

Genomic Cancer Clinical Trials Initiative Newsletter

Welcome to the Genomic Cancer Clinical Trials Initiative (GCCTI) update. The GCCTI was established by Cancer Australia in 2013 and is led by the NHMRC Clinical Trials Centre in partnership with Zest. The aim of the initiative aims to facilitate the development of clinical trials that involve cancers from multiple primary sites and multiple Cancer Cooperative Trials Groups (CTGs). The main activities of the GCCTI are to develop capacity, ideas, and grant applications. Studies developed with the GCCTI that have been successfully funded include EMBRACE and AUTO-CHECK.

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Highlights from the October 2020 GCCTI workshop

The GCCTI Project Team in collaboration with the GCCTI Scientific Steering Group (SSG) hosted a bi-annual workshop on Friday 30 October 2020, with 57 participants in attendance

The workshop focused on innovative ideas and new concepts including the sharing of existing studies and ideas between Cancer Cooperative Trial Groups (CTGs) relevant to GCCTI, to support the prioritisation of concepts for grant applications in 2020 and beyond.

Presentations and discussion included:

- Updates on current grant opportunities and recent changes
- Systemic therapy and radiotherapy across multiple tumour types
- Understanding, interpreting, applying and explaining difficult results of genetic profiling
- Ideas for new areas, molecular targets, and/or drugs for development including progress on current projects

Further details of the presentations and discussions that took place at the workshop will be available to download from the GCCTI website soon.

Ideas/concepts/proposals in development

The GCCTI is currently collaborating with stakeholders to progress the following studies, each led by different investigators:

| Idea/concept/proposal | Summary |
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| <p>BCL-XL in mesothelioma</p> <p>Potential collaborators: ALTG, ANZGOG</p> | <ul style="list-style-type: none"> • Preclinical studies found that high BCL-XL and BCL-2 are associated with poor survival. BCL-XL inhibition in combination with cisplatin demonstrated significant responses in vitro and in vivo (mice), supporting extension into human trials. • Current proposed study is focused on lung cancer and mesothelioma, but there may be other potential targets such as head and neck, oesophagus, germ cell and urinary tract cancer. • GCCTI are undertaking some discussion and scoping to determine if and how collaboration with GCCTI might be of assistance, given its potential across multiple CTGs and tumour types. |
| <p>FLT3 TKI to reduce myelotoxicity of chemotherapy</p> <p>Potential collaborators: ALLG, AGITG, ANZGOG</p> | <ul style="list-style-type: none"> • 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. • GCCTI are undertaking some discussion and scoping to determine if and how collaboration with GCCTI might be of assistance (focusing on the platinum-resistant group), given its potential across multiple CTGs and tumour types. |
| <p>Immune check point inhibitors after chemotherapy for squamous cell tumours</p> <p>Potential collaborators: ANZGOG, AGITIG, ANZUP, TROG</p> | <ul style="list-style-type: none"> • To investigate the effect of consolidation immune checkpoint inhibition following radical therapy in mucosal squamous cell cancers. This would be investigated within a group of mucosal squamous cell cancers, including cervical, oropharyngeal, anal, vulval, vaginal or penile. • These cancers account for ~5% of cancers worldwide, with preponderance in LMIC. This group encompasses both common, less common and rare tumours (where clinical trials |

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| | <p>are challenging and information to guide treatment decisions is scarce).</p> <ul style="list-style-type: none"> • This study is being led by the UK based MRC Clinical Trials Unit at UCL. The study would be coordinated in Australia by the NHMRC Clinical Trials Centre in collaboration with ANZGOG, AGITG, ANZUP and TROG. • A grant application in Australia awaits confirmation of funding from the global study team. The GCCTI maintains an interest in the study and looks forward to re-engaging with collaborators |
| <p>Anti-ROR1 Therapy</p> <p>Potential collaborators: ANZGOG, BCT</p> | <ul style="list-style-type: none"> • Phase II single arm basket trial in patients with platinum resistant ovarian cancer using cirtuzumab, an anti-ROR1 monoclonal antibody, regardless of subtype or ROR1 expression status. • Revised from the original concept which was presented as a Phase II single arm basket trial in platinum-resistant ovarian cancers of cirtuzumab, recruiting patients with high ROR-1 expression, regardless of subtype. |

The GCCTI project team will work with interested CTGs and members to explore and strengthen existing and new concepts for grant submission. For more information, please get in touch with the GCCTI Chair, Martin Stockler.

Update on GCCTI supported studies

EMBRACE

The EMBRACE study is a Phase II clinical trial of the PARP inhibitor, olaparib, in HR-deficient metastatic breast and relapsed ovarian cancer in patients without germline mutations in BRCA1 and BRCA2. This trial aims to determine the activity of olaparib in each tumour cohort (TNBC and HGSOc) as determined by the objective tumour response rate, according to RECIST v1.1.

The application was successful in securing Cancer Australia funding in December 2016 and is led by Dr Katrin Sjoquist, Paul Waring et al., in collaboration with ANZGOG and BCT.

EMBRACE pre-screening recommenced 17 May 2019 following local RGO approval for an amended protocol to expand the current inclusion criteria with reference to breast cancer, which will assist with screening and recruitment.

The study is open and recruiting. There are currently 10 active sites, with 1 more site expected to be opened in 2020. >125 patients have completed pre-screening, of which 12 have been recruited.

COVID-19 and other challenges have resulted in delayed accrual, now estimated to end in the second half of 2020.

For more information about EMBRACE, please visit the [ANZCTR website](#) or contact embrace@ctc.usyd.edu.au.

AUTO-CHECK

AUTO-CHECK is a translational research study looking at the molecular determinants of autoimmunity and immune adverse events in advanced cancer patients treated with immune checkpoint inhibitors. The hypothesis of this study is that a group of patients with a genetic susceptibility to autoimmunity are more likely to develop an immune-related adverse event (IRAEs) after treatment with immune checkpoint inhibitors.

This study was funded in January 2017 by Cancer Australia and is led by Prof Matthew Cook (CIA) and Dr Sonia Yip.

AUTO-CHECK collected bio-specimens from 6 multi-site investigator-initiated trials across 4 CTGs (ALTG, ANZGOG, ANZUP and COGNO), with trials spanning 5 tumour types (endometrial, glioblastoma, mesothelioma, NSCLC, renal cell) – each trial using immune checkpoint inhibitors.

Recruitment closed on 20 December 2019. Overall 256 of a planned 300 patients were recruited. This will not affect the statistical analysis of AUTO-CHECK since it will be exploratory, descriptive analyses.

Over 450 real-time blood shipments from 86 (unique sites: 48) sites to the ANU central lab were arranged during the study. These blood collections ended on 30 June 2020. Molecular analyses of blood samples are ongoing.

For more information about AUTO-CHECK, please contact autocheck@ctc.usyd.edu.au.

GCCTI 1-day Grant Development Workshop Friday 26 February 2021 – Save the Date

Date: Friday 26 February 2021

Time: 9:00am – 3:30pm

Location: Virtual workshop via Zoom

The GCCTI are pleased to confirm **Friday 26 February 2021** as the date for its next 1-day grant development workshop.

Building on discussions at GCCTI's recent workshop in October 2020, this 1-day grant development workshop will focus on strengthening grant submissions for 2021 and beyond.

Further details will be circulated in due course.

GCCTI Support

The primary aim of GCCTI is to facilitate the development of mutation-specific clinical trial concepts that involve cancers from more than one primary site and across more than one CTG.

If you'd like to discuss an idea for a cancer clinical trial that includes multiple primary types and multiple CTGs, please complete and submit the [idea generation template](#) and forward it to the GCCTI Project Team through Natasha Black at Natasha.Black@zest.com.au. We look forward to hearing from you.

You can also access a range of information and resources from the GCCTI website: <http://gccti.org.au>

Season's greetings

The GCCTI Project Team would like to thank you for your continued support and collaboration. We wish you a safe and relaxing break over the holiday season, and look forward to working with you in 2021.



Get in touch
Consulting@Zest.com.au

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