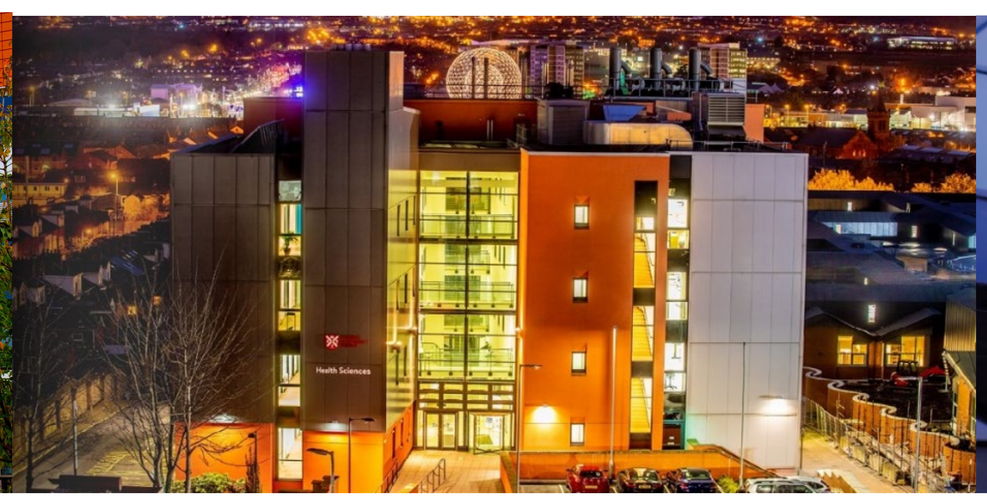


Our Aim

To effectively translate discovery research into biomarker-guided, biologically-informed clinical trials in collaboration with other ECMCs, industry, national and international partners and public/patients to improve regional and national access to early phase trials for patients, thereby improving treatment outcomes.

Research Themes

1. Improving patient care and outcomes through better access to experimental cancer medicine clinical trials by:

- Increasing the number of interventional clinical trials to develop a balanced portfolio across cancer type and treatment modality.
- Increasing capacity for early phase trials in haematological malignancies.
- Improving access to molecularly stratified trials for patients both locally and across the ECMC network.
- Expanding drug-radiotherapy combination studies by building on the success of the delivery of ADRRAD and involvement in development of the cross-ECMC CONCORDE trial.
- Developing new collaborative partnerships with Cancer Trials Ireland and the establishment of the All Ireland Cancer Research Institute.

2. Development of innovative experimental cancer medicine trials arising from our discovery science

- Evaluation of PARP inhibition in SF3B1 mutant uveal melanoma and other SF3B1 mutant malignancies.
- Targeting epigenetically-driven drug resistance in metastatic colorectal cancer

3. Excellence in translational and biomarker experimental cancer medicine research

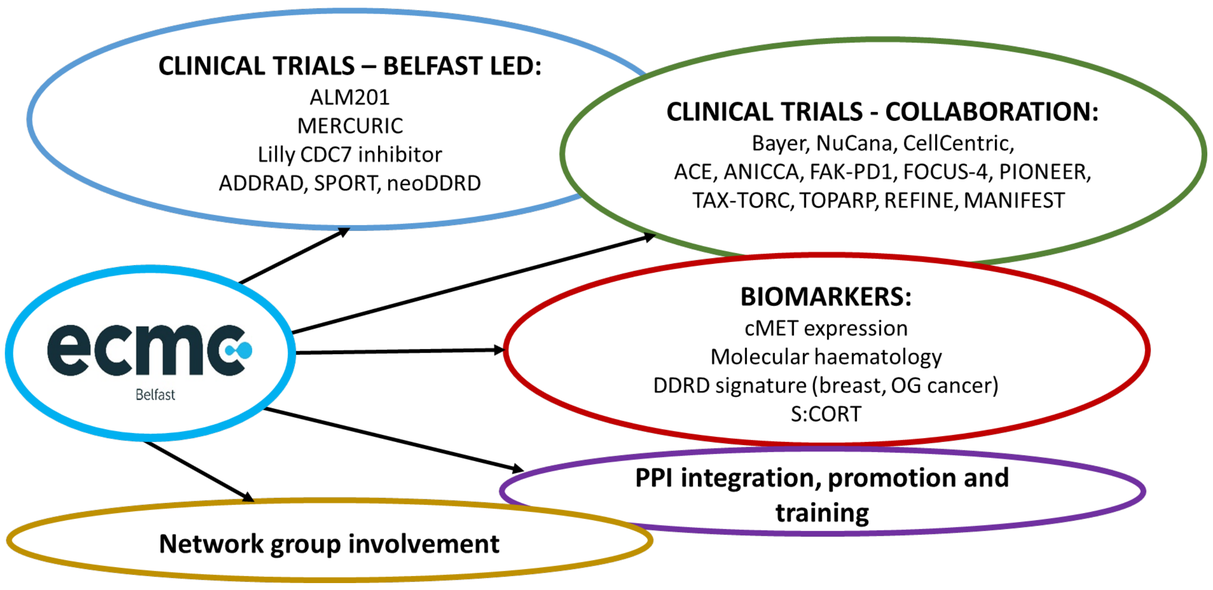
- Predicting response to adjuvant SoC chemotherapy in colorectal cancer.
- Predicting response to neoadjuvant therapies in breast cancer: Neo-DDIR.
- Development of innovative digital pathology and data analysis solutions.

4. Development of novel therapeutic agents for cross network early phase trials

- The novel dUTPase inhibitor CV6-168.
- Inhibitors of FLIP.

5. Data science to support experimental cancer medicine trials

Achievements in the past quinquennium:



Our Challenges

- Re-set post Covid – service and staffing pressures
- Navigation of regulatory divergence post EU-Exit

Working Together in the ECMC Network

Looking forward to ECMC Network facilitation of more collaborations, more cross-centre PPI and on-going involvement in:

- ECMC North collaboration
- ECMC Nurses Group
- Junior Investigator Group
- ECMC Centre Business Leads Groups

Belfast team members (left-right: back) Dr Kienan Savage, Prof Gerry Hanna, Mr Stuart McIntosh, (middle) Dr Melanie Morris, Ruth Boyd, Prof Vicky Coyle, Dr Judy Bradley, Prof Mark Lawler joined by (front) Dr Catherine Elliott, Cancer Research UK, during a recent visit

Other Future Developments

- ASTFOX trial : A Phase I study of the IAP antagonist ASTX660, in combination with standard of care FOLFOX chemotherapy in metastatic colorectal cancer

FIRST PATIENT FIRST VISIT 2023
Belfast, Glasgow, Leicester ECMC
Glasgow CTU
Translationally rich – Precision Medicine Centre, Belfast
Funding – CRUK CRC, Astex Pharmaceuticals

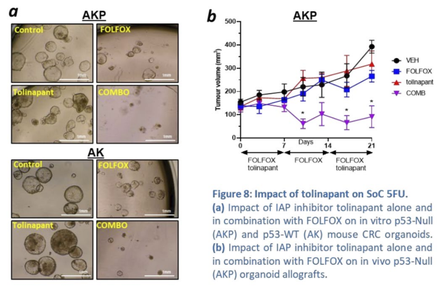
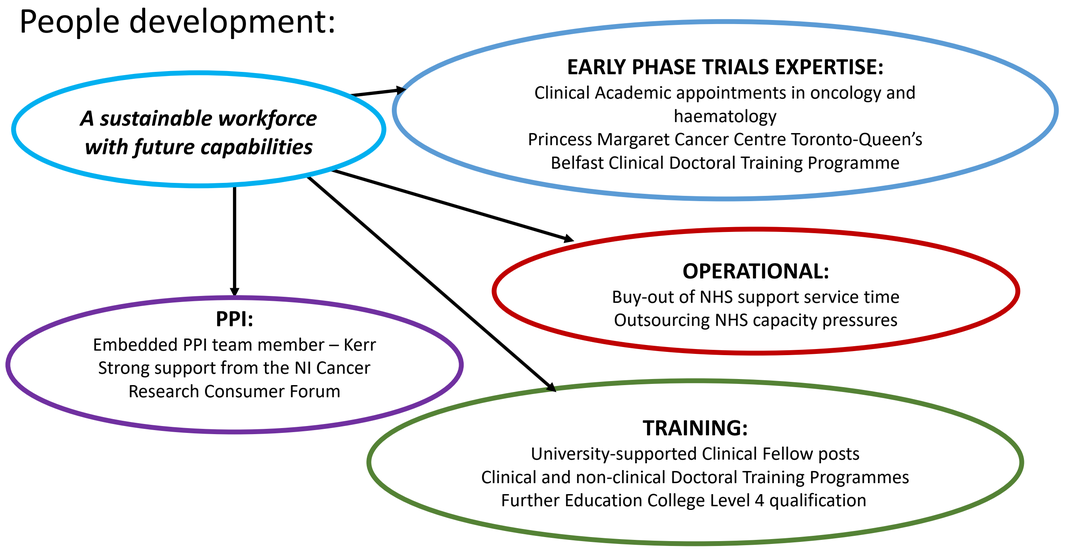


Figure 8: Impact of tolinapant on SoC 5FU. **(a)** Impact of IAP inhibitor tolinapant alone and in combination with FOLFOX on in vitro p53-Null (AKP) and p53-WT (AK) mouse CRC organoids. **(b)** Impact of IAP inhibitor tolinapant alone and in combination with FOLFOX on in vivo p53-Null (AKP) organoid allografts.

- Scheduled roll-out of NHS NI-wide digital integrated care record
- People development:



- i-REACH Institute of Research Excellence for Advanced Clinical Healthcare – the first BRC-type infrastructure in NI.

- Enhanced public awareness, Science Cafes, early career researcher PPI training

Jointly funded by: CANCER RESEARCH UK; Little Princess Trust; NIHR National Institute for Health and Care Research; Ymchwil Iechyd a Gofal Cymru Health and Care Research Wales; CHIEF SCIENTIST OFFICE; HSC Public Health Agency Research and Development

Next steps for the Birmingham ECMC

Driving forward the next generation of studies focused on the context of mutations

Vision

The **Birmingham ECMC** will be an integrated cancer research hub, linking the laboratory with the needs of people with cancer. We will bring together our discovery science, experimental medicine and clinical trials expertise, to accelerate benefits for patients. Working with the **ECMC network** and beyond, we will drive research across three themes: **Precision Medicine** (PM), **Immunotherapy**, and **Biomarkers and Liquid Biopsy**. We will realise our vison by leveraging our expertise and leadership in genomic medicine and methodologies, immunobiology applied to cancer and our technical and scientific expertise in cancer genetics.

Where Next for Precision Medicine (PM)?

Following on from the National Lung Matrix Trial (NLMT) that we led on, and which demonstrated the scale and scope of what can be achieved by the ECMC network working as one, Middleton is the translational lead of DETERMINE and Beggs the genomics lead. **DETERMINE**, led clinically by the **Manchester ECMC**, is a 'next generation' PM platform study, which will recruit at adult and paediatric ECMCs. We are providing its sophisticated laboratory analyses, investigating the impact of the context of targeted alterations on patient outcomes, to establish the rationale for their use.

The main aims of DETERMINE are:

1. To analyse the **mutational processes** generating oncogene driven cancers across the full spectrum of age of onset and site of origin
2. To analyse the **epigenomic characteristics** of oncogene driven cancers across the full spectrum of age of onset and site of origin

Secondary aims:

1. To generate a **molecular portrait** of rare adult and paediatric/TYA cancers harbouring canonical oncogenic alterations
2. To analyse the impact of how the molecular landscape of oncogene driven cancers **influences response to agents** targeting that genetic alteration

We are currently analysing the extensive ctDNA collection from NLMT focusing particularly on genomic drivers of primary progression vs robust response and acquired mechanisms of resistance. This analysis examines the influence of the genomic context on which the targeted alteration is inscribed on the outcome with agents targeting that alteration.

It was very apparent from NLMT that there was no benefit from targeting some of the common drivers in squamous lung cancer (LUSC). We therefore looked for alternative therapeutic vulnerabilities which has led to a trial of precision metabolic medicine, the CRUK funded **KETO-LUNG trial**.

Socio-Economic Diversity and the Criticality of Engaged PPI

KETO-LUNG, led by Birmingham ECMC Director, Middleton, is a feasibility trial exploring the impact of the addition of a ketogenic diet to standard chemo-immunotherapy in LUSC harnessing the unique metabolic vulnerability of LUSC with its exquisite dependency on anabolic glycolysis. This trial effectively inaugurates **Metabolic Precision Medicine** – disease-specific stratification for a targeted metabolic intervention by histology. This trial was developed with significant input from people with lived experience of cancer, including a PPI co-investigator, and is being delivered at **8 ECMC's in areas of socio-economic deprivation**. Expertise across this network of sites is integral to the successful prosecution of this complex intervention trial. We will analyse metabolic and redox shifts using tumoral 13C tracing at our **Metabolic Tracer Analysis Core** for the first time in any trial in advanced disease using biopsy samples. This technology could prove invaluable to other metabolic intervention trials being run across the network. The trial will be important in informing patients, their carers and physicians on the value of dietary changes in cancer.

The Very Real Issue of irAEs

A key focus area is the toxicity caused by immunotherapy used to treat people with solid cancers and we are developing predictive tests for immune-related Adverse Events (irAEs) in patients treated with Immune Checkpoint Inhibitor (ICI). We have shown that lung cancer patients developing severe irAEs have a pre-treatment lack of B regulatory cells, a key cellular population suppressing autoimmunity. **ICI Genetics**, led from Birmingham, is a national programme uncovering genetic (germline, inherited) causes of irAEs. We envision that these platforms will form the basis of an ECMC consortium, to develop much-needed biomarkers predictive of severe irAEs. This is likely to include Bregs, SNPs and combinations of the two. Validation and development of clinical grade biomarkers will be essential, and our GCP labs are well placed to deliver these. In Haem-Onc, we are uncovering the cellular specificities of the drivers of GVL and GVHD in order to disentangle these in order to improve outcomes and tolerability of allo-HSCT. We plan to start clinical testing and service evaluation of an immune effector cell-associated neurotoxicity syndrome (ICANS) cognition battery later this year

We will stive to develop ameliorative therapies, working closely with people with lived experience of cancer through the NCRI Lung Cancer Clinical Studies Group (Middleton, Chair), and have the ambition to broaden the scope to include other toxicities, including chemotherapy induced peripheral neuropathy (CIPN). We are currently working up a large programme of work in CIPN combining whole genome GWAS of oxaliplatin treated patients to look for germline drivers of neurotoxicity with rat models of oxaliplatin-mediated neuropathy and its prevention using agents in our previously published work in spinal cord injury models and which mimics pathologically CIPN.

Tackling the Poor Outcome of Immune ICB in pMMR CRC

Metastatic pMMR colorectal cancer (CRC) is largely recalcitrant to immune checkpoint blockade (ICB) therapy and based on our clinical and scientific excellence in CRC, we are using this disease as a paradigm to try and understand some of the mechanisms underlying resistance to immunotherapy specifically in those with liver metastases (LM) and to ask whether these might be therapeutically tractable. We have two main aims:

1. To improve the response to ICB in people with pMMR CRC and LM by converting CRC cells into surrogate antigen-presenting cells, using organoids and co-cultures as our experimental platform
2. To improve the response to ICB in people with pMMR CRC and LM by targeting the pivotal suppressors of an active T cell attack in LM, using patient derived tissue explants

These studies aimed at clinical translation will resonate beyond CRC given the poor response to ICB in those with immunogenic cancers and liver metastases.

In collaboration with Tejpar (Leuven) we have developed a biomarker validation strategy in pMMR CRC patients in the context of a platform trial of signal-of-activity studies of neoadjuvant immunotherapies (**FOXTROT-IO**, Co-Lead Middleton) in collaboration with Astra Zeneca. One such biomarker is our previously described co-ordinated immune response cluster (CIRC), a Th1-centric metagene. High expression of the CIRC in pMMR overlaps with expression in dMMR CRC. We plan to prospectively explore the predictive value of the CIRC and a range of other potentially predictive biomarkers using pathological response in the context of FOXTROT-IO.

Supporting the ECMC Network

Our Biomarkers and Liquid Biopsy theme provides the ECMC network with technical infrastructure and analysis expertise, to develop clinical grade biomarkers. We will use our expertise in technology development, clinical trial analysis and data management, to set new standards for biomarker development, and promote ECMC network collaboration. **Genomics Birmingham** offers novel genomic analysis services, which are utilised nationally in clinical trials and PM consortia. We will ensure that trial biomarker data from all biological samples are banked within a repository accessible to all ECMCs, promoting integrated data analysis. Together with CRUK, we are making data available on our accessible platforms, linking molecular datasets with patient clinical outcomes.

Understanding Genomic Diversity and Fostering Therapeutic Inclusivity

There is both a clinical and an ethical need to develop targeted therapies for underserved populations. A key objective of our Precision Medicine platform studies is to enlarge the number of people with cancer who can be usefully treated with targeted therapy. In line with this, we will focus increasingly in expanding targeted therapy options to populations that are underserved and/or those that have been less intensively genomically characterised.

We have formed an important strategic collaboration with the **Leicester ECMC**, drawing on their experience of engagement with ethnically diverse communities, to foster genomic equality, therapeutic inclusivity and participation for diverse ethnicities in Precision Medicine. Inclusive participation is essential to understanding differences in both efficacy and toxicity across populations. We are heavily involved in the **FOXTROT-GLOBAL** platform, to test pre-operative therapies in low- and middle-income countries. The first study will be a neoadjuvant programme of anti-PD-L1 in dMMR CRC patients in Nigeria.

We will complement Leicester's expertise in trial access in underserved populations with our genomic and bioinformatic capabilities to understand the available stratified medicine options for these individuals. We are currently working with various national and international partners to understand the genomic specificities of common cancers in ethnically diverse populations. This will better enable us to identify novel precision medicine options for underserved populations and to start to unravel through genome-wide association studies, differences in cancer treatment responses and in the toxicity of such therapies.

Birmingham ECMC - where Equality, Diversity and Inclusion inform what we do

Dimensions of Faith and Language

As one of the first **minority-majority cities** in the UK, Birmingham is well placed to explore the dimensions associated with faith and language. We are initiating interdisciplinary research between genomics, immunology and public health, to explore the impact that faith has on an individual's cancer journey. This will also have a wider reach with field work proposed in Africa. Additionally, we are well placed to leverage established links developed through the **NIHR Global Health Research Unit on Global Surgery** and its global hubs (Ghana, India, Mexico, Nigeria, Rwanda, South Africa). We are interested in exploring the role that language plays in treatment outcomes and recognise that effective community engagement and involvement will be essential. The dimension of language is especially important when considering the whole person, for whom certain symptoms may not have a literal translation in native tongue. As a developing area, we are very keen to establish new collaborations across the ECMC network.

Birmingham ECMC Senior Team

- Professor Gary Middleton - Director
- Professor Andrew Beggs - Deputy Director, and Biomarkers and Lipid Biopsy Lead
- Dr Manoj Raghavan - Precision Medicine Lead
- Dr Francesca Kinsella - Immunotherapy Lead
- Karen Turner - CRUK Senior Research Nurse and PPIE Lead

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Cambridge Experimental Cancer Medicine Centre

Who we are – our leadership and two of our funded staff

Bristi Basu, Academic Consultant in Experimental Cancer Therapeutics;
Cambridge University Hospitals NHS Foundation Trust
Cambridge ECMC co-lead
Bristi's research focus is in drug development and translating pre-clinical findings on lead candidate agents into early phase clinical trials of novel therapeutics, particularly in hepatobiliary and pancreatic tumours.

Duncan Jodrell, Professor of Cancer Therapeutics, University of Cambridge
Cambridge ECMC co-lead
Duncan's work endeavours to integrate and optimise the pre-clinical development and science-led clinical application of novel therapies and novel therapeutic combinations, including first into human (phase I) and associated studies.

Jane Bushen, Bio-sampling Team Lead;
Cambridge University Hospitals NHS Foundation Trust
Jane manages the Bio-sampling team at the Cambridge Cancer Trials Centre (CCTC), which deals with the blood, urine and tissue samples from patients who have consented to clinical trials. Some of these samples are used to support translational research.

Michele Bianchi, Research Nurse
Early Cancer Institute, University of Cambridge
Michele (Mick) coordinates diagnostic research studies focused on early detection of upper GI cancers. He is also part of a joint NHS and University service that runs the Barrett's oesophagus and Familial Gastric Cancer surveillance programmes.

What we're going to do

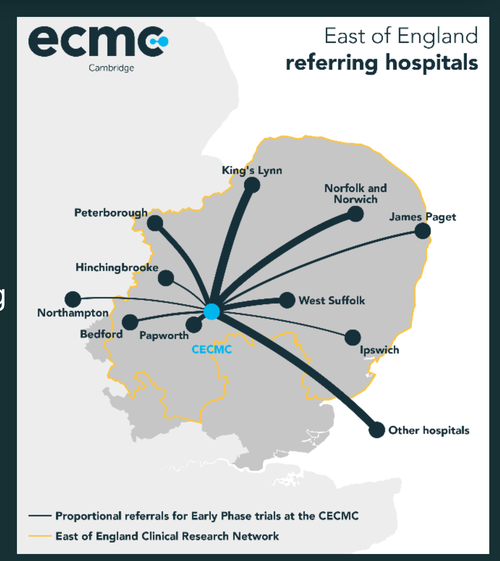
Our Mission
Champion research excellence in experimental cancer medicine for patient benefit.

Our Strategy
Build on our track record of:
- globally competitive translational research
- expertise in early phase trials using novel designs
- delivering impactful clinical biomarkers and diagnostic services

1. ***Early Cancer*** **innovations for risk prediction, detection and interception with minimally invasive technologies**
2. ***Personalised cancer medicine*** **by accelerating access to genomic profiling and innovative trial designs**
3. ***Innovative cancer imaging*** **inventing probes, tracers and methods to diagnose, monitor and treat cancer more effectively**
4. ***Maximise big-data use*** **integrating multimodal data streams - right treatment, right patient, right time**
5. ***Early collaboration*** **with PPI, academic and industry partners to deliver novel therapeutics and technologies**

Regional delivery network

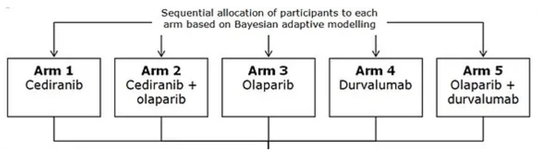
The CECMC is at the centre of CRN-E, the 2nd largest geographically in England, a diverse population of around 3.9M. CUH is the major recruiter to CRN-E cancer studies, recruiting >50% of patients in 2021/22.



Spotlight on CECMC trials

CI: Stewart **Phase**: II
Target participants: 76
Recruiting at: Cambridge, Glasgow.

By utilising a period when patients would otherwise remain untreated, WIRE enables investigation into the therapeutic effects and safety of individual or synergistic combinations of systemic anti-cancer agents without any delay in potentially curative nephrectomy.



Its primary aim is to evaluate changes in multiple molecular, genetic and imaging-based factors in relation to the tumour and host response to the drugs being tested, as well as to develop new models of RCC for better pre-clinical testing of promising Investigational Medicinal Products (IMPs) in the future.

The results will guide and facilitate greater understanding of the optimal combinations of anti-cancer drugs to prioritise for later phrase clinical trials, as well as potential development of predictive biomarkers or methods of tracking response.

Sponsor: Cambridge University Hospitals NHS Foundation Trust; **Funders:** Mark Foundation for Integrated Cancer Medicine & Cancer Research UK Cambridge Centre

CI: Jodrell **Phase**: I
Target participants: 55
Recruiting at: Cambridge, Glasgow, Leeds and Southampton.

Based on preclinical research performed in the CRUK Cambridge Institute, the ATRiUM clinical trial is evaluating the combination of an ATR inhibitor with gemcitabine, with a clinical line-of-sight to patients with pancreatic cancer. Detailed translational research studies will identify both pharmacodynamic and predictive biomarkers. It is hoped that the latter will identify sub-groups of patients, most likely to benefit from the combination. ATRiUM uses a model based, combination trial design assessing varying doses of both gemcitabine and AZD6738.

AZD6738 dose (mg) and frequency	Gemcitabine dose (days 1, 8 and 15, q. 28 days)			
	500 mg/m²	625 mg/m²	800 mg/m²	1000 mg/m²
120 continuous				
120 intermittent		(Cohort 5a) ✓		
80 continuous		(Cohort 4a) ✓		
80 intermittent		(Cohort 3a) ✓	(Cohort 4b) ✓	
40 continuous		(Cohort 2a) ✓	(Cohort 3b) ✓	(Cohort 4c) ✓
40 intermittent		(Cohort 1a) ✓	(Cohort 2b) ✓	

29 patients have been registered and recruitment is ongoing in the four UK Centres.

Sponsors: Cambridge University Hospitals NHS Foundation Trust and University of Cambridge; **Funders:** CRUK Cambridge Centre; Astra Zeneca

Cambridge Cancer Research Hospital

The seven storey 26,000 m² Cambridge Cancer Research Hospital will soon start construction on the Cambridge Biomedical Campus, bringing together cutting-edge NHS clinical space with three new University of Cambridge research institutes, so patients will benefit from the latest innovations in cancer science.

The project is being 'co-produced' by staff, patients, and partners, working together on service design and improvement on an equal basis.

Learn more about the CRH

Advancing precision cancer medicine

The Mark Foundation Institute for INTEGRATED CANCER MEDICINE
GE HealthCare

The ICM partnership with GE Healthcare aims to combine commercial, clinical and academic expertise to create a comprehensive clinical decision-making support platform for use in MDT settings. This platform will bring together in one place different types of data collected from cancer patients from diagnosis through treatment, no matter where this data is collected. Then advanced machine learning methods, developed by MFICM researchers, will integrate the data sources to help clinicians understand what scans or test results mean when analysed together, so they can make faster, better-informed and personalised treatment decisions. A successful proof of concept has been developed using retrospective data from the OV04 Ovarian cancer translational study (CI: Brenton) and AI-based radiomics methods (Crispin-Ortuzar) to provide insights into tumour progression and subsequent prognosis.

This work is being carried out in collaboration with CUH and local district general hospitals to ensure that the approach and platform will be able to implemented broadly across the NHS and elsewhere.

Get in touch

ECMC in Cambridge

ECMC@cancer.cam.ac.uk

Connect with us on Twitter: @CambridgeECMC

Latest events

Poster author: Kate Donoghue, Programme Manager for Cambridge ECMC, University of Cambridge

Jointly funded by: CANCER RESEARCH UK; Little Princess Trust; NIHR National Institute for Health and Care Research; Ymchwil Iechyd a Gofal Cymru Health and Care Research Wales; CHIEF SCIENTIST OFFICE; HSC Public Health Agency Research and Development

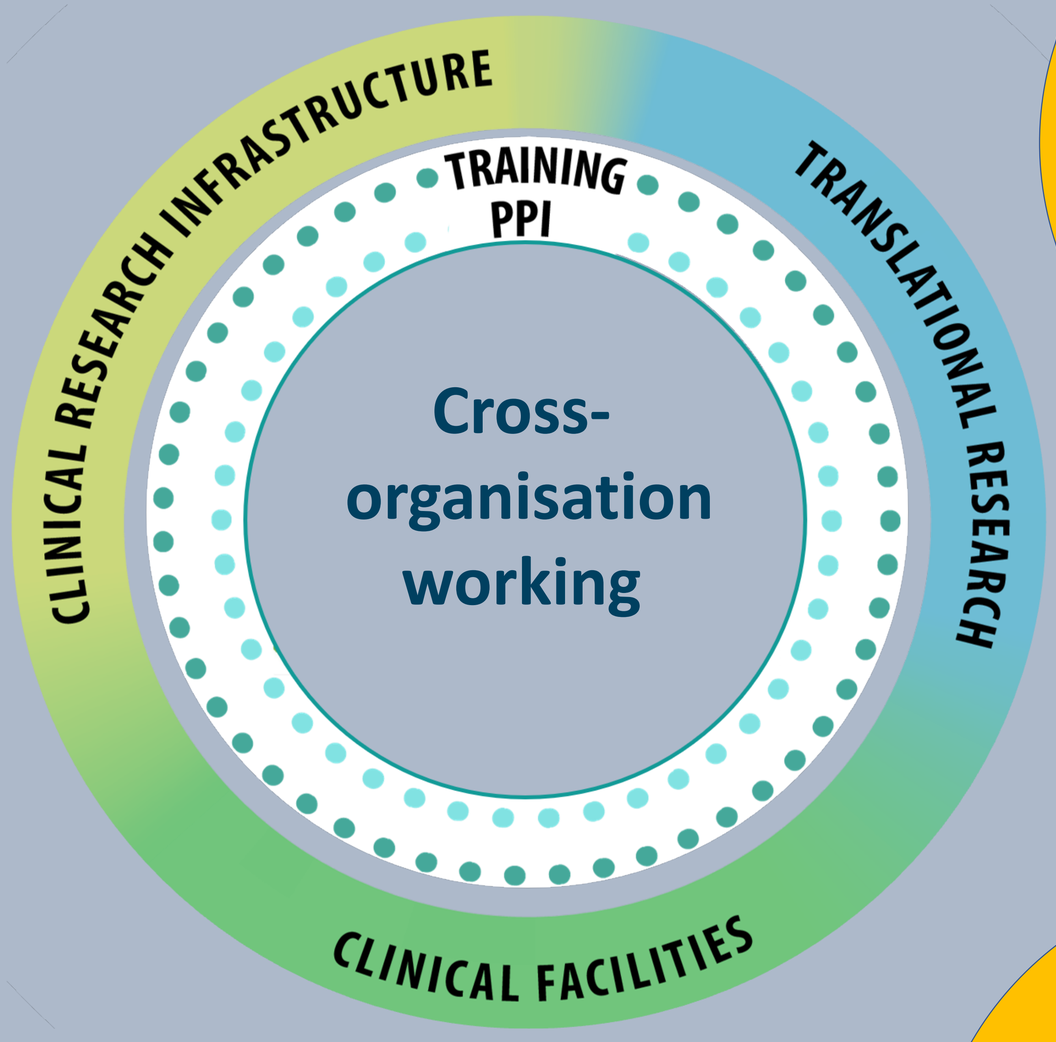
CARDIFF UNIVERSITY
PRIFYSGOL CAERDYDD

ecmc Cardiff

Highlights

Haematology | **Solid**

Cancer focus



Patient centred

Future Directions

Advanced Therapies

- Cellular
- Virotherapy
- Toxicity /Resistance
- Operational delivery
- Upskilling workforce

Data Integration/ Smart Biomarkers

- Trial matching
- Federated learning
- Imaging/molecular Biomarkers
- Data linkage and standardization
- Complex data handling (AI)

Nurse-led Research

- Improving patient experience
- Quality of life (QoL)
- Digital tools for recruitment and monitoring
- Academic training

Impactful PPI

- Broaden Patient access
- Dedicated resourcing
- Training and networks
- Commercial engagement

Drug RT combinations

- Imaging and Radiomics
- Immunotherapy responses
- Translational tissue collections

Joanna Zabkiewicz, Robert Jones, Oliver Ottmann
Contact: CardiffECMC@Cardiff.ac.uk

ecmc Jointly funded by: CANCER RESEARCH UK · Little Princess Trust · NIHR | National Institute for Health and Care Research · Ymchwil Iechyd a Gofal Cymru Health and Care Research Wales · CHIEF SCIENTIST OFFICE · HSC Public Health Agency Research and Development

Paediatric Network – Cardiff

Ceri Hogg, Rhian Thomas-Turner & Madeleine Adams

The Centre

- Cardiff Paediatric ECMC is located at the Noah's Ark Children's Hospital for Wales (NACHfW).
- The dedicated children's hospital was opened in 2005 and was the first purpose-built children's hospital in Wales.
- Children with cancer are treated on Rainbow Ward and Teenagers and Young Adults (TYA) of age 16-25 years are treated at the Teenage and Young Adult Unit.
- Cardiff is a Principal Treatment Centre (PTC) for new cancer referrals in South Wales.
- We have a designated Children and Young Adult Research Unit (CYARU) which is the first purpose-built research unit for children and young adults in Wales.

Aims

- Working closer with national colleagues
- Establishing ourselves within the ECMC network.

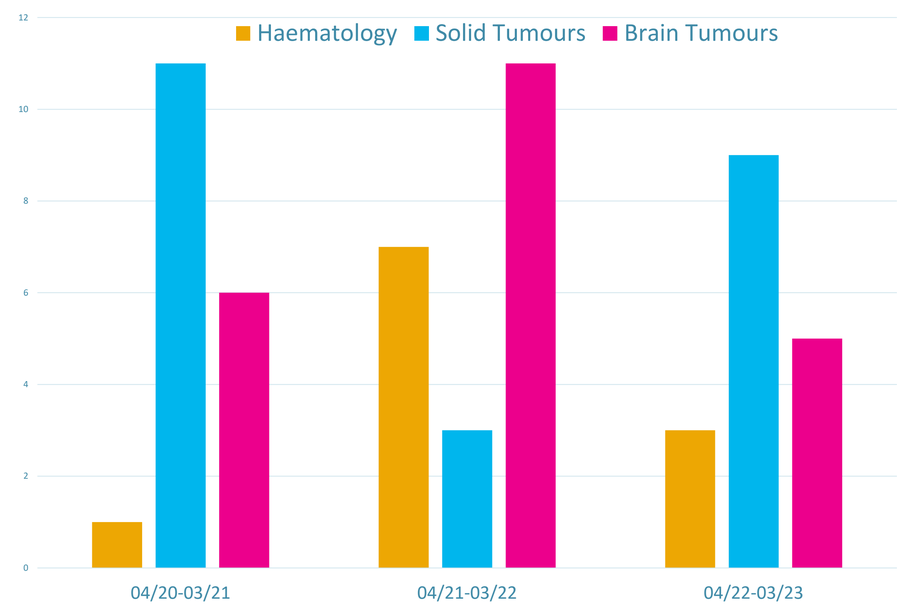
Challenges

- Small centre
- Establishing ourselves nationally
- Pan age establishment

Advantages

- Equity of access closer to home.
- Devolved nation representation

Relapsed patients over the last 3 years



Quinquennium Plan

Early

- Launch portfolio of EP studies.
- Focus on recruitment of TYA and paediatric patients.
- Work with ECMC centres to establish QoL studies.
- Continue to contribute to regional ECMC networks.
- Further develop WGS and molecular testing to facilitate trial activity.

Mid point

- Build on recruitment across all ages
- CUBRIC - Cardiff University Brain Research Imaging Centre - collaboration.
- Strong international (EPPSG) and national (NCRI/ ALL) links for trial development.
- Development of digital tools.

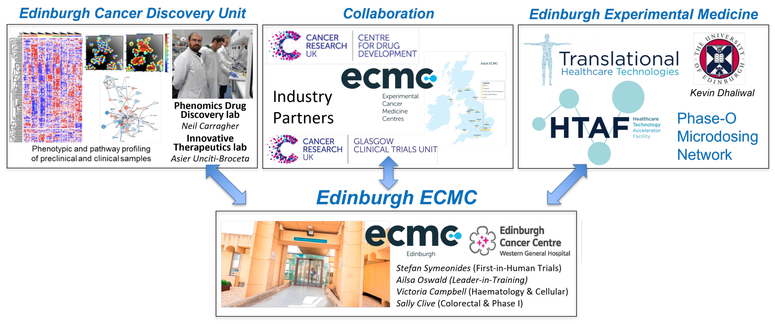
Year 4/5

- Maintain ECMC adult collaborations
- Establish full compliment of EP studies.
- Development of strong links with adult laboratory colleagues.
- Full portfolio to provide equal access for paediatric and TYA patients in Wales.

Jointly funded by: CANCER RESEARCH UK; Little Princess Trust; NIHR | National Institute for Health and Care Research; Ymchwil Iechyd a Gofal Cymru Health and Care Research Wales; CHIEF SCIENTIST OFFICE; HSC Public Health Agency Research and Development

Themes

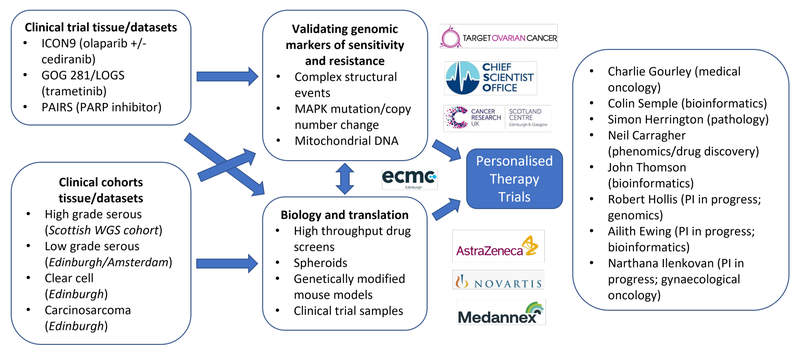
1 First in Human Drug Development



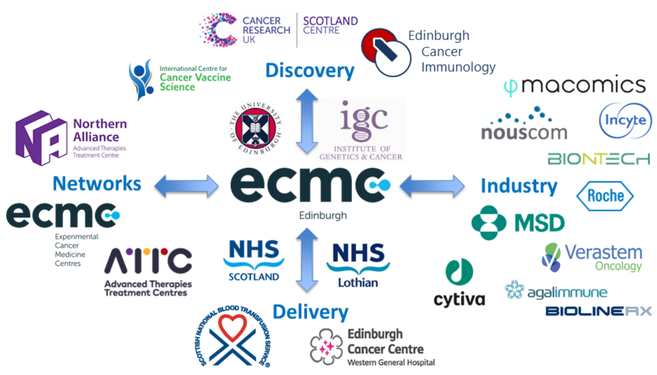
2 Brain Cancer

- Paul Brennan (neurosurgeon)
- Steven Pollard (bioscience)
- Margaret Frame (bioscience)
- Neil Carragher (drug discovery)
- Asier Unciti-Broceta (drug discovery)
- Adam Waldman (neuroradiology)
- Gerry Thompson (neuroradiology)
- Sara Erridge (clinical neuro-oncology)
- Faye Robertson (PI-in-progress; clinical neuro-oncology)
- Karin Purshouse (PI-in-progress; medical neuro-oncology)

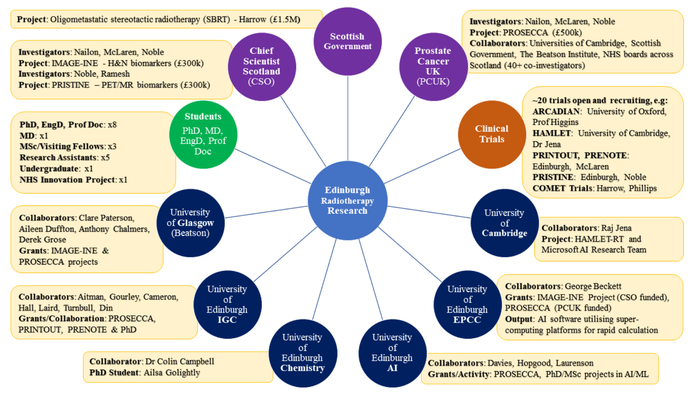
3 Molecular Sub-Types of Ovarian Cancer



4 Cancer Immunotherapy



5 Personalisation of Radiotherapy



6 Emerging Themes

Haematological Malignancies

- Phase I, cellular and translational

Prevention & Early Detection

- Colorectal and Hepatocellular

Mission Statement

"The Edinburgh ECMC will be a core node for UK and international **drug development**, focusing on **first-in-human** trials of exciting new therapies, and the development of robust selection markers to **personalise** patient treatment.

We will build on an ethos of inclusive **collaboration**, **innovation** and efficient trial **management** to provide a **world-class**, **accessible, equitable** service for **all** patients **throughout** the country."

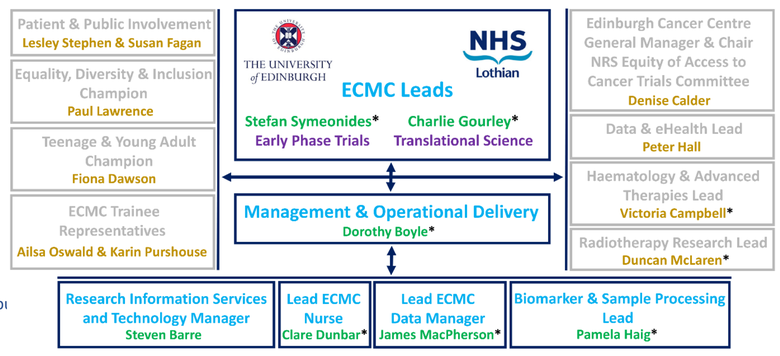
ecmc Edinburgh

Goals

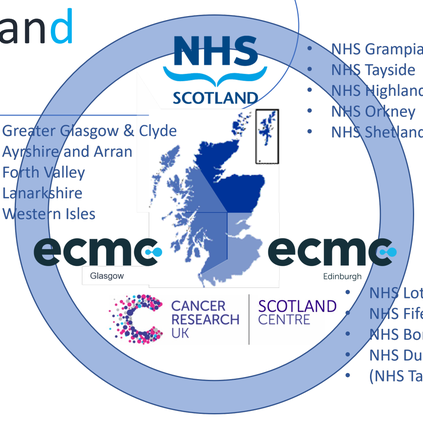
"The Edinburgh ECMC will:

- Translate **CRUK Scotland Centre** research into the clinic
- Personalise treatment through **clinical samples** and **data**
- **Collaborate** closely: Scotland, ECMC network & Industry
- Improve access for **all** patients
- Accelerate trial **set-up** and **efficiency**
- Expand early phase **researchers** and **trials**
- Ensure the new **Edinburgh Cancer Hospital** has experimental cancer medicine at its core"

Leadership Team



Scotland

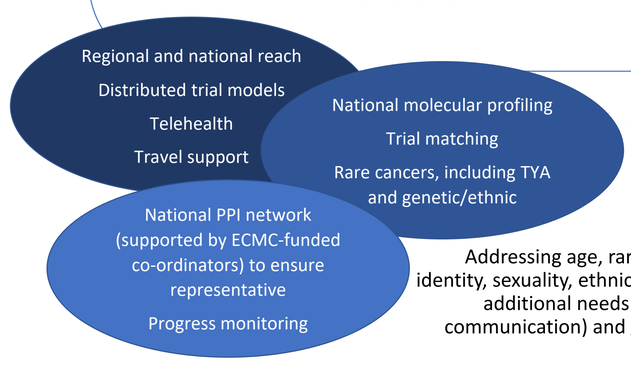


National phase I service:

- Coordinated trial portfolio (esp rare & molecularly-selected)
- Shared referral form
- Shared assessment sheet
- Weekly joint trial matching meeting
- National Molecular Tumour Board
- National MDT for CAR T
- National cancer trials nurses group
- National PPI network
- Telehealth & distributed care

Whole-Scotland approach to accessing clinical trials & technologies, whoever you are & wherever you live

Inclusion



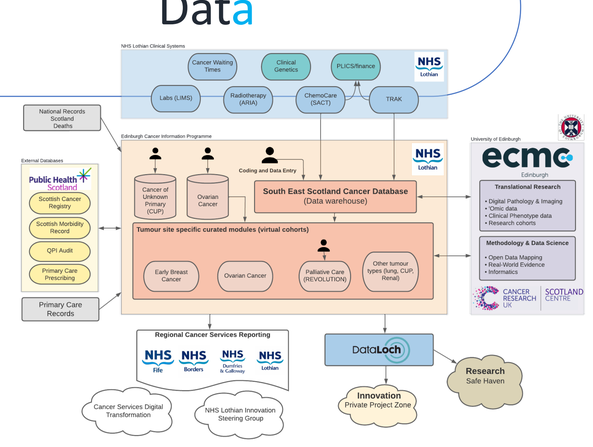
Paul Lawrence *(ECMC EDI Champion)*
Fiona Dawson *(TYA Champion)*

Addressing age, rarity of disease, gender, identity, sexuality, ethnicity, social deprivation, additional needs (physical, intellectual, communication) and **geographic inequality**

2022 Scottish Government report on Equity of Access to Cancer Trials (Denise Calder)

Environment

Data



ECMC Network & ECMC North

ecmc North — Newcastle, Sheffield, Leeds, Manchester, Belfast, Liverpool, Glasgow, Edinburgh

An initiative bringing ECMCs in the North together to foster closer collaborations and sharing of resources, complementing ECMC Network activities

- **8** Created by Newcastle, Sheffield and Leeds ECMCs; expanded to include Manchester, Belfast, Liverpool, Glasgow and Edinburgh
- **21** Number of meetings held to discuss scientific and operational collaborations, share best practice and provide peer support
- **3** Events organised by ECMC North: Scientific Showcase, Bone Oncology Workshop, COVID-19 Educational Event
- **1** The ECMC North group obtained external funding for development of an interactive ECMC COVID-19 Community Hub

1+1 Collaborative clinical trials: ECMC North provided the ideal platform for rolling out the TARGET National trial and are developing our first ECMC-North early phase trial of high dose Mannose in colorectal cancer

2023-2028

- Establish an ECMC North Biomarker Research Forum to share biomarker portfolios, protocols/validation plans and to horizon scan upcoming biomarker technologies to support ECMC North Trials.
- Increase new clinical trial activity, starting with the Mannose trial and the EVIDENT ex vivo screening platform.
- Develop an ECMC North Pathology Research Forum

Sharing knowledge and experience to enhance collaborations

- Regular meetings to share experience and approaches to continued trial activity during the COVID-19 pandemic
- Shared clinical trial information - developed a precursor to EC Trial finder
- Exchange of ideas and shared best scientific and operational practice – provided a forum for exploring novel trial ideas and problem solving

Local

Edinburgh & Glasgow
80 Cancer Research PIs

CANCER RESEARCH UK | SCOTLAND CENTRE

THE UNIVERSITY of EDINBURGH

igc INSTITUTE OF GENETICS & CANCER

- Host and Tumour Profiling Unit
- ECRC Tissue Group
- Edinburgh Cancer Discovery Unit
- Bayes Centre & DataLoch

NHS Lothian

Edinburgh Cancer Centre Western General Hospital

Re-structured early phase and radiotherapy teams
Direct **co-ordination** with R&D and support services

Expanded facilities:

- Dec 2020: new **Clinical Trials Data Centre**
- June 2021: new **Clinical Trials Facility** (50% expansion)
- Oct 2021: new **Haematology Centre** with dedicated cellular therapies unit and ITU facilities
- **Regional** investment across SESCRN hospitals

Expanded **Research Information Services**:

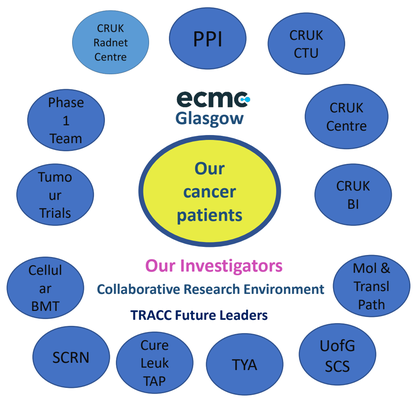
- Portfolio oversight and set-up coordination
- Real-time reimbursement
- NHS savings identified to **reinvest**

ecmc

Jointly funded by: CANCER RESEARCH UK | Little Princess Trust | NIHR National Institute for Health and Care Research | Ymchwil Iechyd a Gofal Cymru Health and Care Research Wales | CHIEF SCIENTIST OFFICE | HSC Public Health Agency Research and Development

Glasgow Adult ECMC

From Discovery Science to Clinical Evaluation

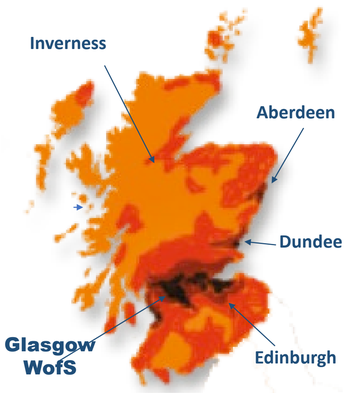


Research Environment

- Beatson - CRF
- CR-UK CTU
- SCRN
- Cure Leukaemia TAP
- Scottish Stem Cell Transplantation / CAR-T
- SNBTS
- NA-ATTC
- IMPACT
- Bio-Repository
- Glasgow Tissue Research Facility
- GPOL & Molecular Genetics
- CR-UK CDD Biomarkers Hub
- CR-UK Centre
- CR-UK BI
- UoG
- (SCS, SII, Cardio-Oncology)
- POG
- CR-UK RadNet
- Molecular Pathology
- Digital Pathology
- MRC Mouse Genetics Network
- Imaging Centre of Excellence
- Stratified Medicine Scotland–Innovation Centre
- The Living Laboratory, Glasgow
- McNab Centre for Cancer Innovation
- **PAEDIATRIC ECMC**

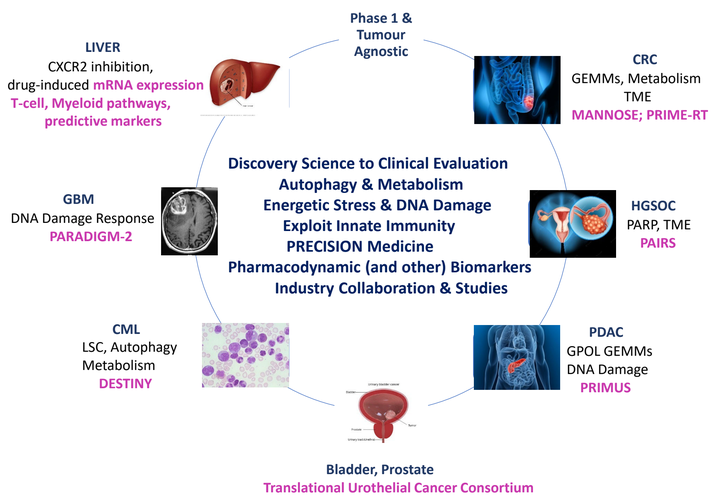
- **Access to early phase trials & experimental medicine for other Scottish Cancer Centres**
- **Equity of access for geographically–remote communities**
- **Inclusion of areas of high deprivation**

- **WoS Population: 2.5 million**
- **8,438 new patients per year**
- **Beyond WoS (5.5 million)**



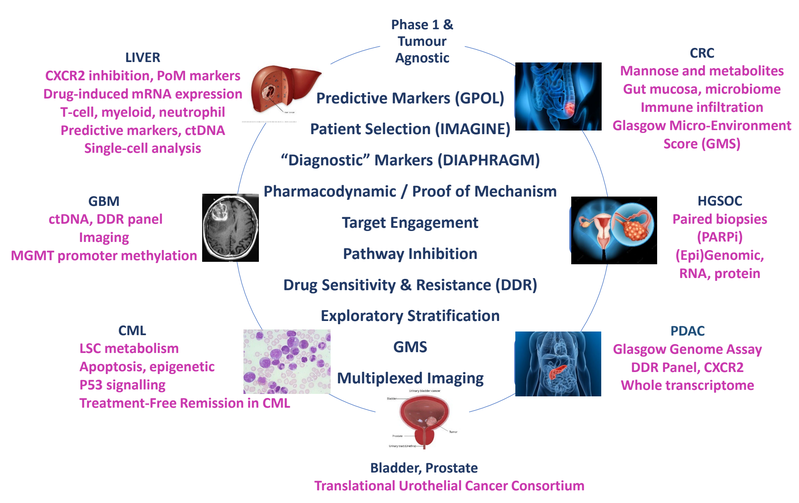
Bringing Discovery Science to the Clinic and to the Network

Cytotoxics, ADCs, Molecular Targeting, Immune Evasion, Precision Platforms, Cellular Therapies



Bringing the Laboratory – Clinical Interface to the Network

Biomarker Studies



Contributing to the Network

a pan-Scotland approach

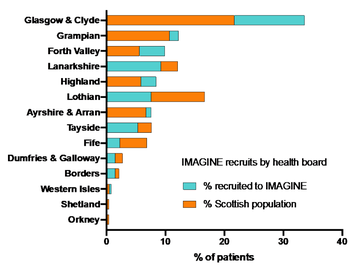
"whoever you are & wherever you live"

Partnership Initiatives
Coordinated trial portfolio
(rare & molecularly-selected)
Shared referral form
Shared assessment sheet
Weekly joint trial matching meeting
National Molecular Tumour Board
National cancer trials nurses group
National PPI network
Telehealth & **distributed care**

Delivering Equitably to a Diverse Population

Inclusion across Scotland

"whoever you are & wherever you live"



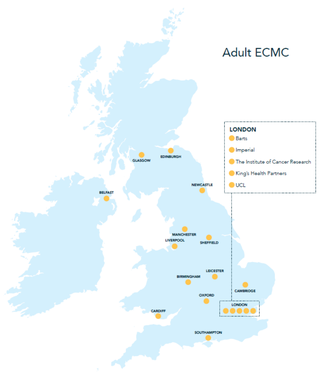
Across all Health Boards
Across all deprivation indices

Accelerating Activity

"decentralised trials"
apply lessons learned to TAPISTRY in Scotland

Collaborations & Alliances

Collaboration with every Adult ECMC



ecmc North

Newcastle, Sheffield, Leeds, Manchester, Belfast, Liverpool, Glasgow, Edinburgh

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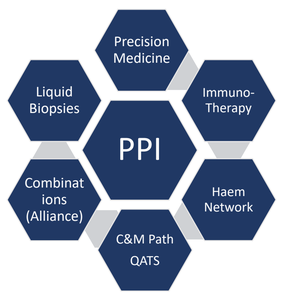
Establish an ECMC North Biomarker Research Forum to share biomarker portfolios,
Increase new clinical trial activity, starting with the Mannose trial and the EVIDENT *ex vivo* screening platform.
Develop an ECMC North Pathology Research Forum.
Collaborations around digital healthcare products made available through the CRUK UpSMART digital accelerator program.

ECMC Working Groups



Not just the Working Groups

Accelerated set-up pilot
JING Faculty & Committee
Industry Alliances (Discovery, Biomarker, & Clinical)
DEFINE-CONSORT
International Collaborations & Alliances

Patient & Public Involvement

Co-Investigator - Elspeth Banks
ECMC Network Steering Committee Member; ECMC PPI Group, support to Edinburgh PPI

PPI Panel and PPI Oversight Group
we provide support, mentoring, development programmes involved at all stages of trial design, development, delivery, TMGs co-applicants– early phase trials grants

Future plans
Involve TYA service for PPI representation
Build relationships with patients groups in Dundee, Aberdeen, Inverness
Engagement and outreach to other centres (regular newsletters, e.g. every 4-6 months)
Embed PPI within each of our strategic research themes
Increase diversity of PPI team (e.g. Ethnic minority groups, socio-economic diversity)
Continue to enhance our PPI strategy -
discussion, observations, and feedback, from our PPI panel and PPI oversight group
Involvement in broader PPI forum across our research environment and pan-Scotland

Future Workforce

Train, Retain, Recruit

TRACC Intercalated MB/BDS-PhD students
9 UoG/UoE medical students, 1 UoG dental student
TRACC Clinical Lecturers and CRTFs
11 UoG/UoE lecturers from various cancer-focused disciplines
Clinical (Trials) Research Fellowships
ECMC, Gyn, BMT / ATIMPs, Lymphoma, GI & Brain – NIHR Associate PI
Senior & Intermediate Fellows
Surgery Radiotherapy Medical Oncology Hemato-Oncology

From Undergraduate

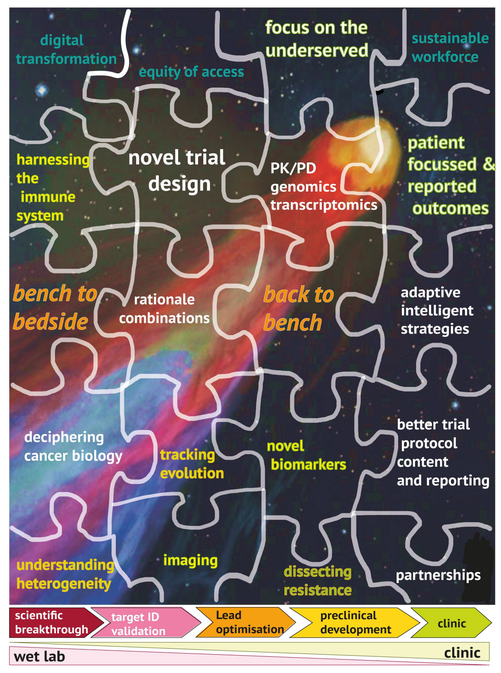
To Senior PI

Bench to Bedside and Back Again!

Drug Development Unit at The Institute of Cancer Research and Royal Marsden

Committed to transform cancer care as rapidly as possible

- **Accelerate clinical translation** through drug development and focused biomarker studies, developing transformative therapeutic strategies across the network.
- **Elucidate cancer biology,** delivering re-iterative bench to-bedside and back-to-the-bench research dissecting treatment resistance, understanding heterogeneity and evolution, validating novel targets, and qualifying impactful biomarkers.
- Improve trial design and conduct by generating consensus driven reporting guidelines **(extensions of CONSORT and SPIRIT guidelines for Phase 1 trials)**
- **Seamlessly transition novel therapeutic strategies to later trials** with partners.
- **Run industry-sponsored and academic trials** (ICR/RMH & CRUK-CDD sponsored), with 30% of the patients we serve being treated on investigator-initiated trials.
- **Adapt and improve trials to PPIE partner recommendations** (eg video PIS; ePROs).
- **Integrate novel technologies** (eg hyperplex immunohistochemistry, digitization, metagenomics, liquid biopsies, single cell analyses, spatial transcriptomics)
- **Train** next generation of medical, paramedical and clinical trial management Units



Improving patients experience in clinical trials

- Incorporating **decentralising trial assessments** within trial protocols when safely feasible
- Supporting **virtual consultations** where possible
- Introducing **advance inconvenience payments** for patients
- Incorporating **PROs/ePROs in dose finding trials** to improve patient experience and investigator's perspectives of type, frequency and severity of adverse events

Improving trial information sharing and consent processes

- **Video based information through a pilot trial**, explaining on what clinical trial participation entail, with information shared digitally by medical, nursing and paramedical staff
- Introducing **virtual consent processes to allow for pre-screening on specific biomarkers,** using archival tissue
- Developing **eConsent processes** within Royal Marsden digital transformation team to establish a process whereby patients' consents are captured digitally while maintaining GCP compliance

Study protocol for a randomised controlled trial of enhanced informed consent compared to standard informed consent to improve patient understanding of early phase oncology clinical trials (CONSENT)

Abhijit Pal[1,2,3], Sarah Stapleton[2], Christina Yap[4,5], Julia Lai-Kwon[1,2], Robert Daly[1,2], Dimitrios Magkos[1,2], Bindumalini Rao Baikady[1,2], Anna Minchom[1,2], Udai Banerji[1,2], Johann De Bono[1,2], Deme Karikios[3], Frances Boyle[3], Juanita Lopez[1,2]

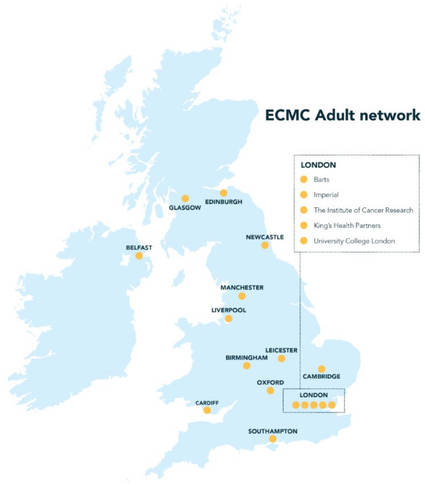
Serving underserved population

- ~14% of our patients treated on Phase 1 trials come from the most economically deprived postcodes in the UK (deciles 1-3)
- Working with PPI/E groups to **reach to underserved patient groups**
- Identifying underserved groups, including **>80Y patients, younger Adults, patients with intra-cerebral malignancies**

Improve trial access for the elderly with the **programme of oncogeriatric assessment and multidisciplinary prehabilitation** to optimise physical health and holistic care

Delivering together

- **Delivering Investigator Initiated Trials, in collaboration with multiple ECMC Centres**, leading several IMPs transitioning to later phase trials (eg: RAF/MEK inhibitor single agent trial led to pivotal trials in low grade ovarian cancer and *KRAS* mutated NSCLC)
- **Improving trial conduct through infrastructure digitalization and sharing best practices** across the network (eg: remote Monitoring, electronic TMF and ISFs, ePROs, Direct Data transfers)
- **Working with network** to improve trial set up, delivery and access (eg:Trial Prioritisation, EC Trial Finder, Expediting trial start up activities, Improved trial costing and budgets)
- **Building Capacity** via structured student internship programmes and partnerships with Universities



NIHR | Biomedical Research Centre at The Royal Marsden and the ICR

Wellcome Trust

CANCER RESEARCH UK

Image: www.dezeen.com/2016/09/26/rogers-stirk-harbours-cancer-treatment-centre-london-guys-hospital/

LTX-315 oncolytic peptide

LTX-315 is a synthetic 9-mer peptide which causes membranolysis on direct injection into a tumour.

A dose-ranging Phase I trial was performed in Guy's CRF, as well as a number of other centres across Europe.

39 patients, with a range of solid tumour types, were treated.

In addition to tumour necrosis and significant increases in intralesional $CD8^+$ T cells, LTX-315 caused abscopal effects (Figure 1).

LTX-315 was generally well tolerated, with only 10% of patients experiencing grade 3 adverse effects (hypersensitivity or anaphylaxis).

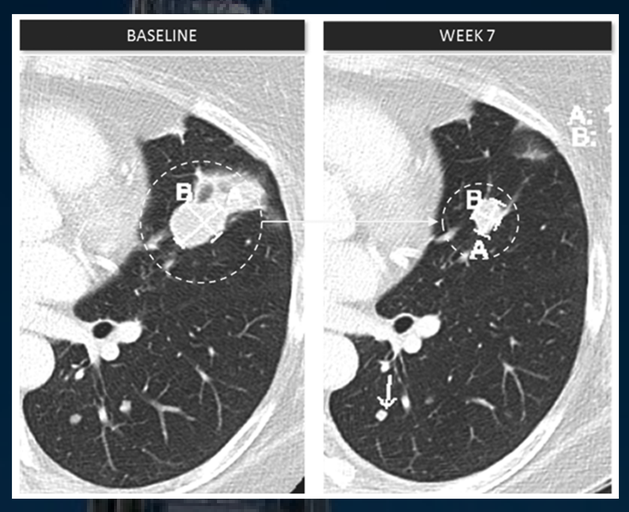


Figure 1. CT scans showing a 64% reduction in the size of a lung lesion in a patient with leiomyosarcoma who received injection of LTX-315 into a gluteal muscle lesion

Funded by Lytix Biopharma AS and NIHR

Spicer J, Marabelle A, Baurain JF et al. Safety, Antitumor **Activity, and T-cell Responses in a Dose-Ranging Phase I Trial of the Oncolytic Peptide LTX-315 in Patients with Solid Tumors.** Clin Cancer Res. (2021) 15:2755-2763. doi: 10.1158/1078-0432.CCR-20-3435

MOv18 IgE antibody - 1st in class

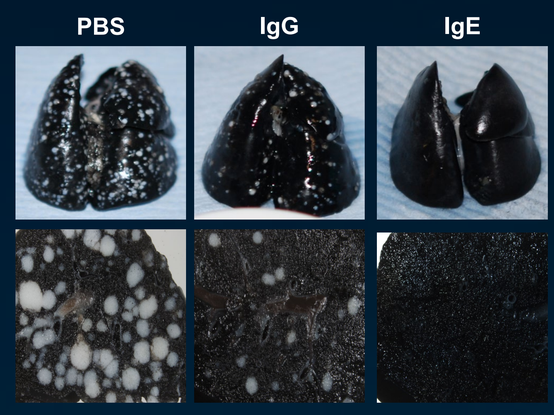


Figure 2. Pulmonary metastases from syngeneic tumours expressing FRα in an immunocompetent rat model. IgE has a greater antitumour effect than IgG

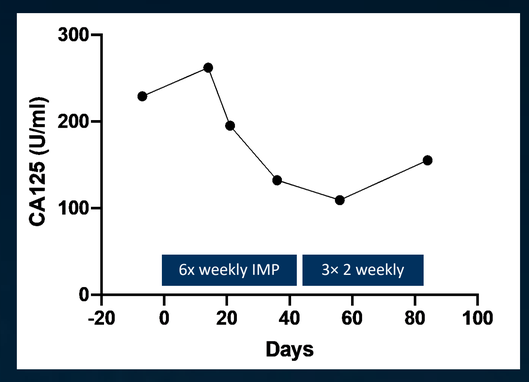


Figure 3. A reduction in the tumour biomarker CA125 was seen in a patient receiving MOv18 IgE at a total dose of 700μg, as well as shrinkage of peritoneal metastases

A first-in-human, first-in-class trial of MOv18, a chimeric monoclonal IgE, was performed in 24 patients with solid tumours expressing folate receptor-alpha (FRα). IgE has been shown to have greater antitumour activity than IgG in immunocompetent rats (Figure 2). The trial found that MOv18 IgE was generally well tolerated, with an anaphylactic reaction occurring in only one patient. One patient experienced shrinkage of peritoneal metastases and an accompanying fall in CA125 (Figure 3).

Funded by CRUK

Spicer J, Basu B, Montes A et al. **Phase 1 trial of MOv18, a first-in-class IgE antibody therapy for cancer.** Cancer Res (2020) 80 (16_Supplement): CT141.

- **Based in the NIHR Clinical Research Facility at Guy's, an MHRA-accredited Phase 1 Unit**
- **Strengths & interests in novel immunotherapies**
- **Recent trials include translation of new therapies discovered at King's**

King's Health Partners ECMC

King's Health Partners

***Phase 1 PIs**: James Spicer (ECMC Lead), Debashis Sarker (co-Lead), Debra Josephs, Rebecca Kristeleit, Arnie Purushotham*

T4 CAR-T

T4 is a CAR T cell trial in which patients' T cells are harvested and modified to express the following receptors:

4αβ – this drives the growth of engineered T-cells in the presence of IL-4. It is used to expand cell populations ex vivo. No manufacturing failures have ocurred (Figure 4).

T1E28z – this chimeric antigen receptor (CAR) binds to all ErbB dimers.

So far, 17 patients with squamous cell carcinoma of the head and neck have been treated. The therapy has been well tolerated and there is some evidence of survival superior to historical controls (Figure 5). The trial has a disease control rate (DCR) of 69%.

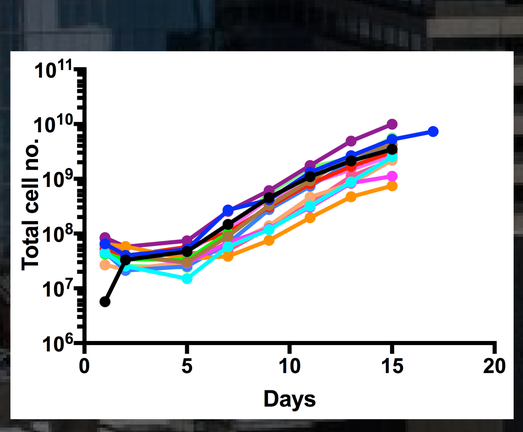


Figure 4. Expansion of engineered T cells in response to IL-4

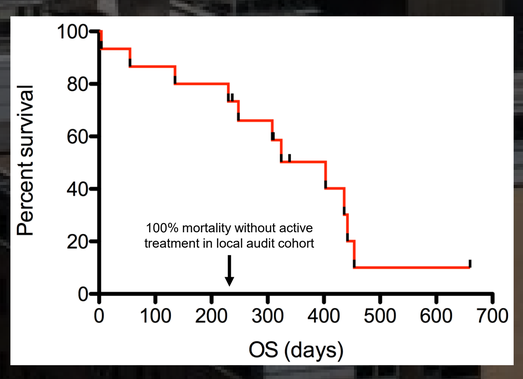


Figure 5. Kaplan Meier curve showing overall survival (OS)

Funded by the JP Moulton Charitable Foundation, Wellcome Trust, NIHR and CRUK

Papa S et al. **T4 immunotherapy of head and neck squamous cell carcinoma using pan-ErbB targeted CAR T-cells** *Cancer Res* (2017) 77 (13_Supplement): CT118

RNA therapeutic

The OUTREACH trial is a first-in-human Phase I study into the effect of MTL-CEBPA on patients with advanced liver cancer. MTL-CEBPA is a small activating RNA therapeutic designed to upregulate C/EBPα, a transcription factor that acts as a tumour suppressor.

38 patients were treated.

Following MTL-CEBPA, 7 patients received tyrosine kinase inhibitors (TKIs), 3 of these had a complete response (Figure 6). Further trials are underway to explore this promising combination.

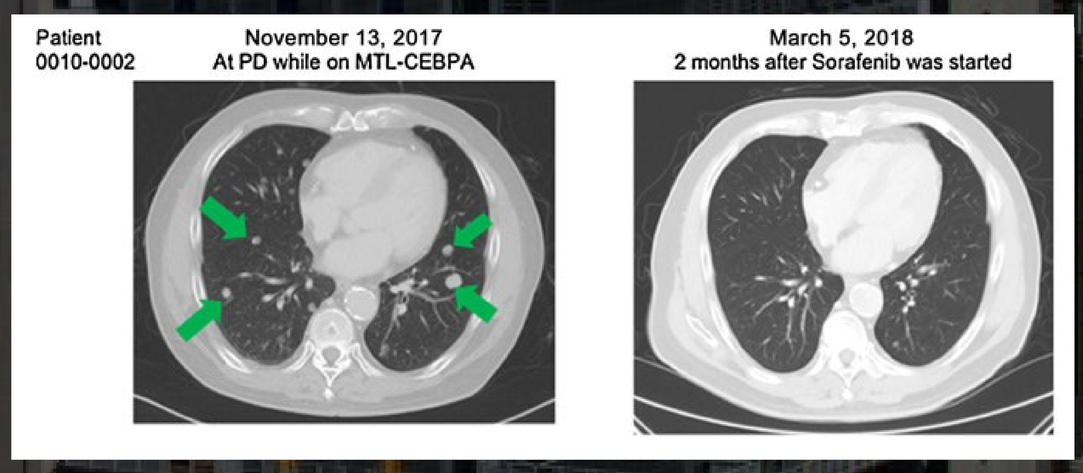


Figure 6. A patient experienced a complete radiological response in their lung metastases (from a primary tumour in their liver) when they were treated with the TKI sorafenib following MTL-CEBPA

Funded by MiNA Alpha Ltd, CRUK, and NIHR

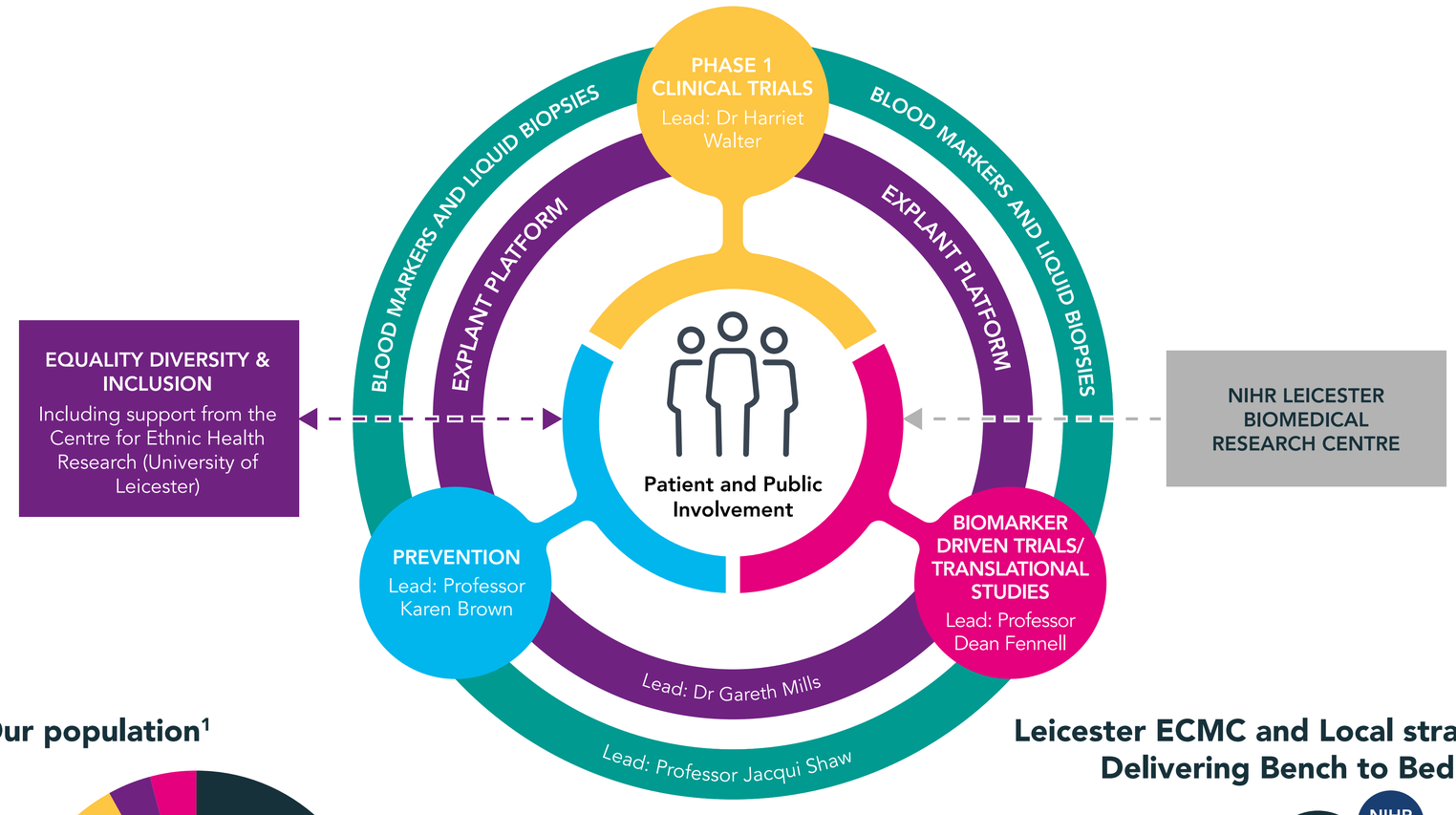
Sarker D, Plummer R, Meyer T et al.. **MTL-CEBPA, a Small Activating RNA Therapeutic Upregulating C/EBP-α, in Patients with Advanced Liver Cancer: A First-in-Human, Multicenter, Open-Label, Phase I Trial.** Clin Cancer Res. 2020 26(15):3936-3946. doi: 10.1158/1078-0432.CCR-20-0414

ecmc Jointly funded by: CANCER RESEARCH UK · Little Princess Trust · NIHR National Institute for Health and Care Research · Ymchwil Iechyd a Gofal Cymru Health and Care Research Wales · CHIEF SCIENTIST OFFICE · HSC Public Health Agency Research and Development

ecmc Leicester

- **Dr Harriet Walter** (ECMC Clinical Lead)
- **Professor Karen Brown** (Professor of Translational Cancer Research, ECMC Co-Lead, Prevention Theme Lead)
- **Professor Anne Thomas** (Professor of Cancer Therapeutics, ECMC prior Lead)

Leicester ECMC Overview

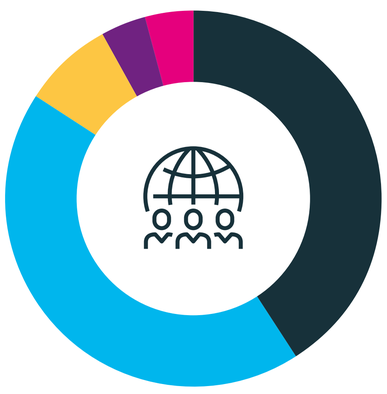


Our population[1]

Population 1.85M

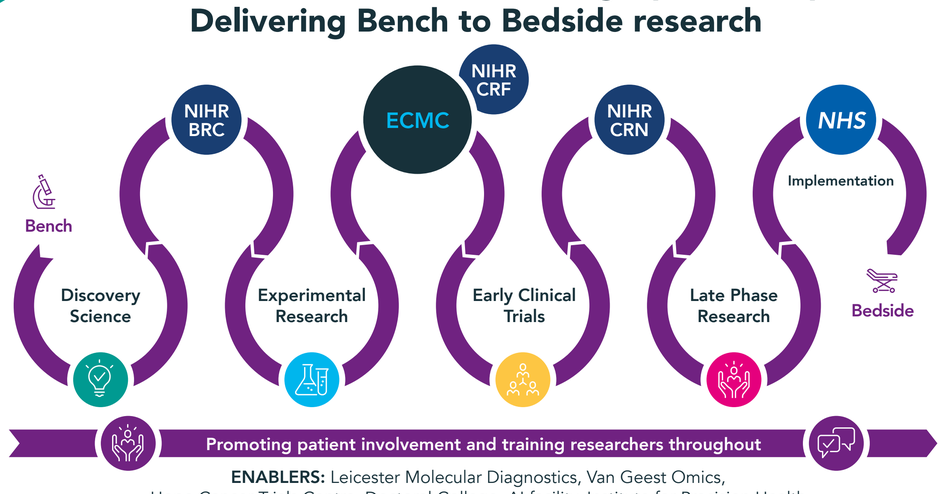
Specialist Cancer Services 3M

Longest Covid-19 lock down



In 2021, 43.4% of usual residents in Leicester identified their ethnic group within the "Asian, Asian British or Asian Welsh" category.

Leicester ECMC and Local strategic partnerships: Delivering Bench to Bedside research



ENABLERS: Leicester Molecular Diagnostics, Van Geest Omics, Hope Cancer Trials Centre, Doctoral College, AI facility, Institute for Precision Health

Aims

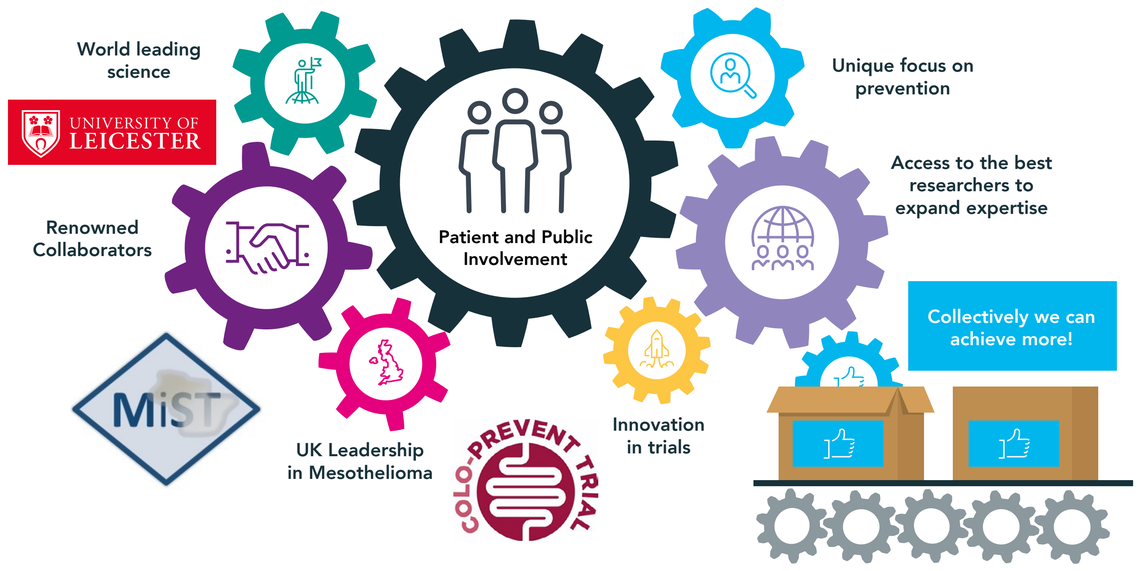
- To embed our areas of research excellence in blood biomarkers and liquid biopsies and our patient derived explant platform across our programme of work.
- To develop a new theme in equality, diversion and inclusion progressing equity of opportunity across our research portfolio and improving outcomes for underserved groups. Work will include:
  - Understanding seldom heard voices.
  - Exploring language as a barrier to taking part in cancer research studies.
  - Exploring attitudes and challenges to participation in window-of-opportunity trials.
- To bring strength to the network in the field of therapeutic prevention.
- To continue our commitment to training and strengthening the workforce through JING, buddy schemes and staff development.

Challenges

- To develop novel approaches for public and patient engagement work with underserved communities.
- Ensuring the UK remains a sustainable and attractive environment for delivering early phase trials.
- Ensuring access to genomic sequencing 'for trials'.

What we will contribute to the network

- To contribute to a step-change in the use of therapeutic interventions for cancer prevention by conducting and supporting the development of pioneering trials.
- To contribute to and promote knowledge transfer within the new translational research forum.
- Sharing of best practice through initiatives such as UpSMART and engagement with underserved communities.



1. Source: Office for National Statistics – 2011 Census and Census 2021. https://www.ons.gov.uk/visualisations/censusareachanges/E06000016/

ecmc Jointly funded by: CANCER RESEARCH UK · Little Princess Trust · NIHR | National Institute for Health and Care Research · Ymchwil Iechyd a Gofal Cymru Health and Care Research Wales · CHIEF SCIENTIST OFFICE · HSC Public Health Agency Research and Development

Manchester ECMC: A Network Driven Approach

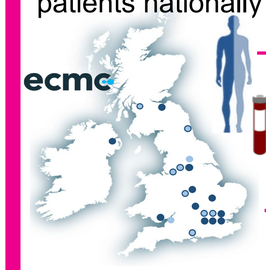
NIHR | Manchester Biomedical Research Centre

Contact: manchesterecmc@manchester.ac.uk

Theme 1: Lead national precision medicine trials

TARGET NATIONAL

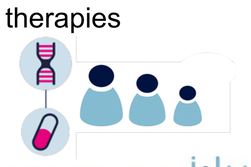
Access to ctDNA testing for 6000 patients nationally



Discussion at virtual National Molecular Tumour Board

TARGET Next Generation

Patients referred for matched experimental therapies



Development of UK database of genomic alterations with associated clinical data

CANCER RESEARCH UK | MANCHESTER INSTITUTE | CANCER BIOMARKER CENTRE

PRECISION MEDICINE (RADIOTHERAPY)

Precision radiotherapy
Advancing drug-RT combination trials (Only site delivering MRI-guided RT & First NHS hospital with proton beam centre)

Theme 2: Digital innovation for patient benefit

UpSMART digital clinical trials

- Data collection (eSOURCE), patient engagement (PROACT) and decision making (eTARGET)

- Trials of tools to measure early toxicity in the kidney (IN-HOME), eye (A-EYE), and immune-related toxicities (NOTION)
- Creation of inclusivity guidelines for development of technology clinical trials ensuring they are designed for all

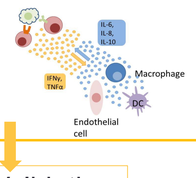
VOCAL

Theme 3: Deliver challenging advanced cell therapy studies

ATTC Advanced Therapy Treatment Centres | iMATCH ADVANCED THERAPY TREATMENT CENTRE

Managing toxicity – Translational Research

- GCP compliant, rapid turn-around cytokines ELISA
- Digital algorithm to establish early warning for evolving cytokine storm



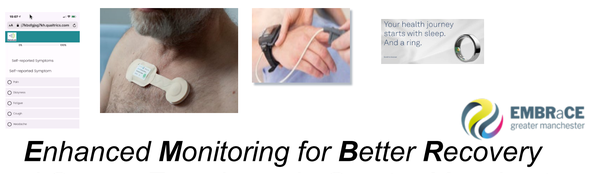
Validation of assay

Transferred to NHS Clinical Laboratory

- Patient Reported Outcome Measures (**PROMS**) in CAR-T
- Patients as co-investigators
- Develop and use PROMs in the Cell Therapy setting

P R O M T

Managing toxicity - Digital Technology

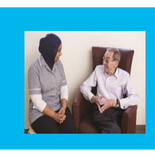


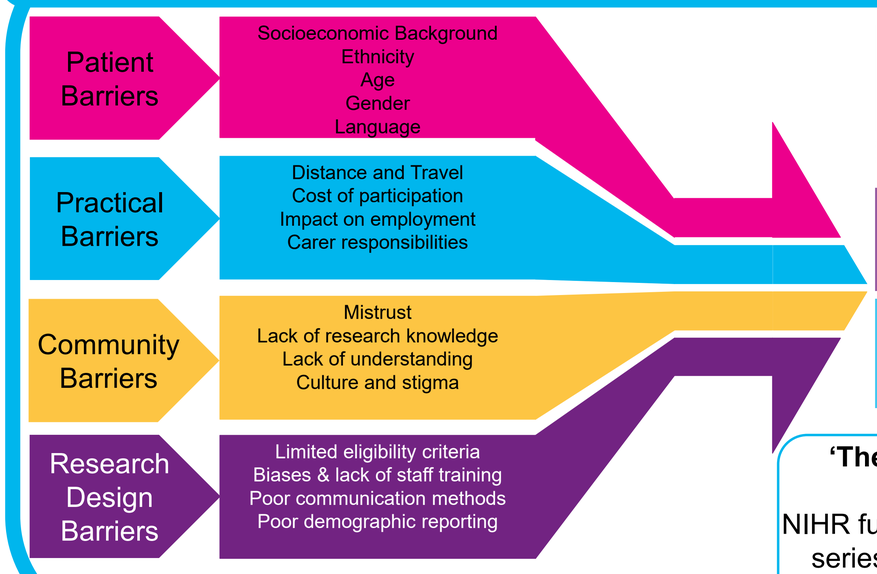
EMBRaCE greater manchester

Enhanced Monitoring for Better Recovery and Cancer Experience in Greater Manchester

Manchester
13 partners
1 city

Theme 4: Ensure equity of access to clinical trials

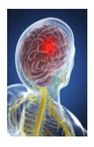




'The Role of Early Phase Cancer Trials':
NIHR funded educational seminar series attended by patients & Health Care Practitioners

Manchester ECMC & The CRUK Biomarker Centre

Biomarker tool box for haematology-oncology clinical trials



- Hodgkin Lymphoma: Improve PET-adapted response assessment
- Primary CNS Lymphoma: Predictive & prognostic biomarkers
- CMML & myelodysplasia: Predict response to oral hypomethylating agents
- Myeloma: Biomarkers to guide use of CelMODs & inobrodib
- AML: Ph1 trial of inodrodib ctDNA methylation to guide patient selection

Biomarkers for Radiotherapy clinical trials

Phase 1b CRAIN Trial in Cervical Cancer
CRUK Combinations Alliance with Astex
ChemoRT plus inhibitor

CRAIN

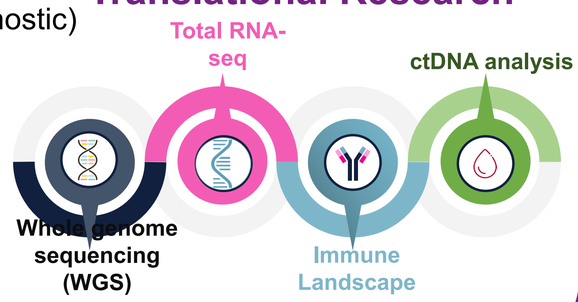
Can treatment response & acute colon toxicity be reported from one blood tube with ctDNA methylation?

Project Exemplar

DETERMINE

- CRUK endorsed umbrella basket platform study for rare adult and paediatric cancers (age and tumour-agnostic)
- Patients as co-investigators
- Incorporating precision medicine, digital tools, advanced therapies and equity of access
- Next generation of molecular tumour boards
- Comprehensive translational research package
- Trial delivery throughout the ECMC network

Translational Research



Key Deliverables

ACCELERATE INNOVATIVE TRANSLATIONAL RESEARCH

- **> 6 biomarkers** to routine use
- TARGET NG Multi-omics informing treatment options
- Digital technologies into **3 new trials**
- Haem-onc biomarker toolbox

GLOBALLY COMPETITIVE RESEARCH DELIVERY

- TARGET National – ctDNA into routine practice
- DETERMINE - Biomarker led treatments for **rare cancers**
- ATMP trials **up by 30%**
- Increased commercial early phase studies in the UK

INCREASE PATIENT CENTRED AND ACCESSIBLE RESEARCH

- Widespread adoption of digital inclusivity guidelines
- PROMS across CAR-T studies
- Increased referrals from under-represented groups **by 10%**
- All TYA patients offered access to ECM trials

ecmc Jointly funded by: CANCER RESEARCH UK | Little Princess Trust | NIHR National Institute for Health and Care Research | Ymchwil Iechyd a Gofal Cymru Health and Care Research Wales | CHIEF SCIENTIST OFFICE | HSC Public Health Agency Research and Development

Sir Bobby Robson Cancer Trials Research Centre

ECMC Innovative Endeavours: Beyond Clinical Trials

ecmc Newcastle

Education and Workforce Projects

- Established effective university links
- Open day events – for general public education which have been fun and engaging
- Careers events for all – Centre events both online and in person, and representation at University and NHS Trust wide events

Find out more about the impact of this work

Careers | Placements | Open Days | Lectures

- Student projects for both Medical and Biomedical Students as part of their degree, or to gain experience in a clinical research environment.
- Student nursing placements
- Internships – Link with a University in France – Offered to students on intercalating degrees. Some have gone on to have a career in Clinical Research.

Patients Care Initiatives

Recruitment of a dietician to provide nutritional support and advice

- **to maintain and optimise their weight to improve their chance of being** recruited to and staying on trial
- to reduce anxiety levels of cancer related weight loss
- **to provide supplements and diet advice**

Recruitment of an Occupational Therapist to provide support on:

- **fatigue management**
- mobility issues
- **psychological adjustment**
- managing breathlessness,
- **equipment provision**
- wheelchair assessment
- **future planning and preferred place of death**

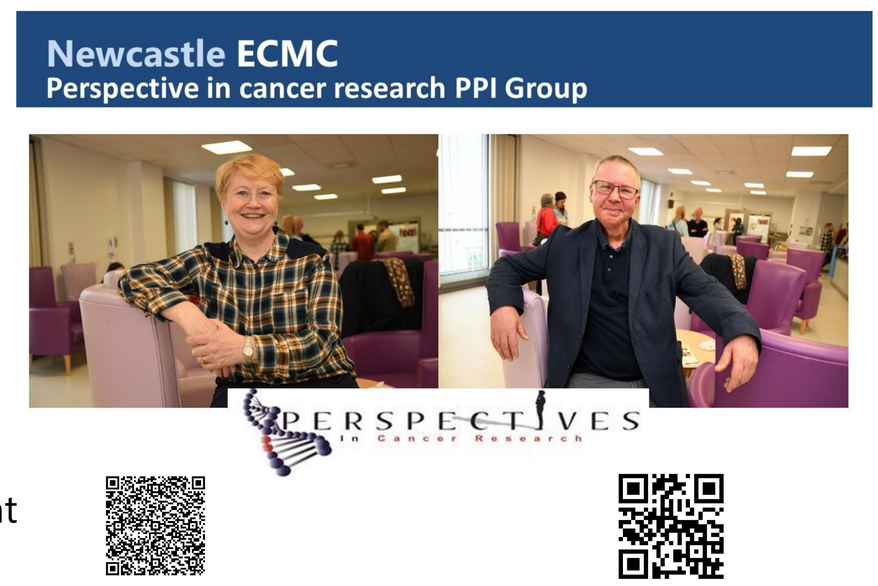
Complimentary Therapy service:

- to continue to provide ongoing support for the patients using different therapies
- **development of a trial to explore complimentary therapy for 'white coat syndrome'** (which can impact on participants meeting trial inclusion)

Patients and Public Involvement Projects

Perspectives in cancer research PPI group ensure the patients voice is at the centre of all we do at Newcastle ECMC:

- 25 members
- Meet once a month
- Review on average 24 research studies pre year (academic and clinical research)
- Support ECMC service improvement projects



Find out more about the impact of PPI at Newcastle ECMC

Access our PPI developed resource

Developed a multi format patient co-designed educational resource that supports patients entire early phase clinical trial journey

- Improved patients comprehension
- Reduced patient anxiety

Developed a new method of electronic consent (2020) - Hospital trust and Sponsor approved

- Utilised a PPI co-designed approach to ensure the patient voice was at the centre, it was **patient friendly** and something they could easily use.

Translational Research

GENETIC SCREENING-PRECISION MEDICINE

CR UK SMP2-Matrix trial (lung cancer)–Top UK recruiters

TARGET-National study using ctDNA-advanced solid tumours

Prospect–NE 'North East's largest Cancer Genome study'

NOVEL METHODS TO DIAGNOSE/MONITOR DISEASE

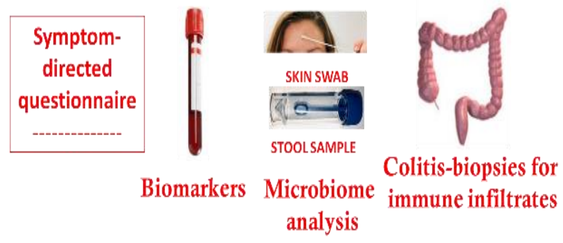
CiRCUITT study ' Circulating tumour cells in thyroid cancer'

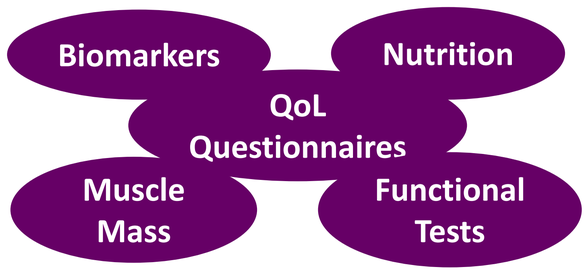
SIDE-EFFECTS OF NOVEL THERAPIES

MEDALLION-Pilot study
'CPI therapy and Immune Dysregulation/ side-effects'

TOLERANCE TO CANCER THERAPIES

Frailty and sarcopenia as predictors of drug toxicities/outcomes studies





Translational Histopathology Laboratory

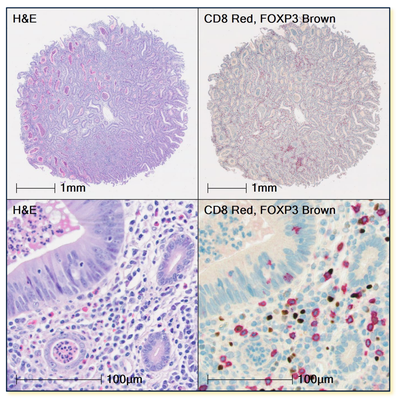
University of Oxford

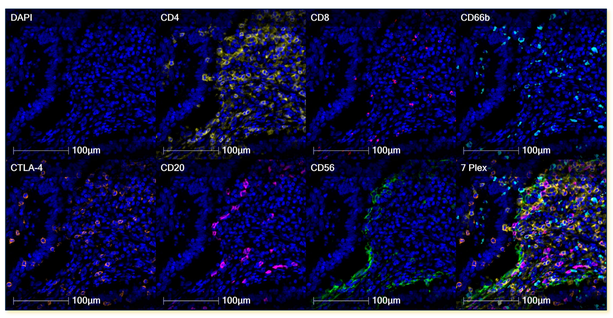
The THL is an outward-facing, core research facility, at the Department of Oncology, University of Oxford.

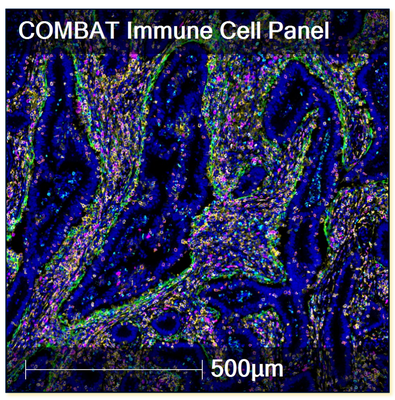
- It is led by a research-active clinical pathologist.
- Supported by a team of experienced histotechnicians.
- Works to GCP standards.
- Delivers projects for academic researchers, clinical trials and biotechnology firms.

Core Services

- Tissue handling, embedding and sectioning.
- Tinctorial histochemical staining (H&E).
- Multi-chromogenic immunohistochemistry.
- Digital slide scanning.
- Pathologist interpretation of H&E / IHC.





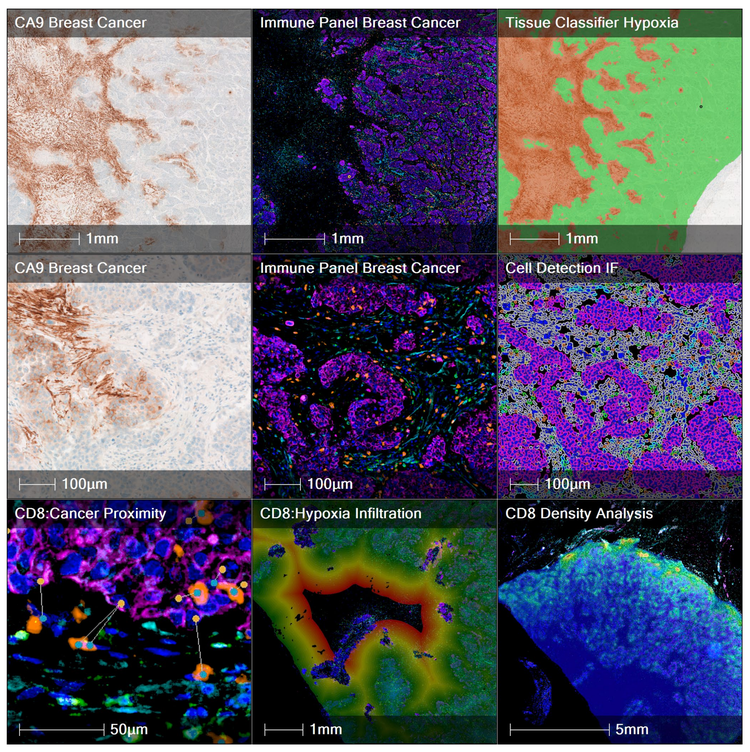


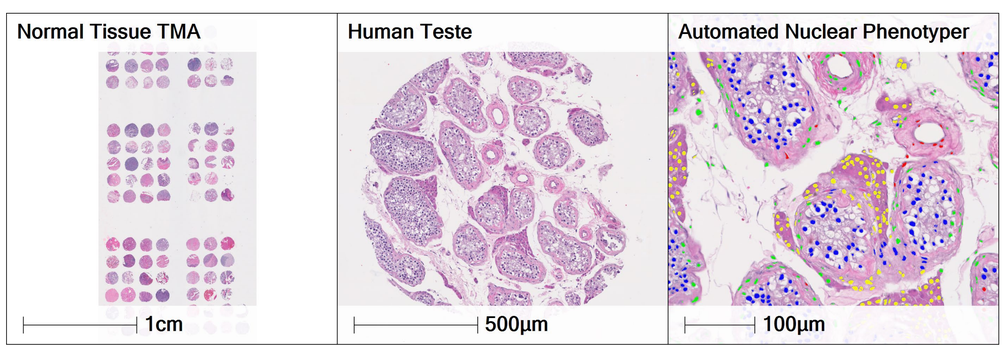
Multiplex Immunofluorescence

- Vectra Polaris system.
- 7-Plex fluorescent immunohistochemistry.
- Bespoke panel design and optimisation.
- High-throughput automated staining.

Image analysis

- Pathologist-led, computer-aided, analysis.
- Indica's HALO image analysis software:
  - Brightfield and immunofluorescence images.
  - Machine-learning automated tissue segmentation.
  - Machine-learning cell phenotyping.
  - Automated cell identification, dye quantification and RNAScope scoring.
  - Colour deconvolution.
  - Image registration.
  - Topological analysis.





Bespoke TMA Creation

- Pathologist-led tissue selection.
- Bespoke tissue arrays.
- Access to extensive collection of archival FFPE material.
- Automated TMA analysis.

thlenquiries@oncology.ox.ac.uk

ecmc Jointly funded by: CANCER RESEARCH UK · Little Princess Trust · NIHR | National Institute for Health and Care Research · Ymchwil Iechyd a Gofal Cymru Health and Care Research Wales · CHIEF SCIENTIST OFFICE · HSC Public Health Agency Research and Development

Southampton ECMC - Introduction

Southampton ECMC is an expert multi-disciplinary team within Cancer Sciences which is one of only three CRUK Centre for Drug Development (CDD) Biomarker Hubs in the UK. We unite discovery and clinical research teams to develop and perform early stage (first-in-human to phase I/II) clinical trials of novel immunotherapeutics and diagnostic tools. Our trials cover a broad spectrum of solid and haematological cancers and are performed in close collaboration with CDD, the Southampton Clinical Trial Unit (SCTU) and commercial partners. Excitingly, we are one of only seven ECMC centres in the UK which are part of both the adult and paediatric networks. Furthermore, as part of the National ECMC Network, we are particularly involved with the ECMC Quality Assurance, Translational Science Network Group, ECMC Junior Investigators Network Group (JING), ECMC Research Nurses Network Group, and the ECMC Immunotherapy Group.

Southampton ECMC - The Team

Director:
Prof. Andrew Davies
Clinical Associate Director:
Dr. Simon Crabb
Laboratory Associate Director:
Prof. Anthony Williams
Senior Research Fellow:
Adam Coleman, PhD

Senior Trial Manager:
Denise Dunkley
Research Engagement Manager:
Liz Allaway
Quality Assurance:
Catherine Pointer, PhD
Lead Scientists:
Nicola Irvine, PhD

Technical team:
Rebekah Allen
Tom Wynn
Alex Stote
CDD Biomarker Hub team:
Thierry Waltrich-Augusto, PhD
Céline Galloway

Southampton ECMC –Recent Achievements

ARGO - A phase II study of Atezolizumab, Rituximab, Gemcitabine and Oxaliplatin in patients with relapsed or refractory diffuse large B-cell lymphoma who are not candidates for high-dose therapy.
Number of Patients Analysed: 57
Number of Samples Analysed: 246
Type of Analysis: Flow Cytometry (2 panels)
Manuscript in preparation

ACCEPT – A Phase Ib/II combination of acalabrutinib in combination with rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone (R-CHOP) for patients with Diffuse Large B-cell Lymphoma (DLBCL)
Number of Patients Analysed: 32
Number of Samples Analysed: 246
Type of Analysis: Flow Cytometry
Manuscript in preparation

RiVa – A phase IIa study of Rituximab and Varlilumab in relapsed or refractory B-cell malignancies
Number of Patients Analysed: 27
Number of Samples Analysed: 169
Type of Analysis: Flow Cytometry (3 panels) + Rituximab PK ELISA
Manuscript in preparation

PROSECO - A UK Multicentre Prospective Observational Study Evaluating COVID-19 Vaccine Immune Responses in Lymphoid Cancer
Number of Patients Analysed: 592
Number of Samples Analysed: approximately 1200 (ELISpot) and 230 (Flow Cytometry)
Type of Analysis: Flow Cytometry + ELISpot
Manuscript in preparation

Southampton ECMC – The Translational Lab

Trial Name	Therapeutic agent	Collaboration	Immunomonitoring
iDx Lung Health (CI: P Johnson)	ELISA assay for 8 serum biomarkers to improve diagnostic performance in risk stratified population screening for lung cancer	SCTU, Oncimmune	ELISA for the detection for autoantibodies against CAGE, GBU4-5, HuD, MAGE A4, NY-ESO-1, p53 and SOX2 lung cancer antigens
AURORA (CI:S Crabb)	Atezolizumab in patients with urinary tract squamous cell carcinoma	UHS, SCTU	Immunophenotyping by Flow Cytometry and peripheral T-cell receptor clonality
P+R-ICE (CI: A Davies)	Pembrolizumab in combination with R-ICE chemotherapy in relapsed/refractory diffuse large B-cell lymphoma	SCTU	TBD
MiNivAN (CI: J Grey)	Combination of 131-I-MIBG, Dinutuximab-β and Nivolumab in paediatric and young adult patients	University Hospital Southampton NHS Trust, Little Princess Trust	Immunophenotyping by Flow Cytometry & ADCC assay
HARE-40 (CI: C Ottensmeier)	RNA vaccine against HPV in HNSCC	SCTU, BionTech	HPV16 E6, E7 & E2 ELISAs, HPV16 E6 and E7 Peptide pool ELISpot & Cytokine assay by Luminex
HMBD-001 (CI: Johann de Bono)	Anti-HER3 monoclonal antibody given IV as a single agent and in combination in patients with advanced HER3 positive solid tumours	CDD	Biomarker detection assays (ELISA)
FAK-PD1 (CI: S. Seymeonides)	Combination of Defactinib an Pembrolizumab in advanced solid malignancies	Glasgow CTU, Edinburgh University	Immunophenotyping by Flow Cytometry RNA-Sequencing

Southampton ECMC – Contacts

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Lead Scientists: Nicola Irvine n.irvine@soton.ac.uk & Thierry Waltrich-Augusto t.waltrich-augusto@soton.ac.uk
Or visit us at http://www.uhs.nhs.uk/ClinicalResearchinSouthampton/Research/Research.aspx
@ECMCSouthampton

Jointly funded by: