Sparking ideas,
speeding progress.

Experimental
Cancer
Medicine
Centres

About us

The ECMC network brings together the talent and the tools that we need to innovate and take the fight to cancer. Our 20 early-phase research centres and 500+ experts work with industry and academic partners to champion ideas, develop treatments and transform patients' lives.

Together, we are:

- An expert network and a dedicated point of entry for industry
- A catalyst for innovation
- Working smarter to speed up progress
- Equipped to lead the way
- Changing lives

CONTENTS

Welcome

At its core, the Experimental Cancer Medicine Centre (ECMC) initiative is a network of expert minds, working in concert across the UK to improve outcomes for all cancer patients. We have been in existence since 2007. In that time over 20,000 patients have participated in its clinical studies – studies that have contributed to the development of effective new treatments for cancer patients such as abiraterone and rucaparib.

Through the efforts of researchers in the UK and beyond, we now understand more about cancer than we ever have before; how it starts, how it develops and crucially how to treat and prevent it. Whilst there have been improvements in treatments and survival rates for many cancers, as the complex nature of the disease unfolds it is clear that we will need to take ever more inventive approaches to continue the pace of this progress. The ECMC network will play a vital part in driving this.

Working in partnership is critical to our success, and that begins with the funders. Since its inception the network has been co-funded by Cancer Research UK, and the health departments of England, Northern Ireland, Scotland and Wales, who have committed to funding the network until 2022, amounting to a lifetime investment of £110m. This is a sound endorsement of the impact our network has made and will continue to make.

At a local level, each ECMC operates as a partnership between a university and one or more NHS trusts, bringing together the expertise needed to devise new strategies to tackle cancer. The network provides a platform for the many experts and professionals who contribute to the design and delivery of experimental cancer studies to come together, share best practice and drive improvements. It is this continued drive for excellence across diverse professional groups that attracts industry and international collaborators, keeping the UK at the forefront of experimental cancer medicine.

Looking forward to the next five years, the network is optimally positioned to meet the opportunities and challenges ahead. We are rebranding the network to better reflect the scale of our shared ambition and to attract commercial partners to the UK. We are expanding the paediatric network, to ensure that as many children as possible have access to early phase trials. We are supporting our junior investigators, to ensure that we have a continuing supply of expert minds to design and deliver the studies of tomorrow. We are improving the efficiency of the network, to get new treatments to cancer patients as quickly as possible. And of course, we are working together to make sure that we exploit developments in the field for the benefit of our patients.

This report is not comprehensive, but provides a window into what the network has achieved. Our progress is dependent on all of the inspirational people collaborating across the UK to conduct ground-breaking research. Together we look forward to the next chapter and the huge difference we can make in the lives of cancer patients around the world.

Dr Aoife Regan
Head of the ECMC Programme Office
On behalf of Cancer Research UK, the National Institute for Health Research in England and the health departments of Scotland, Wales and Northern Ireland.

1,700
ECMC-SUPPORTED EARLY-PHASE TRIALS

£236m
LEVERAGED FROM INDUSTRY*

20,000
PATIENTS RECRUITED TO ECMC SUPPORTED EARLY PHASE TRIALS

13
TREATMENT MODALITIES

ECMC in numbers 2007-2017

The ECMC network provides a unique environment and rich opportunities for academic and industry investigators to conduct pioneering experimental studies.

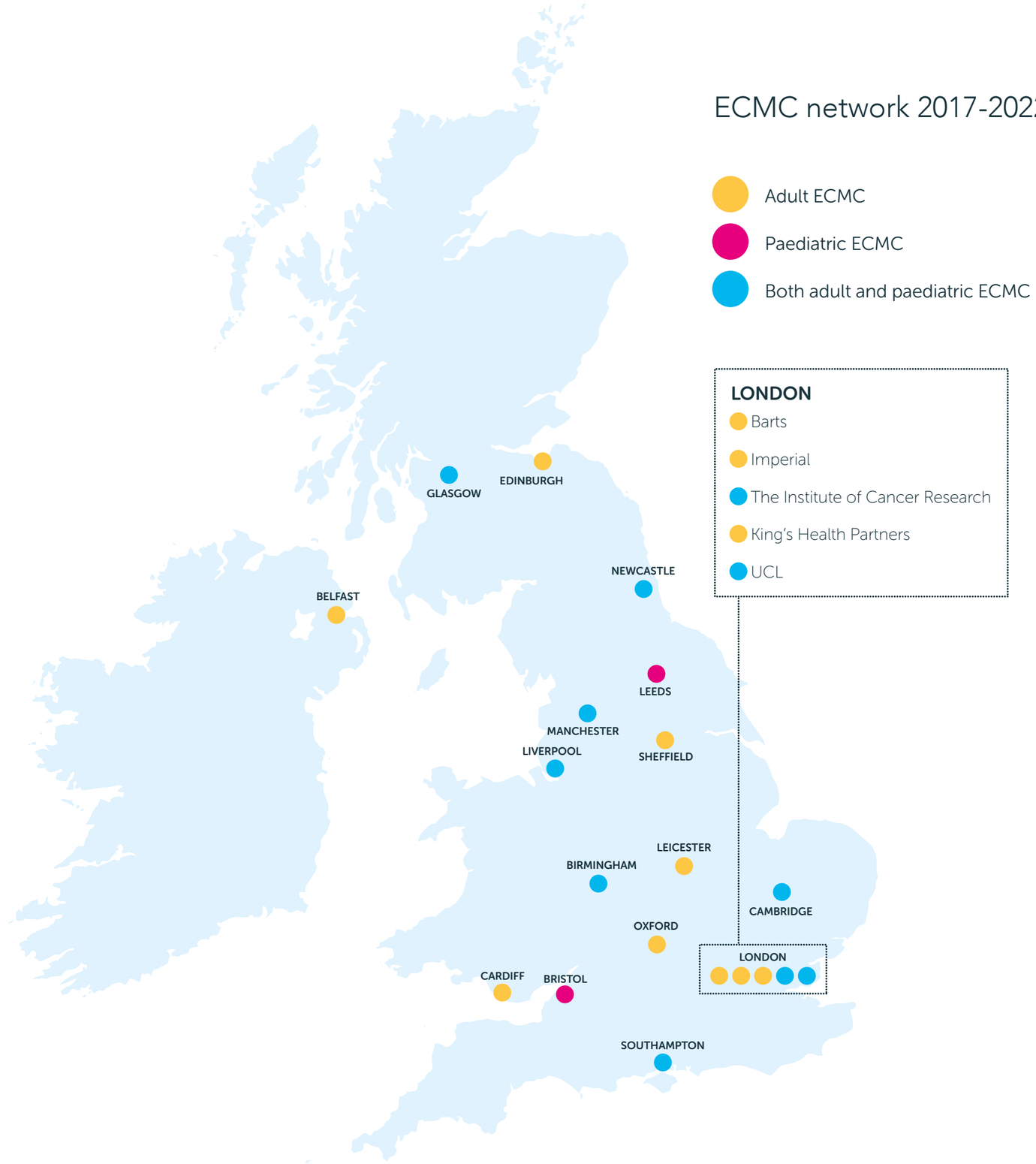
Each ECMC is a centre of excellence in experimental medicine, with unique capabilities and scientific expertise. ECMC offers access to state-of-the-art technology and personnel skilled in using it, ensuring that even the most complex of interventions can be introduced into the clinical setting.

DRUG, IMMUNOTHERAPY, BIOLOGICAL THERAPY, RADIOTHERAPY, MOLECULAR RADIOTHERAPY, CELLULAR IMMUNOTHERAPY, SURGERY, DEVICE, GENE THERAPY, CHEMOPREVENTION, STEM CELL TRANSPLANT, MULTIPLE MODALITIES, COMBINATION

*2012-17.

ECMC network 2017-2022

- Adult ECMC
- Paediatric ECMC
- Both adult and paediatric ECMC



LONDON
- Barts
- Imperial
- The Institute of Cancer Research
- King's Health Partners
- UCL

An expert network

The ECMC is a research network with partnership and collaboration at the heart of our success.

We give industry a dedicated access point to over 500 UK-based expert minds at the forefront of early-phase cancer research.

The success of the ECMC network is made possible through the commitment, enthusiasm and collaboration of many inspirational people, working together to innovate and share best practice.

Dr Stefan Symeonides

Junior Investigator Network Group, Edinburgh

"I became an oncologist because I was always interested in the biology of the human body.

Of all the diseases that affect people, cancer is the one where all of the normal molecular mechanisms have gone wrong. There is so much we need to learn to overcome it. I also find the day to day job incredibly rewarding.

Helping isn't just about giving someone a new drug to treat their cancer, you're helping people that are going through a fundamentally life-changing situation. Every minute that you spend in work, you're doing something useful and helping patients.

I first attended a Junior Investigator Network Group (JING) residential as a trainee where I had the opportunity to present my ideas for my first clinical trial. I received great advice from the more senior faculty members, who had a lifetime of experience in running such trials across the ECMC network.

The ECMC support us in carrying out the first step in drug development – exploiting the science of our research centres and directing it into our network of Phase I clinical trial units for the benefit of patients around the whole UK.

The JING supports the people who make this happen by providing the specialised training that doesn't otherwise exist, thus enabling the next generation of oncologists to develop their careers."

"Every minute that you spend in work, you're doing something useful and helping patients."

DR STEFAN SYMEONIDES

Transforming treatments for very young children with cancer

Newcastle and all paediatric ECMCs

Treatment of cancer in very young children has long presented a major clinical challenge, as developmental physiological changes can markedly impact drug disposition. Data are particularly scarce in children under three months of age. To address this, Newcastle ECMC worked with centres from the paediatric network to generate real world data on scientifically-based carboplatin dosing guidelines for the treatment of neonates - the first time these much needed data have been generated. This evidence will shortly lead to the publication of national guidelines for monitoring carboplatin treatment in paediatric retinoblastoma.

It's a truly cross-network endeavour: the team relied on getting quality samples from all paediatric centres. To ensure quality they ran training programmes for research nurses in sample taking, data capture, sample storage and shipping. Now, samples from across the paediatric network are routinely analysed providing clinical teams with personalised dosing advice for their young patients within 6-24 hours of sample collection.

The Newcastle team, led by Dr Gareth Veal, received the 2013 Quality in Care Excellence in Oncology's 'Best Innovation in Service Provision' national award for this revolutionary study. Data generated over a number of years have resulted in changes to dosing regimens for neonates and infants for several important anticancer drugs.

Pioneering personalised medicine in the UK

Birmingham and all adult ECMCs

The National Lung Matrix Trial (NLMT) offers eligible patients with non-small cell lung cancer, recruited from all locations across the network, access to the UK's first and largest NHS-supported, precision medicine trial. This pioneering trial is led by Professor Gary Middleton, and sponsored by the Cancer Research UK (CRUK) Birmingham Clinical Trials Unit. A study of this complexity and scale would not be possible in the UK without the expertise and infrastructure the ECMC network offers.

Through CRUK's Stratified Medicine Programme 2 (SMP2), patients are genetically screened and eligible patients matched to the most appropriate arm of the NLMT, each one testing a different drug that targets a specific genomic signature. The network has worked together to set up and run this pioneering study, with members across all disciplines sharing best practice along the entire pathway.

Establishing data flow across all ECMC locations was a significant challenge. Newcastle overcame this by implementing a manual, easy-to-use data sharing process, and provided the tool and training to new ECMC locations coming on board. "It's a fantastic example of the ECMC collaborating and sharing to expedite processes at other sites and help the network as a whole" says Tosin Sule, Senior Business Analyst, from CRUK's SMP2 team.

The ECMC network is ensuring that the UK oncology community is set-up to run ever more complex, data rich trials, bringing the best possible treatment options to people with cancer faster than ever before.

A catalyst for innovation

Every day, we're taking on the most complex, challenging questions in our field, pooling our knowledge and experience to explore new ways to understand and fight cancer.

Raising the bar for CAR T-cell therapy

King's Health Partners

The development of chimeric antigen receptor T-cells (CAR T-cells) was long viewed as "a boutique activity", says Professor John Maher at King's Health Partners (KHP) ECMC, who pioneered the technology that underpins many CAR T-cell development programmes today.

It's a markedly different landscape now, with CAR T-cells – where a patient's own T cells are removed, engineered in vitro to kill their cancer cells, and returned to the body – showing promise in haematological cancers. John hopes to extend this to solid tumours, and is pioneering a new CAR-T therapy with three distinct features he hopes will prove beneficial in head and neck tumours.

First, John's team are injecting CAR T-cells directly into tumours rather than the bloodstream, reducing on-target, off-tumour toxicity.

Second, the T4 immunotherapy construct is designed against multiple conformations of the ErbB receptor family – a well-validated target of blockbuster drugs cetuximab and Herceptin. T4 recognises eight related ErbB targets, making it theoretically much more difficult for a tumour to become resistant.

Third, they are using an innovative expansion step that primes CAR T-cells to have heightened responsiveness to interleukin-4, increasing their enrichment to generate several billion CAR T-cells from as little as 40ml patient's blood.

The team has high hopes for the results of their Phase I study currently recruiting in the network – success would rally the CAR T-cell community to progress this pioneering treatment in other cancer types.

Professor Sarah Blagden

ECMC Lead, Oxford

"I am a hybrid between a researcher and a clinician which allows me to guide the translation from basic research into innovative cancer studies. My work is unpredictable, but that is what I find most rewarding. If you have the privilege of running a lab with its own surprises and disappointments, then you will have a working life that never fails to amuse, bemuse and challenge.

I have been the ECMC Lead for Oxford since November 2015. Oxford has wonderful science and it's really exciting to bring it into the clinic. The network is exceptional in how collaborative and progressive it is – no other country has a network to match ECMC. Moving forward, I think we need to be more self-promoting so that others become more aware of what we are doing and achieving.

The UK used to have a reputation for being slow in setting up studies, but that has changed in recent years and we are now offering timelines that are competitive with the USA and Europe. I think it is time to engage more effectively with pharma, offering them a means of testing their novel compounds in multiple locations with a streamlined regulatory process. The next few years will be a time of great change within ECMC, and I am excited to be part of it."

"The network is exceptional in how collaborative and progressive it is – no other country has a network to match ECMC."

DR SARAH BLAGDEN, ECMC LEAD

Taking cutting-edge imaging into the clinic

Cambridge

Cambridge ECMC was the first site in Europe to take a radically innovative imaging technology – hyperpolarised Carbon-13 magnetic resonance imaging (13C-MRI) – into the clinic. It's an alternative way of looking at tumour metabolism and is 10,000-fold more sensitive than conventional MRI.

In preclinical studies 13C-MRI detected rapid metabolic changes linked to cancer treatment, long before changes in tumour size were detected. The MISSION study is exploring the potential clinical applications of the technology across a range of cancers – breast, glioma, lymphoma, ovarian and prostate.

The team hope that over the next two years the study will demonstrate clinical application in cancer, and that they can move into larger scale, multisite trials.

Lead investigator, Dr Ferdia Gallagher, says: "I see the technology being used alongside other methods – biopsies, circulating biomarkers, circulating tumour DNA and hope that it will become more routine, and rolled out to district general hospitals in years to come."

Working smarter to speed up progress

Our collaborative approach is accelerating the process of anti-cancer drug development globally, reducing costs and timescales and increasing our effectiveness.

Translating new innovations faster

University College London and other adult ECMCs

University College London (UCL) ECMC in collaboration with 10 other ECMCs is working with industry partners Tarveda and Ipsen to investigate the feasibility of using circulating tumour cells (CTCs) as prognostic and therapeutic response biomarkers in neuroendocrine tumours (NETs). Conducting repeat biopsies in this patient group can be challenging and UCL-led studies have shown that changes in CTCs, expressing CD56 and synaptophysin, within 3-5 weeks post therapy are predictive of overall outcome.

These promising results mean that CTCs are now being incorporated as prognostic and predictive biomarkers into clinical trials of novel agents for the treatment of NETs.

From observation to impact

The Institute of Cancer Research, Cambridge, Glasgow, Belfast, Cardiff

The TAX-TORC study demonstrates just how quickly a study can go from being an idea to being be rolled out across the network. The speed of set-up was thanks in part to the collaboration with AstraZeneca through the CRUK Combinations Alliance.

TAX-TORC stems from translational research by Dr Udai Banerji at The Institute of Cancer Research (ICR), showing that ascites from women with ovarian cancer who didn't respond to chemotherapy had elevated levels of p-S6 kinase. His findings were published in 2012 and in 2013, a trial opened to study whether TORC1/2 inhibitors, which block the pathway upstream of p-S6 kinase, alongside the standard treatment paclitaxel would prevent or delay resistance occurring. The team saw encouraging results in ovarian cancer (leading to a randomised Phase II study, OCTOPUS), and spectacular responses in two lung cancer patients.

"We're excited for multiple reasons," says Udai. "The science is holding up, and I'm hopeful we'll find a biomarker to enrich the population further and see even higher response rates. We saw encouraging clinical activity and started doing disease-specific expansion cohorts, with the help of other ECMCs. It was truly a national study and recruited around three to six months early."

A world first in glioblastoma

Glasgow, The Institute of Cancer Research, Birmingham, Manchester, Cambridge, Edinburgh & Dundee

OPARATIC was the first study to test the PARP inhibitor olaparib in glioblastoma showing that it could both penetrate the blood brain barrier, and the tumour itself.

"This means olaparib could be beneficial in this patient group," says Lead Investigator Professor Anthony Chalmers from Glasgow ECMC. "And it also shows that we shouldn't write off potential new drugs for glioblastoma when conventional preclinical testing suggests they do not cross the blood brain barrier."

The trial also adapted the dosing schedule for the drug, reducing previously seen bone marrow toxicity and making the combination with temozolomide safe.

The results of this game-changing study have led the team to open two additional trials testing olaparib in patients with newly diagnosed glioblastoma: in combination with radiotherapy in elderly patients in PARADIGM, and in combination with both radiotherapy and temozolomide in patients under 70 in PARADIGM-2.

The UK Therapeutic Cancer Prevention Network

Experimental medicine is not just about the design and testing of new treatments, it is about making the most of the treatments we already have.

The UK Therapeutic Cancer Prevention Network (UKTCPN) is a group of basic and translational scientists, clinicians, epidemiologists, statisticians and specialists in primary care, diet and nutrition – who came together in 2013 to explore opportunities for the network in this important field.

"The UK has excellent epidemiologists and experts in late-phase trials – but there was no forum for us to get together. The UKTCPN brings us together to come up with new ideas, work on large collaborative grant proposals and attract more research funding into the area," explains UKTCPN Co-Chair and Leicester ECMC Lead, Professor Karen Brown.

Professor Dion Morton, the group's other Co-Chair and Lead at Birmingham ECMC, believes that screening patients is key to early disease management: "The challenge for clinicians is to develop effective therapies that will substantially reduce the risk in people with precancerous conditions, before they progress to cancer."

Making progress in drug repurposing is a priority for the UKTCPN. However, studies have shown GPs and patients are reluctant to use well understood drugs like tamoxifen for cancer prevention. The group is working with funders and regulators to tackle some of the barriers to the development of preventive medicines, for example the lack of a well delineated development pathway.

The group is also working at an international level through collaboration with Cancer Prevention Europe (CPE). The UKTCPN, as a core partner and steering group member, will work to ensure therapeutic prevention is well represented in the research remit.

Equipped to lead the way

We're continually investing in our network so we have the facilities and the resources to lead the global fight against cancer. We've created a network of facilities that set the benchmark for our industry and equip us to lead the way in experimental cancer research.

Predicting response to therapy

Belfast

The DNA damage response deficiency (DDRD) assay story began when researchers in Belfast identified a unique gene expression signature found in 20-30% of solid tumours that appeared to be a hallmark of sensitivity to DNA-damaging chemotherapy. With access to the Northern Ireland Biobank they successfully developed a DNA microarray test for this signature which uniquely works on formalin fixed paraffin-embedded samples.

The assay is being tested in clinical trials to predict response to chemotherapy across multiple cancer types, including upcoming collaborations with Cambridge and Oxford ECMC in oesophageal and colorectal cancers, and with collaborators in the USA in breast cancer.

But perhaps the most exciting application could be in the rapidly advancing field of immuno-oncology. Professor Richard Kennedy, Belfast ECMC Lead, explains: "It turns out that the biology that underpins DNA damaging agents is actually the same biology that sensitises tumours to immune checkpoint inhibitors. It may be that this group of patients is the subgroup that's responding to these new drugs. That's where the excitement is."

SUPPORTED THE DEVELOPMENT AND GROWTH OF **SIX NETWORK GROUPS**

30 NETWORKING EVENTS AND WORKSHOPS SUPPORTED

1500+ ATTENDEES

40 CROSS-CENTRE PLACEMENTS SUPPORTEFD

Dr Ruth Challis

Quality Assurance and Translational Science Network Group, Southampton

"Southampton has been a hub for immunotherapy research for the last 30 years, and with the latest explosion in the immuno-oncology field I feel both privileged and inspired to be working at the cutting-edge of oncology research.

In recent years I've seen a changing landscape in experimental medicine: more trials coming to our ECMC, higher regulatory standards and an increased requirement for auditing. We're being increasingly challenged to develop novel tactics that will allow us to validate complex new technologies, ensuring trials can open quickly.

The Quality Assurance and Translational Science (QATS) Network Group supports us in coming together to share best practice and address these complexities as a network, rather than working in isolation.

It is truly motivating to be able to offer novel treatments to patients by working in partnership with industry to gain access to drugs that otherwise would have been shelved, and to new combinations of therapies through the CRUK Combinations Alliance.

We're able to offer more options to patients than ever before, and these experimental treatments could soon become a reality for cancer patients worldwide."

"We're able to offer more options to patients than ever before, and these experimental treatments could soon become a reality for cancer patients worldwide."

DR RUTH CHALLIS

Forging new collaborations

Sheffield and Manchester

Cross-centre placements enable researchers to exchange knowledge and adopt standardised processes and procedures.

Professor Caroline Dive at Manchester ECMC has hosted network members from Sheffield, ICR and Newcastle, all keen to learn about the lab's unique 'fast-track' approach to biomarker method validation and apply this back at their host ECMC.

Dr Fiona Taylor is a Clinical Research Fellow based in Sheffield: "I went on a cross-centre placement to Manchester ECMC to understand how to prepare cell free DNA (cfDNA) for next-generation sequencing. I got to observe working practices in a GCLP accredited lab, which are essential if I am to translate a biomarker into clinical practice.

My visit promoted closer working between our groups. Now I'm collaborating with colleagues in Manchester to perform low coverage whole-genome sequencing and targeted mutation analysis of cfDNA from patients in the STOMP trial, investigating olaparib in small cell lung cancer."

Transforming patient care

Our network has shown it has the world-class reach and the resources to take ideas in the lab and translate them into new cancer treatments with real benefits for patients. Ideas born in our UK laboratories are already making a huge difference in the lives of cancer patients around the world.

"We're looking towards a future where we can make cancer a chronic disease for our patients, rather than a life-shortening disease."

ALISON PASS

Alison Pass

Research Nurses Network Group, Sheffield

"I've worked as a research nurse in Sheffield ECMC for nine years, so I've been here since the inception of the ECMC initiative. Communication and collaboration across the network has progressed in that time, and the Research Nurses Network Group has played a big role in this; we've got representation from each ECMC which gives us a broad perspective across the UK. The group offers a strong learning environment through training sessions and cross-centre placements so that we all have a better understanding of why we do what we do, not only from a practical perspective but also scientifically.

When we take a drug into people for the first time we haven't got the detailed information you'd have for later phase trials. It's difficult to tell patients what the adverse effects may be, when often we don't know. Having a network of nurses across the UK that we're able to tap in to for support and expertise really enhances the care we can offer our patients.

Over the past few years, it's been amazing to see a much wider appreciation of the value that research brings to patient outcomes. Clinicians, teaching staff and academics are engaging with each other in deeper, more meaningful ways. As the trials coming into our ECMC have become more advanced, there has been a shift towards personalisation, and looking at patients as individuals.

We're looking towards a future where we can make cancer a chronic disease for our patients, rather than a life-shortening disease."

Trailblazing surgical technique

Imperial College London

The trailblazing iKnife technique provides biochemical information in real time to surgeons operating on patients with cancer, helping them to excise tumours with a clear margins and reduce damage to healthy structures.

Pioneered by Dr Zoltan Takats, iKnife makes use of aerosols created during surgery, and is engineered to be as similar as possible to a normal operating set-up. iKnife is being tested in breast and ovarian cancer with the aim of obtaining regulatory approval. "The ECMC network gave us infrastructure support at Imperial and access to expertise without which we would have had to find out practically everything from scratch" says Zoltan. "It freed up funding and made the delivery of this project much, much quicker."

A breakthrough in bladder cancer

Barts

The ECMC provides a fertile environment for ground-breaking studies that are bringing more treatment options to cancer patients worldwide. A recent multi-centre, international study led by Barts ECMC tested atezolizumab, a new checkpoint inhibitor drug developed by Roche, in Phase I trials across 20 sites in the UK, and internationally.

The results were striking: after six weeks of treatment, tumours had shrunk in nearly half of a subset of patients that were PD-L1-positive. As a result, the drug received breakthrough designation status by the FDA and was fast-tracked for approval.

In May 2016, atezolizumab became the first drug approval for bladder cancer in the US for more than 30 years; it's currently under review by the European Medicines Agency.

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