Genomic Cancer Clinical Trials Initiative

GENOMIC CANCER CLINICAL TRIALS INITIATIVE

FEBRUARY 2020 WORKSHOP REPORT

This report was finalised on 27 April 2020

Genomic Cancer Clinical Trials Initiative

Contents

INTRODUCTION

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

GCCTI is led by the NHMRC CTC in partnership with Zest. Scientific and technical input is provided by the NHMRC CTC, with project management, stakeholder engagement and communications undertaken by Zest.

The GCCTI project team, in collaboration with the Scientific Steering Group (SSG), held a one-day grant development workshop, at the Hotel Pullman Sydney Airport on **Friday 28 February, 2020.**

PURPOSE OF WORKSHOP

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

The February 2020 workshop focused on strengthening grant submissions for the 2020 rounds, as well as generating ideas for grants to submit beyond 2020. The workshop included:

- **presentations on current grant opportunities, guidelines, assessment criteria and recent changes**
- **mock grant review panels, providing participants with an opportunity to present grant proposals, to receive feedback form expert peers**
- **updates on current and imminent studies of genomic profiling to guide cancer treatment**
- **discussion of ideas for grants to submit beyond 2020**

As an introduction, Professor Martin Stockler (Chair of the GCCTI Scientific Steering Group and project team) opened the workshop by providing an overview of GCCTI's aims, achievements to date and future focus.

The morning session included a series of presentations from representatives of key funding bodies, to provide updates on the key grant programs in Australia. There were also discussions on the practical aspects of developing a grant, such as the grant review process, addressing assessment criteria, and considerations in the development of budgets and timelines. One presentation included a review of 2019 grant application outcomes, and what this means for success strategies in 2020.

This was followed by a group activity, where participants presented their developing grant proposals, for feedback and advice from their peers in the format of a mock grant review panel.

The afternoon session included a series of updates on current and imminent studies of genomic profiling to guide cancer treatment (LUMOS, ASPIRATION, MOST and BCL-XL). The workshop then concluded with a plenary discussion of the various ideas and proposals discussed throughout the day, including potential opportunities for GCCTI to support ideas for new areas, molecular targets, and/or drugs for development.

The full workshop agenda is presented in Appendix I

WORKSHOP WELCOME

Overview of GCCTI (Martin Stockler)

The primary aim of the GCCTI is to support the national cancer cooperative trials groups (CTGs) by developing mutation-specific clinical trials concepts and grant applications involving cancers from more than one primary site and more than one CTG.

The scope and key deliverables of the GCCTI from 2018-21 include:

- **Development of mutation-specific clinical trial concepts and protocols** that involve collaboration with more than one CTG and other key clinicians/groups
- **Submission of grant applications** for funding of these trials, including preparation of budgets
- Incorporation of **quality of life and pharmaco-economic measures, where applicable** (developed collaboratively with the Cancer Australia Chair in Quality of Life and Health Economics Technical Services)
- **Hosting bi-annual workshops** with all CTGs and key stakeholders to identify potential targets for the development of mutation-specific cancer clinical trial protocols

There are also a number of additional outcomes and benefits as a result of the GCCTI:

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

An outline of the future focus of GCCTI over this period included:

- Continued engagement with the Cancer Australia supported Technical Services
- Understanding and adapting to the changing grant processes and cycles
- Increased focus on consumer engagement
- Leveraging opportunities for international collaboration.

There are a number of ways that individuals can engage with the GCCTI, as follows:

- Developing and submitting concepts/ideas to GCCTI
- Working with GCCTI and other CTGs to design trials based on identified concepts
- Contributing to idea generation and prioritisation through attendance at GCCTI workshops and communicating with other CTGs, researchers and the GCCTI project team
- Input into grant applications by joining GCCTI supported grant development teams

CURRENT GRANT OPPORTUNTIES, GUIDELINES, ASSESSMENT CRITERIA AND RECENT CHANGES

This session involved four presentations covering current grant opportunities, guidelines, assessment criteria, recent changes and success strategies for 2020 grant applicants.

NHMRC Grants Programs (Davina Ghersi)

This session was presented by Adjunct Professor Davina Ghersi from the National Health and Medical Research Council (NHMRC), with a focus on the NHMRC Clinical Trials and Cohort Studies Grants 2020. Davina started by providing an overview of the NHMRC's restructured grants program, which are categorised into four grant types:

- **Investigator Grants** will consolidate separate fellowship and research support into one grant scheme that will provide salary funding to the highest performing researchers at all career stages, and a significant research support package.
- **Synergy Grants** will provide $5 million per grant for outstanding multi-disciplinary research teams to work together to answer complex questions.
- **Ideas Grants** will support innovative and creative research projects, and be available to researchers with bright ideas at all career stages, including early and mid-career researchers.
- **Strategic and Leveraging Grants** will support research that addresses identified national needs. This will include an enhanced *Targeted Calls for Research* scheme and a dedicated funding stream for Clinical Trials and Cohort Studies.

A maximum of two applications per round can be submitted by any individual across the Investigator, Synergy and Ideas Grant schemes. A maximum of two grants can be held concurrently, by any individual, with some exceptions. Grants aim to supports high-quality clinical trials and cohort studies that address important gaps in knowledge, leading to relevant and implementable findings for the benefit of human health.

Grant Connect

Workshop participants were encouraged to visit the Grant Connect website to download key documents for review prior to commencing proposal development. Grant Connect is the Australian Government's grants information system, which publishes current and forecasted grant opportunities and awards. Key documents include the latest Clinical Trials and Cohort Studies Grants Guide to applicants on preparing an application, Clinical Trials and Cohort Studies Peer Review Guidelines, SPIRIT Statement (or STROBE) and PRISMA.

Assessment of proposals and Category descriptors

Workshop participants were strongly encouraged to familiarise themselves with the category descriptors early on in the process of preparing an application. Category descriptors form the criteria applied by the Grant Review Panel (GRP), and are a key part of the assessment. An overview of the criteria applied under each respective category description was presented,

including *Significance* (40%), *Research Quality* (40%), and *Team Quality and Capability* (20%).

Other suggestions for successful grant applications included:

- Using a systematic review (such as PRISMA flow chart and checklist) to demonstrate the significance of the proposed research was noted as the ideal, including how the systematic review was completed, and reference to how this information has informed the proposed methodology or trial design.
- Referencing having reviewed relevant clinical trials registries to ensure that the proposal is novel, and does not duplicate current research studies.
- Demonstrating that there is need for a study addressing the proposed question.
- Articulating the anticipated end users of the study results including the relevance of the research question to them.
- Providing a table of milestones and performance indicators with corresponding dates. The approach should be specific to the proposed research and provide for effective monitoring of progress at twelve month intervals.
- Being realistic and honest with recruitment targets, including sample size and potential collaborators.
- Ensuring that a diverse representation of individuals is included in the research team, including but not limited to, involvement of early to mid-career researchers, diverse gender representation, and Aboriginal and Torres Strait Islanders.

Workshop attendees were also encouraged to participate on grant review panels to understand better the review process.

MRFF Grants Programs (Saraid Billiards)

Saraid Billiards, Director at the Health and Medical Research Office provided an overview of NHMRC's role in the context of the MRFF Grants Program. It was acknowledged that the MRFF Grants Program is administered by NHMRC on behalf of the Commonwealth Department of Health (the Department).

Saraid outlined the MRFF 10 year investment plan which was broken up into four themes; patients, researchers, research missions and research translation. Applications for MRFF funding were processed through the grant administration services; NHMRC or Business Grants Hub (BGH) with opportunities available on Grant Connect. Assessment panels were comprised of national and international representation with a broad range of expertise such as health services delivery and implementation and consumers.

The assessment criteria used in the review of the majority of MRFF applications was noted to align with NHMRC's established approaches and was broken into four criteria; Project impact (weighting 40%), project methodology (40%), capacity, capability and resources (20%) and overall value and risk of the project (not weighted).

Applicants should read the Grant Opportunity Guidelines and ensure they address the objectives, review the funding available, be realistic, undertake the assessment criteria and scoring matrix, and note that only one application is accepted per grant opportunity.

Saraid noted that the Clinical Trials Activity goal was to increase CT activity in Australia, help patients access CTs, and enable researchers to bring international trials to Australian patients, supported by a budget of $614.2 million budget over 10 years. Two initiatives that are currently under assessment include; 1) Rare Cancers, Rare Diseases and Unmet Need and 2) International Clinical Trials Collaborations (ICTC). Future CT grant opportunities that may include CTs include EPCDR – Medicinal Cannabis and the recently signed MOU with Texas Medical Centre. A consultation is planned for the Genomics Health Futures Mission draft roadmap as well as an evaluation of CT activity.

Saraid concluded by highlighting a number of important documents recently released and to watch out for including; the MRFF 2019-2020 implementation plan, the upcoming grant rounds, new policies, new MRFF website, the Medical Research and Innovation Priorities and the Medical Research and Innovation Strategy.

March 2020 update: In light of COVID-19 there are a number of uncertainties that the Office is working through.

Cancer Australia Grants (Gayle Jones)

This session was presented by Dr Gayle Jones, Research and Clinical Trials Manager at Cancer Australia. The presentation focussed on the Priority-driven Collaborative Cancer Research Scheme (PdCCRS) – 2020 Funding Round.

Priority-Driven Collaborative Cancer Research Scheme (PdCCRS)

As Cancer Australia's annual national research grants funding scheme, the PdCCRS is designed to collaboratively fund cancer research projects in areas of identified priority. It brings together government and other funders of cancer research to coordinate, co-fund and maximise the number of Australian cancer research grants funded, and to help avoid potential duplication of funded research in Australia. Workshop participants are encouraged to download the full details of the PdCCRS through Grant Connect.

Key discussion points included:

- Confirmation of the PdCCRS Research Priorities – Cancer Australia's research priorities in 2020 remain the same as for 2019, with specific priorities in primary prevention interventions and in cancer health services research. There are additional priorities in Gynaecological and Lung Cancer, and Funding Partner specific priorities. Full details are available on Grant Connect.
- The PdCCRS 2020 Funding Round includes two research categories: Standard Grants (Category A) and Early Career Researcher Grants (Categories B-D). Workshop participants are encouraged to review the specific applicant criteria under each of the respective categories, available on Grant Connect.

- The joint application process with NHMRC remains the same in 2020 with the PdCCRS aligned with the two NHMRC funding body schemes: Ideas Grants and Clinical Trials & Cohort Studies Grants.
- The PdCCRS question forms for both Standard Grants and ECR Grants have undergone some changes to the application forms, following input from relevant stakeholders:
    - CSO Categories are now in a table format for the single primary subcategory and the single secondary subcategory if relevant
    - Consumers named under the PdCCRS question relating to consumer involvement will now need to sign or insert their electronic signature in the consumer declaration panel on the form
- Key dates are noted below:

Activity	**Date/Time**
Grant Round Opens	4 March 2020
Minimum data due in NHMRC's granting system	CTCS applications: 1 April 2020 17:00 AEDT Ideas applications: 8 April 2020 17:00 AEST
NHMRC RGMS Grant Round Closes	CTCS applications: 29 April 2020 17:00 AEST Ideas applications: 6 May 2020 17:00 AEST
PdCCRS Grant Round Closes	13 May 2020 17:00 AEST
NHMRC Peer Review	August – September 2020
PdCCRS GRC Teleconferences	October – November 2020
Announcement of successful applications	December 2020
Funding Agreement Negotiations	January – February 2021
Earliest Start Date for Projects	February 2021
Latest Start Date for Projects	30 June 2021

March 2020 update: Due to the restrictions imposed on the clinical and research sector by the COVID-19 pandemic, the closing dates for submission of applications have been deferred in line with the NHMRC closing dates for Ideas grants and Clinical Trials and Cohort Studies grants. Please refer to addenda posted to the PdCRRS grant opportunity on GrantConnect.

Success Strategies for Grant Applications (John Simes)

John Simes outlined the new environment for Clinical Trials and Cohort Studies: a reduced funding package ($70m), a lower success rate (~5%), and a peer review process that is less able to judge specialised science and more based on a general approach and well-argued case for the non-specialist. There appears to be more emphasis on changes in practice and policy, as opposed to future research. Milestones and deliverables will require careful

planning; submissions will need to strike a balance between an ambitious vision (needed to demonstrate greater impact) and goals which are conservative enough that they are deliverable.

John outlined some key strategies that investigators should employ to help achieve high scores on the category descriptors.

For the *Significance* element (weighting 40%):

- Address important gaps in knowledge, leading to relevant and implementable findings for the benefit of human health, including knowledge, health, economic and social impacts
- Demonstrate improvements in health and wellbeing, health care practice or policy, providing reliable evidence of the effects of health-related interventions on health outcomes (or appropriate surrogates)
- Articulate the differences with previous research (including a systematic review), to provide a strong justification for the proposed research
- Demonstrate that the research question meets the needs of research end-users: consumers, community members, policy makers and clinical practitioners

For the *Research Quality* element (weighting 40%), the study should:

- Have strong design and research methodologies, appropriate to the research question
- Be comparable with the best international research in the field
- Be highly feasible, with all of the required techniques and resources established
- Be highly appropriate for research end-user involvement
- Have well-thought out and effective milestones and performance indicators

John also described some common problems or pitfalls of applications, including: a treatment effect that is implausibly large, a lack of pilot data, an overly optimistic compliance with treatments, insufficient completeness or follow-up, incorrect allowance for factors in sample calculations, a lack of clinical trial experience, and budgetary issues.

Points of discussion included:

- Low success rate in 2019 of trials through NHMRC Trials and Cohort Studies Scheme, and Cancer Australia
- MRFF have been a more successful source of funding in recent times. MRFF often require ‘shovel ready’ grants largely written in anticipation of funding rounds; recognise these are for niche areas.
- NHMRC trials are likely to be high impact practice changing studies
- Most projects awarded by Cancer Australia are basic science and/or translational research. Several trials for Cancer Australia were cut by NFFC by NHMRC
- Applicants need to prepare for a panel audience with a general, breadth of expertise, as opposed to being specialists in their field. The Clinical Trials Panel need to be able to judge a range on a range of disease areas and settings

- Where the study is linked to clinical trials (biological studies) and where the trial is not the primary objective of the grant, consider submitting the study through Ideas Grants (see eligibility ruling up front). In this scenario it will be judged on its innovation/ novelty as much as changing practice
- Consideration should also be given for lobbying future MRFF areas of research – e.g. MRFF is considering calls for research identified by consumer groups; MSAC submissions of current gaps in evidence, etc.

MOCK GRANT REVIEW PANELS (GRPs)

This session was facilitated as two group discussions, where attendees were provided the opportunity to present their grant proposals (through a one-page synopsis) to expert multidisciplinary panels comprised of other attendees, for discussion and feedback.

Proposals were at varying stages of development. There was robust discussion and feedback was provided, helping presenters to further develop and refine their concepts. Panel members considered the following questions when providing feedback to the presenters:

- What were the strengths of the proposal?
- What were the limitations?
- Which aspects of the proposal were not adequately covered?
- Was the sample size justification convincing?
- Were important potential biases and methods for their mitigation specified?
- How persuasive was evidence to support the study's feasibility?
- How evident was the research team's capacity and capability to deliver the project?

A summary of the ideas presented during this session can be found further down in this report, in the *Ideas for Grant Submission (in 2020 and beyond)* section.

CURRENT AND IMMINENT STUDIES OF GENOMIC PROFILING TO GUIDE CANCER TREATMENT

This workshop session included updates on the following studies: LUMOS, ASPIRATION, Most, and BCL-XL in mesothelioma.

LUMOS (Hao-Wen Sim)

LUMOS or Low and Intermediate Grade Glioma Umbrella Study of Molecular Guided Therapies - Pilot Study was presented by Dr Hao-Wen Sim on behalf of the LUMOS investigators. This is a 12-month pilot by COGNO with Professor Hui Gan as the Study Chair and the University of Sydney as the sponsor. The accrual target is 10 in Australia with 5 planned sites.

Background Grade 2 and 3 gliomas are the second largest group of malignant brain tumours in adults. Although the outcomes for G2/3 gliomas at progression/recurrence closely approach the poor outcomes for glioblastoma, there are virtually no trials for patients with relapsed G2/3 gliomas. LUMOS is an umbrella study specifically for patients with G2/3 gliomas to match patients with targeted therapies based on molecular testing using contemporaneous tumour tissue.

Aim This pilot study will generate preliminary feasibility data to support the full study. The full LUMOS study is intended to be an on-going multi-year study funded through a mixture of grants, philanthropic and industry funding. Key to attracting this funding will be providing proof-of-concept by demonstrating that this novel and ambitious concept is feasible.

Design LUMOS – Pilot Study will enrol a cohort of patients with contemporaneous tissue at the time of progression after prior radiotherapy and chemotherapy, to determine the feasibility of undertaking molecular phenotyping with a molecular panel to aid subsequent treatment selection.

Key Inclusion Criteria

- Adults, aged 18 years and older, with histologically confirmed grade 2 or 3 glioma at initial diagnosis. Has available tissue from resection for progressive disease for molecular profiling either within 6 months of study enrolment or following enrolment.
- Availability of tissue from resection for progressive disease for molecular profiling either within 6 months of study enrolment or following enrolment.
- Prior to last craniotomy and surgery, evidence of progressive disease as defined as evidence of new contrast-enhancing tumour and/or 25% increase in the size of the T2/FLAIR area compared to prior imaging after prior treatment with radiotherapy and chemotherapy.

The study was submitted to HREC ethics in September 2019 and 5 sites were selected for the pilot. MRFF grant was successful for 12 months and site activation was planned for Q1 2020.

ASPIRATION (Antony Mersiades)

ASPiRATION is an observational and interventional cohort study to assess the clinical impact of comprehensive genomic profiling (CGP) in patients with newly diagnosed metastatic non-squamous NSCLC (mNSCLC). This study is a collaboration between ALTG, the Australian Genomic Cancer Medicine, NHMRC Clinical Trials Centre and Lung Foundation Australia with support from the Australian Government and Roche.

Background ~20-25% of patients diagnosed with mNSCLC have actionable oncogene drivers, such as EGFR, ALK, and ROS1 for which there are clinically proven, highly effective, PBS subsidised targeted therapies. SOC molecular testing is currently based on national minimum paradigm and test requirements for PBS drug access, such as EGFR molecular testing, with limited broader oncogene panel testing in development and offered ad hoc. Comprehensive Genomic profiling (CGP) is expected to identify actionable genomic alterations in an additional estimated 16.9 % of patients however it is expensive with limited access. In many cases, treatments with proven activity and FDA approval exist, but are not currently available in Australia outside of clinical trial, self-funded or compassionate access avenues. Outcomes will determine the clinical value of CGP over SOC testing for molecularly defined subgroups and if found of value will provide a platform for national CGP testing in lung cancer.

Aim To investigate the clinical impact of comprehensive genomic profiling (CGP) in the management of metastatic NSCLC and assess the feasibility of CGP implementation nationally.

Primary objective To investigate whether routine CGP can be integrated into Australian clinical practice for mNSCLC patients by assessing the: 1) impact of CPG in generating actionable genomic information to personalise clinical decision making and 2) feasibility of routine CGP, including time to receipt of CGP results to inform clinical care.

Design A national multi-centre prospective observational cohort study, led by the ALTG, in collaboration with the AGCMC (MoST Study) co-ordinated through the NHMRC CTC.

Key Exclusion Criteria Any previous treatment for advanced and/or metastatic non-squamous non-small cell lung cancer; comorbidities or conditions (e.g. psychiatric) which may contraindicate participation and/or ability to comply with the protocol; and life expectancy less than 12 weeks.

There are currently 15 planned trial sites across Australia (13 with MoST; and two ALTG specific). Commencement of funding was January 2020 with the first patient planned to be screened in July 2020. It is estimated that 1,000 patients will be screened over 2 years (2020 – 2022) with follow up 2 years after (2022 – 2024), with analysis and publication end of 2024.

BCL-XL in Mesothelioma (Surein Arulananda)

BCL-XL inhibition in combination with cisplatin is effective in malignant pleural mesothelioma due to its dependency on the BCL-XL pro-survival protein. This study is a collaboration

between ALTG and Lung Foundation Australia, and sponsored by Roche, Astra Zeneza, Bristol-Myers Squibb, MSD and Pfizer.

Background Lung cancer has an incidence rate of 2.5 per 100,000 people and has the lowest 5 year survival of all cancers in Australia with a median survival of 12 months. Furthermore, systemic treatments have been limited to chemotherapy. Malignant pleural mesothelioma (MPM) is a lethal malignancy with limited therapeutic options. Evasion of cell death is one consequence of over-expression of pro-survival BCL-2 proteins.

Design Using the H-Score method, the association between the BCL-2 family protein expression and survival in 326 MPM patients were evaluated. *In vitro* assays were performed to evaluate the efficacy of BCL-Xl inhibitors with cisplatin in MPM cell lines. BCL-Xl inhibitors in combination with cisplatin were tested *in vivo*.

Results Patients with high BCL-2 expressing tumours had a worse OS, and high BCL-XL expression had a non-significant trend towards inferior OS. Potent cell killing was observed *in vitro* with BCL-Xl inhibition using A-1331852 and ABT-263. Enhanced apoptic-mediated cell killing occurred when ABT-263 or A-1331852 were titrated with cisplatin. In the xenograft model, significant anti-tumour response and improved survival was observed with the combination of cisplatin and A-1331852 or ABT-263.

Conclusion High BCL-Xl and BCL-2 are associated with poor survival in MPM. BCL-XL inhibition in combination with cisplatin demonstrated significant responses *in vitro* and *in vivo*, supporting expansion to human trials.

MoST (David Thomas)

David Thomas provided an update on the MoST/ AGCMC study. If you would like more information, please contact David at d.thomas@garvan.org.au

IDEAS FOR GRANT SUBMISSION IN 2020 AND BEYOND

The final workshop session included a plenary discussion of the ideas and concepts discussed throughout the day, but with a particular focus on the ideas presented at the mock grant review panels, and the questions and opportunities that could arise from these.

QUIZESCENCE+5-FU (Carolyn Grove)

This is an ALLG phase Ib feasibility study originally developed to treat relapsed/refractory acute myeloid leukemia patients. However the approach of using the oral FLT3 inhibitor quizartinib to prevent chemotherapy induced myelosuppresion is applicable to solid malignancy.

Overview Chemotherapy-induced myelosuppression is a major complication for cancer patients causing high rates of morbidity and mortality. Furthermore myelosuppression is frequently managed by delaying and/or reducing the scheduled dose, and, as a consequence, the efficacy of the treatment can be compromised. Since chemotherapy is the cornerstone for treating many types of cancer, the development of compounds that inhibit myelosuppression would provide relief from its harmful side effects and allow for more effective cancer treatments.

It was found that the FLT3 tyrosine kinase inhibitor quizartinib rapidly induces quiescence of murine multipotent progenitors (MPPs), providing them with significant protection when exposed to cytotoxic compounds such as fluorouracil (5-FU), gemcitabine and cytarabine (1). MPPs are highly proliferative FLT3 expressing cells that are responsible for maintaining life-long blood production, and since they are markedly depleted by chemotherapy their loss is a significant component of myelosuppression.

It was therefore proposed that quizartinib has an unrealized potential as a protector of the hematopoietic system for cancer patients undergoing cytotoxic chemotherapy. The ability of quizartinib to prevent myelosuppression could be a significant benefit to cancer patients receiving chemotherapy where the tumour cells are not dependent on FLT3 signalling, and therefore would continue to cycle and retain sensitivity to chemotherapy.

Hypotheses

1. Quizartinib priming protects the human hematopoietic system from myelosuppression caused by bolus administration of 5-FU or gemcitabine.
2. Quizartinib priming in combination with 5-FU offers an effective treatment for **non**-FLT3-ITD AML patients
3. Quizartinib priming in combination with drugs such as 5-FU may avoid myelosuppresion, allowing exploration of higher doses or novel combinatorial therapies to improve outcomes

Design The plan is to investigate this hypothesis in a phase I clinical trial treating those with solid organ malignancy usually amenable to 5-FU treatment. The treatment is based on findings from preclinical studies that identified the most effective doses of quizartinib and 5-FU for treating mouse models of AML. The dosages are also based on data from clinical studies that have employed quizartinib and 5-FU as single agent therapies.

Accelerating Personalised Opioid Prescribing into Practice (Aaron Wong)

Overview Moderate to severe cancer pain affects most (53%) cancer patients. Opioids are the backbone of cancer pain management, however are prescribed in a trial-and-error approach. Most (80%) patients experience adverse effects (nausea, sedation, confusion, itch, constipation) which leads to the practice of opioid switching in 20% of these already unwell patients due to intolerable toxicity or inadequate analgesic effect. Personalising treatment is important, as opioid switching requires cancer patients to return repeatedly to health services with poorly controlled pain. It is likely that genetic differences account for varied inter-individual responses to opioids.

This research group successfully piloted the feasibility of establishing an Opioid Pharmacogenomic Registry of 50 patients, by prospectively collecting data on matched symptom, pharmacokinetic, and genomic data from metastatic cancer patients with pain over 5 sites over 8 months.

The proposed project, which is in its early stages of development, aims to expand the Opioid Pharmacogenomics Registry using a focused approach to recruit more participants based on learnings from the initial pilot, and to analyse participant data to determine the degree of pharmacogenomic influence on opioid response through interrogating known and exploratory correlations within the data. Through these associations, the project team aims to be able to formulate evidence based guidance around opioid prescribing based on known pharmacogenomic factors.

Molecular Profiling of Oesophageal/ Gastro-oesophageal Cancers (Andrew Barbour)

This idea aims to determine the benefits of comprehensive genetic profiling versus conventional panel testing. The idea is not suitable for GCCTI as it involves only one cancer and only one CTG however, it was useful for CTGs to hear about the idea as it initiated a productive group discussion.

Circulating DNA and Transplant Rejection (Alex Dobrovic)

This proposal aims to use circulating DNA to predict and understand transplant rejection. There is potential link to cancer in that monitoring cancer by monitoring circulating DNA is a growing field, with new evidence suggesting that it can be helpful in distinguishing early and late stage cancer, particularly colorectal. Although this idea doesn't directly involve cancer and therefore doesn't fit GCCTI criteria, it is a great example of an interesting idea which generated some useful discussion about the questions and opportunities that could arise.

WORKSHOP EVALUATION

Thirty-seven (37) participants attended the GCCTI February 2020 Grant Development Workshop, a significant increase from the 26 participants who attended the last GCCTI Grant Development Workshop held in March 2019. Participants represented the following groups/organisations from across the country:

- NHMRC CTC, University of Sydney
- Clinical Cancer Trial Groups (CTGs);
    1. Australasian Gastro-Intestinal Trials Group (AGITG)
    2. Australasian Leukaemia and Lymphoma Group (ALLG)
    3. Australian Lung Cancer Trials Group (ALTG)
    4. Australian & New Zealand Children's Haematology/Oncology Group (ANZCHOG)
    5. Australia New Zealand Gynaecological Oncology Group (ANZGOG)
    6. Australian and New Zealand Urogenital and Prostate Cancer Trials Group (ANZUP)
    7. Australia and New Zealand Sarcoma Association (ANZSA)
    8. Breast Cancer Trials (BCT)
    9. Cooperative Trials Group for Neuro-Oncology (COGNO)
    10. Melanoma and Skin Cancer Trials (MASC)
    11. Palliative Care Clinical Studies Collaborative / Cancer Symptom Trials (PaCCSC / CST)
    12. Psycho-oncology Co-operative Research Group (PoCoG)
    13. Primary Care Collaborative Cancer Clinical Trial Group (PC4)
    14. Trans-Tasman Radiation Oncology Group (TROG) Cancer Research
- St. Vincent's Hospital, NSW
- The Children's Hospital at Westmead, NSW
- Sir Charles Gairdner Hospital, WA
- Royal Adelaide Hospital, SA
- Austin Health, VIC
- Peter MacCallum Cancer Centre, VIC
- Garvan Institute of Medical Research, NSW
- Chris O'Brien Lifehouse, NSW
- University of Technology Sydney
- Murdoch University, WA
- University of Melbourne
- University of Queensland
- Department of Health
- Cancer Australia

Workshop participants were encouraged to complete a post-workshop evaluation form, with twenty (20) responses received (54%); a decrease in completion rate from the last workshop held in October 2019 (71%). However the absolute number of completed evaluation forms remained the same as the last workshop (20).

Similar to the previous two workshops, the majority of the responders were clinical researchers (60%) and representatives of the CTGs (35%), as well as some academic researchers.

Understanding of the workshop's aim and purpose

95% of respondents indicated that they had a clear understanding of the aims and purpose of the workshop (55% 'agreed' and 40% 'strongly agreed'), which is consistent with previous workshops. One respondent was undecided.

Usefulness and relevance of the presentations

95% of respondents indicated that they found the content of the workshop presentations useful and relevant (40% 'agreed' and 55% 'strongly agreed'), an improvement from 90% at the last workshop. One respondent was undecided. One respondent noted:

"Great presentations on potential trial ideas. Thought provoking."

Organisation of the workshop

All respondents (100%) found the workshop to be well organised (30% 'agreed' and 70% 'strongly agreed), an improvement from 96% at the October 2019 workshop.

Topics/ aspects most interesting/ useful

Participants were asked to comment on which workshop topics and aspects they found most interesting. Participants found all aspects of the workshop interesting and useful, including:

- Updates on current grant opportunities, guidelines and different funding bodies
- Mock grant review panel session
- Update on current and imminent studies of genomic profiling
- Innovative ideas generation session
- Grant proposals and possibilities for collaboration
- Hearing about work being carried out by other CTGs

Participants noted the following comments as part of the feedback form:

"The small group facilitated discussion was very useful"

"Informative insights in to upcoming grant opportunities"

Additional suggestions to enhance future workshops included:

Participants were asked for any comments on how workshops could be improved moving forward; the following suggestions were provided:

- Summary of concepts to be presented ahead of time or following the meeting to take back to the CTG members
- More time for group discussions, particularly in the afternoon
- Further discussion on study design

APPENDIX I: WORKSHOP AGENDA

Venue Pullman Hotel, Sydney Airport (191 O'Riordan St, Mascot, NSW 2020)

Date Friday 28 February 2020

Time 9.30am – 3.30pm

Purpose Strengthening grant submissions for the upcoming 2020 rounds, as well as generating ideas for grants to submit beyond 2020.

Time	Item	Presenter
9:15–9:30am	**Arrivals and registration**	
9:30–9:40am	**Welcome and introductions**	*Stuart Baker*
9:40–9:50am	**Overview of GCCTI and achievements to date**	*Martin Stockler*
9:50–11:00am	**Update on current grant opportunities, guidelines, assessment criteria and recent changes**	
	• Update on NHMRC Grants Programs	*Davina Ghersi*
	• Update on MRFF Grants Programs	*Saraid Billiards*
	• Update on Cancer Australia Grants	*Gayle Jones*
	• Success strategies for grant applications	*John Simes*
11:00–11:15am	*Morning Tea*	
11:15–12:45pm	**Mock Grant Review Panels (GRPs)**	*Small Groups*
	Attendees present synopses for 2020 grants proposals to receive feedback from the mock grant panels of expert peers, according to the standard NHMRC processes. Each proposal allocated 15 minutes for presentation, discussion and feedback.* **proposed grants for presentation need not be eligible for GCCTI support*	
12:45–1:15pm	*Lunch*	
1:15–2:00pm	**Update on current and imminent studies of genomic profiling to guide cancer treatment**	
	• LUMOS	*Hao-Wen Sim*
	• ASPIRATION	*Antony Mersiades*
	• MOST	*David Thomas*
	• BCL-XL in mesothelioma	*Surein Arulananda*
2:00–3:15pm	**Ideas for grants to submit beyond 2020**	*Group Discussion*
	Especially those including multiple cancer types and multiple cooperative groups	
3.15–3.30pm	**Wrap-up and close**	*Martin Stockler*