The digital Experimental Cancer Medicine Team

Engaging patients, Driving decisions

2020 Report

Contents

World leading scientific research, including pioneering work in precision medicine and cancer treatment is brought together through the Manchester Cancer Research Centre (MCRC) partnership, a unique collaboration that brings together the expertise, vision and resources of its partner organisations: Cancer Research UK Manchester Institute, The University of Manchester and The Christie NHS Foundation Trust, all of which have formidable individual reputations in the field of cancer research.

Introduction

When writing the 2019 annual report, none of us foresaw the unprecedented headwinds which erupted into our personal, family, work and societal lives with the COVID-19 pandemic. Firstly, our thoughts are with all those including members of digital ECMT who have lost friends and family in an untimely way to this illness. The seismic impact of such an event on all aspects of life cannot be understated. Secondly, our thanks are to members of digital ECMT and our collaborators, who despite the challenges of home working, home schooling and home-staycations have overcome these to meet many and exceed some of the goals we set for 2020 ahead of the pandemic.

2020 marked the closure of the iDECIDE 5-year collaboration with AstraZeneca. At its inception, this collaboration sought to develop REACT- an interactive data review platform which enables researchers, sponsors and investigator sites conducting early phase clinical trials to interrogate the emerging data to better understand the efficacy, toxicity, pharmacokinetic and tolerability profile of investigational medicinal products. A key met goal for 2020 was the release of a free-to-use version of REACT (see page 29 for link 1) which in addition to the above functionalities also included links to cBioPortal for molecular profiling interrogations and the option for individual and population data reviews. Yet the iDECIDE collaboration became so much more than REACT. During 2020 we completed a clinical trial of PROACT which captures (by word, voice or video) patient reported experiences of their participation in an early phase cancer clinical trial to better understand the utility of this digital platform. We further developed eTARGET which enables molecular tumour board to meet virtually, capturing clinical, molecular and demographic data and decisions as to which clinical trial the patient is best suited. To assist in this, a proprietary clinical trial matching tool was developed by digital ECMT which provides investigators with options of potential trials cited in public domain databases based on a limited set of clinic-genomic features. Both products have been released to other cancer centres. 2020 also marked the year when we established easy access to patient groups to take soundings of new digital clinical trials concepts.

But 2020 was also a year when a new 5-year collaboration was birthed - "UpSMART". This "CRUK accelerator programme" (funded by Cancer Research UK, Fondazione AIRC and Fundación Científica de la Asociación Española Contra el Cáncer), brought some 23 early phase cancer clinical trials units across Europe together to form a consortium for sharing and developing new digital platforms which aid in the capture and interpretation of experimental cancer medicine clinical trial data. With the infrastructure now built, our goal was to release one digital platform during 2020 (REACT). This goal was exceeded with a second digital product released in 2020 and a third early in 2021- all of which can be found on the UpSMART Accelerator website (see page 29 for link 2).

Furthermore, the digital ECMT did not stand idle in applying its skills to COVID-19. In collaboration with centres across the UK, coordinated by Manchester, digital ECMT scientists developed an initial algorithm to predict when cancer patients presenting with COVID-19 are more likely to require admission to hospital. This digital product "CORONET" was also released as a free-to-use web tool (see page 29 for link 3). Additionally, the team commenced a major collaboration with Prof. Tom Wilkinson based at University Hospital Southampton (UHS) Trust, adapting and deploying our REACT/ACUITY analytics platform to support the COVID-19 research, enabling correlations to be made between clinical variables and patient outcomes dynamically (read more of this on page 21).

Looking forward to the next 12 months, we will see the initiation of our new 'digital ECMT 2021-2025 strategic ambitions', covered on P.7 of this report. This is an ambitious plan extending the scope of the digital ECMT's research beyond the clinical trial and into broader cancer healthcare. Additionally, we will start our participation in the CCE_DART 'Building Data Rich Clinical Trials (DART)' research programme funded by a Horizon 2020 EU grant. Its purpose is to deliver novel methods for the design and implementation of newer, more efficient and effective clinical trials in oncology and our role will be to lead two of the work packages, the first, developing complex biomarkers using Ethical AI and the second, patient reported outcomes using digital technologies.

Professor Andrew Hughes
Chair of Experimental Cancer Medicine,
The University of Manchester

Introduction
(continued)

digital ECMT – 2021-2025
strategic ambitions

Firstly, on behalf of the entire digital ECMT, I would like to thank Andrew sincerely for his wonderful leadership, mentorship, and steadfast support of the research team over the past five years, which as a team we have all benefited from. Under Andrew's stewardship, the digital ECMT has now established itself as a core research group within the CRUK Manchester Institute and is nationally and internationally recognised for its clinical trial research innovation, direct collaboration with patients as co-researchers and the development of a significant decision science capability. The past 5-year research programme has seen the successful delivery of the iDecide programme, for which Andrew initiated and secured a large research grant from AstraZeneca, which established the 'Technology' Clinical Trial model of engaging patients and a way of delivering new patient centred care pathways. Importantly, Andrew also led and secured funding for the pan-European UpSMART programme enabling the development and distribution of digital assets to experimental cancer medicine centres/early drug development units across Europe. This was a significant achievement for the digital ECMT and has successfully positioned us on the EU academic research stage. Andrew will be missed by all of us on the team, however, we all wish him the very best of luck and every success in his retirement, no doubt equally as busy....and, of course, he now has a Sextant with our coordinates, should he need to find us!

Dr. Dónal Landers
Strategic Director,
Digital Experimental Cancer Medicine Team

> 66 The dECMT continues to be at the vanguard driving digital solutions to improve the care of cancer patients. The innovative strategy driven from within the CRUK Manchester Institute Cancer Biomarker Centre is exciting and I am sure its delivery will step change how biomarker and clinical data are combined for a holistic appreciation of each patient's cancer to optimise their treatment. 99
>
> **Prof Caroline Dive CBE, FMedSci**
> *Interim Director CRUK Manchester Institute (MI) and Director CRUK MI Cancer Biomarker Centre and PI on the UpSMART Accelerator Award*

Developing and delivering technology-based patient-centred research is challenging, but through hard work we have made significant progress with the establishment of our 'technology' Clinical Trial methodology, AI research, and Systems development capability. The last 5 years have certainly been a voyage of discovery for the entire digital ECMT in establishing our research team and our research credentials both locally within the Manchester research community and externally at national and international levels. As mentioned previously, leading and being part of two large EU research programmes and delivering a successful 5-year iDecide programme has given us a solid foundation from which to build our next 5-year strategic plan.

The next five years will be equally ambitious and will see the implementation of our new strategic plan, developed in 2020, which will extend our research beyond the clinical trial and into the broader cancer clinical care setting ranging from cancer screening to late-stage cancer treatment.

Our new vision is "digitally empowering patients and healthcare professionals to innovate and design new cancer care pathways", which is supported by our new mission statement "To provide next generation patient cancer care through comprehensive data-driven evidence to enable:

- the transformation of clinical decision-making;
- evolve the role of the patient and;
- improve patient outcomes."

These important statements of intent continue to re-enforce our goal to deliver tangible clinical benefit in the clinic and in the patient's home. As a team we have agreed that we will achieve this by listening to our patients and healthcare professionals, understand their needs and work proactively with them to:

- Develop algorithms (AI) to support patient care;
- Build digital solutions to address their needs;
- Evaluate our technologies under clinical trial conditions (technology clinical trials).

digital ECMT – 2021-2025
strategic ambitions (continued)

Our research will be delivered through our five key research themes, to which we will align our research programmes, projects and team resources - as shown on the right (Figure 1).

Through our strategy development process, we have identified three 'Big ideas' that we want to achieve in the next 5 years. The first is the establishment of a 'Data Bank' AI Laboratory at the CRUK Manchester Institute CBC/MCRC, the second is delivery of ACUITY to support the Next Generation MTB/MDT leveraging multi-omic, clinical and real-world data to identify optimal treatment options for patients, and the third, a 'Christie patient' new model of care, in which we engage differently with patients and empower them to play a greater part in their treatment.

To deliver these big ideas we plan to collaborate extensively with our colleagues in the MCRC, The Christie and further afield. Next year, we hope to put a formal collaboration in place with The Christie to translate our research into the clinic in areas such as Acute Kidney Injury monitoring in the home, ACUITY observational cancer studies and ethical AI algorithm development and validation.

> 66 The digital ECMT is a superb exemplar of novel team science in digital technology with positive disruption in the way we best care for our cancer patients. It represents the future of oncology whereby ethical AI can be used to achieve bespoke precision medicine.
>
> The best of the team's innovations will augment Real World Evidence studies in The Christie and MCRC as an international lead in digital cancer sciences and ensure adoption of best digital care practice in the UK and worldwide. 99
>
> **Professor Rob Bristow MD PhD FRCPC FMedSci**
> *Director, Manchester Cancer Research Centre*
> *Director, CRUK Manchester Centre.*
> *Senior Group Leader, Translational Oncogenomics, CRUK Manchester Institute*
> *Chief Academic Officer & Honorary Consultant, The Christie NHS Foundation Trust*
> *University Professor of Cancer Studies, Div. Cancer Sciences, FBMH*
> *MAHSC Cancer Domain Research Lead, The University of Manchester*

If you have an innovative idea and are interested in collaborating with the digital ECMT, please get in touch with us (see the back page for contact options).
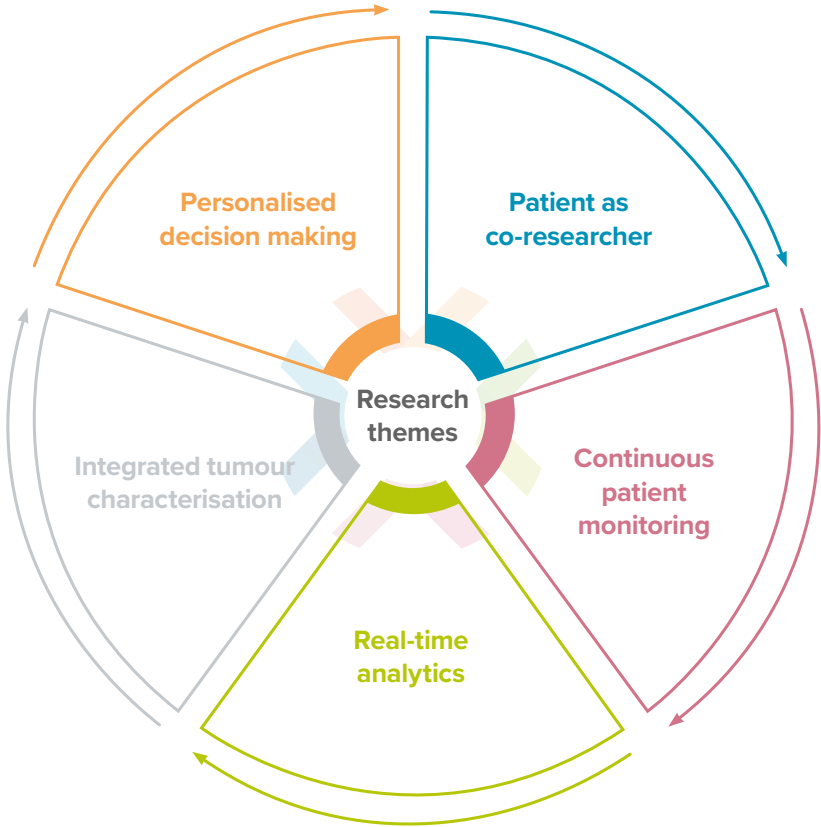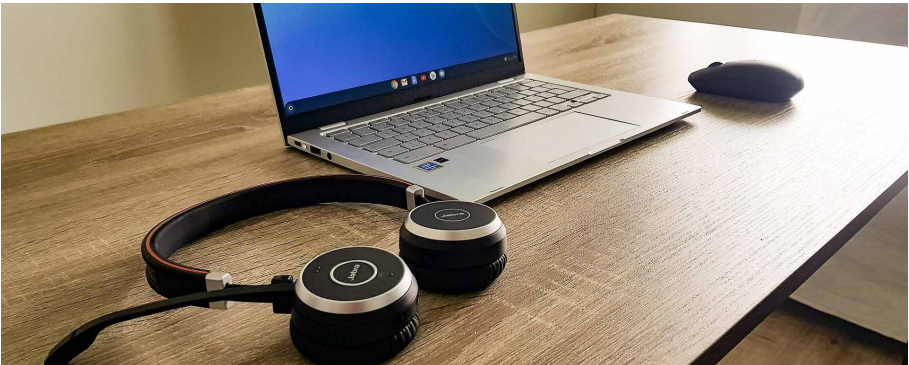
Figure 1: digital ECMT Research themes

The Team

From the end of Q1 in 2020, the entire team have worked from home and met with other team members via video conference only (as illustrated by our team photo on the right). Wider CRUK MI events and discussions with external collaborators have been similarly 'virtual'. But despite these challenges, the team has maintained a delivery focus and found ways to adapt to this new norm.

The team is vital to successful delivery of the digital ECMT 2021-2025 strategy. To support this delivery a new organisational structure has been put in place building on our core capabilities.

Following Andew Hughes' retirement, Dónal Landers will take over the strategic leadership role of the team.   He will be supported by the Senior Management Team in the form of: Paul Fitzpatrick – Head of Technology Solutions; Laura Stephenson – Portfolio Manager; Andre Freitas (Lecturer, department of Computer Science at The University of Manchester) – Artificial Intelligence Group Lead, and Donna Graham (Medical Oncology Consultant at The Christie and Honorary Clinical Lecturer at The University of Manchester) - Technology Clinical Trials Group Lead.

Dr Akshita Patil, who joined us as UpSMART Accelerator Project Manager has yet to experience meeting colleagues in person, since her recruitment, selection and induction all took place online!
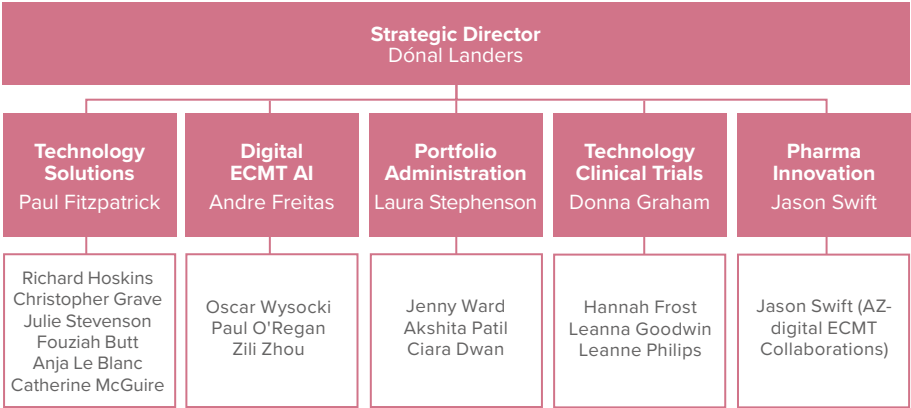
Ciara Dwan successfully attained the digital ECMT Project Manager position late in 2020 – ready to join the team at the beginning of 2021. Despite this very different working model, the team are proud of the many achievements in 2020, as set out in this report.
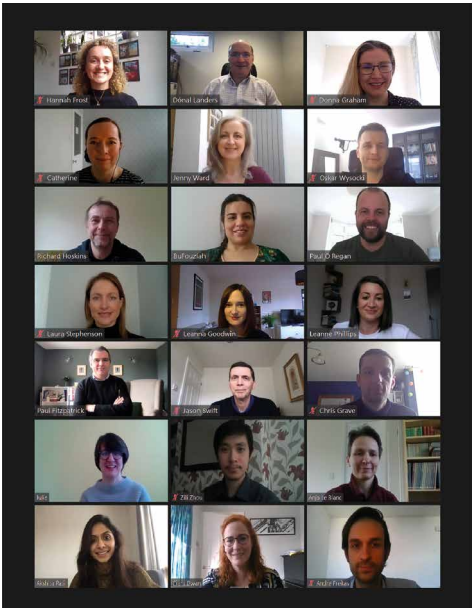
" Joining the digital ECMT at a time everyone is swiftly transitioning into the digital world has been a great experience - I virtually met everyone! It is exciting to be part of a team advancing such a variety of research projects and working towards transforming early phase clinical trials for patients, researchers and clinicians. "

Dr Akshita Patil
UpSMART Accelerator Project Manager

digital ECMT organisational structure 2021

| Strategic Director Dónal Landers				
Technology Solutions Paul Fitzpatrick	**Digital ECMT AI** Andre Freitas	**Portfolio Administration** Laura Stephenson	**Technology Clinical Trials** Donna Graham	**Pharma Innovation** Jason Swift
Richard Hoskins Christopher Grave Julie Stevenson Fouziah Butt Anja Le Blanc Catherine McGuire	Oscar Wysocki Paul O'Regan Zili Zhou	Jenny Ward Akshita Patil Ciara Dwan	Hannah Frost Leanna Goodwin Leanne Philips	Jason Swift (AZ-digital ECMT Collaborations)

The Technology Clinical Trial
Delivering tomorrow's clinical trials today

The 'technology' clinical trial is core to our research. It enables us to translate our scientific work to beyond the patient bedside and directly into their homes. It begins with the identification of an important clinical problem and creating an innovative solution directly with our patient community. We test the 'technology' formally within a specifically designed non-CTIMP study model.

This provides the digital ECMT with a formal way of evaluating technology in its broadest sense – medical devices, software-as-a-device, software systems and Ethical AI – and enables us to assess its feasibility and clinical benefit as part of a patient-centred care pathway. Our 'technology' clinical trial capability continued to grow and develop in 2020 despite the challenges of the COVID-19 pandemic.
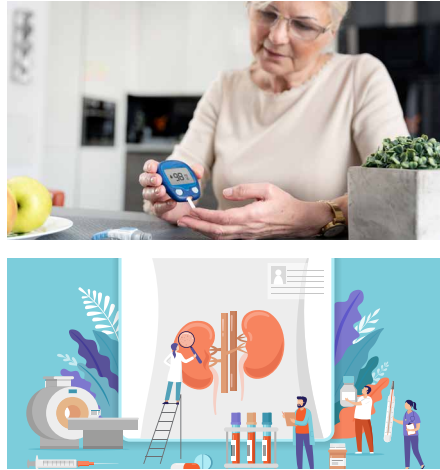
Additionally, despite the contact limitations of COVID-19 and inaccessibility of our Design Lab, based in The 'NIHR Manchester Clinical Research Facility', we continued to access our patient forum opportunities - directly interacting with patients via virtual focus groups run on a video platform. This feedback from patients, specific to testing a research theme and our trial design are highly valuable and inform decisions for such specifics as – the Patient Information Sheet, acceptable frequency of sampling, device selection, Instructions for use of kit and practical tools to help with sampling. This feedback can save a trial which may otherwise have failed due to lack of consideration of the patient's viewpoint . We do not underestimate its significance and the immense value gained.

Our research has focused upon four areas – **In-Home**, **NOTION**, **A-EYE** and **PROACT**:

In-Home

Phase 1 clinical studies often have eligibility criteria that prevent patients with reduced renal function from accessing the trial drug. Often these criteria are not reflective of the mechanism of the drug or the toxicity profiles and these drugs remain untested in these populations until they are in mainstream circulation. Improved monitoring of renal function could potentially lead to earlier detection of adverse renal events and improve patient outcomes, alleviating the risk of patients with reduced renal function going on to clinical trials.

The In-Home study is a feasibility study to evaluate more intensive in-home monitoring of creatinine. Part A is specifically assessing whether patients will take samples at home (based on a pin-prick of blood, creatinine sensor and input to a bespoke app) and to a specific schedule. Despite the challenges with COVID-19, which necessitated a pause to clinical trial recruitment for over 4 months, Part A is now wrapping up; 13 patients have completed the study and an impressive compliance rate was achieved along with favourable feedback on the process. As we move confidently to Part B, the study becomes more focused on whether this intensive monitoring is more effective at identifying acute kidney injury compared with standard of care testing.

> " Through the first phase of our study we have been able to detect several episodes of AKIs in our study participants which otherwise would have detected later at routine blood taking appointments. We have been able to relay these results back to the clinical teams in real time. We have found that the measuring and monitoring has been well tolerated and accepted by our participants. "
>
> **Dr Leanne Phillips**
> *Clinical Research Fellow in Nephrology, digital ECMT*

> " The In-Home study is a great example of ongoing collaborative research to advance care in overlapping comorbidities, in this instance Cancer and Kidney care (Onconephrology). The ability to test a diagnostic algorithm in the home setting with application of novel technology seems apt for current times as it allows medicine to move closer to home, reduce avoidable hospital visits even in complex care dealing with high-risk patients. Early results are promising, as we proceed to next stages of evaluation. With further progress, we believe positive findings from the In-Home study could be translated to practice in relatively short timescales. "

Professor Sandip Mitra, Consultant Nephrologist
Manchester University Hospitals Foundation Trust Professor of Nephrology, University of Manchester National Clinical Chair for Renal Services

> " digital ECMT are a very innovative and collaborative team, developing digital solutions to bring together clinical and biomarker data and optimise the learning from clinical studies. We look forward to progressing our collaboration with them to assess the feasibility of micro-blood sampling in the patient's own home to monitor cytokine levels as an early signal for adverse events. "

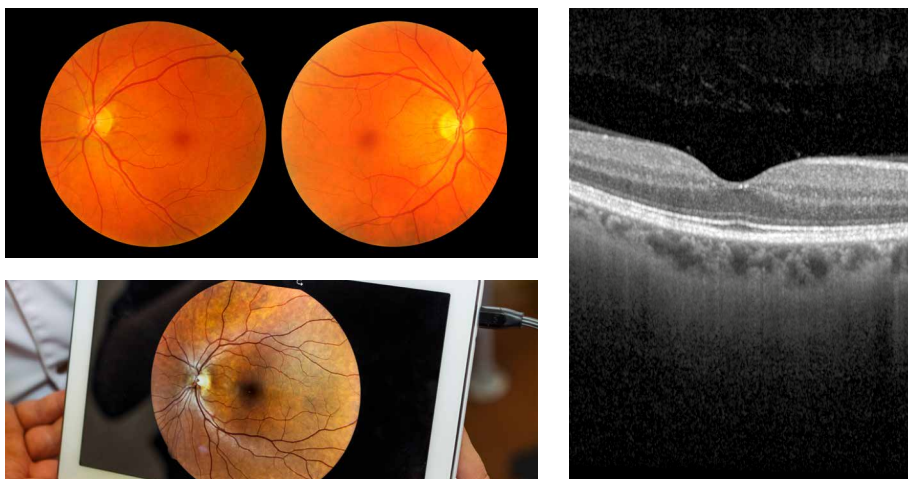**Dr Elaine Kilgour**
Cells and Protein Team Leader
CRUK Manchester Institute Cancer Biomarker Centre

NOTION

Immune related adverse events are side effects from cancer immunotherapies. These adverse events are very common with up to 90% of patients experiencing side effects on combination immunotherapies. Early evidence suggests that changes in cytokines correlate with the development of immune related adverse events. Therefore, monitoring of cytokines may help detect the onset of side effects and help manage them better for patients.

The NOTION study (iN-hOme sampling of cyTokines in Immunotherapy patieNts) is a feasibility study to assess whether patients will take blood samples at home. The blood samples will be analysed retrospectively to assess whether changes in patients' cytokines correlate to the development of immune-related adverse events. The NOTION study is a great example of collaborative working. During 2020, we have partnered with the Immuno-Oncology group at The Christie to develop the study protocol and research package. Additionally, we have worked closely with the CRUK MI CBC Cells and Protein Team, Tumour Immunology & Inflammation Monitoring Lab to validate the lab method for detection of cytokines from a dry-blood spot sample. The study is currently undergoing review by the sponsor in view to submission for ethical approval in 2021.

A-EYE

The ophthalmo-oncology project was initiated to try and address resourcing issues which can leave cancer patients, particularly those on early phase cancer clinical trials, without specialist eye treatment and support. Novel cancer therapies often have unknown toxicity profiles that can include changes to the eye. Often ophthalmology expertise is lacking and only engaged after patient's eye toxicities have become advanced, furthermore, lack of expertise often means that waiting times for patients are significantly delayed.

Through the University of Manchester sponsored A-EYE study, data will be collected from all-comers attending for an eye scan at the Manchester Royal Eye Hospital. Using their anonymised scan and relevant clinical data, including diagnosis, the aim is to develop and test an algorithm to detect eye toxicities from eye scans. Towards the end of 2020, the study protocol and research package were finalised and submitted for ethical review, of which a successful outcome was achieved at the beginning of 2021. Additionally, using publicly available data, our AI Team have developed an initial algorithm for the detection of retinal pathologies and have incorporated vital expert ophthalmologist knowledge to ensure the development of an ethical and explainable AI model.

PROACT

PROACT (Patient Reported Outcomes About Clinical Tolerability) is a system that gives patients and caregivers a way to share their experiences on trial with their research team. Participants have control over what they want to share in video, audio, or text messages, and when they would like to share them. This PROACT trial, which opened to recruitment in 2017 at The Christie and expanded to include Patients at Clatterbridge in 2019, aimed to understand the implications of setting up and using the PROACT system in multiple early phase studies, at multiple sites. It also aimed to characterise how patients used the system, and to also understand whether it is practical to give PROACT accounts to primary caregivers.

Following slow recruitment and then a halt to clinical research in Q1 2020 due to COVID-19, the PROACT study closed. Despite this, meaningful insights were gained. Research nurses identified several benefits to PROACT, most of which related to providing timely support as well as signposting to external guidance when needed. Clinical trial participants shared a wide range of experiences, from tolerability, information about the drug or schedule, benefits of the drug, logistics, or to simply say 'thank you'. All of these delivered a rich understanding of patient and carer perspectives. Critically, this approach was also an efficient method for capturing the emotional status of participants through their own words.

Use of communications systems such as PROACT can provide researchers with an early glimpse into patient and carer experiences that could affect adherence and decisions around compliance in the future. As virtual trials become a reality, and participants have less face-to-face interaction with their medical team, these early insights are likely to become increasingly important.

Decision Science
Supporting the way we interpret clinical trials and make decisions

This year saw the establishment of our new digital ECMT AI team, which will be led by Andre Freitas. This is an important step in the team's evolution and supports our strategic goal of building a strong decision/data science capability within the team. This has already led to some very important research collaborations, such as our research work with University Hospital Southampton on COVID-19 with Prof. Tom Wilkinson and his respiratory team. We are also constantly investigating new ways of improving the way we make decisions that fully involve the patient. This is becoming more relevant as we progress research in Ethical AI technologies as we witness the harmful effects of social algorithms on our society, which consume and use our own data to generate profit from advertising. We, in healthcare, are not immune from this, but have the opportunity to learn and apply medical ethics to AI research, which, in turn supports their ethical design, explainability and interpretability in how they are applied and implemented in our clinical Decision Support Systems (DSSs). We are actively seeking additional grant funding opportunities to further develop our research interests and capabilities.

We have a number of areas of ongoing Ethical AI research, which apply to new hybrid clinical oncology specialities – respiro-oncology, nephro-oncology, ophthalmo-oncology and immuno-oncology.

Innovate Manchester Advanced Therapy Centre Hub (iMATCH)

As part of the iMATCH consortium, led by Prof. Fiona Thistlethwaite (Medical Oncology Consultant and Director of iMATCH), the digital ECMT in collaboration with Dr. Elaine Kilgour's (Team Leader, Tumour Immunology and Inflammation Monitoring Lab., Cancer Biomarker Centre) team are responsible for the development of systems to safely manage patients receiving ATMP through rapid turn-round monitoring capabilities and integration into digital algorithms to establish early-warning systems to flag evolving toxicities. The team has been tasked with developing a novel cytokine assay and an algorithm to predict/detect the early onset of Cytokine Release Syndrome or Cytokine Storm in patients who receive these novel therapies. An initial version of the algorithm is currently under development utilising our new AI capabilities. The NOTION (iN-home sampling Of cyTokines In immunOtherapy patieNts) study, currently in development will begin to assess the feasibility of utilising Dry Blood Spot technology in patients in 2021 to extend this capability to the patient's home. This work overlaps with our COVID-19 research with University Hospital Southampton (see below).

> 66 digital ECMT are a very engaged partner in the iMATCH consortium and we are really excited to be progressing this partnership further. We have worked together over the last 3 years to develop our rapid turn-round cytokine assay and are looking forward to the next step of applying it within the NOTION clinical trial. 99
>
> **Professor Fiona Thistlethwaite**
> *Medical Oncology Consultant ECMT, Honorary Professor - The University of Manchester, iMATCH Director*

eTARGET / digital ECMT Cancer Trial Matching Tool

eTARGET, our decision-support solution, previously reported on, has been further developed to include enhancement of eTARGET and the deployment of the Patient Matching tool, to help identify precision medicine trials for patients with actionable mutations. Histopathology data and corresponding images can now be uploaded to eTARGET and the concept of sites have been introduced to support national Molecular Tumour Boards (MTBs) involving more than one cancer centre. These changes will enable the tool to be deployed to support multi-site precision medicine clinical trials.

As part of the Cancer Research UK (CRUK) UpSMART Accelerator programme, the digital ECMT has created and developed Trial Matching software (digital ECMT Cancer Trial Matching Tool) to support clinical decision making, which matches a cancer patient's tumour genetic profile to optimal clinical trials, supporting our precision medicine research (see page 29 for link 4).
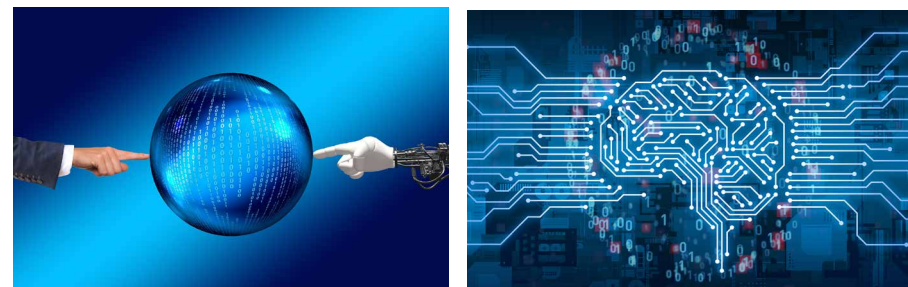
digital ECMT research in response to the COVID-19 Pandemic

CORONET — COVID-19 Risk in Oncology Evaluation Tool

Through a research grant achieved by Dr. Rebecca Lee, funded by The Christie charity, the digital ECMT are collaborating with Dr. Rebecca Lee and Dr. Anne Armstrong, on the "CORONET — COVID-19 risk in Oncology Evaluation Tool". (see page 29 for link 3) Cancer patients are at an increased risk of death from COVID-19 but can present very differently with some patients having mild illness and others having very severe outcomes. In addition, cancer and its treatments can affect blood tests making it difficult to establish what is related to COVID-19 vs. their underlying cancer. A series of routinely captured parameters have been identified that predict outcome from COVID-19 in cancer patients when they present with symptoms to hospital. The Decision Support System (DSS) is designed to aid clinicians with decisions on which cancer patients should probably be admitted to hospital based on outcome predictions.

> " I have really enjoyed collaborating with digital ECMT, we have been able to swiftly respond to the COVID-19 pandemic, developing a digital support tool to aid healthcare workers with their decisions as to whether to admit patients with cancer and COVID-19. The discussions we have had have considerably developed my thinking regarding use of artificial intelligence in healthcare and understanding of how we can implement safe and explainable tools in the clinic. "
>
> **Dr Rebecca Lee**
> *Clinical Lecturer Medical Oncology, The University of Manchester*

University Hospital Southampton COVID-19 Research

Shortly after the start of the COVID-19 pandemic the team commenced a collaboration with Prof. Tom Wilkinson based at University Hospital Southampton (UHS) Trust, recognised internationally for their COVID-19 research (ACCORD clinical trial). The digital ECMT's REACT/ACUITY system was adapted and deployed to ingress the UHS's EHR (Electronic Health Record), ICU (Intensive Care Unit), lab, investigational and scientific data. An additional COVID-19 UHS Dashboard was separately developed to enable correlations to be made between clinical variables and patient outcomes dynamically to support the Research Evaluation Alongside Clinical Treatment in COVID-19 (REACT COVID-19) observational and biobanking study. The delivery of a clinical analytics platform as an endpoint to clinical information pathway with the UHS has been a significant achievement for the collaboration — Prof. Tom Wilkinson (CI for the ACCORD clinical trial) enabling the development and application of novel AI methods to interrogate the large dataset.

> " Developing the capability to curate, analyse and visualise the rich clinical data from COVID -19 clinical care at UHS has enabled our clinical and research teams to rapidly generate novel insights into this new, life threatening disease. The unique digital platform and the skills of the Manchester team have powered real-time understanding of disease underpinning both clinical pathways and novel research findings and has been transformational in this regard. "
>
> **Professor Tom Wilkinson MA Cantab MBBS PhD FRCP FERS**
> *Professor of Respiratory Medicine and Honorary NHS Consultant Physician*
> *Consultant Physician*
> *Clinical and Experimental Sciences*
> *Southampton University Faculty of Medicine*

UpSMART Accelerator Award update

The digital Experimental Cancer Medicine Team, along with our EU colleagues, including those from Fondazione IRCCS Istituto Nazionale dei Tumori Milano and Instituto de investigación Oncologica de Vall d'Hebron, Barcelona were awarded a CRUK Accelerator Award, UpSMART, to enable SMART Experimental Cancer Medicine Trials. The 5-year UpSMART Accelerator Award began in March 2020 and we have made fantastic progress on all of our key milestones, despite our plans/activities being impacted by COVID-19. The ambition of 'digitalising up' the network and making digital healthcare products (DHPs) available across early cancer clinical trial centres is being realised as we progress research in each of the UpSMART work packages (Figure 2 below). We onboarded IGR (Paris) as a collaborating centre in June 2020, making a total of 24 centres in the UpSMART consortia.

During 2020, we worked closely with our Italian and Spanish counterparts to establish an understanding of each of the collaborating and participating centres' existing digital capabilities and experience. This Information Gathering Exercise enabled us to build a repository of in-house developed DHP, commercial DHPs and excel workbooks/ trackers in use across the UpSMART participating centres to help acquire and interpret clinical trial data from experimental cancer medicine clinical trials. We further categorised DHPs according to their maturity and purpose, utilising a framework produced by our Technical Hub (Work package 4). Out of the 29 identified DHPs, we have prioritised 10 to do further scoping and software development if necessary, for open-source release across the UpSMART network.

UpSMART Accelerator Work Packages

1	**2**	**3**	**4**
DHPs for Data acquisition	DHPs for Data interpretation	Training on setup and conduct of Clinical Trials for DHPs	Technical Hub for deployment & adoption of DHPs

Figure 2: UpSMART Accelerator Work Packages

> 66 During the COVID-19 pandemic, it became clear how important being digital is for our Early Phase Clinical Trials Units. Participating in initiatives like UpSMART is accelerating our digitalization and paving the way to implementing the use of medical devices in our trials. 99
>
> **Dr Elena Garralda**
> *Spain Principal Investigator, UpSMART Accelerator Award, Vall d'Hebron Institute of Oncology, Barcelona, Spain*

Digital Healthcare Products Achievements in Year 1:

"REACT" (REal Time Analytics for Clinical Trials) – the REACT DHP was made available to the network under a free-to-use licence and early adopter sites have been identified for its uptake.

The "Coronet" tool has been made available across the network (see page 29 for link 3) - a machine learning algorithm that acts as a decision support DHP to clinicians to assist in determination as to whether a cancer patient presenting with respiratory symptoms requires admission. In line with the spirit of the Accelerator Award, we requested that data be contributed back to the CORONET team to help support the further evolution and value of the tool. To date, 2 datasets have been contributed from across the UpSMART network.

One of the next goals for the Accelerator Award is to conduct a multi-national, multi-centre clinical trial with a primary objective to assess the performance characteristics of a DHP. This will allow the network to collaborate across the EU and embed the training material produced by work package 3 (setup and conduct of a clinical trial with a DHP). We are currently exploring opportunities across the UpSMART network and beyond.

The implementation of a Scientific Advisory Board, with experts from early phase translational research and data science & technology, is underway. The broader insight of relevant experts will be invaluable and help us ensure the strategy remains relevant and at the forefront of technology implementation to drive forwards early phase oncology clinical trial delivery.

Collaborations and Grants / Awards in 2020

> " We've been delighted to bring forward this international collaboration as the Italian Hub for the UpSMART Accelerator programme. Our first year of activity mainly focused on already existing and novel technical solutions to collect and represent patient reported measurements (PRMs) in the clinical research setting, bringing together high-level IT and clinical expertise. Main achievement to date has been the engagement of dedicated IT team to create a customized PROACT App. "
>
> **Dr Matteo Duca**
> *S.C. Oncologia Medica 1*
> *Fondazione IRCCS Istituto Nazionale Tumori*

We continue to recognise the importance of partnering with research, academic, clinical, and industry partners, as well as patients, to build on the collective expertise to deliver digital innovations to early clinical trials and beyond to transform decision-making and the patient's role. And whilst 2020 saw the end of the 5-year "iDECIDE" research programme, a successful collaboration between four strategic partners in cancer research; the CRUK MI Centre for Cancer Biomarker Sciences, The University of Manchester, The Christie and AstraZeneca; the digital ECMT has built on this to extend its collaborations and multi-centre academic research grant involvement.

The Christie NHS Foundation Trust

Our partnership with The Christie is pivotal to ensuring we have a patient-centred focus to our research activities and gives us the opportunity to translate our research into real clinical benefit for patients through involvement and the development of new patient care pathways.

- We work alongside the Experimental Cancer Medicine Team (ECMT) to ensure the delivery of our 'technology' clinical trials with our research practitioner, Leanna Goodwin based within this team. Three of the 4 work package leads for the UpSMART Accelerator programme (Dr Donna Graham, Dr Louise Carter and Alison Walker) are based within the ECMT which gives us a real opportunity to deliver meaningful

solutions that drive valuable clinical benefit. However, 2020 really saw a step change in our approach, as Dr Donna Graham joined our research team to provide strategic and clinical leadership to our goals in driving forwards the success, value and opportunity of our 'technology' clinical trials.

- Partnerships with research areas outside of the ECMT have also been important to establishing our 'technology' clinical trial capability. The NOTION trial, birthed from the iDECIDE programme, has been developed by digital ECMT and the Advanced Cell Therapy Team at The Christie with The Christie acting as sponsor for this trial. As mentioned earlier (p18), there is a strong strategic fit between this work and the broader goals of the iMATCH programme, led by Prof. Fiona Thistlethwaite of which we're a partner. The learnings from this trial will therefore be translated to the iMATCH programme and support in the development of methods to safely manage patients receiving ATMP therapies.

- In 2020, we started our collaboration with Dr Rebecca Lee and Dr Anne Armstrong, based at The Christie, along with clinicians throughout the UK to develop the first version of the CORONET tool, which aids health care professionals in decisions on

whether to admit patients with cancer presenting with COVID-19 and the likely severity of illness. We have also been able to gain value from the collaborative nature of the UpSMART network to highlight awareness of this tool to cancer hospitals in the UK, Spain and Italy, which has in return led to the contribution of further data-sets that are being used to evolve the CORONET tool and will lead to the release of subsequent versions.

University of Manchester

The digital ECMT continues to collaborate with several groups at The University of Manchester to enhance our research capability, including the Research IT group and Computer Science group. This provides us with flexibility to access the right expertise and resources appropriate to the current activities within the portfolio.

Over the last few years, we have worked hard to build our core skills in the area of decision and data science and we recognise the potential for Ethical AI in advancing cancer care particularly in the early phase setting. We are therefore extremely pleased that from the start of 2021, Dr. Andre Freitas will formally join the digital ECMT to lead the AI team and leverage this capability in new grant funded collaborative opportunities with a focus on the development of Ethical AI and the investigation of novel algorithmic methods to deliver direct patient benefit.

University of Manchester/Manchester Royal Eye Hopsital

A-EYE research

An opthalmo-oncology collaboration with Prof. Tariq Aslam to address a deficiency in retinal monitoring in cancer patients on novel therapies. The goal is to develop a new patient care pathway in an oncology setting, leveraging Innovative technologies and Ethical AI as part of a DSS to detect early drug induced retinal pathology in a cancer patients. The first step in achieving this goal is the A-EYE study due to start in early 2021, which will develop new AI methods to detect general retinal pathology and specific pathology caused by precision medicine drugs.

CRUK Manchester Institute

The Cancer Biomarker Centre is recognised both nationally and internationally for its innovation in cancer biomarker research and discovery. A specific area of development, led by Dr. Elaine Kilgour is immune biomarker development, e.g. cytokines. The purpose of this collaboration is to research whether cytokine monitoring can be done in the home from dry blood spots (NOTION study), thus enabling home based immune biomarker monitoring for therapies such as anti-PD1/PD-L1, CAR-T etc. The translation of these types of assays into the patient's home is technically complex in terms of sample management,

which includes patient education, care pathway process development and logistics.

University Hospital Southampton

With all the uncertainty that COVID-19 brought with it in Q1 of 2020, we were fortunate to be able to find an opportunity to formally collaborate with Professor Tom Wilkinson (Honorary Consultant in Respiratory Medicine) and his team at University Hospital Southampton to extend our research beyond early phase cancer clinical trials. We were able to actively make a positive contribution, during the global pandemic, to UHS and support the delivery of their REACT COVID-19 prospective observational study using REACT/ACUITY and our digital ECMT AI team to support their data synthesis and analysis. This has been a significant achievement for both teams in the context of both the clinical-technical collaboration and also from a research perspective in terms of COVID-19 publications.

Cancer Core Europe - CCE_DART Horizon 2020 project

Building on the partnership that was embedded in 2020 with our Spanish and Italian colleagues on the UpSMART programme, we were invited to join a consortium in a bid to secure EU funding from Horizon 2020. The application for CCE_DART (Building Data Rich clinical Trials) was led by Vall d'Hebron and partner sites across Europe. At the end of 2020, it was confirmed

that the application was successful and will initiate in Q1 2021. The programme is for 3 years and consists of 18 work packages of which the digital ECMT will lead on two, firstly, the discovery of multi-layer complex biomarkers and secondly, the development of online tools for Patient Reported outcome (PRO) measurements (in conjunction with the National Cancer Institute – NKI Amsterdam).

2020 news and research activities

Title/Event	Type	Location	Date
Conferences/workshops/publications			
Experimental Cancer Medicine Centres Showcase event Oglesby Cancer Research Building, Manchester	Poster Presentation	Manchester	January
BRC Scientific Advisory Board eTARGET presentation	Poster presentation	Alderley Park	January
Festival of Genomics	Poster presentation	London	January
Digital Pharma Discussion Forum	Invited presentation	London	January
CPSA EU – Clinical Trials Europe Digital Biomarkers: What's the point?	Invited presentation	Cambridge	February
iDECIDE collaboration – Newsletter – "In HOME" recruits first patients for home-based monitoring of kidney function	Newsletter		April
European Health Data & Evidence Network (EHDEN) General Assembly	Consortium call	Online	April
International Medical Press – Antiviral Therapy Evaluation of drugs for potential repurposing against COVID-19 using a tier-based scoring system	Publication		August
PRISME Forum - Technical Meeting Advisory Committee Keynote Presentation by Donal Landers	Presentation	Online	November
Focus Groups			
NOTION Technology Trial Feedback on sampling instructions and labelling information	Online Focus Group	Zoom call	August
Christie Marketing and Engagement Quality of Life	Online Focus Group	Zoom call	October

Title/Event	Type	Location	Date
Education/awareness			
Using modern IT in clinical trials – MRes The Christie How smartphones can make patients players rather than spectators in their clinical trial	Education Lecture	The Christie, Manchester	February
ECMC North Conference Presentation - Digital Tools and remote visits – opportunities to safely deliver early phase trials	Presentation	Online	October

Links

1. UpSMART REACT

More information on the REACT clinical trial visualisation and analytics tool on the UpSMART website.

https://decmtdneupsmartwebsite.azurewebsites.net/?page_id=7

2. UpSMART website

Primary source of information for the UpSMART consortia providing details of the Accelerator Award and information on the Digital Healthcare Products (DHPs). Updated as and when new products become available.

https://upsmart.digitalecmt.com

3. CORONET

COVID-19 risk in Oncology Evaluation Tool.

https://coronet.manchester.ac.uk/

4. Digital ECMT Cancer Trial Matching Tool

Trial Matching software to support clinical decision making – matching a cancer patient's tumour genetic profile to optimal clinical trials, supporting our precision medicine research.

Trial-matching software available upon request.

https://trialmatch.digitalecmt.com/

Contact us

We work together in partnership to transform decision-making and the patient's role.

If you are interested in collaborating with us in research under any of the themes on the right, please contact us:
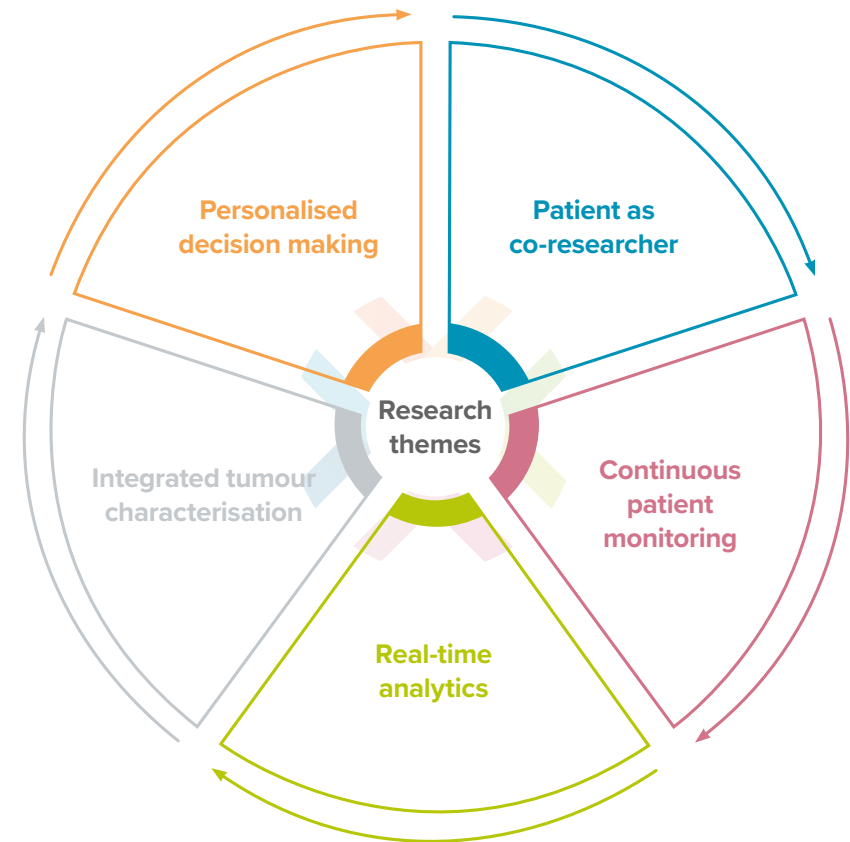
Lets work together!

To get in touch
please contact us at info@digitalECMT.org

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Research themes

Personalised decision making

Patient as co-researcher

Continuous patient monitoring

Real-time analytics

Integrated tumour characterisation