



More than \$600,000 funding for clinical trial support in 2007

For the past seven years the Queensland Cancer Fund, through the Queensland Co-operative Oncology Group (QCOG), has been providing grants to support data management for phase III collaborative group studies conducted in hospitals throughout Queensland. Recently the members of the QCOG Management Committee made a recommendation for \$649,000 to be allocated to data management support in 2007. The budget also includes an allocation for seeding grants to assist institutes/research facilities endeavouring to commence a program of collaborative cancer clinical trials. The 10 Queensland research centres that will be receiving a Data Manager grant in 2007 are listed below.

Since the Cancer Clinical Trials scheme commenced in 2000, there has been a significant increase in the level of clinical trial activity in hospitals that have received funding. During the past 12 months there have been 339 patients recruited into eligible phase III co-operative group studies, with more than 450 patients on active follow-up. This represents an increase of 30 per cent compared to the previous year. The potential for more

patients to be recruited into clinical trials is enormous, but often limited by lack of funding for data management support and infrastructure. QCOG together with the Queensland Cancer Fund have been making ongoing representations to the government to seek a co-funding agreement, which if successful, will have a very positive impact on Queensland's contribution to cancer clinical research.

Institutes receiving data manager grants

- Royal Brisbane and Women's Hospital
Medical Oncology, Radiation Oncology, Gynae Oncology
- Princess Alexandra Hospital
Radiation Oncology, Medical Oncology and Haematology
- Mater Children's Hospital
- Royal Children's Hospital
- Southern Zone Radiation Services – Mater Centre
- Townsville Hospital
- Toowoomba Hospital

QCOG Group debates value of cytoreductive surgery

A small group of colorectal specialists, predominantly surgeons, met late last year at the Queensland Cancer Fund to discuss the topic of cytoreductive surgery and hyperthermic intra-operative intra-peritoneal chemotherapy (HIPEC).

Described as a radical technique which uses heated chemotherapy drugs to target cancer cells and wipe out all micro-metastatic disease cells immediately following debulking of the tumour mass, HIPEC is being used in a limited number of hospitals in the world. One centre in New South Wales has

been developing the technique; is it now Brisbane's time to develop a cytoreductive surgery and HIPEC centre?

Dr Rick Abraham provided a brief overview of data presented at the recent ASCO Annual Meeting held in Atlanta, June 2006. Results from a review of HIPEC for colorectal peritoneal carcinomatosis based on two randomised studies, one non randomised and 11 observational studies showed that morbidity ranged from 23-44%. Operation times varied from 5-9 hours with a re-operation rate of 4-11%. Overall survival was 13-32 months but

increased to 28-42 months in the group having complete resection with no residual disease (CCR-0). Where CCR was equal to zero, five year overall survival was reported as 22-49%. From the discussion at the meeting HIPEC is now the standard therapy for psuedomyxoma and peritoneal mesothelioma.

Professor Alex Crandon and Dr Allan Palmer discussed their experience with cytoreductive surgery from eight cases performed at Brisbane Private (n=7) and Mater Adult Hospitals (n=1). The patients

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ranged in age from 52-77 years. Pathology comprised five ovarian cancers, one peritoneal cancer, one peritoneal mesothelioma and one pseudomyxoma peritonei. Operation times varied from 3.5 to 17.5 hours, with up to four units of blood transfused and 3.5 to 10.5 litres of fluid replacement. One case of HIPEC has been performed. All eight patients were admitted to ICU post operatively for a period of 4-8 days with only one death occurring within 30 days of surgery - a 77 year old patient with unresolved bowel obstruction secondary to recurrent ovarian cancer. The procedure is expensive, complicated and time consuming and requires a large multi-disciplinary team involving not only the medical and nursing staff, but also the support of ancillary staff and hospital management.

Dr Brian Meade talked about his experience with HIPEC whilst working at North Hampshire Hospital, Basingstoke, UK in 2004. Initially they experienced high rates

of mortality and post-operative complication in the first 30 cases from 100 that were performed, indicating that correct patient selection was a key aspect. In addition, they were able to work with a large team of doctors on a rotating surgical roster every 2-3 hours.

Despite the many reports of good outcomes from this procedure, there is still a lack of quality comparative data. Dr David Morris is trying to establish a randomised trial to compare cytoreduction and systemic chemotherapy (SC) vs. SC alone vs. HIPEC. The challenge will be to accrue sufficient patients in a reasonable time, even with three centres operating in Australia.

By far the biggest challenge to the establishment of a Brisbane based facility will be funding. There is limited opportunity to establish a centre in a public hospital due to the pressures of waiting lists, overcrowded operating theatres and availability of ICU beds. In the private hospital, however, the

high costs associated with the procedure are not reimbursed adequately through private health insurance. Whilst these challenges are not insurmountable, it will require a dedicated team to work together to investigate thoroughly the opportunities for establishing a cytoreductive surgery and HIPEC centre in Brisbane. It was agreed that this proposal should be progressed further and that another workshop should be held in the near future.

Dr Andrew Stevenson

On behalf of the QCOG Colorectal Cancer Group

Challenges of cytoreductive surgery/HIPEC

- High morbidity and mortality
- Selected patients only
- Lack of quality data from RCT's
- Lengthy procedures
- High costs
- Extensive operating theatre logistics

The emerging role of lapatinib (Tykerb®) – The next anti-HER2 strategy

Lapatinib is an orally active, potent receptor tyrosine kinase inhibitor targeting both ErB1 and ErB2 receptors. Potential clinical use to date has focused on its activity in metastatic HER2+ breast cancer following disease progression on trastuzumab.

A phase II study of lapatinib monotherapy in 140 patients with locally advanced or metastatic HER2+ breast cancer whose disease has progressed after treatment with an anthracycline, taxane, capecitabine and trastuzumab showed a response rate of 4.3% which is not dissimilar to the early results when trastuzumab was in early development. Clinical benefit, defined as CR/PR/SD \geq 16 weeks, was reported in 10.7% of patients.¹⁻²

Preliminary data from a phase II lapatinib monotherapy study as first line treatment for locally advanced or metastatic HER2 + breast cancer (no prior trastuzumab) in 13 patients has reported PR for five patients (38%) and SD for at least eight weeks in six patients.³

Results from the pivotal phase III randomised trial (EGF100151) of lapatinib were presented at the American Society of Clinical Oncology (ASCO) meeting in June 2006. Patients with HER2+ LABC or metastatic breast cancer who developed progressive disease following prior anthracycline, taxane and trastuzumab treatment were randomised to receive either lapatinib (1250mg daily) plus capecitabine (2000mg/m² on days 1-14) (L+C) vs. capecitabine alone

(2500mg/m² on days 1-14) (C).⁴ The primary end point was time to progression (TTP) and the target patient accrual was 528. At the first planned analysis the study was closed as the primary end point had reached statistical significance with a TTP for L+C of 8.5 months compared to 4.5 months for C alone (p=0.00016). The overall response rate was 23% in the combination arm and 14% in the C arm (p=0.113). The side effect profile for L+C vs C was favourable with the most common toxicities (all grades) including diarrhoea (58% vs 39%, hand-foot syndrome (43% vs 34%) and rash and/or skin reaction (35% vs 30%). Interestingly there was a lower reported incidence of CNS relapse in the L + C compared

to C alone (4 vs 11 respectively) which did not reach statistical significance ($p=0.110$). There were only five cardiac events reported (4 L+C and 1 C), all considered asymptomatic, (\leq grade 2) reversible and there were no withdrawals due to a decrease in LVEF.

In summary, the combination of L+C produced a significantly longer median TTP in HER2+ refractory metastatic breast cancer patients compared with C alone, with a well tolerated safety profile. The low rate of cardiac toxicity and fewer patients developing CNS relapse in the combination arm have increased enthusiasm to incorporate lapatinib into clinical trials in earlier stages of HER2+ breast cancer.⁴

A phase II study with lapatinib in metastatic HER2+ breast cancer patients with new or progressive brain metastases showed a 5% (2/38 patients) partial response (PR) rate using RECIST criteria, one patient just fell short of a PR and five additional patients achieved SD > 16 weeks duration. A large international trial addressing the same question has just closed to accrual.⁵

In view of the cardiac toxicity associated with trastuzumab, a review was conducted analysing cardiac function in 3,127 patients treated with lapatinib in 18 phase I-II lapatinib trials including 10 monotherapy trials and combination trials including lapatinib and capecitabine, letrozole, paclitaxel, cisplatin, or oxaliplatin/5-fluorouracil.⁶ All patients were assessed for normal cardiac function prior to commencing lapatinib treatment. Cardiac monitoring was performed every eight weeks during treatment. Among the 1674 breast cancer patients, only 1.3% of patients experienced a decrease in LVEF, including a 1.2% asymptomatic and a 0.1% symptomatic reduction. The reduction in LVEF was detected by week eight in 65% of patients. The cardiac events improved in

57% of cases. In most cases there were confounding factors such as prior anthracyclines/trastuzumab or medical history.

New trials

TEACH (Tykerb® Evaluation After Chemotherapy) Study

This new international trial led by Paul Goss is the first Phase III trial to investigate whether adjuvant lapatinib will improve disease free survival in women with early stage HER2+ breast cancer, including those with node positive and node negative disease. Trastuzumab is now a part of standard adjuvant therapy along with chemotherapy. However, many women have received adjuvant therapy without trastuzumab. Although these patients remain at elevated risk of relapse, there is no data to date to support initiating delayed trastuzumab treatment in these patients. The TEACH trial compares efficacy and safety of 12 months of lapatinib 1500mg daily versus placebo in women treated for early stage HER2+ breast cancer who have not received trastuzumab and have no clinical or radiological evidence of disease. There is no limit on the time since completion of adjuvant therapy.

ALTTO Study (Previous APHRODITE Study)

International collaboration between BIG (Breast Cancer International Group) and NCCTG expected to commence mid 2007 and to recruit ~8000 women. This is a phase III trial study comparing trastuzumab alone vs lapatinib alone versus trastuzumab followed by lapatinib versus lapatinib concomitantly with trastuzumab in the adjuvant treatment of patients with HER2+ early stage breast cancer. There are two designs each with four arms:

Design 1 – Initiation of targeted therapy after adjuvant anthracycline-based chemotherapy WITHOUT the addition of taxanes

- Herceptin for one year
- Lapatinib for one year
- Herceptin plus lapatinib for one year
- Herceptin (three months) → three month no drug → lapatinib (six months)

Design 2 – Patients scheduled to receive paclitaxel weekly x 12 after anthracycline-based chemotherapy

- Herceptin for one year
- Lapatinib for one year
- Herceptin plus lapatinib for one year
- Herceptin (three months) concurrent with taxane → three month no drug → lapatinib (six months)

This is the final study design. Due to the limited data that is available on lapatinib, in particular the lack of data in the first line metastatic setting and limited data on the combinations, it is anticipated from the opinions voiced at the meeting that accrual to these studies in Brisbane will be limited pending further data.

Dr Nicole McCarthy
Medical Oncologist

References

1. Kaplan EH, Jones CM, Berger MS. Proc Am Soc Clin Oncol 2003;22.
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Timing of thoracic radiotherapy for limited stage small cell lung cancer – are we finally getting the answer?

Small cell lung cancer is an aggressive disease with untreated patients having a median survival of less than six months. Chemotherapy which is the mainstay of therapy has improved the prognosis although most patients still die of their disease. Disease which is limited to the chest has been shown to do better when treated with a combination of both radiotherapy and chemotherapy. However, the exact sequencing of the two modalities has been the subject of much debate for the past 15 years. It is far more practical to commence chemotherapy once the diagnosis has been established, given the fact that most radiotherapy departments have significant waiting lists. There has however been the suggestion that early integration of radiotherapy with

chemotherapy may result in improved survival for patients with limited disease.

Recently an interesting meta-analysis looked at the time factor from the commencement of any therapy until the end of the radiotherapy (SER), and its effect on survival¹. Four trials were analysed including those that had five year survival data and had both early and late radiotherapy schedules. The investigators found a significantly higher five year survival rate in patients who had a shorter SER ($p=0.0003$). However this was offset by a significantly higher rate of severe oesophagitis ($p<0.0001$). These results confirm what many clinicians have believed for some time, but implementation of this outcome is a long way away in most radiation oncology

departments in Australia. In very few hospitals are patients with small cell lung cancer able to commence both chemotherapy and radiotherapy simultaneously, and this is likely to remain until radiotherapy resources improve. Whilst small cell lung cancer remains mostly an incurable disease, it is a reality that their outlook now depends on being able to be treated in a centre which does not have a waiting list for radiotherapy.

Assoc Prof Bryan Burmeister
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Reference:

1. De Ruyscher D, Pijls-Johannesma M, Bentzen SM et al. J Clin Oncol 2006; 24: 1057 - 1063.

The Cancer Council Queensland – new name, same values

The Queensland Cancer Fund has announced it will soon change its name to The Cancer Council Queensland.

The state's leading anti-cancer organisation will also adopt the daffodil – the international symbol of hope - as its new logo from May 1 this year.

Supporters are encouraged to join in the celebrations for this exciting change, with events planned in towns and cities across the state to commemorate the occasion.

While our name and logo will change, our values, services and commitment to the Queensland community will stay the same.

The decision to change to The Cancer Council Queensland was made after extensive consultation with volunteers, partners and supporters, and will enable us to work closely with interstate counterparts.

We will be able to take every opportunity to highlight cancer support services in the community such as the Cancer Helpline, available on 13 11 20 in each state.

The change will also help reduce costs associated with organising national events including Daffodil Day, meaning more money is spent on research, support and education.

Money donated in Queensland will continue to be invested in

Queensland, and the generous donations we receive from Queenslanders will allow us to invest more than \$8 million in cancer research across the state in 2007.

While all materials printed from now on will have The Cancer Council Queensland name and logo, materials bearing the Queensland Cancer Fund name and logo will continue to be used.

If you have any questions or comments regarding this change, please visit our website at www.qldcancer.com.au/namechange, email us at namechange@qldcancer.com.au or call us on (07) 3258 2331.

Improved survival with the addition of rituximab to CHOP-like chemotherapy for good-prognosis diffuse large B cell lymphoma (DLBCL): results of the MInT study.

This was a ground-breaking randomised control trial involving 824 'young' (age 18-60 years) DLBCL patients with stage II-IV disease (or stage I bulk) from 18 different cooperative groups¹. The Australasian Leukaemia Lymphoma Group component was coordinated by Drs Gill and Ma, and contributed approximately a tenth of all patients. Patients were randomised to six cycles of CHOP-like chemotherapy with or without rituximab. Entry criteria were confined to nil or one age-adjusted IPI risk factor. The 'best-risk' patients i.e. stage 1 with no bulky disease, and poorer-risk patients, i.e. more than one risk factor, were excluded. Median follow-up was three years. Patients assigned chemotherapy and rituximab had increased overall survival, progression free survival and event-free survival as compared to chemotherapy alone (see Figure 1). Nearly twice as many patients failed chemotherapy compared to chemotherapy with rituximab, suggesting that the increased cost of immunotherapy might in part be offset by the reduced need for salvage therapy and autologous stem cell transplantation.

As a consequence of the international dimension, it was necessary to include a number of different CHOP-like regimens, including CHOEP (etoposide 100mg/m² i.v. or 200mg/m² p.o. on days two and three) which had been previously reported to be more efficacious than CHOP in young good-risk patients². Although not a planned end-point, the benefit of CHOEP over CHOP was confirmed, but interestingly this benefit was not observed with the addition of rituximab.

A favourable group (no bulk and no IPI=0) could be defined with improved EFS. Trials are now underway in these patients to reduce the number of CHOP cycles to four whilst keeping six of rituximab. This move is a potential indication of future trends where immunotherapy approaches will hopefully reduce the requirement for chemotherapy. Those young patients with less favourable disease (bulk and/or IPI=1) are being randomised to R-CHOP-21 or 'dose-dense' R-CHOP-14 in a Deutsche Studiengruppe für Hochmaligne Non Hodgkin Lymphome (DSHNHL) study. The finding that bulky disease (>7.5cm) emerged as a prominent risk factor (despite

the use of radiotherapy to sites of bulk) questions the role of radiotherapy in this setting and will be the subject of an additional randomisation by the DSHNHL. Lastly, owing to limited international availability, MInT did not utilise functional imaging for response definition. Use of FDG-PET will assist the management of these patients, with more accurate response assessment that will hopefully reduce the need for radiotherapy. In addition, the widespread availability of FDG-PET in Australia has encouraged the ALLG to perform a study assessing the role of FDG-PET directed therapy in DLBCL. This study is currently under development.

Dr Maher Gandhi
Consultant Haematologist
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References

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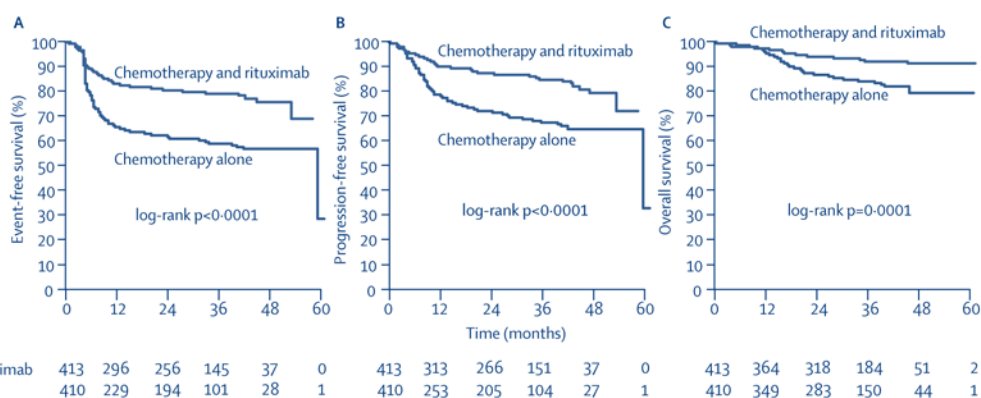


Figure 1: (A) Event-free survival, (B) progression-free survival, and (C) overall survival of 823 patients assigned to CHOP-like chemotherapy alone (n=410) or to CHOP-like chemotherapy and rituximab (n=413)

How is lung cancer managed in Queensland?

The answer to this question is to be addressed through the conduct of the first population based survey of all cases of lung cancer diagnosed over a six month period during 2004. Patients will be identified from notifications to the Queensland Cancer Registry and survey forms will be sent to the nominated treating doctor, including where applicable, surgeons, respiratory physicians, medical oncologists, radiation oncologists and general practitioners. Data collection will commence at the beginning of this year and continue for approximately nine months.

This project is being undertaken as part of the Queensland Integrated Lung Cancer Outcomes Project (QILCOP) and will provide, for the first time, a complete

picture of how lung cancer is diagnosed and treated in Queensland. This is particularly important in identifying those patients that are not included in QILCOP and will help us to understand better the role of multidisciplinary care in the treatment of patients with lung cancer. It will be greatly appreciated if all doctors who receive a survey form can complete it to the best of their ability and ensure that it is returned to the Queensland Cancer Registry. Any questions regarding the project can be directed to the QILCOP Team or Project Co-ordinator Heather Day ph: (07) 3258 2306.

**Assoc Prof Kwun Fong and
Dr Rayleen Bowman**

On Behalf of the QILCOP Team

A joint initiative of the Queensland Integrated Lung Outcomes Project (QILCOP) and the Queensland Cancer Fund

Clinical Practice Survey of lung cancer in Queensland

Chemotherapy questionnaire

To be completed by the clinician responsible for the management of the patient identified below with primary lung cancer.

PATIENT IDENTIFICATION

Name	
Address	
Date of Birth	

Instructions for completion

- Please answer all questions. If the answer is unknown, please indicate 'unknown' next to the question.
- If additional space is required, please attach a separate sheet.

Have you been sent this questionnaire by mistake?
If so, please indicate the problem below, detach this sheet and return it to:
Queensland Cancer Registry
Locked Bag 1450
Spring Hill QLD 4004

This patient's cancer in the lung was a secondary from a different primary site.

I was not responsible for the chemotherapy for this patient's lung cancer.
I suggest you send the questionnaire to:
Doctor's name: _____
Address: _____
Phone No: _____

I do not know of this patient.

If you have any further questions about completing the questionnaire please contact the project co-ordinator
Ph: (07) 3258 2332 Fax: (07) 3258 2345

This questionnaire is adapted with the kind permission of The Cancer Council NSW

Lung cancer special interest group

It has been sometime since the Lung Cancer Group held a meeting, so the new year will start with our first meeting on Tuesday, February 20, 2007 from 6.30pm at the Queensland Cancer Fund. The topic for the meeting will be chemo-radiation for NSCLC with a range of interesting presentations and discussion on a

proposed protocol for a multicentre clinical trial to be undertaken in Queensland.

For further information regarding the meeting please contact the QCOG Professional Officer.

Dr Keith Horwood

Chairman, QCOG Lung Cancer Group

Have you joined QCOG?

For further information regarding membership of QCOG or to join the mailing list to receive further newsletters and updates, please contact:

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Oncology Group**



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