Experimental Cancer Medicine Centres (ECMC) Network

A year of progress 2014/15

Introduction

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

Launched in 2007, the Experimental Cancer Medicine Centres (ECMC) Network is jointly funded by Cancer Research UK and the health departments for England, Scotland, Wales and Northern Ireland

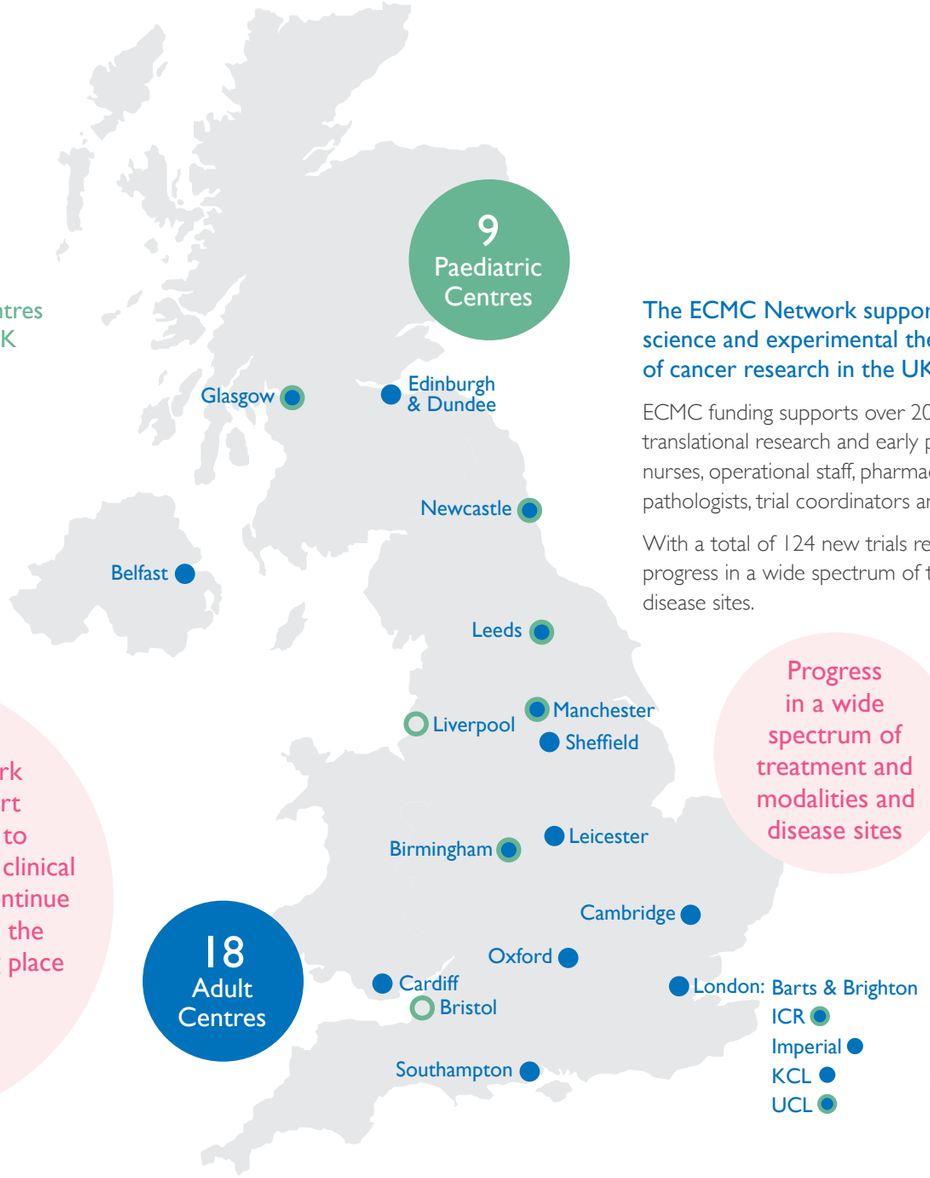
The ECMC initiative supports the infrastructure needed to both deliver world-leading early phase clinical trials and to enable a network of experts to translate scientific discoveries into new cancer treatments for patients.

This booklet highlights just some of the ground-breaking achievements made in the ECMC Network during the financial year 2014/15.

"We're delighted that our ECMC Network has been able to support this important initiative to streamline the regulation of clinical research, so patients can continue to reap the benefits from the world-class research taking place throughout the UK"

Prof Peter Johnson
Cancer Research UK

The capacity of the ECMC Network



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 124 new trials reported, the year 2014/15 saw progress in a wide spectrum of treatment and modalities and disease sites.

Progress in a wide spectrum of treatment and modalities and disease sites

NEW TRIAL BY TREATMENT ADDED TO THE NETWORK (2014/15)

SMALL MOLECULES	105
IMMUNOTHERAPY	13
BIOMARKER	5
OBSERVATIONAL	3
IMAGING	3
GENE THERAPY	1
RADIOTHERAPY	1
DEVICE	1
CHEMOTHERAPY	1
OTHER	12

NUMBER OF TRIALS BY CANCER TYPE SUPPORTED BY THE ECMCS (2012/15)

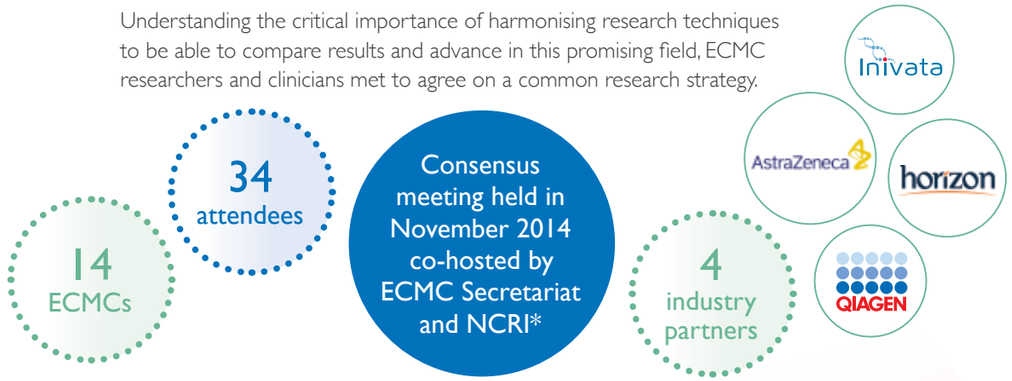
HAEMATOLOGY	181
ANY ADVANCED CANCERS	140
LUNG	76
BREAST	71
COLORECTAL	46
MELANOMA	37
PROSTATE	32
MULTIPLE TUMOUR TYPES	30
PANCREAS	28
BRAIN & NERVOUS SYSTEM	28
OVARIAN/FALLOPIAN TUBE	25
RENAL	23
HEAD & NECK	17
LIVER	17
SOFT TISSUE	15
OESOPHAGEAL	14
BLADDER	12
MESOTHELIOMA	8
UTERINE/ENDOMETRIAL	6
STOMACH	5
BONE	5
OTHER	57

A Network committed to innovation

CASE STUDY: Harmonisation of cell-free DNA (cfDNA) practices

Cell-free DNA (cfDNA, sometimes referred to as circulating tumour DNA or ctDNA) is a promising blood-based biomarker. Research in cfDNA is growing with many new trials collecting plasma for analysis, but to date, there is no consensus on techniques, analysis, priority research questions and clinical strategy to validate cfDNA as a diagnostic or prognostic marker for cancer.

Understanding the critical importance of harmonising research techniques to be able to compare results and advance in this promising field, ECMC researchers and clinicians met to agree on a common research strategy.



Outcomes of the meeting:

- An agreed set of recommendations on analysis, techniques and 'gold' standard practice needed to advance research in cfDNA
- The development of a systematic review and sample sharing study funded by the ECMC initiative
- A shared plan to develop standard operating procedures (SOP) to share across the ECMC Network and beyond to the UK and international research community

* National Cancer Research Institute

Scientific excellence that benefits patients

This year saw some great examples of the groundbreaking work that ECMC Network staff can deliver, with a broad range of innovative trials taking place within the Network

HIPROC
A Phase I/Ib trial to test a hedgehog inhibitor (LY2940680) in combination with paclitaxel in patients with ovarian cancer (Glasgow, Imperial, Barts & Brighton ECMCs)

TRACERx
A biomarker study to track genomic lung cancer evolution (18 ECMCs)

Immunobody
A phase I study to test a DNA vaccine encoding a human modified IgG1 antibody in melanoma (Leeds, Manchester, Newcastle, Southampton ECMCs)

CASE STUDY: NIMRAD

The NIMRAD trial aims to understand the effect of combining radiotherapy with the drug nimorazole for people with locally advanced head and neck cancers. Radiotherapy is commonly used to treat patients suffering head and neck cancer and this study assesses the impact of adding a drug (nimorazole) that targets cells with low levels of oxygen (more difficult to kill with radiotherapy). The study is a national multi-site trial funded by Cancer Research UK (CRUK) and led by Manchester ECMC with the participation of 6 ECMCs: Birmingham, Cambridge, Glasgow, ICR, Leeds, and Sheffield.

In addition, with the collaboration of Belfast, Birmingham, Cambridge, Cardiff, Glasgow, ICR, Leeds, Newcastle and Sheffield ECMCs, Manchester ECMC also led NIMRAD-TRANS to prospectively qualify hypoxia gene signatures to predict nimorazole plus radiotherapy benefit in head and neck cancer patients.

Collaboration

PIONEER is a Phase I study of olaparib in combination with chemo-radiation in locally advanced pancreatic cancer. Under the NIHR Alliance initiative, the Glasgow ECMC has developed this multi-site study to assess whether adding olaparib (**AZD2281**) to a capectiabine-based chemo-radiation regimen improves the effects of treatment in this subgroup of patients with locally advanced pancreatic ductal adenocarcinoma.

KHP
Glasgow
Leicester
Belfast

Oxford
Belfast
11 European partners

MERCURIC study (funded by the European Union) is a phase Ib/II trial to assess a novel therapeutic strategy and search for novel biomarkers in colorectal cancer.

Belfast
Leicester
Birmingham

This study to analyses the effects of **Vitamin D treatment** on growth control biomarkers in human primary colorectal tumours (CRT). Once the optimal dose of Vitamin D is defined in Belfast ECMC, the trial will expand to include the Birmingham and Leicester ECMCs.

Using **Selumetinib in Iodine Refractory Differentiated Thyroid Cancer**. This is sponsored by Sheffield and co-ordinated by Leeds CTRU.

Leeds
Oxford
Glasgow

A Phase I trial to test the safety and benefit of **pre-operative stereotactic body radiation (SBR) therapy** for previously untreated borderline operable pancreatic cancer.

Leeds
Sheffield

Belfast
Cardiff
Glasgow
Southampton
Edinburgh & Dundee
Oxford

The **Opportune** study, which is a randomised Phase II window study to test **GDC0941 plus Anastrozole versus Anastrozole alone** in patients with ER+ primary breast cancer.

KHP
Barts &
Brighton

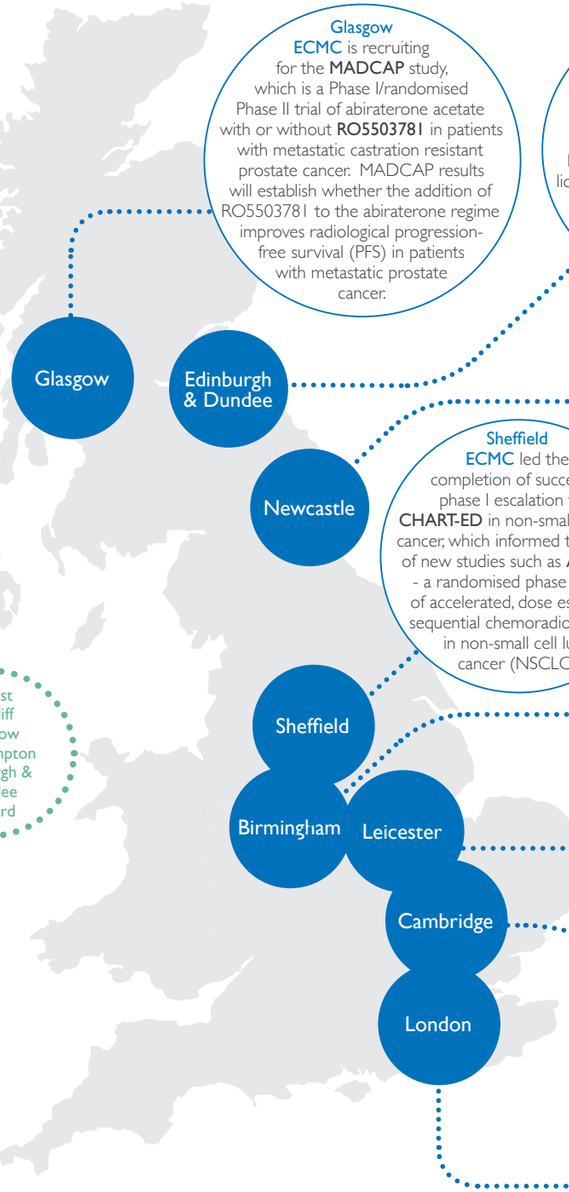
Newcastle
Southampton
Birmingham
UCL

The creation of a UK network for pre-clinical drug therapy assessment using "organoids". **Organoids**, derived from the tumours of cancer patients closely replicate key properties of the original tumours and are amenable to large-scale drug screens.

Developing a technique of preparing patients for **transplantation using a radio-labelled monoclonal antibody** that targets the bone marrow allowing very precise delivery of high radiation doses to the site of disease, in this case the clonal plasma cells.

A Phase I trial for patients with locally advanced or metastatic tumours. Patients will receive the drug **vandetanib** in combination with targeted radiotherapy (**131I-mIBG**) to determine the recommended dose of vandetanib for Phase II.

London
Manchester
KHP



Innovation

Glasgow ECMC is recruiting for the **MADCAP** study, which is a Phase I/randomised Phase II trial of abiraterone acetate with or without **RO5503781** in patients with metastatic castration resistant prostate cancer. MADCAP results will establish whether the addition of RO5503781 to the abiraterone regime improves radiological progression-free survival (PFS) in patients with metastatic prostate cancer.

Edinburgh & Dundee ECMC developed **Olaparib** from Phase I to Phase III. The European Medicines Agency approved Olaparib for use in Europe in December 2014. It is licenced for women with advanced ovarian cancer, fallopian tube and peritoneal cancer who carry a faulty **BRCA1** or **BRCA2** gene.

Newcastle ECMC ran a successful investigator-led imaging trial called **FLAIRE** using **18F-FLT PET CT** to assess response to radiotherapy. The trial has completed recruitment and the results show that **FLT PET CT** imaging during radiotherapy is a potential biomarker for early response to treatment.

Sheffield ECMC led the completion of successful phase I escalation trial **CHART-ED** in non-small cell lung cancer, which informed the design of new studies such as **ADSCaN** - a randomised phase II study of accelerated, dose escalated, sequential chemoradiotherapy in non-small cell lung cancer (NSCLC).

The **EBV+** cancer program led by **Birmingham ECMC** developed a therapeutic vaccine comprising a recombinant vaccinia virus, **MVA-EL**, to boost immunity to EBV antigens. A phase I trial was conducted and successfully showed that MVA-EL is safe and immunogenic across diverse ethnicities.

The **Leicester ECMC** team, in collaboration with Imperial ECMC, have shown that cell free DNA (**cfDNA**) monitoring can detect emergence of resistance to endocrine therapy in patients with **ER+** breast cancer.

The **ECMC-funded biomarker programme** has collected more than a 1,000 normal and tumour specimens from melanoma patients and normal tissue from healthy volunteers. The resources allowed researchers at **KHP** to describe humoral responses in melanoma patients with BRAF mutations, resulting in the **identification of novel immune biomarkers** for predicting malignant disease outcomes.

In collaboration with GI Solutions and Medtronic, this trial has developed a **non-endoscopic diagnostic test for Barrett's oesophagus** using a device called the Cytosponge combined with the Barrett's specific biomarker TFF3. The positive results from the intial trials have encouraged the **Cambridge** team to perform a randomised controlled trial of Ctyosponge-TFF3 in primary care.

ICR ECMC was the lead site on the ECMC Combinations Alliance trial **ComPAKT** with **AZD2014**, a novel oral m-TORC 1/2 inhibitor. After successful treating 56 patients, the trial has progressed to Phase II, as well as a new Phase I/II trial called **TAX-TORC** combining **AZD2014**

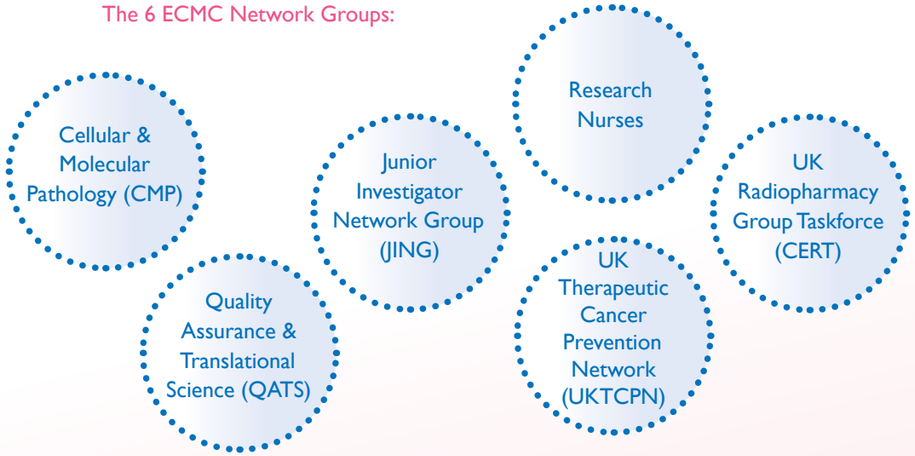
Networking

The ECMCs have established themselves and become a key component of the cancer research infrastructure in their locations throughout the UK.

The number of multi-site trials has increased by a third since the launch of the ECMC Initiative in 2007.

The collaborative nature of the Network would not be possible without the sense of community that stems from the different ECMC professionals. The ECMC community share best practices, through the 6 ECMC Network groups, training opportunities across ECMCs and collaboration in major initiatives such as the Lung Matrix Trial.

The 6 ECMC Network Groups:



Developing Partnerships

Both adult and paediatric ECMCs continue to use their infrastructure and work carried out through the ECMC initiative to leverage additional funds from pharmaceutical companies, biotech companies, government and other partnerships.

As a result, this year has seen **48 companies** involved in setting up new partnerships with the ECMCs which has resulted in over **£73,400,000** of leveraged funds.

CASE STUDY: The Trial Harmonisation Programme

The Trial Harmonisation Programme in an initiative to streamline trial delivery for UK-wide early phase cancer studies by establishing a single operational framework across all ECMCs. This ambitious Programme aims to enable the consistent and unified management of trials processes across the Network.

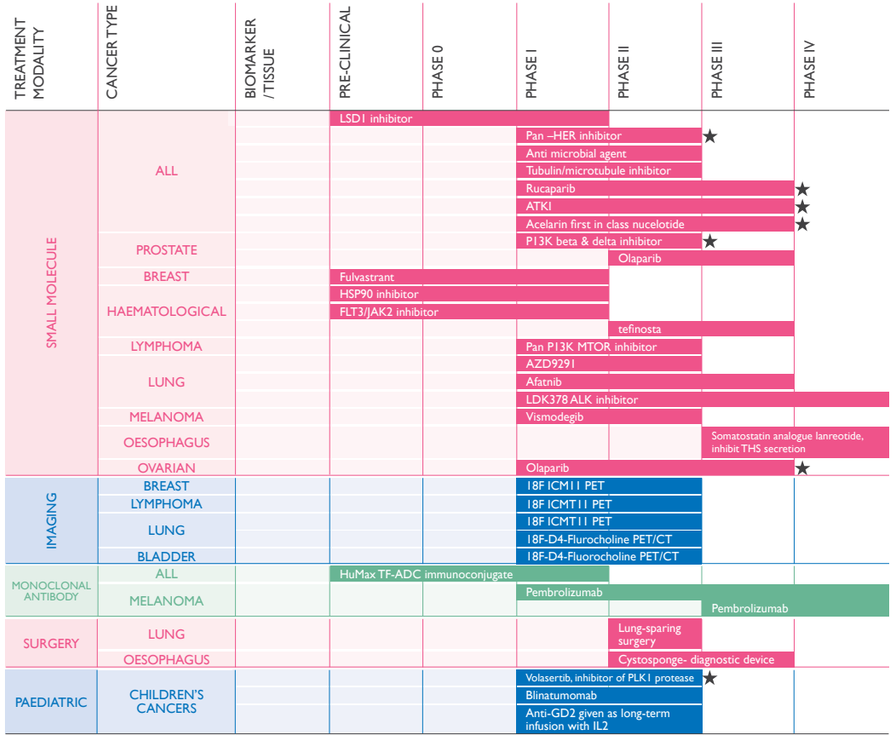
Recognising the importance of standardising practices and reducing set up times to ensure that the UK remains competitive in the global market, we have worked in partnership with the Health Research Authority (HRA) to streamline pharmacy and medical exposure reviews across the Network.

During 2014/15, the ECMC Network volunteered to pilot this initiative which will later be rolled out to the rest of the country. The resulting success was well received by researchers, clinicians, R&D staff and industry stakeholders.

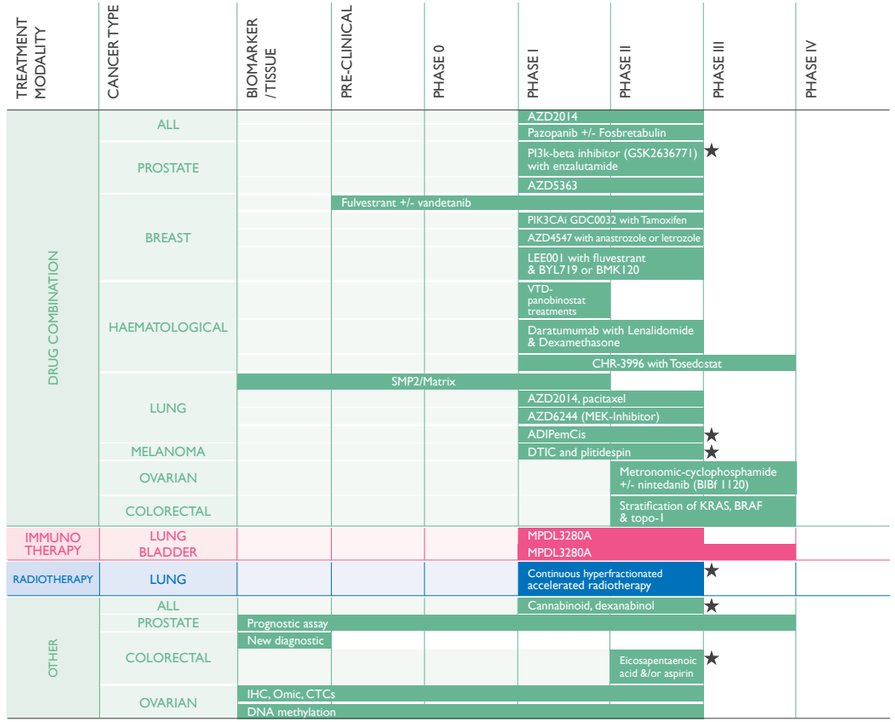
A diverse trial portfolio

This year we have seen the development and progression of some exciting trials throughout the ECMC Network.

Our trial portfolio covers a broad range of cancer types as well as treatment modalities. See below a snapshot with some examples of the diversity of trials taking place in the Network in 2014/15.



Over 2500 patients were recruited onto 389 trials supported by the ECMC Network in 2014/15



ECMC

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ECMC-Experimental-Cancer-Medicine-Centres

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