Government of **Western Australia**
North Metropolitan Health Service
Sir Charles Gairdner Osborne Park Health Care Group

Sir Charles Gairdner Hospital and Osborne Park Health Care Group

Human Research Ethics Committee

Project Summaries for Approved Projects

July to September 2023 Quarter

Project summaries for proposals approved by the SCGOPHCG Human Research Ethics Committee – July to September 2023 quarter.

The material contained in this document is made available to assist researchers, institutions and the general public in searching for projects that have ethics approval from the SCGOPHCG HREC. It contains summaries of projects approved in the July to September 2023 quarter.

Project Title	Diagnostic Efficacy of PET/CT Guided Percutaneous Biopsy for Retroperitoneal Sarcomas
Coordinating Principal Investigator	Professor Rupert Hodder
Institution	Sir Charles Gairdner Hospital
Approval Date	03 July 2023
Retrospective cohort study of Western Australia's Soft Tissue Sarcoma Unit. 10 Year experience of utilising PET/CT prior to percutaneous biopsy to identify "hot" areas when selecting biopsy sites for suspected Retroperitoneal Sarcoma. Comparison between conventional CT guided percutaneous biopsy. Comparison to final histology from operative specimen will be conducted to assess efficacy. The additional time taken for PET/CT will be analysed to determine whether this negatively impacts time to surgery.	

Project Title	The impact of surgery and consequent lymphoedema on forearm bone density and structure in breast cancer patients
Coordinating Principal Investigator	Professor Bronwyn Stuckey
Institution	Sir Charles Gairdner Hospital
Approval Date	06 July 2023
We will compare the bone density by DXA and the bone structure by pQCT in both forearms – affected v non-affected side. We will assess the degree of skeletal muscle mass and fluid deposition in the affected v non-affected forearm as measured by whole body DXA v bio-impedance. We will calculate the absolute risk of fracture by conventional methods. The decision to use bone preserving medications to prevent bone loss and fractures is based on assessment of absolute fracture risk, taking into account BMD at the spine or femoral neck, age and previous minimal trauma fracture. Regional loss of bone strength, e.g. in the forearm is not considered in the decision to treat.	

If this study finds changes in BMD or structure in the forearm which put the affected forearm at risk, a rethink of the threshold for bone preserving intervention in the setting of breast cancer survival management will be needed and we believe would lead to a reduction in wrist fracture, and the burden to the individuals and the health system.

Project Title	Assessing the suitability of oncology patients to be managed by a Symptom Urgent Relief / Rapid Access Clinic: A cohort study and economic analysis.
Coordinating Principal Investigator	Dr Linda Coventry
Institution	Sir Charles Gairdner Hospital
Approval Date	06 July 2023

This study aims to evaluate the Symptom Urgent Relief Clinic (SURC) / Rapid Access Clinic (RAC) for medical oncology patients at a major metropolitan tertiary teaching hospital. The SURC / RAC opened on 7th February 2022 and this nurse led clinic delivered three models of care: A follow-up phone service; a phone / face to face clinic; and a fast track from the Emergency Department (ED) to SURC / RAC pathway.
This study is important as EDs are experiencing unprecedented burden, that has been exacerbated by the COVID-19 pandemic. Alternate models for emergency care of cancer patients are required. This study will have two components, a cohort study will evaluate usage of the SURC / RAC and an economic analysis will be conducted.
The primary outcome measures will be the (i) number of episodes of care delivered by the SURC / RAC; and (ii) an economic evaluation of the SURC / RAC.

Project Title	ADOPTION: AI in medical imaging – developing personalised therapy in oligoprogressive prostate cancer
Coordinating Principal Investigator	Ms Mikaela Dell'Oro
Institution	Sir Charles Gairdner Hospital
Approval Date	06 July 2023

The study will evaluate data which consists of the participants PET/CT scans (PSMA and FDG) throughout the course of their therapy, clinical data available, treatment regimens and patient outcomes such as overall survival to follow their response. AIQ Solutions provides the tools to facilitate the AI model, however, all anonymised analyses will be performed through UWA and no identifiable data will be released.
Prostate specific membrane antigen (PSMA) PET/CT imaging has recently been added to the Medicare Benefit Schedule, for the restaging of men with biochemical recurrence of prostate cancer [1]. With the expected increase of [68Ga]Ga-PSMA-11 PET/CT imaging, a unique opportunity presents to retrospectively evaluate radiomics which support therapeutic

pathways and timing of treatment initiation for long-term control of patients suffering from metastatic prostate cancer (MPC) [2]. Currently clinicians are required to manually identify and assess tumour activity which can be both labour-intensive and prone to both intra- and interobserver variability [3, 4]. Using tools such as TRAQinform IQ™, AI models can be developed to quantify and track all individual lesions on PET scans, deriving radiographic features such as activity and volume to predict patient prognosis.
Biochemical recurrence is estimated to occur in > 25% of patients with prostate cancer following primary curative therapy. As a result, there is an increasing number of MPC patients presenting for metastasis-directed therapy (MDT) such as stereotactic ablative radiotherapy (SABR), [177Lu] Lu-PSMA-617 radionuclide therapy (Lu-PSMA) and systemic therapies including hormone therapy and chemotherapy. However, questions still surround how best to prioritise metastatic deposits for localise and systemic treatment. Measuring the response/progression of individual lesions overtime would provide a comprehensive view of disease burden, allowing clinicians to quantify and predict effectiveness of treatment for individual lesions, thus improving patient quality of life. Furthermore, lesion-specific imaging features such as volume, lesion intensities (SUV, a measure of tracer uptake such as SUVmax and SUVmean) could be investigated using AI models to predict patient response in terms of overall survival (OS) and progression free survival (PFS).
This project is classified as negligible risk, as per the NHMRC definition (NS§2.1). The project requires the collection of retrospective imaging and clinical data for 200 study participants with extracranial metastatic lesions referred for CyberKnife (a robotic form of SABR), Lu-PSMA or systemic therapy. This study will have no impact on the treatment of participants. As obtaining of consent from 200 past participants who have completed treatment would be impractical, a waiver of consent is required.

Project Title	Diagnostic accuracy of ROTEMSigma® to predict clotting factor deficiency after separation of cardiopulmonary bypass? A retrospective cohort study.
Coordinating Principal Investigator	Dr James Preuss
Institution	Sir Charles Gairdner Hospital
Approval Date	06 July 2023

The aim of study is to assess the accuracy of ROTEM SIGMA to identify patients with a poor ability to form clots after separation from the artificial heart and lung machine during open heart surgery.
Data, which has already been collected and published, from 180 patients will be used to assess ROTEMSigma's ability to accurately identify patients with clotting abnormalities. There will be no change to the anaesthetic or surgical procedure and there will be no additional blood tests taken.

Project Title	Stepping up: The future of step tests in adults with Cystic Fibrosis- investigating the impact of Trikafta on exercise capacity using step tests.

Coordinating Principal Investigator	Miss Tamara Hatton
Institution	Sir Charles Gairdner Hospital
Approval Date	13 July 2023

The aim of this study is to retrospectively assess the impact of Trikafta® on exercise capacity using two novel step tests. The secondary aim is to compare responsiveness of the two tests, given a ceiling effect with the A-STEP was noticed.
We hypothesise that Trikafta® will improve exercise capacity as demonstrated by an improvement in step test results. In addition, we hypothesise the effect size for the change in exercise capacity will be greater when using the MCST than the A-STEP as performance on the MCST is less often limited by a ceiling effect.

Project Title	DZ2022E0005: A Phase 3, Open-Label, Randomized, Multi-Center Study of DZD9008 versus Platinum-Based Doublet Chemotherapy as First-Line Treatment for Patients with Locally Advanced or Metastatic Non-Small Cell Lung Cancer Harboring Epidermal Growth Factor Receptor Exon 20 Insertion Mutation
Coordinating Principal Investigator	Dr Samantha Bowyer
Institution	Sir Charles Gairdner Hospital Peter MacCallum Cancer Centre Royal Melbourne Hospital The Prince of Wales Hospital
Approval Date	03 August 2023

This is a phase 3, open-label, randomized, multi-centre study assessing the efficacy and safety of DZD9008 versus platinum-based doublet chemotherapy in participants with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) Exon20ins mutation, who are newly diagnosed or have not received prior systemic therapy in advanced stage. Participants enrolled will be randomized to DZD9008 or platinum-based doublet chemotherapy in a 1:1 manner, stratified by baseline brain metastasis (with/without).
The study consists of 3 phases: Screening Phase, Treatment Phase and Follow-up Phase. Participants will undergo response evaluation criteria in solid tumors (RECIST 1.1), pharmacokinetics and safety evaluations (including physical examinations, ophthalmic assessments, cardiac function testing, documentation of adverse events, vital sign measurements and laboratory tests).

Project Title	Changes in lipoprotein(a) levels following acute myocardial infarction

Coordinating Principal Investigator	Dr Nick Si Rui Lan
Institution	Sir Charles Gairdner Hospital
Approval Date	09 August 2023

This will be a longitudinal observational study. Patients with AMI will undergo blood tests as per the below table for this study. Initial blood tests whilst the patient is hospitalised will be performed on samples collected as part of routine clinical care. Following discharge from hospital, patients will be asked to attend a PathWest specimen collection centre (can be performed at their local centre) for the day 7 and day 28 follow-up blood tests; results will be sent to the investigators. The assay that is used by PathWest to measure Lp(a) is the Randox/Denka Seiken assay.
We aim to evaluate the change in Lp(a) levels following AMI, by measuring Lp(a) at serial time points. The hypothesis is that Lp(a) levels are lower at the time of AMI and will increase after the event.

Project Title	Individualised cytokine analysis in critically ill patients with septic shock or pancreatitis
Coordinating Principal Investigator	Dr Matthew Anstey
Institution	Sir Charles Gairdner Hospital
Approval Date	07 September 2023

This research aims to use new laboratory technologies (isoplexis) that are able to characterise a patient's immune response at a cytokine level, in order to understand the inflammatory profiles that occur in the "sickest of sick" patients in the ICU. Being able to characterise this immune response will set the stage for future work to use drugs targeted at the particular part of the immune response causing inflammation and ongoing harm to the body.
We plan to measure the immune response in three groups of patients: healthy volunteers, and patients admitted to ICU with severe sepsis (infections) or pancreatitis). This immune response will be measured over time. The analysis will compare the groups of patients, as well as linking the results to clinical and laboratory variables that clinicians usually use to diagnose and treat patients.
The teams involved are multi-disciplinary, including immunology, intensive care, surgery, infectious diseases and laboratory science.
The conditions being explored remain high mortality conditions (and sepsis is a common condition), and for those patients who survive, they end up spending long periods of time recovering from their illnesses. Finding new therapies to reduce the severity of illness will have significant implications for the patients themselves, as well as the burden on the WA hospital system.

Project Title	Safety, tolerability and efficacy of the use of EvusHeld® as pre-exposure COVID-19 prophylaxis in kidnEy and simuLtaneous pancreas kiDney transplant recipients – the Australia and New Zealand experience
Coordinating Principal Investigator	Dr Wai Lim
Institution	Sir Charles Gairdner Hospital Fiona Stanley Hospital Royal Perth Hospital Westmead Hospital Royal North Shore Hospital
Approval Date	07 September 2023
The major pandemic caused by the emergence of a novel coronavirus COVID-19 in 2019 has led to over 6 million deaths worldwide. With the discovery and global availability of vaccine candidates and antiviral therapies, the tide of the pandemic is slowly turning, with the response of the majority of countries transitioning from strict lockdowns and quarantine to living with the virus in the community. Although antiviral treatments are effective in reducing the spread and severity of COVID-19 infection, novel preventative treatment option may provide additional protection against COVID-19. This study aims to describe the characteristics of kidney and simultaneous pancreas kidney (SPK) transplant recipients who have received Evusheld® as pre-exposure prophylaxis against COVID-19 infection, and to develop a predictive model that identifies kidney and SPK transplant recipients who have received Evusheld® at risk of developing moderate and severe/critical COVID-19 infection.	

Project Title	Use of archival samples to analyse the tumour microenvironment in GIST (gastrointestinal stromal tumour)
Coordinating Principal Investigator	Professor Ruth Ganss
Institution	Sir Charles Gairdner Hospital Harry Perkins Institute of Medical Research - North PathWest Fiona Stanley Hospital PathWest QEII
Approval Date	07 September 2023
This project will obtain spatial transcriptomic profiles from retrospective formalin-fixed & paraffin-embedded (FFPE) GIST biopsies. Digital spatial profiling (supported by Visium, Vizgen Merscope or NanoString CosMx platform technologies available in WA) will allow us to understand the interactions within the microenvironment in GIST including TLS. Where appropriate we will also undertake RNA sequencing, RNA in-situ profiling and antibody binding assays. These studies will help define the functional heterogeneity of the microenvironment in GIST as well as provide insight into the role of the immune landscape on tumour growth, disease progression and treatment response. By correlating the presence and extent of specific microenvironment characteristics with GIST grade, patient survival and	

treatment response we will be able to identify useful patient stratification strategies that could help inform clinical decision making.

Project Title	Subarachnoid Haemorrhage Aneurysm RErupture Prediction And Patient Expressed Results Study 3 - Investigating the utility of routinely assessable biomarkers of early brain injury at admission for pre-treatment re-bleed prediction following aneurysmal subarachnoid haemorrhage
Coordinating Principal Investigator	Dr Arosha Dissanayake
Institution	Sir Charles Gairdner Hospital
Approval Date	12 September 2023

This is a retrospective 1:4 exact matched case-control study nested within a 14-year cohort of 1007 consecutive patients who suffered 1009 consecutive episodes of aSAH from the rupture of a single saccular aneurysm all managed at Sir Charles Gairdner Hospital. Cases of pre-treatment re-bleeding include 84 patients from this cohort who will be matched based on aneurysm size, parent artery location, theinitial clinical grade at admission measured using the World Federation of Neurosurgical Societies clinical grade as a measure of conscious state compromise and the initial Fisher radiological grade of the aSAH to 336 controls.
We will retrospectively assess each patient's clinical, biochemical and imaging biomarkers of EBI available at the time of admission following aSAH. We will then perform univariate analysis, multivariate conditional logistic regression analysis, area-under-the-receiver-operator-characteristic analysis and 3-knot cubic spline function analysis to find which factor(s) are most useful for predicting the risk of pre-treatment re-bleeding after admission with aSAH.

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