ANZ GOG

20 years improving life for women through cancer research

2000-2010
THE FIRST 10 YEARS

OUR PURPOSE

Our purpose is to improve outcomes and quality of life for women with gynaecological cancer through conducting and promoting cooperative clinical trials and undertaking multidisciplinary research into the causes, prevention and treatments of gynaecological cancer.

ACKNOWLEDGEMENT

We acknowledge the traditional owners of country throughout Australia, and their continuing connection to land, sea and community. We pay our respects to them and their cultures, and to elders both past and present and all Aboriginal and Torres Strait Islander people, from whatever nation they may come.

In particular, we acknowledge the Gadigal people of the Eora nation, and the people of the Kulin nation as the traditional owners of the lands and waters where our offices are located.

For Māori, the indigenous people of Aotearoa New Zealand we acknowledge Papatuanuku as our Earth Mother, and it is from her bond with Ranginui, the sky father, that we, and all the plants and creatures on earth, descend.

From this whakapapa or lineage, we are connected by a common bond and for us as Māori this translates into an obligation as kaitiaki or guardians to care for and protect our land and resources and to maintain their life-sustaining properties for the benefit of present and future generations.

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AUSTRALIA NEW ZEALAND GYNAECOLOGICAL ONCOLOGY GROUP

FIRST GROUP MEETING HELD 16-17 JUNE 2001 AT BRIGHTON-LE-SANDS IN SYDNEY.

TOTAL ANZGOG MEMBERS AT THE TIME – 113.
22 SITES SIGNED UP TO PARTICIPATE IN CLINICAL TRIALS:

LOCATION	HOSPITAL SITES
ACT	The Canberra Hospital
NSW	Royal Prince Alfred Hospital Royal Women's Hospital, Prince of Wales Royal North Shore Hospital Westmead Hospital Liverpool Hospital St George Hospital Newcastle Private Hospital
VIC	The Royal Women's Hospital Mercy Hospital for Women Peter MacCallum Cancer Centre Monash Medical Centre Border Medical Oncology
TAS	Royal Hobart Hospital
QLD	Royal Brisbane and Women's Hospital The Wesley Hospital
SA	Royal Adelaide Hospital King Edward Memorial Hospital
NZ	Auckland Hospital Christchurch Hospital Palmerston North Hospital Wellington Hospital

"It was becoming clear by the 1990s that women who were on clinical trials had better outcomes than those who did not have access. Originally, the gynaecological group of COSA was active but this all fell away especially after the Australian Society of Gynaecologic Oncologists (ASGO) got up and running so there was a clear need for a new multidisciplinary group. The aim was to ensure that everyone interested in the care of women with gynaecological cancer had the opportunity to join. Our vision was simple; have every State represented and become relevant nationally and internationally."

PROF MICHAEL QUINN AM
ANZGOG CHAIR | 2008-2012
FORMER PRESIDENT - IGCS
FORMER CHAIR - GCIG

Prof Michael Quinn AM (left) with Assoc Prof Philip Beale.

A HISTORY OF ANZGOG'S FIRST 20 YEARS

ANZGOG is the peak, national gynaecological cancer research organisation for Australia and New Zealand. We conduct clinical trials across 59 hospital sites and have grown from 200 members in 2000 to 1050 members in 2020. ANZGOG's members are dedicated to expanding the research portfolio in treatment, surgery, radiation oncology, quality of life and survivorship. Together with our staff, donors and partners, our members work to improve life for women through cancer research.

2000-2010

ANZGOG was first established because, unlike the USA, Canada and Europe, there was no gynaecological collaborative trials group in Australia and New Zealand and this needed to change. The plan was to establish a vibrant multidisciplinary clinical trials group that would improve access for women in Australia and New Zealand to cutting-edge clinical trials that, in time, would define new standards of care and improve outcomes. It was unanimously agreed that this was the best way to improve outcomes for patients with gynaecological cancers.

It is important to acknowledge the enormous contributions made by the founders of ANZGOG – Prof Michael Friedlander AM, Prof Michael Quinn AM, and Prof Danny Rischin. It was through their perseverance, determination, and dedication that ANZGOG was able to establish critical, collaborative relationships with international groups such as Gynecologic Oncology Group (GOG) and Gynecologic Cancer InterGroup (GCIG), enabling us to access the main stage of global gynaecological cancer research. These collaborations gave women in Australia and New Zealand access to new treatments through international trials, but also kick-started ANZGOG's capacity to produce its own home-grown clinical trials.

We also recognise the significant support that the NHMRC Clinical Trials Centre (CTC), at the University of Sydney have given us throughout our past, particularly in these first 10 years.

ANZGOG is a great organisation that managed to progress in its first 10 years, participating in 14 trials involving over 1470 patients. The early work done gave us a great foundation on which to build and move forward. This has been possible because of the energy, commitment, and enthusiasm of all its members.

2010-2020

This next 10 years shows how we have become the peak national gynaecological cancer research organisation with over 1,000 members, driving key strategic pathways for new research developed by Australian and New Zealand investigators, while continuing our international collaborations, education and engagement with people affected by gynaecological cancers.

ASSOC PROF PHILIP BEALE
CHAIR | ANZGOG
AS AT JUNE 2021

“I spent countless hours knocking on doors of everyone I knew to secure research funding.

The group gained confidence and started to apply for funding to undertake more trials after GOG182. Patients and their families donated money and the long hours writing grants started to pay off.”

PROF MICHAEL FRIEDLANDER AM

THE BEGINNING OF ANZGOG

In 1999, a small group of gynaecologic, medical and radiation oncologists met and unanimously agreed that we needed to establish a gynaecologic trials group in Australia and New Zealand. There was no funding available for collaborative trial groups and despite a lot of effort to secure funds in Australia it was clear that this would not be forthcoming. There was little appreciation of the importance of clinical trials within the health bureaucracy or funding bodies at that time and we recognised we needed to obtain funding from outside Australia if we were to have any chance of success. Through the help of Ted Trimble as well as the support of the Chair of the GOG I was able to join the US GOG as the Principal Investigator for Australia with all other centres in the country included as affiliates of the Prince of Wales Hospital and this provided access to funding from the US which kick-started ANZGOG.

Danny Rischin and Michael Quinn were integral to the founding of the organisation. There was an enormous amount of work done to secure new opportunities to carry out research trials. It dominated many years of my life but I look back with very good memories of how we all worked together with a common aim. Before long, success started to breed success and we didn’t look back.

John Zalcberg provided invaluable advice early on as he had set up the GI Cancer Group, AGITG, only a few years earlier. I also need to acknowledge Haryana Dhillon, whose support was pivotal in setting up ANZGOG. She was just great and worked so hard to help us get ANZGOG off the ground. The Clinical Trials Centre (CTC – University of Sydney) was also very helpful, particularly John Simes as Director and Julie Martyn as ANZGOG Program Manager. We were a small group of people working hard to make sure ANZGOG continued to grow.

“GOG182 was the first large international clinical trial in ovarian cancer carried out in Australia and as Principal Investigator for ANZGOG as well as Chair of the group, I was ultimately responsible for our performance. I recall the enormous effort and time we all put into the trial and this was an important foundation for the future success of ANZGOG. We quickly learned what was expected of us and we ensured that we met all our obligations and I am still very proud of how we met this challenge.”

PROF MICHAEL FRIEDLANDER AM
INAUGURAL CHAIR - 2000-2008 | ANZGOG
PRINCIPAL INVESTIGATOR | GOG182

Prof Danny Rischin

ANZGOG TRIALS 2000 - 2010

“ ANZGOG has grown from a fledgling organisation to a well-respected trials group with a strong trial portfolio and recognised gynaecological cancer research expertise.

In the early days, much of the work was done by a limited number of people, but now there is broader involvement with many younger investigators interested in conducting gynaecological cancer trials and being involved in ANZGOG.

The group has evolved from predominantly participating in GCIG trials to having an increasing number of ANZGOG-initiated projects, with several based on basic research conducted in Australia. ”

PROF DANNY RISCHIN
INAUGURAL CHAIR | ANZGOG RESEARCH ADVISORY COMMITTEE

CLINICAL TRIALS

GOG182

STUDY	GOG182
TITLE	A phase III randomised trial of paclitaxel and carboplatin versus triplet or sequential doublet combinations in patients with epithelial ovarian or primary peritoneal carcinoma
SUMMARY	Three new drugs appear promising for the treatment of ovarian and peritoneal cancer. These drugs are topotecan (Hycamtin), gemcitabine (Gemzar), and liposomal doxorubicin (Caelyx). This particular study will test different ways of combining each of these drugs with one of the standard treatment programs. The doses and schedules for each combination have been adjusted to have similar side effects and overall duration of treatment. All of the drugs in this study are also used individually for the treatment of ovarian cancer. The combination of carboplatin and paclitaxel is one of the standard treatments for ovarian cancer. It is hoped that adding a third drug to the combination of carboplatin and paclitaxel will improve the overall success of the treatment program.
ANZGOG PI	Prof Michael Friedlander AM
PI INSTITUTION	Prince of Wales Hospital
CANCER TYPE	Ovarian
PHASE	Phase III
TYPE OF TRIAL	Intervention
DRUG/S	Paclitaxel, carboplatin, gemcitabine hydrochloride (Gemzar), pegylated liposomal doxorubicin hydrochloride (Caelyx), topotecan hydrochloride (Hycamtin)
LEAD GROUP, COUNTRY	GOG, US-led international trial; ANZGOG-led in Australia and New Zealand
COLLABORATIONS	IMN, MRC-UK, SWOG, NCI
SPONSOR	The University of Sydney
OPERATING CENTRE	NHMRC Clinical Trials Centre
NUMBER OF SITES	26 ANZ
RECRUITMENT	4,312 Total, 184 ANZ
FUNDING	GOG, ANZGOG

> *"At the time GOG182 was conceived, a number of phase II trials were reporting close to 100% response rates with triplet combinations such as carboplatin, paclitaxel and gemcitabine. On the basis of these trials, more aggressive first-line regimens were being incorporated into clinical practice. It was essential to determine whether the addition of more drugs to the carboplatin and paclitaxel backbone made a difference and improved outcomes."*

PROF MICHAEL FRIEDLANDER AM
PRINCIPAL INVESTIGATOR | GOG182

WHAT WAS THE FOCUS OF GOG182?

GOG182 was a phase III randomised trial of paclitaxel and carboplatin versus triplet or sequential doublet combinations in patients with epithelial ovarian or primary peritoneal carcinoma.

It was the first collaborative group trial undertaken by ANZGOG and the largest trial ever carried out in women with advanced ovarian cancer.

The trial ran at multiple sites around Australia and New Zealand. It enrolled 184 patients and, despite the fact that many sites had no experience with the rigour and trial oversight required in GOG trials, the standard at all sites was very high, passing all rigorous on-site GOG audits.

WHAT DID GOG182 FIND?

GOG182 demonstrated the importance of confirming the positive results of phase II trials and testing combination therapies in phase III trials.

The trial cemented carboplatin and paclitaxel every 3 weeks as the optimal first line treatment for advanced ovarian cancer. This combination remains standard of care 20 years later despite other promising treatment strategies that have been explored in the interim.

There have been a number of additional sub studies and many publications generated by this trial, which have informed the design of future trials.[1,2,3,4]

WHY WAS GOG182 IMPORTANT?

GOG182 brought together a number of other international trials groups and was one of the first GCIG trials. The trial helped to cement the importance of international collaboration to answer important questions.

GOG182 has also been a critical part of the ANZGOG journey. Without the funds and support received from the GOG and CTEP, ANZGOG would not have been established in 2000 and it would be years before we could access funding for a collaborative gynaecological cancer trials group in Australia.

> *"It was virtually impossible to obtain funding in Australia to establish ANZGOG in the late 1990s. GOG182 was the catalyst for ANZGOG and its success as a clinical trials group. Funds provided by the Cancer Therapy Evaluation Program (CTEP) and the US Gynaecologic Oncology Group (GOG) were essential to ANZGOG's establishment. The trial gave ANZGOG a seat at the GCIG table and demonstrated that we have the ability and capacity to carry out complex collaborative clinical trials."*

[1]Bookman MA, Brady MF, McGuire WP et al. Evaluation of new platinum-based treatment regimens in advanced-stage ovarian cancer: a Phase III Trial of the Gynecologic Cancer Intergroup. J Clin Oncol. 2009;27(9):1419-25
[2]Rose PG, Java JJ, Salani R et al. Nomogram for Predicting Individual Survival After Recurrence of Advanced-Stage, High-Grade Ovarian Carcinoma. Obstet Gynecol. 2019;133(2):245-254
[3]Olawaiye AB, Java JJ, Krivak TC et al. Does adjuvant chemotherapy dose modification have an impact on the outcome of patients diagnosed with advanced stage ovarian cancer? An NRG Oncology/Gynecologic Oncology Group study. Gynecol Oncol. 2018;151(1):18-23
[4]Rungruang BJ, Miller A, Krivak TC et al. What is the role of retroperitoneal exploration in optimally debulked stage IIIC epithelial ovarian cancer? An NRG Oncology/Gynecologic Oncology Group ancillary data study. Cancer. 2017;123(6):985-993

CLINICAL TRIALS

GOG191

STUDY	GOG191
TITLE	A phase III trial to evaluate the efficacy of maintaining haemoglobin levels above 120 g/L with erythropoietin versus above 100 g/L without erythropoietin in anaemic patients receiving concurrent radiation and cisplatin for cervical cancer
SUMMARY	The standard therapy for cancer of the cervix is treatment with chemotherapy and radiation. One of the possible side-effects of this standard treatment is a significant drop in haemoglobin. When haemoglobin levels are low, oxygen is not circulated and taken into the body's tissues and organs, as it should be. A low haemoglobin level can make patients feel very tired and could also negatively impact response to treatment with radiation and chemotherapy. The purpose of this study is to determine if a product called erythropoietin (Eprex or Procrit) will raise haemoglobin levels and improve control of the disease. It is unknown whether the administration of the erythropoietin will improve outcomes. On this study all patients will receive the chemotherapy drug cisplatin and radiation therapy. Transfusion will be given if haemoglobin level is very low. Other patients will receive the cisplatin and radiation therapy with the addition of erythropoietin. Transfusion will be given if the haemoglobin level is very low or if it falls abruptly from bleeding.
ANZGOG PI	Dr Michelle Grogan
PI INSTITUTION	Prince of Wales Hospital
CANCER TYPE	Cervical
PHASE	Phase III
TYPE OF TRIAL	Intervention
DRUG/S	R-HuEPO (Eprex/Procrit), cisplatin
LEAD GROUP, COUNTRY	GOG, US-led international trial; ANZGOG-led trial in Australia and New Zealand
COLLABORATIONS	NCI, CCTG
SPONSOR	The University of Sydney
OPERATING CENTRE	NHMRC Clinical Trials Centre
FUNDING	GOG funded by National Cancer Institute

> *"The study closed prematurely, with less than 25% of the planned accrual due to potential concerns for thromboembolic event with R-HuEPO – no patients in ANZ were recruited prior to trial being suspending. The GOG-191 trial was officially closed to recruitment on 17 January 2004 as per memorandum received from GOG dated 29 January 2004."*

ASSOC PROF PHILIP BEALE
CHAIR | ANZGOG

CLINICAL TRIALS

ANZGOG 02-01

STUDY	ANZGOG 02-01
TITLE	A phase II trial of weekly docetaxel (taxotere) for patients with relapsed ovarian cancer who have previously received paclitaxel
SUMMARY	Docetaxel is an active drug in ovarian cancer and is approved for use in ovarian cancer in Australia. In the initial trials in ovarian cancer, docetaxel was administered at a high dose every 3 weeks, but in other cancers a lower dose given weekly has subsequently been shown to have similar effectiveness with less side effects. The aim of this trial is to determine whether the weekly schedule of docetaxel has similar effectiveness but less side effects in women with relapsed ovarian cancer who have previously received chemotherapy.
ANZGOG PI	Prof Danny Rischin
PI INSTITUTION	Peter MacCallum Cancer Institute and Mercy Hospital for Women
CANCER TYPE	Ovarian
PHASE	Phase II
TYPE OF TRIAL	Intervention
DRUG/S	Docetaxel
LEAD GROUP, COUNTRY	ANZGOG-led trial in Australia and New Zealand
SPONSOR	The University of Sydney
OPERATING CENTRE	NHMRC Clinical Trials Centre
NUMBER OF SITES	10 ANZ
RECRUITMENT	37 ANZ
FUNDING	Sanofi-Aventis

INTERNATIONAL COLLABORATIONS
THE EARLY YEARS

International collaborations were essential to enable women to access clinical trials as there was no collaborative gynaecological cancer clinical trials group in Australia and New Zealand before ANZGOG.

GYNECOLOGIC ONCOLOGY GROUP (GOG)

There were early attempts to start a trials group in Australia and New Zealand from 1992. Prof Michael Friedlander AM regularly went to the USA to take part in meetings by the recognised US cancer clinical trials group, the Gynecologic Oncology Group (GOG). Joining this group would enable significant clinical trials to be available in ANZ. The first approach for Australia to join GOG was unsuccessful. Prof Friedlander AM continued to attend GOG meetings regularly throughout these early years and met a lot of people including Ted Trimble who represented the Cancer Therapy Evaluation Program (CTEP).

After almost 10 years, ANZGOG obtained provisional membership in 2001. Ted Trimble was instrumental in helping obtain funding from the USA which helped to kick start ANZGOG.

GYNECOLOGIC CANCER INTERGROUP (GCIG)

Connecting internationally was vital to making new treatments available for women. The Gynaecologic Cancer InterGroup (GCIG) has a multi-country membership and meets twice per annum to discuss collaborations around the world on clinical trials in gynaecological cancers.

At Prof Michael Friedlander's instigation, Prof Michael Quinn and Prof Danny Rischin started attending the regular GCIG meetings. One of the major goals was to provide opportunities to ANZ investigators to develop new concepts and where appropriate to take them to GCIG for international collaboration.

INTERNATIONAL GYNECOLOGIC CANCER SOCIETY (IGCS)

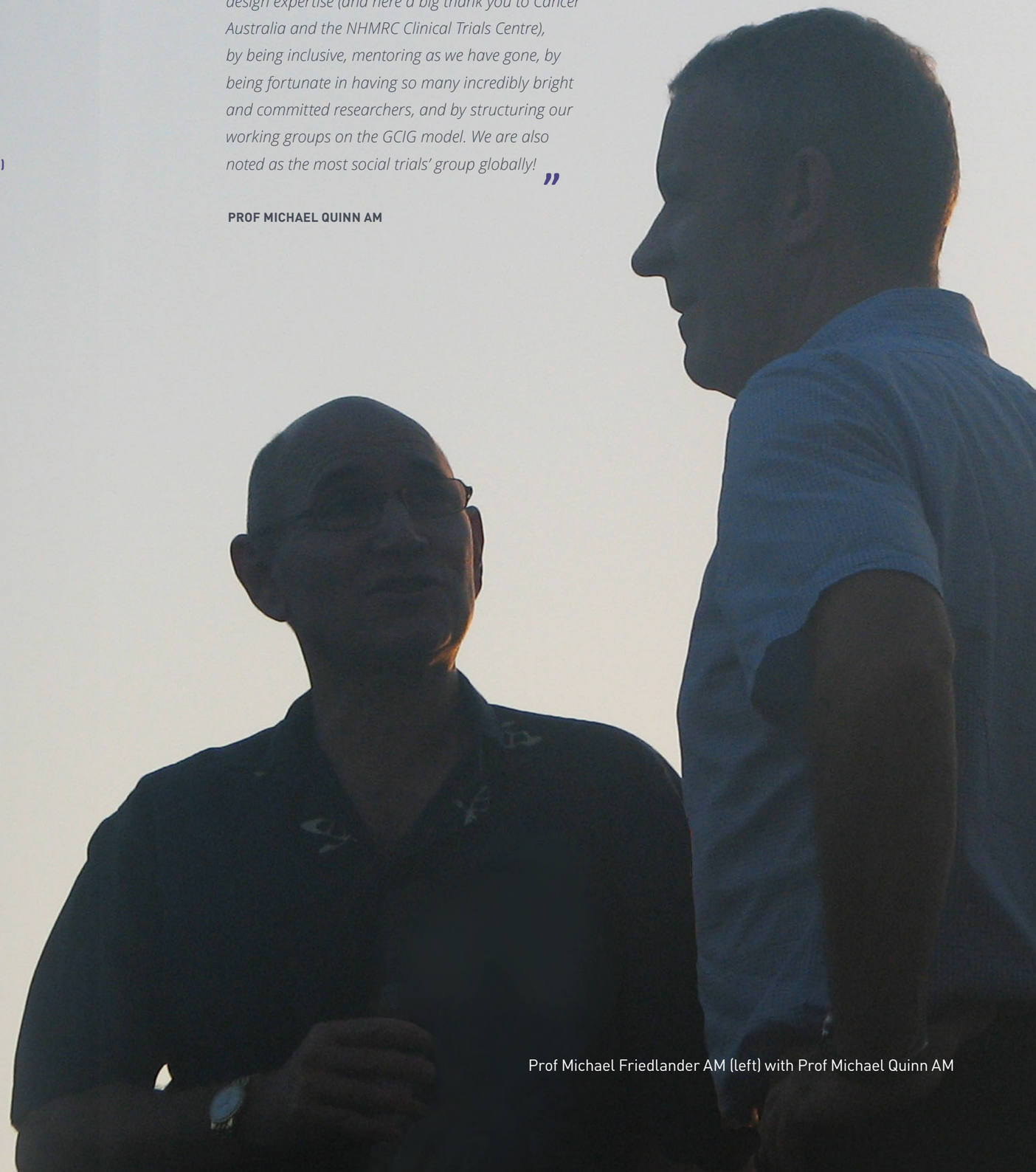
ANZGOG's reputation grew quickly after gaining a seat at the international tables. Co-founder and former Chair of ANZGOG Prof Michael Quinn [2008-2012], later became Chair of GCIG (2012-2014) and President of the International Gynecological Cancer Society (IGCS).

Today, ANZGOG has several members who hold positions on the GCIG and IGCS committees and on their councils, demonstrating our leadership in gynaecological cancer research.

The collaboration of many ANZGOG members on international research committees and organisations continues to underpin the knowledge, education and strategic directions of our clinical research program.

> *"In reality, we were pretending that we had a formal ANZ group, taking it in turns to pay the annual dues to the GCIG. We worked hard to establish ANZGOG, and we were very pleased when we could finally advise GCIG about the formation of ANZGOG."*
>
> **PROF DANNY RISCHIN**

> *"We have gone from the new kids on the block to world leaders, basically by accessing funds and trial design expertise (and here a big thank you to Cancer Australia and the NHMRC Clinical Trials Centre), by being inclusive, mentoring as we have gone, by being fortunate in having so many incredibly bright and committed researchers, and by structuring our working groups on the GCIG model. We are also noted as the most social trials' group globally!"*
>
> **PROF MICHAEL QUINN AM**



Prof Michael Friedlander AM (left) with Prof Michael Quinn AM

CLINICAL TRIALS

GOG199

STUDY	GOG199
TITLE	A prospective study of risk-reducing salpingo-oophorectomy and longitudinal CA-125 among women at increased genetic risk of ovarian cancer
SUMMARY	Women who are genetically predisposed to ovarian cancer are at very high risk of developing this disease. Although risk-reducing salpingo-oophorectomy (RRSO) and various screening regimens are currently recommended to reduce ovarian cancer risk, the optimal management strategy has not been established nor have multiple additional issues been adequately addressed. This is a prospective, international, two-cohort, nonrandomized study of women at genetic risk of ovarian cancer, who chose either to undergo RRSO or screening, at study enrolment. Primary study objectives include quantifying and comparing ovarian and breast cancer incidence in the two study groups, assessing feasibility and selected performance characteristics of a novel ovarian cancer screening strategy (the Risk of Ovarian Cancer Algorithm), evaluating various aspects of quality of life and nononcologic morbidity related to various interventions in at-risk women, and creating a biospecimen repository for subsequent translational research.
ANZGOG PI	Prof Kelly-Anne Phillips
PI INSTITUTION	Peter MacCallum Cancer Centre
CANCER TYPE	Ovarian
TYPE OF TRIAL	Observational
LEAD GROUP, COUNTRY	GOG, US-led international trial; ANZGOG-led trial in Australia and New Zealand
COLLABORATIONS	Clinical Genetics Branch, Cancer Genetics Network
SPONSOR	The University of Sydney
OPERATING CENTRE	NHMRC Clinical Trials Centre
NUMBER OF SITES	4 ANZ
RECRUITMENT	2,605 Total Worldwide, 83 ANZ
FUNDING	GOG, ANZGOG

"I was offered the opportunity by ANZGOG to be the national PI on GOG199 when I was a relatively junior researcher. This opportunity enabled me to build my research career and develop and strengthen my national and international collaborations.

I am particularly grateful for the mentorship of Prof Michael Friedlander AM who provided wise and practical support to me throughout the trial."

PROF KELLY-ANNE PHILLIPS
PRINCIPAL INVESTIGATOR | GOG199

WHAT WAS THE FOCUS OF GOG199?

GOG199 was a prospective study of risk-reducing salpingo-oophorectomy (RSSO) and longitudinal CA-125 screening in women with ovarian cancer.

GOG199 commenced a few years after the discovery of the BRCA1 and BRCA2 genes. At the time there was little information about the value of potential strategies to manage ovarian and fallopian tube risk – specifically screening with a combination of ultrasound of the ovaries and a CA-125 blood test, and risk-reducing bilateral salpingo-oophorectomy.

It was not feasible to do a randomised clinical trial of these two approaches, as it was unlikely that many women would agree to being randomly assigned to one or the other. Instead, GOG199 was an observational study in which women would choose the approach they wished to take, with the option for those who initially chose screening to swap to surgery at any time.

The study aimed to explore:

a) why women might choose one approach over the other

b) what the quality of life (QoL) might be for women in each group

c) how often unexpected cancer would be present in the ovaries

d) whether more intensified screening every 3 months would be more successful than 6 monthly screening.

GOG199 was led through the University of Sydney and the study recruited 2,605 women worldwide (83 of whom were recruited in Australia and New Zealand). Of these, 40% initially chose surgery and 60% initially chose screening.

"This cancer prevention study shows that ANZGOG is committed to research that improves outcomes across the ovarian cancer disease trajectory. GOG199 showed that ANZGOG can conduct successful studies in collaboration with cancer genetics services and can be high recruiters to studies of BRCA1 and BRCA2 mutation carriers. This has resulted in the invitation for ANZGOG to participate in STICs and STONEs in 2018."

WHAT DID GOG199 FIND?

- Women who chose surgery rather than screening were more likely to be older, more worried about ovarian and fallopian tube cancer and more concerned about the limitations of ovarian cancer screening.
- Early cancers were unexpectedly found in the ovaries or fallopian tubes in about 4% of BRCA1 and BRCA2 mutation carriers.
- 3-monthly rather than 6-monthly screening and looking at the rate of rise of the CA-125 blood test, not just the absolute level, seemed to be a promising approach (but needs further research).
- Women who chose RRSO had lower health-related QoL, greater ovarian cancer-related stress, greater anxiety, and more depressive symptoms. However, these improved after surgery, especially cancer-related stress. Screening did not adversely affect QoL. Menopausal symptoms and sexual functioning worsened during follow-up in both groups, but more so among participants who underwent RRSO (of whom very few were taking hormone replacement therapy (HRT) which can help ameliorate these symptoms).

WHAT IMPACT HAS GOG199 HAD?

Ovarian and fallopian tube cancer screening remains experimental and should not be done outside of a clinical study in Australia.

There are negative consequences of putting pre-menopausal women through a surgical menopause in order to minimise their ovarian and fallopian tube cancer risk. GOG199 highlights the importance of thoroughly discussing the impact of surgery to remove the ovaries and fallopian tubes with women before the procedure. It also demonstrates the importance of actively managing menopausal and sexual symptoms after surgery.

WHAT HAVE WE LEARNED FROM GOG199?

GOG199 highlights the important message that for BRCA1 and BRCA2 mutation carriers, at the current time screening is not adequate (and is not recommended by national guidelines) and risk-reducing surgery is strongly encouraged at an appropriate age just before ovarian cancer risk starts to rise above that of the general female population.

GOG199 also collected longitudinal blood samples and tissue from women. These have been used in global collaborations to better understand the genetic variants other than BRCA1 and BRCA2 that play a role in ovarian cancer risk and prognosis.

When functioning normally, BRCA1 and BRCA2 help to prevent cancer. However, when a woman inherits an abnormal copy of one of these genes she is at high risk for ovarian, fallopian tube and breast cancer.

The increased risk for ovarian and fallopian tube cancer does not generally start to become apparent until women are approaching their 40s (for BRCA1) or over 50 (for BRCA2): at younger ages the risk is the same as for the average woman and is very low.

NEXT STEPS

Much more work needs to be done to prove that screening with ultrasound and CA-125 testing can detect ovarian and fallopian tube cancers often enough at an early and potentially curable stage for ovarian cancer screening to become standard of care for BRCA1 and BRCA2 mutation carriers.

Currently, based on the evidence, Cancer Australia does not recommend ovarian or fallopian tube cancer screening for any woman without symptoms, regardless of her level of risk for these cancers.

ANZGOG is now participating in another clinical trial, STICs and STONEs, which is looking at the role of aspirin in prevention of ovarian and fallopian tube cancer in BRCA1 and BRCA2 mutation carriers. Perhaps if aspirin proves useful as a preventive, it could be used to reduce risk initially and risk-reducing surgery could be delayed until after the natural menopause.

CLINICAL TRIALS

CALYPSO

STUDY	CALYPSO
TITLE	A multi-national, randomised, phase III, GCIG intergroup study comparing pegylated liposomal doxorubicin (CAELYX®) and carboplatin vs paclitaxel and carboplatin in patients with epithelial ovarian cancer in late relapse (> 6 months)
SUMMARY	Liposomal doxorubicin (Caelyx) is a new drug which has been shown to shrink or stabilize the size of recurrent ovarian tumors in some patients and can be combined safely with carboplatin. Side effects observed with the combination of liposomal doxorubicin (Caelyx) and carboplatin are different from those observed with paclitaxel and carboplatin. The main purpose of this research study is to find out if treatment of late relapse with liposomal doxorubicin (Caelyx) combined with carboplatin will control the tumor growth at least as well as standard treatment with paclitaxel and carboplatin. This study will look at the side effects of each combination. It is hoped that substituting paclitaxel with Caelyx in combination with carboplatin will improve the tolerance of the treatment program with at least the same efficacy and fewer side effects.
ANZGOG PI	Assoc Prof Paul Vasey
PI INSTITUTION	Royal Brisbane and Women's Hospital
CANCER TYPE	Ovarian
PHASE	Phase III
TYPE OF TRIAL	Intervention
DRUG/S	Pegylated liposomal doxorubicin (CAELYX®), carboplatin, paclitaxel
LEAD GROUP, COUNTRY	ARCAGY/GINECO-led international trial; ANZGOG-led in Australia and New Zealand
COLLABORATIONS	AGO-OVAR, AGO-Austria, NSGO, NCIC-CTG, EORTC, MITO, MaNGO
SPONSOR	The University of Sydney
OPERATING CENTRE	NHMRC Clinical Trials Centre
NUMBER OF SITES	21 ANZ
RECRUITMENT	976 Total Worldwide, 71 ANZ
FUNDING	Schering-Plough (Merck & Co), ARCAGY/GINECO

Prof John Simes

NHMRC CLINICAL TRIALS CENTRE

NHMRC Clinical Trials Centre

THE UNIVERSITY OF SYDNEY

At the time of ANZGOG's formation, the NHMRC Clinical Trials Centre (CTC) at the University of Sydney was already an established organisation with experienced clinical trials staff who could work across projects and trials. This capability made the conduct of trials a much smoother process in the early days of ANZGOG.

ANZGOG and the University of Sydney developed an overarching collaborative agreement which formed the basis for working together on collaborative studies. In the early years the CTC, under Founding Director, Prof John Simes, helped a number of the cancer clinical trials groups become established.

ANZGOG became an independent company limited by guarantee in 2009 and has gone on to sponsor and operate clinical trials independently, in addition to its collaboration with the university.

In the first 10 years of ANZGOG, most trials were 'mailbox' studies, which were led by an international group, with Australia and New Zealand recruiting a local patient population for the trial. The benefit of these trials was a growth of experience in conducting academic investigator-initiated clinical trials, building relationships with experienced senior international investigators and providing new treatments, which may not be available in ANZ for women affected by a gynaecological cancer.

ANZGOG received considerable help from the CTC, with too many people contributing to be able to mention individually. Over the years the CTC team have worked hard to help make ANZGOG the success that it has become.

The CTC staff brought essential skills to these projects, working collaboratively with the ANZGOG volunteer investigators, providing clinical leadership, trial design, project management, biostatistical analysis, data management, monitoring, coordination and systems development.

Today the NHMRC Clinical Trials Centre conducts investigator-initiated collaborative clinical trials across diverse therapeutic areas, including cancer, cardiovascular disease, neonatal health and diabetes.

> *"The CTC, as the coordinating centre, plays an important role in collaborating with ANZGOG to see whether we can deliver high-quality clinical trials that will provide the results we need to see whether the new treatments will in fact lead to better outcomes for patients and therefore lead to advances and changes in practice."*

PROF JOHN SIMES
FOUNDING DIRECTOR | NHMRC CLINICAL TRIALS CENTRE

CLINICAL TRIALS

SCOTROC 4

STUDY	SCOTROC 4
LONG TITLE	A prospective, multicentre, randomised trial of carboplatin flat dosing vs intrapatient dose escalation in first line chemotherapy of ovarian, fallopian tube and primary peritoneal cancers
LAY SUMMARY	Ovarian cancer is treated by chemotherapy consisting of a drug called carboplatin, used either alone, or in combination with another drug called paclitaxel. The dose of carboplatin is calculated at the beginning of treatment in a standard fashion that is based on information such as body weight and kidney function. Normally, patients would then receive 6 cycles of carboplatin at this dose (called 'flat dosing'). However, data from previous studies have suggested that there may be some additional benefit for higher doses of carboplatin. One way of doing this is to increase the dose by small amounts each cycle according to how well the previous cycle was tolerated (called 'intrapatient dose escalation'). This study was designed specifically to test whether 'intra-patient dose escalation' is superior to the more conventional 'flat dosing'.
ANZGOG PI	Dr Geraldine Goss
PI INSTITUTION	Monash Medical Centre, Box Hill Hospital
CANCER TYPE	Ovarian
PHASE	Phase III
TYPE OF TRIAL	Intervention
DRUG/S	Carboplatin
LEAD GROUP, COUNTRY	Scottish Gynaecological Clinical Trials Group (SGCTG)-led international trial; ANZGOG-led in Australia and New Zealand
SPONSOR	The University of Sydney
OPERATING CENTRE	NHMRC Clinical Trials Centre
NUMBER OF SITES	22 ANZ
RECRUITMENT	964 Total Worldwide, 64 ANZ
FUNDING	SGCTG, Cancer Council NSW

> *"SCOTROC 4 was very important because prior data had suggested that outcome from chemotherapy may be improved if the dose of chemotherapy was intensified according to toxicity/tolerance. The trial sought to answer the question of whether maximising the tolerated dose in an individual woman would improve outcome."*
>
> **DR GERALDINE GOSS**
> **PRINCIPAL INVESTIGATOR | SCOTROC 4**

WHAT WAS THE FOCUS OF SCOTROC 4?

SCOTROC 4 was a prospective, multicentre, randomised trial comparing flat dosing with carboplatin compared with intrapatient dose escalation in first-line chemotherapy for the treatment of ovarian, fallopian tube and primary peritoneal cancers.

The aim of the trial was to assess progression-free survival for the two types of dosing.

SCOTROC 4 was led by SGCTG. ANZGOG was a trial partner, with 64 of the 964 patients recruited from 22 sites across Australia and New Zealand.

SCOTROC 4 built on SCOTROC 3 (not an ANZGOG trial), which established that carboplatin alone is an excellent treatment in ovarian cancer. Although we generally prescribe a combination of platinum with paclitaxel, knowledge that single agent carbo is excellent treatment, makes the decision to use this in women who are frailer or to dose reduce the paclitaxel for toxicity, a more clinically acceptable notion.

At the time of SCOTROC 4, most patients receiving carboplatin received the same dose throughout their course of treatment. This is called a 'flat dose'. Some doctors increased the dose at each cycle, as long as the patient didn't experience serious side effects from the previous dose before. This is called 'intrapatient dose escalation'.

> *"I have always had an interest in the relationship between the dose of drugs we use in oncology and their efficacy. Many trials use the maximum tolerated dose of a drug, where in reality patients may need less than that and still respond. If we can achieve the same results with a lower dose, we can minimise toxicity and cost.*
>
> *Although SCOTROC 4 trial asked the opposite question – should dose be intensified according to tolerance – it did establish the principle that maximal dose is not necessarily required for maximal outcome."*

WHAT DID SCOTROC 4 FIND?

This trial was the largest study ever undertaken to investigate the effect of intrapatient dose escalation of chemotherapy.

SCOTROC 4 did not suggest that maximising the dose of carboplatin would improve outcomes for women with ovarian, fallopian tube and primary peritoneal cancers.

The study was published in Annals of Oncology. [5]

WHAT IMPACT HAS SCOTROC 4 HAD ON PRACTICE?

The implications for practice mean that practitioners did not feel obliged to escalate doses of chemotherapy according to tolerance as measured by effects on blood counts. This also meant less concern when dose reductions are needed. The minimum dose required for efficacy is less than the maximal tolerated dose.

WHAT HAVE WE LEARNED THROUGH SCOTROC 4?

SCOTROC 4 trial established that Australia and New Zealand group could contribute on the international stage and conduct important trials.

[5]Banerjee S, Rustin G, Paul J et al. A multicenter, randomized trial of flat dosing versus intrapatient dose escalation of single-agent carboplatin as first-line chemotherapy for advanced ovarian cancer: an SGCTG (SCOTROC 4) and ANZGOG study on behalf of GCIG. Ann Oncol 2013;24(3):679–87.

CLINICAL TRIALS

TARCEVA

STUDY	TARCEVA
TITLE	A randomised, multicentre, phase III study of erlotinib versus observation in patients with no evidence of disease progression after first line, platinum-based chemotherapy for high-risk stage I and stage II-IV ovarian epithelial, primary peritoneal, or fallopian tube cancer
SUMMARY	Following "first-line" chemotherapy, current standard clinical practice does not require any further anti-cancer treatment however patients do have regular check-up visits with their treating doctor. To keep the disease under control as long as possible, it has been proposed that "maintenance" treatment may provide some additional benefits. Experts in treating ovarian cancer are therefore initiating this clinical trial which will evaluate the role of maintenance treatment with a drug called erlotinib. This drug is manufactured by Hoffman La Roche and is also known by its commercial name, Tarceva. Erlotinib targets a specific receptor (the epidermal growth factor receptor) which is found on the surface of both normal cells and cancer cells. By binding to the receptor, erlotinib can prevent cancer cells from growing or dividing, therefore slowing the growth or reappearance of the cancer.
ANZGOG PI	Dr Christopher Steer
PI INSTITUTION	Border Medical Oncology
CANCER TYPE	Ovarian
PHASE	Phase III
TYPE OF TRIAL	Intervention
DRUG/S	Erlotinib
LEAD GROUP, COUNTRY	EORTC-GCG-led international trial; ANZGOG-led in Australia and New Zealand
COLLABORATIONS	AGO, GINECO, MaNGO, NCRI
SPONSOR	The University of Sydney
OPERATING CENTRE	NHMRC Clinical Trials Centre
NUMBER OF SITES	13 ANZ
RECRUITMENT	835 Total Worldwide, 42 ANZ
FUNDING	EORTC, ANZGOG

"What struck me most in the early days [of ANZGOG] was what a collegiate group of clinicians they were as a multidisciplinary group. They were open to collaboration and sharing information and patients. Everyone clearly wanted the best possible outcome for every patient they worked with."

ASSOC PROF HARYANA DHILLON
2000-2004 NHMRC CTC OPERATIONS AND DEVELOPMENT | ANZGOG TRIALS

“Lack of funding impacts the research environment in two ways – no money means fewer clinical trials, leaving us with less evidence on how to improve the chance of a cure and quality of life for our patients. Lack of funding is also detrimental to the enthusiasm of researchers.”

ASSOC PROF ALISON BRAND AM
CHAIR | ANZGOG 2012-2018
TREASURER | ANZGOG 2002-2009

FUNDING RESEARCH

START-UP FUNDING

Funding was non-existent when ANZGOG was formed in 2000. The Group was negotiating to bring clinical trials from the US GOG to Australia and New Zealand for women to take part in, but funding was very hard to find. Everyone was committed and on-board, but money was the issue.

It was gifts by members, community donors and patients of ANZGOG members, that allowed ANZGOG to support basic infrastructure positions that weren't funded through clinical trial grants. These key roles enabled the Group to put work into getting new studies up and running before there was funding from any other special grants.

ANZGOG wishes to acknowledge the generosity of those early donors and their faith in the core group of members determined to get clinical trials operating in Australia. Without these generous gifts, established ANZGOG and beginning these early gynaecological cancer clinical trials would not have been possible and ANZGOG would not be what it is today.

MAJOR DONATIONS ($20K+):

2001	Craig Underhill	$20,000
2001	Consolidated Press Holdings	$40,000
2001-2006	Bristol-Myers Squibb Pharmaceuticals	$51,500
2002	CTEP (US GOG)	$300,000
2002-2005	AMGEN Australia	$30,000
2003	Wilson Family Trust	$50,000
2003	Clemenger Group	$50,000
2003-2005	MaynePharma	$20,000
2003-2010	Lady Fairfax	$250,000
2004	Eli Lilly Australia	$20,000
2004	KE [anonymous]	$20,000
2008-2010	James Potter	$136,500
2009	Comedy for Cancer [via Cathy McRae]	$60,000
2010	Jock Gray	$25,000

2002-2010 PROJECT AND INFRASTRUCTURE FUNDING

The US GOG assisted significantly in the early days of ANZGOG with almost $1 million in funding to support a series of US clinical trials opening in Australia. This developed the relationship with hospital sites and enabled further funding for trials through government project grants and industry support. ANZGOG involvement in international trials was also supported by other international academic groups in Europe and the UK.

GRANTING BODY	PROJECT	2000-2010
Industry Support	Clinical Trials	$331,850
Government Project Grants	Clinical Trials	$1,333,202
Federal Govt Support	Cancer Trials Development	$1,828,040
International Academic Groups	Clinical Trials	$1,879,424
US Gynaecologic Oncology Group	GOG Studies	$963,459
GRAND TOTAL		**6,335,975**

There are 14 academic cancer clinical trials groups (CCTGs) in Australia specialising in the different cancer types (breast, urinary, prostate, lung, gastro intestinal, melanoma, leukaemia - etc). The CCTGs have been fortunate to have Australian Federal Government support for cancer trial development since the mid 2000's. These funds support ANZGOG in developing new studies, fostering ideas from its membership, engaging with cancer consumers and providing information and education to ensure the translation of research results are well known amongst stakeholders.

CLINICAL TRIALS

ICON6

STUDY	ICON6
TITLE	A randomised, placebo-controlled, trial of concurrent cediranib [AZD2171] (with platinum-based chemotherapy) and concurrent maintenance cediranib in women with platinum-sensitive relapsed ovarian cancer
SUMMARY	In this study we are investigating whether we can improve the treatment of cancer with chemotherapy (drug treatment) by adding a new drug called cediranib. Although there are good scientific reasons from laboratory studies why cediranib should work on ovarian cancer cells, it has not yet been tested in a large number of women with ovarian cancer. Some early clinical studies have shown that cediranib does have an effect on tumours, but we don't yet know whether the drug will be effective in treating ovarian cancer and, if it does work, how long treatment should continue for. For this reason, we propose to treat some women with standard chemotherapy drugs alone, some women with the new drug during chemotherapy and some women with the new drug during chemotherapy and continued after chemotherapy has finished, for up to 18 months in total. Because some women will continue to take cediranib after chemotherapy is completed, another role of this study is to find out whether continuing to take cediranib on its own will prolong the benefits of the chemotherapy, without producing side effects that interfere too much with day to day life.
ANZGOG PI	Dr Michelle Vaughan
PI INSTITUTION	Christchurch Hospital
CANCER TYPE	Ovarian
PHASE	Phase III
TYPE OF TRIAL	Intervention
DRUG/S	Cediranib
LEAD GROUP, COUNTRY	MRC/UCL-led international trial; ANZGOG-led in Australia and New Zealand
COLLABORATIONS	NCIC-CTG, GEICO
SPONSOR	The University of Sydney
OPERATING CENTRE	NHMRC Clinical Trials Centre
NUMBER OF SITES	7 ANZ
RECRUITMENT	486 Total Worldwide, 17 ANZ
FUNDING	National Centre for Gynaecological Cancer (Cancer Australia funding partner), MRC

> *"When ICON6 was conceived, we knew that targeting angiogenesis (new blood vessel formation) was effective in ovarian cancer. The available agents required women to have ongoing intravenous infusions every few weeks after chemotherapy. Cediranib was a new tablet-form antiangiogenic agent with promising activity that needed testing in a large randomised trial."*

DR MICHELLE VAUGHAN
PRINCIPAL INVESTIGATOR | ICON6
INAUGURAL NZ DIRECTOR - 2006-2012 | ANZGOG

Dr Michelle Vaughan

WHAT WAS THE FOCUS OF ICON6?

ICON6 was a randomised, phase III placebo-controlled, trial of concurrent cediranib with platinum-based chemotherapy and concurrent maintenance cediranib in women with platinum-sensitive relapsed ovarian cancer.

ICON6 was led by the Medical Research Council (MRC)/University College London as part of a global collaboration involving the MRC/National Cancer Research Institute (NCRI), NCIC CTG = National Cancer Institute of Canada Clinical Trials Group, the Spanish Ovarian Cancer Research Group (GEICO) and Irish Clinical Oncology Research Group (ICORG).

WHAT DID ICON6 FIND?

While ICON6 was running, disappointing results from trials of cediranib in other cancers became available. This resulted in early discontinuation of the trial.

ICON6 had to be reduced in size, and this limited the ability to determine overall survival outcome. In contrast to results in other cancers, ICON6 appeared to show lengthening of average overall survival times by 7 months for women with ovarian cancer receiving cediranib. However, with the reduced numbers of patients in the trial, there was inadequate statistical power to determine whether this was truly the case. The effect of the drug also appeared to reduce over time. [6]

In 2016 the trial was reported as showing a couple of months lengthening of the average time until the cancer progressed, and that continuing the tablets after chemotherapy seemed necessary. Whether the drug meaningfully improves overall survival remains uncertain.

Cediranib is a tablet-form anti-angiogenic agent.

WHAT DID WE LEARN THROUGH ICON6?

There were several learnings from this trial. The first was not to prematurely give up on a new drug before all the information is available.

Another learning was that formal Quality of Life (QoL) research is important, something that is an ANZGOG research priority. The initial trial reported many women stopping cediranib due to the side effects, which could have led to a lack of enthusiasm for continuing investigation of this drug. However, formal QoL analysis, reported in a subsequent paper, reassuringly showed that overall quality of life was no worse in patients taking cediranib.

NEXT STEPS

The next step has been combining this drug with the other effective oral maintenance agents: poly ADP ribose polymerase (PARP) inhibitors. Laboratory and early clinical evidence suggests that these two different classes of drugs could work better together in women with recurrent ovarian cancer. This has led to ICON9 – a trial that is ongoing and in which ANZGOG is participating. ICON9 is testing whether taking cediranib as well as the PARP inhibitor olaparib improves outcomes in women with recurrent ovarian cancer, without significantly reducing quality of life.

We continue to accrue women to ICON9, which if positive will improve the outcome of women with recurrent ovarian cancer.

[6]Ledermann J, Embleton AC, Raja F et al. Cediranib in patients with relapsed platinum-sensitive ovarian cancer (ICON6): a randomised, double-blind, placebo-controlled phase 3 trial. Lancet Oncol 2016;387:1066–74.

CLINICAL TRIALS

HOSTT

STUDY	HOSTT
TITLE	A phase III study to evaluate the impact of maintaining haemoglobin levels above 120g/L versus above 100g/L in anaemic patients with carcinoma of the cervix receiving concurrent cisplatin and radiation therapy
SUMMARY	This research study will assess whether correcting anaemia (decreased red blood cells) will improve the effectiveness of radiation therapy and chemotherapy in treating cervical cancer. Many women with cervical cancer present with anaemia due to bleeding from their tumour. It is also one of the unwanted side effects of radiation and chemotherapy treatment of cervix cancer. When red blood cells, which carry oxygen throughout the body to nourish the tissues, are low in number, which is the case in anaemia, you can feel tired (fatigued), short of breath and have a rapid heart rate. Increasing the number of red blood cells may reduce or eliminate many of these symptoms and may improve the effectiveness of treatment.
ANZGOG PI	Dr Michelle Grogan
PI INSTITUTION	Royal Brisbane Women's Hospital
CANCER TYPE	Cervical
PHASE	Phase III
TYPE OF TRIAL	Intervention
DRUG/S	Red Cell Concentrate (RCC) transfusion to maintain haemoglobin at pre-specified levels
LEAD GROUP, COUNTRY	ANZGOG and National Taiwan University Hospital-led trial
SPONSOR	The University of Sydney
OPERATING CENTRE	NHMRC Clinical Trials Centre
FUNDING	Co-funding from NHMRC CTC and National Taiwan University Hospital (Pilot Phase)

"In 2007, ANZGOG involvement in this trial ceased due to poor accrual and mounting costs."

PROF DANNY RISCHIN
INAUGURAL CHAIR | ANZGOG RESEARCH ADVISORY COMMITTEE

CLINICAL TRIALS

ICON7

STUDY	ICON7
TITLE	A randomised, two-arm, multi-centre Gynaecologic Cancer InterGroup trial of adding bevacizumab to standard chemotherapy (carboplatin and paclitaxel) in patients with epithelial ovarian cancer
SUMMARY	In ICON7 we are studying whether we can improve the benefits of chemotherapy by adding a new drug called bevacizumab to 'standard chemotherapy'. Bevacizumab (also known as Avastin) is what we call a 'targeted therapy' rather than a chemotherapy drug. It acts more specifically on cancer cells than normal cells. As cancers grow they need to develop their own new blood supply to survive and this development of new blood vessels is known as angiogenesis. Bevacizumab works by blocking one of the main factors that cancer cells produce to make these blood vessels. This may then reduce tumour blood flow, which may interfere with the tumour's ability to grow and spread to other parts of the body. We believe this may be an important new way to treat cancer.
ANZGOG PI	Assoc Prof Philip Beale
PI INSTITUTION	Concord Hospital, Royal Prince Alfred Hospital
CANCER TYPE	Ovarian
PHASE	Phase III
TYPE OF TRIAL	Intervention
DRUG/S	Carboplatin, paclitaxel, bevacizumab
LEAD GROUP, COUNTRY	MRC/UCL-led international trial; ANZGOG-led in Australia and New Zealand
COLLABORATIONS	NCIC-CTG, NSGO, ARCAGY-GINECO, AGO-OVAR, GEICO, MRC/NCRI
SPONSOR	The University of Sydney
OPERATING CENTRE	NHMRC Clinical Trials Centre
NUMBER OF SITES	22 ANZ
RECRUITMENT	1,528 Total Worldwide, 76 ANZ
FUNDING	MRC

WHAT WAS THE FOCUS OF ICON7?

ICON7 was an international, phase III, open-label, randomised trial to examine the effect of adding bevacizumab (Avastin) to standard chemotherapy in first-line treatment for women with epithelial ovarian cancer.

ICON7 was undertaken at 263 centres in 11 countries across Europe, Canada, Australia and New Zealand. Participation in Australia and New Zealand occurred at 22 sites, contributing 76 patients out of the total trial cohort of 1528 patients.

ICON7 ran in parallel with US collaborative study GOG-0218, which focused on the same research question. Involvement in ICON7 meant that ANZGOG was part of a global commitment to addressing an important question in ovarian cancer treatment.

WHAT DID ICON7 FIND?

ICON7 demonstrated an overall survival benefit for women with poor prognosis ovarian cancer receiving bevacizumab in addition to standard platinum-based chemotherapy. Together, trial outcomes from ICON7 and GOG-0218 led to approval of bevacizumab in Australia for first-line treatment of ovarian cancer (including epithelial ovarian cancer, fallopian tube cancer and primary peritoneal cancer). Use of bevacizumab is now part of routine clinical care for women with high-risk epithelial ovarian cancer.

HOW HAS ICON7 CONTRIBUTED TO IMPROVEMENTS IN OUTCOMES FOR WOMEN WITH OVARIAN CANCER?

These trials and their results played a significant role in moving the field of ovarian cancer treatment forward. Five-year survival for ovarian cancer is improving incrementally across all jurisdictions in Australia, undoubtedly in part as a result of trials such as ICON7 and resulting changes to clinical practice.

Key findings have been published in leading international journals.[7,8,9]Associated publications have focused on translational questions looking at biomarkers to better understand drivers of response to bevacizumab. This is still a work in progress but demonstrates the importance of building on past trial outcomes to deepen our understanding of response and resistance to treatment.

Bevacizumab is a recombinant humanised monoclonal antibody that binds to and inhibits human vascular endothelial growth factor (VEGF). Inhibition of VEGF prevents new blood vessel formation, inhibiting tumour growth and metastasis.

WHAT CAN WE LEARN FROM ICON7?

Participation in trials such as ICON7 helps develop the international standing of Australian investigators and raise Australia's profile as an important contributor to gynaecological cancer research. This creates opportunities both for Australian and New Zealand participation in future global trials and for Australia to identify partners for Australian-led research.

WHY WAS IT IMPORTANT FOR ANZGOG TO BE INVOLVED IN ICON7?

ICON7 represents an important milestone in ANZGOG's history, occurring at a time when global trial activity was increasing. ANZGOG's involvement was an indicator of the growing maturity of its research network and strengthened capabilities and confidence in patient recruitment and quality assurance processes. ANZGOG was keen to commit resources and expertise to facilitate participation as an active partner in a global collaboration, and the quality of the Australia and New Zealand contribution was viewed positively.

Involvement of Australian patients in ICON7 was important to support Therapeutic Goods Administration and Pharmaceutical Benefits Advisory Committee processes. The dosage of bevacizumab was lower in ICON7 than in the GOG-0218 trial, with no real difference seen in effect, demonstrating cost-effectiveness and helping to make the drug more available to Australian women.

"The international standing and reputation of ANZGOG Chair, Prof Michael Friedlander AM, was critical to ANZGOG being invited to be part of ICON7. ANZGOG's growth owes a significant amount to Michael's global position and collaborations. It is critical that our participation in global trials continues to be actively pursued and supported so that future leaders can emerge and develop and so that ANZGOG's important work can continue."

ASSOC PROF PHILIP BEALE
PRINCIPAL INVESTIGATOR | ICON7

[7]Perren TJ, Swart AM, Pfisterer J et al. A Phase 3 Trial of Bevacizumab in Ovarian Cancer. N Engl J Med 2011;365(26):2484–2496.
[8]Oza AM, Cook AD, Pfisterer J et al. Standard chemotherapy with or without bevacizumab for women with newly diagnosed ovarian cancer (ICON7): overall survival results of a phase 3 randomised trial. Lancet Oncol 2015;16:928–36.
[9]Martín GA, Oza AM, Embleton AC et al. Exploratory outcome analyses according to stage and/or residual disease in the ICON7 trial of carboplatin and paclitaxel with or without bevacizumab for newly diagnosed ovarian cancer. Gynecol Oncol 2019; https://doi.org/10.1016/j.ygyno.2018.08.036

ENGAGING WOMEN IN RESEARCH

ANZGOG involves women affected by cancer and their carers in research identification, development and review. Known within the sector as cancer consumers, ANZGOG's Consumer Research Panel (CRP) members are involved in providing advice, research review and consumer input into ANZGOG's research program and clinical trial development. They take part in specialist tumour working groups, all steering committees and concept development workshops held by ANZGOG.

The inaugural ANZGOG Consumer and Community Committee (CCC) was established in 2007 by Karen Livingstone AM, with a wonderful group of women in Australia who served for many years and helped to develop ANZGOG's approach to consumer engagement. Karen Livingstone was appointed the first Consumer Director on the ANZGOG Board [2007-2017]. ANZGOG continues to involve consumers in its governance and strategic planning.

ANZGOG was one of the first clinical trials groups to embed consumer voices into its research and governance committees. It has fostered greater understanding with its clinical members of the benefits of working closely with consumers in research.

ANZGOG clinical trialists working on research seek input and guidance from women affected by cancer to improve the quality of the research and ensure they are representing the needs and expectations of women for the best outcomes.

The consumer committee brought a range of viewpoints from both cancer survivors and carers, disadvantaged and special community groups, as well as an amazing personal skill base and commitment to helping women like themselves know more about clinical trials and how research can improve life for women.

"One of the immediate challenges was to understand clinical speak which was quite foreign, with so many acronyms! In 2008, consumers were not part of the Australian research landscape, and our goal was to ask questions, comment on research concepts and bring a unique perspective. I believed that the CCC enriched the experience of the researcher by not just considering the treatment benefits but focus on the benefits to a woman's quality of life as well."

KAREN LIVINGSTONE AM
INAUGURAL CONSUMER COMMITTEE CHAIR (CCC) | ANZGOG

Members of the Consumer & Community Committee. Left to right – Debbie Lee, Heshani Nesfield, Pennie Stoyles, Helene O'Neill

CLINICAL TRIALS

TRIPOD

STUDY	TRIPOD
TITLE	A single arm phase II trial of intraperitoneal chemotherapy with paclitaxel and cisplatin after optimal debulking surgery for ovarian and related cancers
SUMMARY	Recent studies by the US Gynecologic Oncology Group have found that patients, who are given chemotherapy directly into the abdominal cavity (intra-peritoneal chemotherapy) as well as through a vein, live approximately 16 months longer than those who are given chemotherapy through a vein only. Patients participating in a previous study using intraperitoneal chemotherapy had significant side effects with the treatment and were not able to complete the full course of treatment. Therefore, this study is using slightly reduced doses of the same treatments thereby reducing the risk and/or severity of side effects from the treatment. TRIPOD is a study which will determine if it is possible and safe to treat ovarian cancer patients, in Australia and New Zealand, with chemotherapy given directly into the abdomen as well as through a vein.
ANZGOG PI	Dr Corona Gainford
PI INSTITUTION	NHMRC Clinical Trials Centre
CANCER TYPE	Ovarian
PHASE	Phase II
TYPE OF TRIAL	Intervention
DRUG/S	Paclitaxel, cisplatin
LEAD GROUP, COUNTRY	ANZGOG-led trial in Australia and New Zealand
SPONSOR	The University of Sydney
OPERATING CENTRE	The NHMRC Clinical Trials Centre
NUMBER OF SITES	12 ANZ
RECRUITMENT	38 ANZ
FUNDING	Cancer Council NSW

OVAR16

STUDY	OVAR16
TITLE	A phase III study to evaluate the efficacy and safety of pazopanib monotherapy versus placebo in women who have not progressed after first line chemotherapy for epithelial ovarian, fallopian tube, or primary peritoneal cancer
SUMMARY	The purpose of this study is to determine if a new drug called pazopanib is safe and effective when given to patients with ovarian, fallopian tube or primary peritoneal cancer. Pazopanib is called a "targeted" therapy because it seeks out to block the function of certain proteins in cells. The main proteins pazopanib blocks are called VEGFR, PDGFR and c-Kit. Since these proteins are involved in cancer cell growth, it is hoped that giving pazopanib will further slow or stop the cancer cells from growing.
ANZGOG PI	Prof Michael Friedlander AM
PI INSTITUTION	Prince of Wales Hospital
CANCER TYPE	Ovarian
PHASE	Phase III
TYPE OF TRIAL	Intervention
DRUG/S	Pazopanib
LEAD GROUP, COUNTRY	AGO-led international trial; ANZGOG-led in Australia and New Zealand
COLLABORATIONS	AGO-Austria, BGOG, GEICO, GINECO, ICORG, JGOG, KGOG, MaNGO, MITO, NSGO-CTU
SPONSOR	The University of Sydney
OPERATING CENTRE	NHMRC Clinical Trials Centre
NUMBER OF SITES	13 ANZ
RECRUITMENT	940 Total Worldwide, 65 ANZ
FUNDING	GlaxoSmithKline, Novartis

CLINICAL TRIALS

SYMPTOM BENEFIT

STUDY	SYMPTOM BENEFIT
TITLE	Does palliative chemotherapy improve symptoms in women with recurrent ovarian cancer? Measuring subjective improvement as well as objective response to estimate the benefit of palliative chemotherapy in women with platinum resistant or refractory ovarian cancer
SUMMARY	In this research study we will investigate quality of life issues related to having ovarian cancer and undergoing chemotherapy. We are interested in knowing how women are doing during chemotherapy for ovarian cancer and whether symptom improvement occurs with treatment. We will also look at factors that might help us decide how well women will respond to their treatment.
ANZGOG PI	Prof Michael Friedlander AM
PI INSTITUTION	Prince of Wales Hospital
CANCER TYPE	Ovarian
TYPE OF TRIAL	Quality of Life
LEAD GROUP, COUNTRY	ANZGOG-led international study
COLLABORATIONS	GCIG clinical trial groups from 11 countries, Sydney Quality of Life Office, University of Sydney, GCIG Symptom Benefit Committee
SPONSOR	The University of Sydney
OPERATING CENTRE	NHMRC Clinical Trials Centre
NUMBER OF SITES	23 ANZ
RECRUITMENT	948 Total Worldwide, 143 ANZ
FUNDING	NHMRC Project Grant, OCRF, ANZGOG

"The impact of the Symptom Benefit Study has been huge and achieved far more than we ever expected and way beyond the successful development and validation of an instrument."

PROF MICHAEL FRIEDLANDER AM
PRINCIPAL INVESTIGATOR | SYMPTOM BENEFIT

WHAT WAS THE FOCUS OF THE SYMPTOM BENEFIT STUDY?

The primary objective of the Symptom Benefit Study (SBS) was to develop and validate an instrument to measure symptom benefit from palliative chemotherapy.

The SBS was initiated after the third International Ovarian Cancer Consensus Conference. Response rates to palliative chemotherapy were very low (<10%) and did not represent an adequate endpoint in clinical trials. The most important question to emerge from the discussion on platinum-resistant ovarian cancer was whether palliative chemotherapy controls or reduces symptoms associated with recurrent ovarian cancer. There were no data available to support the palliative benefit of chemotherapy or good instruments to measure symptom benefit in clinical trials in women with recurrent ovarian cancer.

This Gynecologic Cancer Intergroup (GCIG) study, led by ANZGOG, recruited 948 women with recurrent ovarian cancer from 11 countries, including 143 women from Australia and New Zealand.

WHAT IMPACT HAS THE SYMPTOM BENEFIT STUDY HAD?

The SBS answered many questions beyond the development of MOST.

It was the catalyst in changing the attitudes of the GCIG to the importance of patient-reported outcomes in all clinical trials in gynaecological cancers besides platinum resistant ovarian cancer. All subsequent GCIG Ovarian Cancer Consensus meetings have endorsed the importance of patient reported outcomes and many publications and position papers have emerged from the SBS working group on patient reported outcomes as endpoints in clinical trials.

The Symptom Benefit Study was designed to validate a Patient Reported Outcome Measure (PROM): known as MOST (Measure of Ovarian Symptoms and Treatment concerns).

MOST is a 35-item questionnaire about current symptoms and concerns.

WHAT HAVE WE LEARNED THROUGH THE SYMPTOM BENEFIT STUDY?

The SBS was a challenging study to carry out as it was quite unlike any other GCIG study and there were very few people in the group with expertise in quality of life. Many lessons were learned.

The study has changed views within ANZGOG and in the GCIG about the importance of PROMs not only as endpoints in clinical trials but in clinical practice.

We now have a deeper appreciation of the need to go beyond simply reporting on mean change in quality of life scores in clinical trials, but to include other measures to assess benefit including quality adjusted progression free survival, time without symptoms of toxicity which are now used as endpoints in maintenance trials.

Like all good research the SBS also raised new important questions that need to be addressed in the current era of maintenance therapies as well as incorporation of new treatments such as PARP inhibitors and immune checkpoint inhibitors which did not exist in 2004 when the committee was formed.

Prof Madeleine King

WHAT WAS ANZGOG'S ROLE IN THE SYMPTOM BENEFIT STUDY?

The SBS would not have gone ahead or achieved the success it has without the support of ANZGOG as the lead group. The SBS put ANZGOG centre stage in GCIG and beyond due to the success of the study and the recognition of the expertise of ANZGOG in the field of patient-reported outcomes.

NEXT STEPS

The SBS has reported widely and continues to generate publications.[10,11,12,13,14,15,16,16,17,18,19,20,21]

The SBS has led to further studies such as MOST–OPAL (discussed separately in Part Two of this ANZGOG historical publication) and has led to new large ANZGOG trials:

- SBS2 which is investigating the integration of MOST into clinical practice
- The MOST follow up study which is investigating the role of nurse-led follow up using the MOST following completion of first-line chemotherapy.

"ANZGOG's Symptom Benefit story is one of great achievement that still holds much promise for the future making quality of life the focus. It demonstrates how ANZGOG are leading the way in improving care for women with ovarian cancer."

PROF MADELEINE KING
CANCER AUSTRALIA CHAIR IN QUALITY OF LIFE
ANZGOG RESEARCH ADVISORY COMMITTEE MEMBER

[10]Friedlander ML, Stockler M, O'Connell R et al. Symptom Benefit Study Group. Symptom burden and outcomes of patients with platinum resistant/refractory recurrent ovarian cancer: a reality check: results of stage 1 of the gynecologic cancer intergroup symptom benefit study. Int J Gynecol Cancer. 2014 Jun;24(5):857-64.
[11]Sjoquist KM, Friedlander ML, O'Connell RL et al. Hope, quality of life, and benefit from treatment in women having chemotherapy for platinum-resistant/refractory recurrent ovarian cancer: the gynecologic cancer intergroup symptom benefit study. Oncologist. 2013;18(11):1221-8.
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ANNUAL SCIENTIFIC MEETINGS

The aim of ANZGOG's Annual Scientific Meetings (ASM) was to provide a platform for the discussion of recent clinical trial results and to discuss what clinical trials should be conducted in Australia and New Zealand. These meetings were the cornerstone of the group's member engagement and collaboration activity.

The ASMs were successful events made by the enormous efforts and contributions of many. ANZGOG would like to thank Chair, Prof Andreas Obermair, and the rest of the ASM Steering Committee during these years for preparing a fantastic ASM program.

ANZGOG's ASMs were not only for education but also symbolised the collegiate nature of the group.

CLINICAL TRIALS

PORTEC-3

STUDY	PORTEC-3
TITLE	Randomised phase III trial comparing concurrent chemoradiation and adjuvant chemotherapy with pelvic radiation alone in high risk and advanced stage endometrial carcinoma
SUMMARY	The standard treatment after surgery for endometrial cancer in high risk patients is currently surgery followed by radiotherapy. External beam radiation therapy of the pelvis destroys potential cancer cells in the pelvic area. Many studies have shown that radiation treatment significantly reduces the risk of tumour recurrence in the pelvic area. The addition of chemotherapy during and after radiotherapy may increase its efficacy, and the continuation of chemotherapy after completion of radiation may kill tumour cells in the abdomen or elsewhere in the body. Studies among patients with other cancer types have shown that the addition of chemotherapy reduces the risk of tumour recurrence at distant sites in the body. This has not yet been established for endometrial cancer patients. The objectives of this trial are to investigate whether the addition of chemotherapy during and after radiotherapy further increases the chances of survival and reduces the risk of tumour recurrence in the pelvis and distant sites. The risk and severity of side effects and quality of life during and after treatment will also be evaluated and compared. This trial will help the researchers understand the safety and effectiveness of the treatment.
ANZGOG PI	Prof Linda Mileshkin
PI INSTITUTION	Peter MacCallum Cancer Centre
CANCER TYPE	Endometrial
PHASE	Phase III
TYPE OF TRIAL	Intervention
DRUG/S	Cisplatin, paclitaxel, carboplatin
LEAD GROUP, COUNTRY	LUMC GCIG/Dutch Gynaecological Oncology Group (DGOG)-led international trial; ANZGOG-led in Australia and New Zealand
COLLABORATIONS	NCRI, MaNGO, CCTG, Fedegyn
SPONSOR	The University of Sydney
OPERATING CENTRE	NHMRC Clinical Trial Centre
NUMBER OF SITES	16 ANZ
RECRUITMENT	686 Total Worldwide, 122 ANZ
FUNDING	NHMRC Project Grant, Cancer Australia

> *"ANZGOG was an important contributor to PORTEC-3. The trial took a while to gain momentum internationally. In the end, Australia and New Zealand were the third highest recruiters to the trial, with strong recruitment in both Australia and New Zealand. We benefitted from very strong collaborations between medical oncology and radiation oncology – there was a lot of enthusiasm."*
>
> **PROF LINDA MILESHKIN**
> **PRINCIPAL INVESTIGATOR | PORTEC-3**

WHAT WAS THE FOCUS OF PORTEC-3?

PORTEC-3 trial was a randomised phase III trial comparing post-operative radiation plus chemotherapy (concurrent and adjuvant) to radiation therapy alone in women at high-risk of relapse after surgery.

A total of 686 women participated in the trial, which was active at 103 sites internationally. PORTEC-3 was led by the Dutch Gynaecological Cancer Intergroup. Australia and New Zealand contributed 122 patients to the trial.

Dr Pearly Khaw, ANZGOG Radiation Oncologist, insisted on radiation oncology QA before the trial started. This resulted in her undertaking the QA for the entire trial.

PORTEC-3 used standard treatment of radiation to the pelvic region. One group also received chemotherapy (cisplatin) at the same time as radiation, followed by 4 cycles of adjuvant chemotherapy (carboplatin and paclitaxel).

WHAT DID PORTEC-3 FIND?

Initial results from PORTEC-3 did not show a benefit in terms of overall survival. However, a post-hoc updated analysis showed a significant overall survival benefit of adjuvant chemoradiotherapy vs radiotherapy in women with high-risk endometrial cancer alone after an additional year of follow-up.[22]The benefit in failure-free survival seen in the initial analysis continued in the post-hoc analysis.

> *"It took a long time to see the survival benefit in PORTEC-3. This has been an important lesson – trials take time – especially practice changing trials. It's important for us to be aware of and plan for that."*

WHY WAS PORTEC-3 IMPORTANT?

PORTEC-3 has embedded the use of adjuvant chemotherapy into the management of advanced endometrial cancer. Historically treatment of endometrial cancer has had a strong surgical focus. However, the incidence is increasing, and a proportion of women are not cured by surgery. Trials like PORTEC-3 provide additional options for managing this cancer.

PORTEC-3 has also generated a number of important Australian-led sub-studies. These include the patient preference sub-study and translational studies.

WHAT HAVE WE LEARNED FROM PORTEC-3?

PORTEC-3 was one of ANZGOG's first trials and provided a lot of important lessons about the value of international and national collaboration.

A key lesson driven by Australia was the importance of radiation oncology quality assurance. Pre-trial benchmarking picked up quality issues that were addressed before the trial itself began.

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EVOLUTION OF ANZGOG

Improving life for women through cancer research

> *"ANZGOG has become the most important clinical trials group in gynaecological cancer in the southern hemisphere in only 10 years."*
>
> **PROF MICHAEL QUINN AM**

THE OUTBACK STUDY

ANZGOG'S FIRST HOMEGROWN INTERNATIONAL STUDY

An important achievement for ANZGOG was recognition of its research leadership when the OUTBACK study was approved by the Gynecologic Cancer InterGroup (GCIG) as a multi-country clinical trial led by ANZGOG. The trial was conducted in Australia, New Zealand, USA, China and Saudi Arabia. This was the first time that the US Gynecologic Oncology Group (GOG) had joined a cervix cancer trial that they were not leading.

The OUTBACK study received ethics approval in 2010. The results of the trial were presented at ASCO in June 2021 by Principal Investigator Prof Linda Mileshkin and assisted in changing treatment practice in the USA and internationally.

A significant milestone in ANZGOG's history.

20 YEARS OF RESEARCH
PART TWO: 2010-2020

CLINICAL TRIALS – 2010-2020

ANZGOG MEMBER STUDIES	INTERNATIONAL COLLABORATIONS
OUTBACK	ICON8
PARAGON	OVAR2.21
ANZGOG 1103	VELIA
MOST (OPAL)	STATEC
FeMMe	VIP
OvQuest	ICON9
REZOLVE	MOCCA
ECHO	STICs and STONEs
PHAEDRA	AtTEnd
EMBRACE	
iPRIME	
SOLACE2	
PRECISE	
TIPS	
IGNITE	

ANZGOG RESEARCH PROGRAMS

OASIS INITIATIVE – The OASIS Initiative undertakes signal seeking phase II clinical trials that match targeted new drug therapies with molecular subtypes of ovarian cancer, seeking evidence of clinical response to treatment which could rapidly translate to changes in treatment practice for women.

TR-ANZGOG – ANZGOG's world-class translational research initiative designed to add value to ANZGOG gynaecological cancer clinical trials. TR-ANZGOG supports the collection and use of biospecimens from ANZGOG trials for further research.

FUND FOR NEW RESEARCH – ANZGOG's grants program fosters innovative new research ideas that lead to investigator-led clinical trials. With philanthropic support, we have been able to support 14 innovative new studies from 2015 to 2019 inclusive.

Improving life for
women through
cancer research

The Australia New Zealand Gynaecological Oncology Group (ANZGOG)
is the peak national gynaecological cancer research organisation for Australia and New Zealand.
We are recognised as a world leader and collaborative partner in clinical trials research.

The Australian Business Number (ABN) is 69 138 649 028.
The Australian Company Number (ACN) is 138 649 028.
ANZGOG is an Australian public company limited by guarantee. ANZGOG is endorsed as a deductible gift recipient under Section 30-15 of the Income Tax Assessment Act 1997.

FUNDING CANCER RESEARCH

WomenCan is a trading name of ANZGOG and conducts fundraising for ANZGOG's research, awareness and education activities.

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