgia USA - 2 - 6 June 2006

*Dr Kathryn Field
Advanced Trainee Registrar
Western Hospital*

ASCO was held this year from 2nd - 6th June, 2006, in Atlanta, Georgia. Breast cancer featured strongly in the plenary and special sessions, with exciting new developments and future horizons becoming apparent. Overall, and not just in the field of breast cancer, the understanding and application of targeted therapies was a central theme of the meeting, and it seems likely that these modalities of treatment, together with therapies tailored to the specific molecular nature of an individual's cancer, will be the way of the future. The highlights of the breast cancer-related sessions are presented below.

Lapatinib

Lapatinib is an oral dual-tyrosine kinase inhibitor with specificity for the EGFR (ErbB-1) and HER-

2 (ErbB-2) receptors. Phase I and II studies have shown promise in pretreated patients with HER-2 +ve metastatic breast cancer.

Much excitement was generated from the presentation of the EGF100151 study (Geyer et al). This international randomized phase III study, for HER-2 +ve patients with progressive metastatic or IIIb/IIIc T4 locally advanced breast cancer refractory to trastuzumab, compared Lapatinib and Capecitabine to Capecitabine alone. A pre-planned interim analysis resulted in enrollment stopping after 321 patients had been randomized, due to a clinically meaningful, statistically significant benefit seen in the study arm for the primary endpoint of TTP. With a median of 60 weeks follow up, median TTP was 36.9w vs 19.7w favouring the combination, HR

0.51 (95% CI 0.35, 0.74), $p=0.00016$. Median OS has not been reached but so far there is no difference in OS (29 deaths in each arm).

The first site of relapse was the CNS in 4 patients in the combination vs 11 on capecitabine alone, suggesting that lapatinib may help to prevent CNS metastases, a common and difficult problem in HER-2 +ve patients. The main toxicities seen were diarrhoea, hand-foot syndrome and rash, but minimal grade 4 toxicity. Left ventricular function was closely monitored (4 vs 1 decline in LVEF) but there were no withdrawals due to decreased LVEF.

These data suggest an emerging new standard of care for HER-2 positive patients refractory to trastuzumab. Results of future trials using lapatinib in the adjuvant setting, including the APHRODITE and neo-APHRODITE studies, will be eagerly awaited.

HERA Study - 2 year Update

Since the groundbreaking HERA study results were presented at ASCO last year, the median follow-up is now 2 years. 861 patients in the control arm have chosen to receive trastuzumab and so both intention-to-treat (ITT) and censored analyses are possible. Results from the third arm of the study (2 years of adjuvant trastuzumab) are not expected until 2008.

The most striking new data are those now demonstrating a 3 year overall survival benefit favouring the trastuzumab arm. Using an ITT analysis, the 3y OS is 92.4% vs 89.7%, HR 0.66, (95% CI 0.47, 0.91), $p=0.0015$. This corresponds to an absolute difference of 2.7% at 3 years. The OS (censored) shows very similar results - 92.4% vs 89.2%, HR 0.63, $p=0.0051$.

The 3y DFS (ITT) is 80.6% vs 74.3%, HR 0.64 (0.54, 0.76), $p=0.0001$ again favouring the 1 year trastuzumab arm. Despite overall DFS events numbering 152 in the trastuzumab arm vs 233 in the observation arm, CNS metastases as 1st site of metastatic disease occurred in 26 vs 22 - a higher number in the trastuzumab arm, consistent with previous studies.

An OS benefit for adjuvant trastuzumab had already been demonstrated in the NSABP-B31 and N9831 North American adjuvant studies, so the HERA data will further add to the incentive for HER-2 positive patients to be treated in the adjuvant setting with trastuzumab.

STAR Trial (NSABP P2)

The results of the STAR trial were presented in a plenary session. This primary chemoprevention study randomized over 19,000 high risk postmenopausal women to tamoxifen 20mg/d or raloxifene (a related SERM) 60mg/d, for 5 years. The median follow-up is now 4 years. The cumulative incidence of invasive breast cancer was identical for both arms; however the rate of non-invasive (in-situ) breast cancers was higher in the raloxifene arm - rates per 1000 women 2.11 vs 1.51, RR 1.41 (95% CI 1.00, 2.02). The mechanism or reason for this is unclear. The rate of uterine cancer was slightly lower in the raloxifene arm - 0.5% vs 0.8% but the RR of 0.62 (0.35, 1.08) was not statistically significant. The rate of thromboembolic complications appears lower for raloxifene - for DVT 1.69 vs 2.29/1000 and for PE 0.96 vs 1.41/1000. However there were no differences in rates of strokes, cardiac events or fractures. Cataracts were relatively increased in the tamoxifen arm (12.2/1000) vs raloxifene (9.72/1000). QOL analyses suggested overall similar results between the two groups with no statistically significant differences although the side effect profile differs slightly between the two.

In summary, raloxifene appears to be as effective as tamoxifen in primary prevention of invasive breast cancer in this high risk post-menopausal population; however it is less effective than tamoxifen for preventing LCIS/DCIS.

Other Brief Highlights

Bilateral salpingo-oophorectomy (BSO)

protects against BRCA-associated breast and ovarian cancer. (Kauff et al, Abstract #1003). 886 women with BRCA-1 or 2 mutations were prospectively followed; with a median follow-up of 40 months BSO significantly decreased the rate of ovarian cancer from 4.9% to 0.55% - HR 0.09 (0.03-0.34) and breast cancer from 9.8% to 6.3% - HR 0.48 (0.26-0.90).

Concurrent trastuzumab and radiotherapy

appears to be safe, in a subset analysis of the N9831 adjuvant Trastuzumab trial (Halyard et al, Abstract #523). Radiotherapy was allowed to be given concurrently with trastuzumab and 1460 of these patients were evaluable. Rates of cardiac and other adverse events (AE's) were compared with the study population not receiving radiotherapy, and across treatment arms. There

were no significant differences across the arms in radiotherapy-associated AE's. Radiotherapy also did not increase the frequency of cardiac events. In fact the incidence of cardiac events appeared lower in the patients having radiotherapy (eg in AC → TH → H arm: CE 1.5% with radiotherapy and 6.3% without radiotherapy). Late AEs will require more time to assess and analyze.

The Women's Health Initiative randomized **phase III study of calcium and vitamin D** (over 36,000 women participated) showed no difference in the rate of invasive breast cancer when compared with placebo. This was presented at a Plenary session.

Serum HER-2/neu levels can predict clinical outcome in trastuzumab-based therapy. Using a pooled analysis of seven 1st line herceptin trials for metastatic breast cancer with 307 evaluable patients, Ali et al (Abstract #500) found that a >20% decrease in serum HER-2 levels was associated with a statistically significantly higher ORR, TTP and OS; the data are impressive. As targeted alternatives to trastuzumab become available (eg lapatinib), such testing will become clinically relevant in the near future. Other markers that may be used in the future to predict trastuzumab resistance or responsiveness include PTEN, c-myc and topoisomerase II alpha.

Triple negative (basal-like) breast cancer – a number of sessions discussed chemotherapy options for these patients. One take-home message was to consider BRCA mutational analysis in these women, based on data from Kandel et al (Abstract #508) where patients with triple negative breast cancer were found to have a rate of BRCA mutation 2.6 times the expected rate, taking into consideration their family histories.

Hormone therapy

- Intergroup Exemestane Study (IES) – first mature analysis excluding the patients who were later found out to be ER-ve, the OS HR was 0.83 (0.69 – 1.00), p=0.05, indicating an OS benefit for this subgroup in switching to exemestane after 2–3 years of tamoxifen
- ARNO 95 study – with a median F/U of 30 months, switching to anastrozole after 2y tamoxifen significantly improves both DFS

and OS – for OS, HR 0.53 (0.28, 0.99), p = 0.045

- MA.17 – updated with results from patients who crossed to letrozole after the study was unblinded – HR for DFS was 0.31 (0.18, 0.55: p<0.0001) favoring patients who crossed over to letrozole compared to those who stayed on no treatment. There is a suggestion of OS advantage in the subset with node +ve disease but further data is awaited.
- Overall it is considered that postmenopausal women should receive an aromatase inhibitor; whether up front or in sequencing with tamoxifen, to date, is up to the individual.

To summarize, I learnt a lot not just about breast cancer at my first ever ASCO meeting, but about many other tumour streams; and more importantly:

a) to allow at least half an hour to get from one session to the next – the Georgia World Congress Centre is huge!

b) after boycotting Starbucks in Australia for many years, there is no choice but to drink it in America and I have to admit, it's not bad!

The Colebatch Fellowship Reducing the Burden of Breast Cancer

*Assoc Professor Kelly-Anne Phillips
Cancer Council Victoria Dr John Colebatch Clinical Research Fellow
Peter MacCallum Cancer Centre*

The Dr John Colebatch Clinical Research Fellowship

This Fellowship is named in memory of Dr John Colebatch (1909–2005) to mark his contribution to The Cancer Council Victoria and his pioneering work in the field of paediatric haematology and clinical trial practice in Australia.

The 2006 inaugural Dr John Colebatch Clinical Research Fellowship has been awarded to Associate Professor Kelly-Anne Phillips who is a consultant medical oncologist and Associate Professor of Medicine in the Department of Medical Oncology and Haematology at the Peter MacCallum Cancer Centre.

Dr Phillips' fellowship research program involves work on reducing the burden of breast cancer, it has two distinct categories of research: cancer genetics and clinical trials. The cancer genetics work will focus on prevention and treatment issues for women who are at high-risk for the development of breast cancer because they have a strong family history of the disease. The second

category of research in clinical trials will focus on the two important side effects of successful breast cancer treatment, cognitive dysfunction and premature menopause. Dr Phillips will also continue her clinical practice and her work in treating patients will complement and enhance her research.

The Fellowship is for 5 years commencing in January 2006 and will provide over \$700,000 to Peter MacCallum Cancer Centre to cover the fellowship salary and overheads as well as a conference travel allowance and research infrastructure support.

The overall aims of the fellowship are to develop and support medical researchers undertaking a program of clinical research and to provide the fellow with the mentorship and research environment to further develop their careers as leaders in cancer research.

The funding for these fellowships has been made available due to the generous donations from the Victorian public.

Breast cancer is diagnosed in about 3,000 Victorian women each year. As the inaugural Dr John Colebatch Clinical Research Fellow of The Cancer Council Victoria my research focus is on reducing the burden of breast cancer. The research has two broad aspects: 1) improving prevention and treatment strategies for women who are at high-risk for breast cancer because they have a strong family history of the disease, and 2) understanding and minimising potential long-term side-effects of successful breast cancer treatment, specifically cognitive dysfunction and premature menopause.

Improving Prevention & Treatment for High-Risk Women

Women who have a strong family history of breast cancer are at substantially increased risk for development of this disease. Predictive genetic testing for the breast cancer predisposition genes, BRCA1 and BRCA2, is being routinely undertaken in Familial Cancer Centres throughout Australia. However, relatively little is currently known about the *clinical implications* of having an inherited predisposition. To guide clinical practice, more information is needed

regarding how to reduce cancer risk in such women, and, if the disease does develop, whether it should be treated differently from non-hereditary breast cancer. The three studies outlined below will help answer these questions.

kConFab Follow-Up Study

Since 1997, the parent kConFab study (www.kconfab.org) has recruited families with multiple cases of breast cancer and/or ovarian cancer and collected biological specimens and baseline data at the time of recruitment. The kConFab Follow-Up Study was commenced in 2001. This long-term follow-up study is prospectively and systematically collecting updated epidemiological, lifestyle, screening, prophylactic surgery and outcome data on over 10,000 individuals every three years, using mailed self-report questionnaires and verification of pathology and operative reports. Over the next 5 years, these data will be mature enough to conduct meaningful analyses examining the lifestyle factors that modify breast cancer risk in high-risk women. For example, there is currently considerable uncertainty in the literature about whether it is safe for such women to use the oral contraceptive pill, whether delaying first pregnancy increases or decreases breast cancer risk, and whether alcohol intake affects breast cancer risk in this setting. Results from this study will assist in optimising the clinical risk management strategies of individuals attending Familial Cancer Centres and hence reduce the morbidity and mortality of hereditary breast cancer.

GOG0199: Prospective Study of Risk-Reducing Salpingo-Oophorectomy and Screening In Women at High Genetic Risk for Breast and Ovarian Cancer

Women with a strong family history of breast and ovarian cancer, and/or mutations in BRCA1 or BRCA2 are at high risk for the development of these two cancers. Risk-reducing salpingo-oophorectomy has been shown in retrospective studies to reduce ovarian cancer risk by about 90% and breast cancer risk by about 50% in mutation carriers. However, such surgery is not acceptable to all women and many women undergo screening instead, particularly while still pre-menopausal. The impact of screening these women is uncertain and it is unclear whether early

stage ovarian cancers are being diagnosed with such an approach. Similarly, there are scant prospective data to inform the true risk of subsequently developing breast cancer following such surgery. In addition there are many important questions regarding quality of life, sexual functioning and menopause related symptoms following risk-reducing surgery that have not yet been addressed.

GOG0199 is an international prospective, non-randomised study addressing the relative merits of ovarian cancer screening (using a mathematical algorithm to improve interpretation of screening tests) versus risk-reducing salpingo-oophorectomy in women at high familial risk for breast and ovarian cancer. In Australia, it is being run by the Australian and New Zealand Gynaecologic Oncology Group (ANZGOG), and over 100 women are expected to be recruited through Australian Familial Cancer Centres. The main aim is to prospectively determine the incidence of breast and ovarian cancers in high-risk women and compare rates between those choosing surgery versus screening. Other important aims include assessing quality of life, determining the prevalence of occult ovarian cancers in surgical specimens and establishing a longitudinal serum, plasma and tissue repository for use by other researchers.

BRCA Prognosis Study

This study is part of an international collaboration that is prospectively examining whether the prognosis of breast cancer in BRCA1 and BRCA2 mutation carriers is different from that in non-hereditary breast cancer. Although this question has been addressed in a number of studies to date, all have methodologic flaws and, unlike this study, none has assembled a population based inception cohort from which both mutation carriers and non-carriers can be drawn.

The characteristic histologic and molecular phenotype of BRCA1-associated breast cancers suggests that they proceed via a distinct molecular pathogenesis pathway and this may be expected to have implications for their prognosis. However, these tumours have a mixture of potentially favourable (medullary subtype, absence of erbB-2 over-expression) and unfavourable (high grade, oestrogen receptor negative, p53 mutation positive)

prognostic features. In addition, preclinical evidence suggests that tumours due to mutations in BRCA1 or BRCA2 may be more sensitive to therapeutic agents that cause double-strand DNA breaks. Such a differential therapeutic effect between BRCA-associated and non-hereditary breast cancers, if confirmed, might be expected to influence prognosis. The results of this study will have important implications for the treatment of breast cancer patients with BRCA1 and BRCA2 mutations.

Minimising Long-Term Side Effects of Breast Cancer Treatment

Given that most Australian women diagnosed with breast cancer will be cured, focus on research into long-term side effects is important in order to optimise their quality of life. The two studies outlined below address the important potential long-term side effects of premature menopause and cognitive dysfunction.

IBCSG 34-05/SWOG0230: Phase III Randomised Trial of an LHRH Analogue to Prevent Chemotherapy-Induced Premature Menopause

Approximately one quarter of all breast cancers occur in premenopausal women, and the vast majority of these are potentially curable. Premature menopause is an important, undesired potential side effect of adjuvant breast cancer chemotherapy for young women with hormone receptor-negative breast cancer. It can result in significant long-term health implications such as osteoporosis, and also results in infertility. The risk of premature menopause is influenced by the age of the patient and the type of chemotherapy she receives, particularly the cumulative dose of alkylating therapy such as cyclophosphamide. Several phase II studies of LHRH agonists have shown promising results in terms of possible prevention of premature chemotherapy-associated premature ovarian failure, however this needs confirmation in a phase III study. IBCSG 34-05 is a randomised study of the efficacy of goserelin in reducing the risk of premature menopause in premenopausal women receiving adjuvant chemotherapy for hormone receptor-negative early-stage breast cancer. It is open in Australia through the Australian and New Zealand Breast Cancer Trials Group. If positive, this study will change clinical

practice, and result in decreased morbidity for young women undergoing adjuvant chemotherapy for breast cancer.

Cognitive Function Sub-study of BIG1-98

There is increasing evidence that a subgroup of women experience cognitive dysfunction after breast cancer treatment. The risk factors and aetiology are unclear, but hormonal factors may play a role. Aromatase inhibitors have now been shown to be superior to tamoxifen in terms of disease free survival when used as adjuvant treatment for postmenopausal breast cancer patients. However, because of the greater oestrogen deprivation associated with aromatase inhibitors, they may have a worse impact on cognitive function. This study is comparing the cognitive function of postmenopausal women who received adjuvant tamoxifen with those who received adjuvant letrozole on the BIG1-98 randomised trial of adjuvant hormonal therapy for early-stage breast cancer. This study will be the first adequately powered study to examine the difference between tamoxifen and an aromatase inhibitor on cognitive function. The results will assist women and their doctors to make informed choices about adjuvant hormonal therapy.

As the inaugural Dr John Colebatch Clinical Research Fellow, I look forward to being able to contribute to reducing the burden of breast cancer for Victorian women.

I thank The Cancer Council Victoria and its donors for this opportunity.

The Dunlop Fellowship Development of Targeted Therapies for Cancer

*Associate Professor Grant McArthur
Sir Edward Dunlop Clinical Research Fellow
The Cancer Council Victoria*

The Sir Edward Dunlop Clinical Research Fellowship

This Fellowship is named in memory of Sir Edward 'Weary' Dunlop (1907–1993) to mark his contribution to Australia and, in particular, to the work of The Cancer Council Victoria.

The Dunlop Fellowship is the third prestigious Cancer Council fellowship recognising Sir Edward. It has been awarded to Associate Professor Grant McArthur who is Consultant Medical Oncologist, Head of the Translational Research Group and Head of the Molecular Oncology Laboratory at the Peter MacCallum Cancer Centre.

Dr McArthur's fellowship research program involves the development of targeted therapies for cancer. He will work on three different streams of research concurrently.

These streams of research all relate to the development of new treatments for cancer and encompass understanding the fundamental biology of the target and integrating this with strategies to clinically

develop novel targeted therapeutics. Dr McArthur's will also continue his clinical practice as a medical oncologist, specialising in targeted therapies and his work with patients will complement and enhance his research.

The Fellowship is for 5 years and commenced in January 2006. It will provide over \$700,000 to Peter MacCallum Cancer Centre to cover the fellowship salary and overheads as well as a conference travel allowance and research infrastructure support.

The overall aims of the fellowship are to develop and support medical researchers undertaking a program of clinical research and to provide the fellow with the mentorship and research environment to further develop their careers as leaders in cancer research.

The funding for these fellowships has been made available due to the generous donations from the Victorian public.

The development of imatinib and trastuzumab have changed the paradigm for the systemic therapy of cancer. Targeting specific molecular abnormalities in human cancer by identifying genomic abnormalities that activate oncogenes such as c-ABL, c-KIT or ERB-B2 has led to dramatic results fundamentally changing the clinical course of cancer in these patients. We are now on the verge of an explosion in novel targeted therapies, however significant challenges remain to develop these therapies in a rapid manner particularly identifying patients that will get greatest benefit from these costly therapies.

With the generous support of The Cancer Council Victoria's Sir Edward Dunlop Clinical Research Fellowship, my research program will encompass:

- Novel applications of targeted therapies to the treatment of neoplasia;
- The use of positron emission tomography in monitoring response to targeted therapies; and
- Development and application of biomarker assays to predict response to targeted therapies.

Novel Applications of Targeted Therapies to the Treatment of Neoplasia

A major goal of my teams research program is to develop novel applications of targeted therapies for both common and less common malignancies. The overall approach is not disease focused, but rather is focused on the target and the application of targeted therapies to a variety of diseases. As such the research program encompasses both haematological malignancies and solid tumours.

Although targeting oncogenes that are protein kinases that harbour activating mutations has been highly successful, there are a number of other interesting targets that are not directly mutated that hold promise. For example agents that inhibit the vascular endothelial growth factor receptor have shown significant activity in renal cell cancer although the target is not mutated. This approach of identifying pathways important in cancer and targeting molecules that modulate activity of the pathway is a potential new application of targeted therapies.

Targeting c-MYC and Ribosome Biogenesis

High levels of protein synthesis characterize malignant cells, particularly tumours with dysregulated expression of the oncogene c-MYC. We have shown that the mTOR-inhibitor rapamycin can inhibit global protein synthesis, promoting cell cycle arrest and cell differentiation. Interestingly the c-MYC oncoprotein is selectively reduced in response to rapamycin and further research efforts will focus on combining rapamycin analogues with other agents to reduce activity of c-MYC.

Targeting DNA damage responses

The activity of both cytotoxic chemotherapy and ionising irradiation in malignant disease is dependent on altered checkpoint responses of malignant cells when compared to normal cells. We specifically hypothesise that further modulation of checkpoint responses through the use of agents that target checkpoints will enhance the response of malignant cells to cytotoxic chemotherapy and ionising irradiation. Two targets are being investigated: 1) CDK2 and 2) CHK1.

CDK2 is a cyclin-dependent kinase involved in the regulation of normal G1-S progression and DNA replication. However its activity is also

modulated during DNA damage responses. We have demonstrated a role of CDK2 in DNA repair and that cells with loss of function of BRCA1 or ATM display heightened sensitivity to small molecule inhibitors of CDK2. We now plan to extend these novel observations to evaluate small molecule inhibitors of CDK2 in a variety of preclinical models of combination with chemotherapy and irradiation.

CHK1 is a central protein kinase in regulation of the G2-checkpoint. In pre-clinical models we have demonstrated that a small molecule inhibitor of CHK1 modulates the G2-checkpoint following irradiation and cytotoxic chemotherapy enhancing DNA damage and increasing tumour responses.

The use of Positron Emission Tomography in Monitoring Response to Targeted Therapies

In partnership with Professor Rod Hicks our team have recently demonstrated the utility of using Positron Emission Tomography to monitor response of tumours in vivo to novel target therapeutic agents, both clinically and in animal models. Importantly our research strategy utilizes a variety of metabolic tracers that enable us to probe a number of biological process in vivo. Currently we utilise Fluoro-deoxyglucose (FDG), Fluorine-L-Thymidine (FLT), Fluoro-ethyltyrosine (FET) and Fluoro-azomycin-araboside (FAZA) to monitor glucose transport and metabolism, cell proliferation, amino acid transport and hypoxia respectively. This will have the greatest utility in the evaluation of targeted therapy agents that do not induce rapid tumour progression. This approach may significantly accelerate the development of these agents, as currently proof of biological activity of novel agents typically requires either demonstration of rapid tumour regression or improvements in longer-term clinical endpoints such as time-to-progression or overall survival.

Development and Application of Biomarker Assays to Predict Response to Targeted Therapies

One crucial component in the development of targeted therapeutics is to address whether the agent successfully modulates the target in vivo. A second key component to the development of

these agents is to determine if the molecular profile of the tumour can predict response to the agent. This issue was critically important in the development of Trastuzumab in breast cancer, where only ERB-B2 over-expressing tumours responded to this agent. Therefore successful development of targeted therapeutic agents requires access to biomarker assays such as assays that assess target phosphorylation for drugs that inhibit protein kinases, or mutation analyses that predict activation of the target.

Our initial approach is to validate biomarker assays using pre-clinical models and archival tumour specimens from the Peter MacCallum Cancer Centre and in the near future the Victorian Tissue Bank Initiative. Having validated these assays we are extending these assays into

clinical trials to demonstrate target inhibition and to address the hypothesis that activation of specific pathways in individual patients will lead to selective application of targeted therapeutics in subsets of patients.

Summary

The advent of targeted therapies for cancer is enabling us to use basic knowledge of the pathogenesis of cancer to develop new treatments for patients. In partnership with my basic and clinical research colleagues and our patients in Victoria, Australia and overseas we are entering an exciting new phase in the battle against cancer.

Report of the National Breast Cancer Centre

New Website Feature – Herceptin® Update

NBCC has added new information to its website (www.nbcc.org.au) to keep consumers, health professionals and the media updated on the latest developments about the use of Herceptin® in the treatment of women with early breast cancer.

The Herceptin® Update outlines the status of the drug through the process of assessment involved in the inclusion of any treatment on the Pharmaceutical Benefits Scheme. The information will be regularly updated as the process continues.

Sign-up for NBCC Summaries of New Research

New research is published on a daily basis about all aspects of breast and ovarian cancer – from causes, prevention, early detection and diagnosis through to treatment, supportive care and follow-up.

NBCC has identified a need to provide clear, concise summaries of relevant research to help consumers and health professionals better understand its implications for the future of breast and ovarian cancer detection and care. This will include drawing attention to research of potential significance and providing an interpretation of

research that makes the news and what it means for Australia.

NBCC will be trialling a process of featuring these summaries on its website over an initial period of four months. If you would like to be alerted by email when a new research summary is featured on the website, please contact Janice O'Brien on 02 9036 3350 or email janice.obrien@nbcc.org.au with your details.

Multidisciplinary Care for Advanced Cancer

A working group, chaired by Professor David Currow, is currently developing a draft set of *Multidisciplinary Care Principles for Advanced Disease*. The Group has reviewed NBCC's *Principles of Multidisciplinary Care* and identified areas where the Principles should be revised for patients with advanced disease.

The Working Group met in March to discuss the next steps for this project. While the project will focus initially on breast and ovarian cancer, it is anticipated the Principles developed by the group will also be applicable to other cancers.

For further information about this project, contact Jane Francis on 02 9036 3045 or jane.francis@nbcc.org.au.

Reprinted from *Wongi Yabber* May 2006; 12(2): 5.

Report of The Cancer Council Australia

*Glen Turner
Communications Manager
The Cancer Council Australia*

Changing of the Guard at The Cancer Council Australia

After eight years of running Australia's largest federated health charity, The Cancer Council Australia CEO Professor Alan Coates has retired and passed the baton to the former Chair of the organisation's Medical and Scientific Committee, distinguished ex-Adelaide oncologist, Professor Ian Olver.

President of The Cancer Council Australia, Mrs Judith Roberts AO, said the transition was a good opportunity to both celebrate Professor Coates's extraordinary contribution while welcoming Professor Olver as the ideal candidate to position the organisation to address the future challenges of leading national cancer control in the non-government sector.

"We are extraordinarily fortunate to have had eight years of service from a scientist, advocate and communicator of Professor Coates's calibre and then to be able to seamlessly anoint Professor Olver as his successor," Mrs Roberts said.

"Under Professor Coates's stewardship, The Cancer Council Australia has evolved into one of the nation's most important peak bodies and has influenced a major increase in commitment to cancer control at the federal government level.

"Professor Olver is ideally placed to continue Professor Coates's invaluable work and to use

his own unique skills and experience as one of the nation's leading oncologists and healthcare administrators to take the organisation forward to meet the challenges of an expected 30% increase in cancer incidence over the next five to 10 years as Australia's population ages."

"One-stop-shop" for Primary Care Cancer Resources

A new web-based directory of cancer resources for primary care professionals provides quick and easy access to national, state and territory information. The new directory, developed by The Cancer Council Australia's General Practice Committee, will provide a single access point to a range of cancer resources including guidelines and advice on prostate, breast, bowel, ovarian and skin cancer, as well as issues associated with screening and psychosocial care for cancer patients.

The directory will be updated as new resources become available or revised resources are released - ensuring that primary care professionals have access to the most current information.

The primary care resources directory can be accessed via The Cancer Council Australia website at www.cancer.org.au/primarycare.

Reprinted from Wongi Yabber May 2006; 12(2): 3-4.

The National Cancer Control Initiative (NCCI) Report

*Professor Mark Elwood
Director
National Cancer Control Initiative*

This is the last newsletter from the National Cancer Control Initiative. The NCCI is disbanding, sadly, on the 31 May 2006. Since its inception in 1997, NCCI has contributed greatly to strategic developments in cancer in Australia, and has during this process produced some 36 reports based on wide consultation, and about 75 peer-reviewed papers. NCCI conducted the largest consultation to yield a national consensus on cancer priorities, developed a practical core clinical data set, produced the first evidence-based rationale for the requirements for radiotherapy, set up implementation programs based on the lung cancer and psychosocial guidelines, developed a primary care program in cancer, and jointly produced the 'Optimising Cancer Care in Australia' report. The closure of NCCI is very regrettable, and I do not think we are being conceited if we say that this is not only unfortunate for those of us who have worked with and supported NCCI, but also for the progress of effective cancer strategies in Australia. NCCI has made a major contribution and has developed considerable expertise and resources that are highly relevant to ongoing issues in cancer care. Inevitably, much of this experience will be lost. Our position all along has been that while we

support the development of Cancer Australia as a larger and more comprehensive focus for strategic efforts in cancer, it would have been simple and inexpensive to ensure that NCCI continued until it could be incorporated into or linked with Cancer Australia in an effective way. However there has been no action to ensure linkage. Some of the NCCI staff have accepted other positions, while for others there is still some uncertainty. We are making what arrangements we can to allow some aspects of continuity, for example we are trying to ensure that the NCCI website (www.ncci.org.au) continues for a reasonable time as a portal through which people can still get access to published reports and other material produced by NCCI. A final report is being prepared for the Department of Health and Ageing.

ACN would like to thank Professor Mark Elwood and his staff for their generous cooperation with a number of projects over the last nine years and wish them well for the future.

Reprinted from Wongi Yabber May 2006; 12(2): 2.

Australian Cancer Network (ACN) Activities

Work is continuing with discussion and dissemination of **Accreditation** and **Credentiailling** documents. There will be further fine tuning necessary.

The draft **Guidelines Implementation** document has met with significant approval after being piloted in Victoria. Its distribution is being planned by the National Institute of Clinical Studies (NICS). The generous support of Dr Heather Buchan of NICS has been integral to progress and is appreciated by ACN.

There is to be a major meeting with NICS in October when all three documents will be featured in discussion and decision-making, which should further embed guidelines and the evidence-based approach and hopefully further eradicate unnecessary variation in practice.

Reprinted from Wongi Yabber May 2006; 12(2): 1.

Clinical Oncological Society of Australia (COSA) Report

*Ms Margaret McJannett
Executive Officer, COSA*

COSA has been continuing to move forward on a number of issues on behalf of its membership. Key activities include:

Annual Scientific Meeting (ASM)

The Australian Health & Medical Research Congress, site of this year's COSA ASM, continues to gain momentum. The impressive confirmed speaker list now exceeds 150 speakers and many of them are speaking on cancer related topics.

Specifically within the COSA program, there is the normal range of symposia and sessions meeting the wide range of needs of the membership. We are in process of confirming the international speakers and COSA program. A draft program will be posted on the COSA website shortly. Please note this year's meeting will be held at the Melbourne Convention Centre, November 29-1 Dec. There will be a Consumer Forum held on Tuesday 28 November.

Professional Development Packages for Cancer Professionals

The Commonwealth DoHA called for tenders late in 2005 to look at educational needs of cancer health professionals. A consortium involving Centre for Innovation in Professional Health Education (CIPHE), COSA, TCCA, NBCC, and the RACGP successfully tendered for Phase 1 of the project, scoping current cancer professional development resources and associated needs of cancer professionals, GPs and counsellors.

A reference group is guiding the project, which includes an online survey targeting relevant professionals.

COSA Enabling Grant

Working parties have been convened to make recommendations about how to allocate funds for each component of the grant:

Protocol Development, Information Systems and Quality Assurance. Scoping exercises for each component are in progress. The protocol development working party has developed its recommendations and will be reviewed by the Steering Committee in due course.

Executive Committee has been established to oversee the work of this grant and meet more frequently than the Steering Committee. Members include: Dr Steve Ackland, Chair, Professor Alan Coates, CEO TCCA, Ms Haryana Dhillon, Project Coordinator, Ms Margaret McJannett, EO, TCCA / COSA, and Dr John Seymour and Associate Professor Martin Stockler.

Responses have been made on behalf of the Cooperative Groups through COSA to NSW Health regarding the Policy Directive on Clinical Trials - Risk Management, Insurance and Indemnity, and to the Cancer Institute NSW regarding Streamlining of Ethical Review of Cancer Research in NSW.

Alan Coates Honoured for Scientific Leadership

COSA joins the chorus of clinicians and health professional groups congratulating Professor Alan Coates for winning the prestigious Distinguished Service Award for Scientific Leadership, bestowed by the American Society for Clinical Oncology (ASCO). We have particular reason to celebrate, as ASCO is our US counterpart and the conferring of this award on Professor Coates, a member of our Executive, builds on the already strong relationship between our two organisations.

We are fortunate that Professor Coates will remain active within COSA and in cancer research after he retires from his Cancer Council Australia career later this month.

Reprinted from Wongi Yabber May 2006; 12(2): 3.

Key Published Articles Listing—Breast Cancer

Title	Author & Journal
Multicycle dose-intensive chemotherapy for women with high-risk primary breast cancer: Results of International Breast Cancer Study Group trial 15-95	Basser RL, O'Neill A, Martinelli G, et al. Journal of Clinical Oncology Jan 2006; 24(3): 370–378.
Randomized trial comparing axillary clearance versus no axillary clearance in older patients with breast cancer: First results of International Breast Cancer Study Group Trial 10-93	Rudenstam CM, Zahrieh D, Forbes JF, et al. Journal of Clinical Oncology Jan 2006; 24(3): 337–344.
Axillary surgery: Clinical judgement required [Editorial]	Henderson IC. Journal of Clinical Oncology Jan 2006; 24(3): 325–326.
Risk-reducing surgery in women with familial susceptibility for breast and/or ovarian cancer	Antill Y, Reynolds J, Young MA, et al. European Journal of Cancer 2006; 42: 621-628.
Tamoxifen after adjuvant chemotherapy for premenopausal women with lymph node-positive breast cancer: International Breast Cancer Study Group Trial 13-93	IBCSG. Journal of Clinical Oncology Mar 2006; 24(9): 1332–1341.
Estrogen-receptor status and outcomes of modern chemotherapy for patients with node-positive breast cancer	Berry DA, Cirincione C, Henderson IC, et al. The Journal of the American Medical Association Apr 2006; 295(14): 1658–1667.

Key Published Articles Listing—General

Title	Author & Journal
Religious perspectives on withdrawal of treatment from patients with multiple organ failure	Ankeny RA, Clifford R, Jordens CFC, et al. The Medical Journal of Australia Dec 2005; 183 (11/12): 616–621.
Clinical Cancer Advances 2005: Major research advances in cancer treatment, prevention and screening – A report from the American Society of Clinical Oncology	Herbst RS, Bajorin DF, Bleiberg H, et al. Journal of Clinical Oncology 1 Jan 2006; 24(1): 190–205.
Promoting the implementation of best-practice guidelines using a matrix tool	Luxford K, Hill D & Bell R. Disease Management & Health Outcomes 2006; 14(2): 85–90.

Forthcoming Meetings

Date / Place	Meeting / Contact
<p>8–12 July 2006 Washington DC, USA</p>	<p>UICC World Cancer Congress – <i>Bridging the gap: Transforming knowledge into action</i> American Cancer Society, 1599 Clifton Road, NE, Atlanta Georgia 30329-4251 USA Ph: +1 404 417 5998 Fax: +1 404 728 0133 E-mail: secretariat2006@cancer.org Website: www.worldcancercongress.org</p>
<p>14–15 July 2006 Adelaide, SA, Australia</p>	<p>9th CNSA Winter Congress Pre-conference workshop on 13 July Ph: (02) 9280 0577 E-mail: cnsa@pharmaevents.com.au Website: www.cnsa.org.au</p>
<p>19–22 July 2006 Cairns, QLD, Australia</p>	<p>28th Annual Scientific Meeting of the ANZ Breast Cancer Trials Group (ANZBCTG) Contact: ANZ BCTG Operations Office Ph: (02) 4985 0136 Fax: (02) 4985 0140 E-mail: asm@anzbctg.newcastle.edu.au Website: www.anzbctg.org</p>
<p>27–29 July 2006 Cancun, Mexico</p>	<p>3rd Inter-American Breast Cancer Conference Organised by Miller School of Medicine, University of Miami. Secretariat: Imedex, 70 Technology Drive, Alpharetta 30005, Georgia USA Ph: +1 770 751 7332 Fax: +1 770 751 7334 E-mail: meetings@imedex.com Website: www.imedex.com</p>
<p>9–12 August 2006 Sanctuary Cove, QLD, Australia</p>	<p>Annual Scientific Meeting of the Medical Oncology Group Australia (MOGA) MOGA Conference Secretariat c/o Pharma Events, PO Box 265, Annandale NSW 2038 Ph: (02) 9280 0577 Fax: (02) 9280 0533 E-mail: moga@pharmaevents.com.au</p>
<p>3–9 September 2006 Sunshine Coast, QLD, Australia</p>	<p>The Australia and Asia Pacific Clinical Oncology Research Development (ACORD) Workshop – <i>A Workshop in Effective Clinical Trials Design</i> ACORD Workshop, Level 6, 52 Phillip Street. Sydney NSW 2000 Ph: (02) 8247 6207 Fax: (02) 9247 3022 E-mail: mog@racp.edu.au</p>
<p>27–29 September 2006 Brisbane, QLD, Australia</p>	<p>8th Behavioural Research in Cancer Control Conference Hosted by the Queensland Cancer Fund</p>

Forthcoming Meetings

Date / Place	Meeting / Contact
27 Sep – 1 Oct 2006 Toronto, Ontario, Canada	14th International Conference on Cancer Nursing Organised by the International Society of Nurses in Cancer Care (ISNCC), Cheshire, UK Ph: +44 11 6270 3309 Fax: +44 11 6270 3673 E-mail: conference@isncc.org Website: www.isncc.org
29 Sep – 3 Oct 2006 Istanbul, Turkey	31st Annual Congress of the European Society for Medical Oncology (ESMO) ESMO Head Office, Via la Santa 7, 6962 Viganello-Lugano, Switzerland Ph: +41 91 973 1900 Fax: +41 91 973 1902 Website: www.esmo.org
8–12 October 2006 Leipzig, Germany	European Society for Therapeutic Radiology and Oncology (ESTRO) Ph: +32 2 775 9340 Fax: +32 2 779 5494 E-mail: info@estro.be Website: www.estro.be/estro/index.html
19–20 October 2006 Melbourne, VIC, Australia	NICS Using Evidence: Using Guidelines Symposium National Institute of Clinical Studies, Level 5, 499 St Kilda Road, Melbourne VIC 3004 Ph: (03) 8866 0400 Fax: (03) 8866 0499 E-mail: info@nicisl.com.au Website: www.nicisl.com.au/ www.usingevidence.com.au
26–29 October 2006 Christchurch, New Zealand	57th Annual Scientific Meeting of the Royal Australian and New Zealand College of Radiologists (RANZCR) Website: www.ranzcr.edu.au
1–4 November 2006 Rome, Italy	5th Biennial International Sentinel Node Society Meeting - Sentinel Node Biopsy: New Boundaries Conference Secretariat: CQ Travel SRL, Via Pagliano, 3-20149 Milano, Italy Fax: +39 02 4391 1650 Email: infoeventi@ieo.it
5–8 November 2006 Bangkok, Thailand	3rd General Assembly Conference of the Asia Pacific Organization for Cancer Prevention (APOCP) – Empowering cancer prevention in the Asia Pacific Asia Pacific Organization for Cancer Prevention (APOCP), Nagoya, Japan Ph: +66 1 809 7664 Fax: +66 2 955 9986 E-mail: ktajima@aichi-cc.jp Website: www.apocp.org

Forthcoming Meetings

Date / Place	Meeting / Contact
5–9 November 2006 Philadelphia, Pennsylvania, USA	48th Annual Meeting of the American Society for Therapeutic Radiology and Oncology (ASTRO) American Society for Therapeutic Radiology and Oncology (ASTRO), 12500 Fair Lakes Circle, Suite 375, Fairfax Virginia 22033 USA Ph: +1 703 227 0170 Fax: +1 703 502 7852 E-mail: meetings@astro.org Website: www.astro.org
7–10 November 2006 Mumbai, India	3rd Asia Pacific UICC Reach to Recovery International (RRI) Breast Cancer Support Conference Secretariat: c/o Ms Vimal Kamath, C/7 Bhagya Nagar, Shivaji Park, Mumbai 400 016 India Ph: +91 22 2444 9808 E-mail: vimalk_9@rediffmail.com Website: www.jagruti.org.in
7–10 November 2006 Prague, Czech Republic	18th International Conference on Molecular Targets and Cancer Therapeutics Jointly organised by EORTC, NCI and AACR. EORTC-NCI-AACR Conference secretariat, Federation of European Cancer Societies, Avenue E. Mounier 83, B-1200 Brussels Ph: +32 2 775 02 01 Fax: +32 2 775 02 00 E-mail: ENA2006@fecs.be Website: www.aacr.org
29 Nov – 1 Dec 2006 Melbourne, VIC, Australia	33rd Annual Meeting of the Clinical Oncology Society of Australia (COSA) COSA Office, Medical Foundation Building, Level 5, 92 Parramatta Road, Camperdown NSW 2011 Ph: (02) 9036 3100 Fax: (02) 9036 3101 E-mail: cosa@cancer.org.au Website: www.cosa.org.au
29 Nov – 2 Dec 2006 Venice, Italy	13th Congress of the European Society of Surgical Oncology (ESSO) ESSO 2006 Conference secretariat, Federation of European Cancer Societies, Avenue E Mounier 83, B-1200 Brussels Ph: +32 2 775 0205 Fax: +32 2 775 0200 E-mail: ESSO2006@fecs.be Website: www.fecs.be
14–17 December 2006 San Antonio, Texas, USA	28th Annual San Antonio Breast Cancer Symposium Website: www.sabcs.org

Cancer Council Events Calender

AUGUST

- 25 Volunteer on Daffodil Day
www.daffodilday.com.au
- 26 Daffodil Ball
www.daffodilday.com.au



SEPTEMBER

- 1 Cancer Council Mazda Raffle tickets on sale – Ph: 1300 65 6 585
- 20 Sep – 4 Oct Tour for a Cure – Trek Mont Blanc
www.tourforacure.org.au

OCTOBER



Host a Girls Night In Month
www.girlsnightin.com.au

- Relay for Life – Carlton, Swan Hill
www.relayforlife.com.au
- 14–27 Tour for a Cure – Race Around Asia
www.tourforacure.org.au
- 23 Pink Ribbon Day
www.pinkribbonday.com.au
- 21–22 Relay for Life – Shepparton
www.relayforlife.com.au
- 28–29 Relay for Life – Echuca, Murrumbena
www.relayforlife.com.au



NOVEMBER



- Relay for Life – Ararat, Ballarat, Bass Coast, Dandenong Ranges, Frankston, La Trobe Valley, Whitehorse
www.relayforlife.com.au
- 10–22 Tour for a Cure – Trek India
www.tourforacure.org.au
- 12–25 Tour for a Cure – Cycle Vietnam
www.tourforacure.org.au

DECEMBER

- 6 Cancer Council Mazda Raffle drawn

Shop online at www.cancervic.org.au/shop

For information on our events or other ways to help, such as our regular giving or bequester club programs, call 1300 65 65 85 or visit www.cancervic.org.au

The Cancer Council Victoria

The Cancer Council Victoria is a public institution set up by an Act of Parliament in 1936. It operates as a charity, relies heavily on volunteer support, and raises and spends \$3-\$4 per head of population annually. It is governed by the Council and Executive and other committees. It's mission is to lead, coordinate and evaluate action to minimise the human cost of cancer for all Victorians. The Cancer Council houses three research divisions (behavioural science, clinical research, epidemiology) and units undertaking public and professional education, cancer registration, cancer information and support services, anti-smoking campaign (QUIT), finance, administration and fund raising. It employs about 300 staff. The Cancer Council also auspices a cooperating network of cancer specialists through the Victorian Cooperative Oncology Group and resources an expert Medical & Scientific Committee to dispense studentships, scholarships, fellowships and research grants to other academic, research and medical institutions.

Centre for Clinical Research in Cancer — Victorian Cooperative Oncology Group

The Centre for Clinical Research in Cancer (CCRC) formed in 1997, provides a coordinated and effective resource for collaborative clinical research and development in Victoria. The Centre provides administrative and research support for the Victorian Cooperative Oncology Group, which brings together Victoria's cancer specialists. The Centre fosters and facilitates the development and promotion of a range of collaborative clinical measures to optimise cancer management.

The Victorian Cooperative Oncology Group (VCOG) established in 1976, provides advice to the Cancer Council Victoria, through the CCRC, on all clinical aspects of cancer control, in particular research, screening, diagnosis, treatment, palliative medicine, cancer genetics and professional education. The strategic role of 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. VCOG consists of a primary committee, 9 cancer-site and 3 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. VCOG has established unique linkages between public and private health care professionals, institutions and governments.

