Genomic Cancer
Clinical Trials Initiative

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October 2022 Ideas Generation Workshop Report

The Genomic Cancer Clinical Trials Initiative (GCCTI) is a grant funded by Cancer Australia and delivered in partnership between NHMRC Clinical Trials Centre and Zest.

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Introduction

The Genomic Cancer Clinical Trials Initiative (GCCTI) was established and funded by Cancer Australia in 2013. The GCCTI is a technical service that supports the national cancer cooperative trials groups (CCTGs) funded under Cancer Australia's *Support for Cancer Clinical Trials* program. The GCCTI aims to develop **mutation-specific/molecularly-targeted clinical trials concepts** and **grant applications involving cancers from more than one primary site and more than one CCTG**.

GCCTI is led by the National Health and Medical Research Council Clinical Trials Centre (NHMRC CTC) in partnership with Zest. Scientific technical expertise is provided by the NHMRC CTC, and project management, stakeholder engagement and communications expertise are provided by Zest.

The GCCTI project team held a one-day hybrid **Ideas Generation Workshop** on **Friday 28 October 2022** via Zoom and at the Hotel Pullman Sydney Airport**.**

Purpose of the workshop

The GCCTI annual workshops aim to provide a forum for Australia's leading cancer researchers, CCTGs, and the GCCTI Scientific Steering Group (SSG) to discuss and generate ideas and opportunities for studies and grants involving cancers from multiple primary sites and multiple CCTGs.

The October 2022 workshop provided a forum for key stakeholders to:

- Learn about the latest changes in grant opportunities for clinical cancer research
- Explore new topics and generate ideas with applicability to multiple cancer types and CCTGs
- Discuss ideas and proposals for studies that could involve multiple cancer types and CCTGs
- Identify opportunities for collaboration across cancer types and CCTGs

The workshop program is included in the Appendix

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Overview of the GCCTI

The main aim of GCCTI is to help support the national cancer CCTGs by developing mutation-specific/molecularly-targeted clinical trials concepts and grant applications involving cancers from multiple primary sites and/or multiple CCTGs.

The scope and key deliverables of the GCCTI are to:

- Develop mutation-specific/molecularly-targeted clinical trial concepts and protocols that involve more than one cancer and more than one CCTG
- Submit grant applications for funding of these trials, including budget preparation
- Include quality of life and pharmaco-economic measures with input as appropriate from the Cancer Australia Technical Services for Quality of Life (CQUEST) and Health Economics (CREST)
- To host annual workshops welcoming all CCTGs and key stakeholders to identify potential targets for the development of mutation-specific cancer clinical trial protocols

The intended outcomes and benefits include:

- **Molecularly-focused networks** of researchers, clinicians and scientists
- **Increased capacity** to conduct genomic cancer clinical research
- **Strategies for managing challenges** associated with trials of targeted treatments
- **Structures to support the conduct** of trials that include multiple primary sites and multiple CCTGs

Continued engagement with Technical Services, including:

- Cancer Quality of Life Expert Service Team (CQUEST)
- Cancer Research Economics Support Team (CREST)
- Asia-Pacific Clinical Oncology Research Development Initiative (ACORD)

There are several ways that individuals can engage with GCCTI:

- Developing and submitting concepts/ideas to GCCTI
- Working with GCCTI and CCTGs to develop and design trial concepts
- Contributing to idea generation and prioritisation by attending GCCTI workshops and communicating with other CCTGs, researchers and the GCCTI project team
- Inputting into grant applications by joining GCCTI supported grant development teams

Session 1: Grants update

Update on Medical Research Future Fund (MRFF) grants programs

A/Prof Ruth Webster (Director, Health and Medical Research Office)

The second 10-year MRFF plan includes $6.3 billion of funding for medical research over 10 years (2022–23 to 2031–32). In addition to enhancing and expanding existing MRFF initiatives, the recent update also allocated funds for a new MRFF initiative to support early to mid-career researchers to enable them to work on greatest health challenges.

Updates to the MRFF

- Despite a change in government, the strategy and priorities of MRFF remain unchanged
- Aim to extend grant application opening periods and align grant periods with common opening and/or closing periods, where possible
- MRFF Consumer Reference Panel established to provide advice to the CEO of the Health and Medical Research Office on strategies for strengthening consumer involvement in MRFF implementation – meetings held and guidelines are being updated to reflect the advice from the Consumer Reference Panel
- Assessment criteria are currently undergoing updates. Although the fundamentals have not changed, it was advised that prior to writing a grant application, applicants should familiarise themselves with the refined MRFF assessment criteria descriptors and guidance for applicants (Sections 5 and 6)

Reminders when applying for MRFF funding include:

- Read beyond the title and into each grant opportunity, including the objectives and outcomes, eligibility criteria and selection criteria
- Meet the objective of the overarching MRFF initiative and the intention for the grant model
- Include assessment criteria that are focused on outcomes
- Be aware of any specific grant models which may be specified in the grant opportunity guidelines

How a researcher can contribute and engage with the MRFF:

- Feedback with suggestions and provide ideas
- Strengthen consumer involvement
- Contribute to consultations; upcoming consultations include:
    - Australian Medical Research Advisory Board (MRAB) will be consulting the sector on consumer and clinician involvement in research; health and medical research workforce development; and research quality
    - AMRAB regularly engage with NHMRC Council on working together to consider alignment and complementarity; engagement with the community
- Stay informed and connected (newsletters, webinars, website and social media)
- Consider promoting research by writing an easily understandable and engaging media summary (as part of the grant application)
- Informing MRFF about any upcoming announcements, media or events relating to a grant
- Nominate for membership of a Grant Assessment Committee here

Update on Cancer Australia grants

Dr Alan Woods (Acting Director, Research and Investment, Cancer Australia)

Priority-driven Collaborative Cancer Research Scheme (PdCCRS)

The PdCCRS is Cancer Australia's annual national research grants funding scheme, in which the agency joins with other government and non-government organisations to collaboratively fund national cancer research projects in areas of identified priority. To date, the PdCCRS has awarded 466 grants ($164 million in funds) since 2007.

How to apply for PdCCRS in 2023:

- Grants are managed through an online grants management system (NHMRC's Sapphire system), which will handle applications, reviews and the post-award process
- As previously reminded, ensure all possible research priorities that directly align with the proposal are selected in the application portal; your application can only be considered

for funding by Cancer Australia and/or Funding Partners if the relevant research priorities are selected

- Consumer involvement is a scoring component to PdCCRS grants; having at least two named consumers is recommended to provide alternative viewpoints; evidence of their input should be detailed in the response to the consumer question and any evidence of their consultation included as part of the consumer declaration is encouraged

Other points to note:

- Quarantined funding is available for the following priorities: prevention research; health services research; lung cancer research; clinical trials
- Ideas grants closes in early May 2023 (one week after closure of the NHMRC Ideas Grant round) and grants are announced in December 2023
- Clinical Trials and Cohort Studies closes in early September 2023 (one week after closure of the NHMRC Clinical Trials and Cohort Studies Grant round) and grants are announced in March/April 2024
- Cancer Australia released the draft Australian Cancer Plan which is available here. Members were encouraged to engage and provide feedback which was open for public consultation from 3 November to 16 December 2022

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Session 2: Statistical sharing and borrowing in clinical trials

Statistical information borrowing in clinical trials: baskets, platforms and other designs

Prof Ian Marschner (Professor of Biostatistics, NHMRC Clinical Trials Centre)

Clinical trials provide information about specific treatments administered to specific populations. At times however, information may already be available in a relevant population(s) which may improve the ability to answer the aim of a trial or help supplement the primary information, known as information borrowing. The information borrowed may be from different subgroups, tumour types, or a different trial design (e.g. randomised vs non-randomised).

Information borrowing provides increased information, but also the potential to introduce bias, therefore, information borrowing is reliant on statistical modelling and analyses. A classic example of information borrowing is using information from the control treatment of past studies to supplement control information from the present study. Information borrowing is becoming increasingly common and allows for flexible trial designs, such as in:

- Basket studies – a targeted therapy evaluated on multiple tumour types with a common sub-type
- Umbrella studies – multiple targeted therapies for a single tumour type
- Platform studies – infrastructure for comparative evaluation of multiple treatments by interim analyses, without pre-specifying all treatments to be studied and the ability to add or drop treatments
- Adaptive studies – when any of the above studies have designs that adapt over time in response to the accumulating data

Basket studies

There are three main ways to analyse data obtained from basket studies:

- As independent tumour types – most methodologically pure, but possibly small sample sizes; it assumes there is a different average response rate for each tumour type
- Pooling across all tumour types – this assumes an identical response rate for each tumour type
- Borrowing information across tumour types – by sharing information across relevant tumour types; it assumes an underlying identical average response rate but each tumour type has an adjusted response rate which deviates by a random amount from the identical response rate. Sharing information between multiple tumour types increases statistical efficiency while still allowing for differences between tumour types

Platform studies

The information shared in platform trials usually relates to the control treatment:

- Concurrent controls – primary information to compare treatments randomised during the same period
- Non-concurrent controls – supplementary information from time periods in which concurrent randomisation was not available. Non-concurrent controls increase power but may also introduce bias

Analogous to basket studies, there are three main ways to analyse data obtained from platform studies:

- Restrict to randomised evidence – using the study stages that only have direct randomised comparison of treatments of interest (concurrent controls only); this preserves randomisation and protects against temporal confounding
- Pooling concurrent and non-concurrent controls – may introduce bias due to time trends and other factors
- Aggregate direct comparisons and indirect comparisons – supplements concurrent controls with non-concurrent controls

Bayesian and Frequentist designs

These statistical philosophies are both scientifically valid for basket, platform and adaptive designs (both fixed and innovative designs). The main difference between the two approaches is in their treatment effect summary; Bayesian analyses typically report a posterior distribution (a probability distribution) to summarise what is known about the treatment effect, while Frequentist analyses typically report a best estimate, a confidence interval and a p-value, which may be used to test the null hypothesis of no treatment effect.

Session 3: Microbiome and molecularly targeted cancer treatment

Harnessing the power of the microbiome in the cancer field

Prof Emad El-Omar (Professor of Medicine, UNSW Microbiome Research Centre)

There have been numerous reviews discussing the role of the microbiome in cancer. Recently, the potential role of the microbiome in cancer prediction, prevention and treatment has begun to emerge.

Microbiota in the gut

- The pH of the gut is one of the factors that determines an individual's response to chronic *H. pylori* infection later in life; those with a low pH (high acidity) are more susceptible to the duodenal ulcer phenotype and those with high pH (low/no acid) are more susceptible to the gastric cancer phenotype[1]
- More recently, transplanting human gastric microbiota into germ-free mice has been demonstrated to provide a novel animal model for studying human gastric diseases[2]
- Medications, including non-antibiotic drugs, may directly kill human gut bacteria; anti-psychotics, morphine and proton pump inhibitors (PPIs) have the greatest effects.[3]
    - Prolonged treatment with PPIs is associated with an increased risk of colorectal cancers.[4] PPIs are commonly prescribed in oncology patients to help prevent side effects of cancer therapy, however, the risk/benefit of PPIs should be considered before prescribing

Microbiota in the mouth

- The microbiome within the mouth affects oral diseases such as oral cancers, caries and periodontitis, and systemic diseases such as obesity, diabetes, liver diseases, pancreatic cancer and colon cancer

Australian studies

- The MothersBabies study – a longitudinal, Australia-wide study analysing microbiome from vaginal, stool, oral, skin, urine and blood samples. The aim of the study is to determine the relationship of preconception microbiome with: pre-eclampsia, gestational diabetes, excessive gestational weight gain, perinatal mood disorders, pre-term labour and birth, and paediatric health outcomes in the first two years of life
- The Healthy Optimal Australian Microbiome (HOAME) study – analyses the microbiome of Australians, e.g. professional athletes and centenarians, and their outcomes, e.g. dementia

Faecal microbiota transplantation

- There is some evidence of faecal microbiota transplantation (FMT) being beneficial for inflammatory bowel disease. Further, the 'super donor concept' is being used to standardise delivery throughout a study, this involves a sample (e.g. faeces) being taken from only one healthy donor showing 'normobiosis' and delivered to all participants
- FMT also promotes response in immune cell infiltrates and gene expression profiles[5] and overcomes resistance to anti-PD-1 therapy[6] in melanoma patients

1. Amieva MR and El-Omar EM. *Gastroenterology* 2008; 134(1):306–23. 2. Kwon S *et al. Gut* 2022; 71(7):1266–76. 3. Maier L *et al. Nature* 2018: 555;623–8. 4. Abrahami D *et al. Gut* 2022; 71(1):111–8. 5. Baruch EN *et al. Science* 2021; 371(6529):602–9. 6. Davar D *et al Science* 2021; 371:595–602.

Neoadjuvant immunotherapy, the gut microbiome and circulating immune subsets: implications for efficacy and toxicity

Prof Georgina Long (Co-Medical Director of Melanoma Institute Australia) and Ms Rebecca Simpson (PhD candidate, The University of Sydney)

The gut microbiota modulates immune process both locally and systemically and is likely to influence both response and toxicity development during immunotherapy. Unlike other factors involved in treatment efficacy, the gut microbiome is readily amenable to modification.

A recent publication (Simpson *et al. Nature Med* 2022; 28(11):2344–52) highlighted the roles of native gut microbiota signatures, dietary intake and systemic inflammation in determining the response to and toxicity from immune checkpoint inhibitors. It involved prospectively profiling the baseline gut microbiome and dietary patterns of patients from Australia and the Netherlands (n=103) and performing integrated data analysis with additional melanoma patients from the USA (n=115) who were treated with immune checkpoint inhibitors.

Ruminococcaceae- vs *Bacteroidaceae*- dominated ecotypes

Those with *Ruminococcaceae*-dominated microbiomes (majority of the population from the Netherlands) vs *Bacteroidaceae*-dominated microbiomes had:

- Higher rates of response (p=0.003)
- Significantly higher microbial diversity (p<0.0001)
- Higher relative abundance of methanogens (p=0.0029)
- Association with higher fibre consumption (p=0.0331)

Those with *Bacteroidaceae*-dominated microbiomes (majority of the population from the USA) vs *Ruminococcaceae*-dominated microbiomes had:

- Lower rates of response (p=0.003)
- Enhanced potential for microbial degradation of intestinal mucin (p=0.0001)
- Elevated levels of C-reactive protein (CRP; p=0.018)

Further, when the *Bacteroidaceae*-dominated cohort was stratified, a significant reduction in the relative abundance of *Faecalibacterium prausnitzii* (a key fibre that is critical for the maintenance of barrier function and promoting local immune regulation in the gut) was associated with non-responders (which was not evident in those with *Ruminococcaceae*-dominated microbiomes; p=0.0056).

When comparing different cohorts across countries and cancer types, and further, when accounting for the reproducibility of results in the clinic, the assemblage of microbial communities is an important factor to consider.

Circulating immune subsets

Baseline patient data suggested that underlying microbe–immune interactions prime patients for treatment outcomes. Using mass cytometry, and detecting up to 40 markers simultaneously, peripheral blood mononuclear cells (PBMCs) collected from patients pre- and post-treatment (baseline and Week 6, respectively), were profiled.

Preliminary results show that within the Australian subset (n=71):

- Pathological responders had a higher ratio of regulatory T cells to CD8+ effector memory T cells (Tem) prior to treatment (baseline, p=0.0461)
- Neoadjuvant treatment with ipilimumab/nivolumab for 6 weeks reduced regulatory T cells (p=0.0029) and an expansion of CD8+ Tem (p=0.0096); this was evident irrespective of pathological response status

Harnessing the microbiome – potential targets and multicancer trails

Dr Katrin Sjoquist (Medical Oncologist, Clinical Lead, NHMRC Clinical Trials Centre)

The microbiome is associated with a range of health issues including allergic diseases, gut inflammation and bowel disorders, cardiovascular disease, diabetes, among others. There are studies that have used non-dietary interventions targeting the gut microbiome to treat these health issues. However, interest in the microbiome and its relation to oncology is only emerging. The relationship between the human microbiome and cancer evolution and treatment is complex due to the differing tumour types, location, and settings.

Evidence for interventions to manipulate the microbiome for therapeutic benefit were summarised. Studies involving interventions targeting the microbiome in cancer therapy are generally early phase and focused on immunotherapy.[1–3] However, the relationship between the microbiota, immunity and cancer therapy, and how it affects immunotherapy response still remain unclear. Discussions focused on current unanswered questions and directions for future research and collaboration.

1. Dizman N, *et al*. *Nat Med.* 2022; 28:74–12. 2. Baruch EN, *et al. Science.* 2021; 371(6529):602–9. 3. Davar D, *et al. Science.* 2021; 371(6529):595–602.

Session 4: ctDNA guiding treatment of multiple cancer types

ctDNA guiding adjuvant chemotherapy in early stage colon cancer: are we moving the needle?

A/Prof Jeanne Tie (Medical Oncologist. Senior research fellow, Peter MacCallum Cancer Centre and Walter and Eliza Hall Institute of Medical Research)

Treating minimal residual disease (MRD) using adjuvant chemotherapy helps improve survival in patients with colorectal cancer. However, to date, there is no assay that accurately measures MRD. This translates to imprecise staging of patients where many are treated and only a few saved.

Circulating tumour DNA (ctDNA) has been used to detect MRD after curative treatment (e.g. primary removal), where detection has been associated with recurrence and has been demonstrated in patients with:

- Stage 2 colon cancer (no chemotherapy; HR: 18, p<0.001, n=178)[1]
- Stage 3 colon cancer (chemotherapy; HR 3.8, p<0.001)[2]
- Locally advanced rectal cancer (HR 11, p<0.001)[3]
- Early stage colorectal cancer (2–8 weeks post-surgery, ± adjuvant chemotherapy; HR 14.1, p<0.0001, n=154 and 6 months post-surgery and/or any adjuvant chemotherapy; HR 20, p<0.001, n=254)[4]

DYNAMIC was a multicentre, randomised, phase 2, non-inferiority trial of patients with stage 2 colon cancer (n=455). Patients were randomised to have treatment decisions guided by either ctDNA results or standard clinicopathological features. For ctDNA-guided management, a ctDNA-positive result at 4 and/or 7 weeks after surgery prompted oxaliplatin-based or fluoropyrimidine chemotherapy. Patients who were ctDNA-negative were not treated and were observed). The primary endpoint was regression-free survival at 2 years.[5]

ctDNA-guided management was non-inferior to standard management (93.5% and 92.4%, respectively). Three-year recurrence-free survival was 86.4% among ctDNA-positive patients

who received adjuvant chemotherapy and 92.5% among ctDNA-negative patients who did not.[5]

It was concluded that ctDNA dynamics (post-surgery or post-chemotherapy) reflects treatment benefit and ctDNA clearance can be used as a surrogate marker for adjuvant treatment benefit. Further, there are now trials exploring the use of novel adjuvant therapies in those who are ctDNA negative.

1. Tie J, *et al. Sci Transl Med.* 2016; 8(346):346ra92. 2. Tie J, *et al. JAMA Oncology.* 2019; 5(12):1710–7. 3. Tie J, *et al. Gut.* 2019; 68(4):663–71. 4. Cohen SA, *et al. Ann Oncol.* 2022; 33(suppl 7):S683–4. 5. Tie J *et al. N Eng J Med.* 2022; 386:2261–72.

ctDNA captures distinct clonal dynamics following alternating osimertinib and gefitinib therapy in advanced EGFR T790M positive non-small cell lung cancer: results from the OSCILLATE trial

Dr Lavinia Tan (Medical Oncologist and PhD candidate, Peter MacCallum Cancer Centre)

OSCILLATE was a single arm, phase 2 trial to investigate whether alternating osimertinib and gefitinib would alter selection pressures that drive clonal evolution to delay the development of osimertinib resistance in advanced, non-small cell lung cancer (NSCLC) with the epidermal growth factor receptor (*EGFR*) T790M mutation. OSCILLATE enrolled 47 participants with tumour and/or plasma positive for *EGFR* T790M following progression on first or second-generation *EGFR* tyrosine kinase inhibitor (TKI). Serial ctDNA analysis revealed distinct clonal dynamics with decrease and clearance of both the activating *EGFR* and T790M mutations predictive of treatment response and clinical outcomes. Importantly, the alternating regime was associated with frequent loss of T790M ctDNA in 73% of participants and no evidence of the *EGFR* C797S resistance mutation at disease progression. Despite achieving this goal, the study did not reach the pre-specified target 12-month progression-free survival (PFS) of 65% required to warrant further evaluation. These data highlight the clinical importance of resistance mechanisms beyond suppression of selected genetic mutations in driving therapeutic escape to highly potent targeted therapies.

Incorporating ctDNA studies in cancer trials

Dr Sonia Yip, PhD (Translational Research Lead. Senior Research Fellow, NHMRC Clinical Trials Centre)

ctDNA is shed from the tumour into the blood of an individual. ctDNA is a subset of the broader population of cell-free DNA (cfDNA) shed from any cell type into the blood.

Study design

Studies of ctDNA can be incorporated into a trial as an exploratory objective, where samples are collected prospectively and the laboratory analyses are then conducted retrospectively. Study design considerations include the selection of blood timepoints, alignment with other study assessments and whether results are returned to the treating clinician/participant.

Another trial design is where ctDNA results obtained in real-time are then used to:

- Determine participant eligibility, stratification; or
- To guide treatment of participants

Study design considerations include turn-around time from blood draw to return of results.

Pre-analytical considerations

The choice of blood collection tube type needs to be considered i.e. specialised tubes vs EDTA tubes common in the clinical setting. From the literature, the quantity, quality, and test results downstream are comparable between the tube types provided EDTA tubes are processed and that the double-spun plasma is frozen within 1–2 hours of phlebotomy.

Other sources of cfDNA

- Ascites
- Microbiome blood-borne microbial DNA (mbDNA) profiles could discriminate between numerous types of cancer[1]

1. Poore GD, *et al*,. *Nature.* 2020; 579:567–74.

Workshop evaluation

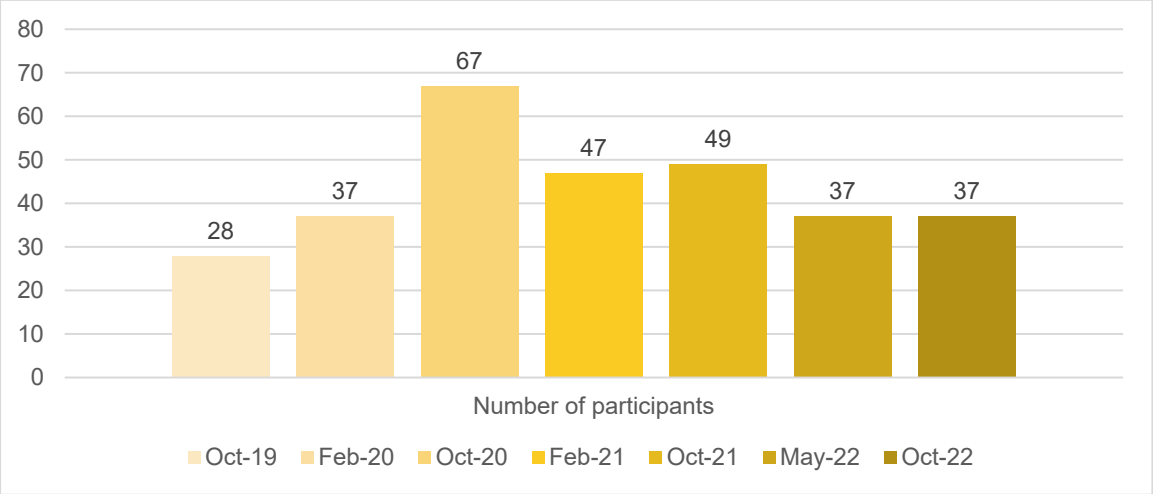
Introduction

The GCCTI is committed to continuous quality improvement and values workshop participants' feedback to help identify opportunities to improve future workshops. Workshop participants completed an online or paper survey to provide feedback.

Participation and survey response rate

Thirty seven participants attended the GCCTI October 2022 workshop; 17 participants (46%) attended in-person and 20 participants (54%) attended virtually.

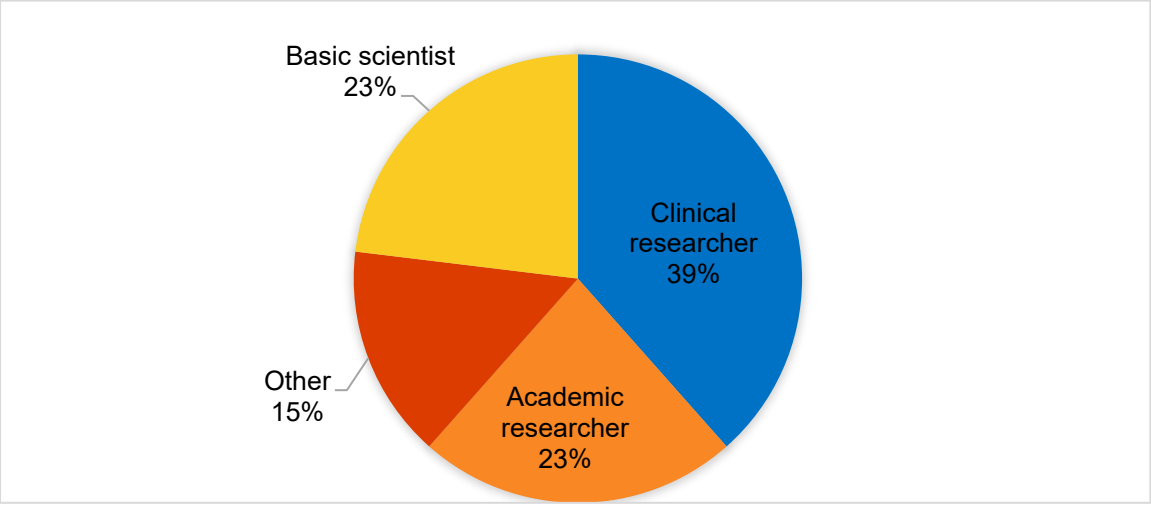
Figure 1: Number of participants at GCCTI workshops (frequency)



Twelve of the 37 participants who attended the workshop completed the survey (a 32% response rate), a decrease in the response rate from the previous workshop, which was 51%.

The majority of survey respondents identified as clinical researchers (42%), followed by academic researchers and basic scientists (25% each).

Figure 2: Participant roles (frequency and proportion)



Organisations/groups in attendance

Participants from organisations/groups across Australia attended.

- Cancer Australia
- Commonwealth Department of Health
- Fiona Stanley Hospital, WA
- Garvan Institute of Medical Research, NSW
- Melanoma Institute Australia
- NHMRC Clinical Trials Centre, NSW
- Peter MacCallum Cancer Centre, VIC
- Prince of Wales Hospital, NSW
- Princess Alexandra Hospital, QLD
- Royal Melbourne Hospital, VIC
- The University of Melbourne, VIC
- The University of Sydney, NSW
- University of NSW (UNSW), NSW
- University of Newcastle, NSW
- University of Queensland, QLD
- University of Technology Sydney (UTS), NSW
- Westmead Institute for Medical Research (WIMR)
- Cancer service – CQUEST
- Cancer Cooperative Clinical Trials Groups (CCTGs)
    1. AGITG
    2. ANZCHOG
    3. ANZGOG
    4. BCT
    5. MASC
    6. PC4
    7. PaCCSC & CST
    8. PoCoG
    9. TOGA

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Understanding the workshop's aim and purpose

100% of respondents indicated that they had a clear understanding of the aims and purpose of the workshop.

73% of respondents ‘agreed’, and 27% of respondents ‘strongly agreed’.

Usefulness and relevance of the presentations

100% of respondents indicated that they found the content of the workshop presentations useful and relevant.

64% of respondents ‘agreed’, and 46% of respondents ‘strongly agreed’. One respondent noted:

“Very friendly atmosphere”

Organisation and format of workshop

100% of respondents indicated that the workshop was well organised

55% of respondents ‘agreed’, and 45% of respondents ‘strongly agreed’.

100% of respondents indicated that the hybrid format of the workshop was successful

64% of respondents ‘agreed’, and 46% of respondents ‘strongly agreed’. This is the first workshop run in a hybrid format. Many respondents indicated that hybrid meeting allowed flexibility for those who may not have been able to attend otherwise.

“Hybrid gave flexibility as needed to shift attendance from F2F –
I would not have been able to attend today without hybrid model”

“but always better with everyone in person”

Topics/aspects most interesting/useful

Participants were asked to comment on which workshop topics and aspects they found most interesting. Participants found all elements of the workshop equally interesting and useful. Respondents noted:

"Enjoyed breadth of topics spanning biostatistics, preclinical research, clinical research and attendance/engagement of clinicians, researchers, statistician."

"Found all talks interesting. The talks about grants were very practical and informative. The topics of microbiome and ctDNA are very topical and interesting."

"The discussion of basket/platform trials was very helpful. Also the microbiome also interesting as it wasn't an area of cancer research I was across"

Additional comments/suggestions to enhance future workshops

Participants were asked for suggestions to further improve workshops; the following suggestions were provided:

- Many participants agreed the hybrid meeting format was beneficial and provided flexibility to those who may have otherwise not been able to attend
- Longer breaks to allow for synergies and informal discussions
- Speakers to stay longer beyond their presentation for informal discussion
- Participants enjoyed learning about a topic from multiple perspectives, e.g. science to clinical trials

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Appendix: Workshop agenda

Venue Pullman hotel, Sydney Airport AND Zoom

Date Friday 28 October 2022

Time 9.00am – 3.30pm

Purpose The October Workshop aims to facilitate development of clinical studies based on molecular characterisation that involve cancers from more than one primary site and more than one Cancer Cooperative Trials Groups (CCTGs).

Time	Session	Presenter
9:00–9:15am	*Registrations*	
9:15–9:30am	**Welcome and introductions**	*Martin Stockler*
	Overview of GCCTI and achievements to date	*Martin Stockler*
	Working with GCCTI	*Martin Stockler*
9:30–10.00am	**Grants Update: what's new and helpful for grant-writers**	
	• MRFF – Cancer Clinical Trial Grant Opportunities • Cancer Australia - Priority-driven Collaborative Cancer Research Scheme	*Ruth Webster* *Alan Woods*
10:00–10:45am	**Statistical sharing and borrowing in clinical trials**	
	Statistical information borrowing in clinical trials: baskets, platforms, and other designs	*Ian Marschner*
10:45–11:00am	*Morning Tea*	
11:00–12:30pm	**Microbiome and molecularly targeted cancer treatment**	
	Harnessing the power of the microbiome in the cancer field	*Emad El-Omar*
	Neoadjuvant immunotherapy, the gut microbiome and circulating immune subsets: implications for efficacy and toxicity	*Georgina Long/ Rebecca Simpson*
	Harnessing the microbiome – potential targets and multicancer trails	*Katrin Sjoquist*
12:30–1:15pm	*Lunch*	
1:15–2:45pm	**ctDNA guiding treatment of multiple cancer types**	
	ctDNA guiding adjuvant chemotherapy in early stage colon cancer: are we moving the needle?	*Jeanne Tie*
	ctDNA captures distinct clonal dynamics following alternating osimertinib and gefitinib therapy in advanced EGFR T790M positive non-small cell lung cancer: results from the OSCILLATE trial	*Lavinia Tan*
	Incorporating ctDNA studies in cancer trials	*Sonia Yip*
2:45–3:05pm	**Progressing ideas**	*Group Discussion*
3:05–3:20pm	**Reflection, plans, feedback, and advice** *Review of GCCTI objectives and planning* *Stakeholder feedback and advice*	*Group Discussion*
3:20–3:30pm	**Wrap-up and close**	*Martin Stockler*