

Spring 2021 Edition

UCLH

EARLY PHASE CANCER TRIALS NEWSLETTER



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Welcome to the First Edition

Welcome to the first edition of our new newsletter showcasing early phase cancer trials at the NIHR University College London Hospitals Clinical Research Facility (UCLH CRF).

We are excited to share information and provide updates on early phase cancer trials, share outcomes on these trials, updates from our Principal Investigators, alongside metrics and the latest news and key publications.

THE CHALLENGES OF RUNNING AN EARLY PHASE CANCER TRIALS PROGRAMME DURING THE COVID-19 PANDEMIC

This past year has been demanding on all of us, but the plight of cancer patients during the pandemic is still being understood.

By Dr. Rakesh Popat

Consultant Haematologist
Cancer Lead NIHR UCLH Clinical Research Facility

The impact on cancer research has been profound with many trials being halted whilst a race to develop COVID-19 vaccines and effective treatments has pushed forward. So what became of cancer clinical trials? Drug development in many areas has fallen behind schedule which means that potentially effective cancer treatments have been delayed getting to clinic.



At UCLH, we tried to maintain our early phase cancer clinical trials programme where possible. We acknowledged that cancer continues despite COVID-19 and patients will still need access to novel agents when their standard treatments have failed. It was a moral duty to try and keep our programme going.

However, this was not easy. The hospital was under great pressure due to the volume of sick COVID-19 patients, and the resources that we needed to run clinical trials continues to be limited.

We worked closely together as clinicians to prioritise the trials that had the biggest potential benefit to patients without putting them at excessive risk and worked with our service support departments to ensure that these studies were feasible to run. We also had to maintain the safety of our patients, recognising that many travel from far to reach us.

For a couple of months at the beginning of the 1st wave, we stopped recruiting due to concerns to the risks to patients.

However, from June we slowly restarted the early phase cancer trials programme at the NIHR UCLH Clinical Research facility with enhanced safety measures.

Patients required negative COVID swabs prior to attendance and were treated where possible in single rooms to minimise infection. We also minimised additional visits by careful planning of appointments and implemented telephone clinics where possible.

This whole process has been made possible by many teams across the hospital pulling together despite the on-going pressures of the pandemic.

Behind the scenes our study co-ordinators have continued to work hard setting up new trials. This was vitally important to ensure that we had a pipeline of trials opening so we didn't emerge from the pandemic with nothing on offer. We were also keen to continue to contribute to the global drug development process as well as the translational laboratory science that goes on alongside.

One of the aspects that worries me, is if certain groups of patients may have been disadvantaged from access to cancer trials, particularly during the pandemic. We're going to look at this further as well as improving our external communications to ensure we reach as many communities as possible.

Despite the challenges we face, we will continue to strive to develop more effective cancer treatments for our patients.

"I'm fortunate and grateful that I work in an organisation that embraces research and makes cancer a priority".

PERSPECTIVE - THE IMPORTANCE OF EARLY PHASE CLINICAL TRIALS IN CANCER

By Professor Daniel Hochhauser

Kathleen Ferrier Professor of Medical Oncology
Head of Research Department of Oncology
Co-Director Cancer Theme, UCLH Biomedical Research Centre
Clinical Director CRUK UCL Centre

University College London Hospitals (UCLH) is a major teaching and research facility connected to University College London (UCL), one of the leading international universities. Cancer is a major component within the Trust, and research within UCL is facilitated by several divisions focused within the UCL Cancer Institute, and includes the Divisions of Medicine, Surgery, Life Sciences and Engineering, incorporating institutes such as the UCL Medical Research Council Laboratory for Molecular Cell Biology.

The core strength of UCL is the immense breadth of research projects involved in cancer ranging beyond biological and physical sciences and including health economics, law, and the wider humanities.

The UCLH Biomedical Research Centre (BRC) is a partnership between UCLH and UCL to support world leading clinical translational research. Within the BRC the Cancer Theme aim is to optimise and develop precision cancer medicine.

This is achieved through three workstreams:

- (a) Improving the therapeutic index in non-chemotherapy cancer treatment,**
- (b) Understanding tumour heterogeneity and targeted therapy**
- (c) Cancer immunotherapy.**



The BRC focuses resources and recruitment in areas in which the UCLH/UCL axis has a leading role internationally and can promote excellence in research. It is however the over-riding function of the BRC Cancer Theme, which I co-direct with Prof. David Linch, to invest in research initiatives which lead directly to improvements in patient care. This has been a highly successful strategy and at its core is the NIHR UCLH Clinical Research Facility (CRF) which exists to manage first-in-human studies and early phase clinical trials. Thus, the CRF is absolutely essential for the core function of the BRC Cancer Theme and has been strongly supported over the past 5 years.

Apart from these important early phase studies, the CRF performs a critical function in facilitating academic investigator-initiated studies in which the BRC faculty can translate clinical findings into studies with patients. The intensive medical and nursing facilities together with the crucial underpinning of informatics can only be done within the auspices of a CRF. Finally, participation in pharma-initiated studies gives the opportunity for patients at UCLH to receive investigational therapies within a tightly controlled environment and affords unique opportunities for the BRC to become familiarised with these new agents which are being integrated into clinical care.

Thus, support for the NIHR UCLH Clinical Research Facility is a crucial function of the BRC and will continue to play a major part in our reapplication for the next five years of funding.

Biomedical Research Centres were established to lead research directly into health care improvement and the Clinical Research Facility is the vital connecting bridge between laboratory studies and initiation of larger randomised studies of new anticancer treatments.

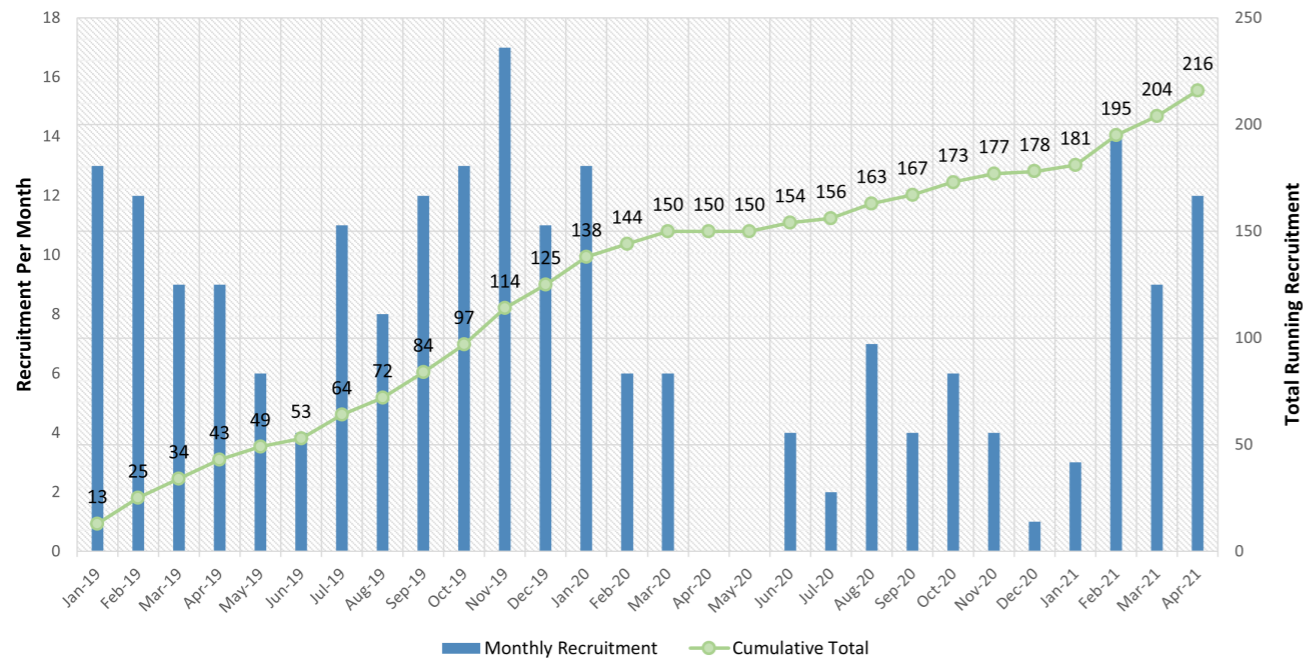
There are several different approaches which have been pursued to initiate new studies on cancer therapeutics within the CRF. Research advances which have originated within UCL are a priority and there are several examples where these have been advanced in collaboration with pharmaceutical partners.

For example, the potent DNA binding drugs synthesised and characterised within the laboratory of Prof. John Hartley and partners with the UCL London School of Pharmacy have been developed into novel agents – antibody/drug conjugates which are now being trialled in the CRF in collaboration with ADCT for use in solid tumours.

A STORY OF EARLY PHASE CANCER CLINICAL TRIALS IN NUMBERS

Despite the difficulties of the pandemic, we kept our portfolio open to enrolment.

The graph below shows our recruitment per month, alongside the cumulative total from January 2019 to April 2021



OUR TRIAL PORTFOLIO

Our growing portfolio of Clinical Trials ensures access to new treatments for patients and helps advance cancer clinical research.



Over the past **two years** we have opened a total of **29** Clinical Trials

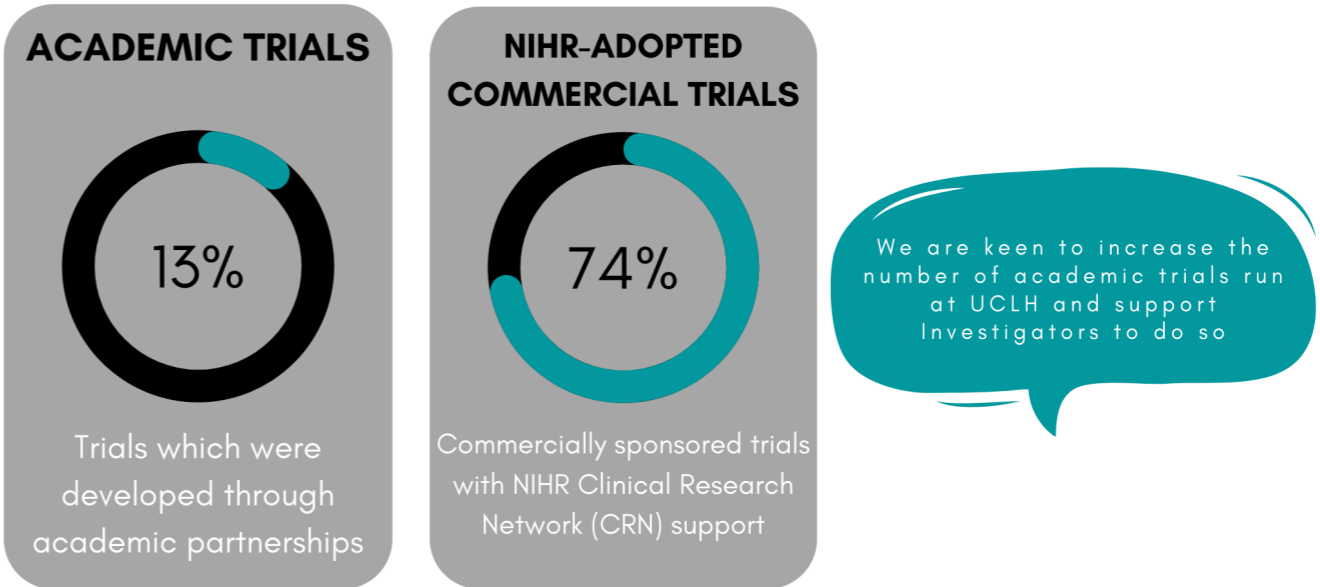
Full Portfolio Numbers:

Number of Trials currently open to recruitment **46**

Number of Trials currently in set-up **21**

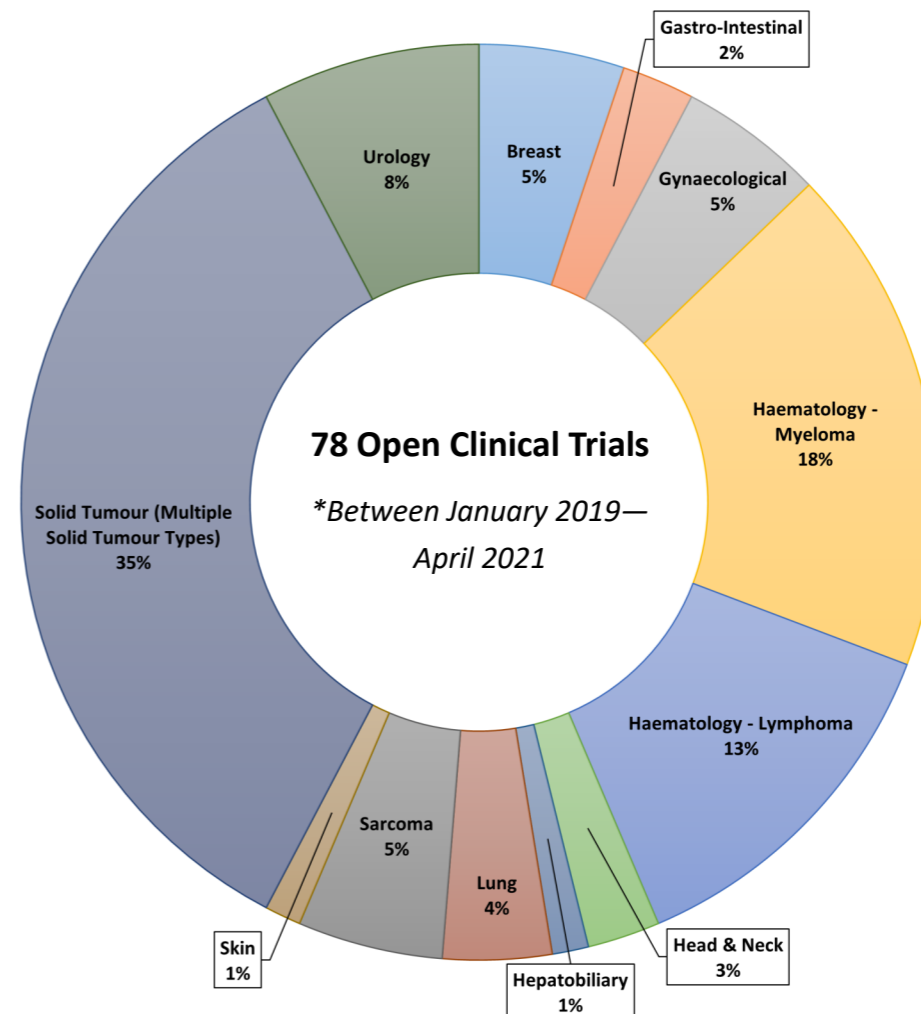
A STORY OF EARLY PHASE CANCER CLINICAL TRIALS IN NUMBERS

Our Current Trial Portfolio



At the UCLH CRF, we have a diverse portfolio of early phase cancer trials looking into an array of treatments across various tumour types.

As of April 2021, our portfolio per tumour group over the last two years* looks like this:



PATIENT AND PUBLIC INVOLVEMENT (PPI)

What is PPI & Why is it so important?

You may have heard the term Patient and Public Involvement (PPI) before, but what exactly does it mean, and why it is so important to researchers?

The simple answer is it's one of the best ways we can understand if the research we are conducting ultimately is relevant for those who it's aimed for, who it will impact, and who it will benefit. This is done through actively including patients and working in partnership with them to deliver these benefits.

We have included extracts from two of our PPI members, who have spoken about what PPI really means to them:

“What’s the point of PPI? Box-tick for funding/approvals ... or useful input?”

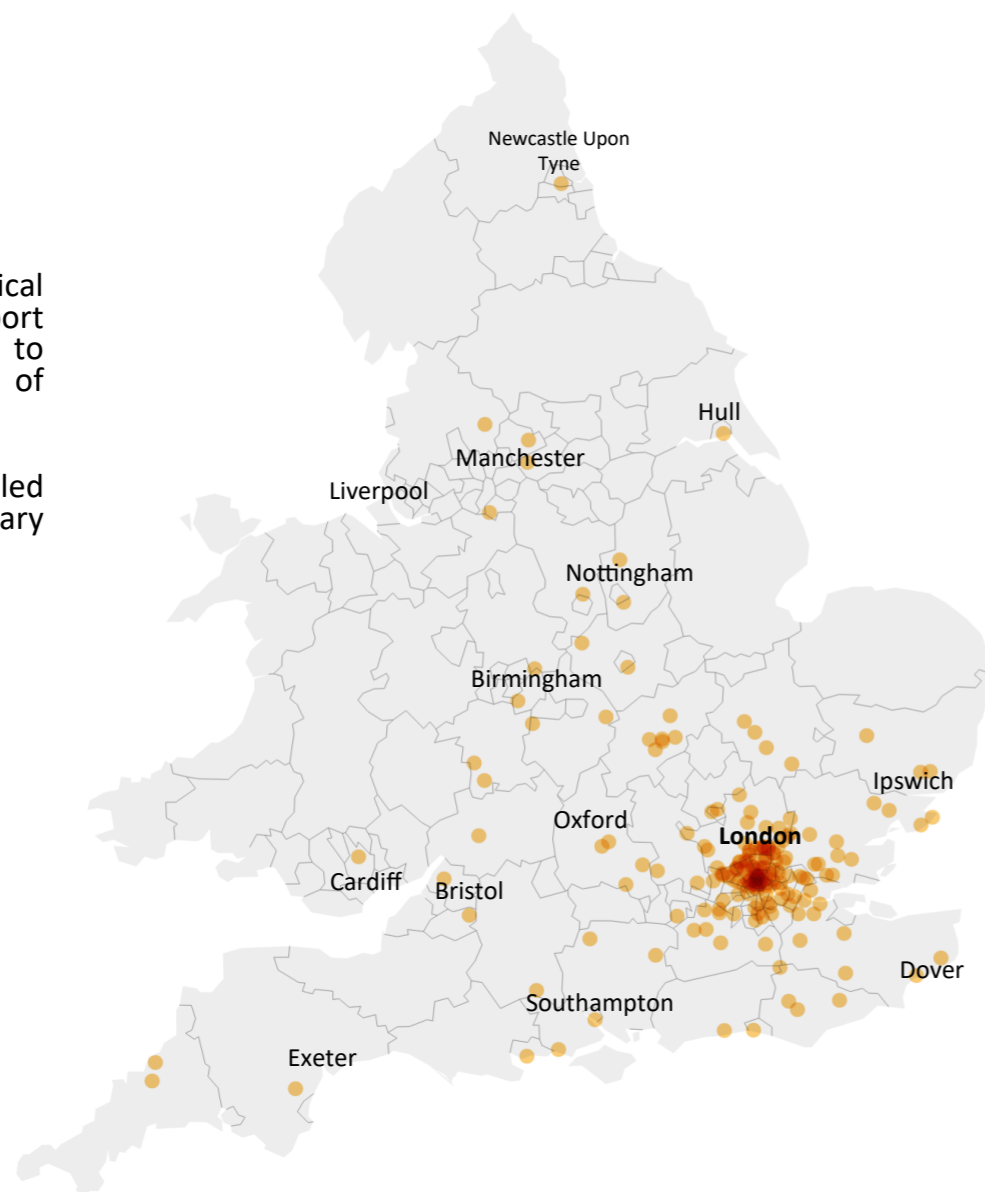
I'd suggest it's a matter of adding perspectives. So when it works, it's a two-way (at least) conversation, that benefits everyone: researchers, clinicians, participants, end-patients, family, carers, and the PPI-ers themselves.

It's not just about symptoms and side-effects; it can highlight all kinds of rational and irrational concerns that can affect recruitment for instance. It can bring a surprisingly different view of results; 'quarter-empty' can become 'three quarters-full'. Sometimes it can offer add-on skills such as communication.

Ultimately, all medical research, at whatever stage, is to do with people; so doesn't it make sense to talk to them? ”

Our diverse range of clinical trials and excellent transport connections allows UCLH to serve a wide geography of patients across the country.

Data from patients enrolled and recruited from January 2019 - January 2021.



Map data: © Crown copyright and database right 2020 • Created with Datawrapper

PATIENT AND PUBLIC INVOLVEMENT (PPI)

What is PPI & Why is it so important?



“For more than a decade I have been involved in PPI work with the Medical Research Council and the NIHR UCLH Cancer Research Facility and I have to say that it has been a thoroughly rewarding and an utterly captivating experience. I presume many of you might be astonished by the use of such flowery vocabulary in my attempt to depict my engagement in PPI activities, so incongruous with the exacting nature of the clinical research area.

Let us not forget that clinical trials are not being carried out in the vacuum, they heavily rely on the human factor. Without patients and the cooperation and encouragement from their families and communities there will be no clinical trials, and without clinical research the progress in the development of new treatments would have not been possible.

Although within the past 10 years many breakthroughs and discoveries have been made that enable to save or prolong lives, cancer remains one of the leading causes of death both in the UK and worldwide.



I have observed the growing need for the incorporation of the patient perspective in clinical research, a call for the better understanding of the trial patients' expectations and goals as well as those of the scientific community. And to make this dialogue possible, we need the support and greater involvement of the wider public in the clinical research decision-making process.

The advancement of medical science depends on it.”

I am a cancer survivor (I was diagnosed with ovarian cancer 13 years ago, when I was in my mid-forties) and I consider myself very fortunate to be alive, the more that I have witnessed the death of few young women from ovarian cancer in my support group shortly after my treatment. It might sound sentimental, but the truth is that I think of them every day. Therefore, the opportunity to make a contribution, however small, to the advancement of cancer research has been very important to me.

During the past 10 years, while mainly working on academic trials in the area of Gynae-oncology, with time passing I have seen my role constantly evolving and the scope of my duties widening.

From being a Patient Representative requiring me to mainly focus on ensuring that the content of the study-related documentation is easily understandable to patients and the public, I have progressed to providing feedback on many aspects of the trial including its design, to assisting with developing study participants' surveys and to disseminating the trial results to the public and study participants, among other things.

JOURNEY FROM CLINICAL FELLOW TO PRINCIPAL INVESTIGATOR (PI)

We provide comprehensive training for our Fellows to allow them to realise their full potential

By Dr. Jenny O'Nions
Consultant Haematologist
NIHR UCLH CRF Principal Investigator

Clinical Research Fellow at the UCLH NIHR Clinical Research Facility

I entered medicine as a graduate-entry student, having already completed a PhD. During my haematology training I wanted to build on my research background and incorporate it into my future clinical career. I was awarded a Marcel Levi Fellowship in 2018 and chose to spend it in the NIHR UCLH Clinical Research Facility (CRF). This was arguably the best decision I made during medical training. It crystallised for me how I could marry my love of clinical medicine with a desire to be directly involved in the evolution of new therapies and improving treatment options for patients.

Training Opportunities in the CRF



The CRF is set-up so that all the elements of trial set-up and execution take place in the same physical space. This close geography means that fellows are working alongside data managers, trial coordinators, laboratory personnel and senior managers as well as the rest of the clinical team. This gave great insight and understanding of the day-to-day responsibilities and challenges of these different roles. I also received 'hands on' training in key aspects of conducting clinical trials, including consenting patients for trials with experimental therapies, assessing causality and reporting adverse events, preparing risk and feasibility assessments, directly participating in site set-up, investigator meetings and dose escalation committee meetings; all essential training for a wannabe trialist. Weekly dedicated CRF radiology and clinical MDTs provided further experience.

As a fellow at the CRF, I was able to develop other skills important in clinical trials, for example attending a course in the use of statistics in medical research and application in study design. I also participated in the Experimental Cancer Medicine Centre (ECMC) Junior Investigator Network Group (JING) meetings, interacting with clinicians, translational scientists, statisticians and expert patients. This provided the foundation to forge links with other investigators, academia and pharmaceutical companies, which is essential in clinical trials.

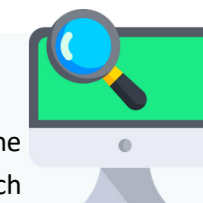
I also engaged in a number of other opportunities; attending the American Society for Haematology (ASH) meeting to present a meta-analysis on the outcomes of blood cancer patients on early phase trials, developing a collaborative translational project with a pharmaceutical company, co-writing a review on anti-CD20 immunotherapy in Follicular Lymphoma and a case series highlighting the challenges of managing ocular adverse events in patients on the DREAMM-1 study.

Principal Investigator at UCLH

The early phase trials programme at UCLH continues to expand. Additional sessions for clinical trials were incorporated in a new leukaemia and myeloid disorder consultant post. I am sure the experience I gained during my fellowship contributed significantly to my successful application for this post and I am now an early phase trials Principal Investigator at UCLH and co-lead for the Trials Acceleration Programme (TAP) at UCLH. Clinical trials are inherent in cancer and fellowships such as mine offer excellent experience in this area, but also enable you to develop the skillset, networks and knowledge to progress in a career as a clinical trialist.

Early phase trials are essential in the translation of scientific insights into improved therapy for patients. The opportunity to be involved in cutting edge trials in the UK is something I am both excited about and proud of.

LATEST NEWS & PUBLICATIONS



New Early Phase Cancer Trials Website Coming Soon

It is with excitement we announce that we are developing a new website which will showcase the early phase cancer trials and research being conducted at UCLH, the NIHR UCLH Clinical Research Facility and highlight emerging research from University College London.

It will act as the central hub for information regarding our early phase cancer trials programme, featuring a complete list of the cancer trials which we are currently running and are open to recruitment, alongside key information about each trial for clinicians, researchers, stakeholders, patients and the public.

Alongside this the website will contain content for patients and the public, to provide an understanding of how early phase clinical trials are run, information on the latest research, and helpful content. We will host a team profile of all our Principal Investigators who run early phase cancer trials, including information about the various teams, departments and networks that ensure smooth running of trials.

The website will help to promote upcoming events, as well as showcasing news and promoting key publications from our team.

The website is scheduled to launch in the Summer of 2021.

Professor Bridgewater was senior author for the Phase 2 FOENIX-CCA2 (TAS-120) Trial oral presentation at AACR

We are pleased to highlight an oral presentation led by Professor John Bridgewater, professor of medical oncology and clinical researcher at UCL Cancer Institute.

The presentation given at the American Association for Cancer Research (AACR) Annual Meeting on the 11th April 2021, looked at the primary results of the Phase II FOENIX-CCA2 Trial (A Study of TAS-120 in Patients With Advanced Solid Tumours), in which UCLH was a recruiting site. The trial evaluated TAS-120 (Futibatinib) in intrahepatic cholangiocarcinoma (iCCA) harbouring a Fibroblast Growth Factor Receptor-2 (FGFR2) fusions/rearrangements.

iCCA, is a subtype of Cholangiocarcinoma (CCA) arising from bile ducts within the liver. This is a rare cancer with a poor prognosis. Alterations of FGFR-2 occur in up to 15% of intrahepatic CCA. Primary results showed TAS-120 resulted in frequent, durable objective responses in patients with iCCA harbouring the FGFR2 fusion/rearrangements.

We would like to congratulate Professor Bridgewater on the achievement and all the team at UCLH who worked on this trial. The abstract can be viewed at the [AACR Annual Meeting 2021 page](#).

ARROW (BLU-667) Trial leads to FDA Accelerated Approval

In December 2020 it was announced the U.S. Food and Drug Administration (FDA) had approved Pralsetinib for the treatment of advanced or metastatic REC-mutant Medullary Thyroid Cancer or metastatic RET Fusion-Positive Thyroid Cancer. The approval came under the FDA's accelerated approval programme from data on the Phase I/II ARROW (BLU-667) clinical trial.

The study is still undergoing at the UCLH site, under the eye of Principal Investigator Dr. Martin Forster.

We would like to congratulate Dr. Forster and all involved in this trial.

ESPRIT Trial first in the CRF to Involve Teenagers & Young Adults

The 'ESPRIT' trial was an academic global phase I study, sponsored by SARC, investigating the tolerance & efficacy of a PARP1/2 inhibitor Niraparib in combination with temozolomide or Irinotecan in patients with recurrent Ewing Sarcoma. Dr. Sandra Strauss was Co-Chief Investigator of the study.

The trial recruited internationally, with UCLH being the only site open in Europe and the first cancer study within the UCLH CRF to recruit Teenagers & Young Adult patients. We are pleased to share the publication which can be found in [ACS Journals](#).