Experimental Cancer Medicine Centre Network

Annual Report 2014-15

CANCER RESEARCH UK

HSC

Ymchwil Iechyd a Gofal Cymru
Health and Care Research Wales

CHIEF SCIENTIST OFFICE

NHS
National Institute for Health Research

The Experimental Cancer Medicine Centre Initiative is jointly funded by Cancer Research UK, the National Institute for Health Research in England and the Health Departments for Scotland, Wales and Northern Ireland.

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INTRODUCTION

Launched in October 2006, the Experimental Cancer Medicine Centres (ECMC) Network is jointly supported by Cancer Research UK (CRUK) and the Health Departments for England, Scotland, Wales and Northern Ireland. 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. The current quinquennium commenced in April 2012, providing a total of circa £35 million over five years to support 18 ECMCs (specialising on adult cancers) across the UK. In addition, the Paediatric ECMC Network is supported by the National Institute of Health Research (NIHR) which funds six centres with an additional three non-funded centres (see Figure 1).

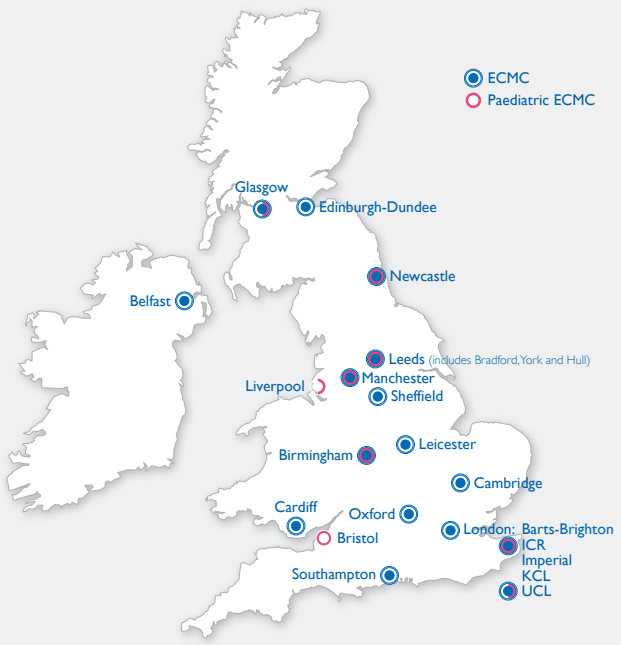
Each ECMC is a partnership between an NHS Trust or Board and a university, which enables the best health researchers and clinicians to work together to generate novel treatments for cancer patients. ECMC funding can be used flexibly to allow Centres to allocate their funding strategically across a number of themes, determined by local need and existing expertise.

Investigators have used the ECMC award creatively to leverage additional funding from NHS Trusts, universities and commercial funders. This has helped to generate further income, which has been invested back into the centres to strengthen their capacity and capability. Locally, this has enabled ECMCs to expand the range of treatments offered to patients. Nationally, it has strengthened the translational research infrastructure of the UK, ensuring that it remains a competitive location for conducting clinical trials.

The interaction with commercial partners remains a significant priority for the Network, with over 70% of all ECMC studies involving a commercial partner as a sponsor and/or funder. As demonstrated by the many examples throughout this report, commercial partners are attracted by the ability of the Network to effectively deliver early phase clinical trials in conjunction with access to world-class translational infrastructure.

This year has seen preparations for the next five-year funding period, starting in April 2017. Central to this has been the development of a new strategy for the Network, which the Secretariat has been leading. The strategy will clarify the role of the ECMC Network alongside other clinical research infrastructure and should enable funders to confidently reinvest in the Network. The strategy not only sets the scientific direction for the ECMC Network but also details the proposed operational framework and governance provisions that will underpin the Network.

Figure 1 The Adult and Paediatric ECMC Networks



Preparations have also begun for the quinquennial review itself, which will take place in Autumn 2016. The review will be held jointly with that of the CRUK Centres and in the case of English ECMCs, it will be informed by the preceding NIHR reviews[1] that will take place in summer 2016. This will ensure that the future ECMC Network is comprised of those Centres with the scientific credibility and track record of delivery of complex studies to time and target.

This annual report is not an exhaustive list of every activity at every Centre; the case studies presented here are representative highlights of the important scientific and clinical achievements delivered by the ECMC Network in 2014-15.

1 The NIHR review will assess the performance of the Biomedical Research Centres (BRC), Biomedical Research Units (CRU) and Clinical Research Facilities (CRF).

A NETWORK THAT DELIVERS

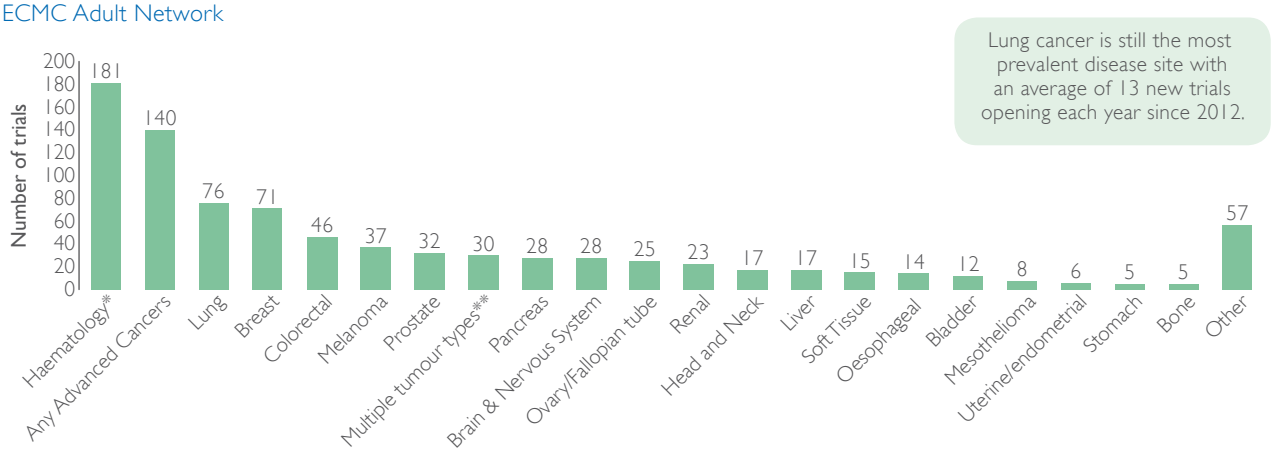
The ECMC Network supports some of the very best science and experimental therapeutics at the forefront of cancer research in the UK. As seen in the figures below, through the 18 Adult and 9 Paediatric ECMCs, this year saw the delivery of trials in a wide spectrum of disease sites. ECMCs deliver excellence in first-in-human trials, combinations and biomarker development but many centres also have specialist expertise in delivery of novel stratification, immunotherapy, radiotherapy combinations or novel imaging biomarkers.

This year the Adult ECMC Network delivered early phase and randomised trials in a broad range of disease sites (figure 2). Whilst the capacity of the Network to deliver high quality trials in prevalent cancer types such as lung (76 trials) or breast (71 trials) cancers remains unchallenged, the ECMCs also have expertise in a range of less common cancers such as brain cancer (28 trials) or liver cancer (17 trials). Conversely, the Paediatric ECMC Network works in most common childhood cancers with haematological and brain cancers taking up the majority of their portfolio (42%).This annual reporting year, the trial portfolio of the ECMC Paediatric Network focuses only on small molecules.

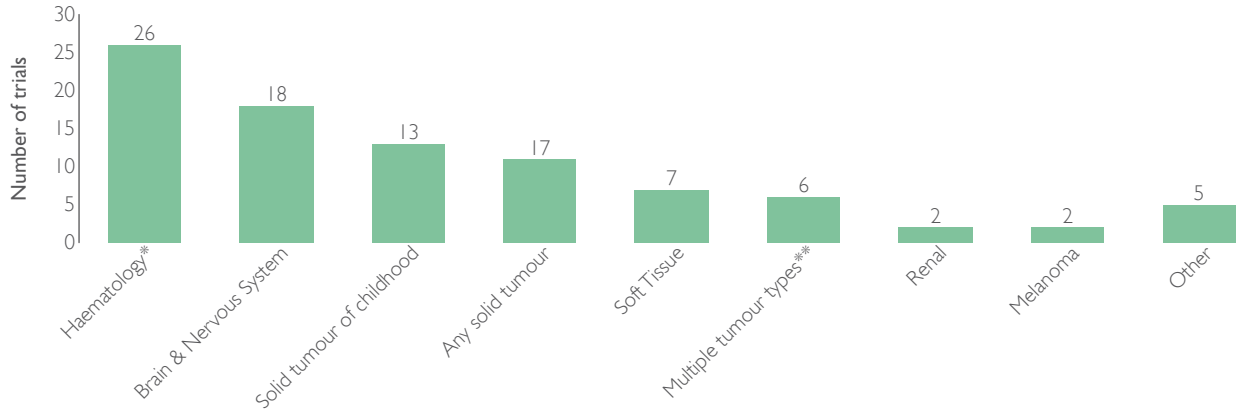
Over the past three years, we have seen a steady increase in the number of new early phase trials supported by the ECMC Network whilst there has been a drop in the number of randomised trials over this same period. These figures seem to follow the general global trend on randomised trials. This is likely to be a consequence of the molecular stratification of patients, which reduces the number of eligible patients to enrol into randomised trials (i.e. lengthening the period to reach statistical significance).

Figure 2 Number of trials supported by disease site in the Adult and Paediatric ECMC Network

ECMC Adult Network

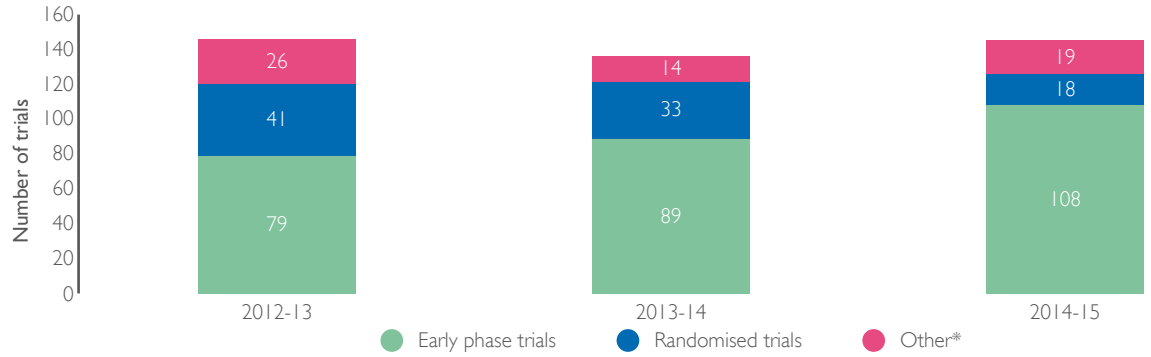


ECMC Paediatric Network



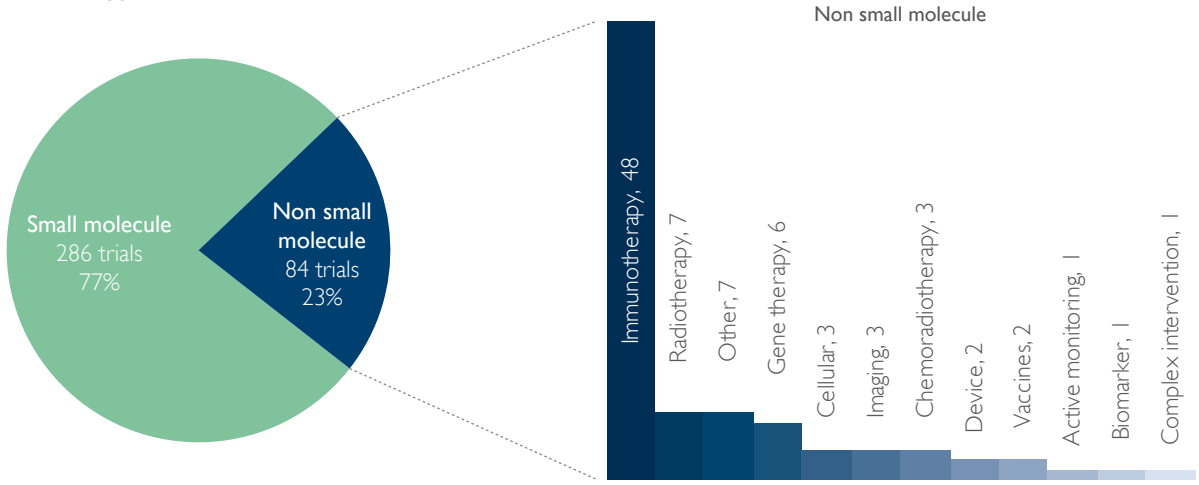
*Haematology includes: Leukaemia, lymphoma, myeloma, Myelodysplastic Syndromes (MDS)
**Multiple tumour types is when the new therapeutic is tested in more than one targeted tumour type

Figure 3 New trials reported according to trial type by the Adult ECMC Network (2012-15)



*Other category includes non-interventional studies and trials that do not fit any other category

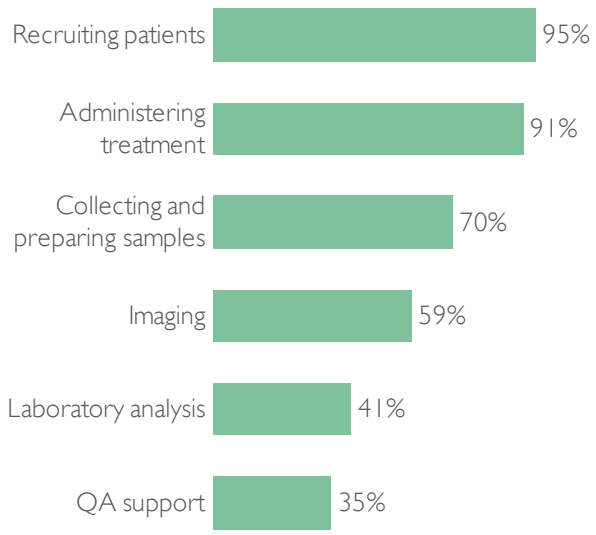
Figure 4 New Early phase and randomised trials hosted by the Adult Network (since 2012) by the treatment type



With regards to treatment modalities, as expected for an early phase trial network, the majority of trials reported this year test small molecules (77% of the ECMC portfolio). Nevertheless, as seen in figure 4, the ECMCs have a broad range of expertise in complex modalities with immunotherapy being the second most common treatment type (48 new trials reported this year).

ECMC funding provides centres with essential clinical staff to enable them to run early phase and translational clinical trials. The supported staff complete a wide range of clinical activities such as recruiting patients or facilitating imaging procedures. Figure 5 summarises these activities as a percentage of total activity reported within the Network (i.e. each member of staff can be involved in a range of activities). The majority of ECMC funding is allocated to patient recruitment and administering of treatments in trials.

Figure 5 Resources used to support studies at the Adult ECMCs



Scientific Excellence in the Network

As seen in figure 6, this reporting year saw some great examples of the cutting edge work that the ECMC Network can deliver. During 2014-15, there was the set up of some truly innovative studies such as TracerX and the National Lung Matrix Trial (NMLT) for lung cancer, MErCuRIC in colorectal cancer or the novel immunobody (i.e. DNA vaccine encoding a human IgG1 antibody with T cell epitopes grafted into its CDR regions) cancer vaccine in melanoma.

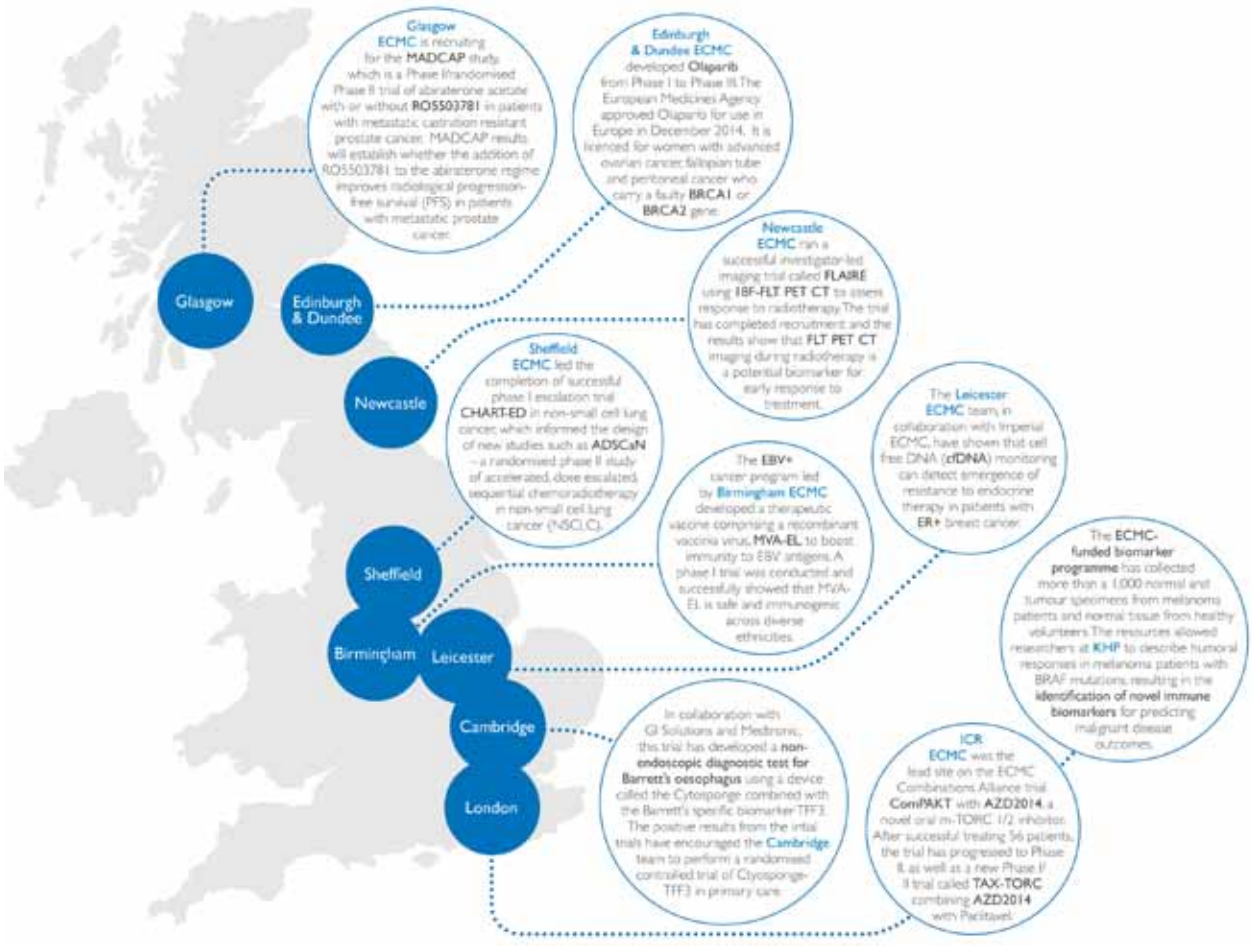
A successful and productive network should be able to demonstrate progression of studies through different phases of development. During 2014-15 there has been significant progression from pre-clinical stages to early phase trials. Of particular interest is the success of the Phase I study with AG014699 (tested at **Newcastle, Oxford, Glasgow** and **Belfast** ECMCs) which has progressed to phase II in melanoma (with **Birmingham** and **Manchester** ECMCs also participating) and to phase II as single agent in breast and ovarian cancer. This novel agent (now known as Rucaparib) entered phase III investigation (i.e. ARIEL3) late in 2013 in high grade serous ovarian cancer and also a translational phase II study in the same indication. **Glasgow** ECMC is the lead European site for ARIEL3 and multiple ECMCs are participating, including **Newcastle** ECMC as the Chief Investigator site for the UK. On the basis of emerging results from ARIEL 2, Rucaparib was given Breakthrough Designation by the FDA in April 2015.

Other excellent examples of progression through the trial phases include the HuMax TF-ADC immunoconjugate developed by **Institute of Cancer Research (ICR)** ECMC, which has now progressed to Phase I/II trial. **Manchester** ECMC trial for AZD6244 (MEK-Inhibitor) in combination with chemotherapy progressed from Phase I to a randomised Phase II in previously treated non-small-cell lung cancer stratified by KRAS status. **University College London (UCL)** ECMC MUK-3: CHR-3996 in combination with Tosedostat in participants with relapsed, refractory multiple myeloma has moved from Phase I to Phase I/IIa dose expansion. Following pre-clinical evaluation of the monocyte-targeted histone deacetylase inhibitor, Tefinostat, **Cardiff** ECMC secured funding for a multi-centre phase II trial (MONOCLE) of this agent in patients with chronic myelomonocytic leukaemia (CMML). **Leeds** ECMC has completed a dose escalation phase of a phase I trial of the cannabinoid Sativex in combination with Temozolamide in patients with relapsed glioblastoma and are now in the expanded cohort stage and opening a drug interaction pharmacokinetic trial. There are also some cases reported of progression on biomarker validation. A particularly good example is the prostate cancer prognostic assay developed by **Belfast** ECMC, which has progressed to final assay lock-down for validation.

Finally, the results of ECMC trials have shaped the development of new trials such as the work carried out at **Edinburgh and Dundee** ECMC on Olaparib in ovarian cancer, which has led to three phase III trials. Similarly, at **Imperial** ECMC ICMT-11-PET study has progressed from proof of concept /first-in-human studies to start testing the protocol in lymphoma, non-small cell lung cancer and breast cancer patients.

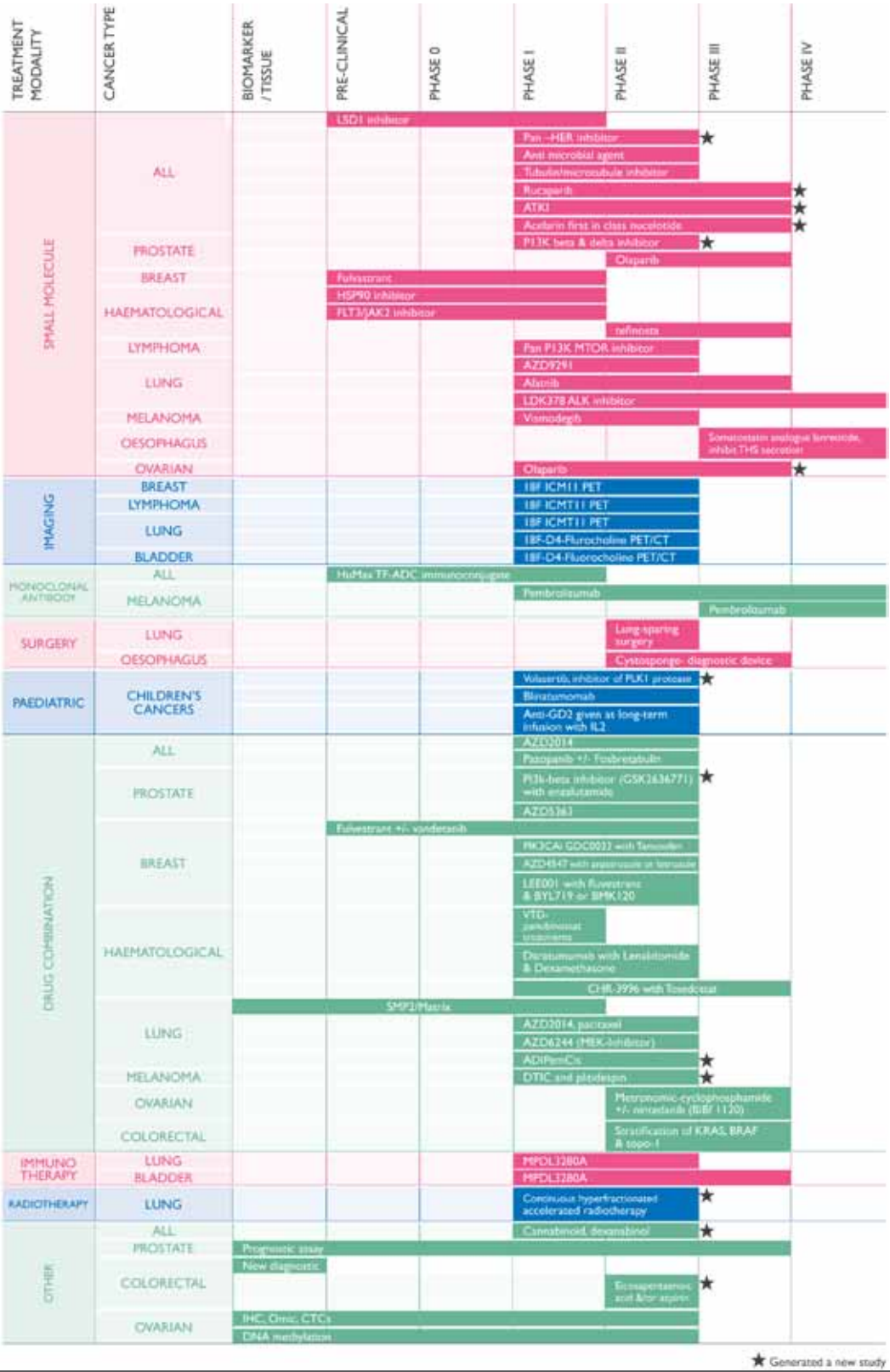
The examples above are not exhaustive but demonstrate that the ECMC initiative has evolved to not only pump prime new activity, but also to support the on-going development of promising studies. Moreover, figure 7 illustrates some examples of the type of trials occurring

Figure 6 Examples of activity in the ECMC Network during 2014-15.



in the Network in a range of cancer types. The richness of hypothesis-driven trials in the Network ensures that the knowledge generated by these early studies can be harnessed to develop new trials (marked as a star in figure 7) with the ultimate aim to maximise patient benefit.

Figure 7 Examples of progression through the R&D pipeline of some of the studies taking place at the ECMC Network during 2014-15.



A COLLABORATIVE INITIATIVE

The first quinquennium established a critical mass of locations capable of delivering high quality studies in multiple disease sites in a diversity of treatment modalities. The emphasis in this quinquennium has been to facilitate the ECMCs to work together as a true network.

Collaboration throughout the Network: from trials to sharing expertise

Through the pooling of expertise in the different ECMCs, the Network is able to deliver trials beyond standard small molecules. Thus, this year saw some examples, illustrated in figure 8, of collaborations on complex studies such as those using radiopharmaceuticals, new surgical techniques and novel drug combinations.

As shown in figures 9 and 10, there is a high degree of collaboration between the ECMCs. The adult and paediatric ECMCs participate in a broad range of multi-site trials with some ECMCs being particularly collaborative. For the adult ECMCs, **UCL**, **Oxford**, **Manchester**, **Glasgow** and **Barts and Brighton** ECMCs have a significant number of multi-site activity. Similarly, **Birmingham**, **Royal Marsden**, **Newcastle**, **Leeds**, **Manchester** and **Great Ormond Street** Hospital (GOSH) ECMCs are also particularly active in multi-site trials in paediatric oncology.

Figure 8 Examples of collaborative activity taking place at the Adult ECMC Network during 2014-15.

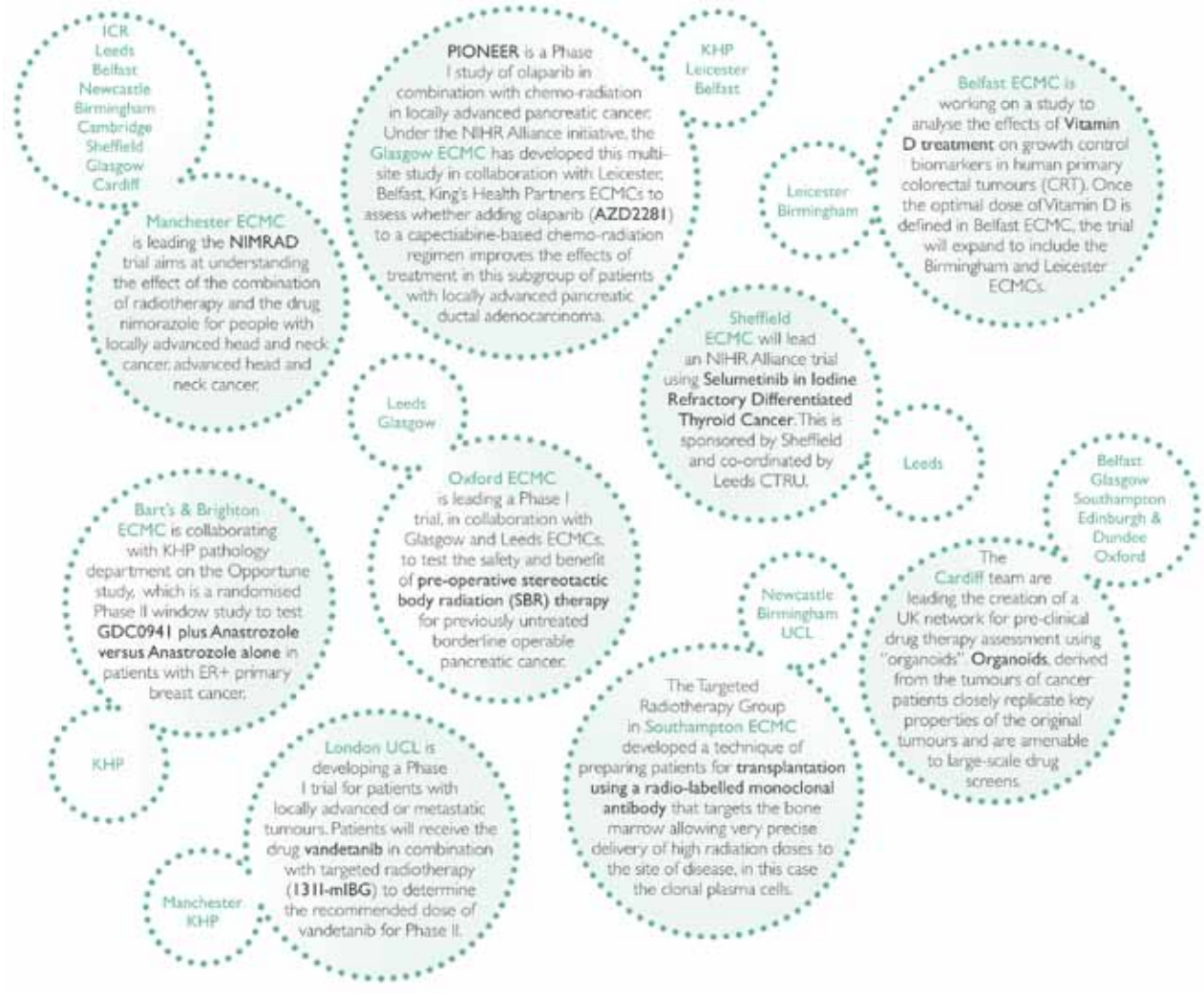


Figure 9 Illustration showing all the existing collaborations on multi-site trials in the Adult ECMC Network in 2014-15.

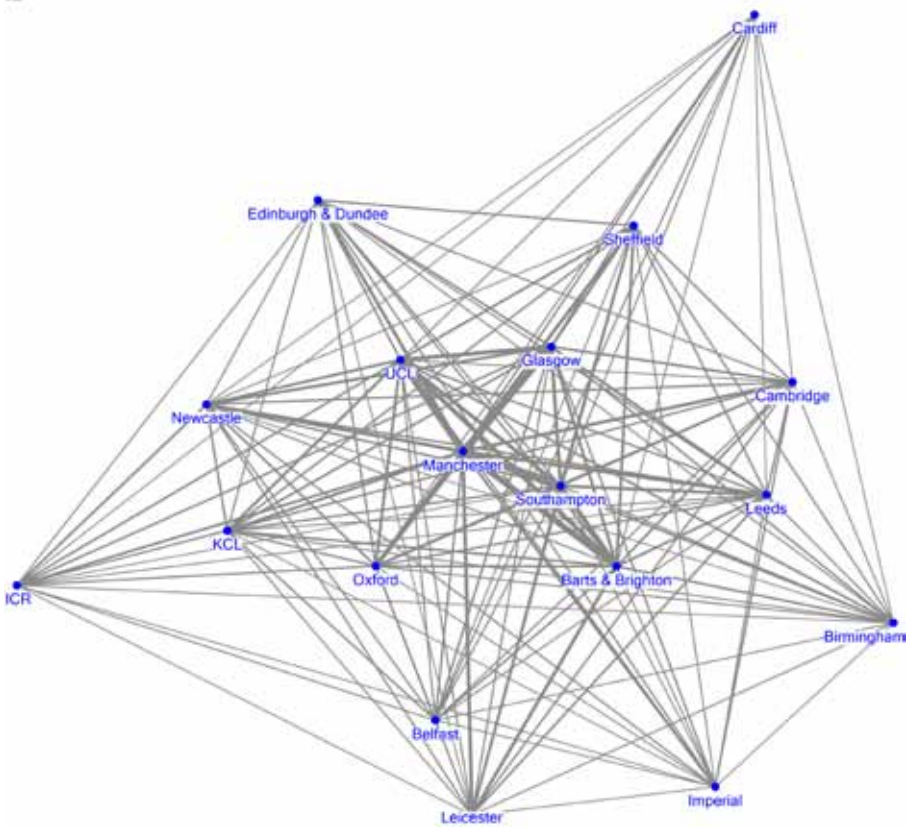
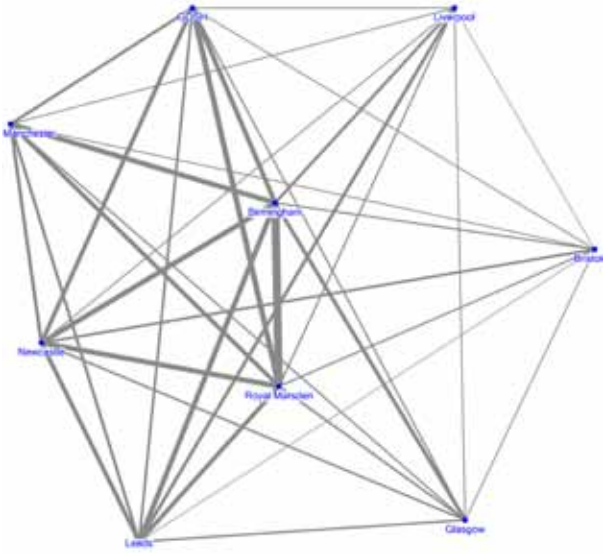


Figure 10 Illustration showing all the collaborations on multi-site trials in the Paediatric ECMC Network in 2014-15.



CASE STUDY:

THE MErCuRIC TRIAL

The MErCuRIC study is funded by the European Community Framework Programme Seven (FP7) and will employ Next-Generation Sequencing (NGS) technologies to identify previously unknown biomarkers with diagnostic and prognostic value in patients with colorectal cancer. This work will allow the consortium to develop novel treatment strategies based on a personalised molecular footprint. This offers significant advantages to the patient (e.g. improved treatment efficacy and reduced side effects) as well as transforming clinical practice through the adoption of leading-edge technology.

Colorectal cancer is the third most common cancer in Europe, and with approximately 200,000 deaths per year, it remains the second most common cause of cancer death. More than half of all colorectal cancer patients develop distant metastases and have 5-year overall survival (OS) of less than 5% because of ineffective treatments.

> "At a local level, the collaborative nature of the research that led up to the successful grant award, involving the CCRCB[2] and the Belfast Health and Social Care Trust, emphasises the importance of a bench to bedside continuum linking the researcher and the clinician, with the patient at the centre of this process"

Professor David Waugh
Director of the Centre for Cancer Research and Cell Biology (CCRB) at Queen's University, Belfast.

This multicentre phase Ib/II clinical trial involves 13 partners in eight different European countries. In the UK, **Belfast** ECMC has been assigned as the country lead with **Oxford** ECMC participating as the Chief Investigator. MErCuRIC will assess a novel therapeutic strategy (combined treatment of a MEK inhibitor PD-0325901 with a MET inhibitor PF-02341066) to combat metastasis, improve survival and change current clinical practice for colorectal cancer patients with KRAS mutant (MT) and KRAS wild type (WT) (with aberrant c-MET) tumours. The consortium will go beyond the current state-of-the- art by employing a novel treatment strategy through the use of in vivo models to discover which patient groups will benefit from particular treatment regimens.

MErCuRIC had its first partners meeting in Vall d'Hebron Institute of Oncology (VHIO) in Barcelona (Spain) in December 2014 and has already opened to recruitment in the **Belfast** and **Oxford** ECMCs. This innovative mechanistically-led trial was presented at the American Society of Clinical Oncology (ASCO) conference in Chicago in June 2015. In addition, Dr Sandra van Schaeybroeck (co-ordinator of the Research Programme at Queen's University in Belfast), presented on the project at the All-Ireland Cancer Consortium (AICC) Conference in May 2015.

MErCuRIC partners attended a successful meeting in VHIO (Barcelona, Spain) in December 2014

2 Centre for Cancer Research and Cell Biology (CCRCB)

Working together in our commitment to excellence

The unique collaborative nature of the ECMC Network creates the perfect medium to share expertise and experience across sites. In this section we present some examples of how sharing and combining expertise has led to important changes with national and international impact.

1. Harmonisation of Cell-Free DNA (CfDNA) practices

Cell-free DNA (cfDNA sometimes referred to as circulating tumour DNA or ctDNA) has shown promise as a prognostic and predictive marker in a number of cancers and has the potential to pave the way for technology to support liquid biopsies. Liquid biopsies have the capability to enable diagnosis and monitoring of disease in cancers where tissues biopsies are difficult or impossible to obtain. This area of work has advanced rapidly but routine use in the clinic is hampered by a lack of standards for sample collection, assay execution and data analysis.

Achieving a national consensus on the use of cfDNA assays could uniquely position the UK to be able to address the critical questions to validate cfDNA as a diagnostic or prognostic marker for cancer.

The ECMC Network, jointly with the National Cancer Research Institute (NCRI), sought to bring together expertise from around the ECMC Network to achieve consensus among research teams investigating cfDNA. The consensus meeting took place in November 2014 and it included 34 attendees from 14 ECMCs and 4 industry partners from AstraZeneca, Qiagen, Horizon Discovery Group and Inivaita. A number of opportunities for research and collaboration were identified with the group making recommendations around analysis, techniques and 'gold' standard practice for research in cfDNA.

Following these recommendations the ECMC Network will be funding a systematic review and sample sharing study, led by Professor Jacqui Shaw (**Leicester** ECMC), across four ECMCs with a view to developing Standard Operating Procedures (SOPs), which can be shared across the Network and beyond. We hope that this process will serve as an example of how the Network can rapidly standardise and adopt promising emerging techniques.

2. Cellular and Molecular Pathology Network Group

Cellular pathology, the science of understanding disease at the level of tissues and cells within the body, remains crucial to our understanding of cancer. It is a key component of the revolution in molecular pathology (the understanding of disease at the level of genes within individual cells) and is underpinning new stratified and personalised approaches to cancer treatment. However cellular molecular pathology expertise is in decline (as demonstrated in figure 11) as academic pathology posts have been undergoing attrition since 2001.

Recognising the vital importance of the role of cellular pathology in the future of cancer research and care, the ECMC Network set up the Cellular & Molecular Pathology Network Group in May 2014. This group was tasked with scoping the extent of the expertise gap and how we could create a culture of innovation and up-skill the cellular pathology workforce in the Network. From surveying the Royal College of Pathologists' membership, the group was able to identify the key supportive elements and barriers to pathologists undertaking research.

The Network Group has become a growing focal point for the pathology community (currently 130 members) and has worked closely with the National Cancer Research Institute (NCRI) for the development of a £620k proposal for a broader initiative, which seeks to reinvigorate pathology across the UK. The Cellular Molecular Pathology (CM-Path) programme proposal, led by Dr Bridget Wilkins (former ECMC Pathology Lead), will stimulate activity across the pathology community for broader engagement and support for research through four workstreams outlined below:

- Skills & Capacity – Integrating molecular pathology and research in the curriculum and up-skill the current consultant workforce in molecular analysis
- Clinical Trials – Improving access to pathology expertise for clinical researchers and review of pathology elements of a proposal for more effective and efficient tissue-based research endpoints

- Discovery – Developing pathology-led discovery strands across a number of cancer research topics
- Technology and Information – Moving towards integrated pathology and molecular analysis reporting and supporting the uptake of new technologies

This work was welcomed by the Royal College of Pathologists, who have been instrumental in engaging the wider RCPath membership and consultant workforce in the proposal. The proposal was submitted to the National Cancer Research Institute (NCRI) Partner funders in June 2015.

Figure 11 Data from the annual Clinical Academic Staff Survey conducted by all medical schools in England, Wales, Scotland and Northern Ireland (Medical Schools Council[3]).

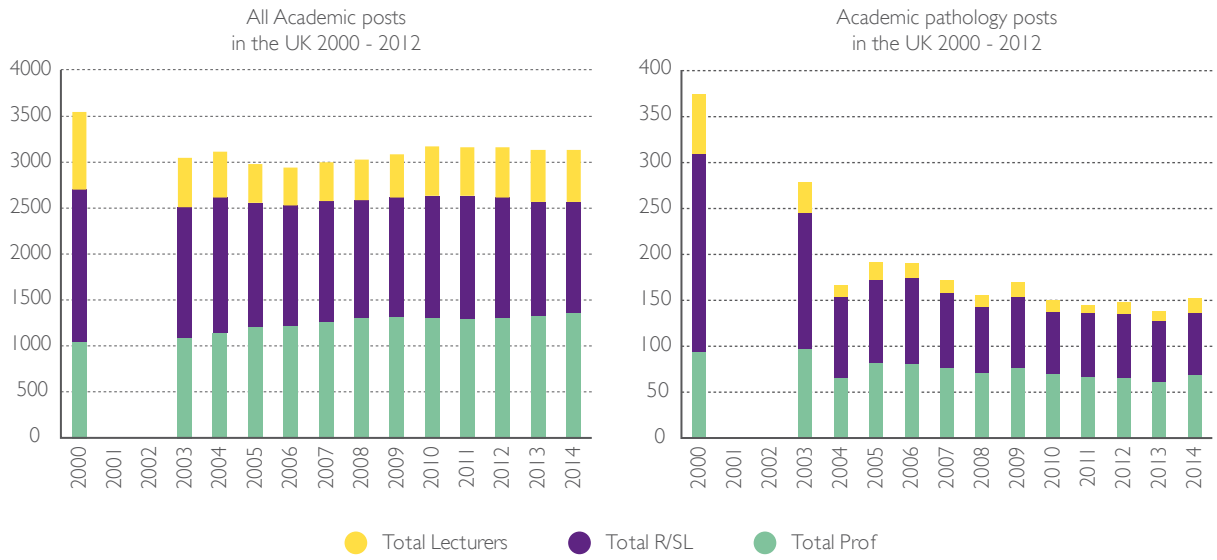
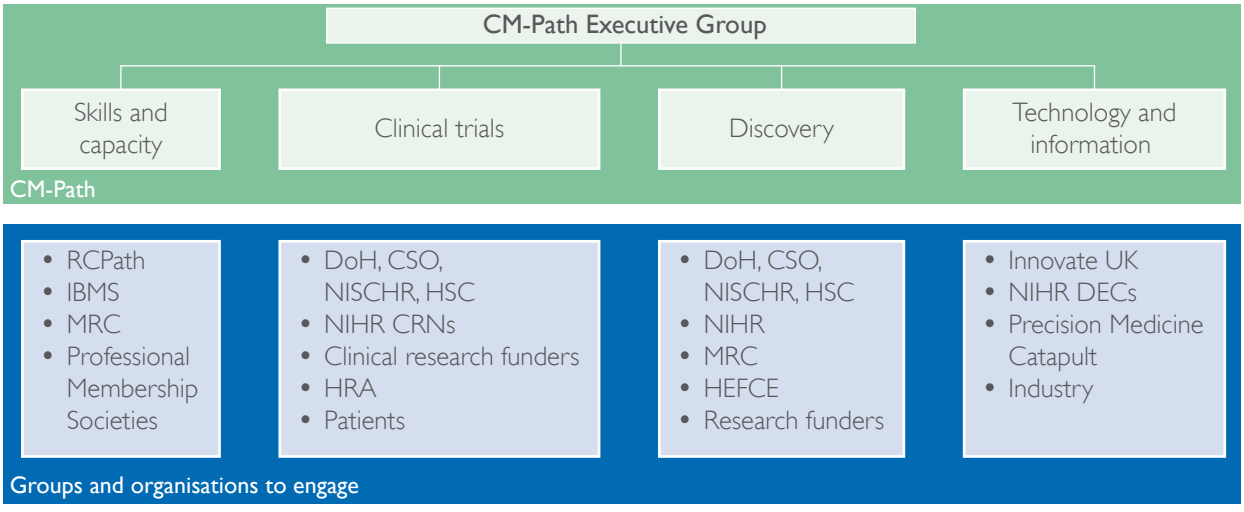


Figure 12 CM-Path proposed structure and reporting lines for workstream activity.



3 Clinical Academic Survey 2000-2012 data published by the Medical Schools Council 2001-2013 http://www.medschools.ac.uk/AboutUs/Projects/clinicalacademia/Pages/Promoting-Clinical-Academic-Careers.aspx

Over **2,500** patients recruited to **389** trials in FY 2014/15

3. ECMC Patient Experience Survey

The ECMC Network thrives to provide best care to patients who volunteer for early phase trials. Research nurses are critical in ensuring patients have a positive experience as they enrol patients, administer treatment and supervise the delivery of ECMC trials. The ECMC Research Nurse Network Group has been central to driving up standards in the patient experience across the Network, for example by ensuring that all locations have appropriate out of hours care pathways for patients on trials.

To help identify areas where further improvements could be made, the Group's steering committee undertook a network wide patient survey to better understand the experience of patients participating in early phase clinical trials. The survey was conducted in 15 ECMC locations during March 2015 with 326 questionnaires returned (ranging from 3 to 72 per location). Analysis of the questionnaires revealed that patients participating in early phase trials were extremely positive about their experience with an overwhelming 99% agreeing that they felt cared for by research staff during their trial. These results were very well-received by the community as they were the first ones to specifically assess the impact of care in patients participating in early phase trials. Individual participating centres were given their results to ensure that actions were taken at local level to improve (when required) identified service gaps.

Whilst the results of the survey were overwhelmingly positive, the nurses do not wish to be complacent. This survey will serve as the baseline for future studies, to ensure that standards are maintained. In addition, the Group will meet in 2015-16 to discuss any issues identified in the questionnaire that had an impact at Network level and should be tackled collaboratively.

Stratified Medicine Programme

The Stratified Medicine Programme (SMP) was set up as a partnership between CRUK and AstraZeneca, Pfizer and the UK government's Technology Strategy Board to explore how the NHS might provide large scale molecular testing for cancer patients. Building on the success and infrastructures of Stratified Medicine Programme part 1 (SMP1) which terminated in 2013, the second part of the initiative (named SMP2) pairs large scale molecular testing with patient treatment. This ambitious initiative is divided into two operational areas, both delivered through the ECMC Network: a collaborative national molecular pre-screening network and the National Lung Matrix Trial, a large national multi-arm umbrella targeted therapy trial.

1. National Molecular Pre-Screening

In the national molecular pre-screening network, patients with late-stage lung cancer are being recruited through all ECMC sites to be tested for a number of genetic aberrations. Samples are sent to one of three Technology Hubs - **Birmingham**, **Cardiff** and **ICR** ECMCs - where they are being tested through a gene panel using next generation sequencing (NGS). Moreover, each participating ECMC contributes to the general success of the programme, providing knowledge and expertise with regards to sample pathways, sample standards, NGS technology, bioinformatics and IT infrastructure to support real time exchange of molecular results.

In the last year the original 10-gene panel used in SMP1 has been replaced by a capture-based NGS 28-gene panel. This has only been possible through continuous collaboration between the technology provider Illumina and the scientists at the Technology Hubs. One of the biggest challenges has been the small size of biopsy samples which required ECMC pathologists (and the molecular geneticists at the Technology Hubs) to work together to optimise sample standards. This was facilitated by the Pathology Working Group that comprises of pathologists and informaticians from all the adult ECMCs. Up until May 2015, 590 samples had been sent for analysis on the new NGS panel with 360 results already released.

2. National Lung Matrix Trial (NLMT)

The NLMT is a multi-arm umbrella trial in which non-small cell lung cancer (NSCLC) patients with stage III or IV disease, or disease not amenable to surgery / radical radiotherapy, are allocated to a treatment arm according to their molecular phenotype. The trial is an academically-led collaborative study between the University of Birmingham, CRUK, AstraZeneca and Pfizer. It is sponsored by the University of Birmingham and coordinated by the Birmingham Cancer Research UK Clinical Trials Unit (CRCTU), with Professor Gary Middleton leading as Chief Investigator.

The NLMT consists of a series of parallel, single-arm phase II trials delivered across the ECMC Network. Each arm tests an experimental targeted drug in a stratified population, with the aim to swiftly determine whether there is sufficient signal of activity in any drug-biomarker combination to warrant investigation in further trials. There are currently 6 arms and 14 drug-biomarker combinations, but the nimble design allows cohorts to be closed when necessary, and to rapidly adopt new arms as new treatments become available.

In the last year the Early Drug Development team within the CRUK CTU at the University of Birmingham finalised the protocol and secured regulatory approval for the trial. It should be noted that the trial is carried out under a single protocol and regulatory submission. This allows for the incorporation of new biomarker-drug combinations by way of a substantial amendment rather than an entirely new protocol and regulatory submission. Thus, the protocol is currently undergoing a substantial amendment to incorporate two new drugs.

The trial is opening nationally in 12 ECMCs (**Birmingham, Cambridge**, **Cardiff, Edinburgh**, **Glasgow**, **ICR**, **Imperial**, **Leeds**, **Manchester, Newcastle**, **Sheffield** and **Southampton**) with **Leicester** ECMC coming on board shortly and four more centres planned to be live by September 2015. Taking advantage of a hub and spoke model - where feeder hospitals are coordinated by the respective ECMC in their region - around 50 NHS trusts are involved in the programme, effectively doubling the size of the network in comparison to SMP1. During 2014-15 **Birmingham**, **Newcastle** and **Southampton** ECMCs opened for recruitment and we hope that the rest will follow during 2016.

The delivery of a complex programme like this is only possible through collaboration between clinicians, researchers, coordinating staff and pharmaceutical partners. Without the ECMC Network driving standards and facilitating collaboration, delivering this programme nationwide would be extremely challenging and would possibly be limited to only a few locations. The ECMC Network is the ideal environment to harness the capabilities across centres and key to the success of the Stratified Medicine Programme.

AN INDUSTRY-FRIENDLY NETWORK

The ECMC Network aims to be industry's partner of choice for hypothesis-driven, biologically rich and technically demanding studies. Centres are able to attract additional funds from pharmaceutical companies, biotech, government and other partnerships such as contract research organisations (CROs) and non-healthcare industries. This reporting year commercial studies have accounted for 77% and 60% of the studies in the Adult and Paediatric Network, respectively.

In the Adult ECMC Network, this year has seen an increase of commercially-sponsored trials by 14% compared to the last reporting year with a subsequent decrease for both academic and academic sponsored/industry funded trials (10% and 2% respectively).

ECMC Partnerships with Industry

Once again in 2014-15 there was ample evidence of commercial companies seeking to collaborate with the ECMC Network. Leveraged funds this year totalled about £73.5 million involving 48 different companies or organisations. These partnerships are varied in scale and scope, ranging from single study collaborations to more extensive strategic partnerships.

We observed an increasing interest from industry in harnessing the immunotherapy expertise available at the ECMC Network. Since 2012 there has been an 85% increase in activity in immunotherapy trials sponsored by industry. Examples seen this reporting year include **Barts and Brighton** ECMC which received funding from

Figure 13 Commercial versus academic sponsor breakdown of new trials

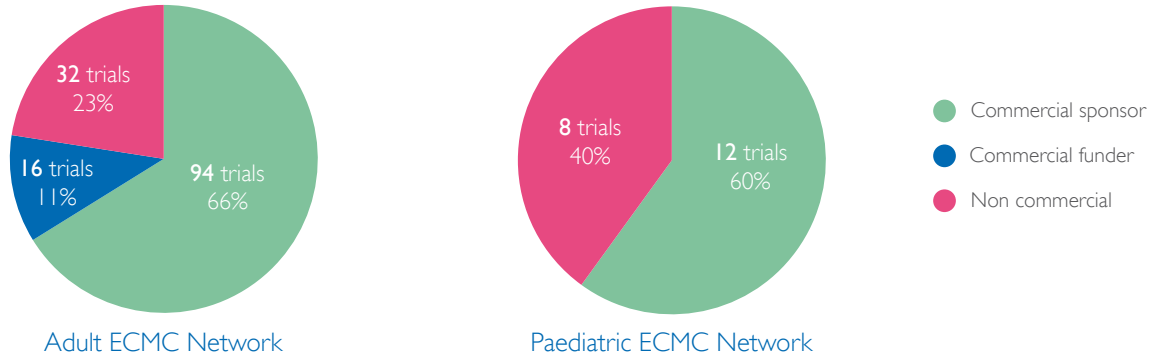


Figure 14 Trends in industry-sponsored trials at the ECMC Adult Network.

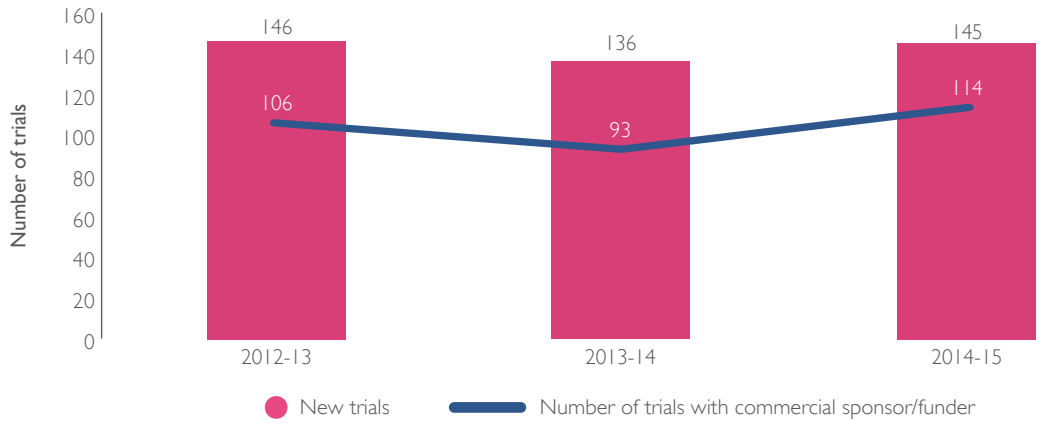


Figure 15 Pharmaceutical and biotechnology companies that have developed new partnerships with the ECMCs during 2014-15

Roche (£1,500,000) for a phase II trial in bladder cancer patients to test the efficacy of MPDL3228A (an anti PD-L1 antibody). Similarly, Merck supported another phase II trial for MK-3745 (PePS2 study) in lung cancer patients at the **Birmingham** ECMC. **KHP** ECMC received funding from Biotecnol Ltd (£457,808) to further develop their pre-clinical work on the tribody novel immunotherapeutic Tb535. **Oxford** ECMC has also received funding from Medimmune (£1,666,667) to evaluate the pre-clinical efficacy of immunotherapies in oesophagus cancer patients.

Imaging is another area that has received increasing interest by industry. Several imaging trials are ongoing in the ECMC Network such as the phase II trial supported by GE-Healthcare Affibody (£1,000,000) to test the [18F]-HER2-Affibody tracer led by **Imperial** ECMC.

Early phase trials are not the only area of collaboration with industry, for example, **Leeds** ECMC is working with Affymetrix-TSB on a biomarker study. The Leeds team will analyse copy number and mutational profiling of 1,400 to 2,000 colorectal tumour specimens from the CR07, Foxtrot and Piccolo trials in search for molecular signatures that will help us find more targeted cancer treatments.

The know-how and experience in setting up trials also attracts companies wishing to conduct phase I trials to test novel drugs such as the trials for lung cancer patients: COMMAND; VS-6060 and VS-5584 carried out by **Leicester** ECMC (funded by Verastem). There are excellent examples of drug combinations trials such as PRICKLE, a phase II study to test gemcitabine and Nab-paclitaxel in pancreas cancer patients led by **Cambridge** ECMC with support from Celgene (£150,000). Similarly, PiSARRO is a phase I trial led by **Edinburgh and Dundee** ECMC to test carboplatin combination chemotherapy with or without APR-246 in patients with ovarian cancer that has been sponsored by Aprea-AB.

CASE STUDY:

PAEDIATRIC ECMC NETWORK

The Paediatric ECMC Network was set up in 2012 to improve access to innovative treatments for children with cancer. The Network consists of nine closely aligned UK tertiary paediatric oncology centres with a broad UK geographical spread, run alongside the NCRI Children's Cancer and Leukaemia Group Clinical Studies Novel Agents Group and linking to key international clinical trial consortia, including the Innovative Therapies for Children with Cancer (ITCC), European early phase trial consortium and others, as well as tumour-specific international clinical trial networks.

Since their inception, paediatric ECMCs have become important recruitment centres for pharma-sponsored, international first-in-child studies. They have consistently delivered trials to time and target and have provided the robust high quality clinical trial data necessary to fulfil regulatory obligations. This has often resulted in companies re-selecting some of these paediatric ECMCs to lead and run subsequent studies. In particular, we would like to highlight the following examples of industry partnership for the 2014-15 period:

1. The recently completed Merck Ridaforolimus (mTOR inhibitor) paediatric solid tumour phase I study The UK recruited over 40% of patients across 12 international sites. (Prof Andrew Pearson, The Royal Marsden, UK Chief Investigator).

2. The Merck Pembrolizumab (PD-1 inhibitor) paediatric solid tumour study has just opened to recruitment at The Royal Marsden, one of just five international sites (Dr Lynley Marshall, Royal Marsden ECMC).

3. Two important first-in-child studies are currently open in UK paediatric ECMCs:

- the Novartis Ceritinib (ALK inhibitor) study for tumours with genetic ALK abnormalities (open in **Birmingham** and **The Royal Marsden** ECMCs) and
- the GlaxoSmithKline (now Novartis) Dabrafenib (BRAF inhibitor) study for tumours with BRAF V600 mutations (open at The Royal Marsden and Great Ormond Street Hospital (GOSH) ECMCs).

Interim results from both of these studies were presented at the recent American Society of Clinical Oncology (ASCO) meeting in Chicago in June 2015, with both new drugs showing great promise in childhood cancers harbouring these specific genetic abnormalities.

ECMC Combinations Alliance

In 2010 the CRUK Centre for Drug Development (CRUK CDD) launched the ECMC Combinations Alliance with the goal to increase the number of combination treatment options available to people with cancer. To this aim, an emphasis is given to more complex combinations such as with radiotherapy trials and indications not typically followed in pharmaceutical development. The Alliance maximises the potential of innovative drugs by utilising the incredible breadth and early phase indication experience in the ECMC Network.

Even with their significant resources, drug companies can only explore a fraction of all possible treatment combinations. Thus, the Combinations Alliance is also driving cross-company collaborations, to establish a position as broker, hence progressing the most promising combinations. Over the last year several new drugs have been offered to the Network by the new commercial partnerships: Biothera offer Imprime PGG (Innate immune modulator), Clovis offer Rucaparib PARP inhibitor) and Rociletinib (EGFR inhibitor) and Verastem offer VS-5584 (PI3K/mTOR kinase inhibitor) and VS-6063

> Partnership and alliances allow us access to some of the best new treatments available, irrespective of where they come from. We owe it to our supporters to work in this innovative way. But, most importantly, we owe it to cancer patients.

Dr Nigel Blackburn
Director of the CRUK Centre for Drug Development (CDD)

Figure 16 Current studies in the Combinations Alliance portfolio.

Study	CI	Sponsor	Combination	Indication
ORCA2	Forster	UCL	PARP inhibitor + Cisplatin + RT	HNSCC
PIONEER	Evans	Glasgow	PARP inhibitor + Capecitabine + RT	Pancreatic
TORCMEK	Schmid & Middleton	Barts	MTOR inhibitor + MEK inhibitor	NSCLC
HIPROC	Glasspool	Glasgow	Hedgehog inhibitor + Paclitaxel	Ovarian
VIRBANT	Thirlwell & Sarker	UCL	RET, EGFR, VEGF inhibitor + Iodine-131 MIBG	Pheos and PG
FACING	Evans	Glasgow	FGFR inhibitor + Cisplatin/Capecitabine	Oesophogastric
DEBIOC	Thomas	Oxford	Mixed Erb Inhibitor + Oxiplatin/Capecitabine	Oesophogastric
RADICAL	Seckl	Imperial	FGFR inhibitor + Anastrozola + Letrozole	Breast
FIESTA	Chester	Leeds	FGFR inhibitor + Gemcitabine/Cisplatin	Bladder
VANSEL	Talbot	Oxford	MEK inhibitor + RET, EGFR, VEGF inhibitor	NSCLC
TAX-TORC	Banerji	ICR	mTOR inhibitor + Taxane	Ovarian/Fallopian
ComPAKT	Yap	ICR	AKT inhibitor + PARP inhibitor	Solid tumours
PATRIOT	Harrington	RMH/ICR	ATR inhibitor + RT	H&N/abdo/pelvic/thorax
PANtHER	Hochhauser	UCL	EGFR inhibitor + FOLFIRI	CRC
DREAM	Saunders	Manchester	MEK inhibitor + VEGFR inhibitor + RT	CRC

Green: in set up, white: open and grey: closed

(FAK inhibitor) as well as the longstanding commercial partnerships AstraZeneca, MedImmune, Lilly and Astex. Over 60 proposals were received this year from across the Network involving various tumour types involving novel:novel and cross company combinations.

There are currently 10 clinical trials ongoing with another 4 in set up, and the scheme has already expanded its remit to include much needed trials of new drugs in combination with radiotherapy (figure 16). In addition, there is now pre-clinical funding support available via the New Agents Committee (NAC) to enable pre-clinical rationale to be generated to support the clinical trial. As a result, there are currently 15 pre-clinical studies in progress funded by NAC. In addition, the RaDCom consortium has been established by the Clinical and Translational Radiotherapy Research Working Group (CTRad) and CRUK to develop ideas and deliver pre-clinical evidence for novel radiotherapy-drug combinations.

Success has now been demonstrated both with delivery of some trials and the opportunities they can offer, such as expansion into wider disease areas shown by TAX-TORC demonstrating efficacy in ovarian and squamous lung. Some good examples showing the varied nature of our work are the novel intra-patient dose escalation in CompAKT and the delivery of the first trial in neuroendocrine tumours in VIBRANT. Broadening the Combinations Alliance portfolio in the future will enable industrial partners to come together and offer their cancer therapies for use in clinical trials in the UK.

THE ENABLING ROLE OF THE ECMC SECRETARIAT

The ECMC Network is a unique model for supporting the delivery of both early phase trials and translational biomarker research with the aim of establishing the UK as a world leader in experimental cancer medicine. The ECMC Secretariat has been key in facilitating a broad range of networking activities. As detailed below, during this year, there have been significant advances in all the Secretariat priority areas with a range of new initiatives (e.g. new grant to support our researchers to attend Flims or creating a patient and public involvement group) and the consolidation of existing activities such as the highly successful JING training workshop and the launch of our new website.

Promoting expertise: Training schemes, network groups and the capability map

1. Network Groups

The Network Groups were developed as platforms to share ideas and/or expertise in areas identified as priorities by our ECMC community. The membership of the different Network Groups can range from a uniform group of affiliated professionals (e.g. QATS and Research Nurses groups) to a multi-disciplinary representation of professionals interested in specific topics (e.g. chemoprevention or radiopharmacy groups).

In 2014-15 the ECMC Network Groups reported activity in a broad range of areas – from training workshops to knowledge hubs to providing support in radiopharmacy trial set up – further enhancing the collaborative nature of the Network.

The UK Therapeutic Cancer Prevention Network Group (UKTCPN)

- The UKTCPN was established to bring together scientists who are involved in research to develop therapies or dietary interventions for the prevention or delay of the development of malignancy. This Network Group is made up of a core steering committee of 20 members (including 2 patient representatives) who help to drive the direction and topics covered by the Group. Established in October 2013, the Network Group has worked to build membership of a further 50 translational scientists, clinical and epidemiology researchers from across the UK actively undertaking pre-clinical or clinical research in therapeutic cancer prevention.

- Moving at pace, this Group has drawn on its broad expertise to put together a programme of work to create a bench to bedside pipeline for discovery and development of re-purposed agents for the therapeutic prevention of cancer. Agents in use in chemoprevention studies are often off-patent, widely available and have well understood safety profiles meaning there is little incentive to invest in discovery or clinical research. To engage the wider cancer research community the UKTCPN will be running a symposia session with international speakers at the NCRI Conference in November 2015, spanning from 'bench-to-bedside' to highlight emerging areas and discuss lessons learnt in the field of chemoprevention. Moreover, plans are in development for a two-day British Association of Cancer Research (BACR) conference to be hosted in Bristol in 2016.

The CRUK, ECMC and UK Radiopharmacy Group Taskforce (CERT)

- The CRUK, ECMC and UK Radiopharmacy Group Taskforce (CERT) was established in 2012 to help provide stakeholders (researchers, funding bodies and regulators) with a common understanding of the regulatory requirements for clinical trials that involve molecular radiotherapies (MRT). The main goal of CERT is to actively influence clinical trial regulations and guidelines to take into account the specialised nature of MRT development, in order to ensure coherent implementation of clinical research using MRT across the UK.

- To help researchers negotiate the regulatory hurdles during trial development, CERT has created a resource area with guidance and advice related to the set up of clinical trials using radiopharmaceutical Investigational Medicinal Products (IMP). This knowledge hub provides a step-by-step process map for MRT trial development as well as examples of approved MRT trials. CERT is also providing support for a national review of MRT research in conjunction

with the Clinical and Translational Radiotherapy Research Working Group (CTRad). Building on a previous review of MRT clinical practice in the UK by the British Institute of Radiology (BIR, for the BIR Report 23[4]), this review seeks to understand the barriers which restrict the UK's ability to perform high quality MRT research. Consultation with the UK MRT community at NHS hospital sites is currently underway which will help draw key conclusions of what is needed to move MRT research forward, taking into account perspectives from basic, translational and clinical research.

The Quality Assurance and Translational Science (QATS) Network Group

- The QATS Network Group has played a significant role in establishing high quality standards in all the laboratories in the ECMC Network. The QATS group continues to support and enable ECMCs to conduct translational research to the appropriate levels of quality and regulatory compliance, utilising validated, cutting-edge techniques.

- The QATS Network Group celebrated its ten year anniversary at the 2014 Annual Network meeting, and used this as an opportunity to thank former Chair Dr Jeff Cummings from the CRUK Manchester Institute for his contribution over the last 10 years to the Group in its various incarnations. Jeff had played a pivotal role in setting up the Group and driving it forward and was chair of the group for a number of years. The focus of the symposium was also to look to the future with talks from key opinion leaders on areas where the QATS community will be most challenged in the next 10 years. Subjects of the talks included the new European clinical trials regulations, cancer biomarkers and pharmacological audit trail in anti-cancer drug development.

- Meeting to discuss the future direction of the ECMC QATS Network Group [February 2015]. This 10th anniversary symposium highlighted the importance of evolving in order to continue to meet the needs of the Network. Whilst the important role that this Group played in the ECMC Network remained unchallenged, it was agreed that the QATS Group should be split into two subgroups - Quality Assurance and Translational Science – to better tackle the diverse set of priorities of both groups.

The Research Nurses Network Group

- The Research Nurses Network Group promotes quality care for patients taking part in early phase research through peer support, training and guidance for research nurses working in early phase and translational research.

- A Research Nurse workshop was organised at the ECMC Annual Network meeting in May 2014 entitled 'ECMC Nurses – Embracing Challenges, Making Changes'. This workshop looked at how different ECMCs are set-up and delegates heard about and discussed examples of inventive work being done by and for research nurses in the ECMCs. On the day, delegates heard examples on the clinical research team including core staff nurses (**Manchester** ECMC); the role of the translational research nurse (**Cambridge** ECMC) and of clinical research practitioners (**Barts and Brighton** ECMC).

2. The provision of training

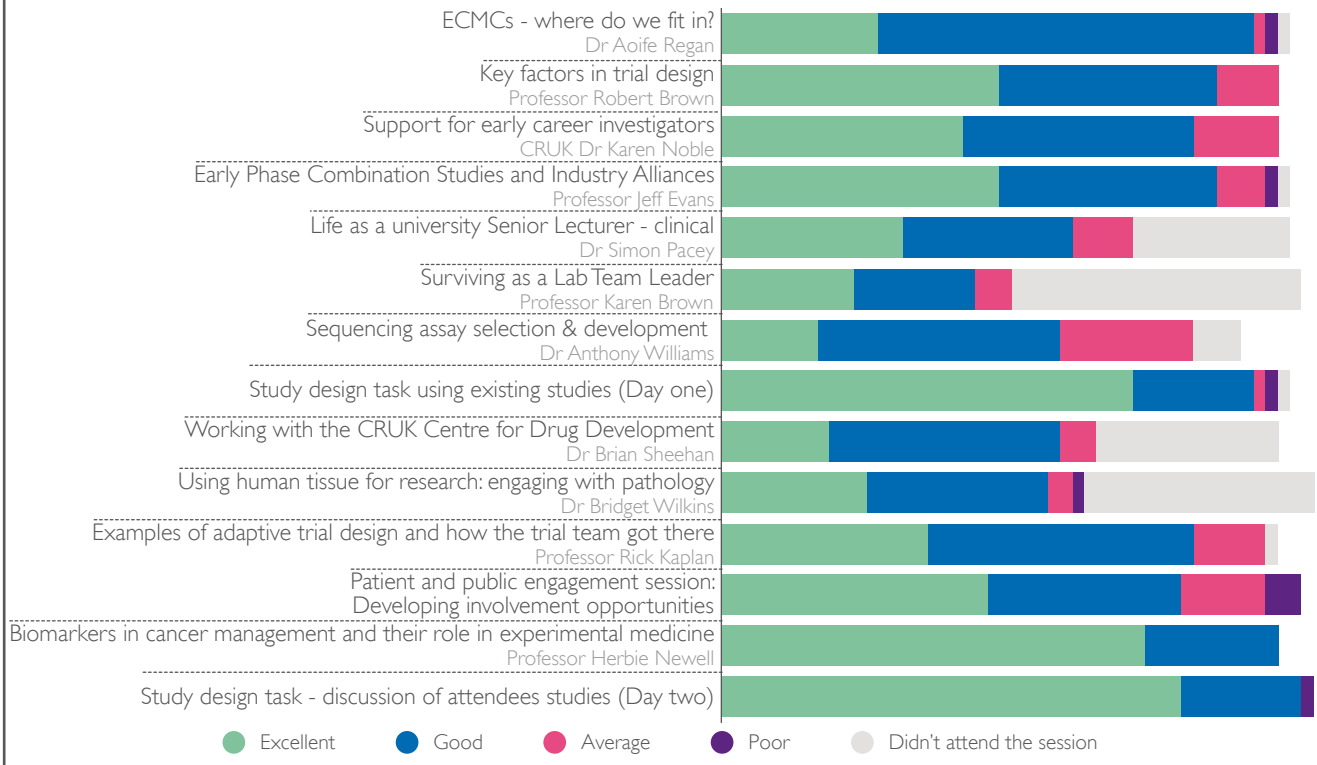
To enhance the existing pool of scientific, clinical and operational expertise across the Network, it is paramount to provide appropriate training to the next generation of experimental medicine professionals. Developing tailored training activities has always been a core activity of the ECMC Secretariat with a range of regular and ad hoc programs developed every year as well as supporting the ECMC Network Groups. In this section we highlight some areas where training has been provided or supported by the Secretariat during the 2014-15 period.

Supporting junior investigators - Junior Investigator Network Group (JING)

Since its set-up in 2012, the ECMC Junior Investigator Network Group (JING) has grown into a thriving community of 200 clinical and non-clinical early career researchers. The third annual residential course in January of this year was attended by 65 junior clinical and non-clinical investigators and supported by a faculty of 39

4 https://membersarea.bir.org.uk/shop/details.asp?id=26&Blue=True

Figure 17 Participant feedback on JING 'Training the Next Generation' residential course (January 2015)



*the 2015 programme contained parallel sessions – grey colour reflects where a different parallel was attended

experienced researchers in the ECMC Network who are recognised international leaders in their fields. The programme, developed by junior investigators for junior investigators, spanned a number of topics for developing early phase and translational studies (e.g. trial design, use of appropriate biomarkers, pathology, imaging, and assays) as well as more interactive sessions on developing their own study ideas and engaging patients in their research. The range of topics covered at the workshop was viewed as relevant and informative, with (as seen in figure 17) the majority of the talks receiving positive feedback.

To further support talented rising clinical researchers in the ECMC Network, the Secretariat has part-funded ten junior investigators from 6 ECMCs to attend the prestigious ECCO, AACR, EORTC & ESMO Methods in Clinical Cancer Research course (otherwise known as Flims), for the June 2015 intake. The ECMC Network will be extending this JING bursary scheme to other clinical trial design, statistics and methods courses for both clinical and non-clinical junior investigators.

Always looking for innovative ways to improve the skills of junior investigators in the Network, JING piloted a scheme with the National Cancer Research Institute (NCRI) Clinical Studies Groups (CSGs) in November 2015 to allow junior investigators to become trainee members to further their networks and gain valuable experience in national trial development. The ECMC Network is currently supporting three trainees in this scheme on the Lymphoma, Prostate and Gynaecological Cancers CSGs and will be piloting an extension of this with CRUK's New Agents Committee (NAC) to have trainee observers on funding committee meetings in the coming year. This will be the first of its kind in getting junior investigators onto funding committees to help understand what goes into a great proposal and key areas funding committees consider when prioritising projects for funding. Applications for trainee observers on NAC has been launched and closed in July 2015.

> We are grateful to the ECMC for providing funding to facilitate these visits. We have since incorporated elements of practice seen at these two ECMCs into our local work flow for our breast tissue banking. Furthermore we plan to disseminate this information to the wider Leeds biobanking teams at one of our regular meetings

Val Speirs
Professor of Experimental Pathology & Oncology, Leeds ECMC

Short-term placements

Since its set-up in March 2012, the Cross-Centre Placements and Skill-Sharing Scheme has awarded 39 placements with the last round including applications linking NIHR Clinical Research Facilities (CRFs) with ECMCs to broaden networking with non-cancer colleagues in experimental medicine. Staff undertaking placements have come from a range of backgrounds including research nurses, trial coordinators, clinical investigators, researchers, technicians and R&D staff and tackled a range of research and training needs from setting up an organoid network to faster biomarker validation techniques or out-of-hours care in early phase units. Many of the placements have forged new collaborations with reciprocal visits or informal mentoring between centres in particular areas of expertise like biobanking, radiopharmacy or quality assurance processes. The application process for cross-centre placements can now be made year-round to allow these to be flexible to the needs of network staff. Consideration is now being given to extending the scheme to support placements outside the ECMC and CRF initiatives, for example in industry.

Research nurses training

The steering committee of the ECMC Research Nurse Network Group identified a need for a training course to cover the basics of delivering early phase trials to share knowledge and boost confidence in newly appointed research nurses.

> We have benefited enormously from being given access to a complete system of SOPs for the setting up of clinical trials. We are now in a position to develop our site specific files for Radiopharmacy with regards to clinical trials including the Product Specification File (PSF) for Investigational Medicinal Products manufactured (IMPS) in the Radiopharmacy.

Jill Tipping
Research Clinical Scientist, Manchester ECMC

The group developed an outline for a training event primarily aimed at research nurses who had been working in early phase cancer research for less than 12 months. Topics covered at the training day included protocol interpretation, screening and recruitment; giving novel agents and links to palliative care. In July 2014, the course entitled 'An introduction to early phase cancer trials: everything you wanted to know but were too afraid to ask' was delivered in London.

As this was a pilot event, feedback on the day was collected in order to ensure that the day was useful and to get suggestions for how the course could be developed and improved for the future. From comments received, delegates found the day useful and appreciated being able to interact with other ECMC staff and discuss how they run their units. The Group's steering committee has reviewed the evaluation forms with the intention of running a second pilot training day in 2015/16 in order to firm up the agenda and course content.

3. Progress on the Capability Map

At the beginning of the current quinquennium work began to develop an ECMC Capability Map. This work was in-line with one of the key strategic aims of the ECMC Network: to attract industry's investment to support experimental cancer medicine studies at centres. Feedback from the Network and industry has consistently suggested the need for a well-designed and maintained resource of this type. The Phase I Capability Map was initially designed to provide means to capture the different and unique capabilities and expertise of each centre. Based on feedback from stakeholders, the Capability Map has continued to evolve to better represent the Network.

The questionnaire to generate the phase II Capability Map was piloted in 2014 at three ECMCs - **Manchester, Belfast** and **KHP** - to gain an initial understanding on possible bottlenecks when filling the requested information as well as testing its utility. Feedback from the pilot centres was taken into account to finalise the questionnaire for the Phase II Capability Map which was rolled out to all the adult ECMCs. The information provided by each centre has been compiled on the

ECMC website. Using this data, the Secretariat will review plans to showcase the unique capabilities of the Network to facilitate collaboration across ECMCs and with industry.

Operational support: Trial harmonisation pathway, strategic partnerships and patient experience

1. The Trial Harmonisation Programme

The ECMC Trial Harmonisation Programme (ETHP) is an ambitious initiative led by the Secretariat to enhance our reputation in early phase clinical cancer research through the efficient delivery of trials and effective management structures. Progress has accelerated considerably over the last year through our partnership with the Health Research Authority (HRA) to streamline several R&D processes in advance of HRA Approval, to develop an ECMC-wide operational framework through the ECMC Operation Guideline and to formalise the collaboration of the Network.

During this last year, there have been significant advances in the programme. We have widely engaged with the health professional community, R&D departments and legal representatives across all ECMC locations. Two joint projects with the HRA to streamline R&D processes within pharmacy and medical exposure reviews have been successfully initiated across the ECMCs (further details in HRA section below). These two areas were selected because they had been identified by the research community as major bottlenecks for trial set-up and fit within the ETHP's aim to deliver faster set up and delivery times for multi-site trials across the Network.

The team also engaged with the R&D community across the Network to help develop the ECMC Operation Guideline. The guideline provides high level guidance of a streamlined operational framework for all ECMC locations during the research pathway. It is anticipated that the guideline will be effective from summer 2015 as part of process embedding and will be underpinned by the legally binding ECMC Collaboration Agreement which is currently in development.

2. Developing national and international collaborations

Health Research Authority (HRA)

The unique set up of the UK-wide ECMC Network has the opportunity to undertake innovative ways of working that allows processes to be tested at a national scale and impact measured in a controlled manner. Working in partnership with the HRA, the pharmacy and medical exposure reviews had been identified by the research community as being key bottlenecks during trial set up. Both of these R&D processes will form part of the technical assurance component of HRA Approval and is anticipated to extend to all trials in the NIHR Clinical Research Network (CRN) by the end of 2015.

Working with pharmacists from the across the Network, the Single Technical Pharmacy Review has been successfully completed with an impact report by the HRA due in summer 2015. From the data cut off date (end April 15), 38 technical reviews have been fully completed with a median turnaround time of 14 days. This equates to 180 duplicated technical reviews avoided at local sites, therefore highlighting potential cost and time savings for each protocol across the Network.

Initial feedback from the pharmacy guardians relating to the new process has been positive, which enabled them to make a cultural shift of reviewing protocols by assessing at a global technical level rather than at a local level. Importantly, the process has allowed pharmacists to provide assurance to each other relating to the protocols reviewed on behalf of each site.

With assistance from Clinical Radiation Experts, Medical Physics Experts and R&D staff across the Network, processes to streamline assessment of research exposures have been agreed following a joint HRA-ECMC Meeting for Medical Exposure Experts in December 2014. Following this meeting, the testing phase has now been launched and a full impact report will also be produced by the HRA by autumn 2015.

It was agreed that the HRA would continue to work with all ECMCs in managing both pharmacy and medical

exposure reviews until the HRA Approval process goes live by end of 2015.

Experimental Cancer Medicine in Europe

In seeking to optimise the ECMC Network there is much we can learn from colleagues in Europe. The French and German governments have both developed a national strategy to facilitate the set up of nationwide academic and commercial early phase cancer clinical trials (i.e. Centres d'Essais Cliniques de Phase Précoce (CLIP2) and the German Cancer Consortium (DKTK in German)), respectively.

The ECMC Secretariat obtained support from CRUK to visit our European colleagues to better understand their unique set up, share experiences with the other secretariats and establish connections with key stakeholders to facilitate future collaborations across Europe in the field of experimental cancer medicine. In April 2015, we visited the CLIP2 and DKTK Heidelberg site to find out how our French and German counterparts match the UK's approach.

Establishing strategic connections with our European colleagues was extremely beneficial, and we are hoping it will lead to more collaborations in the next quinquennium. We are moving towards an exciting time for clinical trials with precision medicine slowly becoming standard practice. This has a direct impact on early phase trials as they are becoming more complex, with more restrictive patient specifications. To obtain enough patients to reach statistical significance for early phase trials, multi-site international clinical trials are likely to become the norm. This visit was a first step towards setting up informal collaborations which aim to place Europe as an attractive place to develop early phase trials for both academic and commercial stakeholders.

3. Patient And Public Involvement (PPI)

Many ECMCs have long established Patient and Public Involvement (PPI) processes in their location. Most ECMCs involve patients and the public in their work as standard practice, often through access to a local or ECMC-specific patient involvement panel or group. These panels facilitate patient and public input for all stages of the research process (i.e. from study development to implementation and dissemination of results). In addition, a number of ECMCs also have patient representatives on their ECMC Steering Committees/Boards or sit on a number of trial-specific steering groups.

In the last year the ECMC Secretariat decided to increase its activity in this area in order to raise awareness of the need for patient involvement in ECMC-funded activity and to help centres to learn from each other. The initiative has been well received by the ECMC community; for example, **Newcastle** and **Belfast** ECMCs have used the cross-centre placement scheme to share best practice for setting up a PPI strategy.

This year the ECMC Secretariat has established an ECMC Patient and Public Involvement (PPI) Group. This group is made up of representatives from the adult ECMCs (nominated by the ECMC Leads) and includes a mixture of staff and PPI representatives. The purpose of this group is to:

- Review/oversee project specific working groups including group objective setting
- Update and share activities from across the Network
- Agree future activities and projects or any areas of priority
- Act as an advisory group (if required) for the whole ECMC Network and to assist on areas that require collective opinion

In advance of the next quinquennium, the ECMC Secretariat is developing a PPI strategy to raise awareness on the need of patient involvement in ECMC-funded activity and to help centres to learn from each other. The first project this group will be looking at is training issues specific to early phase cancer research which is expected to be delivered in 2015-16.

Dissemination of ECMC achievements

A key role of the ECMC Secretariat is to disseminate the fantastic work that is taking place in the Network. A range of communication tools have been developed to ensure we reach the right audiences as well as provide the best

support to our ECMCs. In this section we provide some great examples of the Secretariat engagement with a broad range of audiences to promote the successes of the Network. In particular, this year saw the re-launch of the ECMC website, now housed on a flexible platform which will allow us to develop more innovate communication tools in the coming years.

1. Launch of the new ECMC website

As part of the ECMC Network Strategy, the Secretariat committed to reviewing and developing the ECMC website as a central communication hub to enhance collaboration and promote the Network. To bring the website in alignment with the varied requirements of ECMC stakeholders, the Secretariat developed a proposal based on a comprehensive user assessment. The results from this assessment acknowledged that the existing website was not able to deliver the ECMC objectives successfully. Moreover, there was an overwhelming support from ECMC members to create a website that better catered for the needs of the experimental cancer medicine community.

The new website was officially launched during the ECMC Annual Network Meeting in May 2015. To obtain a balanced view of the new site, we requested feedback from attendees through a questionnaire. Results were overwhelming positive about the new design and user-friendly access, with 82% of responses saying they found the website very useful. The new website will be used by the Secretariat as the core of all the internal and external communication activities of the Network.

Figure 18 The homepage of new ECMC website launched in May 2015

2. Attendance at conferences

NCRI Conference – November 2014 (Liverpool)

The National Cancer Research Initiative (NCRI) Cancer Conference attracts around 2,000 delegates each year and serves as a platform that unites researchers and promotes multidisciplinary sharing and collaboration. Abstracts were accepted for three ECMC Network-led projects, which were presented as posters. The ECMC team had a busy few days promoting the work of the Network at their stand, which, with the help of Multi-Marvin (ECMC mascot), ECMC booklets and capability leaflets, was well attended and sparked lots of interesting conversations and potential new project ideas.

ECMC communication streams (Twitter, e-Bulletin, LinkedIn) were tied in to ensure the success of the ECMC Network debut at the Conference including creating the #MultiMarvinNCRI hashtag encouraging delegates to tweet pictures from around the conference with Marvin which resulted in 43 Multi-Marvin 'selfies' and featured in the NCRI Conference social media round-up.

To help promote the individual capabilities of centres within the Network, leaflets were developed for Centres who were also hosting a stand at the conference to ensure that visitors to those stands were aware that they are an ECMC and have capability in early phase and translational research.

UKCRF Network Conference – July 2014 (Sheffield)

The ECMC Secretariat attended the UK Clinical Research Facilities (UKCRF) Network's 10th Annual Conference entitled 'Excellence, Innovation and Integration; Clinical Research Facilities 2014 and beyond'. At this conference, there was a well-attended ECMC Symposium on the challenges of stratified medicine. The session chaired by Professor Rob Coleman (University of Sheffield) and had the participation of representatives from the ECMC Network.

During the conference, the call of the cross-centre placement scheme was launched where staff at the UKCRFs were given the opportunity to visit an ECMC for the first time. Thus, a research nurse from Cardiff CRF took advantage of this opportunity and arranged a placement at the Institute of Cancer Research (**ICR**) ECMC to find out about developing an escalation strategy for patients and out of hours care, risk management and collaborative care with other wards for early phase patients.

The Clinfield: Building Research Careers Conference - November 2014 (London)

The ECMC Research Nurse Network Group presented the results of the latest survey on out-of-hours safety systems at the Adult Network, an update to a survey first undertaken in 2010. Out-of-hours systems safeguard clinical trial patients' safety when they need support outside working hours, ensuring that out-of-hours staff were made aware the patient is on a trial and that they can access information about that trial. The results from this survey were presented in a poster entitled 'Promoting patient safety in cancer clinical trials: a survey of progress in out-of-hours systems in the ECMC Network' at the Clinfield Conference in London.

3. Social Media

Twitter

The ECMC Secretariat joined Twitter in September 2013 (@ECMC_UK). During 2014/15 @ECMC_UK gained just under 300 new followers. Twitter has been used to raise the profile of the ECMC Network and events that it runs as well as to engage with the research community. During the NCRI Conference in November 2014 '@ECMC_UK' had a high profile presence, this was mostly due to the #MultiMarvinNCRI hashtag which was widely used both during and after the conference. Speakers for ECMC-organised workshops have also been engaged through Twitter, for example Claire Gibbs a speaker at a workshop at the 2015 ECMC Annual Network meeting was contacted through Twitter.

LinkedIn

The ECMC Network also has a presence on LinkedIn with the ECMC Group being created in July 2014. This group currently has 170 members and is used to have discussions, advertise events and promote jobs. The ECMC Group currently has four subgroups: ECMC Junior Investigator Network Group (JING); CRUK, ECMC and UK Radiopharmacy Group Taskforce (CERT), Quality Assurance and Translational Science (QATS) Network Group and an ECMC Bookclub.

E-Bulletin

During 2014/15 five issues of the ECMC e-Bulletin, ECMC Connect, were released. This newsletter reaches about 900 people. This newsletter updates people on the work of the ECMC Network with news stories from both the ECMC Secretariat and the centres themselves. During the past year there have been spotlight articles on subjects such as the TAX-TORC trial, combinations research and administering novel agents. There have also been interviews with Lyn Barrington (patient), Nicola Griffin-Teall (research nurse) and John Chester (ECMC Lead).

LOOKING TOWARDS THE FUTURE

Strategy 2017- 2021 overview

This is a pivotal point in the evolution of the ECMC Network as in the next year the future strategy for the Network will be finalised and the sites that form the next ECMC Network will be chosen. To this end, the Secretariat has been carrying out some scoping exercises to assess whether the focus and structure of the future ECMC Network is fit for the future. With a vision to build a truly collaborative, internationally competitive, national network of early phase experimental cancer medicine centres, the Secretariat has created an ambitious scientific strategy. Whilst we believe that maintaining a good breath of activities in the Network is key to remain competitive, in the next quinquenium we will shift our focus towards the delivery of early phase trials. Nevertheless, aware of the importance that associated activities (i.e. biomarker studies, biobanking and translational science) play in facilitating the bench-to-bedside flow, we will only narrow their remit. Regarding the future structure of the Network, the Secretariat felt that the current set up - a UK-wide network of 18 adult and 9 paediatric centres of similar size - had been a successful cost-effective approach to harness the available knowledge in the different ECMCs whilst promoting collaboration across the Network.

In parallel, the Secretariat has been working with a variety of professionals across the Network to design new structures and processes creating for the first time a nationwide operational framework for experimental cancer medicine. In the next quinquennium, we hope to see that studies approved for recruitment in one ECMC will, with minimum effort, be able to open across the Network.

To support this new way of working, it is proposed that the Secretariat transitions to become a centralised Programme Office. This office will support investigators in the Network, report on activity, provide the secretariat to the governing committees, and promote the Network as a destination for experimental cancer studies. This is a substantial departure from the current ECMC Secretariat, which we will transition to this model over a period of time in advance of the next quinquennium.

The Collaboration Agreement

A key change for the future of the ECMC initiative is to harness the expertise of a dedicated early phase cancer network to become more collaborative with a strategic remit. In order to achieve true networking and to enable efficient processes to support challenging trials and associated translational research, an overall change in governance structures will be required. Through the newly established ECMC Contracts Working Group, their remit is to help develop a legally binding collaborative network that binds all participating members (NHS/ Health Board and University representatives from each ECMC location) to agreed ways of working including responsibilities and overall governance structure.

This year, the terms of references and working deliverables for the ECMC Contracts Working Group were agreed by all members. In addition, in order to speed up the process of discussions across the Network with a commercial partner, a master non-disclosure agreement (NDA) would be first developed by the working group in advance of the collaboration agreement. It is anticipated that sign-off of the NDA will be completed by summer 2015. Thus, there are plans for the NDA to be facilitated by the proposed centralised Programme Office between all ECMC member organisations and commercial partners. Trialling of the NDA process will be planned once NDA sign-off is agreed by all ECMC members. From May 2015, the collaboration principles will be proposed to the Contracts Working Group in order to develop the agreement for ratification and sign-off by all partners by April 2016.

Preparing for the 2016 Quinquennial Review (QQR)

The Experimental Cancer Medicine Centres (ECMCs) funding will be renewed in 2017 and there will be substantial change to the focus and management of the Network. Preparations have already started for the second quinquennial review that will take place in October 2016. The review will not only assess the suitability of the existing ECMCs to continue in the program but will also be open to new UK centres who want to join the ECMC Network.

As ECMC quinquennial and the CRUK Centres triennial reviews were due to take place on the same year it was agreed to combine efforts with CRUK. The decision to organise a joint review aims to avoid the duplication of efforts as well as promoting a better alignment between the strategies of the CRUK Centres and ECMCs in the different UK sites. It is hoped that the joint review will bridge basic science and early phase trials to facilitate access to better treatments for cancer patients sooner.

This year the ECMC Secretariat and CRUK Centres team agreed to a common work plan that will ease existing bottlenecks, promote sharing of expertise and ensure the delivery of a top quality review.

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