



Experimental Cancer Medicine Centres (ECMC) Network

A year of progress 2015/16

Introduction

Launched in 2007, the ECMC Network is a partnership between CRUK and the Health Departments for England, Scotland, Northern Ireland and Wales.

Through collaboration across the experimental medicine community, the ECMC Network's vision is to bring together laboratory and patient-based clinical research to speed up the development of better treatments for cancer patients.

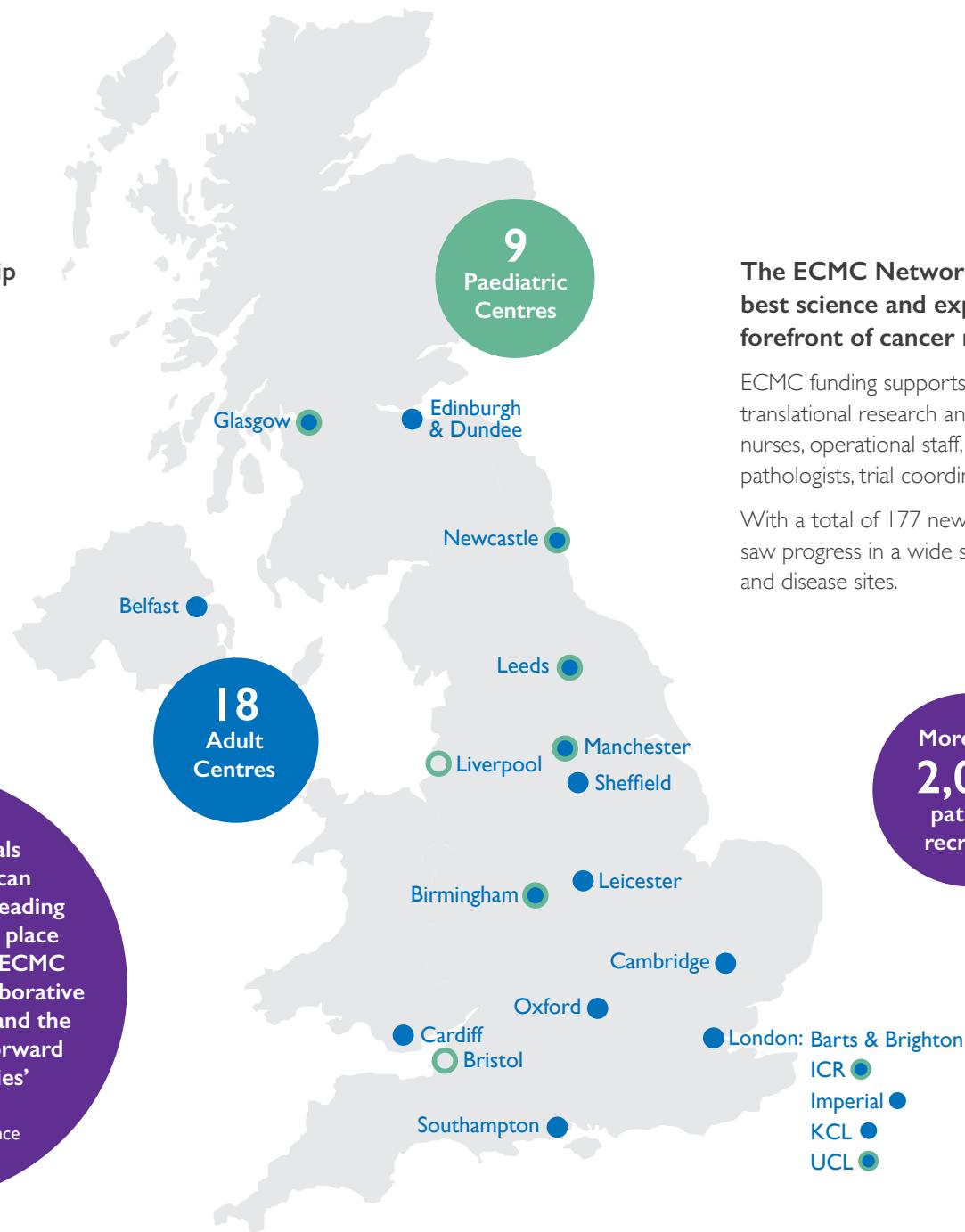
As the Network approaches 10 years of ECMC collaboration, we celebrate having recruited over 18,000 patients onto more than 1,500 new early-phase trials. To date, more than £70m has been invested into clinical and translational research across 35 cancer types.

This booklet highlights some of the ground-breaking achievements made by the Network in 2015/16.

£70m
committed to developing infrastructure for early phase trials to date

'Effective clinical trials ensure that patients can benefit from the world-leading medical research taking place across the country. The ECMC Network shows how collaborative work between charities and the government is driving forward new cancer discoveries'

George Freeman
UK's Minister for Life Science



18
Adult Centres

9
Paediatric Centres

The ECMC Network supports a selection of the best science and experimental therapeutics at the forefront of cancer research in the UK.

ECMC funding supports over 200 staff members involved in translational research and early phase trials, including research nurses, operational staff, pharmacists, physicists, radiographers, pathologists, trial coordinators and quality assurance staff.

With a total of 177 new trials reported, the year 2015/16 saw progress in a wide spectrum of treatment modalities and disease sites.

More than **2,000** patients recruited

More than **20** different cancer types in the portfolio

Over **600** trials active in the Network

The capacity of the ECMC Network

The ECMC Initiative

Each ECMC is a partnership between a university and at least one NHS Trust/Board, which enables the best health researchers and clinicians to work together to generate novel treatments for cancer patients.

ECMC funding can be used flexibly to allow Centres to allocate their funding strategically across a number of themes, determined by local need and existing expertise.

The Network supports over 200 staff members involved in translational research and early phase trials. These expert staff support a broad portfolio of experimental cancer medicine studies of the highest standards.



Delivering innovative treatments for cancer patients.

Ensuring innovative treatments for cancer patients, through the treatment of all cancer types and treatment modalities.

Making the UK the place of choice to deliver trials.

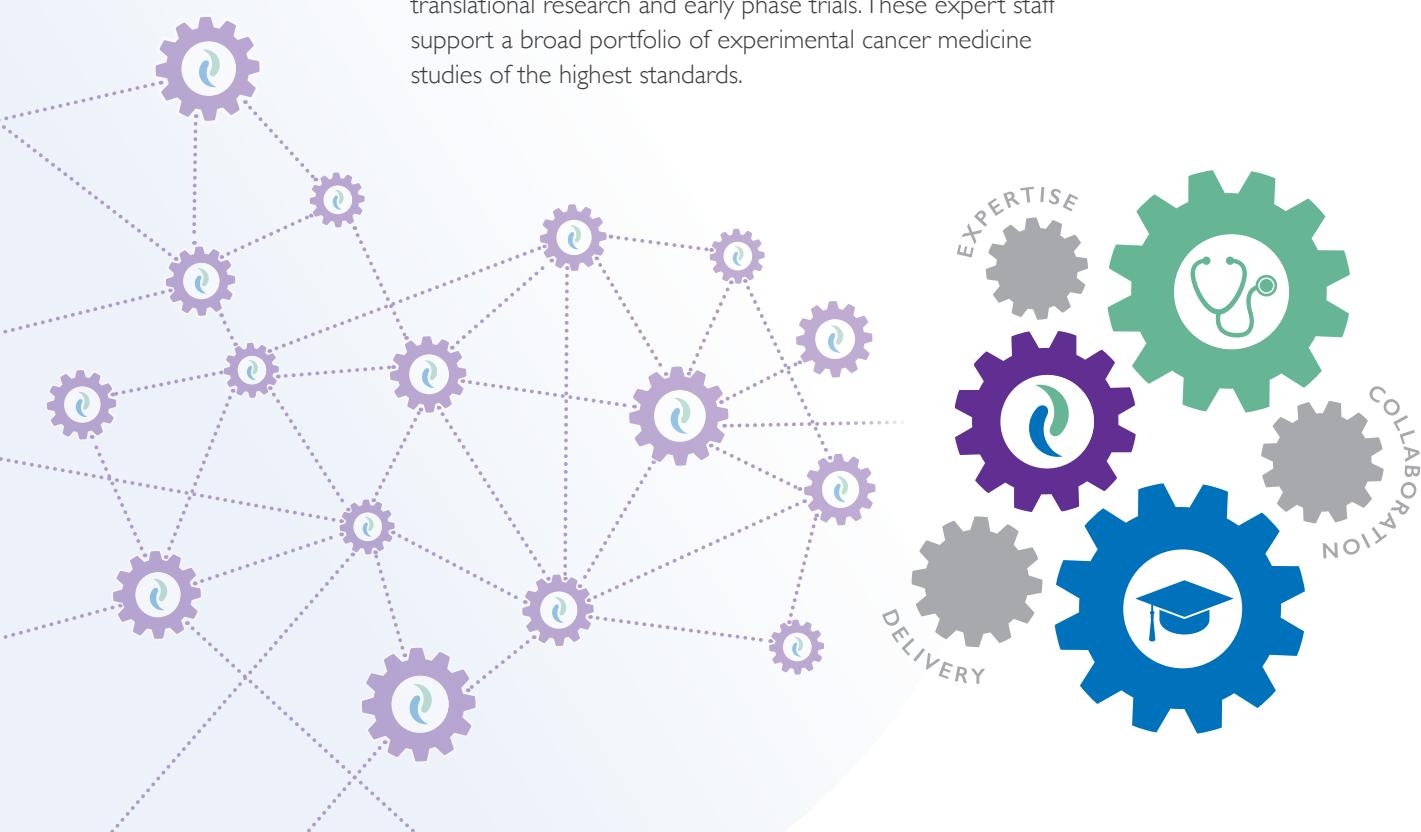
Making the UK a competitive place to perform experimental cancer medicine. By developing new approaches to clinical trial setup we can open the network up to interested companies and match them to relevant ECMCs quickly.

Building the capacity of the Network.

Building the UK's capacity in the field of experimental cancer medicine, by supporting a professional, well-trained and responsive workforce.



Objectives of the Initiative



Innovation

Delivering innovative treatments for cancer patients.

The ECMC Network is proud to display some excellent examples of translational studies and clinical trials that are pushing the boundaries of clinical cancer research.



The **Manchester ECMC** published the results of the first UK Radioimmunotherapy Phase II Trial – the SCHRIFT study – conducted across the UK. This innovative trial made radioimmunotherapy widely available to more cancer patients than has previously been possible. In addition, throughout the duration of the trial, Manchester ECMC collected and analysed blood samples from recruited patients across the ECMC Network to understand the pharmacokinetics of rituximab.

Recent results from the AML17, 18 Pilot, 18 and 19 studies done by **Cardiff ECMC** have provided major new insights into prognostic risk stratification in Acute Myeloid Leukaemia (AML). A sub-set of patients with NPM1 gene mutations, previously classed as a 'favourable risk' abnormality, were found to be at very high risk of relapse – if the mutation remained detectable by quantitative PCR analysis – following a second course of chemotherapy.

The **Newcastle ECMC** have finalised a Phase I dose escalation study of Lapatinib and Pemetrexed in the Second-Line Treatment of Advanced or Metastatic Non-Small-Cell Lung Cancer. The trial also included an exploratory study to measure circulating cell-free thymidylate synthase ribonucleic acid (cfTsmRNA) in all patients and compared it with clinical benefit. Results showed that both Lapatinib and pemetrexed were well tolerated but cfTsmRNA was at the limit of detection and thus, not measurable in all patients. Nevertheless, nonsignificant trends of cfTsmRNA were observed, suggesting that higher levels of cfTsmRNA are associated with poorer outcome.

The ADDRAD single-centre feasibility trial recruited its first patient at **Belfast ECMC**. This trial investigates new combination of hormone therapy, external beam radiotherapy and intravenous radionuclide (radium 223) for men with hormone sensitive, metastatic prostate cancer. The trial also includes translational research in three areas (i) the behaviour and potential predictive capacity of circulating tumour cells, (ii) DNA damage biomarkers as a potential method of facilitating molecular dosimetry, and (iii) new biophysical models of the interactions of bone seeking radionuclides.

The **Birmingham ECMC** supported a translational collaboration between their clinical and scientific teams to focus on liver cancer that resulted in the award of a CRUK programme grant to study the Immunobiome of pancreatic cancer. This grant will allow the Birmingham team to investigate pancreatic ductal adenocarcinoma (PDA) which causes the fourth highest incidence of cancer death in the UK. The programme award will develop new tumour specific antibody and T cell reagents for immunotherapy and will work towards the development of novel early phase clinical studies.

Removing malignant adenomas before they turn into malignant tumours is an obvious clinical priority, but as not all adenomas become malignant. Thus, a better understanding of the molecular events promoting disease progression is required. Building on the existing work describing the importance of KRAS dysregulation in the progression of colon cancer, researchers from **Edinburgh and Dundee ECMC** have identified microRNA-224 (miR-224) as a clinical biomarker for bad prognosis in colorectal cancer patients. The results from this study might open a door for the development of early-stage screening clinical tests.

At the prestigious EORTC-NCI-AACR Annual Meeting in Boston (USA), the **ICR ECMC** presented the results of the Phase I trial of first-in-class ataxia telangiectasia-mutated and Rad3-related (ATR) inhibitor VX-970 as monotherapy or in combination with carboplatin in advanced cancer patients. This study showed that VX-970 was well tolerated and will be further explored in early Phase II studies for multiple tumour types, including triple-negative breast cancer and non-small cell lung cancer patients.

A robust tissue collection study - the ExPAT study – was developed by **Leicester ECMC** to support their chemoprevention programme of work in colorectal cancer. This involved inviting patients undergoing surgery or colonoscopic resection for either colorectal adenomas or cancers, and also working with the pathologists to access fresh tissue without compromising the diagnostic process. The collection of these samples is vital to produce primary cell cultures, spheroid model systems and explant cultures which underpin their chemoprevention programme.

The **Paediatric ECMC Network** is participating in two international first in child immunotherapy Phase I/II trials in relapsed/refractory solid tumours: a study assessing Pembrolizumab in PD-L1 positive patients and one testing Atezolizumab. Both trials represent a potential paradigm change in the treatment for some cancers and will help set the benchmark for how safe and effective these agents are for childhood and adolescent cancer patients. If results are encouraging, these treatments would have the potential to reduce certain long term side effects of chemotherapy regimens on young patients.

Two novel biomarker candidates, macrophage-capping protein (CAPG) and PDZ domain – containing protein GIPCI, were identified for clinical validation from the results of the **Sheffield ECMC AZURE** trial. These biomarkers may facilitate patient selection that will benefit from adjuvant bisphosphonate treatment, which has shown to reduce bone metastasis development and improve the survival of metastatic breast cancer patients.

A new clinical trial has been developed at **Southampton ECMC** that uses a completely new method of preparing patients with AL-amyloidosis for autologous stem cell transplantation. The Southampton's Targeted Radiotherapy Group have developed a novel technique using a radio-labelled monoclonal antibody that allows very precise delivery of high radiation doses to clonal plasma cells. The Phase I study will test the optimal radiation dose that can be delivered safely to patients and will determine if this is associated with a reduction in the production of amyloidogenic protein.

Competitiveness

Making the UK the place of choice to deliver trials.

With a collaborative Network with a track record in delivering innovative clinical studies, there has never been a better opportunity for industry to ensure their challenging studies are completed to time and target.



The Oxford ECMC brought the first partnership with industry facilitated through the ECMC Secretariat. The new streamlined programme aims to facilitate efficient interaction between ECMC Leads and industry. Oxford ECMC noted that US-based pharmaceutical company CytmoX were wishing to develop a multi-centre study using an immunotherapy agent based on the Probody. With the direction of the ECMC Secretariat, a non-confidentiality form was completed and efficiently assessed, which resulted in 11 ECMC locations being identified for collaboration with Oxford ECMC as the lead site. In only 3 working days, an ECMC Non-Disclosure Agreement (NDA) was executed by the ECMC Secretariat between all parties. The speed at which this has been facilitated has acted to enhance the ECMC Network's reputation as being a really promising commercial opportunity in the field of early phase clinical cancer research.

The Leeds ECMC is starting a series of studies evaluating a new medical device for testing patients' blood counts at home. This device is being developed with Philips Healthcare and was made possible by a £900K investment secured through Innovate UK.

The strength of the UK as a centre for early phase clinical trial activity in children, due to the well-established and smoothly functioning **Paediatric ECMC Network**, was reflected when 5 ECMCs – Newcastle, Birmingham, Manchester, GOSH, RMH – were certified by the Innovative Treatments for Children with Cancer (ITCC) as centres for first-in-child studies, following a Europe-wide submission and assessment process by an independent panel of international experts in the field. Only 19 centres were designated across Europe from which the 5 UK centres scored very highly, with some amongst the very top ranked centres by this scoring system. Receiving this certification will certainly impact in pharmaceutical companies willing to perform innovative trials in the UK.

The Glasgow ECMC has been invited to become a member of the Quintiles Early Phase Oncology Network (EPON). Established in early 2016, it consists of approximately 15 centres in Belgium, France, Spain, the Netherlands, and the UK. The aim of this network is to harmonise and streamline the approval and regulatory processes at international level so that study timelines will be shortened, resulting in increased commercial early phase clinical trial opportunities.

Ipsen has supported the set up of a central laboratory analysis at **UCL ECMC** for the national CALMNET trial. This investment was in response to the excellent work performed at the ECMC-funded GCLP laboratory on the development of a novel somatostatin receptor CTC assay. The CALMNET trial will evaluate the role of circulating tumour cells in patients with neuroendocrine tumours receiving Lanreotide Autogel.

Astra Zeneca is supporting the development of D4-choline PET as a pharmacodynamics biomarker for detection of MAPK activity at **Imperial ECMC**. In this study, around 40 patients with triple negative breast cancer treated with selumetinib and selumetinib plus paclitaxel will be studied longitudinally by PET as a pharmacodynamic biomarker. The results of this study might create a paradigm shift in early phase trials, showing proof of target inhibition using novel imaging.

Streamlined delivery

The ECMC Network piloted a component of the Health Research Authority (HRA) approval process with continued **benefits** for Sponsors working with ECMCs

The **ECMC Collaborative Agreement** is a legal arrangement signed between all the associated NHS Trust/Boards and university partners that form the adult ECMC Network. This Agreement defines responsibilities and common ways of working to streamline regulatory processes across ECMCs. This UK-wide Agreement will improve the Network's ability to carry out early phase clinical trials, boosting the research and development of clinical trials in the UK, and therefore bringing innovative new treatments to patients sooner.

Coordinating Network-wide **Expression of Interest (Eoi)** process

Several companies (niche to global) are already working with the Secretariat to help coordinate their **study opportunities** to the Network

Agreed Network-wide **Material Transfer Agreement (MTA)** provisions

A mutual **ECMC Non-Disclosure Agreement (NDA)** template is now available for use across the Network

We offer facilitation of **feasibility/site selection** processes with commercial sponsors

'We're delighted that our ECMC Network is continuing to help cancer patients around the country benefit from world-leading research taking place here in the UK. This initiative will ultimately help potentially life-saving drugs reach cancer patients sooner by accelerating the first step of clinical research'

Sir Harpal Kumar
CEO of Cancer Research UK

The ECMC Network strives to bring cancer treatments through the translational pathway with the aim of reaching cancer patients in the clinic faster.

Below are examples of trials that have shown excellent progression through 2015/16.

Following the successful completion of two ECMC-supported Cytosponge trials (i.e. BEST1 and BEST2), the **Cambridge ECMC** have successfully secured funding for BEST3. This is a cluster randomised design in primary care for 4,000 patients with reflux symptoms comparing Cytosponge with usual clinical care. It is anticipated that this will be the last trial required for NICE to decide whether this technology can become part of routine clinical care in the NHS.

Barts and Brighton ECMC have made significant progress in developing treatments for malignant mesothelioma. Last year, the team completed the ADAM trial, a Phase II multicentre study of arginine deprivation using ADI-PEG20 which was presented at the ASCO conference. Results from this trial led to the opening of a new Phase I trial: the TRAP trial. This novel trial tests subjects with tumour requiring arginine to assess ADI-PEG 20 with pemetrexed and cisplatin (ADI-PemCis) and has recently progressed to Phase II/III trial.

The **KHP ECMC** led the first in human intra-operative Cerenkov Luminescence Imaging (CLI) to guide surgery in breast cancer. Funded by Innovate UK, it is a proof of principle feasibility trial in partnership with industry. The trial provided evidence that CLI can be safely used to determine margins of tumour resection in real time. The results of this work leveraged £3 million in funding from a Horizon 2020 grant and the Guy's and St Thomas Charity, to proceed to an international multicentre randomised controlled trial.

Efficient progression

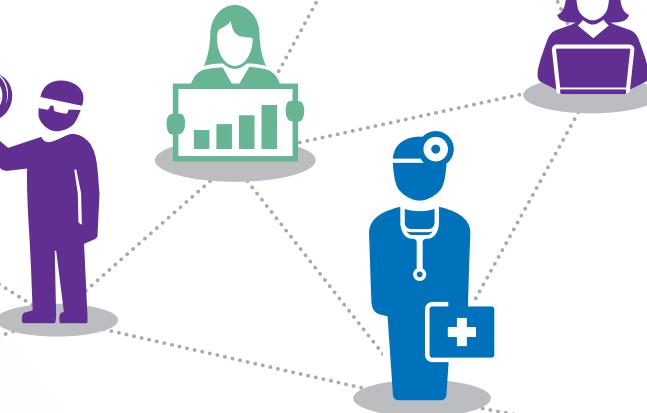
Capacity

Building the capacity of the Network.

The ECMC Network enhances the capacity by encouraging collaboration, and this year saw some great examples of the ground-breaking work that has been carried out across multiple ECMC locations.

Staff members of the **Cambridge** and **KHP ECMCs** held a half-day meeting to share experience and working practices. Staff represented at the meeting included trials managers and research nursing as well as investigators. Outcomes of this meeting included sharing of SOPs, job descriptions and trial portfolios.

Building on relations between **Oxford** and **Belfast ECMCs** through DEBIOC then MErCuRIC has resulted in the CRUK/MRC awarding of the £5M S:CORT programme for the stratification of colorectal cancer patients. This award is heavily reliant on efficient and functional working relationships at strategic, scientific and technical levels initially established through ECMC activity.



The **Edinburgh and Dundee ECMC** has been collaborating with other ECMC groups for several years on the Stratified Medicine Programme 2 (SMP2) which runs throughout the ECMC Network. Edinburgh and Dundee ECMC has shared their expertise in data collection to assist other ECMCs participating in the SMP2. For this purpose, the Edinburgh IT department created a data validation tool for other groups to use so that the data quality on the project can be improved at other ECMCs.

Leicester ECMC has been setting up a "Share Good Practice" project with Cardiff ECMC under the umbrella of the Research Nurses Network Group. This involves allowing a member of the research team to visit Leicester share best practices. This year a researcher visited Leicester ECMC to review the site's approach to funding of phase I studies. The team hopes to expand this innovative project to harmonise best practices across the ECMC Network in the coming year.

The national functional imaging network for childhood cancer has now recruited over a thousand patients across 10 centres, including 6 paediatric ECMCs. This study has recruited well over 100 patients annually since the **Paediatric ECMC Network** was created in 2012, in comparison with an annual recruitment of 60 patients before then. The paediatric Network has been very successful in extending functional imaging across the country, and incorporating these studies into the mainstream of imaging, especially for brain tumour patients. Functional imaging studies have also been successfully embedded within early phase clinical trials of new agents led from the UK such as the BEACON-neuroblastoma study, the ALK Functional Imaging Study or the 5-FU ependymoma study.

A multi-site phase I/IIa study involving **Oxford, Glasgow, Cambridge, Leeds, Birmingham ECMCs** reported partial and complete durable responses with a novel first-in-class immunotherapy drug (IMCgp100) for advanced melanoma. The trial was sponsored by Immunocore Ltd and supported IMCgp100 as a promising treatment for cutaneous melanoma as well as ocular melanoma. More importantly, responses were even observed in patients with advanced melanoma that was resistant to the immune checkpoint inhibitors that have recently become standard of care in many locations.

A Phase II trial conducted in collaboration between **ICR, Glasgow, UCL, Belfast, Leeds, Manchester and Oxford ECMCs** has shown some exciting results. Published at the New England Journal of Medicine (NEJM), the study showed high response rate with the PARP inhibitor Olaparib in patients whose prostate cancers were no longer responding to standard treatments. The results of this clinical trial suggest that a common subset of responsive metastatic prostate cancers (i.e. with defects in DNA-repair genes) can be molecularly stratified for treatment through next-generation sequencing assays.

Network Groups

A key objective of the ECMC Initiative is to build on the expertise available across our ECMC locations, and the Network Groups are central to achieving this goal.

The aims of the ECMC Network Groups are to build upon the UK's capacity for experimental cancer medicine, by bringing together and connecting members of the Network from a range of professions.

Training the next generation

Our Network Groups provide specialist training to better equip the next generation of professionals to tackle the complexities surrounding experimental cancer medicine

Research Nurses

'Introduction to early phase trials' course

Junior Investigator Network Group (JING)

2-day workshop in Newcastle

Providing expert advice

The Network Groups pool expertise in a range of specialist fields that make them the ideal place for multi-disciplinary discussions which act as catalyst for innovative ideas

UK Therapeutic Cancer Prevention Network (UKTCPN)

Parallel session on chemoprevention hosted at NCRI

Quality Assurance & Translational Science (QATS)

New strategy developed

UK Radiopharmacy Group Taskforce (CERT)

Feed into the UK's review of molecular radiotherapy research

Cellular & Molecular Pathology (CMP)

CM-Path Initiative

The National Cancer Research Initiative (NCRI) announced its support for the CM-Path.

In 2014, the Cellular and Molecular Pathology (CMP) Network Group was set up to scope out the extent of the expertise gap in cellular pathology in the UK. The group aimed to create a culture of innovation and to up-skill the cellular pathology workforce in the Network.

In collaboration with NCRI, the group developed the Cellular Molecular Pathology (CM-Path) proposal for a five-year programme, under the guidance of Dr Bridget Wilkins.

The Initiative received support from NCRI, which announced the allocation of £635,000 towards the 5-year programme. The ECMC Network is proud to have initiated the creation of CM-Path, which started this year and is chaired by Dr Karin Oien.

'The ECMC have made a fundamental contribution to the success of stratified medicine programmes in cancer over the past five years, which have been a springboard for further developments like CM-Path'

Dr Karin Oien
Chair of CM-Path

Cellular & Molecular Pathology



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