21st ANNUAL SCIENTIFIC MEETING
Convened by Doctor Lorraine Chantrill
Adelaide Convention Centre
21–23 August 2019
Target survival with the only fully human mAb

*In RAS WT mCRC.

Contraindications:

- RAS/NRAS and/or KRAS metastatic colorectal cancer (mCRC) or for whom RAS status is unknown (see full PI PRECAUTIONS – Laboratory tests) as first-line therapy in combination with FOLFOX by patients who have received front-line fluoropyrimidine-based chemotherapy including irinotecan. Efficacy may be influenced by patient performance status.

Dosage and Administration:

- Refer to full Product Information before prescribing – available from Amgen Australia Pty Ltd, Ph: 1800 803 638.


PBS Information: Authority Required (STREAMLINED). Refer to PBS Schedule for full Authority Information.
Dear Colleague,

Welcome to the 21st Annual Scientific Meeting of the Australasian Gastro-Intestinal Trials Group. The Executive Organising Committee and discipline sub-committees have developed a program that is sure to inform and engage, centred on the theme, “Challenging the enigmatic nature of GI cancers”.

We are fortunate to have highly esteemed international and national expert Invited Faculty presenting on topics carefully chosen to delve deep into the controversies of GI cancer treatment. Together with trial presentations from AGITG members, this year’s program will tackle challenges in the GI cancer landscape and present opportunities for participation in AGITG research.

The Keynote Breakfast sessions that begin each day, feature members of the Invited Faculty in medical and radiation oncology. The Plenaries and Translational Symposia cover a wide range of topics, and will include insights from the Invited Faculty. There will also be a focus on AGITG clinical trials and translational research in three sessions: Early Colorectal Cancer; Advanced Colorectal Cancer; and Upper GI Cancer including Hepatobiliary (HPB), Gastrointestinal Stromal Tumour (GIST) and Neuroendocrine Tumours (NETs).

Of course, the ever-popular New Concepts Symposium and Posters Session are back this year. A few of the workshops that are highlights of the ASM this year include the Colorectal Cancer Multidisciplinary Team Workshop, the Surgical-Radiation Oncology Breakfast focussed on State of the Art Therapies for Rectal Cancer, the Consumer-Study Coordinator Forum, and the Radiation Oncology Workshops in Stereotactic Body Radiation Therapy (SBRT) for pancreatic and liver cancer. The Trainees Workshop has been expanded this year to an intensive session on Tuesday. The meeting will conclude with an International Expert Panel discussion about pancreas cancer, which is not to be missed.

We will acknowledge the many achievements of our members at the 21st Annual Reception and Dinner on Thursday evening. AGITG Chair, Professor Tim Price, will present the John Zalcberg OAM Award for Excellence in AGITG Research to this year’s recipient, announce the successful 2019 Innovation Fund grant project, and announce this year’s Merck-AGITG Kristian Anderson Award recipient. An important part of the evening’s formalities is the presentation of the Best of New Concepts Award, the Best of the Best and Fast Forward Awards and the AGITG Outstanding Site Award.

The meeting would not be possible without the generous support from our sponsors. Our sincere thanks go to the companies that have supported the meeting, enabling essential collaboration, sharing of knowledge, networking and learning to improve patient care.

The AGITG meeting has been the premier forum for the GI cancer research community in Australasia for two decades. We look forward once again to presenting, discussing and debating the best solutions to challenges in GI cancer treatment.

Our sincere gratitude goes to everyone who makes this meeting a valuable and successful event.

Yours sincerely,

Doctor Lorraine Chantrill
Meeting Convenor

Russell Conley
Chief Executive Officer

WELCOME

The Executive Organising Committee for AGITG 2019 thanks our sponsors for their valued and vital support for the meeting.

PLATINUM SPONSOR

Amgen is committed to unlocking the potential of biology for patients suffering from serious illnesses by discovering, developing, manufacturing and delivering innovative human therapeutics. This approach begins by using tools like advanced human genetics to unravel the complexities of disease and understand the fundamentals of human biology.

Amgen focuses on areas of high unmet medical need and leverages its expertise to strive for solutions that improve health outcomes and dramatically improve people’s lives. A biotechnology pioneer since 1980, Amgen has grown to be one of the world’s leading independent biotechnology companies, has reached millions of patients around the world and is developing a pipeline of medicines with breakaway potential.

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Because delivery matters*, we’ve never stopped developing Somatuline® Autogel®

*SOMATULINE® AUTOGEL® was an important attribute of an SSA delivery device according to an international nurse survey 1


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Storage:

- **Administration:**
  - No change to the needle size
  - Ready to use prefilled syringe
  - Administration by deep subcutaneous injection

The most commonly experienced adverse drug effects following treatment with subcutaneous (SC) Somatuline® Autogel® are gastrointestinal disorders (very commonly reported are diarrhoea, loose stools, and abdominal pain) and cholelithiasis (often asymptomatic).

Please refer to full product information for a comprehensive list of side effects.

**Dose:**

- For functional carcinoid tumours and acromegaly.
- For patients with metastatic disease.

Lanreotide as acetate in a pre-filled syringe (60, 90 and 120 mg).

**Interactions**

- **Metabolic:**
  - Patients with compromised liver function may require dose adjustment

**Precautions:**

- **Injection site reactions (pain, mass, induration, nodule, pruritis):**
  - Laboratory investigation changes, weight decreased, decreased appetite, musculo-skeletal pain, myalgia. See full PI for further information.

**Adverse Effects:**

- The most commonly experienced adverse drug effects following treatment with subcutaneous (SC) Somatuline® Autogel® (often asymptomatic).

For further information about Somatuline® Autogel® contact Ipsen Pty Ltd: T (03) 8544 8100 F (03) 9562 5152 E merck.com.au

**PBS Information: Somatuline® Autogel®** Authority required. (Streamlined for Public Hospitals for all indications and Community Access for functional carcinoid tumours and acromegaly.) Private Hospital Authority required. This product is a highly specialised drug listed on the PBS as a section 108 item. Please refer to the PBS schedule for full authority information.

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Bayer is a global enterprise with core competencies in the Life Science fields of healthcare and agriculture. Its products and services are designed to benefit people and improve their quality of life. The company has operated in Australia since 1925 and has a long-term commitment to the health and nutrition of all Australians. Locally, Bayer and Nutricia currently employ almost 900 people across the country and is dedicated to servicing the needs of rural Australia and the local community. Bayer is deeply committed to research and development and has a strong tradition of innovation. The company’s focus on people, partnerships and innovation underpins all aspects of its operations.

bayer.com.au

Ipsen provides specialty medicines and quality services to Healthcare Professional and their patients suffering from debilitating diseases. At Ipsen, our passion is improving the lives of patients. We do this by working together to build partnerships based on trust and mutual respect with Healthcare Professionals. We deliver tailored solutions through our agility and innovation and we strive to be even better tomorrow than we are today.

Ipsen Pty Ltd is the Australian affiliate of a global R & D focused pharmaceutical company.

ipsen.com.au

Merck, the vibrant science and technology company, operates across healthcare, life science and performance materials. Almost 53,000 employees work to make a positive difference to millions of people’s lives every day by creating more joyful and sustainable ways to live. From advancing gene editing technologies and discovering unique ways to treat the most challenging diseases to enabling the intelligence of devices – Merck is everywhere. In 2017, Merck generated sales of €15.3 billion in 66 countries.

Scientific exploration and responsible entrepreneurship have been key to Merck’s technological and scientific advances. This is how Merck has thrived since its founding in 1668. The founding family remains the majority owner of the publicly listed company. Merck holds the global rights to the Merck name and brand. The only exceptions are the United States and Canada, where the company operates as EMD Serono in healthcare, MilliporeSigma in life science, and EMD Performance Materials.

merck.com.au

Server is a privately owned pharmaceutical company governed by a non-profit foundation that is committed to therapeutic progress to serve patient needs. Server has a long-standing commitment to research and development. Worldwide, approximately 25% of branded product turnover is reinvested into research and development through the Server Foundation, with the aim of a 50% investment to fighting cancer by 2020.

Server has significant investment in Oncology and Haematology with broad research and development platforms in cancer cell apoptosis and immuno-oncology with an extensive pipeline of new products in early development. Server Australia is also home to the Asia-Pacific clinical trial hub currently managing 8 cancer clinical trials in Australia. Server is proud to support innovative programming programs with world class institutions including WEHI in Australia to further advance scientific understanding in the area of oncology.

Server Australia oncology products include Lonsurf® (trifluridine/tipiracil), Onivyde® (nanoliposomal irinotecan as succoate), Muphoran (fotemustine) and Oncaspar (pegaspargase).

servier.com.au
**ERBITUX** (cetuximab) FOR THE TREATMENT OF RAS wt mCRC

**mCRC**: metastatic colorectal cancer.
**RAS**: rat sarcoma oncogene, w/t v-hit-type.

**PBS Information:** Authority required. Refer to PBS Schedule for full authority information.


**LONSURF**

- Trifluridine/ tipiracil hydrochloride.
- Contains lactose. ≤ 14%.
- **MINIMUM PRODUCT INFORMATION**

**Product Information please go to www.servier.com.au/PI or telephone 1800 153 590.**

Please review Product Information before prescribing. To access a copy of the Product Information, please go to www.server.com.au/PI or telephone 1800 153 590.

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**References:**
1. Lonsurf Approved Product Information.
4. For continuing treatment (STREAMLINED 8183).
5. Refer to PBS Schedule for full authority information.

** make time for more moments**

Incorporation of trifluridine/ tipiracil hydrochloride in metastatic colorectal cancer (mCRC) with a WHO performance status of 1 or less, previously treated with, or not candidates for fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapies, anti-VEGF agents, and anti-EGRF agents.

**Contraindications:***
- History of hypersensitivity to tipiracil, trifluridine or excipients.
- Pregnancy Category D. Contraindicated in breastfeeding women.
- Lactation: should not be used. Lactation: should not be used.
- Children/adolescents under 18 years of age. Elderly (≥ 75 years).

**Precautions:**
- Very common: Neutropenia, leucopenia, anaemia, thrombocytopenia, diarrhoea, nausea, vomiting, decreased appetite, fatigue. Common: Lower respiratory tract infection, upper respiratory tract infection, febrile neutropenia, lymphopenia, mononcytosis, hyperbilirubinaemia, insomnia, dysgeusia, peripheral neuropathy, dizziness, flushing, headache, flushing, drowsiness, cough, abdominal pain, constipation, stomatitis, oral disorder, hyperbilirubinaemia, Palmar-plantar erythrodysesthesia syndrome, rash, alopecia, pruritus, dry skin, proteinuria, pyrexia, oedema, musculoskeletal pain, hepatic enzyme increased, lipase increased, alkaline phosphatase increased, weight decreased, Uncommon: Septic shock, infectious enteritis, lung infection, biliary tract infection, influenza, urinary tract infection, gingival infection, herpes zoster, tinea pedis, candidiasis, bacterial infection, infection, cancer pain, pancytopenia, granulocytopenia, monocytopaenia, thrombocytopenia, leukocytosis, lymphocytosis, neutropenia, anemia, thrombocytopenia, lymphopenia, eosinophilia, increased blood urea, increased sodium, increased creatinine, increased alkaline phosphatase, increased lactic dehydrogenase, increased aspartate aminotransferase, increased alanine aminotransferase, increased gamma glutamyl transpeptidase, increased bilirubin, increased total protein, increased blood lactate dehydrogenase, increased total protein, decreased C-reactive protein, increased haematocrit decreased. Post-marketing experience: interstitial lung disease.

**Adverse Effects:**
- Very common: Neutropenia, leucopenia, anaemia, thrombocytopenia, diarrhoea, nausea, vomiting, decreased appetite, fatigue. Common: Lower respiratory tract infection, upper respiratory tract infection, febrile neutropenia, lymphopenia, mononcytosis, hyperbilirubinaemia, insomnia, dysgeusia, peripheral neuropathy, dizziness, flushing, drowsiness, cough, abdominal pain, constipation, stomatitis, oral disorder, hyperbilirubinaemia, Palmar-plantar erythrodysesthesia syndrome, rash, alopecia, pruritus, dry skin, proteinuria, pyrexia, oedema, musculoskeletal pain, hepatic enzyme increased, lipase increased, alkaline phosphatase increased, weight decreased, Uncommon: Septic shock, infectious enteritis, lung infection, biliary tract infection, influenza, urinary tract infection, gingival infection, herpes zoster, tinea pedis, candidiasis, bacterial infection, infection, cancer pain, pancytopenia, granulocytopenia, monocytopaenia, thrombocytopenia, leukocytosis, lymphocytosis, neutropenia, anemia, thrombocytopenia, lymphopenia, eosinophilia, increased blood urea, increased sodium, increased creatinine, increased alkaline phosphatase, increased lactic dehydrogenase, increased aspartate aminotransferase, increased alanine aminotransferase, increased gamma glutamyl transpeptidase, increased bilirubin, increased total protein, increased blood lactate dehydrogenase, increased total protein, decreased C-reactive protein, increased haematocrit decreased. Post-marketing experience: interstitial lung disease.

**Interactions:**
- Drugs affecting the platelet activating factor (PAF) receptor: anti-PAF agents, leukotriene antagonists, PAF antagonists.
- Immunomodulating agents: allogeneic stem cell transplantation, lymphadenectomy, chemotherapy (e.g. zidovudine), hormonal contraceptives. Ability to drive and use machines: Possible occurrence of fatigue, dizziness or malaise. Adverse Effects:

**Therapeutic Indications:**
- Adults with metastatic colorectal cancer, previously treated with, or not candidates for fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapies, anti-VEGF agents, and anti-EGRF agents.

**Recommended starting dose of 35 mg/m².dose taken orally twice daily on Days 1 to 5 and Days 8 to 12 of each 28-day cycle, within 1 hour after completion of the morning and evening meals.**

**References:**

**PBS Information:** Authority required for initial treatment (STREAMLINED 8195).

**For continuing treatment (STREAMLINED 8183).**

Refer to PBS Schedule for full authority information.

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**Please review approved Product Information before prescribing.**

To access a copy of the Product Information, please go to www.server.com.au/PI or telephone 1800 153 590.
Roche is a global pioneer in pharmaceuticals and diagnostics focused on advancing science to improve people’s lives.

Roche is the world’s largest biotech company, with truly differentiated medicines in oncology, immunology, infectious diseases, ophthalmology and diseases of the central nervous system. Roche is also the world leader in in-vitro diagnostics and tissue-based cancer diagnostics, and a frontrunner in diabetes management.

The combined strengths of pharmaceuticals and diagnostics have made Roche the leader in personalised healthcare – a strategy that aims to fit the right treatment to each patient in the best way possible.

roche-australia.com

Headquartered in Singapore, Specialised Therapeutics (ST) is a privately-held international pharmaceutical company providing new specialist therapies and technologies to patients in Australia, New Zealand and across South-East Asia. Only therapies that fulfil unmet medical needs are considered by ST.

The current oncology portfolio includes ABRAXANE® (nanoparticle albumin-bound paclitaxel), NERLYNX® (neratinib) as well as the Oncotype DX® breast cancer assay. ST’s oncology pipeline includes novel therapies for cancer related anorexia cachexia (anamorelin), as well as ZEPSYRE® (lurbinectedin) for small cell lung cancer.

In addition, ST has a broader portfolio comprising haematology, neurology and ophthalmology therapies.

stabiopharma.com
AstraZeneca is a global, science-led biopharmaceutical company that focuses on the discovery, development and commercialisation of prescription medicines, primarily for the treatment of diseases in three therapy areas - Oncology, Cardiovascular, Renal & Metabolism and Respiratory. The Company also is selectively active in the areas of autoimmunity, neuroscience and infection. AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide.

astrazeneca.com.au

Bristol-Myers Squibb is a global biopharmaceutical company focused on discovering, developing and delivering innovative medicines for patients with serious diseases. Our people are focused on helping millions of patients around the world in disease areas such as oncology, cardiovascular, immunoscience and fibrosis.

Through the Bristol-Myers Squibb Foundation, we promote health equity and seek to improve health outcomes of populations disproportionately affected by serious diseases and conditions, giving new hope to some of the world’s most vulnerable people. Each day, our employees around the world work together for patients – it drives everything we do.

bms.com/au

GenesisCare are leveraging the experience and expertise of our network to deliver optimal patient treatment whether in a regional centre or capital city. We are investing in treating patients closer to home using state of the art technology, with centres across Australia, the UK and Spain.

genesiscare.com.au

For more than a century, MSD has been inventing for life, bringing forward medicines and vaccines for many of the world’s most challenging diseases. Today, MSD continues to be at the forefront of research to deliver innovative health solutions and advance the prevention and treatment of diseases that threaten people and animals around the world.

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Novartis provides innovative healthcare solutions that address the evolving needs of patients and societies. Headquartered in Basel, Switzerland, Novartis offers a diversified portfolio to best meet these needs: innovative medicines, eye care and cost-saving generic pharmaceuticals.

We have more than 60 years’ history in Australia and employ around 800 associates across our three divisions.

We believe continued R&D is essential to innovation and in Australia we invest around $20M annually in local clinical trials. Our mission is to discover new ways to improve and extend people’s lives.

novartis.com.au

Pierre Fabre Laboratories is the 2nd largest pharmaceutical company in France with a culture of research and innovation, ethical and pharmaceutical rigour, and a commitment to public health for more than 50 years.

Pierre Fabre Laboratories employs more than 10,000 people across 140 countries who share a passion for innovation and excellence in the areas of medication, family health and dermo-cosmetics. In Australia we offer medication for the treatment of fibromyalgia and chemotherapy for the treatment of advanced lung, breast and bladder cancers. We are dedicated to providing optimal outcomes and quality of life for cancer patients and patients suffering from fibromyalgia.

pierre-fabre.com

Sirtex Medical is a global healthcare business with offices in the US, Australia, Germany and Singapore, working to improve outcomes in people with cancer. Our current lead product is a targeted radiation therapy for liver cancer called SIR-Spheres Y-90 resin microspheres. More than 100,000 doses have been supplied to treat patients with liver cancer at more than 1,000 medical centres in over 40 countries.

SIR-Spheres is a Registered Trademark of Sirtex SIR-Spheres Pty Ltd

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Syneos Health™ (Nasdaq:SYNH) is the only fully integrated biopharmaceutical solutions organization. The Company, including a Contract Research Organization (CRO) and Contract Commercial Organization (CCO), is purpose-built to accelerate customer performance to address modern market realities. Created through the merger of two industry leading companies – INC Research and inVentiv Health – we bring together approximately 24,000 clinical and commercial minds with the ability to support customers in more than 110 countries. Together we share insights, use the latest technologies and apply advanced business practices to speed our customers’ delivery of important therapies to patients.

To learn more about how we are shortening the distance from lab to life®, visit:

syneoshealth.com
ORGANISING COMMITTEES

Executive Organising Committee
Convenor: Doctor Lorraine Chantrill, Wollongong Hospital, NSW
Chief Executive Officer: Mr Russell Conley, AGITG, NSW
Medical Oncology Committee Chair: Associate Professor Mustafa Khasraw, Royal North Shore Hospital, NSW
Surgery Committee Chair: Doctor Iain Thomson, Princess Alexandra Hospital, QLD
Radiation Oncology Committee Chair: Doctor Andrew Oar, Gold Coast University Hospital, QLD
Consumer-Study Coordinator Committee Co-Chair: Ms Anne Smith, Christchurch Hospital, NZ
Consumer-Study Coordinator Committee Co-Chair: Ms Jan Mumford, AGITG Consumer Advisory Committee Chair, NSW
Translational Research Committee Chair: Professor Robert Ramsay, Peter MacCallum Cancer Centre, VIC

Medical Oncology Committee
Chair: Associate Professor Mustafa Khasraw, Royal North Shore Hospital, NSW
Associate Professor Rachel Wong, Box Hill Hospital, VIC
Doctor Sharon Pattison, Duned in Hospital, NZ
Associate Professor Jeanne Tife, Peter MacCallum Cancer Centre, VIC

Surgery Committee
Chair: Doctor Iain Thomson, Princess Alexandra Hospital, QLD
Professor Jaswinder Samra, Royal North Shore Hospital, NSW
Ms Belinda Steer, Peter MacCallum Cancer Centre, VIC
Associate Professor Tarik Sammour, Royal Adelaide Hospital, SA

Radiation Oncology Committee
Chair: Doctor Andrew Oar, Gold Coast University Hospital, QLD
Associate Professor Hien Le, Royal Adelaide Hospital, SA
Doctor Julie Chu, Peter MacCallum Cancer Centre, VIC
Doctor Dominique Lee, Princess Alexandra Hospital, QLD
Doctor Meredith Johnston, Liverpool Cancer Therapy Centre, NSW
Doctor Gina Hesselberg, St George Hospital, NSW

Translational Research Committee
Chair: Professor Robert Ramsay, Peter MacCallum Cancer Centre, VIC
Associate Professor Jayesh Desai, Royal Melbourne Hospital, VIC
Associate Professor Oliver Sieber, Walter & Eliza Hall Institute, VIC
Professor John Mariadason, Austin Hospital, VIC
Associate Professor Phoebe Phillips, Prince of Wales Clinical School, NSW
Associate Professor Vicki Whitehall, QIMR Berghofer Medical Research Institute, QLD
Doctor Susan Woods, South Australian Health & Medical Research Institute, SA

Combined Consumer-Study Coordinator Committee
Co-Chair: Ms Anne Smith, Christchurch Hospital, NZ
Co-Chair: Ms Jan Mumford, Chair AGITG Consumer Advisory Committee, NSW
Ms Charnaym Chorlton, The Tweed Hospital, NSW
Ms Chris Aiken, NHMRC Clinical Trials Centre, NSW
Ms Nisha Berthon-Jones, AGITG Clinical Research Manager, NSW
Ms Christine Bishop, AGITG Consumer Advisory Panel, NSW

Members of the AGITG Consumer Advisory Panel were involved in planning the AGITG Annual Scientific Meeting.
The Australasian Gastro-Intestinal Trials Group (AGITG), a multi-disciplinary collaborative group of medical and research professionals, conducts clinical trials and related biological research to improve treatments for gastro-intestinal (GI) cancers: those of the oesophagus, stomach, liver, pancreas, gallbladder, biliary tract, small and large bowel, rectum and anus. Through the tireless efforts of the AGITG membership, we have been instrumental in achieving significant changes in medical practice not only in Australia and New Zealand but worldwide.

Contact Details
1 300 666 769
gcancer.org.au
Lifehouse Building
Level 6, 119 – 143 Missenden Road, Camperdown NSW 2050

Meeting Dates
21 – 23 August 2019

Meeting Venue
Adelaide Convention Centre
North Terrace, Adelaide SA 5000
adelaidecc.com.au

Meeting Managers
Catalyst Event Solutions PL
catalystevents.com.au
GENERAL INFORMATION

Registration
The registration desk is located in Foyer F, on the Ground Floor of the Adelaide Convention Centre (ACC).

Registration Opening Times
Wednesday 21 August  ·  07:00 – 18:00
Thursday 22 August  ·  07:00 – 18:00
Friday 23 August  ·  08:00 – 15:00

Name Badges
All delegates registered for the meeting will receive a name badge at the registration desk. This name badge must be worn at all times to obtain entry to the meeting sessions, the exhibition and the social functions.

Speaker Preparation Room
The Speaker Preparation Room is located in Office F, on the Ground Floor of the ACC. All Speakers are requested to go to the Speaker Preparation Room at least 2 hours prior to their presentation time. This will enable the Technician located in the room, to check through all presentations to ensure that everything is in order and working correctly before being uploaded and made available for each presentation.

Speaker Preparation Room Opening Times:
Wednesday 21 August  ·  06:45 – 17:30
Thursday 22 August  ·  06:45 – 17:30
Friday 23 August  ·  08:00 – 14:30

Meeting Information
Tea Breaks and Lunches
Morning teas, lunches and afternoon teas will be served in Hall F, Ground Floor. Venue staff will assist with pre-requested special dietary requirements. Please make yourself known to a staff member at the designated dietary serving station.

Mobile Phones
As a courtesy to fellow delegates and speakers, please ensure your mobile phone is switched off during the meeting sessions.

Internet Access, sponsored by Specialised Therapeutics
Wireless internet access is available for delegates for the duration of the meeting in all meeting rooms and the exhibition area. Please log in using:
Login: AGITG2019
Password: ABRAXANE

Meeting App
The Meeting App can be downloaded and used on your phone, tablet or laptop. All abstracts can be viewed on the Meeting App. To access please:
• Click on ‘Tap to Start’
• Enter your Event Code: AGITG2019
• Enter your unique password & temporary email that was supplied to you by your conference organiser

Study Coordinators
To assist our Study Coordinators to recognise and connect with each other during the meeting, a ‘gold dot’ will be visible on the name badge of those we have identified as a Study Coordinator. If you are a Study Coordinator and you do not have a ‘gold dot’ please see staff at the Registration Desk. Study Coordinators are invited to meet at the Registration Desk at the start of the Welcome Reception, 18:15, in Foyer F. We hope this will assist you to connect with colleagues and make your ASM experience a great one. If you need any information during the meeting, please ask one of our Event Managers located at the Registration Desk.

Poster Presentations
Posters will be displayed in Hall F, Ground Level for the entire meeting.

Social Program
The following events are included in the registration fee for full registrations.

Welcome Function
Wednesday 21 August  ·  18:15 – 20:15
Hall F, Ground Level

AGITG 21st Annual Reception
Thursday 22 August  ·  18:30 – 19:30
Hall F, Ground Level

AGITG 21st Annual Dinner
Thursday 22 August  ·  19:30 – 22:30
Panorama Ballroom, Level One
The Organising Committee thanks all the sponsors for their support, and invites all delegates to visit the trade exhibition during the meeting.

Exhibition Operating Times
Wednesday 21 August · 10:30 – 20:00
Thursday 22 August · 11:00 – 19:30
Friday 23 August · 10:00 – 14:15
The trade exhibition is located in Hall F, on the Ground Floor of the ACC.

01. Amgen
02. Ipsen
03. Unicorn Foundation
04. Novartis
05. Merck Group
06. Servier
07. MSD
08. Specialised Therapeutics
09. Sirtex
10. Roche
Professor James Abbruzzese is the Chief of the Duke Division of Medical Oncology and serves as the Associate Director for Clinical Research and Training for the Duke Cancer Institute (DCI). Professor Abbruzzese is a leading expert in the clinical study and treatment of pancreatic cancer, and his management experience and vision for clinical research and the Division will substantially support cancer care and research at Duke. Before moving to Duke, he held the Waun Ki Hong Distinguished Chair in Translational Oncology and he was Chairman of the Department of Gastrointestinal Medical Oncology and Digestive Diseases at the University of Texas M. D. Anderson Cancer Center in Houston.

Professor Abbruzzese earned his medical degree with honors from the University Of Chicago Pritzker School Of Medicine and completed his residency in Internal Medicine at Johns Hopkins Hospital. He also completed clinical fellowships in Infectious Diseases at the Johns Hopkins and in Medical Oncology and Medical Oncology Research Laboratory of Neoplastic Disease Mechanisms at the Dana-Farber Cancer Institute of Harvard Medical School. Before his recruitment to Duke University he spent most of his professional career at M.D. Anderson, where he progressed through the ranks to assume leadership positions as Chairman of the Department of Gastrointestinal Medical Oncology and Associate Vice-Provost for Clinical Research.

Among his many accomplishments, Professor Abbruzzese is a Fellow of the American College of Physicians and Fellow of the American Society of Clinical Oncology. He has co-authored more than 400 research publications and is the immediate past Chair of the Clinical Trials and Translational Research Advisory Committee of the National Cancer Institute. He currently serves as the Chair of the NCI Pancreatic Ductal Adenocarcinoma Progress Working Group.

Professor Sharlene Gill is a medical oncologist specializing in gastrointestinal (GI) malignancies at BC Cancer – Vancouver. She received a BSc. in Pharmacy, and MD from the University of British Columbia in 1996 followed by residencies in Internal Medicine and Medical Oncology, subsequently completing a fellowship in GI Oncology at the Mayo Clinic (Rochester, MN) and a Masters of Public Health from the Harvard School of Public Health (Boston, MA) before returning to Vancouver where she is presently Professor of Medicine at the University of British Columbia. In 2017, she also completed an MBA from the Kenan-Flagler School of Business at the University of North Carolina.

Professor Gill’s areas of clinical expertise are in colorectal, pancreatic and hepatobiliary cancers. She is actively engaged in education and research, with over 90 peer-reviewed publications and book chapters to her credit. Her scientific focus is in the areas of health outcomes and clinical trial research. In Spring 2019, Professor Gill will assume the role of Chair for the GI Disease site of the Canadian Cancer Trials Group (CCTG).

Professor Christian Jobin is the Gatorade Trust Professor of Medicine at the University of Florida Gainesville. He received his PhD in Immunology/Microbiology from Université Laval (Quebec, Canada) in 1994. He did a post-doctoral fellowship at the University of North Carolina Chapel Hill working on bacteria host interaction in the intestine.

Professor Jobin's research focuses on establishing the functional impact of bacteria in inflammation and carcinogenesis and deciphering mechanism of action. Using genetically engineered mice and zebrafish, germ-free and gnotobiotic technology in combination with microbial genomics, his lab studies the role of bacteria in cancer. His laboratory showed the key role of genotoxic microbial gene cluster in carcinogenesis.

Professor Jobin has published over 360 scientific papers (Science, Nature, Nat. Comm., Nat. Micro., Immunology, J. Exp. Med., Gastroenterology) and presented his work at various national and international scientific meetings (over 900 conferences). His research, supported by the National Institute of Health has led to numerous awards and honours (Mucosal Immunology Society Award, American Gastroenterological Association Fiterman Young Investigator Basic Research Award, UF Senior Faculty Excellence in Research Award).

Professor Jobin has served on several study sections including American Cancer Society, CCFA Fellowship and Career Awards, NIH tumor microenvironment and he is currently serving on the Gastrointestinal Mucosal Pathobiology study section (GMPB-permanent member). He is the co-leader of the Cancer Therapeutics Host Response research program at the University of Florida Health Cancer Center.

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Associate Professor Manisha Palta
Duke University School of Medicine
United States of America

Associate Professor Manisha Palta is a radiation oncologist and the Director of Clinical Research in the Department of Radiation Oncology at Duke University and is a member of the Duke Cancer Institute. She primarily treats patients with gastrointestinal cancers and is actively involved in clinical research trials.

Associate Professor Palta has always liked helping people, and in college volunteered in the oncology ward. She knew then that she had found her passion. Interacting with patients is her favourite part of the job. She likes to explain how radiation works and how it can benefit them. Her hope is to provide her patients with an explanation that gives them less anxiety and less fear about the treatment.

Associate Professor Palta’s primary clinical focus is the treatment of gastrointestinal malignancies. She is the Principal Investigator of three prospective, investigator-initiated studies. The first seeks to optimize the neoadjuvant regimen for patients with potentially resectable pancreas cancer by incorporating neoadjuvant systemic therapy and stereotactic body radiotherapy (SBRT).

The second is an investigator-initiated study evaluating the addition of immunotherapy, pembrolizumab, into the neoadjuvant treatment of resectable esophagogastric cancers treated with chemoradiation. This project involves 2 tumor biopsy and 5 liquid biopsy collections during the trial for tumor immunophenotyping. Lastly, she is conducting a multi-institutional, prospective, randomized phase II study evaluating quality of life differences with liver SBRT or percutaneous ablation in patients with non-operative hepatocellular carcinoma.

Professor Stephen J Wigmore
Hepatobiliary-Pancreatic Surgical Services and Edinburgh Transplant Unit
Royal Infirmary of Edinburgh
The United Kingdom

Professor Stephen Wigmore is an HPB and transplant surgeon who trained at King’s College Hospital School of Medicine. He worked in London for a couple of years before moving to Edinburgh to work with Sir David Carter and Professor James Garden. He undertook his basic and higher surgical training in Edinburgh. In 2005, he was appointed Professor of Transplantation Surgery at the Liver Unit in Birmingham University.

Professor Wigmore returned to Edinburgh in 2007 as the Chair of Transplantation Surgery. He is currently the Head of Department of Clinical Surgery at the University of Edinburgh. He is the Surgeon to the Queen in Scotland and is the Chair of the Research Committee of the Royal College of Surgeons of Edinburgh. He is the Honorary Secretary of the James IV Association of Surgeons for the British Isles and Rest of the World Section. He is President of the British Transplantation Society and was elected a Fellow of the Royal Society of Edinburgh.

Ms Kate Furness
Monash Medical Centre
Victoria

Ms Furness is a Senior Clinical Dietitian at Monash Medical Centre specialising in oncological upper gastrointestinal and hepatobiliary surgery. Her passion is to provide the best quality, timely and evidence-based nutrition support in the pre- and post-operative phases of major surgeries. This has led to the commencement of her PhD with Monash University. As the research dietitian on the randomised controlled trial “Effect of early and intensive nutrition care, delivered via telephone or mobile application, on quality of life in people with upper gastrointestinal cancer”, Kate’s doctoral research looks at a process and mechanisms of action evaluation to determine the core active ingredients that will enable the sustained implementation of best practice nutrition intervention across broader settings, to improve the quality of life and nutrition status of individuals with upper gastrointestinal cancer.

Ms Furness is also an Associate Investigator on a multicentre randomised controlled trial “Real-time patient-reported outcomes (PRoRs) in clinical practice – a novel approach to improving quality of care for patients with upper gastrointestinal cancer”.

Associate Professor W F Eddie Lau
Austin Health, VIC & Peter MacCallum Cancer Centre Victoria

Associate Professor Eddie Lau is a Consultant Radiologist & Nuclear Medicine Specialist at Austin Health in Victoria and an honorary radiologist at the Peter MacCallum Cancer Centre in Melbourne, Australia. He has academic appointments of Principal Fellow and Clinical Associate Professor at the University of Melbourne.

Associate Professor Lau is a dual trained radiologist and nuclear medicine specialist with more than 15 years’ experience in cancer and multi-modality imaging, including Computed Tomography, Magnetic Resonance Imaging and Positron Emission Tomography. He has over 70 peer-reviewed publications, 6 books/chapters as well as more than 120 presentations on various topics in cancer imaging at national and international conferences.

Associate Professor Lau has received Royal Australian and New Zealand College of Radiologists and National Health and Medical Research Council Project Grants, and is a reviewer for a number of imaging and cancer journals.
Professor Emad El-Omar graduated in Medicine from Glasgow University, Scotland, and trained as a gastroenterologist. He worked as a Visiting Scholar/Scientist at Vanderbilt University, TN, and National Cancer Institute, MD, USA, and was Professor of Gastroenterology at Aberdeen University, Scotland, for 16 years before taking up the Chair of Medicine at St George & Sutherland Clinical School, University of New South Wales, Sydney, Australia.

Professor El-Omar is the Editor in Chief of the journal Gut. His research interests include the gut microbiome, inflammation driven GI cancer and IBD. He is the Director of the Microbiome Research Centre at St George Hospital, Sydney.

Professor Peter Gibbs is a medical oncologist based at the Western Hospital and a laboratory head and divisional director at the Walter and Eliza Hall Institute (WEHI), both in Melbourne. His WEHI team are conducting world-first prospective randomised studies that are examining the impact of circulating tumour DNA analysis informed treatment in the adjuvant setting, including 3 AGITG studies (DYNAMIC-III, DYNAMIC-rectal and DYNAMIC-pancreas). His team also lead international clinical registry efforts in multiple tumour types, now including colorectal, pancreas and oesophago-gastric cancer.

A recent research initiative supported by the registry data collection is the novel concept of randomised registry trials, with studies having now commenced in multiple tumour types. Professor Gibbs’ team have also initiated prospective studies exploring the potential of patient derived tumour organoid sensitivity testing to guide clinical decision making. Professor Gibbs in his clinical role as a medical oncologist has been a lead investigator for multiple international clinical trials.

Ms Tanya Symons has worked in the field of clinical research for over twenty years, initially as a trial manager. In 2000, she set up a clinical trials consultancy, providing training and advice to many of the research active institutions in the UK including over 80 non-commercial organisations, training thousands of health professionals. In 2012, Tanya also redeveloped the UK’s Clinical Trials Toolkit; a national resource designed to support non-commercial researchers conduct investigator-led clinical trials.

Ms Symons has now established her clinical trials consultancy in Australia, working as a consultant for both Commonwealth and State governments and is using her knowledge of international best practice to influence the streamlining and standardisation of research-related systems and processes. She has recently authored a suite of clinical trials guidance for the NHMRC, including the new “Safety Monitoring and Reporting in Clinical Trials Involving Therapeutic Goods 2016”, co-authored the TGA’s Clinical Trials Handbook (2018) and is heavily involved in the clinical research reform agenda in NSW Health.
Clinical research is part of an active global oncology community. Study Coordinators and Research Nurses are vital to the constant development of cancer biology and treatment, and it is essential that they develop knowledge and skills in research development and conduct. The Study Coordinator workshop covers a wide range of topics presented by experts in the field. Attendees will gain a broader insight into the world of oncology research.

- Good Clinical Practice/Risk Based Monitoring/NHMRC Safety Reporting Guidelines – Tanya Symons
- GI related issues, e.g. biology & pathology of GI cancer – Doctor Matthew Burge

Oncology has an active global research community and our understanding of cancer biology and treatment is constantly evolving. It is essential for trainees to develop knowledge and skills in clinical medicine and research methodology. The AGITG Trainee Workshop provides an opportunity for trainees to meet and learn from successful medical, surgical and radiation oncologists as well as scientists, trial co-ordinators and statisticians. Attendees will deepen their understanding of how to conduct successful research and the career opportunities available.

- Statistics 101 – Rebecca Asher
- Protocol Writing – Professor Chris Karapetis
- Creating an Effective Scientific Poster – Flynn Slattery

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- Statistics 101 – Rebecca Asher
- Protocol Writing – Professor Chris Karapetis
- Creating an Effective Scientific Poster – Flynn Slattery

13:00 - 14:30 Study Coordinator Meeting 2 – Riverbank Room 2

Co-Chairs: Ms Nisha Berthon-Jones & Ms Christine Aiken

- Effective Scientific Poster creation – Flynn Slattery
- Site Accreditation – where is Australia up to and when can courses and programs be implemented? – Professor Nik Zeps
- Health services / implementation research (‘bench to bedside’/translation of research into practice) – Professor John Simes

13:00 - 14:30 Trainee Workshop 2 – Riverbank Room 1

Chair: Doctor Lorraine Chantrill

- Trials and Tribulations – Doctor Amitesh Roy, Doctor Lorraine Chantrill & Professor David Watson

15:00 - 17:00 Tour of the South Australian Health & Medical Research Institute with Translational Research 101 Lecture

(For Consumer Advisory Panel, Study Coordinator & Trainee Delegates Only)
Day 1

PROGAM: WEDNESDAY, 21 AUGUST 2019

7:00 - 18:00 Registration Open

7:45 - 8:45

MARCK

Keynote Breakfast Session – Panorama Rooms 1, 2 & 3

Co-Chairs: Professor Sharlene Gill

Colorectal cancer might be a constellation of different disease states with complex biologic dynamics rather than one entity. Clinical research and practice needs to adapt to overcome these complexities. Can we use the available and emerging clinical trial evidence, to identify the most effective and least toxic treatment for the individual patient? This practical session will provide up-to-date information and guidance with an opportunity for question-and-answers. The aim is to enable participants to understand upcoming strategies, clinical and research challenges in the management of colorectal cancer.

9:00 - 10:30

Opening Plenary – Hall G

9:00 - 9:30

AGITG Early Colorectal Cancer Trials – Hall G

Co-Chairs: Associate Professor Jeanne Tie & Professor Peter Gibbs

SPAR: Associate Professor Michael Jameson

A randomized, placebo-controlled phase II trial of Simvastatin in addition to standard chemotherapy and radiation in preoperative treatment for rectal cancer

ASCOLT: Doctor Mark Jeffery

Aspirin for Dukes C and High-Risk Dukes B Colorectal Cancers. An International, Multi-centre, Double Blind, Randomised Placebo Controlled Phase III Trial – COMBINED WITH ASCOLT Translational

RENO: Professor Chris Karapetis

Prospective Study of ‘Watch and Wait’ Strategy in Patients with Rectal Cancer who have Developed a Clinical Complete Response with concurrent chemo-radiotherapy: RENO (Rectal Cancer No Operation)

10:30 - 11:00

Morning Tea – Hall F

11:00 - 13:00

AGITG Early Colorectal Cancer Trials – Hall G

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A randomized, placebo-controlled phase II trial of Simvastatin in addition to standard chemotherapy and radiation in preoperative treatment for rectal cancer

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Prospective Study of ‘Watch and Wait’ Strategy in Patients with Rectal Cancer who have Developed a Clinical Complete Response with concurrent chemo-radiotherapy: RENO (Rectal Cancer No Operation)

13:00 - 14:00

Lunch – Hall F
7:45 - 8:15
Keynote Breakfast Session – Panorama Rooms 1, 2 & 3
The role of SBRT in oligometastatic gastro-intestinal cancer – Associate Professor Manisha Palla
Co-Chairs: Doctor Andrew Orar & Doctor Dominique Lee

Traditional palliative approaches to patients with early metastatic disease has been an active area of research. Recent randomised evidence has demonstrated an overall survival benefit for SBRT in oligometastatic disease in non-small cell lung cancer. To date, no randomised trials have been published exploring SBRT in oligometastatic gastrointestinal cancer. This keynote session will discuss the “Who”, “When” and “Why” of SBRT in oligometastatic gastrointestinal cancers and the opportunity for meaningful research in this controversial domain.

9:00 - 11:00
Translational Science Symposium – Hall G
Sponsored by

Co-Chairs: Professor Robert Ramsey & Associate Professor Vicki Whitehall
GI cancers develop within the complex environment of the patient where there is a relenting battle between the cancer cells and the host. Pioneers like Peto and Vichow recognized that there are roles played by non-tumour cells we now describe as immune, vessel and other stromal cells. More recent appreciation has emerged of another complex population of organisms that impact upon this battle are those of the microbiota; fungi, bacteria and their phages. Together as intact organisms or products, they influence tumour growth, and respond to cytotoxic drugs and immunotherapeutics. The translational session traverses these topics of microbiota, chemotherapies and immune modulators as they impact GI cancers.

11:00 - 11:30
Morning Tea – Hall F

11:30 - 13:15
Translational Science Symposium continues – Hall G
Cutting Edge Translational Science in GI Cancer
Sponsored by

Co-Chairs: Professor Oliver Sieber & Doctor Susan Woods

• “Bench to bedside: engineering bacteria to detect, prevent and treat colorectal cancer” – Associate Professor Daniel Worthley

• “Beside to practice: TNT, NIM, and avoiding surgery for rectal cancer” – Associate Professor Tank Sambour

• “Overcoming our addiction to oncocenes to target oesophageal adenocarcinoma” – Doctor Nicholas Clemens

• “Microbiota, immunotherapy and personalised treatment” – Doctor Michael Bukert

• “DCLKs is a novel driver of gastric cancer” – Doctor Michael Bukert

• “Pooled secondary analysis of clinical trials – making the most of the data” – Doctor Michael Sorich

Panel Discussion

13:15 - 14:15
Lunch and Poster Review – Hall F

13:15 - 14:15
Meet the Experts from the Translational Science Symposium at the Angen Stand

14:15 - 16:00
New Concepts Symposium – Hall G
Sponsored by

Co-Chairs: Professor Tim Price & Doctor Katrin Sjoquist

The New Concepts Symposium sponsored by Specialised Therapeutics Australia is designed as a novel way to reach out to a wider spectrum of the group. This session provides an opportunity for delegates to present embryonic new concepts for feedback and discussion with the audience as well as comments from international guests in terms of perspective, international interest and relevance. A good idea can be tested and a perception gained on whether to take the concept forward to a more formal review by the Upper or Lower GI Working Party. The identification of other AGITG members who may wish to assist in progressing the concept as an AGITG supported protocol is also possible. The winner of the Best New Concept Award will receive a $5,500 prize and a framed certificate. The runner up will receive a $1,500 prize and framed certificate. The Awards are presented at the Annual Scientific Meeting. Prizes and details of the Award recipients are published on the AGITG website and in the Annual Report.

• Concept 1: A randomised phase II study to define the feasibility of organoid sensitivity testing driven treatment for patients with chemotherapy metastatic colorectal cancer – Presenter: Doctor Grace Gard

• Concept 2: Phase I study of AqBo50 with/without AqBo30 in patients with metastatic colorectal cancer following progression on standard chemotherapy and biological therapy – Presenter: Doctor Yoko Tomita & Invited Faculty: Professor Christian Jobin

• Concept 3: A phase II study of oncolytic immunotherapy of metastatic neuroendocrine tumours using intralesional rose bengal disodium in combination with pembrolizumab – Presenter: Doctor Mark McGregor & Invited Faculty Reviewer: Professor Florian Lendick

• Concept 4: Psostrinion expression tomography of cell death for prediction of response to neoadjuvant therapy in rectal and oesophageal carcinoma – Presenter: Doctor Ivan Ho Shon & Invited Faculty Reviewer: Professor Shariene Gill

16:00 - 16:30
Afternoon Tea – Hall F

16:30 - 18:00
Best of Posters / Fast Forward – Hall G
Sponsored by

Co-Chairs: Professor Stephen Clarke & Professor Robert Ramsey

The AGITG Annual Scientific Meeting accepts abstracts for posters for selection by the Executive Committee. Posters are displayed in the exhibition area. Four posters are chosen for Fast Forward presentation in the Best of the Best Session. Each presenter has seven minutes to present with three minutes for questions. Four posters are also chosen for Fast Forward presentation. Each presenter has three minutes to present with two minutes for questions. The AGITG recognises excellence in the Best of the Best Session. Each presenter has seven minutes to present with three minutes for questions. Four posters are also chosen for Fast Forward presentation. Each presenter has three minutes to present with two minutes for questions. The AGITG recognises excellence in the Fast Forward Session. The New Concepts Symposium sponsored by Specialised Therapeutics Australia is designed as a novel way to reach out to a wider spectrum of the group. This session provides an opportunity for delegates to present embryonic new concepts for feedback and discussion with the audience as well as comments from international guests in terms of perspective, international interest and relevance. A good idea can be tested and a perception gained on whether to take the concept forward to a more formal review by the Upper or Lower GI Working Party. The identification of other AGITG members who may wish to assist in progressing the concept as an AGITG supported protocol is also possible. The winner of the Best New Concept Award will receive a $5,500 prize and a framed certificate. The runner up will receive a $1,500 prize and framed certificate. The Awards are presented at the Annual Scientific Meeting. Prizes and details of the Award recipients are published on the AGITG website and in the Annual Report.

• Palliative Oesophageal Chemoradiotherapy: A Phase I Clinical Trial – Presenter: Doctor Swetha Sridharan

• Immunomodulatory effect of Renin-angiotensin inhibitors on T-lymphocytes in mice with colorectal Liver Metastases – Presenter: Doctor Daro Ardila

• A comprehensive patient-reported outcome (PRO) assessment model for colorectal cancer (CRC) survivors: a mixed methods systematic review – Presenter: Doctor Claudia Rutherford

• SPARC expression in pretreatment rectal cancer biopsies is associated with tumour regression following neoadjuvant chemoradiotherapy – Presenter: Associate Professor Christine Hemmings

Fast Forward Session

• Neoadjuvant capcetabine versus infusional 5-fluorouracil for the treatment of locally advanced rectal cancer – Presenter: Doctor Matthew Lof

• Phase I trial of nab-paclitaxel administered concurrently with radiotherapy in patients with locally advanced inoperable pancreatic adenocarcinoma (ART in LAP trial) – Presenter: Doctor Amritha Roy

• Investigating the role of tumour-associated T cells in human colorectal cancer liver metastases – Presenter: Doctor Kevin Fenix

• The effect of overexpressing double stapled anastomoses in oncological colorectal surgery – Presenter: Doctor Simon Wilkins

18:00 - 18:30
AGITG INTEGRATE II Trial (Closed session – Participating Sites Only) – Riverbank Room 3

18:30 - 21:30
AGITG 21st Annual Meeting Reception – Hall F

19:30 - 22:30
AGITG 21st Annual Meeting Dinner – Panorama Ballroom
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<tr>
<th>Time</th>
<th>Event</th>
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<tr>
<td>9:00 - 10:00</td>
<td>Keynote Breakfast Session – Panorama Rooms 1, 2 &amp; 3</td>
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<td>Translating perioperative management of pancreatic cancer into survival benefits: state-of-the-art and new perspectives – Professor James L. Abbruzzese</td>
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<td>Co-Chairs: Associate Professor Mustafa Khasraw &amp; Doctor Melissa Eastgate</td>
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<td>New agents, emerging strategies, and optimization of established regimens are changing the delivery and timing of systemic therapy. Has progress in the treatment of pancreas cancer been slow? Are the new strategies likely to result in improved outcomes for patients or is it complicating clinical management in this setting? This session is designed to help place emerging information into the context of clinical trial data in a practical and interactive fashion in order to provide up-to-date information and guidance.</td>
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<td>10:00 - 10:30</td>
<td>Morning Tea – Hall F</td>
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<td>10:30 - 13:15</td>
<td>AGITG Upper GI Cancer Trials – Hall G</td>
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<tr>
<td>Co-Chairs: Doctor Kate Clarke &amp; Doctor Julie Chu</td>
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<td>ALT-GIST: Professor Desmond Yip</td>
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<td>A randomised phase II trial of imatinib alternating with regorafenib compared to imatinib alone for the first line treatment of advanced gastrointestinal stromal tumour (GIST)</td>
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<td>DOCTOR: Professor Andrew Barbour</td>
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<td>A Randomised Phase II trial of pre-operative cisplatin, 5-fluorouracil and docetaxel, +/-Radiotherapy, based on poor early response to standard chemotherapy for resectable adenocarcinoma of the oesophagus and/or gastro oesophageal junction – COMBINED WITH DOCTOR Translational</td>
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<td>TOPGEAR: Professor Trevor Leong</td>
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<td>A randomised II/III trial of preoperative chemoradiotherapy versus preoperative chemotherapy for resectable gastric cancer</td>
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<td>DYNAMIC-Pancreas: Doctor Belinda Lee</td>
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<td>Circulating Tumour DNA Analysis Informing Adjuvant Chemotherapy in Early Stage Pancreatic Cancer: A Multicentre Randomised Study</td>
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<td>ACTICCA-1: Doctor Jenny Shannon</td>
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<td>Adjutant chemotherapy with gemcitabine and cisplatin compared to observation after curative intent resection of cholangiocarcinoma and muscle invasive gall bladder carcinoma</td>
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<td>CONTROL NETs: Associate Professor David Wyld</td>
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<td>Capcitabine ON Temozolomide Radiotherapy Octreotide Lutetium-27 NeuroEndocrine Tumours Study</td>
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<td>NABNEC: Associate Professor Mustafa Khasraw</td>
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<td>A Randomised Phase II Study Of nab-paclitaxel In Combination With Carboplatin As First Line Treatment Of Gastrointestinal Neuroendocrine Carcinomas</td>
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<td>MASTERPLAN: Doctor Andrew Oar</td>
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<td>A randomised phase II study of MFOLIRINOX And Stereotactic Radiotherapy (SBRT) for Pancreatic Cancer With High Risk and Locally Advanced Disease</td>
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<td>AGITG Upper GI Cancer Research Portfolio – How does this fit in to the International Context? – Professor James L. Abbruzzese</td>
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<td>13:15 - 14:15</td>
<td>Lunch – Hall F</td>
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<td>14:15 - 16:15</td>
<td>Closing Plenary – Hall G</td>
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<td>Co-Chairs: Associate Professor Michael Jameson &amp; Professor Steve Ackland</td>
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<td>Trials and Tribulations in colorectal cancer in 2019</td>
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<td>New treatments for colorectal cancer have been sparse in the last few years. Are there other ways we could look at this diverse group of bowel cancers? Our closing plenary will look at colorectal cancer through different lenses.</td>
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<td>International Faculty Panel: Professor Christian Jobin, Professor Florian Lodick, Associate Professor Manisha Palta, Professor Stephen J Wigmore</td>
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<td>• 2018 John Zalcberg OAM Award Recipient Presentation (on appropriate aspects of their area of interest) – Professor John Simes</td>
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<td>• Registry Trials in CRC and other GI Cancers – Professor Peter Gibbs</td>
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<td>• Next challenges in moving from microbiome into clinical integration (opportunities and barriers) – Professor Christian Jobin</td>
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<td>• Hottest topic in colorectal cancer – Professor Florian Lodick</td>
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<td>Panel Discussion</td>
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<td>16:30</td>
<td>Minibus departs to AGITG ASM 2019 Degustation Adventure, McLaren Vale. Head to North Terrace, in front of the ACC</td>
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<tr>
<td>16:30</td>
<td>Buses depart to the Airport, head to North Terrace, in front of the ACC</td>
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**SAVE THE DATE**

**22ND ANNUAL SCIENTIFIC MEETING 2020**

Sofitel Melbourne on Collins
26 – 28 August 2020
Dear Colleague,

I always leave the AGITG Annual Scientific Meeting energised by the scope of new ideas and passion of my fellow AGITG members. This year, our program addresses the enigmatic nature of rare and underfunded GI cancers, and it is heartening to see so many new concepts and ideas being developed in these areas.

Although survival rates are increasing for many cancers, our work is far from over. AGITG’s nine Research Priorities were set by the Scientific Advisory Committee in 2018 to serve as a guidepost for steering future research in directions we believe have the greatest potential to accelerate the pace of progress. We identified a list of research priorities that will help fill critical gaps in rare GI cancers, including exploring collaborations for tumour streams and basket studies, late-stage trials, particularly in colorectal cancer, clinical trials in HCC and rectal cancer.

Cancer treatment advances are only as good as patients’ ability to access them. But, for far too many patients, high-quality cancer care and clinical trials are out of reach. We have much work to do before everyone with cancer has equal access to the best treatments and the opportunity to participate in research. By working together as a community, I know we can find solutions that will help ensure that the advances that are discussed on the following pages reach every patient who could benefit from them.

There are so many unanswered questions in GI cancer, and your insights are crucial to our work in changing this. I hope that the ideas we share over the next few days will leave you feeling motivated to continue to find the best treatments for our patients.

If you have any research ideas now or beyond the meeting, I encourage you to engage with us to develop them. The annual AGITG Innovation Fund grant provides funding for an Investigator-led pilot study, translational study, or capacity-building project. You can also submit a research concept to our Upper and Lower GI Working Parties at any time for discussion and development – please see our website for more information.

I encourage you to refer your colleagues to join us through our online membership form: www.gicancer.org.au/member-registration. Membership is free and is open to specialists from all relevant disciplines.

Thank you for your continued support of the AGITG. I look forward to learning and sharing new insights with you over the next few days.

Yours sincerely,

Professor Tim Price
Chair AGITG & GI Cancer Institute
Dear Colleague,

One of the key highlights of the Annual Scientific Meeting is always the announcement of the recipients of AGITG grants and awards. Supporting researchers and developing new trial concepts is at the core of what we do, and recognising the multitude of new ideas and insights that are presented and submitted each year is something we take great pride in.

This year the AGITG has implemented new avenues for research development. One of these is the Idea Generation Workshop, which was held in June. Ten presenters brought embryonic research ideas for discussion at the workshop, and participants formed Concept Development Groups to develop the ideas into trial concepts.

It is our goal to develop these ideas into concepts that could be eligible for funding support through the Innovation Fund grant or that could be presented at the New Concept Symposium in the future. Supporting every stage of the research development pathway and funding vital research is a cornerstone of the AGITG’s work. The next Idea Generation Workshop will be held in 2020.

I would like to thank you all for your ongoing engagement with the AGITG. There has been a significant increase in AGITG membership this year. We have also seen an increase in the involvement by AGITG members in the activities of the GI Cancer Institute to support much needed funds for pilot studies and translational research.

Your support of the GI Cancer Institute and our Gutsy Challenge fundraisers is vital to reaching community members and raising awareness and funds. With this backing we will provide two Innovation Fund grants of up to $200,000 in 2020 and hope to achieve our goal of providing three Innovation Fund grants in 2022.

Thank you to all the patients who participate in our research thereby contributing to the GI cancer knowledge base. We also value those patients and their families who have been introduced to us through our members. Your referrals of patients and interested family members regarding supporting our work through fundraising, donations and bequests are always welcome.

If there are any ways that we can improve our engagement with you or our communication of information, please let me or a member of the AGITG team know.

If you have any suggestions or feedback, please contact me at the AGITG office on 1 300 666 769 and russell@gicancer.org.au.

Yours sincerely,

Russell Conley
Chief Executive Officer
The NHMRC Clinical Trials Centre (CTC) is a leader in clinical trials. Through excellence in research and trials, we improve practices, policy and health outcomes for patients globally.

Since the CTC’s establishment in 1988, we have worked with our partners to contribute major advances in clinical care. This includes running over 200 clinical trials involving more than 80,000 patients and 800 international collaborators.

We service the full clinical trial spectrum — from assisting in establishing new groups by creating a research governance structure and terms of reference, identifying important questions related to public health, and concept and protocol development, through to randomisation, data collection, ethics and regulatory compliance, on-site monitoring and audit, and data analyses and manuscript preparation.

The CTC works collaboratively to design and run trials with five of the 13 national cancer cooperative groups in Australia. We have helped recruit thousands of patients locally and globally in breast, oesophageal, gastric, colorectal, lung, gynaecological, neurological and urogenital cancers.

The CTC has collaborated with the AGITG since 1991, conducting 57 trials involving over 5,000 patients around the world. Together, our research has changed treatment practices for patients with gastrointestinal tumours, improving life expectancy and quality of life.

Melbourne's Walter and Eliza Hall Institute is one of Australia’s leading biomedical research organisations, with a strong national and international reputation for performing highly influential basic and translational research.

With more than 1,100 staff and students, the Institute is addressing some of the major health challenges of our time, with a focus on cancer, infection, inflammation, immune disorders, development and ageing. The Institute is at the forefront of research innovation, with a strong commitment to excellence and investment in research computing, advanced technologies and developing new medicines and diagnostics.

The Institute is organised around five themes; Cancer Research and Treatments; Infection, Inflammation and Immunity; Healthy Development and Ageing; New Medicines and Advanced Technologies and Computational Biology.

This Institute is committed to delivering long term improvements in treating and diagnosing diseases, with many national and international clinical trials underway based on research undertaken at the Institute. Around 50 medically trained researchers are embedded within the Institute’s multidisciplinary research teams, and the Institute maintains strong links with clinical partners, including through the Victorian Comprehensive Cancer Centre and the Australasian Gastro-Intestinal Trials Group.

The Centre for Biostatistics and Clinical Trials (BaCT) at Peter MacCallum Cancer Centre provides a full range of service to clinical trials to facilitate the advancement of treatments and improved outcomes for cancer patients. In operation for over 40 years, we are committed to excellence, innovation and adaptability. BaCT uses the latest technologies to ensure efficient and timely clinical trial oversight and data capture, and provides expert statistical support.

BaCT staff can be involved at all phases of study, from collaboration on protocols and trial design from clinical, regulatory and statistical perspectives, to Trial Master File preparation and management, safety reporting management, eCRF design and development, and interim and final statistical analyses, among other tasks. The team implements high-quality biostatistics, clinical, data management, quality assurance, pharmacovigilance and trial centre project management services to a diverse research community.

BaCT is delighted to work with the AGITG on the experimental Phase II MODULATE trial. This trial studies two different combinations of immunotherapy treatments for colorectal cancer.

Survivorship Research Group (SuRG), Centre for Medical Psychology & Evidence-based Decision-making (CeMPED), University of Sydney.

SuRG is part of the CeMPED, a cross school, faculty, ad discipline research group at the University of Sydney.

We have a small, efficient team of four research officers, eight PhD students, and one post-doctoral research fellow, located across our Camperdown and Concord Campuses, who are engaged in research projects related to cancer survivorship and the cancer experience. CeMPED's mission to conduct excellent research across the interface of Psychology, Medicine, and Public Health to answer questions about: the behavioural factors which promote good health and prevent disease; ways to enhance the psychosocial adjustment of patients and carers; ways to increase use of evidence in health care decision making and ways to support patients to be more involved in their own health care. Our own work address these issues within the cancer context. Our team has particular expertise in cancer and cognition having conducted a large international cohort study of Cancer and Cognitive Function in colorectal cancer patients.

We are the Australian Coordinating Centre for the Co.21 CHALLENGE trial of a 3-yr lifestyle intervention in colon cancer survivors. We are excited to be coordinating the OXTOX study, evaluating the efficacy and safety of ibudilast on peripheral neuropathy symptoms in patients receiving oxaplatin. This is work stemming from our collaboration with laboratory-based researchers in the School of Psychology, University of Sydney and builds on the Phase I study of Doctor Christina Teng, Medical Oncologist and PhD Candidate.
RESEARCH PRIORITIES
During 2017 our Board of Directors and management created a revised Strategic Plan for the organisation and its activities including the development of new clinical trials and translational research. In December 2018, our Scientific Advisory Committee set our research priorities, defining those key areas that address the areas of greatest need and are at the forefront of research.

These areas of research urgently need greater attention and have the potential to significantly improve the knowledge base for clinical decision-making and will address vital unmet needs in GI cancer care.

The current list reflects AGITG’s Research Strategy – to undertake a strategic, multidisciplinary, program-based, collaborative clinical trials portfolio to improve outcomes for patients with gastro-intestinal cancer. It focuses on pro-actively building the clinical trial portfolio, maximise recruitment and funding opportunities, foster multidisciplinary national and international collaborations, maintain and support a multidisciplinary membership base and maintain efficient and cost-effective structures and processes for optimal use of resources.

Over time, AGITG’s Research Priorities will evolve with the cancer research landscape and will be periodically updated to reflect advancing science and unmet clinical needs.

Professor Tim Price, Chair of the GI Cancer Institute and the Scientific Advisory Committee, says, “Our research priorities have been developed with the ultimate goal of improving patient outcomes. We are looking to the future to ensure that we continue to conduct innovative and ground-breaking research that improves the treatment options and outcomes for patients with GI cancers.”

AGITG RESEARCH PRIORITIES
Accelerating progress to improve outcomes for people with GI cancer

<table>
<thead>
<tr>
<th>Priority</th>
<th>Description</th>
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<tbody>
<tr>
<td>Thinking “outside the box” for appropriate new areas for research, including pharmacogenomics, pre-habilitation, and nutrition.</td>
<td>Foster innovation and develop novel approaches for: prevention, screening, diagnosis, treatment and control, treatment modalities, genomics, investigating cancer biology.</td>
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<tr>
<td>Rare cancer possibilities, collaborative approach and investigation into potential future funding.</td>
<td>Investigate national and international funding and collaboration opportunities relevant for rare cancers, and develop a rare cancer model for AGITG.</td>
</tr>
<tr>
<td>Developing concepts in the rectal cancer space.</td>
<td>Current treatment favours early diagnosis, therefore developing concepts in rectal cancer is a priority to improve management.</td>
</tr>
<tr>
<td>Clinical trials in HCC and liver SBRT.</td>
<td>Design clinical trials in Hepatocellular Carcinoma (HCC) including treatment strategies with Stereotactic Body Radiation Therapy (SBRT).</td>
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<tr>
<td>Rare cancer international collaborations for tumour streams and rare basket studies.</td>
<td>Engage international collaborators to develop basket and umbrella trials in rare cancers to enhance feasibility.</td>
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<tr>
<td>Mapping and summarising trial activity elsewhere, using this to inform future research opportunities.</td>
<td>Map national and international GI cancer clinical trial activity to ascertain current landscape and pro-actively contribute to idea generation.</td>
</tr>
<tr>
<td>Registry-based trials.</td>
<td>Develop pragmatic clinical trial paradigms to enhance generalisability to real-world patients, site participation and participant recruitment, reduce cost and research waste. Examples of such trial designs include: registry-based randomised trials, adaptive platform trials, observational studies.</td>
</tr>
<tr>
<td>Late-stage trials, particularly colorectal.</td>
<td>Current treatment favours early diagnosis, therefore developing concepts in colorectal cancer is a priority to improve management.</td>
</tr>
<tr>
<td>Incorporation of patient-reported outcomes (PROs) into existing and new studies.</td>
<td>Integration of quality of life or other patient-reported outcomes (PROs) during concept development.</td>
</tr>
</tbody>
</table>
RESEARCH DEVELOPMENT ACTIVITIES

UPPER GI AND LOWER GI WORKING PARTIES

The AGITG’s Upper GI and Lower GI Working Parties represent the disciplines of allied health, medical oncology, surgery, radiation oncology, statistics, translational science and study coordination. The Upper GI Working Party focuses on cancers of the oesophagus, gallbladder and pancreas, stomach and liver, while the Lower GI Working Party looks at cancer of the bowel, rectum and anus.

The Working Parties meet bi-monthly to:
• Identify gaps in research activities;
• Develop and/or facilitate new clinical research concepts;
• Review the scientific merit of research proposals;
• Explore funding and feasibility opportunities in liaison with the Operations Executive Committee;
• Nominate Principal Investigators;
• Nominate Trial Management Committee members

Upper GI Working Party Members include:
• Doctor Lorraine Chantrill – Chair, Medical Oncologist
• Professor Andrew Barbour – Deputy Chair, Surgeon
• Ms Rebecca Asher – Statistician
• Professor Alexander Bousis – Gastroenterologist
• Ms Katie Benton – Upper GI & Surgical Dietician
• Doctor Yu Jo Chua – Medical Oncologist
• Professor Michael Findlay – Medical Oncologist
• Doctor Yoo Young (Dominique) Lee – Radiation Oncologist
• Professor Barbara Leggett – Hepatologist
• Associate Professor Lara Lipton – Medical Oncologist
• Associate Professor John Lubel – Hepatologist
• Professor John Marladasson – Translational Science
• Mrs Jan Mumford – Chair, Consumer Advisory Panel
• Doctor Adrian Nagrial – Medical Oncologist
• Doctor Andrew Oar – Radiation Oncologist
• Associate Professor Nick Pavlakis – Medical Oncologist
• Professor Nik Zeps – Biological Scientist
• Doctor Zee Wan Wong – Medical Oncologist
• Professor Stephen Ackland – Medical Oncologist
• Mr Robin Mitchell – Deputy Chair, Consumer Advisory Panel
• Professor Robert Ramsay – Translational Science
• Associate Professor Jeremy Shapiro – Medical Oncologist
• Associate Professor Oliver Sieber – Translational Science
• Associate Professor Jeanne Tie – Medical Oncologist
• Professor Yu Jo Chua – Medical Oncologist
• Professor Alexander Engel – Surgeon
• Mr David Espinoza – Statistician
• Associate Professor Cherry Koh – Surgeon
• Doctor Connie Diakos – Medical Oncologist
• Doctor Connie Diakos – Medical Oncologist
• Associate Professor Jeanne Tie – Medical Oncologist
• Professor Alexander Boussioutas – Gastroenterologist
• Associate Professor Niall Tebbutt – Chair, Medical Oncologist
• Dr Matthew Burge – Medical Oncologist
• Doctor Connie Diakos – Medical Oncologist
• Professor Barbara Leggett – Hepatologist

Lower GI Working Party Members include:
• Associate Professor Niall Tebbutt – Chair, Medical Oncologist
• Professor Chris Karapotis – Deputy Chair, Medical Oncologist
• Professor Stephen Ackland – Medical Oncologist
• Doctor Matthew Burge – Medical Oncologist
• Doctor Julie Chu – Radiation Oncologist
• Doctor Connie Diakos – Medical Oncologist
• Professor Alexander Engel – Surgeon
• Ms Katie Benton – Upper GI & Surgical Dietician
• Associate Professor Oliver Sieber – Translational Science
• Associate Professor Jeanne Tie – Medical Oncologist
• Professor Yu Jo Chua – Medical Oncologist
• Professor Nik Zeps – Biological Scientist

INNOVATION FUND

BACKGROUND

The AGITG Innovation Fund is made possible through generous contributions from the Spencer Gibson Foundation, the His Honour Alan Bishop Fund and with donations raised through the GI Cancer Institute’s Gutsy Challenge. Expenditure of these funds requires an overall framework that respects their philanthropic origin, and must align with the strategic direction of the AGITG.

GUIDING PRINCIPLES

Innovation funding will be offered to AGITG members to further AGITG led research. Expenditure decisions will be based on scientific merit and with the intention that they lead to enhancement of the AGITG research program. The successful application will be a proposed AGITG sponsored new research study that aims to lead on to a larger scale AGITG sponsored trial to be supported by a peer-reviewed grant source or industry. This can be a pilot phase, interventional study; a translational or biomarker study; or a project aiming to develop methodology, capacity building or infrastructure. Applications that do not meet these criteria will not be considered.

INNOVATION FUND

GUIDING PRINCIPLES

Investigators of unsuccessful applications are encouraged to continue development of the concept in consultation with the relevant AGITG Working Party, where interested members within the Working Party structure are happy to assist with refining the concept.

AWARD PROCESS

An amount of $200,000 has been identified to support a new AGITG sponsored research study. The amount and duration of funding for individual projects will be determined as part of the application process. Applications will be reviewed and prioritised by the Grants Committee, which will provide a recommendation for funding to the Board.

Management of the research funding application process is delegated to the Chief Executive Officer. The award winner will be announced at the AGITG Annual Scientific Meeting.

ASSESSMENT CRITERIA

Assessment criteria will be based on:
1. Scientific Merit of Research Proposal
   • The research proposal:
     - Is an original scientific idea with the potential to impact future clinical practice,
     - Is a translational or biomarker study linked to AGITG trial/s, and
     - Aims to develop AGITG methodology, capacity or infrastructure.

2. Feasibility
   • Study commencement must be within 6 months of receiving the Grant.
   • Study completion must be within the timeframe.
   • Expenditure of the study intervention will not be funded by the AGITG.

3. Alignment with AGITG Research Priorities

4. Ability to lead to an AGITG-sponsored large-scale trial
   • The successful research proposal will aim to progress the study to a large-scale AGITG-sponsored trial.

5. Capacity building for AGITG
   • The research proposal is led by at least one AGITG Member with a minimum of 12 months membership.
RESEARCH DEVELOPMENT ACTIVITIES

NEW CONCEPTS SYMPOSIUM

The New Concepts Symposium is designed as a novel way to reach out to a wider spectrum of the group. This session provides an opportunity for delegates to present embryonic new concepts for feedback and discussion with the audience as well as comments from international guests in terms of perspective, international interest and relevance.

A good idea can be tested and a perception gained on whether to take the concept forward to a more formal review by the Upper or Lower GI Working Party. The identification of other AGITG members who may wish to assist in progressing the concept as an AGITG supported protocol is also possible.

The winner of the Best New Concept Award will receive a $3,500 prize and a framed certificate. The runner up will receive a $1,500 prize and framed certificate both presented at the Annual Scientific Meeting Dinner. Details of the Best New Concepts Award are published on the AGITG website and in the Annual Report. Past winners have later been successful in submissions to the AGITG Innovation Fund which provides up to $200,000 for AGITG pilot research.

ELIGIBILITY CRITERIA

• Fulfils the definition of translational or clinical research
• International competitive science
• Contribution to area of unmet need in Australia
• Feasible as AGITG coordinated research
• Fundable (contestable funding and/or charitable sources)

PROCESS

• Concept submissions will be peer reviewed.
• Four concepts will be chosen for presentation.
• Selected concepts will be reviewed by a statistician with suggestions for improvement provided to the Investigator prior to printing the concept in the program book.
• Following presentation of the concept a critique will be provided by the Invited International Faculty.
• Delegates will then be invited to provide comments and the presenter will have opportunity to respond.
• The process is intended to be constructive and result in refinement of the concept – with the aim of becoming an AGITG sponsored Protocol.
• Investigators of unsuccessful applications are encouraged to continue development of the concept in consultation with the relevant AGITG Working Party, where interested members within the Working Party structure are happy to assist with refining the concept.

IDEA GENERATION WORKSHOP

Strategic Activity: Develop, promote and implement a pro-active approach to idea generation linked to AGITG’s strategic forward plan for practice-changing multimodality trial activity

The AGITG hosted an Idea Generation Workshop on Friday, 21 June 2019 in Sydney. The workshop was targeted at identifying areas of unmet need in relation to gastro-intestinal clinical trials in Australia and globally.

Submission of ideas relating to gaps in current knowledge, or ideas for future clinical trials in gastro-intestinal oncology were invited, in all disciplines and at any stage of development. Applicants were encouraged to submit an idea that they may not necessarily want to drive themselves.

The selection process prioritised ideas that align with the AGITG Research Priorities.

At the Idea Generation Workshop, ten new research ideas were presented. They are now being developed further, and address a wide range of topics including colorectal, gastric, liver and pancreatic cancer, skin toxicity and neuropathy.
TRANSLATIONAL RESEARCH MODEL

Strategic Activity: Develop, promote and implement a pro-active approach to idea generation linked to AGITG’s strategic forward plan for practice-changing multimodality trial activity

This new model (currently under development) aims to develop translational research in collaboration with basic scientists, preclinical and industry partners, by providing access to stored biological specimens acquired from studies that have subsequently closed.

TRANSLATIONAL RESEARCH REPORT

An inventory report will be generated quarterly that lists bio-specimen information. The report will include the following details:

- Trial name. Studies where AGITG is ‘regional’ coordinating centre will be noted on the report, with details of the lead group.
- Recruitment
- Trial status
- Types of specimens expected for collection
- Status of specimen collection
- Translational sub-studies identified and status
- For closed studies: number of samples available (internal viewing only)

PROCESS

AGITG Members that wish to access the biospecimens will submit an application to AGITG detailing:

- Translational concept
- Ethics approval
- Funding approval
- Timeframe for anticipated commencement and completion of the study
- Type and volume of biospecimens required
- Whether the samples will be returned to AGITG

The application will be circulated to the Operations Executive Committee (OEC) and relevant Trial Management Committee (TMC) for consideration.

Concepts will be prioritised based on:

- Scientific merit
- Alignment with AGITG Research Strategy
- Volume of samples remaining

Approved concepts will be required to adhere to the AGITG Publications Policy.

ENDORESED STUDY MODEL

Strategic Activity: Support feasibility studies to inform and enhance large-scale practice-changing trials.

AGITG will encourage investigators to submit concepts requiring ‘endorsement’ or ‘sponsorship’ for consideration via the internal processes in place.

Concepts that are ‘endorsed’ may involve AGITG liaising with the sponsoring institution to:

- Conduct feasibility to gauge interest from a wide network of potential sites to participate in the study
- Advertise the study on the AGITG website
- Invite presentations at the ASM
- CAP review and feedback: lay summary of concept and master Participant Information Sheet and Consent Form

Investigators requesting AGITG endorsement of concepts must agree to the following governance framework:

1. AGITG Working Party reviews and approves the scientific merit of the research proposals. Investigators should advise of any time sensitivities in relation to Working Party review.
2. AGITG Consumer Advisory Panel reviews the relevance of the concept from a consumer perspective.
3. AGITG-CTC Operations Executive reviews and approves the resources allocated to conduct the study including the study budget.
4. A TMC will be appointed to maintain adequate oversight on the trial if necessary.
5. An AGITG Member is an Investigator on the study.
6. The Institution submits six-monthly progress reports using the AGITG reporting template in a timely manner. In addition, the relevant AGITG Working Party throughout the year may request study updates.
7. If the pilot research develops a positive signal that warrants a larger-scale study:
   a. AGITG will have the expectation to review and act as Sponsor of the study, and the Chief Investigator and AGITG will work together to source additional grant or industry funding.
   b. A Coordinating Centre selected by the AGITG will coordinate the large-scale study.
   c. AGITG will request access to the pilot study data for the purposes of developing a larger-scale study.
8. AGITG will be acknowledged in all publications arising from the pilot study to reflect the support provided to the investigator.
9. Execution of an agreement including the above terms.

AGITG Working Party

Review / Approval

- Scientific Merit of Concept / Protocol

Consumer Advisory Panel

Review / Approval

- Concept / Trial meets consumer needs
- Review of PICF to ensure easy to understand

Operations Executive Committee

Review / Approval

- Study Budget
- TMC Formation
- HREC Approved Documents
BACKGROUND
Rectal cancer usually presents with locally-advanced disease that requires ‘short course’ radiotherapy or, more commonly, ‘long course’ pCRT and often adjuvant chemotherapy. While these advances have reduced local relapse to 10% in most patients, those with higher tumour stage, or evidence on staging MRI scan of invasion of local nodes, mesorectal fascia or blood vessels, have substantially higher local relapse rates and poorer overall survival (OS). In addition, distant relapse still occurs in 25-30% of patients, with most dying within 5 years. 60% of high-risk patients have poor tumour responses to pCRT, and this group has double the risk of relapse compared to good responders. Furthermore, about 10% of surviving patients suffer from chronic bowel toxicity from radiotherapy. Adding more drugs (such as oxaliplatin) to pCRT increases toxicities without improvement in cancer survival. Other strategies being explored in phase II and III trials have not yet changed the standard of care.

Retrospective studies have shown improved outcomes in rectal cancer patients if taking statins, including overall survival, pathological tumour response to pCRT and acute and late toxicities of pelvic radiation. Major risk patients have poor tumour responses to pCRT, and this group has double the risk of relapse compared to good responders. Furthermore, about 10% of surviving patients suffer from chronic bowel toxicity from radiotherapy. Adding more drugs (such as oxaliplatin) to pCRT increases toxicities without improvement in cancer survival. Other strategies being explored in phase II and III trials have not yet changed the standard of care.

STUDY SCHEMA
Eligibility
Patients with biopsy-proven rectal adenocarcinoma (or high-grade dysplasia on biopsy with radiological evidence of invasive tumour) planned for concurrent long course pCRT using fluoropyrimidine-based chemotherapy population

STUDY PROGRESS
Australia and New Zealand currently has 10 sites (7 in Australia and 3 in New Zealand) opened for recruitment. Another 5 Australian sites and 3 New Zealand sites are in the process of opening. There are 19 recruited participants as of June 2019.

TRANSLATIONAL RESEARCH
Tissue samples taken from diagnostic biopsies and resected tumour will be collected and analysed to compare between the SIM and placebo groups:
- The association between CD3+ and/or CD8+ T cell infiltrates in the tumour in the pre-pCRT diagnostic biopsies and pathTRG;
- The intensity and distribution of subsets of infiltrating T cells in irradiated normal and malignant tissue in the resected specimen;
- The influence of SIM on systemic inflammation (assessed with the mGPS and NLR).

AIMS
To evaluate the effect of simvastatin (SIM) on the efficacy and toxicity of preoperative chemoradiation (pCRT) in rectal cancer patients, and on systemic and local inflammatory responses.

STUDY DESIGN
This is a randomised double-blind placebo-controlled multicentre phase II trial. The planned sample size is 222 patients (147 from NZ sites and 75 from Australian sites over 4 years). Eligible patients will be aged 18 years with biopsy-proven rectal adenocarcinoma (or high-grade dysplasia on biopsy with radiological evidence of invasive tumour) planned for long-course pCRT using fluoropyrimidine-based chemotherapy. The study treatment is SIM 40mg capsule or placebo capsule taken daily for 90 days, starting 1 week prior to first radiation dose. Treatment allocation will be balanced using minimisation for major prognostic variables. Patients will be allocated in a ratio of 1:1 to SIM or placebo. The primary objective is to compare rates of favourable (grades 1-2) mTRG (by central review) following pCRT with SIM or placebo, considering mTRG in 4 ordered categories: 1, 2, 3, 4-5.
ASCOLT is coordinated by the National Cancer Centre Singapore and is currently open in Singapore, Taiwan, Saudi Arabia, Malaysia, Indonesia, Hong Kong, China, India, South Korea, Australia and New Zealand. This trial is supported by Cancer Australia grant funding. The first Australian site opened in June 2014, first ANZ patient randomised in August 2014. In early 2018, international recruitment target increased from 1200 to 1587 patients, due to a lower than expected event rate. There are 32 ANZ sites, recruitment was extended to approximately 400. ANZ recruitment is at 359 of 1386, internationally (correct as of 20 Jun 2019).

**TRANSLATIONAL RESEARCH**

In Australia, AGITG sites are collecting tumour tissue (formalin-fixed paraffin-embedded tumour tissue blocks) and blood (for recovery of serum and plasma) at 3 time points (Baseline, 6, & 12 months). Singapore and various other countries are also collecting biological samples.

The Australian-led translational research in ASCOLT focuses on the predictive value of key biomarkers identified in retrospective studies, particularly tumour PIK3CA mutation and COX-2 overexpression. Consenting AGITG patients constitute the majority of participants in the serial blood collection protocol that will be a rich source of CRC prognostic markers, including circulating tumour DNA. Several collections of tumour blocks/slides have been completed. Further collection of the serial blood samples and subsequent patient’s tissue blocks is planned.

**STUDY SCHEMA**

<table>
<thead>
<tr>
<th>ASCOLT Dukes / High risk Dukes B colon cancer (or) Rectal cancer subgroups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery</td>
</tr>
<tr>
<td>(Complete resection of tumour)</td>
</tr>
<tr>
<td>Standard therapy</td>
</tr>
<tr>
<td>(at least 3 months of chemotherapy +/- Radiotherapy)</td>
</tr>
<tr>
<td>Eligible patient</td>
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<tr>
<td>Randomisation</td>
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**AIMS**

To assess the effectiveness of Aspirin against placebo control in patients with Dukes C or high risk Dukes B colorectal cancer in terms of Disease Free Survival (DFS) and Overall Survival (OS). The primary endpoint is DFS with secondary objectives including OS at 5 years, DFS and OS in different ethnic groups, cancer sub-groups and compliant vs non-compliant patients.

**BACKGROUND**

The ASCOLT study is an international randomised phase III trial investigating the effect of aspirin as additional adjuvant treatment on disease free survival and overall survival in patients with resected stage II and III colorectal cancer (CRC). This study of aspirin (a cost effective and familiar medication) is testing a critical question aimed at improving the survival of patients in Australia and New Zealand with potentially curable but high risk localised colorectal cancer.

Evidence is emerging that aspirin has anticancer properties, particularly in gastrointestinal cancers. Indirect evidence from five meta-analyses of randomised trials in patients with vascular disease showed that long term use of aspirin reduces the primary incidence of CRC by about 40-50 percent. Randomised trials performed in patients at high risk for colorectal cancer reported that aspirin can reduce the development of polyps (the precursors of CRC) and the incidence of CRC. Although several cohort studies have suggested that aspirin improves survival in patients with localised CRC, prospective evaluation of the benefit of aspirin as an adjuvant agent in patients with a history of CRC has yet to be conducted.

The recruitment target in the ASCOLT trial is likely to have adequate power to identify subgroups that specifically derive benefit from aspirin. In this way aspirin may become another personalised or targeted therapy which is likely to be very cost effective.

**STUDY DESIGN**

ASCOLT is a multi-centre international phase III trial in patients with stage III and high risk stage II colon cancer, stage II and III rectal cancer who have had resection of their primary tumour and have completed standard adjuvant therapy (chemotherapy ± radiotherapy). Within 120 days of completion of the standard therapy patients will be randomised to the study in 1:1 ratio to either:

- Aspirin arm: 200 mg aspirin once a day for 3 years
- Placebo arm: 200 mg matching placebo once a day for 3 years

Patients will be randomised with competitive recruitment to the planned total of 1587 participants. Patients will have 3-monthly follow-up assessments for 3 years (months 3 to 36), followed by 6 monthly assessments for additional 2 years (months 42 to 60). Participating sites are offering an optional 6-monthly extended survival follow-up beyond 60 months, until the last patient at site reaches month 60.
AIMS
To determine the rate of local failure in patients with locally advanced rectal adenocarcinoma who have achieved a complete clinical response after chemoradiation and are then managed by ‘wait and watch’ strategy.

BACKGROUND
Rectal cancer is a common malignancy. The current treatment approach for patients with rectal cancer involves neoadjuvant chemoradiation followed by resection. The resection can lead to surgical complications and long-term consequences.

Complete response is observed in approximately 20% of cases after chemoradiation. A number of recent studies have shown that patients can be observed safely after completing chemoradiation without surgery, provided an apparent complete response has been achieved. Resection is reserved for recurrent cancer cases. This approach potentially avoids unnecessary surgical resection and the resulting complications in this group of patients.

This study will investigate the non-operative management approach prospectively.

STUDY DESIGN
This non-randomised longitudinal cohort study aims to enrol 250 participants over a three-year period, with 50 participants on the ‘Watch and Wait’ arm and 200 participants in the standard arm.

Adult patients with a diagnosis of rectal cancer who planned to receive neoadjuvant long course chemoradiotherapy will be consented for data collection prior to commencing treatment. After completing chemoradiation, study participants will be allocated to a treatment arm based on their clinical response.

In both arms, tissue and blood specimens and Patients Reported Outcome Measures will be collected.

STUDY PROGRESS
The study is currently open to recruitment with three participants recruited at Flinders Medical Centre SA. The Royal Adelaide, Queen Elizabeth and Mt Gambier Hospitals in SA are currently seeking governance approval. Sites in NSW and New Zealand are currently looking into running the RENO study.

TRANSLATIONAL RESEARCH
The study aims to collect tissue blocks for central histology review and translational studies. Fresh tissue, plasma and serum will be collected for biomarker studies.

RENO is partially funded by an AGITG Innovation Fund Grant with support from the Gutsy Challenge.
AIMS
To determine whether ibudilast has the potential to decrease the severity of acute neurotoxicity and chronic chemotherapy-induced peripheral neuropathy (CIPN) in patients with metastatic colorectal cancer receiving oxaliplatin.

BACKGROUND
Oxaliplatin containing chemotherapy medications improve survival in patients with colorectal cancer. Oxaliplatin causes acute neuropathy (paraesthesias or dysesthesias) and chronic chemotherapy-induced peripheral neuropathy (CIPN) in almost all patients. Acute toxicity peaks on day 3 following the infusion. Severity of acute neurotoxicity predicts chronic sensory neuropathy. Chronic CIPN results in sensory ataxia and dysesthesia. CIPN is dose dependent and is the most common dose-limiting factor for patients receiving oxaliplatin. CIPN can continue to worsen in the months after stopping treatment ("coasting"). Recovery is often incomplete, with residual deficits in most patients, minimal improvement on axonal excitability parameters, and 25% of patients left with sustained CIPN of at least moderate severity.

The mechanism of oxaliplatin neurotoxicity is hypothesised to be the accumulation of oxaliplatin in the dorsal root ganglion, leading to axonal degeneration, mitochondrial disruption and/or glial activation.

Ibudilast is a non-selective phosphodiesterase inhibitor with anti-inflammatory properties. In vitro studies have shown that ibudilast can modulate glial activity and cytokine expression, leading to attenuation of neuropathies. Ibudilast has been used in Japan for 20 years to treat asthma, and more recently for post stroke dizziness with phase II data for use in multiple sclerosis as an inhibitor of neuroinflammation. It is not known to be oncogenic.

Ibudilast administered concomitantly with oxaliplatin prevented neuropathic pain and cold hypersensitivity in rodent models, and prevented cognitive impairment compared to placebo with oxaliplatin. There are no known agents to prevent or treat CIPN. If ibudilast can reduce CIPN this will enable better delivery of recommended chemotherapy doses and improve quality of life and functional status of many cancer patients.

STUDY DESIGN
Randomised phase II trial evaluating ibudilast (30mg PO bd) and placebo to determine whether ibudilast can decrease acute neurotoxicity severity and CIPN in patients with metastatic CRC receiving oxaliplatin with either FOLFROX or CAPOX, and to determine whether ibudilast will decrease dose reductions of oxaliplatin due to neurotoxicity.
AIMS
The purpose of this research study is to test the effectiveness, safety, and tolerability of an experimental drug combination; either nivolumab and BBI-608 or nivolumab and BNC105, in 90 patients with advanced bowel cancer who have previously received standard treatment.

BACKGROUND
Colorectal cancer (CRC) is the third most commonly diagnosed cancer in males and the second in females, with an estimated 1.4 million cases and more than 700,000 deaths worldwide. Australia has one of the highest incidences of CRC - in 2016 it is estimated that 17,520 new cases will be diagnosed, leading to 4,094 deaths (https://bowelcancer.canceraustralia.gov.au/statistics). Although overall survival rates for early stage, localized CRC are more than 70%, almost half of all CRC patients develop metastatic disease (mCRC) which is usually incurable. Standard chemotherapy and biologic agents have improved survival, but only to a modest extent and novel approaches are urgently needed.

PD-1 checkpoint inhibition has shown benefit in a number of cancer types. Microsatellite unstable (MSI) CRC shows sensitivity to PD-1 inhibitors, but represents only a small subset (4%) of metastatic CRC(1). Evidence indicates that for the majority of microsatellite stable (MSS)-CRC patients, PD-1 inhibitors are ineffective as monotherapy(2). MSS-CRC is highly immunosuppressive and inhibits the influx of activated PD-1-expressing T cells to the tumour microenvironment (TME). As T cell infiltrates seem to be trapped at the invasive margin of the lesion, it has been proposed that a simple activation of these T cells will not lead to antitumour immune responses without a concomitant modulation of the TME in order to allow the T cells to engage with the tumour.

Therefore, novel therapies trialling immune checkpoint inhibitors (e.g. anti PD-1) in combination with agents that modulate the TME, present a unique and much-needed opportunity to improve the effectiveness of this strategy in both patients with CRC as well as many other cancers. This protocol evaluates PD-1 inhibition in combination with a vascular disrupting agent or a STAT3 inhibitor.

STUDY DESIGN
This is an open-label, multicentre, parallel phase II study designed to assess the efficacy of the combination of nivolumab and BNC105, in 90 patients with advanced CRC. Patients with microsatellite stable adenocarcinoma of colorectal origin that is not resectable are eligible and will be randomised in the ratio of 1:1 using permuted block randomisation with stratification by screening ECOG performance status (0 or 1) to receive nivolumab and BNC105 or nivolumab and BBI-608.

Primary Endpoint:
- Objective response rate (CR or PR) defined by immune RECIST (iRECIST)

Secondary Endpoints:
- Objective response rate (CR or PR) defined by RECIST1.1
- PFS, defined as the time from the treatment commencement to the first date of objectively documented progressive disease or date of death from any cause. Response assessed by the investigator based on immune RECIST (iRECIST)
- The type, severity and relationship to treatment of adverse event, assessed according to the NCI CTCAE v5.0
- Overall survival, defined as the time from the treatment commencement to the date of death from any cause or date of end of study.

STUDY PROGRESS
Lead ethics approval was received on 6 July 2018, the study was opened for recruitment on 13 September 2018, with the first participant randomised on 21 September 2018. As of 28 June 2019, 53/90 participants have been enrolled from 12 participating sites. Recruitment is currently on hold pending the outcome of the interim safety analysis.

TRANSLATIONAL RESEARCH
The study aims to collect archival tumour tissue, fresh tumour biopsies and peripheral blood from each study participant.

STUDY SCHEMA

<table>
<thead>
<tr>
<th>Arm 1</th>
<th>Arm 2</th>
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<tbody>
<tr>
<td>Nivolumab (240mg every 14 days)</td>
<td>Nivolumab (240mg every 14 days)</td>
</tr>
<tr>
<td>BNC105 (16mg/m2/day on day 1 and 8 every 21 days)</td>
<td>BBI608 (240 mg bd continuous)</td>
</tr>
</tbody>
</table>

For 24 months or until disease progression or unacceptable toxicity

Disease assessments (CT scan and tumour marker) every 6 weeks ± 7 days until disease progression

End of treatment visit

30 day Safety Visit

3 monthly Follow-up
AIMS
The objectives of this study involve clarification of the role of circulating DNA (ctDNA) for tumour mutation profiling and optimisation of the techniques and timing to measure ctDNA.

BACKGROUND
Although evaluation of RAS status has been generally based on an assessment of tumour tissue, this approach is associated with several theoretical and practical disadvantages. The relevant tumour sample may have been obtained at a different site and at some time in the past. Consequently, there is frequently a delay associated with obtaining tissue for biomarker analysis, especially if the sample has been archived. Moreover, it is never certain that biomarker status in an archival tissue sample will correlate with the current tumour status. In addition, because of tumour heterogeneity, it is possible that a small tissue sample may not actually reflect the biomarker status of the majority of the tumour.

It has been recognized for some time that tumours can shed tumour DNA (circulating tumour DNA: ctDNA) into the bloodstream, probably as a consequence of apoptosis of tumour cells. Detection of mutations in ctDNA provides an alternative method of biomarker analysis; so called “liquid biopsy”. It offers several advantages as it is immediately available via the patient for analysis; it reflects the current tumour status and presumably presents an average reading for the biomarker status as a composite of all tumour sites.

STUDY DESIGN
LIBERATE is a cohort study and 100 patients will be recruited from 14 sites in Australia. The primary objective is to validate liquid biopsies as an alternative to tissue based assays to determine ras status, and the secondary objective is to compare different modalities of evaluating mutation status in ctDNA. Blood samples for ctDNA will be collected at baseline, then 2-4 days after the first dose of chemotherapy and a final blood sample within 1 week of the first restaging scan. All treatment choices are at the discretion of the clinician and they may include experimental therapies. Extended RAS status determined according to usual routine practice. Baseline demographics, treatment regimen and the results of the first restaging scan will be collected and no other clinical data or follow up is required.

STUDY PROGRESS
Australian lead ethics approval was received on 30 October 2017 and LIBERATE was opened for recruitment in April 2018. There are 14 AGITG sites open around Australia. Recruitment is currently at 91 participants out of the target accrual of 100 (as of 20Jun2019).

TRANSLATIONAL RESEARCH
Three blood samples of 40ml will be collected from each patient and sent to the Olivia Newton-John Cancer Research Institute (ONJCR) laboratory. Tumour tissue will be made available for central analysis, which may include evaluation using novel assays. Central collection of blood and tumour samples is planned for Q4/2019.
**AIMS**

The aim of this study is to investigate the activity of panitumumab monotherapy, or combined with infusional 5-FU, in Ras and BRAF wild type, elderly patients with metastatic colorectal cancer.

**BACKGROUND**

Metastatic colorectal cancer is a disease of the elderly, with a median age at diagnosis of approximately 70 years. To date, limited research has been conducted with anti-EGFR antibodies in elderly patients who, for a number of reasons, may be unsuitable for a combination chemotherapy backbone. First line trials using combination chemotherapy demonstrate that RAS wild type patients, and particularly those with left sided primaries, derive a survival benefit from regimens incorporating anti-EGFR antibodies. Since patients may never receive second and subsequent treatment lines, it makes sense to use anti-EGFR antibodies first line in RAS WT disease. There is an opportunity to investigate the activity of anti-EGFR monotherapy, or combined with “light” chemotherapy in a molecularly selected, hitherto under-investigated elderly patient population.

**STUDY DESIGN**

Non-comparative phase 2 randomised (1:1) open-label multicentre clinical trial. Patients will be stratified by performance status (0 v >1, 2); site of primary tumour (left v right) and number of metastatic sites (1 v >1). Left sided is defined as at, or distal to, the splenic flexure.

**Primary endpoint:** To measure 6 month progression free survival (PFS) (disease progression or death) in the two groups of elderly mCRC patients, one receiving panitumumab monotherapy and the other receiving combination therapy with panitumumab plus 5-fluorouracil and leucovorin (5-FU).

**Secondary endpoints:** To measure the effect of panitumumab monotherapy and panitumumab plus 5-FU on Overall survival (OS), Time to treatment failure, Objective tumour response rate (OTTRR) and Safety.

**Tertiary and correlative objectives:**

- Study associations between clinical outcomes and potential predictive/prognostic tissue and blood based biomarkers including, but not limited to, the percentage of RAS mutant cells, tumour inflammatory biomarkers; and resistance mechanisms, such as HER-2 overexpression

MONARCC is a multicentre trial that aims to recruit 80 patients from 16-17 sites in Australia. Amgen is supporting the study including drug supply for both treatment groups. MONARCC was awarded an AGITG Innovation Grant in 2016 with support from the Gutsy Challenge, and has received additional AGITG funding from the Alan Bishop Memorial Fund.

**STUDY PROGRESS**

MONARCC received central ethics approval in Australia in September 2017. The first site opened in June 2018 and the first patient was randomised in July 2018. As of 18 June 2019, 9 patients enrolled to the study and 17 sites opened.

**TRANSLATIONAL RESEARCH**

Formalin-fixed paraffin-embedded tissue will be collected for translational research from all participants for central review of RAS and BRAF mutation status and for translational studies within the tertiary /correlative objectives. This is required of all participants.

Blood for translational research will be collected from all participants at three timepoints - Cycle 1 Day 1, Cycle 2 Day 1 and at 6 months. Central laboratories will be used to conduct translational research studies including biomarker analyses.

**STUDY SCHEMA**

**Eligibility**

Adults over >70 with at least 1 comorbidity (Charlson comorbidity Index) or aged >75, with previously untreated, RAS and BRAF wild type metastatic colorectal cancer

**Stratification (1:1)**

Stratified in a 1:1 ratio by performance status (0 Vs >1,2); site of primary tumour (left V right) and number of metastatic sites (1 V >1). Left sided is defined as at, or distal to, the splenic flexure.

**Duration of accrual:** 2 years

**Duration of follow-up:** up to 18 months

**Endpoints**

- **Primary endpoint**
  - 6 month Progression free survival

- **Secondary endpoints**
  - Overall survival
  - Time to treatment failure
  - Objective tumour response rate
  - Safety

- **Tertiary/correlative endpoints**
  - Overall treatment utility
  - Feasibility/utility genotypic assessment
  - Patient activity
  - Validation of a prognostic nomogram
  - Exploratory comparisons of anti-tumour efficacy by treatment arm
  - Biomarker analyses of blood and tissue

**Arm A**

- IV Panitumumab 6mg/Kg every 2 weeks until disease progression or unacceptable toxicity
- N=40

**Arm B**

- IV Panitumumab 6mg/Kg every 2 weeks plus Infusional 5-fluorouracil as per the modified De Gramont schedule until disease progression or unacceptable toxicity
- N=40

**Blood collection**

- Blood for translational research will be collected from all participants at three timepoints - Cycle 1 Day 1, Cycle 2 Day 1 and at 6 months.
AIMS
The primary objective of the DYNAMIC-Rectal study is to demonstrate that an adjuvant therapy strategy incorporating ctDNA results in addition to standard pathologic risk will reduce the number of patients receiving adjuvant chemotherapy.

BACKGROUND
Despite guidelines recommending the routine use of adjuvant chemotherapy in locally advanced rectal cancer (LARC), there is little evidence in the modern era to support the routine use of post-operative chemotherapy in patients who received pre-operative chemo-radiation therapy. In fact, the results of EORTC 22921 combined with the results of other smaller studies argue against the routine use of chemotherapy for patients with clinical stage II or III disease who are undergoing pre-operative chemo-radiotherapy. Although the use of adjuvant FOLFOX appears promising in node-positive disease (ypN+), this comes with a toxicity price and the impact on overall survival yet to be proven. Clearly, better predictors of those patients who actually require adjuvant chemotherapy are needed (e.g. ctDNA-positivity indicating presence of minimal residual disease).

Our initial studies have demonstrated across multiple colorectal cancer cohorts, the potential utility of ctDNA as a marker of recurrence risk. The end goal for LARC patients is to integrate ctDNA analysis into routine clinical practice to guide clinical decision making, and most importantly to benefit patients. This initial study is powered to show that a ctDNA-based approach to adjuvant therapy will lead to substantially fewer patients receiving adjuvant therapy, which we believe is the only practical study design with a clinically significant endpoint, within the patient numbers that could be recruited. Importantly, this study will also demonstrate the feasibility of performing such a biomarker-driven study in the rectal cancer population.

STUDY DESIGN
DYNAMIC-Rectal is a prospective, multi-centre, randomised study enrolling a total of 408 patients with locally advanced rectal cancer treated with standard neoadjuvant chemo-radiotherapy followed by surgery. Patients will be randomised 1:2 to be treated as per standard of care (Arm A: SOC) or according to post-op ctDNA results (Arm B: ctDNA-informed). Patient enrolment will be stratified by participating centre and ypN stage.

Primary endpoint: Number of patients receiving adjuvant chemotherapy
Secondary endpoints:
- ctDNA results turn-around time
- 3-year recurrence free survival
- Overall survival

STUDY SCHEMA

STUDY PROGRESS
DYNAMIC-Rectal received central ethics approval in Australia in September 2017. The first site opened in June 2018 and the first patient was randomised in July 2018. As of the 14 June 2019, 55 patients have been enrolled onto the study and 19 sites activated. The study is funded by an NHMRC grant.

BIOMARKER TESTING
Formalin-fixed paraffin-embedded tumour (preferably diagnostic biopsy sample) and matched normal tissue will be collected from all participants to identify somatic mutation(s) for subsequent ctDNA analysis. Thirty to 60mL of blood for ctDNA analysis will be collected from all participants at 4 and 7 weeks post surgery. Up to 4 additional study bloods will be collected during chemotherapy and at the end of treatment from participants randomised to the ctDNA-informed arm that is treated with chemotherapy. ctDNA analyses will be conducted by the Vogelstein Laboratory at Johns Hopkins University, Baltimore, USA.
DYNAMIC-III

Circulating Tumour DNA Analysis Informing Adjuvant Chemotherapy in Stage III Colon Cancer: A Multicentre Phase II/III Randomised Controlled Trial (DYNAMIC-III)

AIMS

The primary aim of the DYNAMIC-III study is to demonstrate that a de-escalation/escalation treatment strategy using ctDNA-informed management is non-inferior to standard of care treatment as measured by the rate of 3-year recurrence-free survival.

BACKGROUND

In the adjuvant setting, post-operative circulating tumour DNA (ctDNA) has been shown to be a marker of minimal residual disease, with the presence of ctDNA predicting recurrence in stage II colon cancers and locally advanced rectal cancers.

For patients with stage III colon cancer, adjuvant chemotherapy improves overall survival but some patients will receive adjuvant therapy and still recur, whereas others will not recur in the absence of any adjuvant treatment. For every patient with stage III colon cancer, a reliable biomarker could improve their adjuvant management decision (treatment regimen and/or treatment duration), allowing therapy to be tailored to each patient’s risk of recurrence and moving away from a generic “one size fits all” approach. Specifically, for the great majority of patients, a biomarker that defines a given patient to be either at very high risk (such as a positive ctDNA test) or at very low risk (such as a negative ctDNA test) of recurrence would allow treatment to be escalated in very high risk cases (enhancing the likelihood of preventing disease recurrence and death) or de-escalated for patients with a very low risk of recurrence (reducing treatment related toxicity, reducing direct treatment related cost, and reducing indirect treatment related costs, such as time off work, with minimal to no risk of compromising survival outcome).

STUDY DESIGN

DYNAMIC-III is a prospective multi-centre, phase II/III randomised controlled study enrolling a total of 1000 stage III colon cancer patients. Patients will be randomised 1:1 to be treated according to post-op ctDNA results (Arm B: ctDNA-informed), or per standard of care (Arm A: SOC). Enrolment will be stratified by participating centre and clinical risk groups (low risk = T1-3N1; high risk = T4 and/or N2).

Primary endpoint:
- For the ctDNA negative cohort: 3-year recurrence free survival
- For the ctDNA positive cohort: 12 month recurrence free survival

Secondary endpoints:
- Proportion of patients with NEGATIVE post-op ctDNA receiving de-escalated treatment (no or less intense chemotherapy compared to pre-planned standard chemotherapy) in the ctDNA-informed arm
- Overall survival
- ctDNA results turn-around time
- Proportion of patients with positive ctDNA at completion of all treatment in the ctDNA-informed positive cohort

STUDY SCHEMA

Exploratory Endpoints:
- Proportion of patients with positive ctDNA at completion of all treatment in the ctDNA-informed arm negative and positive cohort
- Treatment duration and dose intensity
- Health economic impact
- Treatment related hospitalisation

STUDY PROGRESS

DYNAMIC-III received central ethics approval in Australia in March 2017. The first site opened in October 2017 and the first patient was randomised in October 2017. As of 24 June 2019, 203 patients have been enrolled onto the study and 26 sites activated. The study is funded by a philanthropic source, the Marcus Foundation.

BIOMARKER TESTING

Formalin-fixed paraffin-embedded tumour and matched normal tissue will be collected from all participants to identify somatic mutations for subsequent ctDNA analysis. 30-60mL of blood for ctDNA analysis will be collected from all participants 3-6 weeks after surgery (ctDNA-1). Up to four additional study bloods will be collected prior to and during chemotherapy and at end of treatment from patients randomised to the ctDNA-informed arm only. ctDNA analyses will be conducted by the Vogelstein Laboratory at Johns Hopkins University, Baltimore, USA.

Session: AGITG Advanced Colorectal Cancer Trials
Presentation: DYNAMIC-III
Speaker: Associate Professor Jeanne Tie
Institution: The Walter and Eliza Hall Institute of Medical Research
Financial Disclosure: None to declare
Protocol Title: Circulating Tumour DNA Analysis Informing Adjuvant Chemotherapy in Stage III Colon Cancer: A Multicentre Phase II/III Randomised Controlled Trial (DYNAMIC-III)
Study Chair(s): Associate Professor Jeanne Tie and Professor Peter Gibbs
Project Manager(s): Marlyse Debrincat and Roslynn Murphy
Trial Coordinator(s): Marlyse Debrincat (Marlyse.Debrincat@mh.org.au) and Roslynn Murphy (Roslynn.Murphy@mh.org.au)

Day 2 TRIAL ABSTRACTS - DYNAMIC-III

Arm A
Standard of Care (N=500)

Arm B
ctDNA Informed (N=500)

Clinicians choice

ctDNA Negative (N=375)

ctDNA Positive (N=125)

Note: Clinicians and patients in Arm A (SOC) will remain blinded to their ctDNA result for the duration of the study.

Stratification: 1) Participating site 2) Clinical risk (low vs high)

Explores other endpoints:
- Proportion of patients with positive ctDNA at completion of all treatment in the ctDNA-informed arm negative and positive cohort
- Treatment duration and dose intensity
- Health economic impact
- Treatment related hospitalisation

STUDY SCHEMA

STUDY DESIGN

DYNAMIC-III is a prospective multi-centre, phase II/III randomised controlled study enrolling a total of 1000 stage III colon cancer patients. Patients will be randomised 1:1 to be treated according to post-op ctDNA results (Arm B: ctDNA-informed), or per standard of care (Arm A: SOC). Enrolment will be stratified by participating centre and clinical risk groups (low risk = T1-3N1; high risk = T4 and/or N2).

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- For the ctDNA positive cohort: 12 month recurrence free survival

Secondary endpoints:
- Proportion of patients with NEGATIVE post-op ctDNA receiving de-escalated treatment (no or less intense chemotherapy compared to pre-planned standard chemotherapy) in the ctDNA-informed arm
- Overall survival
- ctDNA results turn-around time
- Proportion of patients with positive ctDNA at completion of all treatment in the ctDNA-informed positive cohort

STUDY SCHEMA

STUDY DESIGN

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STUDY SCHEMA

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STUDY SCHEMA

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STUDY SCHEMA

STUDY DESIGN

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Secondary endpoints:
- Proportion of patients with NEGATIVE post-op ctDNA receiving de-escalated treatment (no or less intense chemotherapy compared to pre-planned standard chemotherapy) in the ctDNA-informed arm
- Overall survival
- ctDNA results turn-around time
- Proportion of patients with positive ctDNA at completion of all treatment in the ctDNA-informed positive cohort
The primary objective of the study is to compare the activity, in terms of overall response rate (ORR), of two combination chemotherapy regimens (cisplatin plus 5-fluorouracil (5FU) vs. carboplatin plus weekly paclitaxel) for the first line treatment of patients with inoperable relapsed or metastatic squamous cell carcinoma of the anus (SCCA). The results of the study will be used to inform the design of future III trials testing the addition of a targeted agent to the preferred chemotherapy regimen. The secondary objectives of the study are to provide estimates of differences in survival, toxicity and quality-of-life (QoL) endpoints between the two treatment arms. Exploratory biomarker research will also be undertaken in order to further investigate the role of the epidermal growth factor (EGF) pathway and other molecular pathways in predicting response or resistance to systemic chemotherapy in patients with inoperable relapsed or metastatic SCCA.

BACKGROUND

The optimal palliative chemotherapy regimen for patients with inoperable relapsed or metastatic SCCA is still unknown. Various chemotherapy regimens as either monotherapy or combination chemotherapy have been reported to be active, however, the current available evidence in this setting is based on small phase II trials, retrospective series, and case reports, and there have been no prospective phase III studies or meta-analyses to inform clinical practice.

Current guidelines recommending the use of cisplatin and 5FU in advanced SCCA are mainly based on small phase II data indicating modest survival benefit, however, this combination chemotherapy has never been evaluated within the context of a formal, randomised, clinical trial. Additionally the optimal chemotherapy backbone to which targeted agents can be potentially added is not known. Emerging evidence indicates that targeting the EGF pathway could be potentially beneficial in SCCA.

This study will provide evidence for the optimal first line treatment option, thus setting the standard of care for this disease. It will also establish the optimal chemotherapy backbone to use in combination with new targeted agents in future trials. Additionally this study will be able to confirm the feasibility of conducting an international trial on a relatively rare condition like advanced SCCA that entails global collaboration and global representation. If successful this collaboration will pave way for future collaborative studies.

It is envisaged that biomarker research on blood and tissue samples collected from participating patients will enable the identification of a subpopulation of patients who have increased chances to respond to a particular treatment. Moreover, the collection of fresh blood samples (at baseline and at disease progression) and tumour tissues (archival and also fresh at disease progression upon further patient consent) will also allow exploration of the biology of SCCA, identification of predictive/prognostic biomarkers, and development of selective therapeutic strategies.

STUDY DESIGN

This is an international, multicentre, open label, randomised phase II trial. Patients will be randomised to receive cisplatin plus 5-FU or carboplatin plus weekly paclitaxel. ECOG performance status (PS) (0-1 vs. 2), HIV status (positive vs. negative) and extent of disease (locally recurrent vs. metastatic) will be used as stratification factors. ORR is the primary endpoint. 90 patients are to be recruited internationally (to allow 36 assessable patients per treatment arm).

InterAACT is being coordinated internationally by The Royal Marsden NHS Foundation Trust. Approximately 50 international centres in the UK, Europe, Australia and the US participate in this study. The Royal Marsden NHS Foundation Trust is the lead international sponsor.

STUDY PROGRESS

The study is currently in close-out.

The study opened to recruitment in the UK in January 2014 and subsequently in Australia on 15 March 2016. Five Australian sites participated: Royal Hobart Hospital, Prince of Wales, Flinders Medical Centre, Austin Hospital and Princess Alexandra Hospital. The study met its recruitment target in November 2017, after having enrolled 91 patients. Three (3) patients enrolled in Australia, who have since completed the study.

Trial results were presented at ESMO in 2018 and at the AGITG ASM 2018. Main conclusion: There were no differences seen in overall response rates between the two regimens however median PFS and OS were better with carboplatin and paclitaxel. Median progression free survival with carboplatin paclitaxel was 8.1 months (95% CI 6.6-8.8) compared to 5.7 months (95% CI 3.3-9.0) with cisplatin 5FU. Median overall survival was 12.3 months for cisplatin 5FU (95% CI 9.2-17.7) compared to 20 months (95% CI 12.7- not reached) for carboplatin paclitaxel HR 2.00 (95% CI 1.5-3.4; p =0.014). There were more serious adverse events with cisplatin and 5FU (62%) compared to carboplatin and paclitaxel (36%), p=0.016. Although there was no difference in ORR between carboplatin paclitaxel and cisplatin 5FU the association with less toxicity and longer survival suggests that carboplatin paclitaxel should be a new standard of care in chemotherapy naive advanced anal cancer.

TRANSITIONAL RESEARCH

Explorative biomarker analysis including the collection of archived tumour tissue and blood sample at baseline, and upon progression, is planned.

STUDY SCHEMA

![Study Schema Diagram]

InterAACT Trial

Inoperable, locally recurrent or metastatic squamous cell carcinoma of the anus

Randomisation

Stratified by: PS 0-1 vs 2, HIV +ve (yes vs no) locally recurrent vs metastatic

Arm A

Cisplatin + 5FU
N=max 45

24 weeks treatment

Arm B

Carboplatin + weekly Paclitaxel
N=max 45

24 weeks treatment
INTRODUCTION

There is a large unmet need for patients with metastatic colorectal cancer (mCRC) who have failed standard therapy and remain fit for further treatment. Further treatment with previously used chemotherapy or use of novel agents has modest effect in unselected patients. Predicting treatment benefit using testing of patient derived tumour organoids (PDTO) is a promising new strategy to identify treatments with likely activity. At the Walter and Eliza Hall Institute (WEHI) we have grown >100 mCRC derived PDTOs and have established drug sensitivity protocols. Early data indicates concordance of patient and PDTO response, including standard to chemotherapy and EGFR antibody (EGFRI) treatment. Many investigational agents are also being tested, including new agents under development at WEHI.

We will initially enroll 42 mCRC patients that have failed or are intolerant of oxaliplatin and irinotecan based treatment and of an EGFRI inhibitor (if RAS wild-type), to pilot a randomised study. PDTOs will be derived from a fresh tumour biopsy, molecular and drug sensitivity testing performed. This includes testing for standard mCRC treatments (oxaliplatin, irinotecan, 5FU, lonsurf, EGFRI and regorafenib), chemotherapy agents not routinely used in mCRC (tezolozomide, gemcitabine and pemetrexed), and in selected patients, therapies targeting HER2 over-expression or BRAF mutation. Patients will be randomised to receive PDTO informed treatment or dealers choice (which can include lonsurf). Pending successful completion and learnings from the feasibility component of the study the study will be expanded to a phase III study with an overall survival endpoint. Industry will be approached to provide funding for agents not on the PBS, including pemetrexed, an EGFRI, regorafenib. Agents targeting HER2 overexpression and BRAF mutations may be included, pending drug availability.

All patient treatment and data outcome data will be captured in the TRACC registry, which also captures prior lines of therapy data, patient and tumour data.

RATIONALE

Pre-treatment drug sensitivity testing could be used to inform treatment selection in patients who are fit for treatment, yet have failed standard therapy. Patient derived tumour organoids can be grown in vitro and exposure to potential therapeutic drugs to assess for sensitivity. This may aid in clinical decision making in selection for the most promising available therapy, as early results show concordance between in vitro and clinically meaningful clinical response.

Patient Derived Tumour Organoids (PDTO) are a 3D multicellular in vitro tissue construct that mimics the corresponding in vivo tumour. Typically grown in 384 well plates, many drugs at varying concentrations and drug combinations can be tested. For CRC, a high success rate (now >90% in our hands) of establishing PDTOs has been achieved, with similar success rates reported by others [1,2]. Recent studies have demonstrated the feasibility of personalized high-throughput drug PDTO screening to identify effective therapies for individual mCRC patients [2,3]. Importantly, evidence is accumulating that responses to anti-cancer agents ex vivo in PDTOs and PDTO-based orthotopic mouse tumour xenograft models mirror the clinical response [4]. Scientists at WEHI have to date generated PDTOs from >100 CRC patients and now have established protocols where PDTOs are established within 2 weeks. With drug sensitivity testing completed within a further 2 weeks a result can be provided to treating clinicians by around 4 weeks from date of biopsy.

Currently, there are multiple potential strategies for patients with mCRC refractory to standard treatment. These include rechallenge with standard chemotherapy options, Oxaplatin or an EGFRI inhibitor, for those that are RAS wild type, Maindralult-Goebel et al [4] reported potential benefit from the re-introduction of oxaplatin in a series of 29 patients with mCRC. Objective responses were seen in 6 (21%), progression free survival was 18 weeks and overall survival 42 weeks. Santini et al [5] reported that the re-introduction of EGFR Inhibitors resulted in a response rate and median PFS of 6.6 months in 39 patients that were re-treated with cetuximab +/- irinotecan based treatment.

Non-standard chemotherapy options with gemcitabine, temozolomide or pemetrexed may be considered, although with modest response rates published. An early analysis of 216 patients evaluated in six Phase II studies found that gemcitabine plus a fluoropyrimidine in first-line (n=2) or as third-line (n=3) treatment produced response rates of 30 - 38.2%, with median time to progression 4.8 - 8.3+ months and overall survival of 9.8 - 19+ months [6]. Patients with MGMT loss of expression have modest benefit from temozolomide. [7]. In the largest phase II study [7] that enrolled 45 patients with MGMT promoter methylation, a 10% response rate, disease control rate of 32% and overall survival of 5.1 months was reported. An NSABP phase II study of pemetrexed in treatment naive patients (n=54), reported a response rate of 23%, with three additional (5.6%) unconfirmed partial responses. Median progression-free survival was 5.3 months, median overall survival 11 months [8]. Other treatment options based on prospective clinical trials, if available, are drugs targeting molecular pathways in molecularly selected patients. These include Targeting RAS wild type tumours that over-express HER2, BRAF V600E targeted treatment or regorafenib, each of which produces modest improvements in outcome. [9,10,11]

To better understand biomarkers of treatment response and resistance, in parallel potential biomarkers of drug sensitivity and resistance will be explored in the laboratory, including understanding acquired resistance to ongoing treatment exposure in PDTOs that are initially treatment sensitive. Clinical data will be collected in the TRACC registry.

STUDY PROPOSAL

A pilot randomised feasibility clinical trial at multiple Australian centres. A fresh tumour biopsy will be performed to generate a PDTO, with samples collected into specified media and sent to the WEHI in Melbourne. Testing of sensitivity to a panel of standard and non-standard treatments will be undertaken. Patients will be randomised to receive the best treatment based on PDTO response versus dealers choice (which could include lonsurf). If PDTO treatment data is not yet available and in the opinion of the treating oncologist the patient needs to initiate treatment they will commence treatment with lonsurf to be followed by the PDTO recommended therapy. Patients on the PDTO arm can receive multiple PDTO informed treatments.

All patient treatment and data outcome data will be captured in the TRACC registry, which will also have captured comprehensive patient and tumour data, and details of previous treatment and response. Pending the success of the pilot study funding will be sought to expand to a phase III study with survival endpoints. This research will also inform and support future applications for trials of available and novel agents in the treatment of mCRC, enriched with patients likely to respond to treatment.

STUDY SCHEMA

This study would recruit at multiple AGITG sites. A fresh tumour biopsy will be obtained at local hospitals with subsequent PDTO culture at WEHI. Biopsies will be undertaken after failure of standard therapies (except for lonsurf). Data related to organoid treatment sensitivity to a panel of potentially active drugs will be provided to the treating clinician in a standardized format within 4-6 weeks. Patients in the control arm will initiate treatment at the discretion of the treating clinician. In the PDTO informed arm patients will initiate treatment with the best option as determined by the PDTO or to lonsurf (or other dealers choice) to be followed by the PDTO informed options. Given the novel nature of this research a pilot study is required to ensure feasibility of a large RCT and to inform the statistical plan.

Organoid sensitivity panel*

<table>
<thead>
<tr>
<th>FOLFIRI</th>
<th>FOLFOX</th>
<th>EGFRI</th>
<th>Lonsurf</th>
<th>Regorafenib</th>
<th>Gemcitabine</th>
<th>Pemetrexed</th>
<th>Temozolomide</th>
</tr>
</thead>
</table>

All pathology, clinical, treatment and outcome data captured in the TRACC registry

*The number of available options will depend on industry support for non-funded treatments.
PRIMARY OBJECTIVES
To pilot a randomised controlled study of patient derived tumour organoid sensitivity to inform management of patients with mCRC that have failed standard therapy (except for lonsurf).

SECONDARY OBJECTIVES
• To determine likely recruitment rates
• To determine the optimal time for testing (pre or post second line therapy)
• To obtain preliminary data on the proportion of patients that receive the PDTO informed treatment and the outcome for both study arms (to inform planning for the phase III study)
• To determine the proportion of patients from a non-Melbourne site where a PDTO culture can be established from a fresh tissue biopsy
• To explore the correlation between PDTO drug sensitivity and clinical benefit

INCLUSION CRITERIA
 Patients who have completed second line therapy must be
1. Fit for further treatment
2. Have a life expectancy of > 3 months
3. Have failed or are intolerant of standard therapies (excluding lonsurf)
4. Have adequate major organ function.

Patients who are being consented for biopsy and PDTO culture prior to initiating second line therapy must be likely to fulfil study eligibility criteria at the end of second line therapy

EXCLUSION CRITERIA
 Patients where a biopsy to obtain fresh tissue cannot be safely performed

STATISTICAL ANALYSIS
42 patients will be enrolled over 12 months, patients will be randomised 2:1 to PDTO informed versus dealer’s choice treatment. The primary endpoint is the proportion of patients randomised to PDTO informed treatment who receive a PDTO informed therapy. The study will be considered successful if 15 of 28 patients in the PDTO informed therapy receive a PDTO recommended treatment. Based on current data (>90% success rate) an organoid culture will be successful in at least 34 patients, including 26 in the experimental arm. Treatment duration, best response and progression free survival data will be collected.

Using the method of Mehta-Cain, boundaries for declaring sufficient adherence can be determined based on a one-sided 95% confidence interval for adherence rate of 70% in the PDTO informed treatment population.

With a sample size of 42 patients, 28 patients in intervention arm, we would conclude that PDTO informed treatment cohort has sufficient adherence (at a 75% rate) if more than 15 patients are deemed to have adherence to protocol and DO have PDTO sensitivity driven treatment recommendations.

DISCUSSION POINTS AND COMMENTS
An application has been submitted for funding of an initial single arm study in this patient population which will provide further information regarding the correlation between PDTO response and patient response and will inform the feasibility of the study proposed here, a follow-on pilot randomised study. The initial study will be conducted without industry support. The study proposed here is to address the many feasibility and logistical issues associated with a large randomised study before commencing such a study. A key question is the feasibility of waiting for the PDTO sensitivity testing results, the alternative approach being to commence patients on treatment with lonsurf and then to follow with the PDTO informed treatment, the concern being that again many patients will not be fit for treatment post lonsurf. Alternative approaches would include to rigorously define the patient group, excluding those with poor prognosis features, potentially based on metastatic site (e.g., exclude patients with peritoneal or bone metastases), or unacceptable levels of liver function tests, LDH, NLR, CEA or other criteria.

The optimal timing of the tissue biopsy needs to be determined and can only be tested prospectively. If taken before commencing second line treatment then a result will be available for the study, but the uncertainty is how many patients will not be fit for the next line of treatment. The feasibility of collecting samples at non-Melbourne sites needs to be tested. The statistical plan for the phase III study can only be defined once the percentage of patients in the treatment and control group likely to receive the allocated treatment and preliminary data on outcomes can be reasonably estimated. If moving ahead with a study where the biopsy is taken prior to second line treatment then a reasonable estimate of the proportion of patients likely to make it to the next line of treatment is required.

No current clinical trials were found using link for search words colorectal cancer, organoids, sensitivity, tissue testing.

References:
11. Kopetz, S., et al. ASCO GI 2018
In a murine breast cancer model, treatment with a single dose of cyclophosphamide resulted in a 2-fold increase in tumour uptake of GSAO 24 h after administration of the chemotherapeutic [10]. GSAO has now been labelled with 68Ga for PET CT (Cell Death Indicator, or CDI-PET CT) [11]. CDI-PET CT is currently being assessed in a first-in-human study at Prince of Wales Hospital in Sydney (CT-2018-CTN-00827-7), preliminary results of which indicate highly favourable imaging and biodistribution characteristics (Figure 1), radiation dosimetry and no observed adverse events. This proposal is for a human proof of concept study to determine whether an increase in response to therapy is detectable with CDI-PET CT and whether it correlates with pathological response.

Rationale
Cell death imaging has potential wide application in clinical and research oncology; one important role may be the accurate and timely assessment of response to neoadjuvant therapy such as in rectal and oesophageal carcinomas.

In some carcinomas of the rectum, neoadjuvant chemoradiotherapy (nCRT) prior to surgery is standard of care [12]. Following nCRT, between 10% and 26% of patients achieve pathological complete response (pCR) [13], an observation which has led to the exploration of a “wait and see” approach to surgery in those patients who attain a clinical complete response (cCR) following nCRT [14]. Two meta-analyses reported that patients achieving a cCR, and in whom a “wait and see” approach to surgery was adopted, did not differ from patients who underwent immediate surgery in either disease-free or overall survival, but one meta-analysis demonstrated that the non-surgical group had a higher risk of local recurrence [15, 16]. One limitation raised in the meta-analysis by Li et al. is that cCR may not correlate well with pCR and patients with cCR following nCRT who do not have pCR likely have a high rate of local recurrence [16]. There is no consensus regarding the criteria and techniques used to establish cCR and methods used include digital rectal examination, endoscopy, MRI, FDG-PET CT, transrectal ultrasound and CEA. None are sufficiently accurate alone and are often used in combination [17]. Of the imaging techniques used to assess for cCR, the two most promising are MRI and FDG-PET, however, while MRI and FDG-PET are able to identify non-responders for “wait and see” approach, neither are sufficiently accurate to safely select patients for organ sparing approaches [18].

Similar to rectal carcinomas, neoadjuvant chemotherapy (nCT) or nCRT is standard of care in some carcinomas of the oesophagus and gastro-oesophageal junction (GOJ) [19], with reported rates of complete pathological response to nCRT of 27% [20]. While a “wait and see” approach to surgery may be considered in squamous cell carcinoma of the oesophagus, there is no routine role for this in patients with adenocarcinoma [21]. However, in the CROSS study, 18% of patients in the nCRT arm had a tumour regression grade (TRG 0-4) of (90% vital residual tumour cells in the primary tumour), and these patients do more poorly and are probably exposed to the adverse effects of nCRT for no benefit [22]. Recognising this, Barbou et al. undertook a study to escalate chemotherapy without or with addition of radiotherapy in patients deemed to be non-metabolic responders based on FDG-PET [23]. While FDG-PET following nCT has been shown to detect non-responders [24], in the nCET setting FDG-PET was unable to discriminate between significant residual disease (TRG 3-4) and benign inflammatory changes secondary to nCRT [25]. No one method can accurately and adequately assess response to nCRT and there is no consensus on the best combination of methods. The preSANO trial performed endoscopy, bite on bite biopsies and fine needle aspiration of suspicious nodes, endoscopic ultrasound and FDG-PET CT and found that all missed TRG 0-1 tumours were false negatives rates of 33%, 10%, 28%, 15% for each of these techniques, respectively [26]. A study is currently underway assessing MRI, FDG-PET CT, circulating tumour DNA (ctDNA), endoscopy with bite on bite biopsies, and endoscopic ultrasonography (EUS) with fine needle aspiration of suspected lymph nodes [27].

Direct imaging of tumour cell death represents a new paradigm for assessing treatment response. As discussed in the introduction, the kinetics of tumour cell death are poorly understood due to the lack of effective methods to assess this accurately in vivo. Measurement of tumour cell death soon after commencement of therapy (within hours or days) is expected to give useful information regarding the effectiveness of therapy as greater amounts of cell death would likely translate to better response over multiple cycles of chemotherapy or fractions of radiotherapy. CDI has been shown to detect tumour cell death within 1 day of commencement of treatment in mice [10]. A potential advantage of CDI-PET CT is that it should also report on cumulative cell death following some period of treatment. In principle, the best time to perform imaging for cumulative cell death would be...
following as much treatment as possible but prior to significant clearance of dead cells from the tumour mass in
responders (which results in clearance of the target for CDI). The time course for clearance of dead tumour cells
will generally correlate with reduction in tumour volume. CDI-PET CT, therefore, should be performed prior to
tumour shrinkage becoming evident. From studies performed using CT in an attempt to assess early response,
no significant change in tumour volume is observed at 2 weeks after commencement of therapy regardless of
subsequent histopathological response [28], but may be seen at the completion of nCT (but is very unreliable)
[29]. In order to assess both immediate and cumulative cell death, the initial patients in this proposed study will
undergo CDI-PET CT at 1, 2 and 14 days after commencement of treatment.

In summary, non-invasive assessment of treatment response after nCT or nCRT in rectal carcinoma and
carcinomas of the oesophagus and GOJ remains inadequate. However, there is a significant clinical need for such
capability to allow more individualized treatment approaches, including organ preserving or a “wait and see”
approach to surgery and to allow exploration of alternative treatment strategies in those in whom nCT or nCRT is
ineffective. This concept to directly image cell death using CDI-PET CT in patients with rectal and oesophageal/GOJ
carcinomas may add significantly to the ability to non-invasively assess response to nCT or nCRT and guide
subsequent treatment. In addition, this trial will provide novel proof of concept data more generally regarding
the magnitude and kinetics of tumour cell death following nCRT in vivo in a population with robust histopathological
and clinical outcome data.

**STUDY PROPOSAL**

**Study Design:**
Prospective, single arm, open label observational study

**CDI preparation:**
Unlabelled CDI will be supplied to each study site. Labelling with $^{68}$Ga will be performed at the
study site. Detailed methods will be provided and validation will be performed at site
initiation, however is similar to other clinically used $^{68}$Ga radiopharmaceuticals.

**CDI-PET CT:**
There is no patient preparation required prior to CDI-PET CT scan, although oral hydration is
encouraged. For each CDI-PET CT scan, patients shall be administered approximately
200 MBq (range 150 – 250 MBq). Patients will rest in a shielded room for an uptake
period of 60 minutes. Following the uptake period of 60 minutes a CDI-PET CT scan will be
performed to include all relevant sites of disease (usually from skull vertex to proximal femora).

**nCRT:**
According to local clinical practice / protocol

**nCRt:**
Staging FDG-PET CT (within 28 days of commencement of nCRT) and FDG-PET CT a
minimum of 4 weeks and no greater than 6 weeks after completion of nCRT. CT, MRI, and
other imaging according to local practice / protocols

**Other investigations:**
According to local practice / protocols

**Methodology:**
Screening, consent and confirmation of suitability for nCRT including confirmation of
stage with FDG-PET CT

Perform pre-treatment CDI-PET CT within 7 days of commencement of nCRT

Commence nCRT

The first 8 patients in each sub-study will undergo a further three (3) CDI-PET CTs at 1, 2
and 14 days after commencement of nCRT

Subsequent patients will undergo one (1) further CDI-PET scan at the time point (1, 2 or
14 days) based on analysis of the initial eight (8) patients in each cohort to identify the
optimal timepoint.

Complete nCRT according to local practice / protocol

Perform FDG-PET CT at least 4 weeks after completion of nCRT

Surgery as planned

Analyse the surgical specimen for TRG

Follow-up for overall survival

**STUDY SCHEMA**

*The eight (8) initial patients in each cohort will undergo CDI-PET CT scans 1, 2 and 14 days after commencement of treatment. Subsequent to this, patients will undergo a single CDI-PET CT scan at either 1, 2 or 14 days after commencement of treatment based on an analysis of the initial eight (8) patients in each cohort to identify the optimal timepoint.*

**PRIMARY OBJECTIVES**

- To assess if change in tumour CDI uptake following commencement of nCRT correlates with TRG
- To determine the kinetics of cell death detected by CDI-PET CT following commencement of nCRT
- To determine the magnitude of change of tumour CDI uptake following commencement of nCRT

**SECONDARY OBJECTIVES**

- To assess CDI-PET CT prediction of overall survival in patients’ oesophageal/GOJ and rectal carcinomas
  treated with nCRT
- To assess CDI-PET CT prediction of Ro resection

**INCLUSION CRITERIA**

**Oesophageal/GOJ Sub study:**
1. Able to understand and willing to sign the written informed consent and undergo study procedures
2. Male or female patients ≥ 18 years of age
3. Histologically confirmed oesophageal/GOJ carcinoma
4. Planned for nCRT prior to surgical resection

**Rectal sub study:**
1. Able to understand and willing to sign the written informed consent and undergo study procedures
2. Male or female patients ≥ 18 years of age
3. Histologically confirmed rectal carcinoma
4. Planned for nCRT prior to surgical resection

**EXCLUSION CRITERIA**

1. Chemotherapy or radiotherapy within the previous 6 weeks
2. Pregnant or breastfeeding
3. Contra-indication to nCRT

**STATISTICAL ANALYSIS**

It is hypothesised that the change in tumour CDI uptake will be influenced by response to treatment i.e. non-
responding tumours will have a lower increase in CDI uptake, whereas responding tumours will have a higher
increase CDI uptake. The primary objective, therefore, is to assess whether the change in CDI uptake correlates
with pathological assessment of response measured by the TRG. To assess the correlation between TRG (ordinal
variable, Grade 0–3) and change in tumour CDI uptake (continuous), Spearman’s correlation will be used. With a
total of 46 patients and based on a one-sided hypothesis, a Spearman’s $p = 0.4$ can be detected with 80% power
at a significance level of $p=0.05$. 

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Assessment of kinetics of cell death measured by CDI-PET CT will be determined by measuring the magnitude of change at each time point and gradient of change over time. An interim analysis of the first 8 patients in each subgroup will be undertaken to identify that time point which demonstrates the greatest change in CDI uptake, as the optimal time point for the remaining patients. If more than one time point demonstrates a similar magnitude or gradient of change, additional factors (such as available pathological data and inter-subject variability, which may be reflective of differences in response) will also be considered in selecting the optimal time point. A futility endpoint is not specified as there is no prior human data to inform what constitutes a clinically meaningful change in CDI uptake.

The magnitude of change in tumour CDI uptake will be estimated for all patients. In addition, as it is hypothesised that the change in tumour CDI uptake will be influenced by response to treatment and may vary by tumour type, the magnitude of change in tumour CDI uptake will also be estimated for sub-groups by tumour type and TRG.

No similar studies identified.

References:
INTRODUCTION  
Neuroendocrine tumours (NETs) frequently metastasize to the liver and present treatment challenges, particularly once progressing on somatostatin analogue and peptide receptor radionuclide therapy (PRRT). Liver metastases arising from NETs and other solid organ malignancies are often unresectable due to the location, size and number of lesions. Locoregional techniques such as cryoablation, radiofrequency ablation (RFA), selective internal radiotherapy (SIRT) and transarterial chemoembolization (TACE) are options for patients with unresectable liver metastases, but these therapies are limited in that they are only effective to the directly treated lesions and hence additional treatment options are needed.

RATIONALE  
Intralesional IL rose bengal disodium, an oncolytic immunotherapy, is one such potential additional treatment option under development for solid tumours. In pre-clinical and clinical trials, a 10% w/v solution of IL rose-bengal disodium (PV-10) has been shown to be an effective chemoablative agent. It is rapidly internalized by tumour cells, leading to disruption of lysosomal integrity and oncolysis through immunogenic cell death. It is preferentially retained in tumour tissue for over 72 hours while being rapidly cleared from surrounding normal tissue. Response in un.injected tumours (bystander response) has also been seen in clinical and pre-clinical models of melanoma, pancreatic cancer, colon cancer and breast cancer.

In initial phase 1 trials in melanoma, IL PV-10 led to a response rate of 48% in injected targeted lesion with 27% of non-injected lesions also showing a bystander response (1). Phase 2 data demonstrates a similar ORR of 51% in injected lesions with 33% ORR in un injected bystander lesions, significantly correlating to response in target injected lesions (2). This appears to be due to release of antigenic tumour fragments and damage associated molecular proteins (DAMPs) to the immune system, leading to an adaptive immune response through activation of CD8+ and CD4+ T-cells and enhancing dendritic cell infiltration to draining lymph nodes, with the CD8+ T-cells reactive to autologous or HLA-matched tumour (3-6).

These observations of a component of immune-mediated response provided the basis for ongoing clinical testing of PV-10 in combination with immune checkpoint inhibitors, both in melanoma and in other tumour types. Antibodies targeting PD-1/PD-L1 immune checkpoint pathway have yielded dramatic responses in a number of tumour types, however these responses appear to be more common in tumour types with high PD-L1 expression or a high tumour mutational burden (TMB). NETs have a moderate rate of measurable PD-L1 expression (7) but do possess a low TMB (8) and monotherapy with PD-1 inhibitors has demonstrated only modest antitumour activity in pre-treated patients. The phase 2 KEYNOTE-158 study of pembrolizumab in pre-treated NET, unelected for PD-L1 status, demonstrated an objective response rate (ORR) of 3.7% whilst KEYNOTE-028 achieved an ORR of 10.1% in a small population of PD-L1 positive selected carcinoid and pancreatic NET patients (7, 8). The use of pemetrexed, another PD-1 inhibitor, yielded an ORR of 7.4% in NETs although notably all almost responses were in those with thoracic primary tumours, with pancreatic and GI NETs yielding 3% and 0% response rates respectively (10). Therapeutic approaches that can overcome inadequate tumour recognition by the immune system might significantly enhance response of these “cold” tumours to PD-1 inhibitors.

Combining PV-10 with systemic checkpoint inhibitor antibodies has shown enhanced anti-tumour effect against injected and non-injected tumours in murine models of melanoma, with this effect abrogated when CD8+ cells were subsequently depleted (11,12). PV-10 administered in combination with pembrolizumab in patients with advanced cutaneous melanoma is the subject of a phase Ib/II clinical study (study PV-10-MM-1201, NCT02557321). Interim data from a cohort of 23 Stage III and IV subjects was reported at the Society for Melanoma Research 2018 Annual Meeting, demonstrating a safety profile consistent with established patterns for each drug, with no significant overlap of adverse events or unexpected toxicities attributable to the combination. Overall response rate was higher than expected for either drug as monotherapy, with complete response (CR) observed in non-injected visceral disease, including lung and liver metastases. Preliminary efficacy was 9% CR and 56% PR (65% ORR) by RECIST (3).

Other forms of ablative therapies, such as RFA and cryoablation (RFA, cryoablation) used in combination with immune checkpoint inhibitors have demonstrated synergistic effects in colorectal cancer, hepatocellular cancer and prostate cancer (14-16). Of particular interest, RFA not only increased T-cell infiltration to colorectal cancers, but also increased expression of the immune-dampening PD-L1 protein, providing a rationale for the demonstrated improved anti-tumour response and prolonged survival seen in the combination of RFA and PD-1 inhibition (14).

Safety and early signal of efficacy for intrahepatic injection of PV-10 has been established in two phase 1 trials. In an initial phase 1 study of IL PV-10 administered via percutaneous injection to hepatic tumours (study PV-10-LC-01, NCT00986660), 23 subjects have received at least one treatment cycle: 6 subjects with HCC, 6 with metastatic colorectal carcinoma, 5 with metastatic uveal melanoma (mUM), 2 with metastatic non-small cell lung cancer and 1 each with metastatic cutaneous melanoma, metastatic ovarian cancer, metastatic pancreaticobiliary cancer, and metastatic breast carcinoma. Initial data was presented at Asia Pacific Associating for the Study of the Liver in 2017 (17). These treatments exhibited acceptable toxicity, with four subjects experiencing SAEs deemed at least possibly related to PV-10 treatment: namely photosensitivity reaction, injection site reaction and lethargy resolving without sequelae and a fatal thromboembolic event. Three of the 5 mUM patients received PV-10 on a background of nivolumab or ipilimumab + nivolumab with unexpected toxicity.

In a parallel phase 1 study of IL PV-10 administered percutaneously to hepatic metastases of symptomatic GEP-NET, 8 subjects have received at least one treatment cycle and one subject has received a cycles (study PV-10-NET-01, NCT02693067) with data from cohort 1 (6 patients) presented at ASCO in June 2019. One patient had an SAE of angioedema with facial and hand swelling possibly mediated by photosensitivity, a known side effect of rose-bengal, which resolved with corticosteroids and anti- histamines over 5 days. No other SAEs deemed at least possibly related to PV-10 were observed. Injected tumours exhibited patent retention of Ga-DOTATATE activity in both injected and non-injected tumours observed in several patients. ORR of injected lesions is 90% (progression in 1 subject), with overall disease control of 84%. Chromogranin A (CgA) response: 5 stable, 1 progression; and 1 subject with “carcinoid pellagra” had rash resolution (18).

The proposed study will assess whether combination of hepatic intra-lesional PV-10 combined with systemic PD-1 inhibition with pembrolizumab can enhance both local and systemic response in patients with mNET and liver metastases.

Success in this indication may be informative for other “cold” tumour types in overcoming innate or acquired resistance in patients with disease that is nonresponsive or refractory to checkpoint inhibition.

STUDY PROPOSAL  
Phase 2 single-arm trial (SAT) based on a Simon’s two-stage design; all subjects will receive the combination of hepatic intra-lesional PV-10 combined with systemic PD-1 inhibition with pembrolizumab.

The study will examine the efficacy and safety of pembrolizumab combined with IL PV-10 in patients with biopsy-proven or clinically diagnosed (based on currently accepted standards) neuroendocrine tumour metastatic to the liver that is not amenable to resection or other potentially curative therapy.
STUDY SCHEMA
Subjects will receive their first dose of pembrolizumab (200 mg intravenously) at the start of a three-week lead-in period. On study day 0 (one day prior to the next scheduled dose of pembrolizumab) subjects will receive, under CT or ultrasound guidance, percutaneous injection of PV-10 into 1-2 injectable tumours (each tumour ≥1 cm in diameter, sum of maximum diameters ≤4.9 cm) up to a maximum dose of 15 mL PV-10. They will receive the second dose of pembrolizumab the following day if PV-10 has been well tolerated (on study day 1) and continue to receive pembrolizumab 200 mg every 3 weeks for 24 months or until progression, intolerable toxicity or study withdrawal. Subjects with additional injectable tumours ≥1 cm in diameter will be eligible for additional PV-10 injections 6 weeks or more after any previous injection (one day prior to scheduled pembrolizumab dose), until all injectable tumours have been treated. Subjects exhibiting new hepatic lesions during the study interval may receive PV-10 to such lesions if clinically stable and overall disease status does not merit immediate change of therapy.

Disease evaluations with CT, ¹¹¹Gallium-DOTATATE PET (to probe SSTR expression of injected and non-injected tumours), and serum chromogranin A will be performed at screening and subsequently every 12 weeks starting at the time of initial PV-10 administration until disease progression or a maximum of 24 months. Clinically stable patients with suspected progressive disease may remain on study therapy until progression is confirmed in a second assessment at least 4 weeks after initial evidence of progression is detected.

Efficacy (ORR) will be assessed by RECIST 1.1, with assessments performed q12w starting at the time of initial PV-10 administration. Response will be followed for up to 24 months from initiation of study treatment. Progression-free survival will be followed on the same schedule. Overall survival (OS) will be followed for all subjects for at least 24 months or until objective response assessment is completed for the final subject in the study.

Reduction in NET symptomatology will be probed using EORTC QLQ-C30 and QLQ-GI.NET21 quality of life (QoL) instruments, incorporating:
• Reduction of major NET symptoms (diarrhoea and flushing)
• Reduction of other symptoms of NET (bronchoconstriction, abdominal cramping, peripheral oedema
• QoL assessment will be conducted at baseline (during screening prior to initiation of study treatment); immediately prior to initiation of PV-10 treatment; and q3w thereafter (i.e., prior to next dose of pembrolizumab and/or PV-10).

Correlative analysis will be carried out using serial blood samples collected pre- and post-PV-10 injection, assessing functional activity of CD8+ T-cells and other mononuclear cells, DAMP and cytokine levels, and functional T-cell response to autologous tumour. Optional tumour biopsies pre- and post-PV-10 will also be obtained to assess tumour infiltrating lymphocytes and PD-L1 expression (i.e., changes in TME). These exploratory assessments will be used to investigate potential correlation of these biomarkers to treatment response.

Initial safety assessment will be based on AEs (including laboratory data) observed within 28 days of initial PV-10 administration, with final safety assessment based on all AEs observed within 100 days of final PV-10 administration.

The estimated duration of the study is 34 months for analysis of the primary endpoint (ORR), consisting of a 1 month start-up interval, 24 month enrolment period, up to 6 months treatment and ORR follow-up after initiation of PV-10 (i.e., 7 months after initiation of pembrolizumab) for the last patient in (LPI) and 1 month for completion of primary analysis. Up to an additional 16 months may be required to complete secondary endpoint readout (i.e., up to a total duration of 50 months for PFS and OS at up to 24 months for LPI with 1 month close-out for last patient out, LPO).

PRIMARY OBJECTIVES
The primary objective of this study is to assess efficacy of Intralvesional PV-10, administered into lesions in the liver arising from neuroendocrine tumours (mNET), in combination with systemic administration of an anti PD-1 antibody. Assessment of efficacy of the combination will be based on objective response rate (ORR) of injected and un.injected/bystander lesions according to RECIST 1.1 criteria.

SECONDARY OBJECTIVES
Additional objectives are to further characterize efficacy based on progression-free survival (PFS), overall survival (OS), NET biomarkers, SSTR expression of injected target and un injected (bystander) lesions assessed by ⁶⁸Gallium-DOTATATE/PET/CT and symptom-based assessments of response. Safety and tolerability of the combination will be characterized based on observed adverse events, including abnormal laboratory values.

Exploratory Objectives. Correlative analyses will be used to probe possible changes in immune system signalling and function at the tumour level (TME) and systemic level (in peripheral blood).

INCLUSION CRITERIA
1. Age 18 years or older, males and females.
2. Histologically or cytologically confirmed, or clinically diagnosed based on currently accepted standards, neuroendocrine tumours, metastatic to the liver that are not amenable at the time of enrolment to resection, transplant or other potentially curative therapy. Patients must have at least one common NET symptom (Gl. NET21 score of 2 or more at baseline) including: flushing, diaphoresis, diarrhoea, abdominal discomfort, hyperacidity, dyspnoea or palpitations.
3. The Target Lesion(s) must be determined to be amenable to percutaneous injection by the treating physician.
4. The Target Lesion(s) must have measurable disease, defined as a unidimensionally measurable lesion ≥1.0 cm in longest diameter by helical CT; the maximum diameter of any Target Lesion should be ≤3.9 cm. These lesions should also overexpress SSTR. If the lesion is negative on PET/CT, there is no need to perform further PET/CT scans.
5. Performance status of Karnofsky scale 60%-100% or ECOG performance scale 0-2.
7. Haematopoetic Function
• White blood cells (WBC) ≥2,500/mm³.
• Absolute neutrophil count (ANC) ≥1000/mm³.
• Haemoglobin ≥8 g/dL.
• Platelet count ≥50,000/mm³.
• Coagulation: international normalized ratio (INR) ≤1.3.
8. Blood Chemistry
• Aspartate transaminase (AST) and alanine transaminase (ALT) ≤5 times ULN.
• Alkaline phosphatase (ALP) ≤1.5 times ULN.
• Bilirubin ≤1.5 times ULN.
• Creatinine ≤1.5 times ULN and estimated glomerular filtration rate (eGFR) ≥50.
9. Thyroid Function
• Total T3 or free T3 (serum triiodothyronine), total T4 or free T4 (serum thyroxine) and TSH (serum thyrotropin) ≤ CTCAE Grade 2 abnormality.
10. Renal Function
• Subjects must have adequate renal function in the opinion of the investigator with no clinically significant renal impairment or uncontrolled renal disease, see 8 above.
11. Target Lesion(s) contiguous with, encompassing or infiltrating major blood vessels.

EXCLUSION CRITERIA

1. Target Lesion(s) contiguous with, encompassing or infiltrating major blood vessels.
2. Liver metastases amenable to resection, transplant or other potentially curative therapy.
3. Subjects who have received hepatic surgery, ablation or chemoembolization within 4 weeks of PV-10 administration.
4. Radiation Therapy
   • Subjects who have received hepatic radiation within 4 weeks of PV-10 administration.
5. Chemotherapy
   • Subjects who have received cytotoxic chemotherapy within 4 weeks of PV-10 administration (6 weeks for nitrosoureas or mitomycin C).
6. Investigational Agents
   • Subjects who have received investigational agents within 4 weeks (or 5 half-lives) of PV-10 administration.
7. Phototoxic or Photosensitizing Agents
   • Subjects who have received agents posing a clinically significant risk of photosensitivity reaction within 5 half-lives of PV-10 administration.
8. Concurrent or Intercurrent Illness
   • Subjects with significant concurrent or intercurrent illness, psychiatric disorders or alcohol or chemical dependence that would, in the opinion of the Investigator, compromise their safety or compliance or interfere with interpretation of the study.
   • Subjects with uncontrolled thyroid disease or cystic fibrosis.
   • Presence of clinically significant acute or unstable cardiovascular, cerebrovascular (stroke), renal, gastrointestinal, pulmonary, immunological (with the exception of the presence of hepatitis B virus (HBV), viral hepatitis, or cirrhosis), endocrine, or central nervous system disorders.
   • Current encephalopathy or current treatment for encephalopathy.
   • Variceal bleeding requiring hospitalization or transfusion within 4 months of screening.
   • History of human immunodeficiency virus or acquired immune deficiency syndrome.
   • The clinical or radiological presence of ascites.
   • Active autoimmune diseases or history of autoimmune diseases; these include but not limited to immune related neurologic disease, multiple sclerosis, demyelinating neuropathy, myasthenia gravis, systemic lupus erythematosus (SLE), connective tissue diseases, scleroderma, inflammatory bowel disease, hepatitis, toxic epidermal necrolysis (TEN) and Stevens Johnson Syndrome
9. Fertile subjects who are not using effective contraception (e.g., oral contraceptives, intrauterine devices, double barrier methods such as condoms and diaphragms, abstinence or equivalent measures).

10. Prior treatment with PD-1 or PD-L1 checkpoint inhibitors
11. Systemic steroid requirement >10mg prednisolone equivalent daily or other immunosuppressive medications within 14 days of pembrolizumab administration
12. History of interstitial lung disease
13. Pregnancy
   • Female subjects who are pregnant or lactating.
   • Female subjects who have positive serum β HCG pregnancy test taken within 7 days of PV-10 administration.
14. Long Acting Somatostatin Analogues
   • Subjects who have received investigational agents within 4 weeks (or 5 half-lives) of PV-10 administration.
15. Informed Consent: Signed by the subject prior to screening

STATISTICAL ANALYSIS
Sample size
Based on the KEYNOTE-158 study, the proposed population treated with anti PD-1 monotherapy has an ORR of 3.7% at a median of 10.2 months follow-up. The current phase I trial of intra-lesional PV-10 has shown a 50% response rate in the first cohort of 6 patients. ORR = 50% (95% CI: 0.19 to 0.81). Using this information, to rule out an ORR rate of 4% in favor of 19% (using the lower bound of the confidence interval), based on Simon’s two-stage design, a 5% significance level and 80% power, a total of 34 patients are required.

All analyses will be on the intent-to-treat (ITT) population. The ITT population will be defined as all subjects who have received an intra-lesional injection of PV-10. Since this is an open-label, single-arm clinical trial, descriptive statistics will be employed to analyse the data. Summary statistics for continuous variables will include the mean, standard deviation, median, and range (minimum/maximum); categorical variables will be presented as frequency counts and percentages; and time-to-event variables will be summarized by Kaplan-Meier (K-M) plots and survival proportions.

Efficacy Parameters
This phase 2 study will be conducted in two sequential stages using Simon’s two-stage design. Nine subjects will be enrolled into the first stage of the study, with an interim assessment of efficacy conducted 24 weeks following initial treatment of the ninth subject. If ≥ 1 response is observed among the first 9 subjects, enrolment of 25 additional subjects will be completed into the second stage of the study.

Safety Parameters
Phase 1b testing of PV-10 and pembrolizumab in patients with cutaneous melanoma has established minimal likelihood of additive or unexpected toxicity in the proposed indication; experience with a small sample of patients receiving PV-10 to hepatic metastases of uveal melanoma while on a background of nivolumab or ipilimumab + nivolumab is consistent with this larger patient population and further establishes safety expectations for the proposed study. The Sponsor will conduct ongoing monitoring of safety data. If areas of concern are identified by the Sponsor or any Investigator, these will be discussed by the Sponsor and each Investigator either individually or by teleconference in order to arrive at a consensus regarding appropriate actions to ensure subject safety. If any CTCAE Grade 4 or higher adverse event at least possibly related to study treatment occurs, enrolment will immediately be temporarily stopped. The Sponsor and all Investigators will assess the event and arrive at a consensus decision whether to: (1) permanently halt enrolment; (2) modify dosing or otherwise modify study treatment or assessment schedule; or (3) resume enrolment.
Enrolment will be held if ≥23% of subjects experience a dose limiting toxicity (DLT) in the initial cohort of 9 patients. In the event of a hold, a safety review will be conducted by the Sponsor and enrolment will be restarted only with Sponsor approval (and subsequent EC/IRB notification). Since there are no classic target organ drug
toxicities identified with PV-10 (rose bengal disodium), DLT will be based on occurrence of any persistent, severe treatment-emergent adverse effects, or any treatment-threatening or fatal adverse effects. Toxicity will be evaluated according to CTCAE version 5.0. Because PV-10 is a small molecule agent with a half-life of six hours and no known potential for systemic accumulation, the period of observation for DLT will be 28 days from the first dose of PV-10 and will be defined as occurrence of any of the following the events which are attributed to study therapy (i.e., considered possibly, probably or certain related to study therapy):

- Dose-limiting toxicity is defined as onset of any CTCAE Grade 3 toxicity within 14 days of PV-10 administration that is persistent for 14 days or longer and deemed at least possibly related to PV-10, or any Grade 4 or greater toxicity of any duration deemed at least possibly related to PV-10.

The causal relationship of AEs will be attributed to either PV-10 or pembrolizumab if the respective drug can at least possibly be related to the event. Events with a causal relationship that can at least possibly be related to both drugs will be attributed to both drugs.

The analysis for safety will report all subject adverse events (including abnormal laboratory tests).

**Additional Parameters**

Tumour biomarker, QoL, and exploratory correlative results will be presented for all subjects.

**BIOLOGICAL SUB-STUDY**

**Exploratory Objectives.** Correlative analyses will be used to probe possible changes in immune system signalling and function at the tumour level (TME) and systemic level (in peripheral blood).

**Liquid Biopsy.** Serial blood samples will be analysed by flow cytometry and multiplex immunassay to determine pre- vs post-treatment effects and possible correlation with clinical response. Samples will be collected (a) prior to initiation of pembrolizumab, (b) immediately prior to initial PV-10 administration, (c) 24 hrs after PV-10 administration, and (d) 21-42 days after PV-10 administration.

**Isolated PBMC before and after initiation of study treatment will be analysed to measure the frequency of immune cell populations such as effector T-cells, regulatory T-cells (Treg), NK cells, and myeloid derived suppressor cells (MDSC) using flow cytometry.**

**Serum collected before and after initiation of study treatment will be analysed to measure the frequency of immune cell populations such as effector T-cells, regulatory T-cells (Treg), NK cells, and myeloid derived suppressor cells (MDSC) before and after PV-10 treatment.**

**Immunohistochemistry (IHC) staining will be applied to determine tumour immune profiles before and after clinical treatment. The levels of several crucial immune markers, especially tumour infiltrating lymphocytes (TIL), will be analysed including CD3, CD8, PD-L1, PD-1, Foxp3, and CD68. This will focus on determining whether treatment with PV-10 in combination with PD-1 affects TIL and the immune microenvironment in patients’ tumours.**

**DISCUSSION POINTS AND COMMENTS**

- **Requests for funding for anti PD-1 drug are ongoing**
- **Seeking input/discussion on appropriate measurement of response rate ie functional vs mRECIST vs RECIST**

No similar studies noted for this indication.

**References:**


INTRODUCTION
In Australia, despite the ongoing steady improvement in its survival outcome, colorectal cancer (CRC) continues to pose a major health burden. CRC is estimated to be the second most common cancer diagnosis in both sexes and to be the second most common cause of cancer death in 2019 [1]. While efficacy of several chemotherapy and biological therapy drugs have been established in CRC management, toxicity and development of resistance remain problematic. Adjuvant chemotherapy, for example, is not routinely recommended for those with Stage II disease as its toxicity outweighs its small benefit, despite the 5-year recurrence risk for these patients remaining as high as 20% [2]. Toxicity associated with adjuvant chemotherapy is also a concern for those with Stage III disease and a pooled analysis of international phase 3 clinical trials indicated the mean percentage of chemotherapy re-chosen to be as low as 68% of the planned dose [3]. For those with Stage IV disease, systemic therapy including biological therapy is generally the mainstream of treatment. Unfortunately, the vast majority of these patients experience inherent or acquired resistance to the therapy and for the period of 2011 to 2016, the 5-year survival rate for Stage IV disease was 13% in Australia [4]. These findings together highlight the need for alternative therapeutics for CRC with improved efficacy and reduced toxicity.

AqpB013 and AqB050 are synthetic small molecules designed and synthesized by Dr. G. Flynn as inhibitors of AQP1 [5]. They were developed to target cancer cells that endogenously express AQP1, using in vitro scratch wound and Matrigel spheroid invasion assays [6]. AQP1 expression has been demonstrated by in situ hybridization in colon adenomatous polyps and secondary lesions, but not in the surrounding normal colon mucosa, supporting the theory of its involvement during the early stage of CRC development [8]. AQP1 expression by immunohistochemistry correlates with histological features known to be poor prognostic such as local nodal metastasis and lymphovascular invasion, and at the transcript level, its high expression predicts poor survival in CRC [11]. Therefore, AQP1 is a plausible diagnostic and therapeutic target for CRC and inhibitors of AQP1 may provide an additional systemic therapy option for CRC patients.

RATIONALE
AqB013 and AqB050 are well tolerated with no adverse effects noted [6]. Intratumoral injection of AqB013 alone, similarly, reduced lung metastases and improved survival in the same murine tumor model of melanoma [7]. AQP1 expression is demonstrated by in situ hybridization in colon adenomatous polyps or primary and secondary lesions, but not in the surrounding normal colon mucosa, supporting the theory of its involvement during the early stage of CRC development [8]. AQP1 expression by immunohistochemistry correlates with histological features known to be poor prognostic such as local nodal metastasis and lymphovascular invasion, and at the transcript level, its high expression predicts poor survival in CRC [11]. Therefore, AQP1 is a plausible diagnostic and therapeutic target for CRC and inhibitors of AQP1 may provide an additional systemic therapy option for CRC patients.

STUDY PROPOSAL
This is the first in-human, single-centre, non-randomised, open-label phase 1 study to evaluate safety and tolerability of loop diuretic, bumetanide-derived inhibitors of Aquaporin 1, AqB050 and AqB013 in subjects with metastatic CRC. The study is designed to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of AqB050 monotherapy or combination of AqB050 with AqB013 in subjects with metastatic CRC, who have progressed or are intolerant of the standard systemic therapy, including fluoropyrimidine, irinotecan, oxaliplatin and bevacizumab. For those with RAS wild-type CRC, subjects must have received treatment with EGFR inhibitors and either progressed or be demonstrated as intolerant. Whether AqB050 will be administered as monotherapy or in combination with AqB013 will be determined by their efficacy in the ongoing preclinical studies involving a mouse xenograft model of human colon cancer organoids as well as rat pharmacokinetic and toxicology studies. Either AqB050 monotherapy or combination of AqB050 with AqB013 will be evaluated as oral therapeutics.

The study will be conducted in 2 phases; Part 1 Dose Escalation Phase and Part 2 Dose Expansion Phase. Dose escalation phase is aimed at evaluating the safety, tolerability, pharmacokinetic and pharmacodynamics of either AqB050 monotherapy or combination of AqB050 with AqB013 and determining the maximal tolerated dose (MTD) of repeat daily dosing schedule in subjects with metastatic CRC. Dose expansion phase of the study will be open once the MTD and/or a biologically active dose has been determined in the dose escalation phase. Different administration schedules can be used in the dose expansion phase based on clinical and pharmacokinetic data from the dose escalation phase. The dose limiting toxicity (DLT) evaluation period will be 21 days. Administration of AqB050 monotherapy or combination of AqB050 with AqB013 in both dose escalation and dose expansion phases may continue until evidence of disease progression, intolerance to the study drugs or withdrawal of consent.

Part 1: Dose Escalation
During the dose escalation phase, subjects will be enrolled in cohorts and they will receive daily oral administration of either AqB050 monotherapy or combination of AqB050 with AqB013 (the formulation to be evaluated in the study will be determined prior to study commencement based on pending preclinical data). Each cohort will consist of a minimum of 3 newly enrolled evaluable subjects. Subjects are considered evaluable if
they complete 21 days of treatment or receive less than 21 days of treatment due to DLT. DLT is defined as more than 3 days of Grade ≥ 3 any adverse events by CTCAE v5.0 despite optimal medical support. 3 patients will be initially enrolled in the first cohort (Dose Level 1), the dosing level for which will be determined based on the results of preclinical studies. If there is no DLT in the first 3 subjects within the cohort, subsequent enrollment will occur for a new cohort at the next dose level (Dose Level 2). If safety data show 1 subject in a cohort experiencing a DLT, then the cohort will be increased to a maximum of 6 subjects. If no more than 1 of the 6 subjects experiences a DLT, then the next dose level may be evaluated. If 2 subjects entered in any cohort experience a DLT, then the MTD has been exceeded, and the previous dose level will be considered the MTD. The escalation phase will initially have up to 4 cohorts at 4 dose levels, however, additional cohorts can be introduced if no dose level has ≥ 2 DLTs and MTD is not determined from evaluation of these 4 cohorts. In such a case, a new cohort may be introduced at the next dose level (Dose Level 5). A minimum of 6 evaluable subjects will be treated at the dose level before the dose can be declared as the MTD and enrollment into the dose expansion phase can begin. If a dose level is opened and subjects in the previous cohort subsequently develop unexpected toxicities the cohort will be closed, and the previous cohort will be re-assessed with further subjects enrolled as required. The total sample size for the dose escalation phase will be at least 9-15 subjects if all the subjects enrolled are evaluable and the MTD is achieved within the first 4 dose levels. Dose escalation phase will continue until any of the following events:
• The MTD is identified
• The highest planned dose level is determined to be safe and tolerable

Subjects will cease taking study drugs upon following events; disease progression, significant toxicity (DLT or other toxicity where subjects are assessed to be intolerant of the study drugs by investigators), or withdrawal of consent and they will be reviewed 30 days after the last administration of study drugs for the end of treatment and safety follow-up and then 12 weekly thereafter.

Part 2: Dose expansion
Upon completion of the dose escalation phase of the study, the dose expansion phase will commence to determine the efficacy of AqB050 with/without AqB013. The recommended dose for the dose expansion phase may differ from the MTD depending on the clinical data obtained during the dose escalation phase. Subjects will cease taking study drugs upon following events; disease progression, significant toxicity (DLT or other toxicity where subjects are assessed to be intolerant of the study drugs by investigators), or withdrawal of consent and they will be reviewed 30 days after the last administration of study drugs for the end of treatment and safety follow-up and then 12 weekly thereafter. Up to 23 subjects will be enrolled to the dose escalation phase. This number includes subjects who were already treated at the dose chosen for the dose expansion phase during the dose escalation phase.

Following primary and secondary endpoints will be collected during the dose exploration and dose expansion phases.

Primary endpoints
• Number of participants experiencing dose-limiting toxicities
• Number of participants who experienced adverse events assessed by CTCAE v5.0
• Overall response rate according to RECIST v1.1
• Clinically significant vital signs, physical examinations, electrocardiogram (ECGs), and clinical laboratory tests

Secondary endpoints
• Pharmacokinetic parameters of AqB050 with/without AqB013, but not limited to, maximum observed plasma concentration (Cmax), time to achieve Cmax (tmax), and area under the plasma concentration-time curve (AUC)
• Disease control rate according to RECIST v1.1
• Duration of response according to RECIST v1.1
• Progression free survival
• Overall survival

PRIMARY OBJECTIVES
• To evaluate the safety and tolerability of AqB050 with/without AqB013 in adult subjects with metastatic CRC, who have progressed or are intolerant of the standard systemic therapy.
• To estimate the maximum tolerated dose and/or a biologically active dose, which will be recommended in the subsequent Phase 2 study.

SECONDARY OBJECTIVES
• To characterize the pharmacokinetics of AqB050 with/without AqB013 following administration as an oral capsule formulation.
• To evaluate tumour response assessed by computed tomography (CT) using RECIST v1.1 criteria of AQB050 with/without AqB013.

INCLUSION CRITERIA
Subjects with following characteristics are recruited for the study;
1. Men or women ≥ 18 years old.
2. Subjects with pathologically proven metastatic colorectal carcinoma.
3. Subjects must have progressed or intolerant of the standard systemic therapy, which include fluoropyrimidine, irinotecan, oxaliplatin and bevacizumab. For subjects with RAS-wild metastatic CRC, the must have additionally received systemic anti-EGFR therapy. Disease progression is defined as progression of disease during or within 3 months from the last administration of the last systemic regimen and this would also apply to the adjuvant therapy.

4. Measurable or evaluable disease according to RECIST v1.1.

5. ECOG performance status ≤ 2.

6. Life expectancy of >3 months.

7. Adequate haematological, hepatic and renal functions.

8. Subjects with ability to take oral medications.

9. Subjects have provided informed consent.

EXCLUSION CRITERIA

Subjects with following characteristics are excluded from the study:

1. Active brain metastasis.

2. Unresolved toxicities from prior anti-tumour therapy, defined as not having resolved to Common Terminology Criteria for Adverse Events (CTCAE) v3.0 Grade ≤ 1 with the exception of alopecia. Grade 2 or 3 toxicities from prior anti-tumour therapy that are considered irreversible may be allowed.

3. Anti-tumour therapy (chemotherapy, biological therapy and hormonal therapy, investigational agent) within 28 days of the first administration of the study drugs.

4. Therapeutic or palliative radiation therapy within 2 weeks of the first administration of the study drugs.

5. Major surgery within 4 weeks of the first administration of the study drugs.

6. Men and women of reproductive potential who are unwilling to practice acceptable methods of effective birth control.

7. Women who are lactating/breast feeding or who plan to breast feed while on study drugs.

8. Women with positive pregnancy test.

9. Subjects have provided informed consent.

10. History of any clinically significant disorder, condition or disease that in the opinion of the investigator would

11. History of any clinically significant disorder, condition or disease that in the opinion of the investigator would

12. Subjects must have progressed or intolerant of the standard systemic therapy, which include fluoropyrimidine, irinotecan, oxaliplatin and bevacizumab. For subjects with RAS-wild metastatic CRC, the must have additionally received systemic anti-EGFR therapy. Disease progression is defined as progression of disease during or within 3 months from the last administration of the last systemic regimen and this would also apply to the adjuvant therapy.

13. Subjects have provided informed consent.

14. Subjects with ability to take oral medications.

15. Adequate haematological, hepatic and renal functions.

16. ECOG performance status ≤ 2.

17. Measurable or evaluable disease according to RECIST v1.1.

18. Subjects with ability to give written informed consent and/or to comply with all required study procedures.

19. Subject to give written informed consent and/or to comply with all required study procedures.

20. The final analysis will occur when target enrollment is complete and each subject either completes 6 months on study or withdraws from the study. Descriptive statistics will be provided for selected demographics, safety, pharmacokinetics and efficacy as appropriate. Descriptive statistics on continuous data will include means, medians, standard deviations and ranges, while categorical data will be summarized using frequency counts and percentages. Overall response rate and disease control rate will be presented with 95% exact CI. Progression free and overall survival will be calculated using Kaplan-Meier method.

BIOLGICAL SUB-STUDY

For subjects with available archival tumour samples of distant metastases, following attainment of consent, the tissues may be tested for AQ1P expression and the association with tumour response to AqB050 with/without AqB013 may be explored.

DISCUSSION POINTS AND COMMENTS

We like to obtain feedback from audience on following points;

- Any additional preclinical data required for this phase 1 clinical study to proceed
- How to estimate the sample size required for the dose expansion phase ie whether to use overall response rate (ORR) or disease control rate (DCR) for the calculation. Phase 3 trials evaluating biological therapy (regorafenib, TAS-102) as salvage therapy in metastatic CRC showed significant improvement in DCR, but not ORR compared to the placebo.

No inhibitors of Aquaporin-1 including AqB013 and AqB050 have ever been studied as cancer therapeutics in human.

References:


Palliative Oesophageal Chemoradiotherapy: A Phase I Clinical Trial

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BACKGROUND
Optimal palliative treatment of metastatic oesophageal carcinoma (OC) with dysphagia is controversial. Competing risks include treatment toxicity and duration, symptom management and disease control. We explore a potentially superior chemoradiotherapy (CRT) regimen in a carefully selected patient cohort.

METHODS
Eligible patients for this ethics approved, Phase I clinical trial had biopsy-proven OC including gastro-oesophageal junction (GOJ) carcinoma, dysphagia, low volume metastatic or locally advanced disease and ECOG PS 0–2. The biologic equivalent dose of radiotherapy was kept at 40Gy, whilst the number of daily fractions were reduced in a stepwise manner from 15 to 10 over four schedules. Patients received weekly concurrent CP (carboplatin AUC2 and paclitaxel 50mg/m2) either three (schedules 1–3) or two (schedule 4) times. Dose Limiting Toxicities (DLTs) were radiation pneumonitis or oesophageal rupture. Efficacy was recorded as relief of dysphagia using the Mellow score where 4=complete dysphagia and 0=able to eat all solids.

RESULTS
18 patients, median age 68 years (range 42–81) were recruited. Tumour sites were 1 proximal oesophageal, 2 mid, 7 distal and 8 GOJ. Histologies were 5 squamous cell carcinoma and 13 adenocarcinoma. At baseline 8 patients were severe dysphagia (Mellow 3 or 4). No DLTs occurred within a minimum of 6 weeks following completion of CRT. Three patients required admission for management of nausea related to study treatment. By 3 months, all 16 assessable patients at current time showed an improvement in dysphagia, with a median of 2 points change in Mellow score. Some responses were profound: one patient had a Mellow score improvement from 4 to 0 and at current time showed an improvement in dysphagia, with a median of 2 points change in Mellow score. One patient had a Mellow score improvement from 4 to 0 and another was dysphagia free 2 weeks after completing CRT without any further therapy.

CONCLUSIONS
A short course of CRT with weekly concurrent CP provides good dysphagia relief with manageable toxicity in a selected group of patients with OC. Schedule 4 appears safe and should be tested in larger studies to confirm its efficacy.

Immunomodulatory effect of Renin-angiotensin inhibitors on T-lymphocytes in mice with Colorectal Liver Metastases

Ardila, Dora – Author, PhD research fellow surgical oncology, Department of Surgery University of Melbourne, Austin Health

BACKGROUND
Colorectal cancer is the third most common cancer diagnosed in the developed world. It is the second most deadly cancer, where the majority of colorectal cancer related deaths are due to metastasis to the liver, which is frequently presented at diagnosis. Current literature and our research show that tumor infiltrating immune cells positively or negatively contribute to tumor progression, depending on the cell type. We have shown that inhibitors of the Renin Angiotensin system (RAS), currently used in the clinic to control blood pressure, also inhibit tumor growth by modulating the tumor infiltrating immune cells. Aim: To investigate the effects of RAS inhibition on tumor T lymphocyte distribution in a mouse model of colorectal liver metastases (CRLM).

METHODS
Liver metastases were established orthotopically, to resemble the human disease. The mouse host is immunocompetent ensuring full spectrum of immune responses. Mice received tumor induction and were separated into two groups; control (saline) and RAS inhibitor (Captopril) treatment. Saline or Captopril was administered daily via intraperitoneal injection, from day 1 post-tumor induction to endpoint. Tumor growth was determined using stereology proliferation markers and IHC on days 15 or 21 following tumor induction. Lymphocyte subsets in the tumor and liver tissues were analysed by flow cytometry and immunohistochemistry.

RESULTS
The results show that Captopril significantly decreased tumor viability and impaired metastatic growth. Flow cytometry analysis showed T cells (CD3+CD45+) were significantly increased in the captopril treated group compared to control for both surrounding liver and tumor at day 15. These results were also confirmed by IHC. Interestingly, flow cytometric analysis indicated that a T cell phenotype double negative for the CD4 and CD8 markers was significantly increased in the captopril treated group while the CD3+CD4+ T cells were significantly decreased compared to control group for both surrounding liver and tumor.

CONCLUSIONS
RAS inhibitors reduce tumor growth and modulate the immune response by increasing the infiltration and altering the phenotype of T lymphocytes. The exact nature of these changes needs to be further characterized, especially the identity and function of the double negative CD3+ T cell population need to be elucidated.

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Doctor Dora Ardis
Doctor Dora Vallejo-Ardila

Doctor Dora Vallejo-Ardila, M.D, is an international PhD research fellow in surgical oncology at The University of Melbourne under the Supervision of Professor Christopher Christophi, Head of the Department of Surgery, Austin Health. She graduated in medicine and general surgery from the Industrial University of Santander, Colombia. She gained considerable international experience working in high profile research environments in the United States, Brazil and Germany. Her scientific interest is strongly influenced by her background as both, physician and researcher. In her studies, she aims to unify experimental and clinical research with potential life-saving technologies, to provide better outcomes for patients suffering from colorectal cancer liver metastasis.
A comprehensive patient-reported outcome (PRO) assessment model for colorectal cancer (CRC) survivors: a mixed methods systematic review

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BACKGROUND

PROs are important cancer clinical trial endpoints. PROs are also used in clinical practice to guide patient-centred care. CRC is a common malignancy in the developed world. Advances in screening, early diagnosis, and effective treatments have led to improved survival rates, and a growing population of long-term CRC survivors with unmet needs. To better understand survivors’ long-term disease and treatment impacts and to monitor key PROs as part of routine survivorship care, we aimed to develop a comprehensive survivorship PRO assessment model for evaluating PROs in CRC.

METHODS

Four electronic databases were searched for: (1) longitudinal studies reporting pre-treatment PRO predictors of survival in CRC identified through univariate or multivariate models, or prevalence of PROs ≥1 year post-treatment completion; and (2) qualitative studies reporting CRC symptoms, treatment side-effects, and HRQOL impacts ≥1-year post-treatment. Two reviewers independently applied inclusion criteria and extracted: (1) PRO predictors of survival and (2) survivors’ long-term impacts. We used meta-synthesis methods to collate and summarise the evidence across studies. We aggregated grouped findings into specific patient-reported themes, providing a summary of the evidence for each theme and generating a framework of the CRC survivor long-term outcomes and experiences.

RESULTS

Physical and psychological functioning, pain, fatigue and appetite loss had prognostic significance above and beyond clinical predictors of survival in CRC. CRC survivors experience ongoing bowel symptoms and functioning impairments ≥1-year post-treatment. Patients often self-manage symptoms and functioning impairments (e.g. modify diet, wear nappies). Our PRO model includes six PROs (symptoms, physical, social, psychological and sexual functioning, impact on relationships), three patient-reported experiences (supportive care needs, healthcare experiences, return-to-work), and six mediating factors (disease stage, age, comorbidity, health behaviours, access to supportive care, financial toxicity).

CONCLUSIONS

CRC survivors experience symptoms that can predict survival and impair functioning. Currently, patients self-manage symptoms, with few supportive care services available targeting symptoms. Post-treatment CRC care should routinely monitor symptoms and functioning. Earlier detection and treatment of these problems may improve HRQOL and even extend survival. Our empirically-derived PRO model guides the comprehensive assessment of PROs in CRC clinical practice and future clinical trials.
The effect of oversewing double stapled anastomoses in oncological colorectal surgery

**BACKGROUND**
Up to a third of patients suffer a postoperative complication following colorectal resectional surgery with complication rates of 28% undergoing surgery for colon cancer in USA and in Australia and New Zealand, complication rates of 20% for colon cancer and 27% for rectal cancer. The most feared complication of the intestinal anastomosis is leakage, occurring in up to 3-19% of patients. Anastomotic technique is potentially controllable variable in anastomotic failure, however there is minimal evidence examining the effect of oversewing staple lines on anastomotic outcomes to guide surgical decision making. Accordingly, our aim was to determine whether oversewing a double stapled anastomosis has any impact on post-operative surgical outcomes in colorectal cancer surgery.

**METHODS**
A retrospective analysis of prospectively collected data from two Victorian hospitals was performed on patients having had a colorectal cancer resection between January 2010 and July 2017. Patients with oversewn anastomoses were compared with those patients where no oversewing was performed. Complications (surgical and medical) were investigated using logistic regression. Further subgroup analyses on colonic resections were performed.

**RESULTS**
Analysis of the eligible 2001 patients demonstrated that patients with an oversewn DSA were less likely to have an anastomotic leak (p=0.093), or return to theatre (p=0.014). An oversewn DSA did not influence in-patient mortality, 30-day mortality or other surgical complications. Univariate analysis showed anastomotic leaks were less likely for oversewn patients and females but more likely with rectal cancers, open surgery or laparoscopic converted to open surgery, and increasing BMI. Subgroup analysis of the 884 colonic resections demonstrated oversewn patients were less likely to return to theatre (OR 0.250, 95%CI 0.070-0.893), have medical complications (OR 0.298, 95%CI 0.106-0.842) or a small bowel obstruction (OR 0.087, 95%CI 0.009-0.820). Univariate analysis showed hybrid or laparoscopic surgery, left side tumours, and a history of arrhythmia increased risk of anastomotic leak for colonic resections. Multivariate analysis showed all these factors had independent associations with anastomotic leak.

**CONCLUSIONS**
Oversewing a double-stapled anastomoses in colorectal cancer surgery is a protective factor against anastomotic leaks and reduces reoperative surgical rates.
Phase I trial of nab-paclitaxel administered concurrently with radiotherapy in patients with locally advanced inoperable pancreatic adenocarcinoma (ART in LAP trial)

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Flinders Center for Innovation in Cancer, Flinders University, Flinders Medical Center, The Queen Elizabeth Hospital, Genesis Care, Institute of Cancer Research

BACKGROUND
Locally advanced pancreatic adenocarcinoma (LAPC) carries a poor prognosis with median overall survival of 12-18m. The optimal treatment is controversial. Nab-paclitaxel is active in advanced pancreatic cancer and has exhibited radio-sensitising anti-tumour efficacy.

METHODS
We conducted a investigator-initiated open-label, phase I dose escalation trial of nab-paclitaxel with standard external beam radiotherapy (EBRT). All patients had biopsy-proven, untreated, localised, inoperable pancreatic adenocarcinoma; Patients received nab-paclitaxel on a weekly schedule for 6 weeks, concurrently with EBRT. A 3+3 cohort design was employed, with doses of nab-paclitaxel increasing from 25 mg/m2 (cohort 1), to 50 mg/m2 (cohort 2), 75 mg/m2 (cohort 3) and 100 mg/m2 (cohort 4). This principal objective of the trial was to establish the maximum tolerated dose (MTD) of nab-paclitaxel given concurrently with radiotherapy. Secondary objectives included safety evaluation, response rates, PFS, median and 1-year OS.

RESULTS
Fourteen patients were recruited to the study. Median age of patients was 69 (range 40-86), 69% had a head or neck of pancreas tumour. Majority of patients had grade 1 or 2 toxicities with nausea (92%), fatigue (69%), diarrhoea (54%) and vomiting (54%) being the most common ones. Three patients were recruited in each of the first three cohorts, without any dose limiting toxicities (DLT). In cohort 4, DLT of febrile neutropenia and enterocolitis was observed in patient 1. The cohort was expanded with a subsequent DLT of febrile neutropenia and enterocolitis again was observed in patient 5. Both DLT events lead to death (grade 5). The MTD and recommended phase II study dose has been established as 75mg/m2. Following chemo-radiotherapy DCR was 67%, mPFS of 4.7 months (95% CI 2.5-27.5), 1 year SR of 43% and mOS 11.4 months (95% CI 6.37-25.2).

CONCLUSIONS
The combination of weekly nab-paclitaxel and fractionated radiation was generally well-tolerated at doses of nab-paclitaxel below 100 mg/m2. There were two treatment related DLTs leading to death in the nab-paclitaxel 100 mg/m2 cohort. The MTD and recommended phase II study dose for nab-paclitaxel combined with radiation therapy in the treatment of LAPC is 75mg/m2. Clinical trial registry number: ACTRN1261300137352 Specialised Therapeutics provided nab-paclitaxel and a research grant.

Investigating the role of tumour-associated T cells in human colorectal cancer liver metastases

Doctor Amitesh C Roy
Doctor Amitesh C Roy is a consultant medical oncologist at Flinders Centre for Innovation in Cancer and is a senior clinical lecturer at the Flinders University. He trained at the tertiary cancer centres in Adelaide and Royal Marsden Hospital, UK and holds a master’s degree in translational medicine from the University of Edinburgh as well as associate fellowship of the Royal Australasian College of Medical Administrators. His main area of research interest is in GI malignancies with involvement in various clinical and translational research projects nationally and internationally.

Doctor Kevin Fenix
Doctor Kevin Fenix is a Hospital Research Foundation early career research fellow based at the Basil Hetzel Institute for Translational Research. He is studying novel tumour-infiltrating immune cell subsets in colorectal cancer liver metastasis patients. His goal is to harness the knowledge gained from this work to develop novel prognostic markers for liver metastasis risk assessment, and targets for immunotherapy. During his PhD Kevin studied the role of chemokine receptors and T cell trafficking in response to infection.

Fenix, Kevin Aaron – Author1,2
1Flinders University, 2Βasil Hetzel Institute for Translational Health Research

BACKGROUND
Colorectal cancer (CRC) is the third leading cause of cancer-related death worldwide, with secondary hepatic malignancy increasing the CRC mortality rate from 30% to 70%. Currently, there are no prognostic tools to determine the risk of liver metastasis in CRC patients. The presence of tumour infiltrating CD8+ T lymphocytes (Immunoscore) can potentially predict patient survival, however CD8+ T lymphocytes represent a diverse population with distinct functional properties. The aim of this project is to characterise the frequency, phenotype and function of tumour-associated CD8+ T cells in CRC patients and investigate the correlation of specific cell subsets with prognostic clinical endpoints.

METHODS
In this study, we collected CRC primary tumours and liver metastases from patients operated at two major South Australian hospitals (Royal Adelaide Hospital and Queen Elizabeth Hospital) and performed flow cytometry to characterise tumour-associated T cells. The prognostic value of identified cell subsets was determined by immunofluorescence using a 200 patient CRC tissue-microarray.

RESULTS
We found evidence for the enrichment of distinct T cell subset with a tissue-residency signature within both primary CRC tumours and liver metastases. Our tissue-microarray analysis suggests that the presence of tissue-resident T cells in primary tumours of TNM stage II patients is associated with shorter progression-free survival and with a higher risk of liver metastasis.

CONCLUSIONS
These results suggest a novel immune-tumour interaction promoting metastatic progression in early stage CRC. The presence of tissue-resident T cells will be developed and validated as a prognostic biomarker for the risk of metastatic progression in early stage CRC patients.
These were presented in the sarcoma session at ASCO 2019 (poster discussion). The Primary endpoint data analysis was completed in December 2018. Below are the Results and the Conclusion.

As of the 31 December 2017, ALT GIST closed to recruitment after reaching the revised recruitment target of 76 evaluable patients. 78 patients were enrolled from 37 sites internationally (14 AGITG sites across Australia and Singapore, 7 SSG sites in Scandinavia and 16 EORTC sites across Europe). As of the 21 June 2019, 38 patients remain on treatment, 28 patients are currently in follow-up and 12 patients are deceased. Seventy-six eligible patients (ALT 40, IM 36) enrolled from June 2015 to September 2018 were evaluable for the OTR. The patients (pts) were predominately male (n=51, 67%). Median age was 58 (range, 28-84) in the ALT arm and 65 (range, 35-82) in the IM arm. KIT was mutated in 63, PDGFR in 2, and wildtype in 5 tumors. Relative dose intensity in the ALT arm 102% for IM and 82% for REG and was 65% (95% CI, 45-74%) and 64% (95% CI, 48-78%), respectively. Seven (18%) pts in ALT arm and 10 (28%) in IM arm discontinued treatment due to progressive disease. Seven pts (18%) in the ALT arm stopped protocol therapy due to unacceptable toxicity, and none in the IM arm. Fifteen (38%) pts in the ALT arm and 14 (38%) in the IM arm had serious adverse events, mostly grade 3. Progression free survival (PFS) at 1 year was ALT 0.86 (95% CI:0.69,0.94) and IM 0.83 (95% CI.0.65-0.92), p logrank=0.57.

CONCLUSION
There was no meaningful difference in the primary endpoint of OTR and in PFS between the groups in this first analysis of ALT-GIST, and no unexpected safety signals. The study is ongoing and other endpoints will be reported in due course.

TRANSLATIONAL RESEARCH
Collection of FFPE diagnostic tumour tissue and blood for research at multiple time points. Determination of exon mutation profile of primary tumour and protein expression relating to cKIT and PDGFR signalling pathways. Planned research into circulating serum plasma growth factor and cytokine levels, plasma drug levels and circulating tumour cells and free circulating DNA load.

AIMS
This study aims to determine if an alternating regimen of Imatinib and Regorafenib has sufficient activity and safety to warrant further evaluation as a first line treatment for metastatic GIST.

BACKGROUND
Despite highly active current treatment for metastatic gastrointestinal stromal tumour (GIST) with the use of Imatinib, most people will ultimately relapse and die of multifocal metastatic disease. Regorafenib, a multi-targeted tyrosine kinase inhibitor (TKI) with activity against angiogenic, stromal and oncogenic receptor tyrosine kinases, has demonstrated activity in the treatment of GIST and is approved for third line therapy of advanced GIST. Using an alternating regimen of Imatinib and Regorafenib with brief drug free intervals may allow tumour stem cells to re-enter the cell cycle and become susceptible once more to drug therapy.

STUDY DESIGN
This is a non-comparative randomized phase II design of 76 evaluable patients allocated 1:1 (38 in the alternating group and in the control), stratified by site, receipt of previous adjuvant therapy (prior adjuvant therapy vs no prior adjuvant therapy), and receipt of Imatinib for metastatic disease for less than 21 days (yes or no). The primary objective is objective tumour response (complete or partial response) as determined by RECIST v1.1 or before 9 months from the time from either (i) randomization (if patients have not yet commenced treatment) or (ii) commencement of therapy (if patients are randomized during the first cycle of Imatinib). Secondary endpoints include progression free survival, clinical benefit rate (SD + PR + CR) following 3 cycles (24 weeks) of treatment, time-to-treatment failure, safety/toxicity/tolerability and overall survival.

STUDY PROGRESS
This study is collaboration between the AGITG, NHMRC Clinical Trials Centre (NHMRC CTC), European Organisation for Research and Treatment of Cancer (EORTC) and Scandinavian Sarcoma Group (SSG). Australian lead ethics approval received September 2014 and opened to recruitment February 2015. The study opened to recruitment internationally on 3 March 2016. As of the 31 December 2017, ALT GIST closed to recruitment after reaching the revised recruitment target of 76 evaluable patients. 78 patients were enrolled from 37 sites internationally (14 AGITG sites across Australia and Singapore, 7 SSG sites in Scandinavia and 16 EORTC sites across Europe). As of the 21 June 2019, 38 patients remain on treatment, 28 patients are currently in follow-up and 12 patients are deceased.

The Primary endpoint data analysis was completed in December 2018. Below are the Results and the Conclusion. These were presented in the sarcoma session at ASCO 2019 (poster discussion).
This study represents a paradigm shift in the administration of pre-operative therapy for oesophageal adenocarcinoma (OAC). This study focussed on metabolic non-responders to pre-operative therapy in so far as the management of this group will be changed to a different therapy to try to improve response and potentially survival. This study was the first to use the combination of DCF +/- RT in non-responding patients with OAC generating safety and efficacy data. It will determine whether changing therapy can salvage a response and provide valuable data regarding the potential to individualise therapy related to the tumour characteristics – so called “tailored therapy”. Finally, the routine pre-treatment tumour and blood banking gives our group a unique opportunity to search for OAC biomarkers that may be indicators for FDG-PET response, response to the regimens used and possibly assessment of survival. These are the basis of an NHMRC-funded genomics project. The primary aim was to assess whether changing the pre-operative therapy regimen to DCF +/- RT after the first cycle of CF chemotherapy for early metabolic non-responders will induce a histological response. Study endpoints include: major histological response (<10% residual viable tumour), and secondary endpoints of PFS, OS, toxicity, HRQoL, and feasibility of response-based therapy. In addition banking of tumour tissue and blood before and after treatment for future molecular analyses investigating biomarkers of response was undertaken.

BACKGROUND
Over the last 30 years, the incidence of OAC in Australia has increased more than any other cancer. Surgery forms the mainstay of curative treatment, however survival remains poor. Preoperative chemotherapy (CTX) with or without concurrent radiotherapy (CRT) have resulted in modest improvements in outcome. Patients who demonstrate a histological response in the resected specimen following pre-operative therapy (CTX or CRT) have consistently better survival than non-responders. Recent data suggests that a reduction in the level of tumour activity seen on a PET scan performed 14 days after the start of CTX compared with a baseline PET scan (”early metabolic response”), is predictive of a histological response and improved survival. Increasing the proportion of responders to pre-operative therapy remains one of the major challenges facing patients with localised OAC. We believe it is time to undertake the first clinical trial aimed at improving outcomes for early metabolic non-responders by changing their therapy after the first cycle of standard CTX to include docetaxel +/- radiotherapy.

STUDY DESIGN
This is a randomized phase II study for patients that are PET-non-responders to induction chemotherapy. Patients will be randomised equally to the two treatment groups. Additionally; information on a third group of patients who respond to induction chemotherapy will be collected to help inform a future phase III trial. A sample size of 30 patients per arm will have 80% power with 95% confidence to exclude an uninteresting histological response rate of 5% in favour of a 20% response rate in each arm. A formal comparison for response rates between the two randomised groups is not planned. This study will have 48 months accrual and 36 month follow up.

STUDY PROGRESS
The study was opened by Princess Alexandra Hospital in 2009, it was then awarded an NHMRC grant in 2010, which enabled it to become a multi-centre trial coordinated by the AGITG/NHMRC Clinical Trial Centre. The study opened at 9 sites. Recruitment was closed on 31 December 2015 after 124 eligible patients were registered, of which 66 were randomised. The study recruited its last patient on 29 December 2015 and the last patient completed treatment on 19 February 2016. The study completed follow-up 31 March 2019. A primary analysis of study data has been completed, and an abstract was accepted for the ESMO 2016 Congress. In April 2018, secondary analyses were performed on 3 year PFS and presented in a poster discussion at ESMO 2018. Final analysis, including OS, was completed in March 2019. A manuscript, outlining primary and secondary results has been submitted for publication.

TRANSLATIONAL RESEARCH
Tissue banking (normal and tumour) was performed routinely for consented patients at two time points: (1) at pre-treatment endoscopy or EUS and (2) at surgery. These biopsy specimens were collected and stored as fresh tissue at the central lab. Buffy coat, Serum and plasma for biomarkers will be collected and sent as fresh whole blood to the central lab for processing. This unique tissue collection forms the basis of a NHMRC project grant application to undertake a comprehensive genomic study in OAC using whole genome sequencing, RNAseq, and methylation to identify biomarkers of treatment benefit and novel treatment targets.

STUDY SCHEMA

<table>
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<tr>
<th>DOCTOR</th>
<th>PET Scan</th>
<th>Response</th>
<th>No Response</th>
<th>Randomisation</th>
<th>CF</th>
<th>DCF</th>
<th>DCF &amp; RT (45gy in 25f)</th>
<th>Endoscopy prior to surgery to assess macroscopic tumour response</th>
<th>Surgery</th>
<th>Surgery</th>
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<tbody>
<tr>
<td>Screening</td>
<td>Registration</td>
<td>Initial Chemotherapy CF</td>
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<tr>
<td>Patients with resectable adenocarcinoma of the oesophagus or OG junction</td>
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TRIAL ABSTRACTS · TOP GEAR

Protocol. A second interim analysis testing for both efficacy and futility was triggered in September 2017 when TOP GEAR opened to recruitment in September 2009 and reached its phase II recruitment milestone of 120 patients. The phase III component that will recruit a further 450 patients to provide a total sample size of 570 patients. Conducted in two parts. Part I is the phase II component of the trial that will recruit 120 patients, while Part II is the phase III component that will recruit 450 patients. Therefore, TOP GEAR is a multicentre, prospective, randomised, stratified, phase II/III clinical trial. Eligible patients will be from the AGITG, the European Organisation for the Research and Treatment of Cancer (EORTC) and the Canadian Cancer Trials Group (CCTG).

This is an international, intergroup trial led by investigators from the AGITG and the NHMRC Clinical Trials Centre, in collaboration with the Trans-Tasman Radiation Oncology Group (TROG), the European Organisation for the Research and Treatment of Cancer (EORTC) and the Canadian Cancer Trials Group (CCTG).

The primary objective is to investigate whether preoperative chemoradiotherapy is superior to preoperative chemotherapy alone in patients undergoing adequate surgery (D1+ dissection) for resectable gastric cancer.

BACKGROUND

Gastric cancer remains a significant global public health problem. Although in developed countries its incidence has dramatically decreased, on a worldwide scale it is still a leading cause of cancer related deaths. Surgery is the only potentially curative treatment for gastric cancer. Although the survival rates for patients with early stage disease (stage IA and IB) are high, this subgroup of patients constitutes only 20% of those undergoing resection. The majority of patients will have locally advanced or metastatic disease at presentation, which has an extremely poor prognosis. The current five-year survival rate for gastric cancer in Western countries is approximately 20%, a figure that has improved little over the past 30 years. Despite this rather grim outlook, there have been several important recent advances utilising chemotherapy and radiotherapy in the adjuvant setting that have generated renewed interest and debate in the treatment of resectable gastric cancer.

Since the publication of the Intergroup 0116 and MAGIC studies and the presentation of the Dutch CRITICS trial, clinicians have been faced with the dilemma of which adjuvant strategy to employ. Opinions remain divided regarding the relative efficacy of chemoradiation vs chemotherapy and clinical practice varies amongst different institutions. The important question that needs to be addressed is whether chemoradiotherapy is superior to chemotherapy alone in the neoadjuvant treatment of resectable gastric cancer.

STUDY DESIGN

This is an international, intergroup trial led by investigators from the AGITG and the NHMRC Clinical Trials Centre, in collaboration with the Trans-Tasman Radiation Oncology Group (TROG), the European Organisation for Research and Treatment of Cancer (EORTC) and the Canadian Cancer Trials Group (CCTG). TOP GEAR is a multicentre, prospective, randomised, stratified, phase II/III clinical trial. Eligible patients will be randomly allocated to either preoperative chemotherapy or preoperative chemoradiotherapy. The trial will be conducted in two parts. Part I is the phase II component of the trial that will recruit 120 patients, while Part II is the phase III component that will recruit a further 450 patients to provide a total sample size of 570 patients.

STUDY PROGRESS

TOP GEAR opened to recruitment in September 2009 and reached its phase II recruitment milestone of 120 patients on 24 June 2014, triggering a safety and feasibility analysis that was reviewed by the AGITG Independent Data Safety Monitoring Committee (IDSMC) in March 2015 with recommendation to continue the trial as per protocol. A second interim analysis testing for both efficacy and futility was triggered in September 2017 when 300 patients had been followed up for a minimum of 6 months after completion of adjuvant chemotherapy. The analysis was reviewed by the AGITG IDSMC in June 2018 with the recommendation to continue the trial as per protocol and no concerns regarding efficacy, futility or safety. The phase III component of the trial is ongoing.

In keeping with emerging evidence for standard treatments for this patient group, an amendment to the TOPGEAR protocol was made in July 2017 to allow for the inclusion of EOX and FLOT chemotherapy regimens. As of 25 June, there are 488 patients on trial across 56 active sites across Australia and New Zealand (19 sites), Canada (13 sites) and Europe (24 sites).

An extension to the existing NHMRC grant was approved to allow recruitment to continue until the end of 2020. The extended accrual period of this study has enabled a reduction in the sample size to 570 patients, by enabling the detection of more observed events. This can be achieved while maintaining the same statistical power of the original trial design.

TRANSLATIONAL RESEARCH

TOP GEAR includes a translational research sub-study led by Associate Professor Alex Boussioutas. Where possible, both pre- and post-treatment tissue samples are collected (fresh and/or snap frozen and/or FFPE). In addition, a series of blood samples are collected prior to treatment, during treatment and at regular intervals during follow-up, ideally until recurrence. Specific aims to address as part of this clinical trial are:

a. Are there biomarker and biological determinants of chemotherapeutic and radiotherapeutic response in gastric cancer?
b. Are there biological differences in remnant disease that differs from the primary lesion and could be useful to target specific therapeutics?

AIMS

The primary objective is to investigate whether preoperative chemoradiotherapy is superior to preoperative chemotherapy alone in patients undergoing adequate surgery (D1+ dissection) for resectable gastric cancer.

STUDY SCHEMA

Eligibility

Adults over 18 years with histologically proven adenocarcinoma of the stomach or gastroesophageal junction that is:

a. Stage IB (T2N1 only) – IIEC, i.e. T2 – N1 and/or N+, v.
b. Considered operable following initial staging investigations

Stratification

• Age: <50yrs vs 50yrs – 70yrs vs >70yrs
• Primary tumour site: gastroesophageal junction (esophagogastric junction (Ivor-Lewis)) vs gastroesophageal junction (total gastrectomy) vs upper third vs middle third vs lower third vs tumour extends into 2 or more of the above adjacent sites
• Clinical tumour stage: T1-2 vs T3-4
• Clinical nodal stage: N-ve vs N+ve
• Site/Institution
• PET
• EUS
• Laparoscopy
• Chemotherapy regimen

Endpoints

Primary endpoint
Overall survival
Secondary endpoints
Disease free survival
Pathologic response rate
Treatment administration

Duration of accrual: 10 years
Duration of follow-up: up to 5 years

Group 1 (Control Arm)
ECF (or EOX) x 3 OR
FLOT x 4 Repeated every 14 days + SURGERY (D1+)
+ ECF (or EOX) x 3 Repeated every 21 days
OR
FLOT x 4 Repeated every 14 days

Group 2
ECF (or EOX) or EOX x 2 Repeated every 21 days
OR
FLOT x 3 Repeated every 14 days + PREOP CRT
5 Gy + CI 5-FU (or X) + SURGERY (D1+)
+ ECF (or EOX) or EOX x 3 Repeated every 21 days
OR
FLOT x 4 Repeated every 14 days

Follow-up: 5 years
Aims
The primary aim of the DYNAMIC-Pancreas study is to demonstrate that risk-stratified treatment using circulating tumour DNA (ctDNA)-informed management following curative-intent surgery for localised pancreatic cancer can provide a more tailored approach to the patient and maintain outcomes as measured by the rate of 2-year recurrence-free survival, whilst exploring the possibility of reducing chemotherapy-related toxicity.

Background
Pancreatic cancer is an aggressive disease with few long-term survivors. In the majority of cases, long-term survival can only be achieved with surgical resection of localised disease. Following resection of pancreatic adenocarcinoma, routine use of adjuvant chemotherapy improves survival outcomes, however there are currently no biomarkers that define patients that are more or less likely to benefit from treatment. Inferior survival outcomes have been demonstrated with ctDNA detection pre- and post-pancreatic cancer surgery, with relapse occurring despite standard adjuvant therapy in patients with detectable ctDNA following surgery, whilst patients with no detectable ctDNA post-surgery had reduced recurrence rates. Thus, a reliable biomarker for patients with resected pancreatic cancer could improve their adjuvant management decision (treatment regimen/treatment duration), allowing therapy to be personalised to each patient’s risk of recurrence.

This ctDNA-directed study will place greater focus on tailoring our approach to treatment, answering important questions around who and how we treat, as well as how many drugs need to be administered concurrently in order to achieve better outcomes. Also of great importance is the potential of a ctDNA-directed approach to reduce the unnecessary use of treatment (treatment de-escalation) in lower-risk patients (reducing treatment-related toxicity, duration of therapy, direct treatment-related cost, and reducing indirect treatment-related costs, such as time off work) without compromising survival outcomes.

Study Design
DYNAMIC-Pancreas is a prospective, multi-centre, randomised controlled study enrolling 438 participants with localised adenocarcinoma of the pancreas undergoing either neo-adjuvant (peri-operative) therapy followed by “curative” surgery (Ro or Ri) or immediate “curative” surgery who would routinely be offered adjuvant chemotherapy.

This study will enrol two participant cohorts, with the major focus being on the cohort that receive neo-adjuvant treatment (N=350), where participants will be randomised after surgical resection to receive either standard of care adjuvant treatment or treatment guided by their ctDNA status. Participants who have received radiotherapy prior to surgery will be eligible but will be stratified. Participants will also be stratified by Ro and R1 resection status. Participants who undergo immediate resection can be enrolled into a separate non-randomised single-arm biomarker-guided cohort (n=88) in order to gain further insight into the use of this strategy.

Primary Study Endpoint: 2-year recurrence-free survival
Secondary Study Endpoints:
- ctDNA results turn-around time
- Proportion of participants completing planned study treatment
- Proportion of participants with positive ctDNA after surgery
- Proportion of participants with positive ctDNA at completion of all treatment

Exploratory Endpoints:
- Chemotherapy duration, dose intensity and drug intensity (2 vs 3 drug combinations)
- Health economic impact
- Treatment-related hospitalisation

Study Progress
DYNAMIC-Pancreas received central ethics approval in Australia in July 2017. The first sites opened in March 2019 and the first patient was enrolled in March 2019. As of 21 June 2019, 6 patients have been enrolled onto the study and 11 sites activated. The study is funded by a philanthropic source, the Marcus Foundation.

Translational Research
Formalin-fixed paraffin-embedded tumour tissue will be collected from all participants to identify somatic mutations for subsequent ctDNA analysis. Blood collections (30-60mL) for ctDNA analysis will be obtained from all participants 4-6 weeks after surgery (ctDNA-1). Up to three additional study bloods will be collected - prior to chemotherapy, during chemotherapy and at end of treatment from all participants. ctDNA mutation analyses will be conducted by the Vogelstein Laboratory at Johns Hopkins University, Baltimore, USA.

Study Schema

<table>
<thead>
<tr>
<th>Cohort A: SOC</th>
<th>Cohort A: mFOLFIRINOX 3 months*</th>
<th>Cohort B: Biomarker informed</th>
<th>Cohort B: mFOLFIRINOX</th>
<th>Cohort C: Biomarker informed</th>
<th>Cohort C: mFOLFIRINOX</th>
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<tbody>
<tr>
<td>Post-Op ctDNA</td>
<td>Randomise 1:1</td>
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<tr>
<td>N=150 Neo-adjuvant post-surgery Cohort</td>
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Blood collection time point: ctDNA-1A = Week 4-6 post-surgery
Clinic selects intended chemotherapy regimen at enrolment, prior to randomisation results

* Duration of therapy, dose reductions/modifications as per institute practice
† Recommendation for a total of 6 months of treatment with at least 2 months in the post-operative (adjuvant setting)
AIMS
The primary objective of this study is to evaluate the impact of gemcitabine and cisplatin compared to standard of care on disease-free survival (DFS) in patients with operable biliary tract cancer (BTC). Secondary objectives are safety and tolerability of the treatment, disease free survival at 24 months, overall survival (OS), quality of life, function of biliodigestive anastomoses, rate and severity of biliary tract infection, patterns of disease recurrence, and locoregional control. An evaluation of the quantity and quality of information patients have gained after the informed consent as well as of the involvement of patients in the decision-making process (shared decision making) will be undertaken.

BACKGROUND
Complete surgical resection represents the only potentially curative treatment for BTC, but even after curative intent (R0) resection, the 5-year survival rate is low. Optimisation of post-operative adjuvant therapy is imperative.

In view of positive data obtained in a large randomised phase III trial in advanced BTC, (Valle, Wasan et al. 2010), the combination of cisplatin and gemcitabine for 24 weeks was chosen for this clinical trial for evaluation against standard of care. In 2017 the BILCAP trial reported positive results for post-operative adjuvant capecitabine, thereafter adopted as standard of care, and the ACTICCA-1 trial has been amended accordingly.

Data on prognostic factors for BTC are rare. Now that adjuvant chemotherapy is the standard of care, predictive markers are of particular importance. Within the current trial tumour tissue will be collected together with the clinical data.

STUDY DESIGN
This is a multicentre, prospective, randomised, controlled phase III trial designed to assess the clinical performance of gemcitabine with cisplatin vs. standard of care after curative intent resection of BTC. There are two recruitment phases resulting from the change in standard of care from observation to capecitabine.

ACTICCA-1 is an international investigator-initiated clinical trial, sponsored internationally by the University Medical Center Hamburg-Eppendorf and coordinated internationally by the University Cancer Center Hamburg. 781 patients are to be randomised in Germany, Netherlands, Denmark, Austria, United Kingdom and Australia. The expected Australian contribution is 50 patients from 15 centres.

STUDY PROGRESS
Recruitment commenced internationally in 2016. 187 patients were randomised in phase I (gemcitabine and cisplatin compared with observation). Following the outcome of the BILCAP study, standard of care for this patient population changed and recruitment was put on hold to amend the protocol accordingly. In Australia protocol V6, 21 June 2017 was approved by central ethics in September 2017 and recruitment recommenced in early November 2017.

As of 27 June 2019, ACTICCA-1 has recruited 13 patients and opened 12 sites in Australia. 46 sites have been opened in Germany, Netherlands, Denmark, Austria and UK. 436 patients enrolled and 403 randomised.

TRANSLATIONAL RESEARCH
Translational research will be performed to evaluate the prognostic and predictive impact of tissue markers in biliary tract cancer with particular regard to adjuvant chemotherapy with gemcitabine and cisplatin.

AUSTRALIAN SUB-STUDIES
An Australian-led surgical sub-study will evaluate the prognostic significance of mode of presentation and the risk/benefit of extent of surgery in gallbladder cancers. The surgical sub-study has been added to the latest protocol amendment and data will be collected via the main trial electronic Case Report Form.

STUDY SCHEMA

ACTICCA-1 Trial
Scheduled curative resection of biliary tract cancer

↓
Surgery

Eligible for randomisation
Not eligible for randomisation

↓
Gemcitabine + Cisplatin
Cápecitabine

Follow-up
The aims of CONTROL NETS are to 1) determine the relative activity of capecitabine + temozolomide (CAPTEM) plus Lutetium-177 Octreotate peptide receptor radionuclide therapy (PRRT) and capecitabine (CAP) in the treatment of pancreatic neuroendocrine tumours (pNETs) and mid gut neuroendocrine tumours (mNETs); and 2) to inform future comparative phase III RCTs to determine the optimal therapies in pNETs and mNETs.

BACKGROUND
Neuroendocrine tumours (NETs) are a heterogeneous group of malignancies that can arise at any site in the gastrointestinal tract, that are known by their ability to over express somatostatin receptors. Originally called carcinoid tumours, these tumours are rising in incidence. In patients with incurable disease, several systemic options have demonstrated activity but few have been compared in prospective, randomized controlled trials (RCTs). Lutetium-177 PRRT and CAPTEM have shown promising activity in initial single arm trials. Prospective RCTs are needed to build on these early trials to determine the optimal role of these therapies in clinical practice.

STUDY DESIGN
CONTROL NETS consists of two non-comparative parallel group Phase II randomized open label trials of Lutetium-177 Octreotate (177Lu-Octreotate) peptide receptor radionuclide therapy (PRRT) and capecitabine (CAP)/temozolomide (TEM) chemotherapy (chemo): (i) versus CAPTEM alone in the treatment of low to intermediate grade pancreatic neuroendocrine tumours (pNETs); (ii) versus PRRT alone in the treatment of low to intermediate mid gut neuroendocrine tumours (mNETs).

In Cohort A, CAPTEM chemo alone is chosen as the control therapy as it has the highest reported activity of the modern chemo regimens and is becoming the chemo regimen of choice in many parts of the world.

In Cohort B, PRRT is the control therapy due its high activity and the lack of benefit seen with TEM in previous studies in mNET patients.

STUDY PROGRESS
The trial received initial ethics approval in March 2015. Following several unsuccessful attempts at NHMRC and Cancer Australia grant funding for the full n=65 pts study, the TMC ratified a decision to amend the accrual target to n=72 for the trial. A protocol amendment to consolidate these changes was approved in March 2018.

CONTROL NETS completed recruitment of 72 patients in November 2018, with patients enrolled at four sites: Fiona Stanley Hospital, The Royal Brisbane and Women’s Hospital, Royal North Shore Hospital and St George Hospital.

All patients have now completed trial treatment. Patients in the mNET cohort met the 12 month PFS primary endpoint in May 2019 with data planned for presentation at ASCO GI 2020. The pNET cohort will meet the 15 month PFS primary endpoint in November 2019 with potential data presentation at ENETS or ASCO 2020.

Follow up for Overall Survival and Health Economics endpoints has been extended to 27 months in the mNET cohort to align with the pNET cohort 18 month follow up – both will now be met in January 2021. Funding to date has been via multiple Unicorn Foundation contributions, a University of Sydney Bridging grant, a Perpetual Impact grant and most recently a Tour de Cure grant (secured by Unicorn Foundation).

TRANSLATIONAL RESEARCH
Patients were invited at the time of study entry to provide written informed consent for donation of an archival tissue (FFPE) sample and to provide blood samples. Planned tertiary translational objectives are the correlation of circulating and tissue biomarkers and study endpoints (relating to survival, response and safety), including but not limited to CgA, Ki-67 & tumour MGMT expression, and the development of a clinically applicable composite response rate score incorporating structural and functional imaging, biochemical, metabolic and symptomatic response. Final Translational Research blood collections are expected in August 2019. Teams are being formalised for individual tertiary objectives and additional funding options are being investigated to cover these analyses.

STUDY SCHEMA

<table>
<thead>
<tr>
<th>STUDY SCHEMA</th>
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<tbody>
<tr>
<td>Patients with low intermediate grade advanced, unresectable pancreatic neuroendocrine tumours (pNETs) or mid gut neuroendocrine tumours (mNETs)</td>
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<table>
<thead>
<tr>
<th>CONTROL NETs</th>
</tr>
</thead>
</table>

- Pancreatic neuroendocrine tumours (pNETs)
- Midgut neuroendocrine tumours (mNETs)

2:1 Randomisation (Experimental-Control)

Stratification by:
- Previous systemic therapy regimens (<1v2)
- WHO tumour grade: Low Grade – G1 (Ki67<2% and/or mitotic count <2) vs. intermediate Grade – G2 (Ki67 3-20% and/or mitotic count 2-20)
- Visceral only vs. visceral with bone metastases & Treating institution

<table>
<thead>
<tr>
<th>Cohort A: pNETs</th>
<th>PRRT/CAPTEM vs. CAPTEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=27</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Cohort B: mNETs</th>
<th>PRRT/CAPTEM vs. PRRT</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=45</td>
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</tbody>
</table>

CAPTEM
Oral capecitabine 750mg/m² b.i.d. days 1-14 and 29-42 and temozolomide 75mg/m² b.i.d. days 10-14 and 38-42 every 56 day cycle, up to 4 cycles or until unacceptable toxicity

n=9

PRRT/CAPTEM
7.8GBq 177Lu Octreotate given intravenously (IV) every 8 weeks for 4 cycles (on Day 10 of chemotherapy) with concurrent CAPTEM, repeated up to 4 cycles or until unacceptable toxicity

n=18 pNETs
n=30 mNETs

Follow up for a minimum of 18 months

<table>
<thead>
<tr>
<th>PFS 12 Months (pNETs)</th>
<th>PFS 15 months (mNETs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Objective tumour response rate</td>
<td>Clinical Benefit Rate</td>
</tr>
<tr>
<td>Safety/Toxicity</td>
<td>Quality of life</td>
</tr>
</tbody>
</table>

Day 3 TRAIL ABSTRACTS • CONTROL NETs

Session: AGITG Upper GI Cancer Trials
Presentation: CONTROL NETs
Speaker: Associate Professor David Wyld
Institution: Royal Brisbane & Women's Hospital
Financial Disclosure: None to declare
Protocol Title: Capecitabine ON Temozolomide Radionuclide Therapy Octreotate Lutetium177 Neuroendocrine Tumours Study.
Study Chair(s): Associate Professor Nick Pavlakis and Professor Harvey Turner
Project Manager(s): Kate Wilson
Trial Coordinator(s): Ailsa Langford (controlnets@ctc.usyd.edu.au)
AIMS
The general aim of NABNEC is to establish if carboplatin and nab-paclitaxel combination is an effective and tolerable chemotherapy treatment for grade 3 advanced gastrointestinal NECs. To explore translational biologic, molecular and functional imaging endpoints, to inform future research and improve outcomes for NEC patients.

BACKGROUND
Neuroendocrine carcinomas (NEC, WHO 2010 grade 3, WHO 2017 grade 3, comprising small cell NEC and large cell NEC, are aggressive rare cancers and are generally rapidly fatal. They arise commonly in the gastrointestinal system. There have been a few retrospective studies but no randomised, prospective controlled trials conducted to establish gold standard chemotherapy for advanced gastrointestinal NECs. Etoposide and carboplatin are historical standard of care by extrapolation from small cell lung cancer trials. Paclitaxel and carboplatin are active in gastrointestinal NECs but there is no data on the role of nab-paclitaxel. This randomised study will determine the role of these therapies in clinical practice and to prospectively study the biology and imaging characteristics of NEC.

STUDY DESIGN
NABNEC is an open label centrally 2:1 randomised multicentre phase II trial. The study treatments are:

**Arm A:** IV nab-paclitaxel (100mg/m²) on Day 1 every week and carboplatin (AUC=5) every 3 weeks until disease progression or unmanageable toxicity

**Arm B:** IV carboplatin AUC=5 on Day 1 and etoposide 100mg/m² on Days 1-3 every 3 weeks until disease progression or unmanageable toxicity

Duration of accrual: 3 years  Duration of follow-up: up to 3 years

Endpoints
- **Primary endpoint:** Objective tumour response rate
- **Secondary endpoint:** Progression free survival
- **Tertiary/correlative endpoints:** Overall survival, Safety, Quality of life
- **Biomarker analyses of blood and tissue**
- **Mutational and DNA methylation profiling**
- **FDG-PET imaging**
- **68GA-octreotate PET/CT imaging**
Aims

The aim of this study is to determine if the addition of stereotactic body radiotherapy (SBRT) to chemotherapy improves locoregional control for patients with high-risk operable, borderline resectable and locally advanced pancreatic cancer.

Background

Pancreas cancer (PC) has the fifth highest incidence of cancer related mortality and accounts for the death of more than 2,900 Australians annually. For the PC patients with high-risk, borderline resectable (BRPC) or locally advanced pancreas cancer (LAPC), the 5-year overall survival is abysmal, at 12%. This is despite having no demonstrable metastatic disease at diagnosis. Approximately half of all PC patients experience locoregional recurrence (LRR). Even with surgery, 40% of patients will experience a LRR in the first 12 months. LRR is a major contributor to the substantial morbidity and mortality of this cancer. SBRT is a significant dose escalation to standard external beam radiotherapy (EBRT) without an increase in toxicity. This is anticipated to increase tumour cell kill and reduce rates of LRR. Reduced LRR rates could reduce the debilitating symptoms associated with LRR and progression, and potentially improve overall survival by preventing or delaying development of metastases. LRR is associated with significant pain and suffering due to gastric outlet obstruction, duodenal erosion and coeliac plexus infiltration, and ultimately results in premature death. MASTERPLAN addresses LRR rates in PC and attempts to improve health outcomes, including overall survival for the nearly 3,300 Australians diagnosed with PC every year.

Study Design

This is a prospective, two arm, multicentre randomised, phase II clinical trial, with randomisation 1:2, patients are stratified by tumour stage and chemotherapy administered. A recruitment target of 120 patients over 48 months from 10 sites in Australia.

Study Progress

MASTERPLAN was submitted to the NHMRC Medical Research Future Fund (MRFF) Low Survival Cancers and Diseases (LSCD) Grant Opportunity in April 2018 and was successfully awarded funding in September 2018. Central HREC Approval was received on 8 March 2019 with 6 initial sites. Governance submission and site contracts are underway. Activation of first site and randomisation of first patient planned for Q3 2019.

Translational Research

Collection of matched tumour tissue and serial research blood from patients for subsequent translational research into: the molecular and genetic drivers of PC, prognostic and predictive biomarkers for clinical endpoints — including circulating tumour DNA and protein signatures (proteomics).
What science can do

GenesisCare is one of the largest providers of radiation therapy and intensity modulated radiation therapy treatments in Australia. Globally, we have over 140 GenesisCare centres and 8,000 highly trained healthcare professionals and support staff.

- Advances in technology have enabled new radiation therapy techniques to be developed, allowing patients to be treated with greater precision and accuracy.
- We leverage our network’s expertise and experience to ensure all patients benefit; whether seen in a regional centre or capital city – bringing treatment closer to home.
- We continually improve patient care and exceed global benchmarks for patient satisfaction. Our patient surveys average 99% satisfaction.
- We participate in internationally-recognised, high-quality clinical trials and are currently participating in over 110 clinical trials throughout Australia across oncology and cardiology in over 35 locations.

genesiscare.com
SIR-Spheres® is a registered trademark of Sirtex SIR-Spheres Pty Ltd.

Indications for Use:
SIR-Spheres Y-90 resin microspheres are indicated for the treatment of unresectable metastatic liver tumors from primary colorectal cancer. This device is a radiopharmaceutical. Federal (USA) law restricts this device to sale by or on the order of a physician.

Resin microspheres may only be distributed to a duly licensed or accredited facility capable of handling therapeutic medical isotopes. This product is radioactive and should thus be handled in accordance with all applicable standards and regulations.

Reference the Package Insert (www.sirtex.com) for a complete listing of indications, contraindications, side effects, warnings, and precautions.

Get Gutsy and take on a challenge

More money raised through the Gutsy Challenge, means more grants available to support your research and the research of your colleagues.

Call 1300 666 769 or visit gicancer.org.au/gutsy-challenge-adventures/
This unique fly in, fly out trekking expedition will take you deep into the heart of the Bungle Bungle. Starting and finishing with a chartered flight over the National Park, the Gutsy Challenge allows trekkers to avoid the long drive, and maximise their experience.

This five day trek follows the gorge as it winds its way between the red and black beehive like sandstone domes. The team will trek with full packs to a base camp on thefirst night and do two days of moderate walks with only a day pack. Returning to the camp each night to be surrounded by the red cliffs of the Bungles at Piccaninny Gorge. On day four, the group will trek to a new camp, following Picaninny Creek south west towards Cathedral Gorge, where they will spend their last night. The final day of the trek starts with a walk to Cathedral Gorge, where it is said the natural acoustics are better than the Sydney Opera House!

AGITG Members Katie Benton and Belinda Steer will lead the Gutsy Challenge, with all funds raised supporting the AGITG Innovation Fund. With only 10 spots available we are taking expressions of interest NOW!

**Gutsy Challenge**

**Bungle Bungles**

**June 2020**

Dates: 21-27 June 2020
Registration Fee: $200
Fundraising Target: $3,500/person
Travel Costs: $3,850/person (excl. flights)
Trip Duration: 7 days
Accommodation: Camping
Minimum Age: 18

Visit our website and complete the form www.gicancer.org.au/bunglebungen or contact us on 1 300 666 769 or info@gicancer.org.au

Kakadu National Park is one of the 10 Natural Wonders of Australia. It covers nearly 20,000 square kilometres of incomparable natural beauty and unique biodiversity. As a Kakadu Gutsy Challenge trekker you will have the opportunity to enjoy the magnificence of this Natural Wonder, come face to face with native wildlife and experience ancient Aboriginal rock art sites.

This adventurous trekking challenge will reveal the extraordinary diversity of habitats of the escarpment. You will be rewarded for your efforts with the spectacular Barramundi Falls and a sunrise wetland cruise. You will trek 45kms of the National Park, share in traditional owner stories and information about the natural land and stay in sustainable, semi-permanent safari camps each night.

AGITG Member Associate Professor Nick Pavlakis will lead the Kakadu Gutsy Challenge over five days. All funds raised from this Gutsy Challenge will support the AGITG Innovation Fund. With only 16 spots available we are receiving expressions of interest NOW!

**Gutsy Challenge**

**Kakadu**

**August 2020**

Dates: 16-22 August 2020
Registration Fee: $200
Fundraising Target: $3,500/person
Travel Costs: $2,890 (excl. flights)
Trip Duration: 5 days
Difficulty: Moderate
Accommodation: Twin share, sustainable safari camps
Minimum Age: 18

Visit our website and complete the form www.gicancer.org.au/kakadu or contact us on 1 300 666 769 or info@gicancer.org.au
L’ETAPE
2019

WE’RE LOOKING FOR RIDERS TO JOIN THE L’ETAPE GUTSY CHALLENGE 2019 TEAM.

L’Etape Australia offers amateur riders an experience as close to riding in the Tour de France you can get this side of Europe. With fully closed roads and a course equal to a mountainous stage of the Tour de France, L’Etape Australia provides a truly unique riding experience.

As part of the GI Cancer Institute’s L’Etape Gutsy Challenge team you will have access to start line accommodation, training guides and a team of inspirational cyclists from all walks of life.

All funds raised from this Gutsy Challenge will support the AGITG Innovation Fund.

Dates: 29 November - 1 December 2019
Registration Fee: $200
Fundraising Target: $5,500/person
Travel Costs: $400 (excluding travel costs to Jindabyne)
Trip Duration: 2 nights
Difficulty: Moderate
Accommodation: Start line cabins at Jindabyne Holiday Park. Twin share.

Contact us on 1300 666 769 or at info@gicancer.org.au to become part of the Gutsy Challenge team or to find out more.

Many patients and their families want to help fund research into GI cancers – but don’t know how.

We are the only organisation working to find better treatments and cures for all GI cancers in Australasia. Community-based support is critical for the future sustainability for funding small scale clinical trials.

To refer a patient or to find out more information, please call 1300 666 769 for a confidential discussion.
From humble beginnings in 2014 our Gutsy Challenge has quickly grown to become a major source of income for GI cancer research and a vital tool to help increase awareness of GI cancers within the community. We can proudly say this growth is due to the dedication and commitment from our members and staff.

Now in its 6th year, our Gutsy Challenge continues to grow rapidly. Enabling us to increase our annual Innovation Fund grant each year and set our sights on raising enough to award two grants of $300,000 in 2020. Without the ‘gutsy’ efforts of the people listed below we would not be where we are today.

We wish to thank the members, staff and industry personnel along with all the people who have supported them in each of their Gutsy Challenges. Collectively these people have raised over $335,000 to date.

Professor Tim Price will lead a team of six gutsy Australians and five gutsy New Zealanders through 70km of New Zealand’s Southern Alps on a challenging week-long trek this November.


Doctor Lorraine Chantrill will lead ten intrepid trekkers along 135km of the West Australian coast. Hiking up to 25km per day the team will trek through the Leeuwin Naturaliste National Park in September.

Support Lorraine and the Cape to Cape Gutsy Challenge team by making a donation here www.gicancer.org.au/CapetoCape

Associate Professor Niall Tebbutt will once more lead a team of six gutsy New Zealanders, scaling the heights of Mt Himlung Himal (7,226m) in May 2020. Mt Himlung Himal is located between the border of Nepal and Tibet.

Support Niall and the Mt Himlung Himal Gutsy Challenge team by making a donation here www.gicancer.org.au/Himlung

All donations are tax deductible and support the AGITG Innovation Fund grant.
GUTSY CHALLENGE - TREASURE ROAD IS AN EXCITING ROAD TRIP IDEAL FOR FAMILIES WITH SCHOOL AGED CHILDREN.

2020 will see our inaugural family friendly fundraising event take place. The fundraising adventure – five fun-filled days and nights in the September, 2020 school holidays - will depart Sydney and finish at an undisclosed destination near Dubbo.

Each days’ route will be revealed once the teams decipher the clues handed out at breakfast each morning.

The Treasure Road kids will each receive a ‘passport’ that they will fill with stickers received upon successfully finding deciphered locations along the way. And each night, stopover towns will welcome participants with open arms and present fun and exciting entertainment.

This adventure gives families the opportunity to enjoy a unique, affordable, fun-filled family holiday in the support of GI cancer research.

Dates: 28 September - 2 October 2020

Registration Fee: $500/vehicle (cost of accommodation, dinners and nightly entertainment and breakfasts included).

Fundraising Target: $4,000/vehicle

Travel Costs:
- Adult: $200
- Child: $100

Trip Duration: 5 nights

Accommodation: Family camping in local showgrounds along the way

Contact us on 1300 666 769 or email us at info@gicancer.org.au to find out more.