Annual Report

2017/18

ecmc

Experimental
Cancer
Medicine
Centres

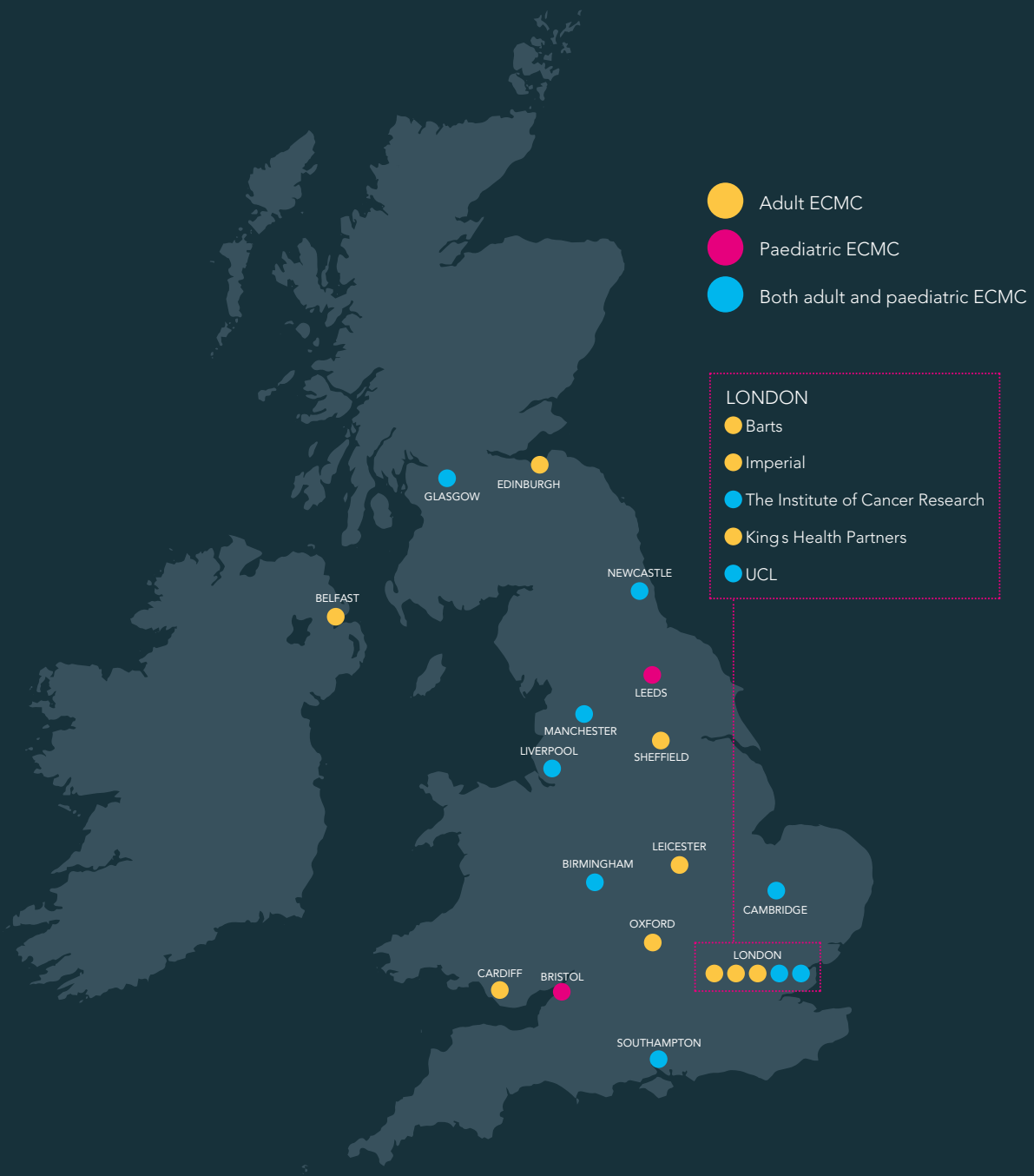

Figure 1 Our centres – 18 adult centres and 11 paediatric locations across the UK

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Executive summary

Jointly funded by Cancer Research UK (CRUK) and the health departments of England, Northern Ireland, Scotland and Wales, the Experimental Cancer Medicine Centre (ECMC) network initiative entered its third quinquennium in April 2017.

The funders have committed £35 million over five years to support 18 adult centres and one paediatric network with 11 locations, which were successful in the last quinquennial review performed by an independent international expert panel in October 2016.

Capitalising on the success of the previous ten years, the ECMC network initiative aims to build a truly collaborative, internationally competitive national network of early-phase experimental cancer medicine centres, translating the most promising innovations from the academic and industry sectors into the cancer medicines of tomorrow.

2017/2018 has been pivotal in setting an increasingly ambitious agenda for the network and laying the foundations for success.

Firstly, our network has kept its prominent position at the forefront of experimental medicine, supporting many valuable academic and commercial collaborations. Across the UK, more than 5,000 patients have been recruited for treatment, in nearly 1,000 studies. Over 200 of these were newly reported by our centres in the past year. Productive engagement with industry is an important priority to bring the most innovative treatments to patients, and in the last year we worked with over 150 industry partners, who benefited from our network's ability to deliver high-quality research with world-class translational infrastructure.

Secondly, to build a network that is more than the sum of its parts, we revolutionised our governance structure to help ensure we are setting a sufficiently ambitious agenda, and we set out to develop a network-wide strategy to enhance our ability to compete internationally. We have identified four strategic areas of focus to underpin the network's activities in this quinquennium:

- Network scientific and clinical strengths
- Relationship with industry
- Operational delivery
- Workforce needs.

The spirit of collaboration as the basis of the network is evident as more than half of the network's trials are multi-site. Additionally, there are several established platforms running across all our centres, such as the Cancer Research UK Combination Alliance, the Stratified Medicine Programme and the National Lung Matrix trial.

Thirdly, to support the ECMC network's mission, the central coordinating team (previously known as the ECMC secretariat) has been restructured into the ECMC Programme Office, with dedicated resources to support network activities and operational effectiveness. New high-impact initiatives led by the Programme Office include a collaborative approach with regulators to address some of the regulatory blocks for experimental cancer medicine, and the creation of a searchable clinical trial database to identify suitable trials for patient referral within the network. The Programme Office plays a key role in facilitating engagement with commercial partners, streamlining operational activities, sharing expertise, coordinating the advancement of new approaches and the dissemination of success stories.

This report is not an exhaustive list of all activity within the network. Here we highlight case studies representing our achievements in 2017/18 and our progress with the network-wide strategy and its implementation.

£35m
funding over 2017-22

5,000
patients recruited

11
paediatric locations

150
industry partners

18
adult centres

A network that fosters scientific excellence

A network founded on scientific excellence

Our network delivers excellence in early-phase interventional treatment trials. Almost 190 new trials were added to the ECMC portfolio in 2017/18, on top of the 743 trials that were already active prior to April 2017 (**Table 1**).

The new studies cover a wide spectrum of disease types in both the adult and paediatric portfolios. Treatment interventions are the most prevalent study type, representing over 85% of the adult portfolio and over 95% of the paediatric portfolio. The portfolio also covers several imaging, device and prevention trials, as well as supporting a novel screening platform study.

The adult network's delivers high quality trials in prevalent disease types (eg breast; genitourinary and gynaecological cancers; thoracic and respiratory; and gastrointestinal), alongside trials in rare cancer such as sarcoma and brain cancers (**Figure 2**). During the past year, the greatest numbers of new studies added to the adult portfolio were for patients with haematological cancers and patients with any advanced cancer.

	Studies added in 2017/18	Studies ongoing prior April 2018
Treatment intervention trials	187	743
Imaging	12	19
QoI/Side effects	6	7
Device	4	1
Prevention	2	1
Screening platform	2	2
Diagnostic	0	2
Total:	**213**	**775**

Table 1 The number of ECMC-supported studies and range of trial types in the adult and paediatric networks in 2017/18. The left-side column shows the number of newly reported trials during 2017/18 and right-side column shows the total number of supported trials as of March 2018. (Treatment intervention trial: drug, biologicals, radiotherapy and surgery trials; QoL: quality of life).

Adult studies by disease category

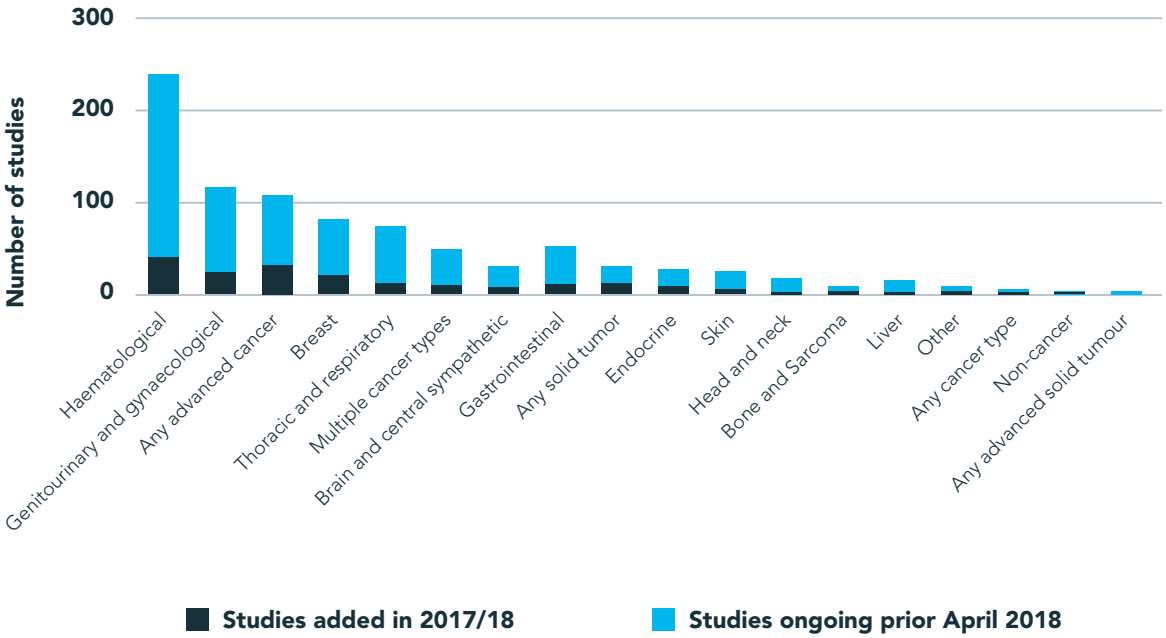
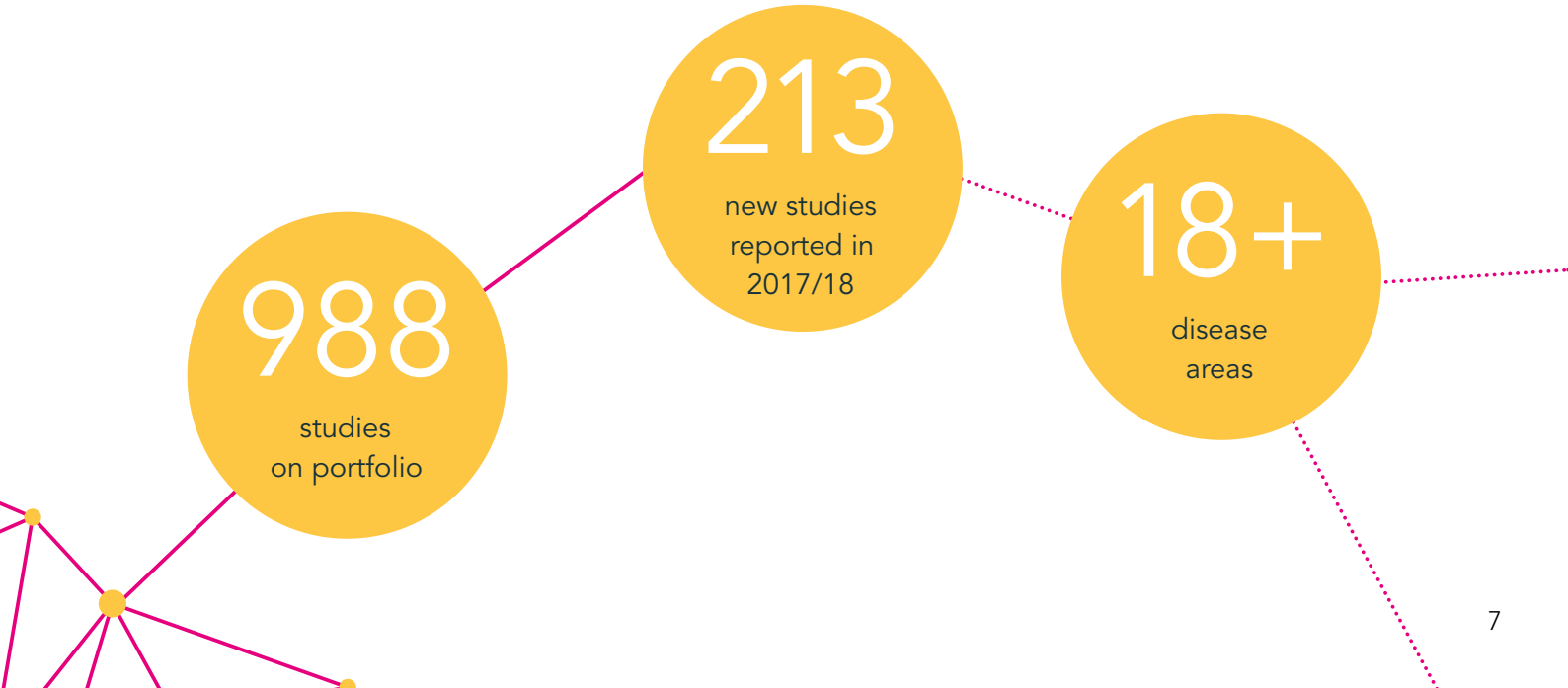


Figure 2 Disease types in the adult ECMC portfolio in 2017/18.



Paediatric studies by disease category

The ECMC Paediatric Network portfolio is focused on the most common childhood cancers; haematological and brain cancers represent the majority of the portfolio – 62% of new trials – in total 26 new trials (**Figure 3**).

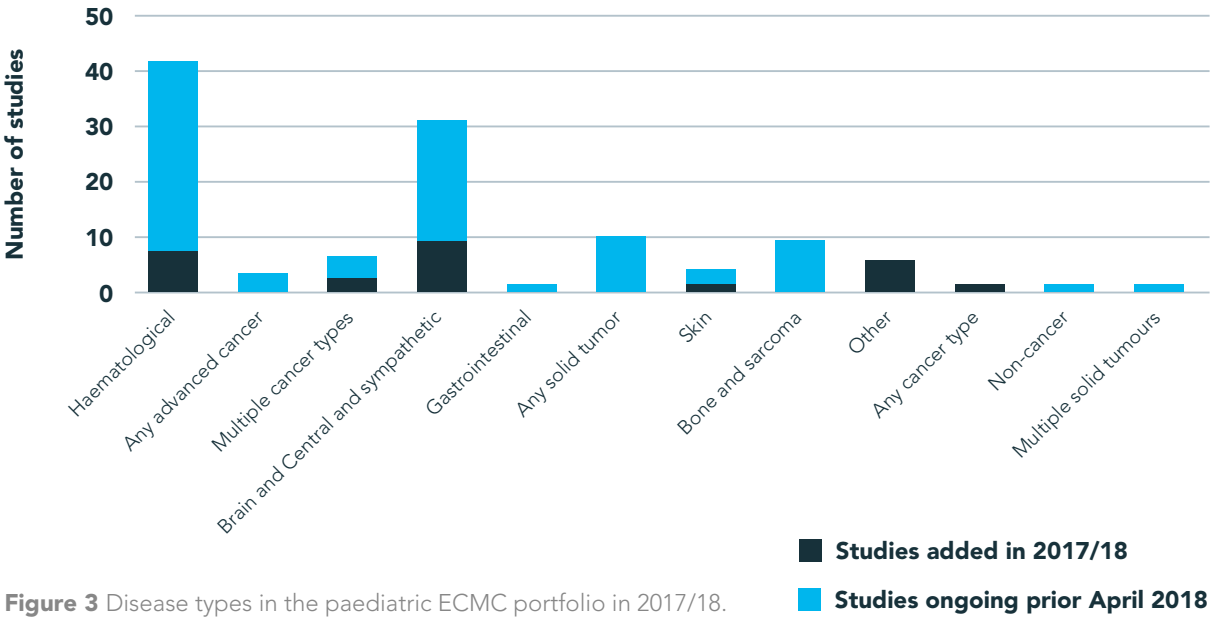


Figure 3 Disease types in the paediatric ECMC portfolio in 2017/18.

Total number of studies by phase

Whilst 70% of the new trials are Phase I and Phase II non-randomised trials (**Figure 4**), ECMC funding also supports biomarker and translational studies to advance treatment development.

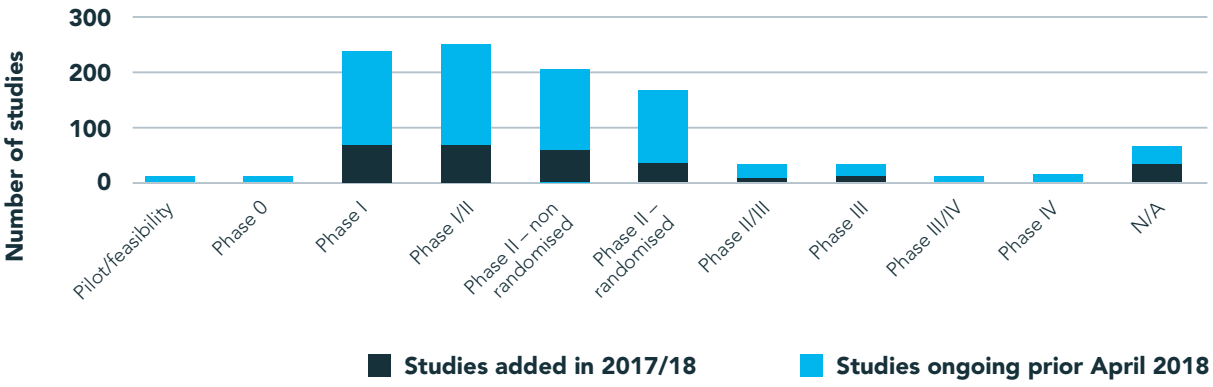


Figure 4 The number of new ECMC-supported studies in the adult and paediatric networks in 2017/18 across different phases (N/A: Trials without phases eg studies of devices, surgical, some radiotherapy trials).

Catalysing innovation in early-phase research

Throughout 2017/18 our researchers took on some of the most complex and challenging questions in cancer. Here we highlight their scientific advances and share examples of novel trials exploring new ways to understand and fight cancer.

The MANTA trial led by **Barts ECMC** (330 patients randomised in 88 sites, in nine countries) demonstrated superior efficacy of fulvestrant plus everolimus versus fulvestrant alone or fulvestrant plus the dual TROC inhibitor vistusertib. These results led to discontinuation of the development of vistusertib in breast cancer.

The **Belfast ECMC** generated several novel high-grade serous ovarian cancer cell lines from ascites removed from patients with cisplatin-sensitive and cisplatin-resistant ovarian cancer. These cell lines have been used to demonstrate selection for an angiogenic phenotype post cisplatin treatment. This research has been widely shared at AACR (2017 and 2018), and ASCO (2018) and a manuscript is in preparation.

The Phase II STAR-TREC trial in early stage rectal cancer patients opened, with the target of accelerating recruitment to demonstrate the ability to perform a future Phase III study incorporating 400 patients. STAR-TREC will evaluate differences in pelvic relapse rates between organ saving and standard surgery. A biorepository for central tissue storage will be established in **Birmingham ECMC** to test stratifiers for deep x-ray therapy and organ preservation. It is envisioned that STAR-TREC will be a practice-changing trial, giving patients access to organ preservation treatments instead of having a radical surgery as per current standard practice.

Edinburgh ECMC was the leading recruiter to the Phase Ib PISSARO study of APR-246, a novel agent aiming to increase the sensitivity of cancer cells to platinum through effects on p53, in relapsed platinum-sensitive high-grade serous ovarian patients. The Edinburgh investigator was then selected to lead the follow-on randomised Phase II trial in platinum-sensitive recurrent and p53-mutated epithelial ovarian cancer.

The REI-EXCISE trial, led by **Imperial ECMC**, is a first-in-women study of mass-spectral analysis of the in vivo surgical diathermy plume. If successful, it has the potential to transform how breast conserving surgery is conducted, with impacts including reducing positive margins, re-operative interventions, improving cosmesis and reducing healthcare costs.

Based on the anti-tumour activity demonstrated in the Phase II **ICR ECMC**-led TOPARP trial in lethal prostate cancer, olaparib was taken forward to a larger randomised Phase-III study. Astra Zeneca's PROfound study is comparing olaparib versus enzalutamide or abiraterone in subjects with metastatic castration-resistant prostate cancer. ICR's work on olaparib led to them identifying that 12% of all patients with advanced prostate cancer have germline DNA repair defects, leading to a change in the National Comprehensive Cancer Network guidelines in 2017.

The **ECMC Paediatric Network** supported the opening of the BIOMEDE Phase II trial for newly diagnosed DIPG, in nine locations. This novel, Innovative Therapies for Children with Cancer (ITCC)-sponsored study is a major step forward in the management of this universally fatal type of brain tumour, in which progress has been stymied by a lack of material for biological studies.

A Phase II study of the CXCR2 inhibitor, AZD5069, in combination with MEDI4736 (anti-PDL-1 antibody) arose out of laboratory studies in **Glasgow ECMC**, and the PD analysis will be performed in the Glasgow ECMC laboratories.

Leicester ECMC developed an explant culture platform, as a pre-clinical tumour model to better predict patient outcomes and response to novel and standard of care therapies. They published a high impact paper (Karekla E. et al. Cancer Research 2017) which details how the explant platform is predictive of both patient outcome and drug responsiveness. They envision that further development will help to generate a model amenable to efficacy assessment of immunotherapies, which are currently lacking.

Newcastle ECMC participated in the Phase I study of 2-hydroxyoleic acid (2OHOA), a novel sphingomyelin synthase activator, establishing a safe dose. As well as acting as a recruiting site, Newcastle developed the assays, and delivered the clinical, pharmacokinetic and pharmacodynamic data for the whole study, which is now complete. The results have led to a Phase II programme in high-grade gliomas, both in adults and children, funded by HORIZON 2020. Newcastle will be involved in pharmacology and pharmacodynamic evaluations, potentially for all European sites, and will be a clinical centre.

The Phase I open-label, dose escalation study of the antibody drug conjugate GSK2857916 in subjects with relapsed/ refractory multiple myeloma and other advanced hematologic malignancies, led by **UCL ECMC** has completed enrolment to its Phase I myeloma cohort. The IMP has FDA and EMA breakthrough designation, based on the Phase I results. The Phase I lymphoma cohort is still enrolling, and Phase II is planned to open this year.

Sheffield ECMC conducted the first combination trial of a radioactive pharmaceutical with immunotherapy in breast cancer. The NEPTUNE study is a Phase Ib/II proof-of-concept trial, combining avelumab and repeat doses of radium-223 in ER+ve, HER2-ve metastatic breast cancer.

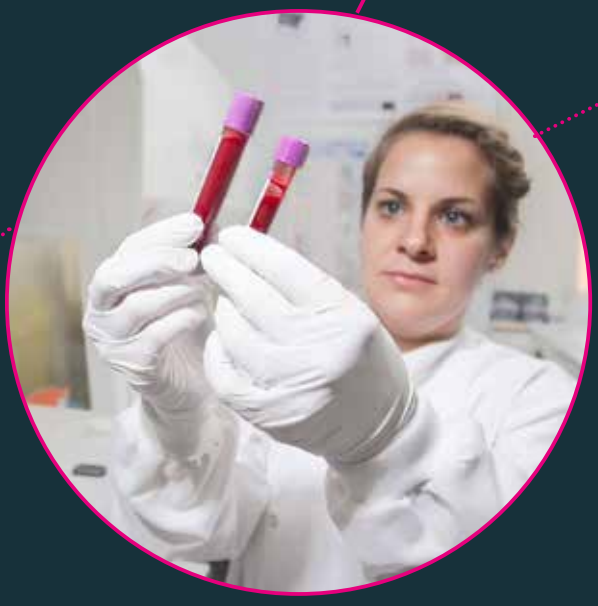
A network that delivers

ECMCs are specialist locations which have the capability to undertake large-scale, world-leading clinical trials. Our network brings together experts and professionals and provides a platform for the successful design and delivery of experimental cancer studies, sharing best practice and driving improvement. We've created a network of facilities and capabilities that set the benchmark for our industry and equip us to lead the way in experimental cancer research.

Below are examples of the network's high performance in delivering trials and accelerating anti-cancer drug development.

Manchester ECMC was the highest EU recruiter, and performed the molecular profiling in the STARTRK trial, enrolling patients with locally advanced and metastatic solid tumours who had any of a NTRK1, 2, 3 mutation or a ROS1 or ALK gene rearrangement (~1% prevalence). These results have led to Ignyta setting up a trial of registrational intent.

Ice-CAP, a Phase I investigator-initiated trial combining ipatasertib (PI3K inhibitor) with atezolizumab (PD1 inhibitor), taking place within the **ICR ECMC**, is the fastest study set up globally as part of the Roche imCORE network.



Newcastle ECMC was the first site to open in the SeluDex study, which is the first ECMC Combinations Alliance study across age boundaries, with simultaneous dose finding and safety cohorts in children and adults with acute lymphoblastic leukaemia. The Newcastle-based PIs in paediatrics, worked alongside Professor Pam Kearns (Birmingham), to gain agreement to include European paediatric sites, facilitating timely recruitment in this rare patient population. Newcastle also developed the fully-validated selumetinib assay to support the trial.

The ALM201 first-in-human Phase I trial of a novel anti-angiogenic agent recruited 20 patients from **Belfast**, **Newcastle** and **Manchester ECMCs** and completed dose escalation on time and on target, with minimal drug-related toxicity seen. The expansion phase will open once **Belfast ECMC's** predictive biomarker has been validated and CE marking obtained.

Since becoming a ECMC in 2017, 28 Phase I and II studies have opened at Clatterbridge Cancer Centre, compared to 16 in 2016. Four of these involve translational elements supported by local **Liverpool ECMC** infrastructure. Liverpool CTU is now leading four new Phase I/Phase II trials in set-up and has developed a host of new funding applications and protocols, submitted to industry and charitable funding streams. ECMC infrastructure has also permitted the set-up of the Liverpool CTU Post-Trial Tissue Bank and LECMC Tissue Collection Project, which will support translational work as a valuable bio-resource for the ECMC network.

Changes to operational procedures and the co-ordination of sampling across multiple projects in **Leicester ECMC**, has led to the number of samples collected and processed by the team rising steadily to approximately 900; all of which are associated with ECMC-returnable projects. Support was extended to 21 studies including early-phase clinical trials and translational research studies split across 12 principal investigators and three hospital sites.

The **Cambridge ECMC**-managed Personalised Breast Cancer Program (PBCP) has completed its feasibility phase, recruiting 250 patients and demonstrating that whole genome sequencing (WGS) data can be delivered in a clinically acceptable time frame. The WGS data are being used to change clinical practice in both early- and late-stage breast cancers. Representatives of the Department of Health and Cancer Research UK have visited this flagship project.

Kings ECMC has opened and is leading the OUTREACH Phase I trial in patients with hepatocellular carcinoma, working with MiNA Therapeutics. Following rapid, recruitment, clinical efficacy has been evident from early on, with data presented at the ASCO 2018 meeting.

A network primed to work with industry

Industry partnerships are vital in driving the development of innovative treatments and working with industry continues to be one of our key objectives.

Our network brings together scientific and clinical experts and key opinion leaders for industry to partner with, to drive the development of cancer treatments of tomorrow. We facilitate industry access to each centre's cutting-edge, early-stage innovation and provide a route to integrate with clinical centres led by outstanding academic leads, which benefits not only the ECMC centres and industry, but also patients.

Industry investment in experimental medicine in the UK is vital to bring innovative treatments to patients. Working with over 150 industry partners, the adult network has supported over 500 commercially sponsored trials and studies across a broad range of cancer types, recruiting over 1,200 patients.

ECMC continues to be the industry partner of choice. Over 68% of new trials in our adult portfolio were commercially sponsored. Likewise, the paediatric network continues to be at the forefront of working with industry, with 50% of its trials and studies commercially sponsored (**Figures 5** and **6**).

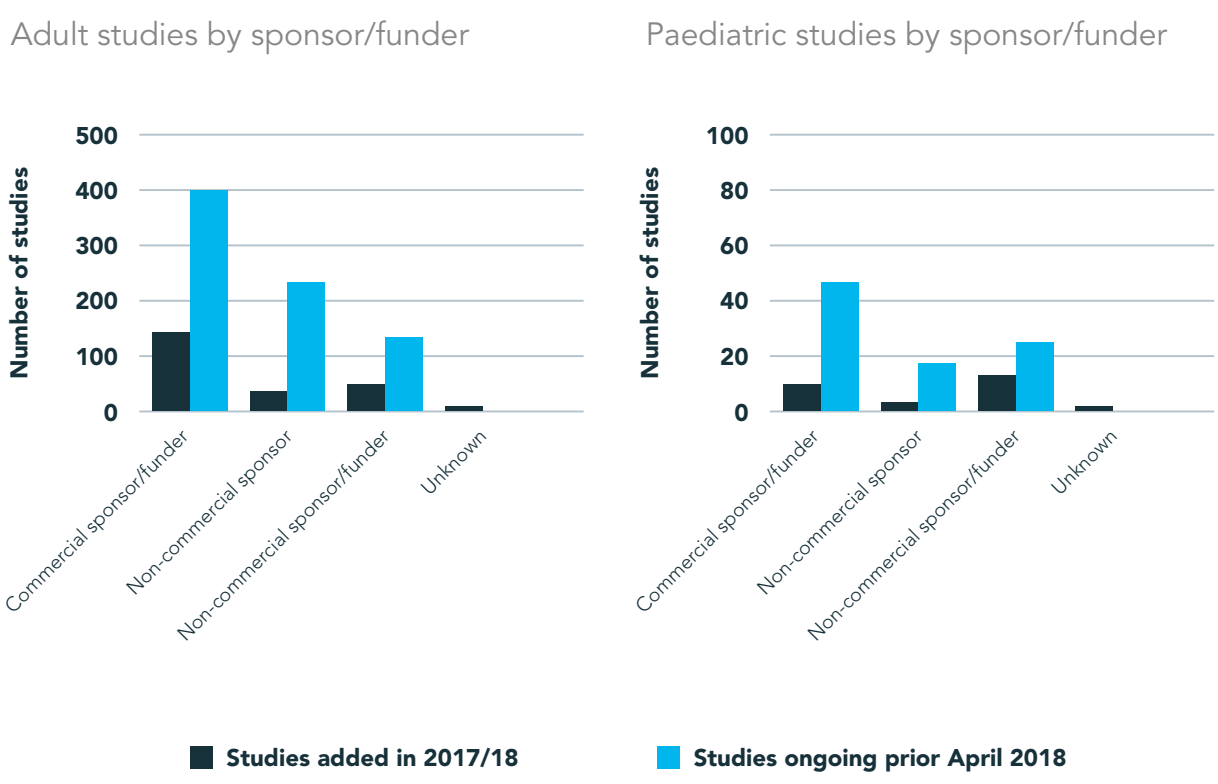


Figure 5 Non-commercial and commercial trials in the ECMC portfolio in 2017/18

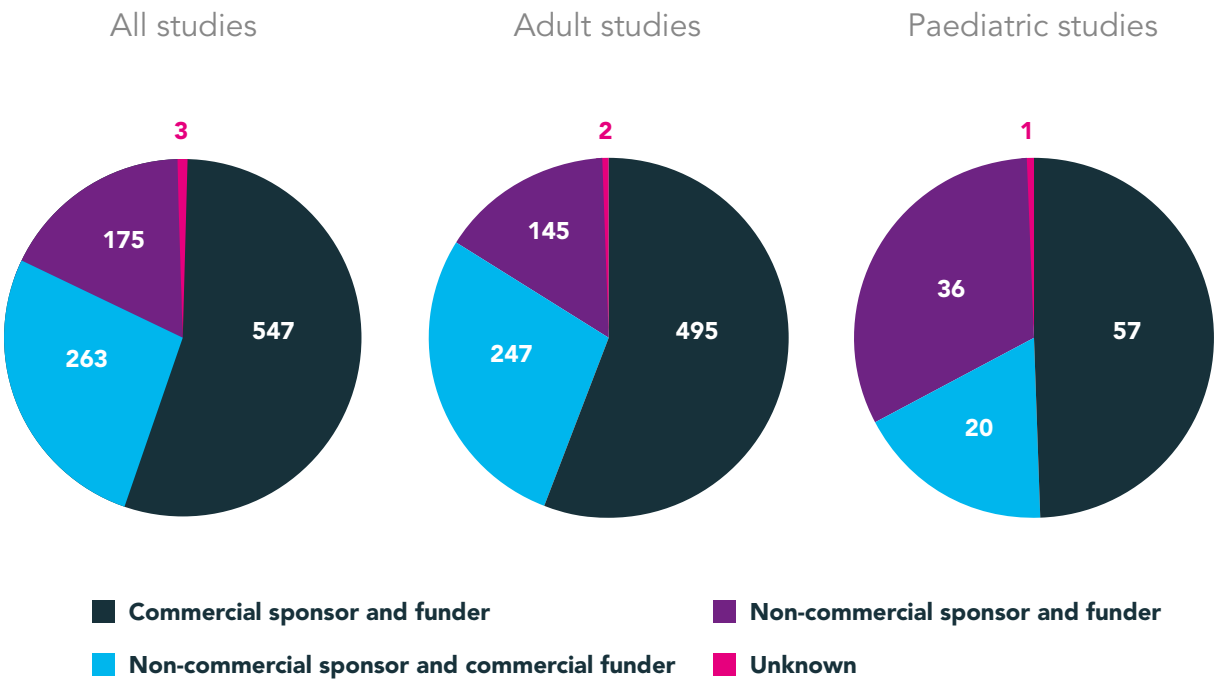


Figure 6 New commercial sponsored, commercial funded and non-commercial sponsor trials in the ECMC portfolio in 2017/18

Working together with industry

Our industry partnerships are crucial to ensure patients in the UK gain access to innovative treatments at the earliest opportunity.

Cambridge ECMC's Department of Oncology, the Department of Mathematics, and Microsoft Research are collaborating to develop machine learning algorithms to detect both image and non-image features that predict for late toxicity following radiotherapy for head and neck cancer, prostate cancer, lung cancer, and brain tumours.

Cardiff ECMC was selected by Novartis as its lead UK Phase I site for studies in haematological malignancies. The first study opened in August 2017 – CPDR001X2105: a Phase Ib assessment of two immune checkpoint inhibitors (PDR001 and MBG453) in acute myeloid leukaemia. Further Novartis studies are currently in setup, most notably ABL001 in relapsed/refractory CML.

Imperial ECMC is exploring with Novartis whether new HIPPO inhibitors, can be given systemically to pre-clinical models of breast cancer. Evidence from in vitro experiments has shown that the HIPPO pathway, specifically Vgll1 and 3, is involved in resistance to endocrine therapy.

In collaboration with Verastem and Merck, via the Combinations Alliance, the FAK-PD1 study (combining defactinib and pembrolizumab in patients with advanced solid malignancies) has opened. **Glasgow ECMC** CTU is co-ordinating the trial and performing PD analyses to determine whether inhibition of FAK can enhance PD-1 blockade immunotherapy in patients with NSCLC, mesothelioma, and pancreatic cancer.

Leicester ECMC has setup three new haematology partnerships, to run translational studies, with Roche: Obinutuzumab (anti-CD20) antibodies in DLBCL patients; Astex – effect of IAP inhibitors on DLBCL; Bioinvent – expression of CD32b and mechanisms of novel CD32b antibodies in DLBCL.

A Phase Ib trial with an MPS-1 inhibitor (BOS172722), is now open to recruitment for triple negative breast cancer patients. BOS172722 was initially discovered and developed in the ICR, supported by Cancer Research UK. **ICR ECMC** is the lead site and lead recruiter for this trial, with its biomarker team providing full pharmacokinetic analysis in this trial.

Autolus (a UCL spinout) secured a £59m investment to take CAR-T cell therapy into blood cancer trials. Two new Phase I/II studies in paediatric acute lymphocytic leukaemia (ALL) and adult diffuse large B-cell lymphoma (DLBCL), AMELIA and ALEXANDER for AUTO3 (an autologous T-cell product, genetically modified to express two separate CARs which recognise CD19 and CD22) have opened at **UCL ECMC**.

A partnership with Blueprint Medicines and **KHP ECMC**, has resulted in a first-in-man Phase I trial of BLU-554, a potent, highly-selective oral FGFR4 inhibitor in patients with hepatocellular cancer and either FGF19 amplification or FGF19 expression by IHC. The study has shown acceptable tolerability, pathway engagement and anti-tumour activity in heavily pre-treated FGF19+ patients.

Oxford ECMC's leadership role in establishing the UK's RNA Alliance has resulted in the formation of a collaboration including other ECMC centres (Glasgow, Cambridge), Cancer Research UK Cancer Research Technology, and an industry-funded programme of drug discovery developing first-in-class inhibitors to RNA-binding proteins.

The **ECMC Paediatric Network** is involved in the Novartis Phase I/II studies of dabrafenib and trametinib, and has provided Phase I and dose expansion data leading to the development of a global study of the combination in BRAF-mutated high-grade glioma and a planned randomised study in BRAF-mutated low-grade glioma.

Edinburgh ECMC has an ongoing partnership with MSD to run several pembrolizumab trials both in single agent and in combination, in ovarian, lung, renal, head and neck, gastric, oesophageal, and prostate cancer. To support delivery, MSD has provided direct funding to the trials unit, for data management resource. By leveraging this commercial support, Edinburgh has been able to overcome an often rate-limiting resource shortage in opening and running trials.

Birmingham ECMC has forged several industry partnerships, including:

- Securing funding from Gilead UK and Ireland Fellowship Programme to implement a study of the validation and pilot implementation of a single multiplex gene panel to detect key mutations and copy number variation in chronic lymphocytic leukaemia (CLL).
- Partnering with Illumina UK to pilot the TruSight Tumour15 and Trusight Tumour170 panels into translational laboratories, and to introduce tumour mutational burden panel testing into routine clinical use.
- Working with ArcherDx to introduce a fusion gene panel into routine use.

The ARGO randomised Phase II study examining the addition of the checkpoint inhibitor, atezolizumab to conventional R-GemOx chemotherapy in patients with relapsed and refractory diffuse large B-cell lymphoma is being led out of **Southampton ECMC**. This study will run at 30 UK sites and aims to recruit 120 patients in 24 months. The Southampton ECMC laboratory is conducting multiple translational endpoints. acceptable tolerability, pathway engagement and anti-tumour activity in heavily pre-treated FGF19+ patients.

Working together to increase capacity and drive delivery

New governance structure to increase ambition

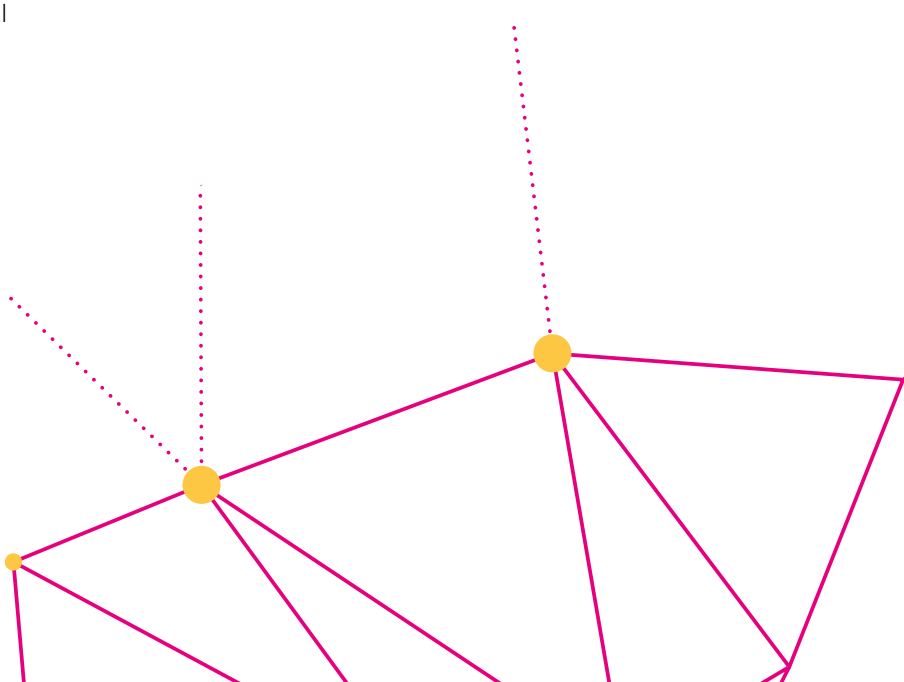
In 2017 we introduced a new governance structure to help to ensure we are setting an appropriately ambitious agenda and to streamline strategic discussions and decisions. This has taken the form of a Network Steering Committee, Strategy Group and a Paediatric Strategy Group.

The ECMC Network Steering Committee (NSC) brings clinical and scientific experts (UK-based and international), industry and academic Sponsors and a patient representative together, along with the ECMC funders, to provide oversight of the activities and performance of the ECMC network and steer our strategic direction. The NSC inaugural annual meeting for the third quinquennium (2017-22) was held in February 2018. In this forum, the NSC recognised the network was unique in bringing the best UK experts together to deliver cutting edge experimental medicine in the UK.

The ECMC Strategy Group (SG) reports to the NSC. It is composed of ECMC leads, who are charged with developing the future scientific and clinical direction of the network. Ruth Plummer (Newcastle) was elected as group chair, with Sarah Blagden (Oxford) and Udai Banerji (ICR) as vice-chairs. The group met for its first biannual meeting in November 2017, to create a cohesive network strategy to position the network at the forefront of the international experimental cancer medicine.

For the first time we have established a peer group for paediatric activities in the **Paediatric Strategy Group (PSG)**. The group is chaired by James Spicer, an ECMC lead from the adult network, who provides an independent perspective and facilitates cross-talk between the adult and paediatric communities. Our vice-chair, Darren Hargrave, is from the ECMC paediatric community and provides specific paediatric insights. The group held its first biannual meeting in February 2018 to discuss the future direction of the paediatric network by collaboratively addressing the agreed strategy through development of network-wide initiatives.

The **ECMC Delivery Group** will support the delivery of themes identified by the Strategy Group and will be constituted in the coming year.



New network-wide strategy to enhance international competitiveness

Within our new ECMC governance structure, the ECMC Strategy Group (SG) leads in developing an overarching network strategy.

Our high-level vision is to build a truly collaborative, internationally competitive national network of early-phase experimental cancer medicine centres, translating the most promising innovations from the academic and industry sectors into the cancer medicines of tomorrow.

The centres which form our network were selected through international competitive peer review in October 2016 as the best for experimental cancer medicine in the UK, based on previous achievement and future strategy in the areas of scientific excellence, operational effectiveness and network activities.

The new quinquennium offers us an opportunity to build on our centres' individual strengths and fully realise the potential of a cohesive network, which is more than the sum of its parts. The breadth of scientific and clinical knowledge and expertise within the network, the extensive cancer infrastructure available in the UK, and the integration with the National Health Service (NHS) puts the ECMC network in a unique position to establish our self as an international leader and speed the process of innovation from bench to bedside. Moreover, the integration of adult and paediatric components is a unique advantage to ensure maximal patient impact

The SG has identified four main areas of focus to build the network's success:

- Scientific and clinical strengths of the network
- Relationship with industry
- Organisational and operational effectiveness
- Workforce needs.

We will focus on maximising our outputs in these four areas throughout the quinquennium. In 2017/18 we prioritised strategic initiatives to support the network's strengths, focusing on creating a searchable database of early-phase trials to maximise patient referral, and forming a collaborative working group with the research community, funders, regulators, industry partners to promote a consensus view on innovative trials. These two examples are described in detail in p33 and 35.

Continued delivery of world class early-phase research

One of our key objectives is to build on the expertise across the ECMC locations, by bringing together and connecting members of the network, and promoting initiatives which have strong emphasis on collaboration.

This year we demonstrated again how team work across our network builds capacity and capability in experimental cancer medicine. As shown in **Figure 7**, there is a high degree of collaboration between the ECMCs, with 53% of the trials being reported as being delivered across multiple ECMCs. The adult and paediatric ECMCs participate in a broad range of multi-site trials with a significant volume of multi-site activity. This year saw several examples, illustrated in the case studies on p22, of collaborations on complex studies, which demonstrate the capability the network and its centres have in delivering trials.

In addition, the network offers training and skill-sharing opportunities through several means, some of which are highlighted in the case studies on p22. While each ECMC has unique and world-leading expertise within early-phase clinical research, collaboration across the ECMC network enhances our ability to generate new treatments for cancers and deliver them efficiently and to the highest quality.

Collaboration in trial delivery

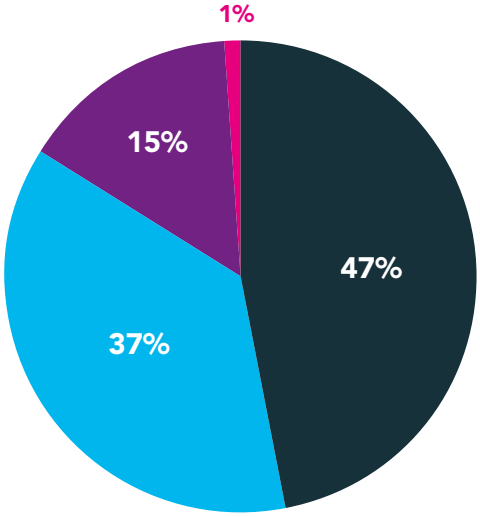


Figure 7 ECMCs work collaboratively to deliver trials. The pie chart shows 2017/18 trials in which single, 2-4 ECMCs, 5-9 ECMCs, 10 or more ECMCs reported participation. Over 50% of the trials are delivered collaboratively.

Showcasing collaborations in the network

Cambridge ECMC sponsors CaNCaP03, a Phase I study assessing the pharmacodynamics biomarker effects of olaparib (PARP inhibitor) +/- degarelix (GnRH antagonist) prior to radical prostatectomy. Cambridge collaborates with UCL and Cardiff ECMCs to deliver the trial.

Southampton ECMC hosted the **Manchester ECMC** Cell and Protein Team and Science Strategy Leads for two-days to demonstrate practices in validation and quality control of immune-monitoring assays for clinical trials. Manchester will hold a reciprocal visit later in 2018.

Oxford ECMC's leadership role in establishing the UK's RNA Alliance has resulted in the formation of a collaboration including other ECMC centres (**Glasgow, Cambridge**) and CRT and an industry-funded programme of drug discovery developing first-in-class inhibitors to RNA-binding proteins.

The **Birmingham ECMC**-run National Lung Matrix trial has continued to develop thanks to the support of the ECMC network. The trial is now open at 20 UK sites, including 16 ECMC centres. 218 patients with locally advanced or metastatic non-small cell lung cancer have been recruited to the 20 cohorts based on the molecular profiling of tumours by the Stratified Medicine Programme (SMP2).

Manchester ECMC improved the inclusion of exploratory biomarkers in early trials, to maximise information gained on patient selection, target modulation and response. It implemented a newly developed flowchart to select appropriate levels of assay validation within Clinical and Experimental Pharmacology, which has reduced the time-lines for agreement of biomarker validation plans. This process has been shared with Cancer Research UK and several ECMCs.

As part of her Cancer Research UK Clinical Trials Fellowship, an ECMC investigator from **Leicester ECMC** spent three months at **Southampton Clinical Trials Unit.** During this time, she worked on several trial proposals, involving both the University of Leicester and University of Southampton. This collaboration continues with several projects involving junior investigators from both sites.

Cardiff ECMC and **Manchester ECMC** co-lead the FAKTION Phase Ib/II trial which evaluates the safety and efficacy of fulvestrant in combination with an AKT inhibitor (AZD5363) in patients with incurable ER-positive breast cancer. The Cardiff ECMC-supported laboratory analyses plasma ctDNA and FFPE tissue samples with next generation sequencing.

Newcastle ECMC has collaborated with **Belfast, Glasgow** and **Edinburgh ECMCs** to open the Cancer Research UK Centre for Drug Development-sponsored first-in-human study of a novel CDC7 inhibitor. This study illustrated the benefits of the network, with Belfast leading the trial, Newcastle validating the PK assay and developing novel PD assays to incorporate in the trial design.

Our burgeoning paediatric network

The ECMC Paediatric Network was set up in 2012 to improve access to innovative treatments for children with cancer.

Our paediatric network aims to improve the clinical trials landscape for children in the UK. It is comprised of eleven centres around the UK. Cambridge and Southampton joined in 2017, strengthening our translational research and immunotherapy capabilities.

The network works closely with the Cancer Research UK-funded Paediatric Biobank in Newcastle, which is the only dedicated biobank in the UK for paediatric samples. It also collaborates closely with the Newcastle Cancer Centre Pharmacology group, which provides essential pharmacokinetic outputs for early-phase clinical trials and advanced imaging expertise for the network. We have a Paediatric Network Manager, who is based in the ECMC Programme Office, to support the operational and strategic activities of the network.

The eleven centres work together to develop and drive strategic and operational activities that enhance early experimental clinical trials for children. We aim to ensure that every child in the UK has equal access to experimental medicine. To this end, the network is arranged into four regional sub-networks (North East/Scotland/ Northern Ireland; North West/Yorkshire; Midlands/ South West/Wales and London/South East). These regional networks will ensure that when a new clinical trial opens, it includes at least one centre per region, leading to a better geographical spread of paediatric trials throughout the UK and less travel for children and their families.

The regional networks will also house a regional discussion panel where clinicians can discuss what experimental treatment options are available across the region for relapsed patients. This provides clinicians with greater knowledge of recruiting clinical trials regionally, in addition to supporting information collection in relation to relapse patients. This benefits not just the patient but also our clinical and scientific understanding from a paediatric perspective.

A data manager based at the Clinical Trials Unit in Birmingham will support these networks, and facilitate data collection about relapse cases, a vital resource for which there is no current national collection.

The ECMC Paediatric Network provides the organisational framework to implement a new precision medicine initiative for children, Stratified Medicine Programme-Paediatrics (SMPaeds). This is a Cancer Research UK-funded UK-wide prospective screening programme for children with relapsed cancer. It aims to enrol each paediatric patient whose brain cancer or other solid cancer has relapsed or is refractory to standard treatment, with a view to offering them an appropriate treatment option through clinical trials testing new targeted anti-cancer therapies.

SMPaeds will use a comprehensive multi-omic characterisation of tumour and germline DNA and will work as a screening platform for enrolment onto national and international clinical trials, which require molecular pre-screening, including the ITCC E-SMART trial. E-SMART is a European partnership between academia and pharma companies that provides a basket of molecularly targeted new agents, to which patients will be allocated based on molecular abnormalities identified by screening in SMPaeds. E-SMART is the model for the future precision medicine strategy for paediatric oncology in Europe and collaboration across the ECMC network will maximise its impact in the UK.

Network-wide initiatives

The varied and impressive skills held within the collaborative ECMC network, make it the perfect ecosystem for the development of complex initiatives such as the ECMC Combinations Alliance (CA) and the Stratified Medicine Programme (SMP).

These programmes are pushing ground-breaking work and, in turn, are supporting the mission of the ECMC initiative to provide better and faster treatments to cancer patients in the UK.

Combinations Alliance

The Combinations Alliance (CA) aims to increase the number of novel treatment options available to people with cancer through facilitating the network partnering with industry. This Cancer Research UK model utilises ECMC expertise to explore the potential of novel agents in combination, either with other drugs (licensed or novel) or with radiotherapy, across a range of cancers.

The CA Team identifies industry partners who then offer up their agents to the network. Innovative clinical trials proposals are then generated and refined through a series of meetings and workshops with the ECMC scientific and clinical communities.

During 2017/18, the ECMC network was invited to participate in two formal expression of interest (EOI) calls, involving three CA partners: Plexxikon, AstraZeneca and Astex, offering nine novel agents (**Table 2**). This generated a total of 54 clinical trial proposals, representing engagement from each adult ECMC, in either a Sponsor or collaborating capacity, across multiple cancer types and included several cross-company proposals. Following triage, EOIs will be submitted to a Cancer Research UK funding committee in 2018/19.

Currently the CA portfolio comprises 22 trials; eight (FAK-PD1, HIPROC, PARADIGM2, PATRIOT, RADICAL, SPIRE, TAX-TORC and TORCMEK) were presented at international meetings in 2017/18.

The CA is governed by a Joint Steering Committee with core membership comprising representatives of the ECMC network, industry partners and Cancer Research UK. We refreshed its membership during 2017/18 to ensure a breadth of expertise and geographical spread. Of note, Darren Hargraves (UCL) joined as representative of the ECMC Paediatric Network.

ECMC Trial Managers meet regularly to exchange operational lessons learned from the CA portfolio of trials and ways to improve timely set-up and delivery.

The CA continued its association with the Radiotherapy Drug Consortium (RaDCom) initiative, supporting attendance to the FDA-AACR-ASTRO Regulatory Science and Policy Workshop on the Clinical Development of Drug-radiotherapy Combinations in February 2018. With representation from Ricky Sharma (Oxford), Tim Illidge (UCL) and Kaye Williams (Manchester), the purpose was to address the lack of drug development for products intended specifically for use with radiation therapy and define a path forward.

The success of the CA has been strengthened through continued engagement with the network to better understand how both the adult and paediatric communities can feed into and off the model, along with timely portfolio delivery to sustain existing and attract new industrial partners.

Partner	Agent
Plexxikon	Bromodomain inhibitor (PLX51107) Selective inhibitor of TRK and FMS kinases (PLX9486)
AstraZeneca	STAT3 (AZD9150) ATM inhibitor (AZD0156) ATR inhibitor (AZD6738) BTK inhibitor (Acalabrutinib) Anti PD-L1 (Durvalumab (Imfinzi) with or without Tremelimumab) Anti CTLA-4 (Tremelimumab in combination with Imfinzi or another AZ/Medi molecule)
Astex	Inhibitor of apoptosis proteins (IAPs) (ASTX660)

Table 2 Combinations Alliance partner drug offerings in 2017/18

Project/ Trial	CI	Sponsor	Source/ Partner	Combination	Indication
Set-up					
PaGoDA	Dean	Glasgow	Plexxikon	TMS/FMS kinase + gemcitabine	Pancreatic
PoLERISE	Crabb	Southampton	Plexxikon	CSF1R, KIT and mutant FLT3 kinases + Enzalutamide*	Prostate
Recruiting					
SELUDEX	Menne	Birmingham	AstraZeneca	Selumetinib + Dexamethasone	Paediatric & adult ALL
WISTERIA	Mehanna	Birmingham	AstraZeneca	Wee1 inhibitor + cisplatin + RT	Head & neck
FAK-PD1	Symeonides	Glasgow		FAK inhibitor + Anti PD1/ PDL1*	Solid tumours
PARADIGM-2	Chalmers	Glasgow	AstraZeneca	PARP inhibitor + RT/TMZ	GBM
SPIRE	Crabb	Southampton	Astex	SGI-110 + Cisplatn/ Gemcitabine	Bladder
ORCA2	Forster	UCL	AstraZeneca	PARP inhibitor + Cisplatin + RT	HNSCC
PIONEER	Evans	Glasgow	AstraZeneca	PARP inhibitor + Capecitabine + RT	Pancreatic
TORCMEK	Schmid and Middleton	Barts	AstraZeneca	MTOR inhibitor + MEK inhibitor	NSCLC
PATRIOT	Harrington	RMH/ICR	AstraZeneca	ATR inhibitor + RT	H&N/Abdo/pelvic/ thorax
Follow-up					
VANSEL	Talbot	Oxford	AstraZeneca	MEK inhibitor + RET, EGFR inhibitor	NSCLC
PANtHER	Hochhauser	UCL	AstraZeneca	EGFR inhibitor + FOLFIRI	Colorectal
TAX-TORC	Banerji	ICR	AstraZeneca	mTOR inhibitor + Taxane	Ovarian/fallopian/lung
ComPAKT	Yap	ICR	AstraZeneca	AKT inhibitor + PARP inhibitor	Solid tumours
DEBIOC	Thomas	Oxford	AstraZeneca	Mixed Erb inhibitor + Oxiplatin/Capecitabine	Oesophogastric
RADICAL	Scki	Imperial	AstraZeneca	FGFR inhibitor + Anastrozole + Letrozole	Breast
Closed					
HIPROC	Glasspool	Glasgow	Lilly	Hedgehog inhibitor + Paclitaxel	Ovarian
FIESTA	Chester	Leeds	AstraZeneca	FGFR inhibitor + Gemcitabine / Cisplatin	Bladder
VIBRANT	Thirlwell and Sarker	UCL	AstraZeneca	RET, EGFR, VEGF inhibitor + Iodine-131 MIBG	Pheos and PG
FACING	Evans	Glasgow	AstraZeneca	FGFR inhibitor + Cisplatin/ Cepecitabine	Oesophogastric
DREAM	Saunders	Manchester	AstraZeneca	MEK inhibitor + VEGFR inhibitor + RT	Colorectal

Table 3 Combinations Alliance portfolio

Cancer Research UK Stratified Medicine Programme 2

Cancer Research UK is a leader in precision medicine driving forward national molecular diagnostics and targeted therapies, making them more routinely available. The Stratified Medicine Programme Phase 2 (SMP2) is a collaborative programme with partners from across different sectors (**Figure 8**). Genetic pre-screening on SMP2 selects advanced non-small cell lung cancer patients to the multi-arm, multi-stage National Lung Matrix Trial (NLMT).

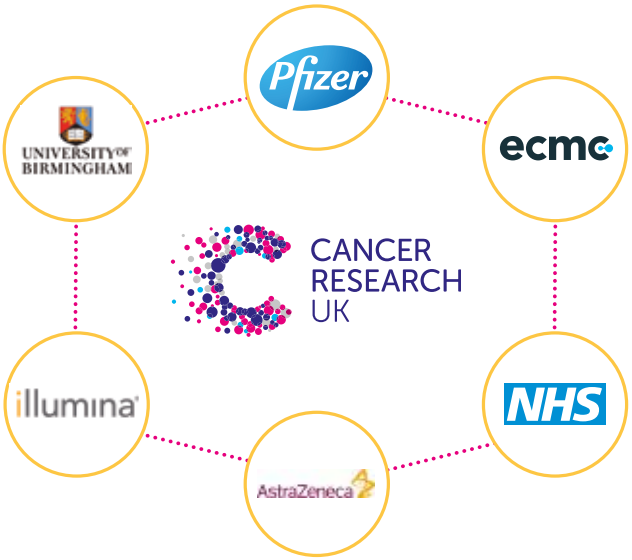


Figure 8 The Stratified Medicine Programme Phase 2 collaboration partners

The SMP2 has been running since 2014 and is now open to recruitment at all 18 adult ECMCs. Through a hub and spoke model, it can reach more than 70 hospitals across the UK.

Through the ECMC network, the SMP2 programme has been able to establish infrastructure and share learnings required for a successful national precision medicine initiative. The programme will now be able to use this experience and knowledge to expand the SMP2 network further, providing access to more patients.

Once patients are consented, their tumour samples are analysed in the three SMP2 Technology Hubs (Birmingham, Cardiff and ICR ECMCs). These use the Illumina next-generation sequencing (NGS) panel test for a number of genomic aberrations that assess whether a patient is able to join the NLMT.

To date over 3,500 patients have been tested through SMP2. Based on learnings from the start of the programme, the programme has implemented a series of changes to improve the quality control failure rate, NGS pass rate and testing turnaround times. These include optimisation of the NGS panel, streamlining the bioinformatics pipeline and changes to the sample requirements.

All these improvements have allowed over 2,000 patients to be identified as molecularly eligible for one or more of the NLMT arms. Site specific reports are now released on a weekly basis, matching each result to NLMT cohorts, which increases the visibility of the results and improves patient tracking.

Further improvements are planned for the upcoming year, including work now underway to optimise sample processing pathways to improve the quality of samples for downstream NGS analysis, upgrading of the NGS panel from 28 genes to greater than 150 genes, as well as opening the potential for more therapeutic options on NLMT. This will be a significant change across the whole programme, in line with some of the wider changes underway as part of NHS England's Genomic Reconfiguration, involving several ECMCs.

The National Lung Matrix Trial

The National Lung Matrix Trial (NLMT) is a signal-seeking trial sponsored by the University of Birmingham as a collaborative study together with SMP2 partners. The trial utilises an adaptive design of a series of parallel, single-arm Phase II trials, where each arm tests an experimental targeted drug in a stratified population, to determine if further investigation of any drug-biomarker combination is warranted.

NLMT opened to recruitment three years ago with eight arms and 21 drug-biomarker combinations. Its adaptive design allows for a flexible response to the ever-changing landscape of NSCLC, such as arm closure based on emerging evidence. It also allows for new arms to be brought on board with existing and new pharma partners in the upcoming year.

All 18 of the original ECMCs are now open to NLMT recruitment. During 2017/18 over 100 new patients were enrolled to the study. As the network of sites participating in SMP2 pre-screening platform expands, we expect to include these sites in the NLMT, allowing equity of access to patients. To date, more than 230 patients have been recruited and received treatment across all eight arms of the trial.

The ongoing delivery of complex programmes such as SMP2 and NLMT are only possible through collaboration between clinicians, researchers, coordinating staff and pharmaceutical partners. The ECMC network is the ideal environment to support this collaboration and harnessing the capabilities within the network is the key to the success of the Stratified Medicine Programme.

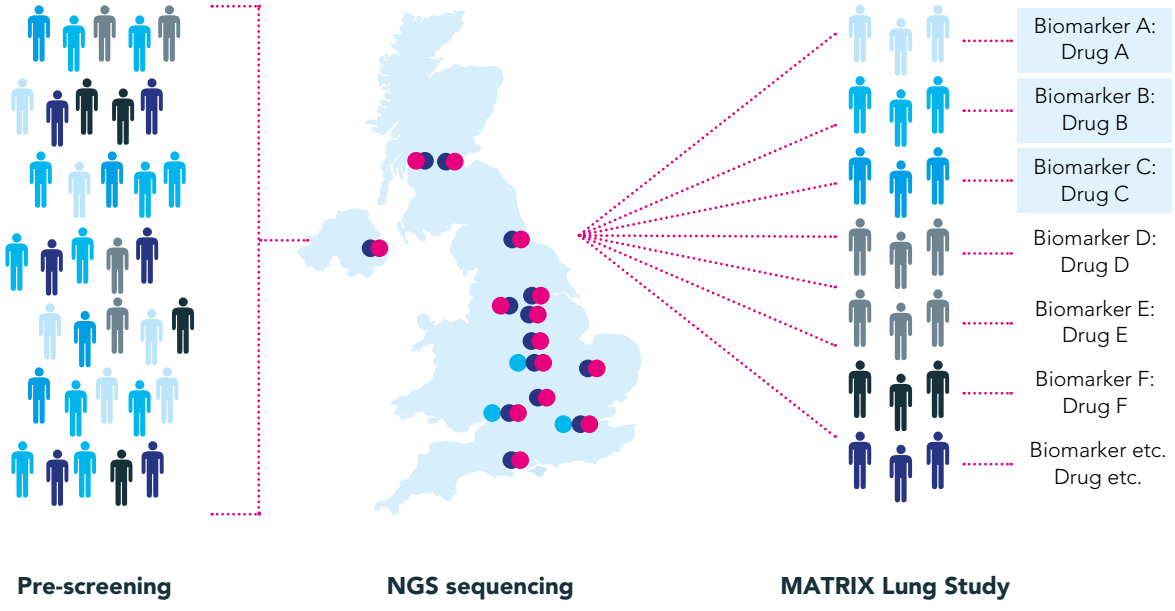


Figure 9 Overview of the Stratified Medicines Programme and the National Lung Matrix Trial

Patient and public involvement in the network

All ECMCs recognise the importance of involving people affected by cancer in our work and the positive impact it can have on research.

Common patient and public involvement (PPI) activities taking place across the network include patient representatives on governance boards and trial specific steering committees, and patient input into research documents such as protocols and patient sheets.

ECMCs are making efforts to take a more holistic approach to PPI, including measuring the impact of PPI in research, ensuring that patient representatives come from a diverse background, and trying to connect PPI with commercial studies.

Running alongside all these activities are engagement events, for example symposiums and open days, which both raise the profile of research in a location and are a way to recruit members to patient groups or panels. A report detailing all the PPI activities stated by the ECMCs for 2017/18 can be found on the ECMC website[1].

PPI in colorectal cancer

The Northern Ireland Cancer Research Consumer Forum (NICRCF)'s members are passionate about maintaining patient perspectives at the forefront of project decisions, sustaining project timelines, and raising awareness to facilitate recruitment and success.

NICRCF is a PPI partner in both the EU FP7 funded **MErCuRIC programme**/Phase I trial in colorectal cancer and **S:CORT** Stratification in Colorectal Cancer, a MRC/Cancer Research UK co-funded stratified medicine consortium.

Patient Sounding Board

The ECMC team in **Cardiff** created a patient sounding board of eight patients who meet twice a year, or as and when new projects require review.

Patients were recruited by clinicians overseeing their treatment for haematological malignancies (related to bone marrow transplants) and were able to give their viewpoint based on their experience and knowledge. This patient subset has a particularly poor prognosis and represents a key area for developing novel drug design and early-phase trials.

Science Café

In 2017/18 **Imperial** held four Science Café events at the Maggie's Centre, a patient friendly environment.

In December 2017 the EpiPredict group held a workshop with junior researchers who were new to PPI. The researchers created presentations, blogs and a video about their work, which were presented at a Science Café meeting. The activities received positive feedback from both the PPI members and researchers, and have helped the EpiPredict group become more aware and involved with PPI at Imperial.

Raising awareness of research amongst hard to reach groups

Leicester has an ethnically diverse population, which includes hard to reach groups for whom language is frequently a barrier. **Leicester ECMC** has successfully made an impact in communicating with Polish and African-Caribbean communities.

The team held a research awareness event at the Leicester Polish Centre. Hands-on activities demonstrating randomisation, targeted therapies and the 'taste test' generated a lot of interest, and participants agreed that their knowledge of research was enhanced.

Leicester has a successful partnership with Leicester University's Centre for Black Minority Ethnic Health which facilitates access to several communities and the opportunity to organise and attend events.

[1] http://www.ecmcnetwork.org.uk/news/announcement/hear-about-great-ppi-work-being-done-across-ecmc-network

Enabling role of the ECMC Programme Office

The ECMC Programme Office (PO) has been key in facilitating a broad range of network activities from promoting expertise (network groups), supporting efficient trial delivery, patient recruitment and better regulatory environment to disseminating the success of the network.

A streamlined process to facilitate commercial opportunities

The PO has established a streamlined process to quickly respond to commercial opportunities, which is used by the adult network and enables industry access to the network infrastructure.

Organisations, ranging from major pharmaceutical companies to smaller biotechnology firms and Clinical Research Organisations, complete the ECMC PO confidential engagement form. Following a quick review of suitability of the opportunity, the PO works with the partner to guide them through the streamlined process to facilitate an Expression of Interest (EOI) call to assess the capacity and capability of the network. Successful EOIs are progressed to signing a non-disclosure agreement (NDA).

In 2017/18 the PO facilitated the signing of three non-ECMC NDAs and one unmodified ECMC NDA. When the adult ECMC NDA, the first UK wide compatible template, is accepted by commercial and non-commercial partners in its unmodified form, it allows efficient access for interested ECMC Leads to discuss a study opportunity with a commercial partner, therefore enabling feasibility assessment to be completed in a timely manner and supporting faster study set up in the UK. This multi-party NDA allows early access of study opportunities to the ECMC network and can boast a turnaround time of five working days when used in its unmodified form (**Figure 10**).

In the last year, the paediatric network has also begun to capitalise on study opportunities directed to the PO. We are developing a process to review paediatric suitability before distributing an opportunity to the network for consideration.

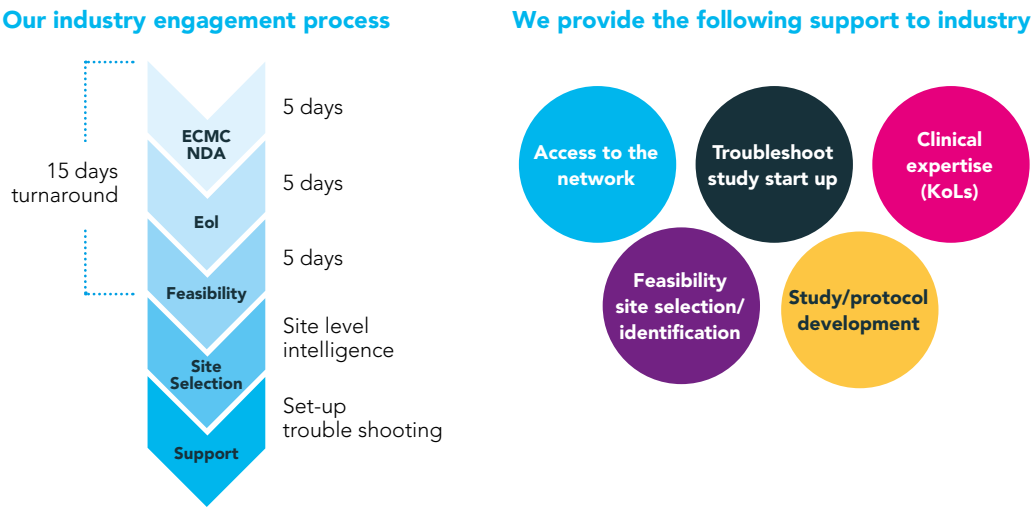


Figure 10 Streamlined process to facilitate commercial opportunities

Identifying 'research-ready' sites for a Phase I antibody trial

Servier Research and Development Limited has engaged with the ECMC PO to bring a new Phase I antibody clinical trial to the network. Early engagement with the PO enabled a rapid EOI to identify interested sites for study feasibility. Servier Research and Development Limited accepted the ECMC NDA in its unmodified form and fully executed the agreement signed with all interested parties.

"I have recently had an excellent experience working with the ECMC Programme Office for assistance identifying appropriate sites for a new Phase I antibody clinical trial in the UK.

The ECMC has a rapid process of identifying 'research-ready' sites who met the criteria for previous experience using this type of IMP. The route was quick and efficient and enabled Servier to speak to several sites very quickly and progress with the feasibility of carrying out this trial. I personally found the service from the Programme Office extremely helpful and very quick and efficient. This service should be further advertised to other companies both in the UK and abroad.

Thanks to PO we are now in discussion with three sites for the set-up of this trial in the UK."

Servier Research and Development Limited

Supporting efficient delivery and patient recruitment – EC Trial Finder

Patients are at the centre of our mission, and one of the goals of the network is to improve procedures for the delivery of clinical trials for patient benefit.

The ECMC leads have identified the lack of national visibility of open trials as one of the main barriers in establishing efficient patient referral. Currently clinicians have access to trial data within their local portfolio management system but do not have visibility of all early-phase trials across the ECMC network. Additionally, the existing publicly available trial databases do not meet the needs of the clinicians (eg molecular stratification search, availability of contact details and timely updates).

In agreement with the ECMC leads, in March 2017 the ECMC PO, in collaboration with Cancer Research UK, launched the creation of the 'Experimental Cancer Trial Finder' (EC Trial Finder). The EC Trial Finder will allow clinical staff in the network to search relevant trials according to specific trial criteria, such as cancer type, recruitment status, molecular profile, treatment type, age; and the search result will include contact details of recruiting site. This should enable clinicians to quickly determine whether there are clinical trials in the ECMC network that their patients may be eligible for and provide the necessary information to allow clinicians to confirm potential trial eligibility and slot availability directly with the individuals who are managing the clinical trial.

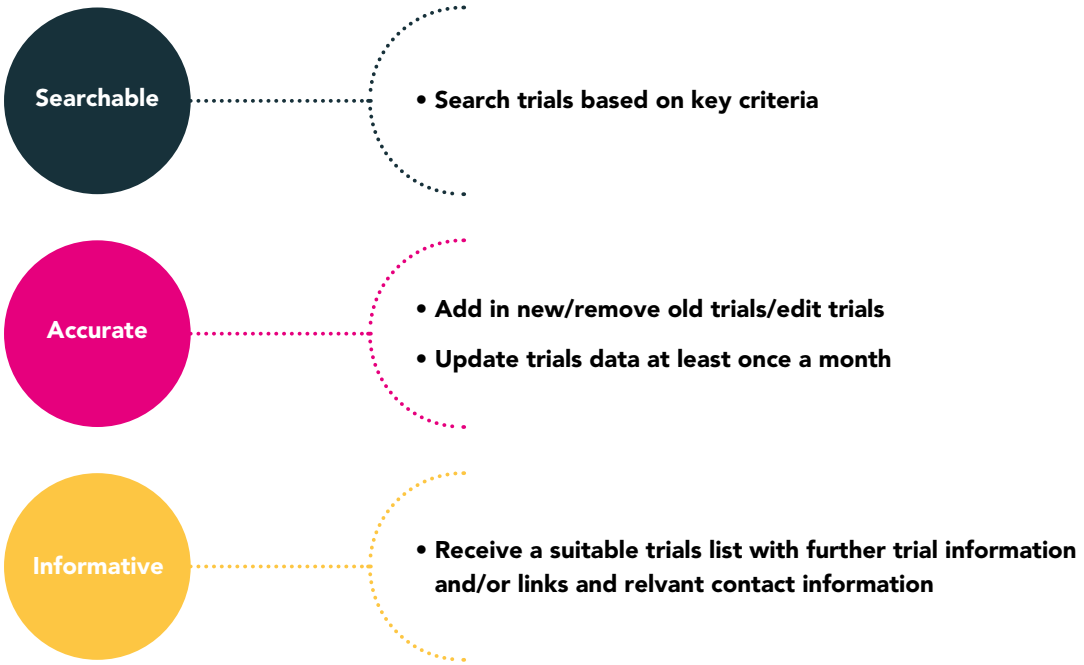


Figure 11 EC Trial Finder - a product which stores details of all early-phase trials running at ECMC and previous ECMC locations to support patient referrals and collaboration

The EC Trial Finder aims not only to improve speed of identification of relevant trials for patients but also to stimulate interest and drive investment in the network from pharmaceutical partners, due to an improvement in the patient recruitment process across the network and in the UK.

The immediate benefits of the EC Trial Finder Project are expected to be as follows:

- Increased opportunity for patient matching and referrals within the ECMC network
- Increased opportunity to enhance patient recruitment volumes and decrease timelines
- Improved communication and collaboration within the ECMC network through better visibility of clinical trials information
- Improved reputation for innovation and profile across the network
- Further build internationally recognised network, attracting future funding and trials to the network.

During 2017/18 an EC Trial Finder working group, comprising representatives from adult and paediatric locations, consulted to define the initial requirements for the database. The working group provides an opportunity for ECMC locations to support the monitoring, evaluation and future development of the EC Trial Finder Database by providing feedback, ideas and contributing to strategic and practical discussions. To aid with information sharing, a legal framework was then put in place with the creation of a Letter of Intent (LoI) defining roles and responsibilities and expectation for the ECMCs taking part to phase one. EC Trial Finder is expected to be released by then end of 2018.

Fostering a conducive regulatory environment for innovative trials

One of the strategic priorities identified by the Strategy Group was to work together with regulatory bodies to create a more conducive regulatory environment for experimental cancer medicine in the UK. The ECMC Programme Office is in a unique position to build on our existing relationships with the network and regulators to build consensus and inform crucial decision making that impacts on the conduct of clinical trials in the UK.

The clinicians and staff of the ECMC network are at the forefront of developing and delivering Complex Innovative Design (CID) trials[1]. These trials are efficient in allowing the evaluation of multiple interventions with faster decision making. CID trials provide patients with the opportunity to be part of cutting-edge research.

The network recognised that successful delivery of CID trials requires close and streamlined interactions between regulators, NHS, pharma partners and academia. Given the importance of of these studies and the complexity in delivering them, the network believes it has a responsibility to influence regulation in this key area.

To this end the ECMC Programme Office held a workshop in February 2018 in partnership with regulatory bodies (Health Research Authority, Medicines and Healthcare products Regulatory Agency (MHRA)) and other stakeholders including the research community (ECMCs, Cancer Research UK, and Clinical Trials Units), devolved administrations and industry associations (The Association of the British Pharmaceutical Industry (ABPI) and UK BioIndustry Association (BIA)). The first-of-a-kind workshop highlighted there was not only a need to develop better definitions for complex trials but also to develop and share a better understanding of the issues associated with the set up and delivery associated with these trials. The workshop attendees agreed to develop a consensus paper for publication, which in turn will provide recommendations for a guidance document. The goal is to publish this early in 2019.

Subsequent to the publication of the paper the group will again collaborate on producing guidance and training for researchers, regulators, patients and industry on the most efficient approach to innovative trials. By leading the international research community on the networked delivery of CID trials, the ECMC network would like NHS patients to be the first to benefit from cutting-edge cancer research.

"I found the day to be incredibly engaging and it was good to see such an interested and motivated group for this important topic".

Dr Kirsty Wydenbach, Deputy Unit Manager and Senior Medical Assessor, Clinical Trials Unit, MHRA

[1] The term Complex Innovative Design Trial in this statement includes: platform, umbrella, basket, bucket, complex, and adaptive study designs

Promoting expertise – the network groups: enhancing the UK's capacity in experimental cancer medicine

A key objective of the ECMC initiative is to build on the expertise available across our locations, by bringing together and connecting members of the network. The network groups are central to achieving this; we highlight their achievements below.

The UK Therapeutic Cancer Prevention Network Group (UKTCPN)

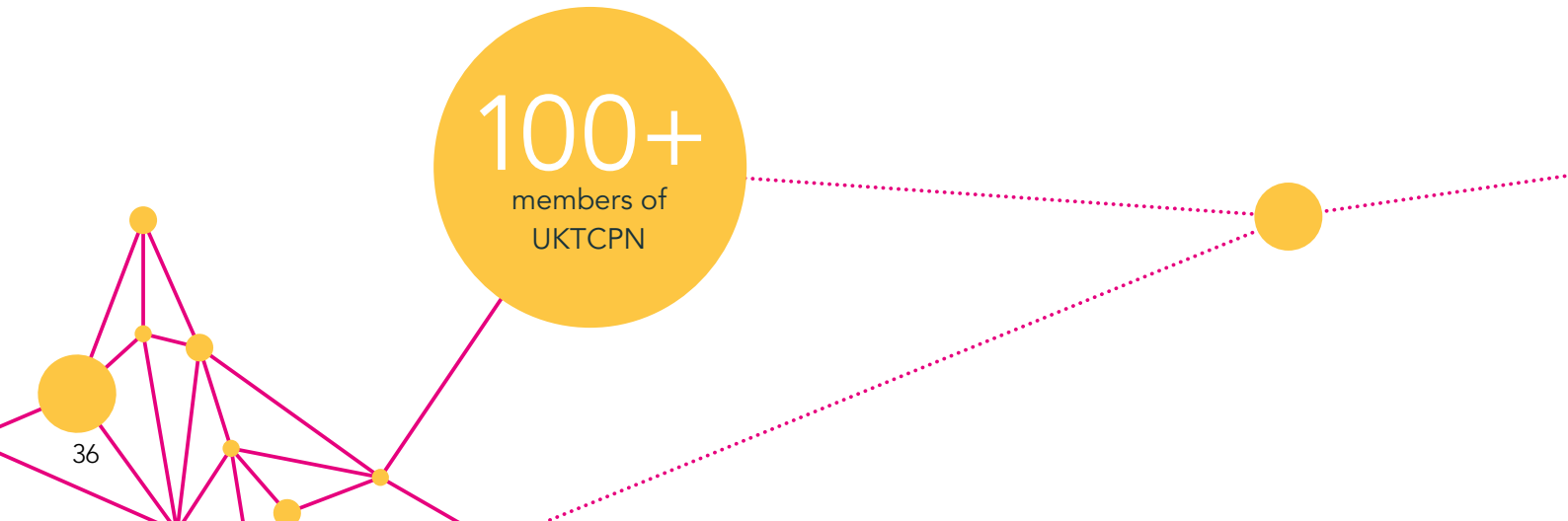
The UKTCPN group, established in 2013, brings together a unique blend of research expertise in therapeutic cancer prevention including basic and translational scientists, clinicians, epidemiologists, statisticians, pathologists and specialists in primary care, diet and nutrition.

This year the group revised the membership of the core steering committee and appointed a new co-chair, Professor Ruth Langley (UCL) who will lead the group together with Professor Karen Brown (Leicester). Professor Dion Morton (Birmingham) who stepped down will continue to advise the group as an ex co-chair. With 16 core steering committee members across the ECMC network, and a circulation list of over 100 professionals in various disciplines related to prevention, the group plans to ensure that therapeutic cancer prevention is well represented in the network.

Last year members of UKTCPN joined the Drug Repurposing Group that was led by the Department of Health and the Association of the Medical Research Charities (AMRC). Together they discussed and reviewed the ways of facilitating access to the off-patent medicines to ensure that the benefits of medical research are translated into practice to improve outcome for patients. Discussions were summarised in the report entitled: 'Facilitating adoption of off-patent, repurposed medicines into NHS clinical practice' that was published in December 2017 and submitted to government. The UKTCPN members also wrote a consensus paper focused on effective drug repurposing for cancer prevention. The paper, 'Unleashing potential: how can we overcome barriers to effective drug repurposing for cancer prevention?' is currently being reviewed and will be published later this year.

The group is also a part of the international consortium Cancer Prevention Europe (CPE) with a mission to reduce morbidity and mortality from cancer in European populations through prevention and earlier diagnosis. CPE reviewed the current state of prevention and suggested the action points for the future in the report 'Time for a European initiative for research to prevent cancer: A manifesto for Cancer Prevention Europe (CPE)' that was accepted for publication in the Journal of Cancer Policy.

The UKTCPN Steering Committee also established a collaboration with International Cancer Prevention Society (ICAPS). Together the two groups started working on the organisation of a two-day conference in London (September 2019) on 'Cancer Prevention by Targeting Inflammation and Immune System' that will explore current developments of immunoprevention of cancer.



Quality Assurance and Translational Science Network Group (QATS)

The QATS group was established in 2007 and supports and enables ECMC network to conduct translational research to the appropriate levels of quality and regulatory compliance, utilising validated, cutting edge techniques.

In the last year the group focused on delivering the successful conference hosted in March 2017 'Opportunities and challenges with emerging biomarker technologies and their application in early-phase trials' at the ICR ECMC in in Sutton. The conference showcased the use of novel technologies in translational research through seminars and the poster session. The interactive workshop and panel discussion provided the opportunity to discuss the challenges of validation of various technologies to GCP standards, such as mass cytometry, multispectral immunofluorescence and NanoString, and sharing the best practice within the network group.

Junior Investigator Network Group (JING)

JING brings together, and helps develop, junior investigators across all disciplines of clinical and translational research within the ECMCs. This group was established in 2012 as the ECMC Leads recognised the importance of ensuring that the future generation of leaders within experimental cancer medicine in the UK are trained appropriately.

In January 2018 the sixth JING: Training the Next Generation event was held in Manchester. Over 100 people from across the ECMC network attended the two-day residential which is aimed at junior investigators wishing to pursue careers in early-phase clinical and translational research. Attendees included trainees, faculty, speakers and public involvement representatives.

During the first day of the meeting, trainees heard presentations on several elements relating to the design of early-phase clinical and translational research proposals such as biomarkers, statistics, surgery, radiotherapy combinations and working with industry. The second day opened with a session run by the Cancer Research UK Patient and Public Involvement team on involving people affected by cancer. The rest of the day was spent in break-out groups with trainees presenting their own study ideas and receiving feedback from their peers and faculty members.

The event received overwhelmingly positive feedback with all attendees, who completed the feedback survey, finding the event a success (excellent: 79%, good: 21%).

In 2018, the steering committee summarized the main outcomes and feedback after the conference and recruited representatives of Quality Assurance Managers and Translational Scientists from all 18 centres to form a 'working group' that will start addressing identified issues.

"Excellent facilitators in each session. I feel it is the face time and feedback during the breakout sessions that are invaluable and make this conference unique from many others."

Quote from trainee

100%
attendees rated JING event good or excellent

100+
junior investigators attended JING: Training the Next Generation 2018

Figure 12 Feedback from JING: Training the Next Generation 2018. Participants told us the most valuable things they learned from the event.

The ECMC Programme Office continued to support trainees to attend the NCRI Clinical Studies Group (CSG) meetings. This scheme gives junior investigators the opportunity to experience the workings of a CSG. The intake who were recruited in 2016 came to the end of their term in 2017/18 and the Programme Office has announced its commitment to provide bursaries for junior investigators from the network who are successful in the next round of this scheme (2018–20).

Over the next year the JING will be looking at how the long-term impact of attending the JING: Training the Next Generation event can be measured and developing a JING alumni programme.

Research Nurse 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 those involved in early-phase and translational research.

To celebrate the tenth anniversary of the ECMC network, the Research Nurse steering committee reflected on the network's successes and future hopes in an article for Cancer Nursing Practice. The article was informed by the feedback from senior research nurses at the ECMCs who were asked to consider the progress they had seen, how their role has changed and what they were most proud of. Key areas that were highlighted in the article were:

- Taking part in a Phase I trial is no longer 'a last resort' for patients who can now take part in an early-phase trial with the option of standard treatment later.
- New roles in this area that research nurses are interacting with such as clinical nurse specialists, radiology teams, allied health professionals and GCP compliance teams.
- Rise in the involvement of patients, carers and members of the public in clinical research design and coordination.
- Research nurses have had to become more skilled in explaining complex trial terminology along with scientific principles and discovery.
- Research Nurses are having to ask patients for more when they take part in a trial from increased frequency for blood and tissue samples to study requirements for fresh tissue biopsies.

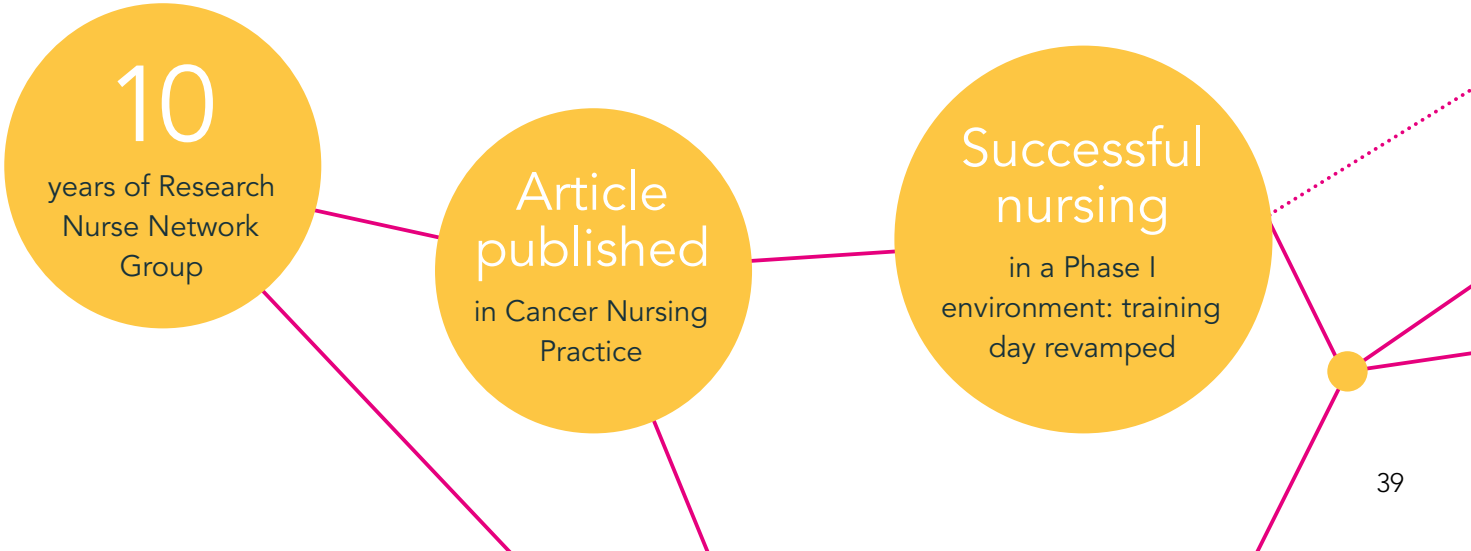
The article recognised that throughout the decade the bedrock of success has remained:

- Effective teamwork
- A working partnership with patients and the public
- Delivering high quality care.

Over 2017/18 the research nurse steering committee revamped their training day for research nurses new to working in early-phase cancer research. The aim of this day is to equip new early-phase cancer research nurses to delivery high quality, patient-centred care, within the regulatory framework. This course has been run previously however based on feedback this year's meeting was designed to be more interactive with plenty of discussion. The steering committee co-produced a booklet to support delegates by demonstrating how early-phase cancer trials differ (or don't) from later phase trials. The revised version of the training day will be run in April 2018.

The ECMC Programme Office has been working to involve the paediatric research nurses in the ECMC Research Nurse Network Group (RNNG). A research nurse contact at each paediatric location has been identified and one of them will join the steering committee. Paediatric research nurses were invited to attend the training day for new research nurses.

Over the next year the RNNG will be looking at how they can raise their profile both within the Network (to promote the involvement of research nurses from the early stages of trial design and development and in other key projects being run by the Programme Office) and externally to promote research as a career option for nurses.



ECMC Patient and Public Involvement Group

The ECMC PO supports an ECMC PPI Group; each adult ECMC is represented on this group with a staff and patient representative who are involved in PPI at their location. One of the main aims of the group is to share best practice, allowing people to hear about and learn from others in the network. The group also recognised the need for resources and/or training for people affected by cancer who were taking part in PPI activities in early-phase cancer research. This was primarily to ensure that they were aware of the differences between early-phase and later phase cancer research which they may be more familiar with. A booklet was produced and version 1 of this booklet was made publicly available in March 2018. In order to ensure that the booklet meets its desired purpose this version of the booklet is out for consultation and all those who read it are encouraged to provide feedback. The booklet and its feedback will be reviewed by members of the group in autumn 2018.

Disseminating the successes of the network

A key role of the ECMC Programme Office is to promote the success of the network.

In 2017, the ECMC network celebrated its tenth anniversary and the focus of these celebrations was the ECMC Annual Network meeting on 10 May 2017. Over 250 delegates, staff from across the network and other stakeholders, attended the day in London.

In the morning, delegates heard keynote addresses from Sir Harpal S Kumar (CEO, Cancer Research UK) and Louise Wood (Department of Health) who both celebrated the achievements of the network and the partnership between Cancer Research UK and the four health departments. Delegates also heard about trials taking place within the network, about the Junior Investigator Network Group and an affecting talk from a patient on the RADICAL trial from the Combinations Alliance portfolio. Following a lunchtime of networking, delegates looked to the future with a choice of three parallel sessions: patient referral, relationship with industry and regulatory environment.

At the meeting, staff who had worked in the network for 10 years or more were recognised and delegates were asked to share their thoughts on the best thing about the network and what they were looking forward to in the new year.

"The partnership isn't just about a joint investment – this approach has created a UK wide network, providing patients from all UK nations with access to early-phase clinical trials. The numbers are impressive, with over 20,000 patients participating in over 1,700 ECMC supported early-phase trials over the last decade"

Sir Harpal S Kumar

The new ECMC brand was also launched at this meeting and had a positive response from both the funders and ECMC members. The new brand was created to better reflect the network, and to help promote engagement with industry. The new identity concentrates on the idea of a network of expert minds and a single point of entry for industry.

With the introduction of the new brand, we updated all ECMC communication and marketing materials, with an all new logo, colours and graphics. Distribution of these new materials to sites, as well as the creation of new centre specific ECMC logos, allowed promotion of the ECMC network like never before. We have continued the dissemination of information about the network through our three main communication channels, Twitter (@ECMC_UK), our website (ecmcnetwork.org.uk) and the newsletter (distributed once every two months), which have all received a fresh design in line with the ECMC rebrand.

Aside from receiving a fresh and rebranded design, the **ECMC website** continues to be a hub for information on ECMC network groups, centres, interviews and news.

Activity from the **@ECMC_UK** twitter account includes promotion of ECMC events, network training days, core messages and interaction with the wider oncology community. This year we have focused on disseminating network achievements and milestones from the network and with our twitter account having recently hit 2,000 followers, our social media content is reaching a wider audience than ever. We continue to tweet daily and live from events and conferences to maintain a high social media presence.

Our **newsletter** features interviews, science news from the network and upcoming events. Regular sign-ups have made this year's newsletters some of the most read yet – being sent out to almost 1,300 recipients and boasting a click-to-open rate consistently over 30%. Particularly well received stories include an interview with Cancer Research UK Chief Clinician Charles Swanton, a round-up of our 2018 Junior Investigator Network Group training event and a report from the first complex trial design consensus paper workshop.

New
ECMC brand launched

250
delegates attended Annual Network meeting 2017

2,000
followers of @ECMC_UK

Looking forward

In 2017/18 we built on the success of the previous ten years and set the basis for a successful third quinquennium.

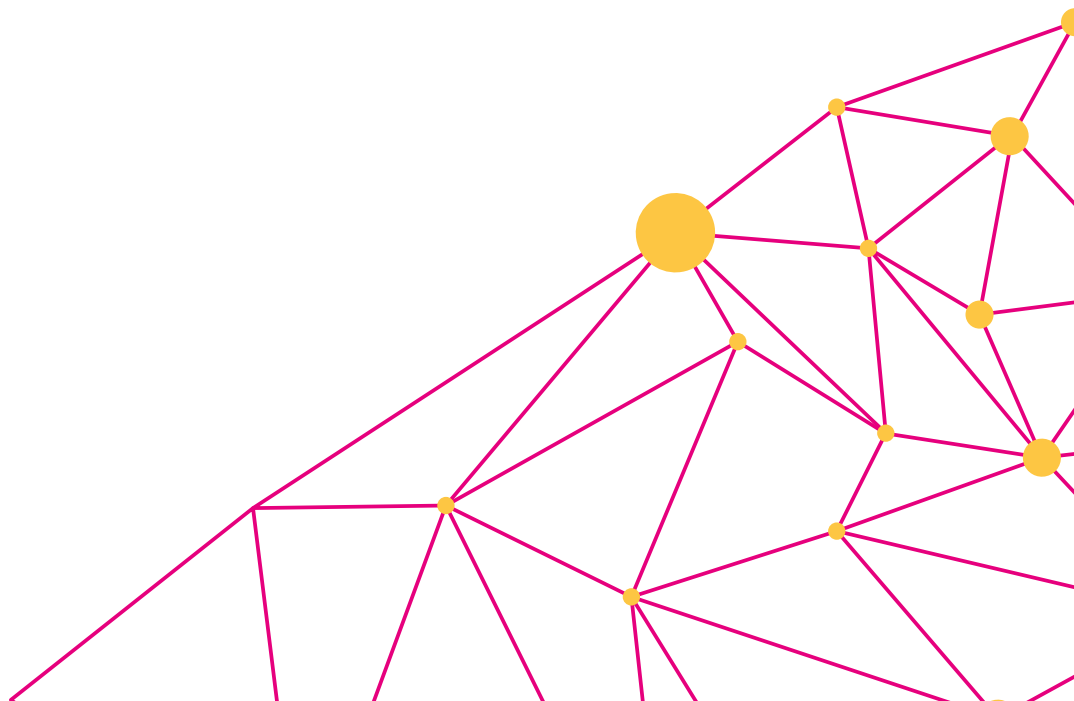
Over the next year the network will push forward our strategic agenda and will respond with agility to the changing environment in experimental medicine, focusing on the delivery of high impact translational and scientifically rich studies to the highest standard. Capitalising on our breadth of knowledge and expertise, we aim to position the network at the forefront of international research, to maximise patient benefit.

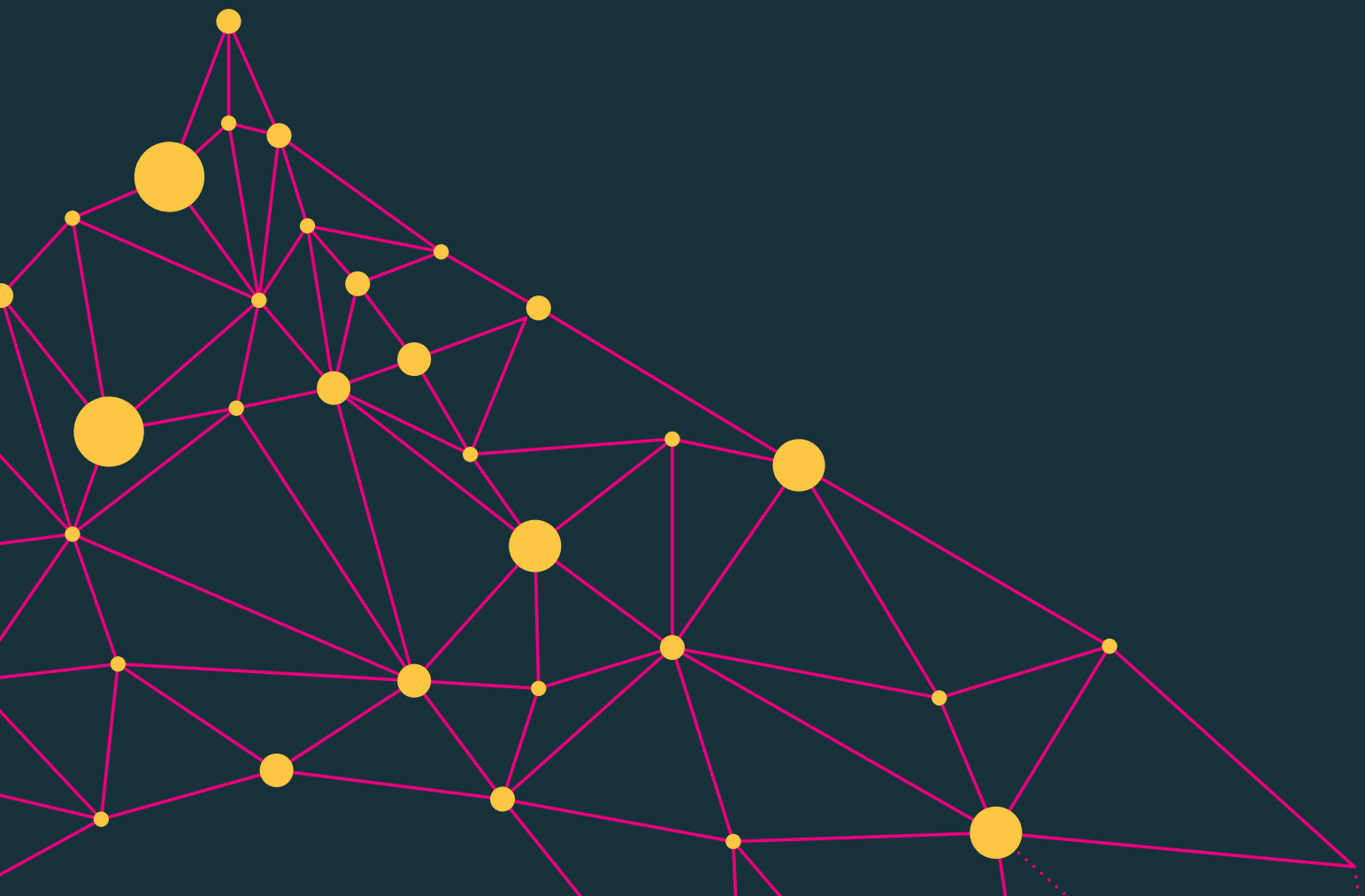
We will continue working closely with our industry partners, to ensure that innovation from the private sector can be translated into medicine in a fast and efficient way, and by means of this interaction, we plan to increase the attractiveness of the UK as destination of choice for the development of innovative treatments.

We will keep driving effective collaboration within the network, to support exchange of ideas and best practice within the network, for a network that is more than the sums of its part.

The work of the network will be supported by the newly created Programme Office. Among the initiatives led by the PO, in the near future we are expecting realisation of two main outputs: the launching of the EC Trial finder, the first national database of early-phase trials running in the network that will allow real time queries of available trials, facilitating patient referral across the UK; and the publication of a consensus paper on innovative trials, written with contribution of ECMC clinicians, regulators, industry partners, research and development colleagues, and patients. The paper will be testimony of the network's ability to coordinate a unified voice in the research landscape, and of the network's and UK's readiness to drive the agenda for experimental cancer medicine.

With growing awareness of the network leading to increased partnership and collaboration both internally and externally we look forward to an exciting year ahead with significant opportunities to advance our capabilities and broaden our reach and impact benefiting not just patients in the UK but also contributing to the advancement of our research standing internationally.





ECMC Programme Office
The Angel Building
407 St John Street
London EC1V 4AD

www.ecmcnetwork.org.uk

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