



# Gynaecological Cancer Update

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July 2006  
Issue Number: 27

Q&A ON THE DHS INTEGRATED  
CANCER SERVICES (ICS)

PAPSCREEN REPORT – NEW  
CERVICAL SCREENING GUIDELINES

NCI STATEMENT ON IP CHEMO

ANZGOG TRIAL OF IP CHEMO  
ANNOUNCED

ASGO, ASCO, ISSVD MEETING  
REPORTS

AOCS UPDATE

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



# GYNAECOLOGICAL CANCER UPDATE

July 2006

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## CONTENTS

Editorial .....	3
Questions and Answers on the DHS Integrated Cancer Services (ICS) .....	4
PapScreen Victoria Update on New Cervical Screening Management Guidelines .....	9
New Position Statement on Cervical Cancer Screening .....	10
NCI Clinical Announcement – Intraperitoneal Chemotherapy for Ovarian Cancer .....	11
ANZGOG Trial of IP Chemotherapy Announced .....	21
Sail Away With ASGO .....	21
Report of the 42nd Annual Meeting of the American Society of Clinical Oncology (ASCO) .....	22
Report on the World Congress of the International Society for the Study of Vulvovaginal Disease (ISSVD) .....	24
Molecular Epidemiology of Ovarian Cancer: The Australian Ovarian Cancer Study (AOCS) .....	25
National Breast Cancer Centre (NBCC) Report .....	27
Ovarian Cancer Program Website Innovation .....	28
Gynaecological Cancer Support Website Updated .....	28
Australian Cancer Network (ACN) Activities .....	29
The National Cancer Control Initiative (NCCI) Report .....	29
Dunlop Fellowship: Development of Targeted Therapies for Cancer .....	30
The Sir Edward Dunlop Clinical Research Fellowship .....	30
Report of The Cancer Council Australia .....	32
Clinical Oncological Society of Australia (COSA) Report .....	33
Cancer Council Events Calender .....	34
Key Published Articles Listing—Gynaecological Cancer .....	35
Key Published Articles Listing—General .....	35
Forthcoming Meetings .....	36

This newsletter is produced by The Cancer Council Victoria's Gynaecological Cancer Committee and sent to health professionals interested in management of gynaecological cancer(s). The Victorian Cooperative Oncology Group's advisory committees on breast, gastrointestinal, head & neck, 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 Mrs Noellyn Ngo, Ph: (03) 9635 5265.

\* \* \* \* \* **Last Issue – No. 26 – December 2005** \* \* \* \* \*

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

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## Editorial

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This large edition of the Gynaecological Cancer Update contains some important articles which will be of interest to most. Firstly, Elise Davies from the Department of Human Services (DHS) has outlined the new Integrated Cancer Services (ICS) framework set up by the DHS and how this is planned to benefit the administration and provision of cancer services to the community of Victoria. The overall aim of the ICS framework is the streamlining of cancer care across the community, to ensure access for all cancer patients to the best possible care. The implementation of this is outlined in the enlightening question and answer session included in this edition.

This edition of the newsletter also highlights two important new issues. The first is a review of the changes to the cervical screening recommendations from the NHMRC presented by PapScreen Victoria. These changes are coming into effect at the beginning of July, and a checklist of the major new changes and how they affect women and their treating doctors is outlined.

The other issue covered extensively, which is of concern to women with advanced ovarian cancer and their treating physicians, is intraperitoneal chemotherapy. This issue is introduced with a copy of the National Cancer Institute (NCI) alert on the use of intraperitoneal (IP) chemotherapy. The NCI alert caused significant angst in gynaecological oncology circles in Australia, as we tried to work out how to incorporate the use of chemotherapy administered in this way into our practices. We wanted to have a coordinated Australia-wide experience, so that there would be consistency of protocols and comparability of data, as we start to use this route of administration. A meeting of interested participants was run through the ANZGOG (Australia and New Zealand Gynaecological Oncology Group) in Noosa in

February. An initial trial proposal for the administration of IP chemotherapy was subsequently modified to reflect feedback obtained at this meeting. A proposed phase 2 trial of intraperitoneal chemotherapy (TRIPOD) based on the American data in the GOG 172 trial is presented in this update, and it is hoped that most Australian gynaecological oncology centres will use this protocol. It will give us information on the feasibility and toxicity of IP chemotherapy in the Australian setting, and until a randomised phase 3 trial does become available, it will give patients access to intraperitoneal chemotherapy as recommended in the NCI alert.

This edition also contains reports on the ASGO meeting by Dr Andrea Garrett; the ASCO meeting by Dr Serene Foo, that highlighted current treatment of endometrial cancer; and the ISSVD by Associate Professor David Allen, that includes a new classification of vulvar dermatoses.

An update on the AOCs study, and the work of the NBCC, Ovarian Cancer Program, ACN, NCCI, The Cancer Council Australia and COSA are also included. Important in these, is information on new consumer websites, which are now updated and running well for the Ovarian Cancer Program and Gynaecological Cancer Support.

We also have an outline of the planned 5-year research of the Sir Edward Dunlop Fellow, Associate Professor Grant McArthur from the Peter MacCallum Cancer Centre, on targeted therapies and PET scanning. It will be very interesting to see the results of this project as it develops.

I am always indebted to the contributors to this newsletter, and I would like to express my thanks again for all their hard work, and also to Noellyn Ngo at The Cancer Council Victoria for her wonderful work in producing this update issue

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

*Cancer & Palliative Care Section  
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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 statewide 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; and
- 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 utilising 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; and
- 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 re-dress 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 statewide 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; and
- 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 statewide system to address the above issues.

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

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## PapScreen Victoria Update on New Cervical Screening Management Guidelines

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**N**ew guidelines for the Management of Asymptomatic Women with Screen Detected Abnormalities were endorsed last July after an extensive review process by the National Health and Medical Research Council (NHMRC). These changes will come into effect on 3 July 2006.

The new guidelines will assist practitioners in managing women with cervical abnormalities but each woman will still be able to choose her own management. The guidelines are not prescriptive. Pap test providers are, however, encouraged to follow the new management guidelines from July onwards.

The main changes relate to:

- New terminology for Pap test cytology
- Women with a low-grade change should have a repeat Pap test in 12 months
- Biopsy-proven CIN 1 does not require treatment
- Women with atypical glandular cell reports need colposcopy
- HPV testing is recommended as a test of cure following treatment of high-grade squamous changes

A full copy of the new guidelines can be accessed at: [www.nhmrc.gov.au/publications/synopses/wh39syn.htm](http://www.nhmrc.gov.au/publications/synopses/wh39syn.htm).

The recent changes may cause confusion for some women. Below is some further information to assist you with enquiries.

### Low Grade Abnormalities on Pap Tests

What are the new recommendations for managing women whose Pap test is reported as a low-grade abnormality?

This is the change that will affect the most women. Around 90,000 women each year receive a Pap test report of low-grade abnormality (variously described as definite CIN1, possible CIN1, HPV effect, non specific minor change, or atypia).

The new recommended management depends on the woman's age (<30 yrs, 30+ yrs) and, for women aged 30+ years, whether or not she has had a normal Pap test result in the preceding two to three years.

It is now recommended that Pap tests reported as low grade **in women <30 years** be followed by a repeat Pap test in 12 months.

- If this repeat Pap test is reported as normal, then a further Pap test should be taken in another 12 months. If this Pap test is normal, it is recommended that the woman returns to 2-yearly screening.
- If this repeat Pap test is reported as a low-grade or high-grade abnormality, it is recommended that the woman have a colposcopy.

The recommended management for **women aged 30+ years** with a low-grade Pap test is as follows:

- If the woman has had a normal Pap test in the preceding two to three years, it is recommended that she have another Pap test in 12 months.
- If the woman has **not** had a normal Pap test in the preceding two to three years, it is recommended she either have immediate colposcopy or a repeat Pap test within 6 months.

For both of the above scenarios in women aged 30+ years where the Pap test is repeated, the recommended management is the same. If the repeat Pap test is abnormal (either low-grade or high-grade), colposcopy is recommended. If the repeat Pap test is normal, then a further Pap test should be taken in another 12 months. If this Pap test is normal, it is recommended that the woman returns to 2-yearly screening.

These recommendations are evidence-based. We now know that the majority of low-grade abnormalities spontaneously resolve without the need for treatment.

## Glandular Abnormalities on Pap Tests

What are the new recommendations for managing women whose Pap test is reported as a glandular abnormality?

The new guidelines recommend that all women whose Pap tests are reported as showing a glandular abnormality be referred for colposcopy. Glandular abnormalities are very rare. They develop within the endocervical region of the cervix, rather than the ectocervix - which is the part visible at the top of the vagina. It can be quite difficult to sample the cells of the endocervical region, and, for this reason, repeat Pap tests may not give an accurate report on the state of the cervix. This is the reason for the new recommendation for colposcopy in these women.

Adenocarcinoma is the type of cervical cancer associated with glandular abnormalities.

## Post-Treatment Management of Women with Biopsy Proven High-Grade Abnormalities

What are the new recommendations for managing women who have been treated for a high-grade abnormality?

Women whose biopsy is reported as CIN 2 or CIN 3 or adenocarcinoma in situ (AIS) receive ablative or excisional treatment to remove the area of abnormality. Despite apparently successful treatment, published studies show that this group of women remains at slightly higher risk of cervical cancer than women who have never had an abnormality. Because of this higher risk, these women have until now been recommended to have annual Pap tests for the rest of their lives. (This has not always been a popular policy with women!)

The new guidelines recommend different management of these women. The new policy is that women who have received ablative or excisional treatment for CIN 2, CIN 3 or AIS should have six tests using three modalities over a two-year interval after the treatment. If these six tests are normal, it is recommended that these women return to the usual screening interval (currently two years). The six tests and three modalities are:

4 to 6 months after treatment	Pap test & colposcopy
12 months after treatment	Pap test & HPV test
24 months after treatment	Pap test & HPV test

This new policy will affect about 15,000 women each year.

## Further Information

To reflect the new recommendations and terminology, PapScreen Victoria has updated its resources for women and health professionals. These are now available, free of charge. To order resources or for any other information about Pap tests and cervical screening visit PapScreen Victoria's new website [www.papscreen.org.au](http://www.papscreen.org.au) or contact the Cancer Helpline - 13 11 20.

## New Position Statement on Cervical Cancer Screening

The Cancer Council Australia has issued a new position statement on cervical cancer screening. The statement provides recommendations relating to cervical cancer screening including:

- Under the provisions of the current National Cervical Screening Policy, women aged 18 to 70 who have ever been sexually active are recommended to have a Pap smear every two years as part of the National Cervical Screening Program.
- In the absence of sufficient evidence to suggest that alternative screening technologies are more effective than the conventional Pap test, a patient centred approach for individual decisions about screening methodologies is recommended.
- In line with emerging evidence, The Cancer Council Australia supports the move towards the introduction of a three-yearly cervical screening interval in Australian women in conjunction with long-term evaluation in terms of invasive cervical cancer incidence and mortality.

The position statement can be viewed on The Cancer Council Australia's website at [www.cancer.org.au/positionstatements](http://www.cancer.org.au/positionstatements).

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

# NCI Clinical Announcement – Intraperitoneal Chemotherapy for Ovarian Cancer

5 January 2006

## Background

Epithelial ovarian carcinoma is the leading cause of death from gynecologic malignancies in the developed world. In 2005, it has been estimated that in the United States, 22,220 women will be diagnosed with ovarian cancer, and 16,210 women will die from the disease.<sup>1</sup> To date, no effective screening regimen for ovarian cancer has been identified. More than half of women with ovarian cancer present with advanced-stage disease (FIGO III/IV) at the time of diagnosis.

Epithelial ovarian cancer appears to arise from the epithelial surface of the ovary. Spread of the disease is often by local extension, by intra-abdominal dissemination to other sites within the peritoneal cavity, and by lymphatic spread to pelvic and para-aortic nodes in the retroperitoneum. The recommended treatment includes primary surgery for diagnosis, staging, and cytoreduction, followed by chemotherapy. Unlike many other solid tumors, effective cytoreduction (“debulking”) conveys a survival benefit among with women with ovarian carcinoma.<sup>2,3</sup> The goal of primary surgery is to reduce the burden of ovarian cancer to no or minimal residual disease. The recommended initial chemotherapy is generally a platinum-and-taxane combination given by intravenous infusion every 3 weeks for 6 courses.<sup>4,5</sup>

As residual ovarian cancer after surgery and initial recurrences are primarily confined to the abdomen, intraperitoneal (IP) administration of chemotherapy was first proposed several decades ago.<sup>6</sup> Certain chemotherapeutic agents, including cisplatin and, more recently, paclitaxel, were found to have distinct pharmacokinetic advantages when given via an intraperitoneal route.<sup>7-9</sup> These include high intraperitoneal concentration of drug, as well as a longer half-life of the drug in the peritoneal cavity, compared to that observed with intravenous (IV) administration. For cisplatin there was a 10–20–

fold greater exposure in the peritoneal cavity over what is achieved with the IV route.<sup>10</sup> In addition, the intraperitoneal administration resulted in prolonged systemic exposure to the chemotherapeutic agents.

## Recent Trials

Over the past 10 years, the results of 7 randomized trials assessing the administration of intraperitoneal chemotherapy for first-line treatment of ovarian cancer have become available.<sup>11-17</sup> (Table 1) These trials represent studies of IP chemotherapy conducted over two decades, with the first patient randomized in 1986. These trials have compared chemotherapy administered via the IV route (conventional therapy) to that administered via a combined IV and IP approach. In all of the trials, the chemotherapy was given after primary surgery. Some of these trials, however, have had complex designs assessing multiple factors in addition to IP treatment. Trial characteristics are summarized in Table 1 and warrant close scrutiny. An 8th trial comparing IP consolidation therapy to no further treatment among women with no evidence of disease after primary surgery and adjuvant chemotherapy has been reported.<sup>18</sup> (Table 2) Median survival reported for the control and experimental arms for the eight trials is shown in Tables 3 and 4. The estimated treatment hazard ratios for progression-free survival, based on available data, are shown in Figure 1. The estimated relative death rates are displayed in Figure 2 for 6 of the 8 studies. (The relative death rate was not reported in the studies by Kimani et al. and Polyzos, et al.) On average, IP therapy was associated with a 21.6% decrease in the risk of death (hazard ratio=0.79; 95% confidence interval 0.70–0.89). Since the expected median duration of survival for women with optimally debulked ovarian cancer receiving standard treatment is approximately 4 years, this size reduction in the overall death rate is expected to translate into about a 12-month

**Table 1. Randomized trials comparing IV versus IP or IP/IV first-line treatment of ovarian cancer.**

Study Identifier / Year Published	Control Regimen	Experimental Regimen	Eligible Patients	No. of Patients
Kirmanian et al, 1994	Cisplatin 100mg/m <sup>2</sup> IV, Cyclophosphamide 600mg/m <sup>2</sup> Q 3 weeks x 6	Cisplatin 200mg/m <sup>2</sup> IP, Etoposide 350 mg/m <sup>2</sup> IP Q 4 weeks x 6	Stage IIC-IV	62
SWOG 8501 / GOG 104 Alberts et al, 1996	Cisplatin 100mg/m <sup>2</sup> IV, Cyclophosphamide 600 mg/m <sup>2</sup> IV Q 3 weeks x 6	Cisplatin 100mg/m <sup>2</sup> IP, Cyclophosphamide 600mg/m <sup>2</sup> IV Q 3 weeks x 6	Stage III, <= 2 cm residual	546
Polyzos et al, 1999	Carboplatin 350mg/m <sup>2</sup> IV, Cyclophosphamide 600mg/m <sup>2</sup> IV Q 3 weeks x 6	Carboplatin 350mg/m <sup>2</sup> IP, Cyclophosphamide 600mg/m <sup>2</sup> IV Q 3 weeks x 6	Stage III	90
Gadducci et al, 2000	Cisplatin 50mg/m <sup>2</sup> IV, Cyclophosphamide 600mg/m <sup>2</sup> IV, Etoposide 60mg/m <sup>2</sup> IV Q 4 weeks x 6	Cisplatin 50mg/m <sup>2</sup> IP, Cyclophosphamide 600mg/m <sup>2</sup> IV, Etoposide 60mg/m <sup>2</sup> IV Q 4 weeks x 6	Stage II-IV, < 2 cm residual	113
GOG 114 / SWOG 9227 Markman et al, 2001	Cisplatin 75mg/m <sup>2</sup> IV, Paclitaxel 135mg/m <sup>2</sup> (24hr) IV Q 3 weeks x 6	Carboplatin (AUC9) IV q 28 days x 2, Cisplatin 100mg/m <sup>2</sup> IP, Paclitaxel 135mg/m <sup>2</sup> (24hr) IV q 3 weeks x 6	Stage III, <= 1 cm residual	462
Yen et al, 2001	Cisplatin 50mg/m <sup>2</sup> IV, Cyclophosphamide 50mg/m <sup>2</sup> IV, Etoposide / Doxorubicin 50mg/m <sup>2</sup> IV Q 3 weeks x 6	Cisplatin 100mg/m <sup>2</sup> IP, Cyclophosphamide 500mg/m <sup>2</sup> IV, Etoposide / Doxorubicin 50mg/m <sup>2</sup> IV Q 3 weeks x 6	Stage III, <= 1 cm residual	118
GOG 172 Armstrong et al, 2006	Cisplatin 75mg/m <sup>2</sup> IV, Paclitaxel 135mg/m <sup>2</sup> (24hr) IV Q 3 weeks x 6	Paclitaxel 135mg/m <sup>2</sup> (24hr) IV, Cisplatin 100mg/m <sup>2</sup> IP, Paclitaxel 60mg/m <sup>2</sup> IP on day 28 Q 3 weeks x 6	Stage III, <=1 cm residual	415

Note: SWOG 8501 / GOG 104 was conducted under the auspices of the NCI / Bristol Myers Squibb (BMS) cisplatin cooperation program . GOG 114 / SWOG 9227 and GOG172 were conducted under the auspices of the NCI / BMS Cooperative Research and Development Agreement for paclitaxel.

**Table 2. Randomized trials comparing surveillance to IP consolidation treatment.**

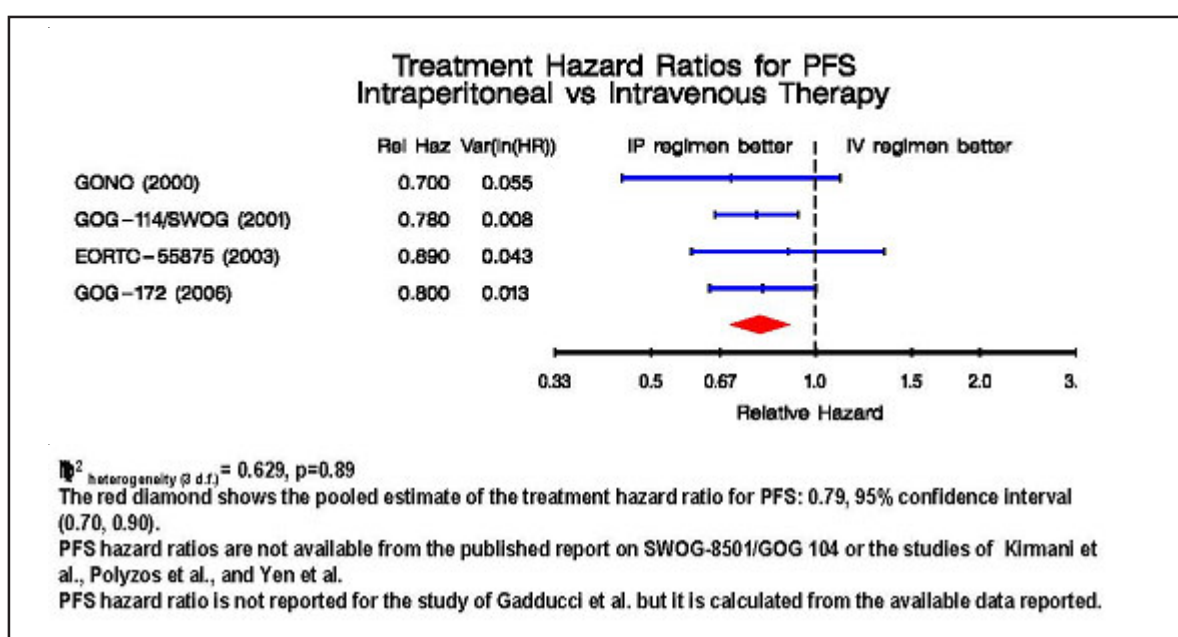
Study Identifier / Year Published	Control Regimen	Experimental Regimen	Eligible Patients	No. of Patients
EORTC 55875 Piccart et al, 2003	Surveillance	Cisplatin 100mg/m <sup>2</sup> IP Q 3 weeks x 4	Stage IIB-III in pathologic complete response following cisplatin-based primary treatment	153

**Table 3. Median survival time for randomized trials comparing IV versus IV/IP first-line treatment of ovarian cancer.**

Study Identifier / Year Published	No. of Patients	Median duration of survival for control regimen (months)	Median duration of survival for experimental regimen (months)
SWOG 8502 / GOG 104 Alberts et al, 1996	546	41	49
Polyzos et al, 1999	90	52	63
Gadduci et al, 2000	113	25	26
GOG 114 / SWOG 9227 / ECOG GO114 Markman et al, 2001	462	51	67
Yen et al, 2001	118	48	43
Armstrong et al, 2006	415	50	66

**Table 4. Median survival time for randomized trial comparing surveillance to IP consolidation treatment.**

Study Identifier / Year Published	No. of Patients	Median survival duration for control regimen (months)	Median survival duration for experimental regimen (months)
EORTC 55875 Picart et al, 2003	153	78	91

**Figure 1**

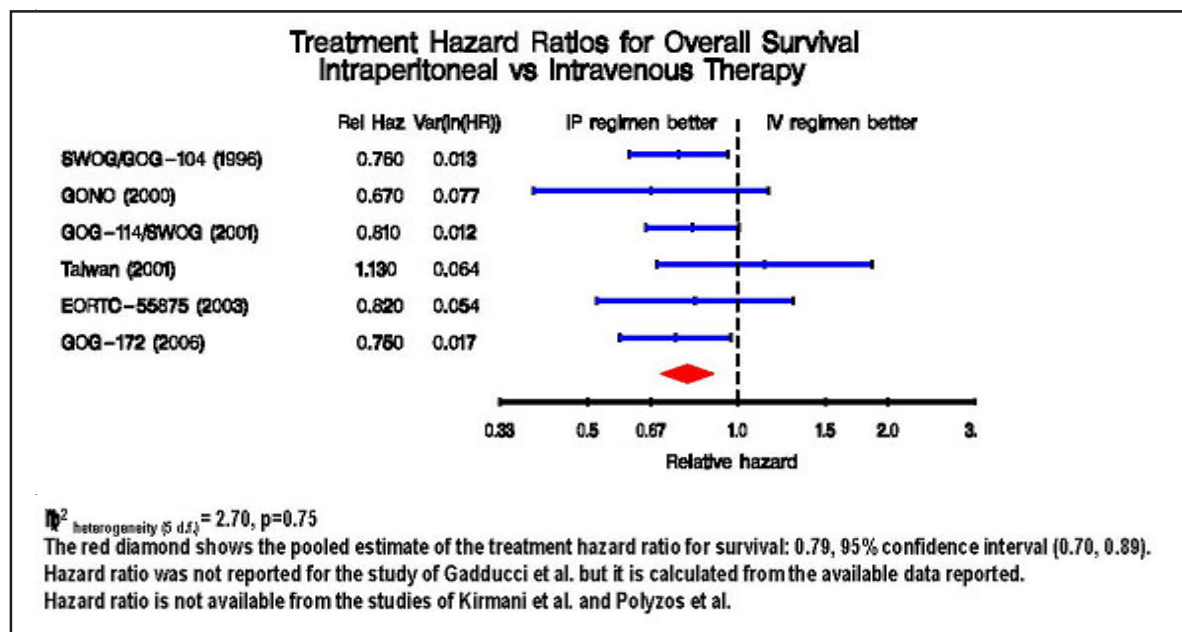


Figure 2

increase in overall median survival. The most recent trial, conducted by the Gynecologic Oncology Group and reported by Armstrong et al. in the *New England Journal of Medicine*, included both IP cisplatin and paclitaxel in the experimental arm. In that study (GOG 172), the improvement in median overall survival was 15.9 months with a treatment hazard ratio of 0.75 (95% confidence interval 0.58–0.97) favoring the IP study arm. The magnitude of improvement in median overall survival associated with IP/IV administration of chemotherapy is similar to that observed with the introduction of either cisplatin or paclitaxel.

### Toxicity

The toxicity observed during these trials may be divided into toxicity associated with the presence of an IP catheter, toxicity associated with the IP administration of chemotherapy and the toxicity associated with the chemotherapy itself. A summary of the toxicity reported across these 8 studies is shown in Table 5. As might be expected, the risk of infection and fever was higher among patients receiving IP treatment and thus having an IP catheter. In addition, patients receiving IP therapy were more likely to have abdominal pain, nausea, and vomiting. In the most recent study (GOG 172) women on the IP arm experienced greater hematologic, metabolic, and neurologic toxicity than those on the IV arm. The increased toxicity observed in this study may

also be due to the IP doses of paclitaxel. In general, however, the toxicity associated with intraperitoneal treatment appeared to be short-term and manageable.

GOG investigators have analyzed the reasons why the prescribed courses of IP chemotherapy on GOG 172 were discontinued.<sup>19</sup> They observed catheter complications in 39 of 118 patients (33%). These included infection in 21 women, catheter blockage in 9, catheter leak in 3, access problems in 5 and drainage per vagina in 1. In addition, they noted reasons for discontinuing IP therapy potentially related to the presence of a catheter among 4 women with abdominal pain, 4 with bowel complication, and 19 women who refused further IP therapy. They did not find any association between the timing of catheter relative to initial surgery or the extent of primary surgery to complication rates, although they did note that women who underwent left colon resection were less likely to start IP therapy.

### Health-related Quality of Life (HRQOL)

HRQOL data are available from GOG 172. Abdominal discomfort improved from baseline to chemotherapy cycle 4 for women on both the IV and IP/IV chemotherapy arms, although the improvement was greater among women on the IV arm.<sup>20</sup> They observed better HRQOL among women on the IV arm compared with women

**Table 5. Reported toxicity.**

Category	Symptom	Study	IV (%)	IP/IV (%)	P-value	
Auditory	Hearing loss ( $\geq$ Grade2)	Alberts et al	15	5	P<0.001	
	Tinnitus ( $\geq$ Grade 2)	Alberts et al	14	7	P=0.01	
Blood / Bone Marrow	Anemia ( $\geq$ Grade3)	Alberts et al	25	26	ns	
		Gadducci et al	8	6	nr	
		Kirmani et al	3	7	nr	
			Yen et al	12	7	ns
	Granulocytopenia ( $\geq$ Grade3)	Alberts et al	69	56	P=0.002	
	Leukopenia ( $\geq$ Grade3)	Alberts et al	50	40	P=0.04	
		Armstrong et al	64	76	P<0.001	
		Gadducci et al	19	24	nr	
		Kirmani et al	21	19	nr	
		Markman et al	62	77	nr	
		Polyzos et al	18	5	P<0.01	
		Yen et al	21	10	P=0.033	
	Thrombocytopenia ( $\geq$ Grade3)	Alberts et al	9	8	ns	
		Armstrong et al	4	12	P<0.001	
		Gadducci et al	2	0	nr	
	Kirmani et al	0	5	nr		
	Markman et al	3	49	nr		
	Polyzos et al	10	3	P<0.09		
	Yen et al	10	7	ns		
Constitutional symptoms	Fatigue ( $\geq$ Grade3)	Armstrong et al	4	18	P<0.001	
		Markman et al	1	3	nr	
	Fever ( $\geq$ Grade2)	Alberts et al	5	6	ns	
		Markman et al	9	4	nr	
	Fever ( $\geq$ Grade3)	Armstrong et al	4	9	P=0.02	
	Markman et al	1	3	nr		
Gastrointestinal	$\geq$ Grade 3	Armstrong et al	24	46	P<0.001	
		Markman et al	17	37	nr	
		Gadducci et al	26	37	nr	
	Nausea / Vomitting (Grade2)	Piccart et al	NA	82	na	
Infection	Grade 1	Piccart et al	NA	26	na	
	$\geq$ Grade 3	Armstrong et al	6	16	P=0.001	
		Markman et al	1	4	nr	
Metabolic	$\geq$ Grade 3	Markman et al	1	10	nr	
	Hepatic	Armstrong et al	<1	3	P=0.05	
	Renal	Armstrong et al	2	7	P=0.03	
	Creatinine clearance ( $\geq$ Grade 3)	Markman et al	1	5	nr	
	Creatinint clearance (Grade2)	Piccart et al	NA	45	na	
Neurology	Neuromuscular effects at end of treatment ( $\geq$ Grade2)	Alberts et al	25	15	P=0.02	
	Neurotoxicity (Grade 2 or 3)	Piccart et al	NA	15	na	
	Neurotoxicity ( $\geq$ Grade3)	Armstrong et al	9	19	P<0.001	
		Markman et al	9	12	nr	
Pain	Abdominal pain (Grade 1 or 2)	Piccart et al	NA	38	na	
	Abdominal pain ( $\leq$ Grade2)	Alberts et al	2	18	P<0.001	
	Abdominal pain ( $\geq$ Grade 3)	Armstrong et al	1	11	P<0.001	

randomized to the combined IV/IP arm during and immediately after treatment. These differences disappeared over time, however, so that at one year, HRQOL and pain scores were similar between the two arms except for paresthesias, which were more likely to persist at moderate levels among the patients on the IP/IV arm.<sup>21</sup> These findings suggest that the additional toxicity, with the exception of paresthesias, that may be observed with IP delivery is generally transient and not a long-term issue for most patients.

### Patient Eligibility

Patients who may benefit from an IP approach are women with advanced ovarian cancer (FIGO stages III) who have undergone optimal surgical cytoreduction to no or minimal residual (no tumor nodule > 1cm in diameter) disease. Retrospective and prospective cohort studies suggest that 25 to 75% of patients are able to undergo optimal surgical cytoreduction.<sup>3</sup> Factors influencing the success of surgical cytoreduction include younger age, decreased co-morbidity, and the availability of a surgeon and supportive team with expertise in the surgical management of ovarian cancer. The presence of extensive adhesive disease in the abdomen should be considered a relative contraindication to IP therapy, as multiple adhesions may well preclude adequate distribution of IP chemotherapy.

### Unanswered Questions

As Table 1 makes clear, these 8 studies have all evaluated somewhat different experimental treatment regimens, although all utilized IP either

cisplatin or IP carboplatin. The use of non-platinum agents varied between the studies, and included cyclophosphamide, anthracyclines, etoposide, and paclitaxel. In 7 of the 8 studies, only cisplatin or carboplatin was given via an IP route, while the most recent study, GOG 172, administered both cisplatin and paclitaxel via an IP route. Fujiwara et al. have recently suggested that substitution of carboplatin for cisplatin may reduce the toxicity of IP platinum.<sup>22</sup> The optimal IP regimen for women with optimally-debulked ovarian cancer remains unclear.

The optimal number of IP treatments is also not known. In SWOG 8501, GOG 114, and GOG 172 the number of IP treatments was often limited due to toxicity. The number of women completing the planned six courses of IP chemotherapy ranged from 71% (GOG 114) to 58% (SWOG 8501) to 42% (GOG 172). (Table 6) Most of the patients who experienced toxicity with IP administration were able to tolerate additional IV chemotherapy. Regardless, intent-to-treat analysis demonstrated a survival benefit even though a large proportion of the patients was unable to complete the full, planned schedule of IP treatments.

We do not know whether women who undergo interval cytoreductive surgery after neoadjuvant chemotherapy, or initial suboptimal cytoreductive surgery followed by several courses of IV chemotherapy, and are then left with no or minimal residual disease, may also derive a survival benefit from IP chemotherapy. In addition, we have no data on women with stage IV disease who underwent optimal cytoreductive surgery. As noted above, one study, EORTC 55875, did find a survival benefit associated with

**Table 6. Completion rate for prescribed courses of chemotherapy (%).**

Study Identifier / Year of Publication	IV regimen (%)	IP/IV regimen for IP administration (%)
SWOG 8501 / GOG 104 Alberts et al, 1996	58	58
GOG 114 / SWOG 9227 / ECOG GO114 Markman et al, 2001	86	71
Gadducci et al, 2000	96	65
EORTC 55875 Piccart et al, 2003	NA	56
GOG 172 Armstrong et al, 2006	90	42

consolidation IP therapy among women without clinical evidence of disease after primary surgery and platinum-based chemotherapy. Without additional evidence from well-controlled trials, therefore, we do not know whether women with no or minimal residual disease after surgery and standard platinum-and-taxane IV chemotherapy should be encouraged to consider IP consolidation therapy.

Segna et al. have reported a small series documenting the feasibility of intra-operative administration of chemotherapy for women with gynecologic malignancies.<sup>23</sup> Several small studies have evaluated intra-operative hyperthermia combined with IP chemotherapy administration.<sup>24,25</sup> To date, however, the use of intra-operative chemotherapy with or without hyperthermia has not been evaluated in a multi-institutional, randomized phase III trial.

There are theoretical concerns that the prolonged half-life of paclitaxel associated with IP administration may delay wound healing.<sup>26</sup> In addition, the administration of IP therapy may exacerbate the development of intra-abdominal adhesions, making subsequent abdominal surgery more risky.

There have been no studies comparing techniques for placement of intraperitoneal catheters, including timing relative to primary surgery, or techniques of administration of chemotherapy in this patient population. As noted above, analysis of data from GOG 172 suggests that delayed placement of an IP port did not decrease the likelihood of complications.<sup>19</sup> Other surgical procedures, such as hysterectomy, small bowel resection and reanastomosis, and right colon resection, did not affect the initiation of IP chemotherapy.

Better ways of introducing large volumes of fluid into the peritoneal cavity are needed. In addition, novel approaches to prevent fibrotic formation around the IP catheter, as well as to prevent catheter-related mechanical trauma from the catheter to surrounding tissue, such as large and small bowel, are needed.

Further trials are warranted, in particular trials to address reduction of toxicity associated with IP administration.

## Recommendations for administering IP chemotherapy

Before primary surgery for presumed advanced stage ovarian cancer, the operating surgeon should discuss with the patient the potential benefits of intraperitoneal chemotherapy, as the surgery may need to be tailored to facilitate subsequent IP chemotherapy. Specifically, performance of a supracervical hysterectomy may avoid surgical entrance into the vagina. If the vagina is opened, then it should be closed with delayed absorbable suture, to avoid leakage of peritoneal instillate from the vaginal defect. Similarly, the abdominal wound can also leak ascites and peritoneal instillate, so it too should be carefully closed with semi-permanent or permanent sutures. In many cases, the port for IP infusion of chemotherapy can be placed at time of primary surgery. Most teams of investigators with expertise in the administration of IP chemotherapy recommend the use of a semi-permanent subcutaneous venous access port connected to a single-lumen venous catheter, such as a 9.6 French polyurethane venous access tubing.<sup>27,28</sup> Peritoneal catheters with fenestrations and Dacron cuffs, which had been used in the past, reportedly are associated with a greater incidence of bowel adhesions and erosion into the bowel.

Ports should be located on the inferior thorax at the midclavicular line, placed to avoid irritation from a brassiere. A transverse incision slightly larger than the port should be made overlying the ribs, after which a subcutaneous pocket should be created directly over the fascia covering the ribs. The port should be sutured with permanent 2-0 suture at four corners to the fascia, to prevent rotation or migration and facilitate access via a Huber needle. Next, the catheter should be tunneled under the cutaneous tissue, above the fascia, to a point 6 cm lateral to the umbilicus. At this point, it can be pulled into the peritoneal cavity through a small hole the size of the catheter. The catheter should be cut to a length of about 10 cm, to ensure that it remains in the abdominal cavity, but reduce the risk of adherence to bowel or kinking. The port should then be flushed with 10 cc of heparin (100 units per cc).<sup>19</sup>

Contraindications to placement of an IP port at time of primary surgery include an uncertain pathologic diagnosis, gross bacterial

contamination of the peritoneal cavity, serious co-morbidity, and serious intraoperative complications. There is no absolute contraindication to placement of an IP port at the same time as bowel resection and reanastomosis, although some surgeons prefer to wait and place the port at a second procedure, in an effort to decrease risks of infection and adhesions. Anaf et al. have described a laparoscopic technique for IP port placement.<sup>29</sup>

Makhija et al. recently reported their own, single-institution retrospective experience of complications associated with the presence of an IP catheter placed as described above for the administration of IP chemotherapy.<sup>28</sup> In their retrospective series, 61 of 313 catheters (19.6%) were placed at time of laparoscopy. Among 301 patients treated between 1989 and 1997 they noted catheter-related complications in 30 women (10%). Of these, 19 women (6.3%) experienced inflow obstruction and 11 (3.6%) experienced infection. Only 21 of 301 (7%) required cessation of IP chemotherapy before its planned completion. In addition, Makhija et al. observed no cases of bowel perforation or small bowel obstruction/ileus.

The optimal volume of infusate is not known. One goal of instilling a large volume of fluid is to ensure that the drug-containing infusate reaches all intraperitoneal surfaces. One liter of fluid per m<sup>2</sup> of body surface area, up to a maximum of 2 liters, may be a useful target for determining the appropriate volume of infusate for an individual patient.

It seems reasonable to recommend reconstitution of the drugs to be administered via an IP route in one liter of normal saline, followed by infusion of that liter quickly into the abdomen, then infusion of an additional liter of normal saline to facilitate intra-abdominal distribution. Should the patient become uncomfortable for any reason, then the second liter need not be entirely infused. There is no need to drain the infused fluid from the abdominal cavity. GOG 172 prescribed the constitution of both paclitaxel and cisplatin in 2 liters of normal saline warmed to 37 degrees Centigrade followed by infusion through a peritoneal catheter as rapidly as possible. After infusion, they encouraged patients to change position at 15-minute intervals for two hours to ensure adequate intra-abdominal distribution.

Patients administered either IP cisplatin or paclitaxel should receive the same supportive-care drugs used with IV administration of these agents. Routine premedications, including H1- and H2-antihistamines and dexamethasone should be given before paclitaxel administration. GOG 172 prescribed dexamethasone 20 mg orally 12 and 6 hours before the infusion of paclitaxel or 20 mg intravenously 30 minutes before the paclitaxel infusion. Both diphenhydramine 50 mg and cimetidine 300 mg (or a suitable alternative) were administered intravenously 30 minutes before the paclitaxel infusion. Hydration and antiemetics should be given before and after cisplatin administration. All GOG protocols in which cisplatin is administered IP mandate the simultaneous administration of at least one liter of normal saline to reduce the risk of cisplatin-induced nephrotoxicity. In addition, delayed nausea is common with IP administration of cisplatin. Antiemetics often need to be maintained for 3 to 4 days after IP infusion.

The largest studies, namely SWOG 8502, GOG 114, and GOG 172, administered an intraperitoneal dose of cisplatin 100 mg/m<sup>2</sup> given every 3 weeks. It would seem reasonable, therefore, to consider the same dose for treatment of patients off protocol, with appropriate dose reduction for toxicity. Patients should be routinely questioned about potential neurotoxicity, and undergo immediate dose reduction for neurotoxicity  $\geq$ CTCAE grade 1. In addition, delivery of IV paclitaxel at a reduced dose (135 mg/m<sup>2</sup>) with a 24-hour infusion pump can reduce the risk of neurotoxicity.

Patients with malignant ascites who are otherwise candidates for IP chemotherapy should undergo drainage of their ascites followed by IP installation of the infusate. In order to keep the vascular compartment full, however, individual patients may need additional IV fluid so that the total volume of fluid administered balances that of the ascites removed. If a woman undergoes removal of 3 litres of ascites, followed by 2 litres of IP infusate, then she will also need at least an additional litre of IV fluid over the next 24 hours.

The optimal management of toxicities associated with IP administration of chemotherapy is not well established. GOG 172 mandated reduction of the dose of IP drug for patients reporting grade 2 abdominal pain. As

noted above, patients should be regularly assessed for potential neurotoxicity, with immediate dose reduction of cisplatin for any degree of neurotoxicity. In GOG 172, treatment was held for grade 3 or 4 peripheral neuropathy and not restarted until neuropathy resolved to grade 2 or less. Again in GOG 172, patients who experienced recurrent grade 2 abdominal pain after dose reduction or who experienced grade 3 abdominal pain were switched to IV chemotherapy. If creatinine rose to greater than 2.0 mg/day, then creatinine clearance was measured. Treatment was held if creatinine clearance was less than 50 cc/min and was resumed only when creatinine clearance was greater than 50 cc/min. There is no evidence that IP cisplatin is more nephrotoxic than IV cisplatin. As noted above, all GOG protocols in which cisplatin is administered IP mandate the simultaneous administration of at least one litre of normal saline to reduce the risk of cisplatin-induced nephrotoxicity.

If a patient is not able to tolerate infusion of the treatment volume, due to unacceptable pain or extremely slow infusion, then the IP route should be abandoned and the patient treated with IV chemotherapy. Similarly, if the patient experiences severe complications related to the presence of an IP catheter, such as intra-abdominal infection, prolonged ileus, bowel obstruction, or bowel perforation, then the complication should be managed appropriately and the route of chemotherapy switched from IP to IV. In general, a malfunctioning IP catheter should not be replaced; instead the physician should switch to IV chemotherapy. IP catheters should be removed at the completion of IP chemotherapy as the patient's medical status permits. In general, IP ports can be easily removed under local anesthesia in the office.

### Summary

Based on the results of these randomized phase III trials, a combination of IV and IP administration of chemotherapy conveys a significant survival benefit among women with optimally debulked epithelial ovarian cancer, compared to IV administration alone. While it is not possible to specify a precise regimen, the three largest studies with the greatest survival advantage delivered cisplatin 100 mg/m<sup>2</sup> IP. The two most recent trials also included taxanes. In all the

published studies, the chemotherapy regimens mandated modification based on patient tolerance.

The benefit appears to be approximately a 12-month improvement in median overall survival (range 0–16 months). Of note, the magnitude of improvement in survival is similar to that noted with the introductions of cisplatin and of paclitaxel in the treatment of women with ovarian cancer. Combined IP/IV administration of chemotherapy, however, may also be associated with a significantly increased short-term risk of toxicity compared with IV chemotherapy. In general, however, the toxicity is short-term and manageable.

Effective surgical debulking is critical to long-term survival for ovarian cancer. Women undergoing surgery for presumed ovarian cancer, therefore, should undergo surgery by a gynecologic oncologist or a surgical team with expertise in the staging and cytoreduction of ovarian cancer. After primary surgery, women with optimally-debulked FIGO stage III ovarian cancer should be counseled about the clinical benefit associated with combined IV and IP administration of chemotherapy. Based on the most recent trials, strong consideration should be given to a regimen containing IP cisplatin (100 mg/m<sup>2</sup>) and a taxane, whether given by an IV only or IV plus IP.

Women with epithelial ovarian cancer and their physicians should be encouraged to participate in prospective clinical trials, in order to identify better treatment for this disease.

### Bibliography

1. Jemal A, Murray T, Ward E et al. Cancer statistics, 2005. *CA Cancer J Clin* 2005; 55: 10–30.
2. Hoskins WJ, McGuire WP, Brady MF et al. The effect of diameter of largest residual disease on survival after primary cytoreductive surgery in patients with suboptimal residual epithelial ovarian carcinoma. *Am J Obstet Gynecol* 1994; 170: 974–979.
3. Bristow RE, Tomacruz RS, Armstrong DK, et al. Survival effect of maximal cytoreductive surgery for advanced ovarian carcinoma during the platinum era: a meta-analysis. *J Clin Oncol* 2002; 20: 1248–1259.
4. Ozols RF, Bundy BN, Greer BE et al. Phase III trial of carboplatin and paclitaxel compared with cisplatin and

- paclitaxel in patients with optimally resected stage III ovarian cancer: a Gynecologic Oncology Group study. *J Clin Oncol* 2003; 21: 3194–3200.
5. [www.nci.nih.gov/cancertopics/pdq/treatment/ovarianepithelial/](http://www.nci.nih.gov/cancertopics/pdq/treatment/ovarianepithelial/)
  6. Dedrick R, Myers C, Bungay P et al. Pharmacokinetic rationale for peritoneal drug administration in the treatment of ovarian cancer. *Cancer Treat Rep* 1978; 62: 1–11.
  7. Markman M. Intraperitoneal antineoplastic agents for tumors principally confined to the peritoneal cavity. *Cancer Treat Reviews* 1986; 13: 219–243.
  8. McClay EF, Howell SB. A review: intraperitoneal cisplatin in the management of patients with ovarian cancer. *Gynecol Oncol* 1999; 36: 1–6.
  9. Markman M, Francis P, Rowinsky E, Hoskins W. Intraperitoneal paclitaxel: a possible role in the management of ovarian cancer? *Semin Oncol* 1995; 22: 84–87.
  10. Howell SB, Pfeifle CL, Wung WE et al. Intraperitoneal cisplatin with systemic thiosulfate protection. *Ann Intern Med* 1982; 97: 845–851.
  11. Kirmani S, Braly PS, McClay EF et al. A comparison of intravenous versus intraperitoneal chemotherapy for the initial treatment of ovarian cancer. *Gynecol Oncol* 1994; 54: 338–344.
  12. Alberts DS, Liu PY, Hannigan EV et al. Intraperitoneal cisplatin plus intravenous cyclophosphamide versus intravenous cisplatin plus intravenous cyclophosphamide for stage III ovarian cancer. *N Engl J Med* 1996; 335: 1950–1955.
  13. Polyzos A, Tasvaris N, Kosmas C et al. A comparative study of intraperitoneal carboplatin versus intravenous carboplatin with intravenous cyclophosphamide in both arms as initial chemotherapy for stage III ovarian cancer. *Oncology* 1999; 56: 291–296.
  14. Gadducci A, Camini F, Chiara S et al. Intraperitoneal versus intravenous cisplatin in combination with intravenous cyclophosphamide and epidoxorubicin in optimally cytoreduced advanced epithelial ovarian cancer: a randomized trial of the Gruppo Oncologica Nord-Ovest. *Gynecol Oncol* 2000; 76: 157–162.
  15. Yen M-S, Juang C-M, Lai C-R et al. Intraperitoneal cisplatin-based chemotherapy vs. intravenous cisplatin-based chemotherapy for stage III optimally cytoreduced epithelial ovarian cancer. *Int J Gynecol Obstet* 2001; 72: 55–60.
  16. Markman M, Bundy BN, Alberts DS, et al. Phase III trial of standard-dose intravenous cisplatin plus paclitaxel versus moderately high-dose carboplatin followed by intravenous paclitaxel and intraperitoneal cisplatin in small-volume stage III ovarian carcinoma: an intergroup study of the Gynecologic Oncology Group, Southwestern Oncology Group, and Eastern Cooperative Oncology Group. *J Clin Oncol* 2001; 19: 1001–1007.
  17. Armstrong D, Bundy B, Wenzel L et al. Phase III randomized trial of intravenous cisplatin and paclitaxel versus an intensive regimen of intravenous paclitaxel, intraperitoneal cisplatin, and intraperitoneal paclitaxel in stage III ovarian cancer: a Gynecologic Oncology Group study. *N Engl J Med* 2006; 354: 34–43.
  18. Piccart MJ, Floquet A, Scarfone G et al. Intraperitoneal cisplatin versus no further treatment: 8-year results of EORTC 55875, a randomized phase III study in ovarian cancer patients with a pathologically complete remission after platinum-based intravenous chemotherapy. *Int J Gynecol Cancer* 2003; 13 (Suppl 12): 196–203.
  19. Walker JL, Armstrong DA, Huang DQ et al. Intraperitoneal catheter outcomes in a phase III trial of intravenous versus intraperitoneal chemotherapy in optimal stage III ovarian or primary peritoneal cancer. A Gynecologic Oncology Group study. *Gynecol Oncol* 2006; 100: 27–32.
  20. Wenzel LB, Huang HQ, Armstrong D et al. Validation of a FACT/GOG-Abdominal Discomfort subscale: a Gynecologic Oncology Group Study. *Proc ASCO*; 2005; Abstract 8101.
  21. Wenzel LB, Huang H, Armstrong D et al. Quality of life results of a randomized study of intravenous paclitaxel and cisplatin versus IV paclitaxel, intraperitoneal cisplatin and IP paclitaxel in optimal stage III epithelial ovarian cancer. *Proc ASCO* 2004; Abstract 5026, p. 455s.
  22. Fujiwara K, Markman M, Morgan M et al. Intraperitoneal carboplatin-based chemotherapy for epithelial ovarian cancer. *Gynecol Oncol* 2005; 97: 10–15.
  23. Segna Ra, Dottino PR, Jennings TS et al. Feasibility of intraoperative administration of chemotherapy for gynecologic malignancies: assessment of acute postoperative morbidity. *Gynecol Oncol* 1993; 48: 227–231.
  24. Ryu KS, Kim JH, Ko HS et al. Effects of intraperitoneal hyperthermic chemotherapy in ovarian cancer. *Gynecol Oncol* 2004; 94: 325–332.
  25. Gori J, Castano R, Toziano M et al. Intraperitoneal hyperthermic chemotherapy in ovarian cancer. *Int J Gynecol Cancer* 2005; 15: 233–239.
  26. Hopkins MP, von Grueningen VE, Holda S et al. The effect of intermittent-release intraperitoneal chemotherapy upon wound healing. *Am J Obstet Gynecol* 1997; 176: 819–823.
  27. Alberts DS, Markman M, Armstrong D et al. Intraperitoneal therapy for stage III ovarian cancer: a therapy whose time has come! *J Clin Oncol* 2002; 20: 3944–3946.
  28. Makhija S, Leitao M, Sabbatini P et al. Complications associated with intraperitoneal chemotherapy catheters. *Gynecol Oncol* 2001; 81: 77–81.
  29. Anaf V, Gangji D, Simon P et al. Laparoscopic insertion of intraperitoneal catheters for intraperitoneal chemotherapy. *Acta Obstet Gynecol Scand* 2003; 82: 1140–1145.

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## ANZGOG Trial of IP Chemotherapy Announced

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A study published in the New England Journal of Medicine in January found significant survival benefits in delivering chemotherapy directly into the abdomen of women with advanced ovarian cancer.

The study of over 400 women compared the results of six cycles of standard chemotherapy delivered intravenously with the same drugs administered directly into the abdomen, known as intraperitoneal (IP) chemotherapy. The study found survival time for women receiving chemotherapy directly into the abdomen increased by 16 months.

The United States National Cancer Institute (NCI) released a clinical announcement in response to this study and other randomised trials into IP chemotherapy. The NCI announcement supports the use of chemotherapy delivered both intravenously and directly into the abdomen but highlighted a number of questions that still need to be addressed, such as the toxicity and catheter complications. Current research is aimed at developing IP regimens that are effective and have fewer side effects.

A meeting was recently held by the Australia New Zealand Gynaecological Oncology Group (ANZGOG) to discuss issues about IP

chemotherapy relevant to the Australian context. As a result of the meeting, ANZGOG will open a phase II trial of IP chemotherapy for primary ovarian, peritoneal and fallopian tube cancers, known as TRIPOD, in July 2006.

TRIPOD will test one such regimen being piloted at the Memorial Sloan Kettering Cancer Centre in New York where women receive six cycles of cisplatin and paclitaxel IP with additional paclitaxel given intravenously. The trial will determine the regimen's feasibility, tolerability and effects on quality of life.

TRIPOD is designed to ensure Australian and New Zealand women have access to a standardised regimen of IP chemotherapy and to contribute knowledge about its feasibility and effects. TRIPOD will also help to place oncology centres in Australia and New Zealand in the best position to participate in future international trials of IP chemotherapy.

For further information about this trial, please contact Dr Corona Gainford at the National Health and Medical Research Council (NHMRC) Clinical Trials Centre, University of Sydney on 02 9562 5366 or [corona.gainford@ctc.usyd.edu.au](mailto:corona.gainford@ctc.usyd.edu.au).

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## Sail Away With ASGO

3–7 May 2006, Hamilton Island, Queensland, Australia

*Dr Andrea Garrett  
Gynaecological Oncology Fellow  
Royal Women's Hospital*

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The annual Australian Society of Gynaecologic Oncologists (ASGO) conference was held in early May and Hamilton Island provided a beautiful setting. Gynaecologic oncologists, medical oncologists, radiation oncologists and pathologists met to exchange ideas and research endeavours. The event was generously sponsored by CSL, Mayne

Pharma, Johnson and Johnson Medical, Commonwealth Bank, Tyco Healthcare, Schering-Plough and Melbourne Pathology. Trade displays showcased new equipment available.

The conference kicked off with the Fellows Pathology session. Dr R Brown (Vic) headed a

fantastic session on histology. Multiple histology slides of common and rare gynaecologic oncology conditions were presented, providing an excellent update.

The content of the lectures covered a wide range of topics with the presenters showcasing their oncology unit's research activities. The 10 Fellows also presented during the main lecture program. These presentations were all of a high standard. The Keith Free Prize is awarded annually to the Fellow with the best presentation. This year the prize was awarded to Dr R Farrell (WA) for her presentation on *"Quality of life and the role of sentinel node biopsy in the treatment of vulval cancer"*.

Laparoscopic surgery has increased within the field of gynaecologic oncology, with obvious advantages to patients and a morning session was devoted to this aspect of oncology surgery. A trouble-shooting session provided an excellent opportunity to improve laparoscopic skills. Dr Leung (WA) presented an interesting concept of multi-disciplinary laparoscopic groups with the interchange of skills among different specialities. This approach need not be limited to laparoscopic surgery only. An update on the LACE trial (an international multi-centre randomised trial comparing laparotomy and laparoscopy in the treatment of endometrial cancer), showed promising preliminary results with recruitment going well.

Intraperitoneal (IP) chemotherapy was up for debate. An NCI statement issued earlier this year stated that IP chemotherapy should be offered to women with ovarian cancer given the survival advantage. However there were major concerns regarding the side effects and acceptability of this route of administration. Gynaecologic oncologists were in agreement with the concept of IP chemotherapy and keen to introduce this mode of treatment into their practice; however debate ensues regarding the most appropriate drugs to use and in what doses. Consensus was not reached; however units around the country would be offering IP chemotherapy to patients in the very near future. Consideration was also being given to various trials in order to determine the best regimen for IP chemotherapy.

The ASGO AGM was held during the conference and this year Dr Russell Land (Qld) was welcomed to the society of gynaecologic oncologists as its newest member, having successfully completed his membership training. Dr K Narayan (Radiation Oncologist, Vic) was also welcomed as an honorary member.

On a lighter note, the social program was enjoyed by all. Despite the weather being overcast for much of the week, delegates spent an afternoon on Whitehaven Beach and the resort also offered snorkelling trips and the use of catamarans. Much of the evening entertainment was provided by a talented gynaecologic oncologist on the piano.

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## Report of the 42<sup>nd</sup> Annual Meeting of the American Society of Clinical Oncology (ASCO)

2-6 June 2006, Atlanta, Georgia, USA

*Dr Serene Foo*

*Medical Oncologist*

*Royal Women's Hospital / Austin Health / Mercy Hospital for Women*

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There are increasing tumour specific meetings but ASCO still remains the premier annual scientific meeting for oncologists. In the gynaecological cancer tracks, there were no real surprises with presentations including the interim ICON 5 data and of course,

ongoing (unchanged) debate regarding intraperitoneal chemotherapy, which I am sure will be covered elsewhere in this edition. It is a real credit to the organising committee of the Noosa weekend in February that we had such stimulating presentations by Drs Maurie

Markman and Abu Nadine. In more detail, some of the abstracts / sessions are as follows:

I personally found that one of the more dynamic sessions was an education session titled "Are all uterine malignancies created equal?" as well as an oral presentation of adjuvant therapy for CS. The discussion of endometrial stromal sarcoma was encompassed within one slide and a reminder about hormonal intervention, but I think it demonstrates the need for international collaboration to advance the management for rare tumours.

Abstract 5001 was a GOG randomised trial of whole abdominal irradiation (WAI) vs. cisplatin-ifosfamide + mesna (CIM) in optimally debulked (<1 cm residual tumour) stage I-IV carcino-sarcoma (CS) of the uterus. Besides initial surgery, there has been no established consensus regarding adjunctive therapy for optimally debulked patients with uterine CS. This study compared PFI, OS, toxicity, and failure patterns using WAI vs. CIM for this uncommon group of female malignancies. Patients were randomised to either WAI (30Gy followed by pelvic boost) or cisplatin 20mg/m<sup>2</sup>/d × 4, ifosfamide 1.5g/m<sup>2</sup>/d × 4 and mesna 120mg/m<sup>2</sup> loading dose, then 1.5g/m<sup>2</sup>/d × 24 h, q 3 weeks × 3 cycles. Of 224 patients were enrolled, 207 (WAI=105; CIM=102) were eligible. Patient demographics and characteristics were similar between arms. FIGO stage (both arms) was: I=64 (31%); II=26 (12%); III=93 (45%); IV=24 (11%). GI toxicity ≥ grade 2 occurred frequently and similarly (31%, both arms). CIM was associated with more ≥ grade 3 anaemia (11% vs 1%) and neurotoxicity (9% vs 0%) compared to WAI. Two deaths were attributed to RT-induced hepatitis. Sites of first recurrence in WAI vs. CIM among the 97 (47%) patients who relapsed were: vagina, 4 vs 10; pelvis, 12 vs 12; abdomen, 23 vs 14; lung, 13 vs 13; other, 13 vs 9. The estimated probability of recurring within 5 years was 58% (WAI) and 52% (CIM). The recurrence rate was 18% lower for CIM patients relative to WAI patients (p=NS). The estimated death rate for CIM is 30% lower relative to WAI (HR: 0.672, 95% CI: 0.458-0.986, p=0.056). The authors concluded that compared to WAI, adjuvant CIM reduces the recurrence rate and prolongs OS in optimally debulked uterine CS patients; however, due to a high relapse rate and poor OS, the imperative for new adjuvant therapies remains. This trial was notable in taking 12 years to accrue and is provocative

given a trend toward a survival benefit with just 3 cycles of chemotherapy (estimated 5 year survival rate of 34% vs 47%). It was also interesting that there were more abdominal failures in the WAI group. Subset analysis showed that age and stage were predictive for higher recurrence rate. Future trials are likely to incorporate both chemotherapy as well as radiotherapy, ie, vaginal brachytherapy.

Along similar themes, there was passionate discussion particularly from Dr Kaled Alektiar, a radiation oncologist from MSKCC who questioned the results of GOG122 evaluating the use of WAI vs. chemo (doxo / cisplatin x 8 cycles) in stage III/IV uterine sarcomas. In the JCO publication in January this year, the conclusion was that chemotherapy significantly improved PFS (50% vs. 38%) and OS (55% vs. 42%) compared to WAI. He went on to dissect the results and very eloquently pointed out that in fact, there were significant imbalances in the 2 arms that were not initially stratified for stage; and the differences even with stage III patients, who had quite different prognosis if they had isolated nodal involvement only, as opposed to patients who had positive cytology / serosal or vaginal involvement. This showed that the **unadjusted** differences in PFS (43% vs 38%, absolute diff 5% and not 12%) and likewise OS (53% vs 42%, absolute diff 11% and not 13%) were much more modest than advertised. There were no differences in the patterns of relapse between the two groups, specifically pelvic / abdominal or extra-abdominal sites. Importantly, only 63% of the chemo patients completed therapy as compared to 85% of the WAI group, cardiac toxicity of 15% vs 0% and 4% and 2% treatment related deaths respectively. He concluded that chemotherapy should definitely be used in advanced disease but not at the expense of radiotherapy, and that sequential chemo-radiotherapy was a logical way forward. GOG 184 randomised patients to radiotherapy followed by either cisplatin / doxorubicin or TAP with G-CSF support.

There was also discussion of newer therapies for LMS including mention of newer biological agents such as phase II data of SU11248 and sorafenib.

Of no surprise was the initial PFS / toxicity data of ICON5/GOG182 which was a 5-arm phase III randomised trial of paclitaxel (P) and carboplatin (C) vs combinations with gemcitabine (G), PEG-

liposomal doxorubicin (D), or topotecan (T) in 3836 patients with advanced-stage epithelial ovarian (EOC) or primary peritoneal (PPC) carcinoma.

Treatment was completed in 80% in all 5 groups. For the regimens evaluated, there is no evidence that adding a third active cytotoxic agent prolongs PFS in EOC with median PFS of 16 months. Analysis of OS and impact of stratification factors are in progress.

Last of all was further discussion of **GOG178** of 3 vs 12-monthly cycles of taxol following attainment of a clinically defined complete response (CR) to platinum.

Of the 146 patients on the 3-C arm, 9 (6%) actually received prolonged PAC (>3-C) following closure of the study by the DSMC. Median (12-C vs 3-C; intention-to-treat analysis):

updated PFS (all patients) 22 vs 14 months,  $p=0.01$ ; OS (all patients) 53 vs 46 months,  $p=0.27$ . Exploratory analysis (Cox models adjusting for stratification factors): 12-C vs 3-C HR 0.59 ( $p=0.03$ ) if baseline CA-125  $\leq 10$  ( $n=175$ ), and 1.25 ( $p=0.34$ ) for baseline CA-125  $>10$  ( $n=121$ ). The treatment vs baseline CA-125 interaction was statistically significant (Cox model  $p=0.03$ ). However, an unplanned exploratory analysis strongly suggested an improvement in survival for patients receiving 12-C of PAC if the baseline CA-125 level was  $\leq 10$  (67 months vs 47 months), those individuals likely to have the smallest volume of clinically-undetectable residual OC when single-agent "maintenance" PAC was initiated. This provocative data was also supported by a number of posters showing predictive value of low nadir CA 125 levels following first line chemotherapy.

ANC	PLTs	Hepatic	Pulm				
Arm	Regimen		Cycles	Gr4	Gr3/4	Gr3/4	Gr3/4
I	P-C6	[Reference Arm]	x8	59%	22%	1%	2%
II	P-C5	+ G 800 (d1, 8)	x8	74%	61%	4%	5%
III	P-C5	+ D 30 (every other cycle)	x8	69%	38%	1%	5%
IV	C5 (d 3)	+ T (d1, 2, 3)	x4 then P-C6 x4	57%	36%	2%	3%
V	C6 (d 8)	+ G 1000 (d1, 8)	x4 then P-C6 x4	56%	58%	3%	4%

Doses in mg/m<sup>2</sup> except C AUC 5 or 6 (C5 or C6); All P 175 (3 hr): All cycles q 21 d

## Report on the World Congress of the International Society for the Study of Vulvovaginal Disease (ISSVD)

20-24 February 2006, Queenstown, New Zealand

*Associate Professor David Allen  
Gynaecological Oncologist  
Mercy Hospital for Women*

The ISSVD was founded in 1970 to promote international communication among gynaecologists, pathologists, dermatologists and related disciplines, to establish international agreement on terminology and definitions of vulvovaginal diseases and to promote knowledge in the field of vulvovaginal

disease. The 2006 congress covered a wide range of issues including benign, pre-malignant and malignant conditions. Topics of interest that were presented included:

- Outcomes of stage IB/II vulvar cancer patients after radical surgical treatment – A study from Turin,

Italy looked at survival in early stage vulva cancer. Inguinal LN involvement is known to be the most important prognostic factor in vulvar cancer. In the study of 90 cases of stage IB/II vulvar cancer, 12% of patients recurred and died. Depth of stromal invasion, tumour diameter and number of nodes removed were shown not to be prognostic factors. It was suggested that future investigation should be directed towards the evaluation of biological markers.

- **False negative sentinel node in patients with vulvar cancer** – This paper, also from Turin, Italy, questioned the safety of relying on sentinel node biopsy alone in the management of vulvar cancer. They reported 2 cases of false negative sentinel nodes and discussed the 5 cases reported in the literature.
- **The neoplastic potential of lichen sclerosis** – This was discussed in a workshop setting with Ron Jones as the moderator. Little new knowledge emerged. The association of squamous cell carcinoma of the vulva with LS is 5% or less.

Benign conditions discussed included vulvodynia, vulvar vestibulitis syndrome and vulvar dermatoses, amongst others. The benign conditions dominated most of the sessions. A new classification for vulvar dermatoses was proposed and this is shown in Table 1. This classification was accepted at the meeting and will be published in the near future.

**Table 1. 2006 ISSVD Classification of vulvar dermatoses: Pathological subsets and their clinical correlates.**

<b>Spongiotic pattern</b>
Atopic dermatitis
Allergic contact dermatitis
Irritant contact dermatitis
<b>Acanthotic pattern</b> (formerly, squamous cell hyperplasia)
Psoriasis
Lichen simplex chronicus
Primary (idiopathic)
Secondary (super-imposed on lichen sclerosis, lichen planus, or other vulvar disease)
<b>Lichenoid pattern</b>
Lichen sclerosis
Lichen planus
<b>Dermal homogenisation / sclerosis pattern</b>
Lichen sclerosis
<b>Vesiculobullous pattern</b>
Pemphigoid, cicatricial type
Linear IgA disease
<b>Acantholytic pattern</b>
Hailey-Hailey disease
Darier's disease
Papular genitocrural acantholysis
<b>Granulomatous pattern</b>
Crohn's disease
Melkersson-Rosenthal syndrome
<b>Vasculopathic pattern</b>
Aphthous ulcers
Behcet's disease
Plasma cell vulvitis

## Molecular Epidemiology of Ovarian Cancer: The Australian Ovarian Cancer Study (AOCS)

*Ms Nadia Traficante, Project Manager, AOCS*

*On behalf of the AOCS Management Group (Prof David Bowtell, Prof Adèle Green, Dr Anna deFazio, Dr Georgia Chenevix-Trench, Dr Dorota Gertig, Dr Penny Webb)*

### Background

**A**OCS began in 2000 as a collaborative study between researchers at the Peter MacCallum Cancer Centre (PMCC), Queensland Institute for Medical Research (QIMR), Westmead Institute for Cancer

Research (Westmead) and University of Melbourne (UoM). In 2001 the US Department of Defense (DOD) awarded the collaborative a Program grant for national molecular epidemiological study of ovarian cancer in Australia, allowing the Australian Ovarian Cancer Study (AOCS) to commence. Funding was

provided to create Epidemiology and Bio-specimen Core facilities, for ascertainment of 1000 cases and 1000 controls from the eastern states (VIC, QLD, NSW, SA) and for the establishment of three projects within AOCs.

Since 2003, a series of 1–3 year grants from Cancer Councils in each Australian state have enabled the formation of a Clinical Follow-Up Core and the collection of detailed clinical information. This funding has been vital as collection of follow up information was not included in the DOD program and the detailed clinical annotation of bio-specimens represents a major strength of AOCs. Cancer Council funding also allowed expansion of collection to TAS and WA so that sample collection is truly national. AOCs was successful in the 2005 NHMRC Project grant round and secured funding through to 2011 for on-going collection of clinical follow-up data, allowing collection of a minimum 5-year clinical follow up on almost all cases. In addition, we were successful in our 2005 NHMRC Enabling Grant application in obtaining funding to manage and maintain the AOCs Core Facilities through to 2010.

## Progress

Recruitment and data / sample collection for AOCs is going well and the study is attracting considerable international attention. As of 25 May 2006, AOCs had recruited a total of 1788 women with invasive or borderline ovarian cancer, far exceeding our initial target. These include 421 women from New South Wales, 304 from Victoria, 507 from Queensland, 206 from South Australia, 257 from Western Australia and 93 from Tasmania. We have collected 1058 fresh tumour tissue samples, 1538 blood samples and have received a total of 1769 completed questionnaires. Patient recruitment from all centres will cease at June 30 2006. Control recruitment commenced in May 2003 is now complete. We recruited a total of 1066 control women that did not have ovarian cancer, received 1064 questionnaires and 928 blood samples, again exceeding our initial target.

As of 31 May 2006, clinical follow-up had been initiated on 2170 patients nationally (this is the total number of recruited participants, including cases that were subsequently found to be benign). The Post-Operative Data form has been completed on 92% of the total patient

population recruited to date. The Primary Treatment Form, including chemotherapy details and response to treatment, has been completed on 85% of cases that have completed their primary treatment and data collection is ongoing. Thus far, only 26 patients (1%) have been lost to follow-up despite the fact that 30–40% of our patients return to regional areas for on-going treatment.

## Research Projects

In addition to case recruitment and bio-specimen collection, DOD funding was also awarded for three major projects within AOCs to (a) examine new epidemiologic factors associated with ovarian cancer, (b) relate germline polymorphisms in hormone metabolism and DNA repair pathways to lifetime risk of ovarian cancer, and (c) identify molecular subtypes of ovarian cancer using DNA microarray-based gene expression analysis. The addition of the clinical follow-up core has allowed further analysis of overall survival, progression-free survival and response to chemotherapy in ovarian cancer patients to be associated with tumour DNA microarray expression profiles and epidemiologic and genetic risk factors. Preliminary analyses for these projects are currently underway and publications are expected in 2006.

In the last 12 months researchers external to AOCs have also applied to access AOCs data and bio-specimens to explore genes associated with X-inactivation in ovarian cancer (QIMR), to evaluate quality of life in ovarian cancer patients (Uni of Sydney and QIMR), to perform proteomic profiling of sera from cases versus controls (PMCC), for SNP-based CGH analysis of chemo-resistant ovarian cancer (PMCC and Westmead), analysis of **p53** mutation status (Hutchison/MRC labs, Cambridge, UK), and a survey of copy number change in ~200 ovarian cancer cases using SNP-based CGH analysis (PMCC in collaboration with Dana Farber).

## Collection of Relapse Ascites from Selected Cases

Resistance to chemotherapy, both intrinsic and acquired, is a major clinical issue in ovarian cancer. AOCs has created an outstanding resource to investigate the molecular pathology

of intrinsic chemo-resistance using tissue samples from women who are refractory to primary treatment. Unfortunately most women who are initially responsive to treatment will become refractory and develop progressive disease. There exists a significant opportunity to leverage work done in AOCs by collecting samples of relapsed / platinum-resistant tumour cells from patients for whom we have primary tissue samples and who were initially responsive. This can be achieved by collecting ascites that requires drainage for palliation and is rich in tumour cells. We are currently collecting ascites with our existing network, and expect to obtain matched samples from approximately 100 women.

We believe that AOCs is now the biggest study of its kind in the world and we are very grateful to everyone who has helped to make this possible.

If you have questions about any aspect of the study please feel free to contact the project managers:

- Nadia Traficante at the Peter MacCallum Cancer Centre (Bio-specimen Core – [nadia.traficante@petermac.org](mailto:nadia.traficante@petermac.org) / 03 9656 1937)
- Jillian Hung at Westmead Hospital (Clinical Follow-Up Core – [jillianh@westgate.wh.usyd.edu.au](mailto:jillianh@westgate.wh.usyd.edu.au) / 02 9845 7031)

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## National Breast Cancer Centre (NBCC) Report

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### 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 [www.nbcc.org.au](http://www.nbcc.org.au) 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](mailto: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](mailto:jane.francis@nbcc.org.au).

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## Ovarian Cancer Program Website Innovation

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At the first National Ovarian Cancer Consumer Forum held in February in collaboration with OvCa Australia (National Ovarian Cancer Network), attendees heard presentations from an ovarian cancer survivor and clinical experts in ovarian cancer. Pod casts of these highly informative presentations are now available on the National Breast Cancer Centre's (NBCC) Ovarian Cancer Program website - [www.ovariancancerprogram.org.au](http://www.ovariancancerprogram.org.au) - for those women and their families who were unable to attend the Forum. Visitors to the website can also access the speakers' PowerPoint presentations from the Forum.

The presentations available as pod casts are:

- A consumer's perspective - Ms Eugenia Koussidis

- It runs in the family: Understanding ovarian cancer risk - Dr Gillian Mitchell, Director of the Familial Cancer Centre at Peter MacCallum Cancer Centre
- Ovarian cancer treatment and challenges - Dr Deborah Neesham, Royal Women's Hospital

A summary of the key issues arising from the Forum is also available on the website as a PDF document. These key issues will inform NBCC's future work in ovarian cancer.

For further information about this project or to request a copy of the full report on the Forum, please contact Jane Francis on 02 9036 3045 or [jane.francis@nbcc.org.au](mailto:jane.francis@nbcc.org.au).

*Reprinted from Ovarian e-upd@te, June 2006, Issue 20.*

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## Gynaecological Cancer Support Website Updated

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The Gynaecological Cancer Support website [www.gynaecancersupport.org.au](http://www.gynaecancersupport.org.au) has been redesigned. The original website was developed in 2004 by a taskforce led by Dr Gerry Wain of Westmead Hospital. The website aims to foster collaborative psychosocial care for women diagnosed with a gynaecological cancer, their families and carers.

The web site provides a resource for:

- Women diagnosed with gynaecological cancer, their families and friends providing supportive information about the emotional and social issues faced when dealing with a cancer diagnosis

- Medical practitioners and women seeking referral to treatment and support services
- Health professionals currently working with women diagnosed with a gynaecological cancer
- General practitioners furthering their professional education (Royal Australian College of General Practitioners accredited e-Learning course)

For further information about the website, please contact Jane Mills on [jane\\_mills@wsahs.nsw.gov.au](mailto:jane_mills@wsahs.nsw.gov.au).

*Reprinted from Ovarian e-upd@te, June 2006, Issue 20.*

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## Australian Cancer Network (ACN) Activities

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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.*

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## The National Cancer Control Initiative (NCCI) Report

*Professor Mark Elwood  
Director, National Cancer Control Initiative*

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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](http://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.*

# Dunlop Fellowship: Development of Targeted Therapies for Cancer

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

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 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-azomycinaraboside (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

## **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.

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.

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## Report of The Cancer Council Australia

*Glen Turner  
Communications Manager  
The Cancer Council Australia*

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### 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](http://www.cancer.org.au/primarycare).

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

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## Clinical Oncological Society of Australia (COSA) Report

*Ms Margaret McJannett  
Executive Officer, COSA*

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**C**OSA 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 (AH&MR) 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, 29 November-1 December. 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.*

## Cancer Council Events Calender

### AUGUST

25 Volunteer on Daffodil Day  
[www.daffodilday.com.au](http://www.daffodilday.com.au)

26 Daffodil Ball  
[www.daffodilday.com.au](http://www.daffodilday.com.au)



### SEPTEMBER

1 Cancer Council Mazda Raffle tickets on sale – [Ph: 1300 65 6 585](tel:1300656585)

20 Sep – 4 Oct Tour for a Cure – Trek Mont Blanc  
[www.tourforcure.org.au](http://www.tourforcure.org.au)

### OCTOBER



Host a Girls Night In Month  
[www.girlsnightin.com.au](http://www.girlsnightin.com.au)

Relay for Life – Carlton, Swan Hill  
[www.relayforlife.com.au](http://www.relayforlife.com.au)

14–27 Tour for a Cure – Race Around Asia  
[www.tourforcure.org.au](http://www.tourforcure.org.au)

23 Pink Ribbon Day  
[www.pinkribbonday.com.au](http://www.pinkribbonday.com.au)



### October con't

21–22 Relay for Life – Shepparton  
[www.relayforlife.com.au](http://www.relayforlife.com.au)

28–29 Relay for Life – Echuca, Murrumbena  
[www.relayforlife.com.au](http://www.relayforlife.com.au)

### NOVEMBER



Relay for Life – Ararat, Ballarat, Bass Coast, Dandenong Ranges, Frankston, La Trobe Valley, Whitehorse  
[www.relayforlife.com.au](http://www.relayforlife.com.au)

10–22 Tour for a Cure – Trek India  
[www.tourforcure.org.au](http://www.tourforcure.org.au)

12–25 Tour for a Cure – Cycle Vietnam  
[www.tourforcure.org.au](http://www.tourforcure.org.au)

### DECEMBER

6 Cancer Council Mazda Raffle drawn

Shop online at [www.cancervic.org.au/shop](http://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](http://www.cancervic.org.au)

## Key Published Articles Listing—Gynaecological Cancer

Title	Author & Journal
<b>Chemotherapy for advanced, recurrent or metastatic endometrial carcinoma (Review)</b>	<b>Humber C, Tierney J, Symonds P, et al.</b> The Cochrane Database of Systematic Reviews 19 Oct 2005; 4: CD003915.
<b>Surgery by consultant gynecologic oncologists improves survival in patients with ovarian carcinoma</b>	<b>Engelen MJA, Kos HE, Willemse PHB, et al.</b> Cancer Feb 2006; 106(3): 589–598.
<b>Managing advanced stage cervical cancer</b>	<b>Allen D &amp; Narayan K.</b> Best Practice & Research Clinical Obstetrics and Gynaecology Aug 2005; 19(4): 591–609.

## Key Published Articles Listing—General

Title	Author & Journal
<b>Public illness: How the community recommended complementary and alternative medicine for a prominent politician with cancer</b>	<b>Lowenthal RM.</b> The Medical Journal of Australia Dec 2005; 183(11/12): 576–579.
<b>Religious perspectives on withdrawal of treatment from patients with multiple organ failure</b>	<b>Ankeny RA, Clifford R, Jordens CFC, et al.</b> The Medical Journal of Australia Dec 2005; 183 (11/12): 616–621.
<b>Clinical Cancer Advances 2005: Major research advances in cancer treatment, prevention and screening – A report from the American Society of Clinical Oncology</b>	<b>Herbst RS, Bajorin DF, Bleiberg H, et al.</b> Journal of Clinical Oncology 1 Jan 2006; 24(1): 190–205.
<b>Promoting the implementation of best-practice guidelines using a matrix tool</b>	<b>Luxford K, Hill D &amp; Bell R.</b> Disease Management & Health Outcomes 2006; 14(2): 85–90.

## Forthcoming Meetings

Date / Place	Meeting / Contact
<b>1–4 July 2006</b> Budapest, Hungary	<b>19<sup>th</sup> Meeting of the European Association for Cancer Research (EACR)</b> EACR 19 Conference Secretariat, Federation of European Cancer Societies, Avenue E. Mounier 83, B-1200 Brussels Ph: +32 2 775 02 05 Fax: +32 2 775 02 00 E-mail: <a href="mailto:EACR19@fecs.be">EACR19@fecs.be</a> Website: <a href="http://www.fecs.be">www.fecs.be</a>
<b>8–12 July 2006</b> Washington DC, USA	<b>UICC World Cancer Congress – <i>Bridging the gap: Transforming knowledge into action</i></b> American Cancer Society, 1599 Clifton Road, NE, Atlanta Georgia 30329-4251 USA Ph: +1 404 417 5998 Fax: +1 404 728 0133 E-mail: <a href="mailto:secretariat2006@cancer.org">secretariat2006@cancer.org</a> Website: <a href="http://www.worldcancercongress.org">www.worldcancercongress.org</a>
<b>14–15 July 2006</b> Adelaide, SA, Australia	<b>9<sup>th</sup> CNSA Winter Congress</b> Pre-conference workshop on 13 July Ph: (02) 9280 0577 E-mail: <a href="mailto:cnsa@pharmaevents.com.au">cnsa@pharmaevents.com.au</a> Website: <a href="http://www.cnsa.org.au">www.cnsa.org.au</a>
<b>20 July 2006</b> Washington DC, USA	<b>Gynecologic Oncology Group (GOG) Corporate Symposium</b> Ph: +1 215 854 0770 Fax: +1 215 854 0716 Website: <a href="http://www.gog.org">www.gog.org</a>
<b>21–23 July 2006</b> Washington DC, USA	<b>Gynecologic Oncology Group (GOG) Semi-Annual Meeting</b> Ph: +1 215 854 0770 Fax: +1 215 854 0716 Website: <a href="http://www.gog.org">www.gog.org</a>
<b>9–12 August 2006</b> Sanctuary Cove, QLD, Australia	<b>Annual Scientific Meeting of the Medical Oncology Group Australia (MOGA)</b> MOGA Conference Secretariat c/o Pharma Events, PO Box 265, Annandale NSW 2038 Ph: (02) 9280 0577 Fax: (02) 9280 0533 E-mail: <a href="mailto:moga@pharmaevents.com.au">moga@pharmaevents.com.au</a>
<b>3–9 September 2006</b> Sunshine Coast, QLD, Australia	<b>The Australia and Asia Pacific Clinical Oncology Research Development (ACORD) Workshop – <i>A Workshop in Effective Clinical Trials Design</i></b> ACORD Workshop, Level 6, 52 Phillip Street. Sydney NSW 2000 Ph: (02) 8247 6207 Fax: (02) 9247 3022 E-mail: <a href="mailto:mog@racp.edu.au">mog@racp.edu.au</a>

Date / Place	Meeting / Contact
<b>27 Sep – 1 Oct 2006</b> Toronto, Ontario, Canada	<b>14<sup>th</sup> International Conference on Cancer Nursing</b> 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: <a href="mailto:conference@isncc.org">conference@isncc.org</a> Website: <a href="http://www.isncc.org">www.isncc.org</a>
<b>29 Sep – 3 Oct 2006</b> Istanbul, Turkey	<b>31<sup>st</sup> Annual Congress of the European Society for Medical Oncology (ESMO)</b> ESMO Head Office, Via la Santa 7, 6962 Viganello-Lugano, Switzerland Ph: +41 91 973 1900 Fax: +41 91 973 1902 Website: <a href="http://www.esmo.org">www.esmo.org</a>
<b>8–12 October 2006</b> Leipzig, Germany	<b>European Society for Therapeutic Radiology and Oncology (ESTRO)</b> Ph: +32 2 775 9340 Fax: +32 2 779 5494 E-mail: <a href="mailto:info@estro.be">info@estro.be</a> Website: <a href="http://www.estro.be/estro/index.html">www.estro.be/estro/index.html</a>
<b>14–18 October 2006</b> Santa Monica, California, USA	<b>11<sup>th</sup> Biennial Meeting of the International Gynecologic Cancer Society (IGCS)</b> Ph: +41 22 908 0488 Fax: +41 22 732 2850 E-mail: <a href="mailto:igcs-11@kenes.com">igcs-11@kenes.com</a> Website: <a href="http://www.igcs.org">www.igcs.org</a> / <a href="http://www.kenes.com/igcs-11">www.kenes.com/igcs-11</a>
<b>15–19 October 2006</b> Perth, WA, Australia	<b>Annual Scientific Meeting of the Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG)</b> Congress West PO Box 1248 West Perth WA 6872 Ph: (08) 9322 6906 Fax: (08) 9322 1734 E-mail: <a href="mailto:conwes@congresswest.com.au">conwes@congresswest.com.au</a> Website: <a href="http://www.ranzcog.edu.au">www.ranzcog.edu.au</a>
<b>19–20 October 2006</b> Melbourne, VIC, Australia	<b>NICS Using Evidence: Using Guidelines Symposium</b> National Institute of Clinical Studies, Level 5, 499 St Kilda Road, Melbourne VIC 3004 Ph: (03) 8866 0400 Fax: (03) 8866 0499 E-mail: <a href="mailto:info@nicsl.com.au">info@nicsl.com.au</a> Website: <a href="http://www.nicsl.com.au">www.nicsl.com.au</a> / <a href="http://www.usingevidence.com.au">www.usingevidence.com.au</a>
<b>26–29 October 2006</b> Christchurch, New Zealand	<b>57<sup>th</sup> Annual Scientific Meeting of the Royal Australian and New Zealand College of Radiologists (RANZCR)</b> Website: <a href="http://www.ranzcr.edu.au">www.ranzcr.edu.au</a>
<b>1–4 November 2006</b> Rome, Italy	<b>5<sup>th</sup> Biennial International Sentinel Node Society Meeting – <i>Sentinel Node Biopsy: New Boundaries</i></b> Conference Secretariat: CQ Travel SRL, Via Pagliano, 3-20149 Milano, Italy Fax: +39 02 4391 1650 E-mail: <a href="mailto:infoeventi@ieo.it">infoeventi@ieo.it</a>

Date / Place	Meeting / Contact
<b>5–9 November 2006</b> Philadelphia, Pennsylvania, USA	<b>48<sup>th</sup> Annual Meeting of the American Society for Therapeutic Radiology and Oncology (ASTRO)</b> 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: <a href="mailto:meetings@astro.org">meetings@astro.org</a> Website: <a href="http://www.astro.org">www.astro.org</a>
<b>5–10 November 2006</b> Kuala Lumpur, Malaysia	<b>18<sup>th</sup> FIGO World Congress of Gynecology &amp; Obstetrics</b> Organised by the International Federation of Gynecology & Obstetrics (FIGO). Contact: Gregg Parker E-mail: <a href="mailto:consec@figo2006kl.com">consec@figo2006kl.com</a> Website: <a href="http://www.figo2006kl.com">www.figo2006kl.com</a>
<b>7–10 November 2006</b> Prague, Czech Republic	<b>18<sup>th</sup> International Conference on Molecular Targets and Cancer Therapeutics</b> 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: <a href="mailto:ENA2006@fecsc.be">ENA2006@fecsc.be</a> Website: <a href="http://www.aacr.org">www.aacr.org</a>
<b>7–12 November 2006</b> Toronto, Ontario, Canada	<b>54<sup>th</sup> Annual Scientific Meeting of the American Society of Cytopathology</b> American Society of Cytopathology, 400 West 9 <sup>th</sup> Street, Suite 201, Wilmington DE 19801-1555 USA Ph: +1 302 429 8802 Fax: +1 302 429 8807 Website: <a href="http://www.cytopathology.org/meetings/index.php">www.cytopathology.org/meetings/index.php</a>
<b>29 Nov – 1 Dec 2006</b> Melbourne, VIC, Australia	<b>33<sup>rd</sup> Annual Meeting of the Clinical Oncology Society of Australia (COSA)</b> COSA Office, Medical Foundation Building, Level 5, 92 Parramatta Road, Camperdown NSW 2011 Ph: (02) 9036 3100 Fax: (02) 9036 3101 E-mail: <a href="mailto:cosa@cancer.org.au">cosa@cancer.org.au</a> Website: <a href="http://www.cosa.org.au">www.cosa.org.au</a>
<b>29 Nov – 2 Dec 2006</b> Venice, Italy	<b>13<sup>th</sup> Congress of the European Society of Surgical Oncology (ESSO)</b> 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: <a href="mailto:ESSO2006@fecsc.be">ESSO2006@fecsc.be</a> Website: <a href="http://www.fecsc.be">www.fecsc.be</a>

### **Contributions Welcome**

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

	<b>Deadline</b>	<b>Issue Date</b>
Mid-year issue	1 June	1 July
Year-end issue	1 November	1 December

Contributions should be forwarded to:

The Editor, Gynaecological Cancer Update  
C/- Centre for Clinical Research in Cancer  
The Cancer Council Victoria  
1 Rathdowne Street  
CARLTON VIC 3053

[Noellyn.Ngo@cancervic.org.au](mailto:Noellyn.Ngo@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.

