

Winter 2021 Edition

UCLH

EARLY PHASE CANCER TRIALS NEWSLETTER



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Welcome to the Winter 2021 Edition

As another year comes to a close, we reflect upon the turmoil that the ongoing COVID-19 pandemic has had on cancer research. At UCLH, we have continued recruiting into early phase cancer trials as a high priority to enable patient access to novel treatments and contribute to drug development. I'm very appreciative to all that have worked hard to achieve this.

In this newsletter we cover areas that we have been working on over the year. Prof. Libri highlights the importance of early phase cancer trials to UCL/UCLH's experimental medicine strategy. In that theme, we highlight a few important trials led by Drs Strauss, Popat and O'Nions that deliver academically led studies with translational elements, highlighting the strong partnership between the Hospital and University. We also describe the challenges in enrolling ethnic minorities into cancer trials and what we're doing to improve this. Finally, two of our clinical fellows outline their career progression after completing attachments with us.

I hope you find this of interest and wish you all a safe and restful time over the holiday period.

*Dr. Rakesh Popat, Consultant Haematologist
Cancer Lead NIHR UCLH Clinical Research Facility*

THE IMPORTANCE OF EARLY PHASE CANCER CLINICAL TRIALS - A PERSPECTIVE

By Professor Vincenzo Libri
Director of NIHR UCLH Clinical Research Facility

I'm delighted to contribute to this edition of the newsletter and emphasise the commitment of our NIHR University College London Hospitals Clinical Research Facility (UCLH CRF) to early phase cancer research. Since inception in 2009, the UCLH CRF has consistently prioritised cancer and haemato-oncology malignancy trials and has delivered some of the most complex and innovative clinical studies, to benefit patients with some of the most challenging, severe, and incurable diseases. We are incredibly proud that cancer research is one of our greatest strengths.



Our cancer trials portfolio is unparalleled and one of the largest in the UK with more than 90 new early-phase trials opened since 2017 (representing 23% of all phase I cancer trials opened at NHS Trusts hosting NIHR-CRFs). Approximately 75 phase I cancer trials are active at any one time, and we work with a multitude of charities and pharmaceutical companies to achieve excellent outcomes, including winning the UCLH Excellence Award 2020 for the category 'Contributions to World Class Research'.

This is all possible thanks to the outstanding partnership between world-class Investigators and an exceptional CRF team made up of passionate, dedicated and highly professional medical, nursing, laboratory, and research governance personnel.

Undoubtedly, 2021 has been one of the most challenging years any of us could have ever imagined due to the extraordinary and unprecedented COVID-19 pandemic. Yet, whilst the pandemic caused the majority of clinical research studies at UCLH/UCL to pause at the peak of the first wave of COVID-19 infections, interventional CRF trials in serious or life-threatening conditions, including cancer and neurodegenerative disorders, continued safely with minimal disruption, and alongside multiple large-scale COVID-19 vaccine trials.

Despite the challenges and immense pressures imposed by the COVID-19 crisis, I was touched by the resilience and dedication exhibited by our team striving to maintain our core activities in the best interest of our patients and families.

My last but most prominent thought is for our wonderful patients without whom none of our research would be possible. Their voluntary participation in trials is admirable. More than ever, we are determined to uphold our promise to expedite the early evaluation of novel treatments for the most challenging, complex, and difficult cancer types, with an ultimate goal of offering a better future to affected patients and their families.

"I wish everyone a very well-deserved break over the Christmas holiday and a happy and productive 2022".

Moving forward, our ambitious objective is to consolidate the CRF as the clinical research 'laboratory' and central hub of the UCLH/UCL translational medicine agenda for cancer treatment and to support more leading-edge research focused on the needs of cancer patients with limited treatment options. This will require a consolidated and strong partnership between investigators and CRF staff and to maximize efforts toward the common goal of delivering innovative and effective treatment to patients.

As we approach the end of the year, I want to reiterate how grateful I am for all the hard work and efforts of our investigators and CRF staff during what has been a demanding 12-months. I am proud of how all within the CRF have come together to help deliver on our cancer translational medicine agenda.

Next year will no doubt bring its own set of challenges, but I am confident in the ability of our CRF community to find and seize the opportunities that will come along with them.

HIGHLIGHT ON OUR ACADEMIC CANCER CLINICAL TRIALS

We are delighted to highlight a few cancer clinical trials which showcase our commitment to supporting academic collaborations



IMMUNOSARC2

Phase I-II trial of sunitinib plus nivolumab after standard treatment in advanced soft tissue and bone sarcomas

Chief Investigator: Dr. Sandra Strauss

We are excited to announce that ImmunoSARC2 has opened to recruitment. This is an innovative Phase I/II study of Sunitinib and Nivolumab in patients with 6 rare subtypes of soft tissue and bone Sarcomas (Dedifferentiated Chondrosarcoma, Extraskeletal Myxoid Chondrosarcoma, Vascular Sarcomas, Solitary Fibrous Tumour, Alveolar Soft Part Sarcoma and Clear Cell Sarcoma), many of which have no defined treatments, and importantly the study is open to Adolescent as well as Adult Patients.

The role of immunotherapy combinations in the management of Sarcoma remains undefined.

This trial showcases the infrastructure developed to support academic collaborations within the UCLH Clinical Research Facility, opening the opportunity to work with wider academic partners and the ability to bring much needed treatments to rare cancers.

ImmunoSARC2 is an academic collaborative clinical trial sponsored by the Spanish Group for Research on Sarcoma (GEIS) with sites in Spain, Italy and UCLH as the only site in the United Kingdom, and provides an opportunity for patients with these rare Sarcomas to access novel therapies and for researchers to better understand the biology related to efficacy, with a number of correlative analyses ongoing.

We are grateful to the Jon Moulton Charity Trust for financial support that has made this unique partnership possible by allowing us to conduct the study at UCLH including providing support for a trial coordinator; Fatjon Dekaj.

IN THE PIPELINE:

We have two new exciting NIHR portfolio academic clinical trials developed within the National Cancer Research Institute (NCRI) Haem-Onc group that are currently in set-up:

PROMMISE

A Platform trial for Relapsed patients to evaluate Ongoing novel therapies in Multiple Myeloma in combination with Standard of care therapies

Chief Investigator: Dr. Rakesh Popat

ProMMise is a Phase I trial for patients with Multiple Myeloma.

The Chief Investigator is Dr Rakesh Popat (Consultant Haematologist and Cancer Lead UCLH CRF), and the study is sponsored by the University of Leeds as part of the Clinical Academic Research Partnership (CARP) programme.



PROMISE

Investigation into the combination of PLX2853 with ruxolitinib in patients with intermediate-2 or high risk myelofibrosis not receiving an adequate response with ruxolitinib alone.

Principal Investigator: Dr. Jenny O'Nions



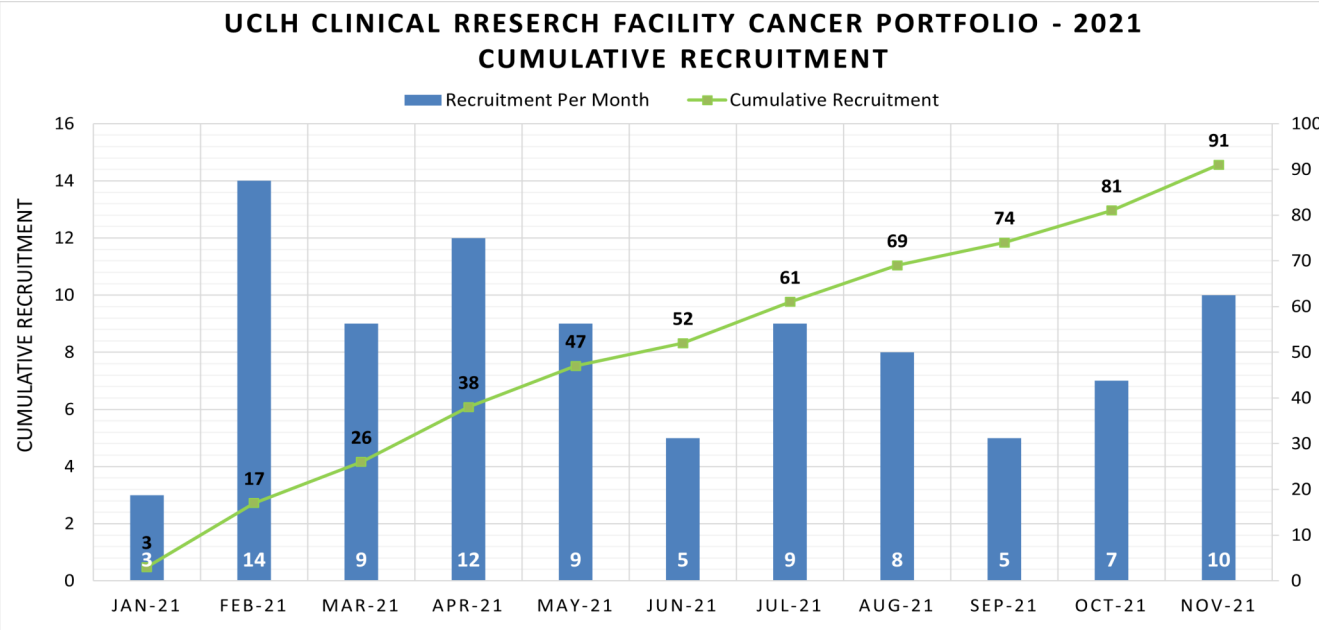
PROMise is a Phase I study for patients with intermediate or high-risk Myelofibrosis.

The Chief Investigator is Dr. Adam Mead (Oxford NHS Trust), and it will be run at UCLH by Dr. Jenny O'Nions (Consultant Haematologist). The study is sponsored by the University of Birmingham as part of the Trials Acceleration Programme (TAP).

A STORY OF EARLY PHASE CANCER CLINICAL TRIALS IN NUMBERS - 2021 REVIEW

2021 has been a challenging year due to the difficulties of the pandemic. Despite this we kept our portfolio open to enrolment ensuring access to new treatments and advancing cancer clinical research.

The graph below shows our 2021 annual recruitment per month, alongside the cumulative total.



OUR 2021 TRIALS PORTFOLIO

Our growing portfolio of cancer clinical trials ensures access to novel treatments for patients



Despite the challenges this past year we have opened

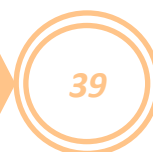


Full 2021 Cancer Trials Portfolio Numbers:

Number of Trials currently open to recruitment

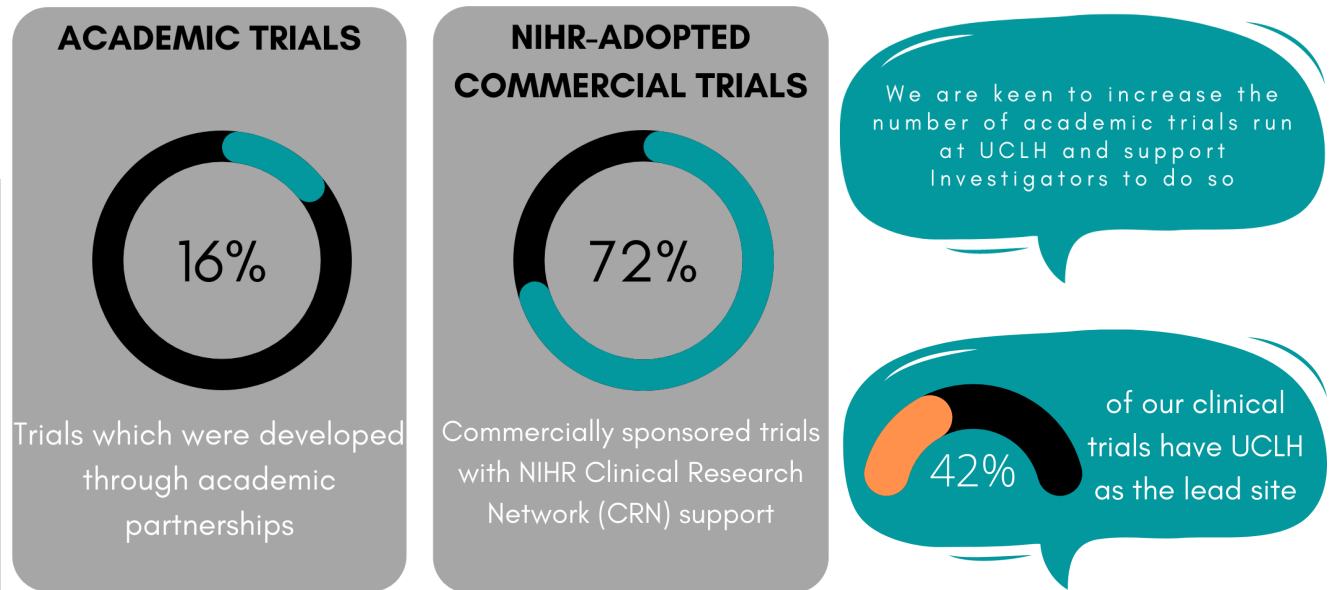


Number of Trials currently in set-up

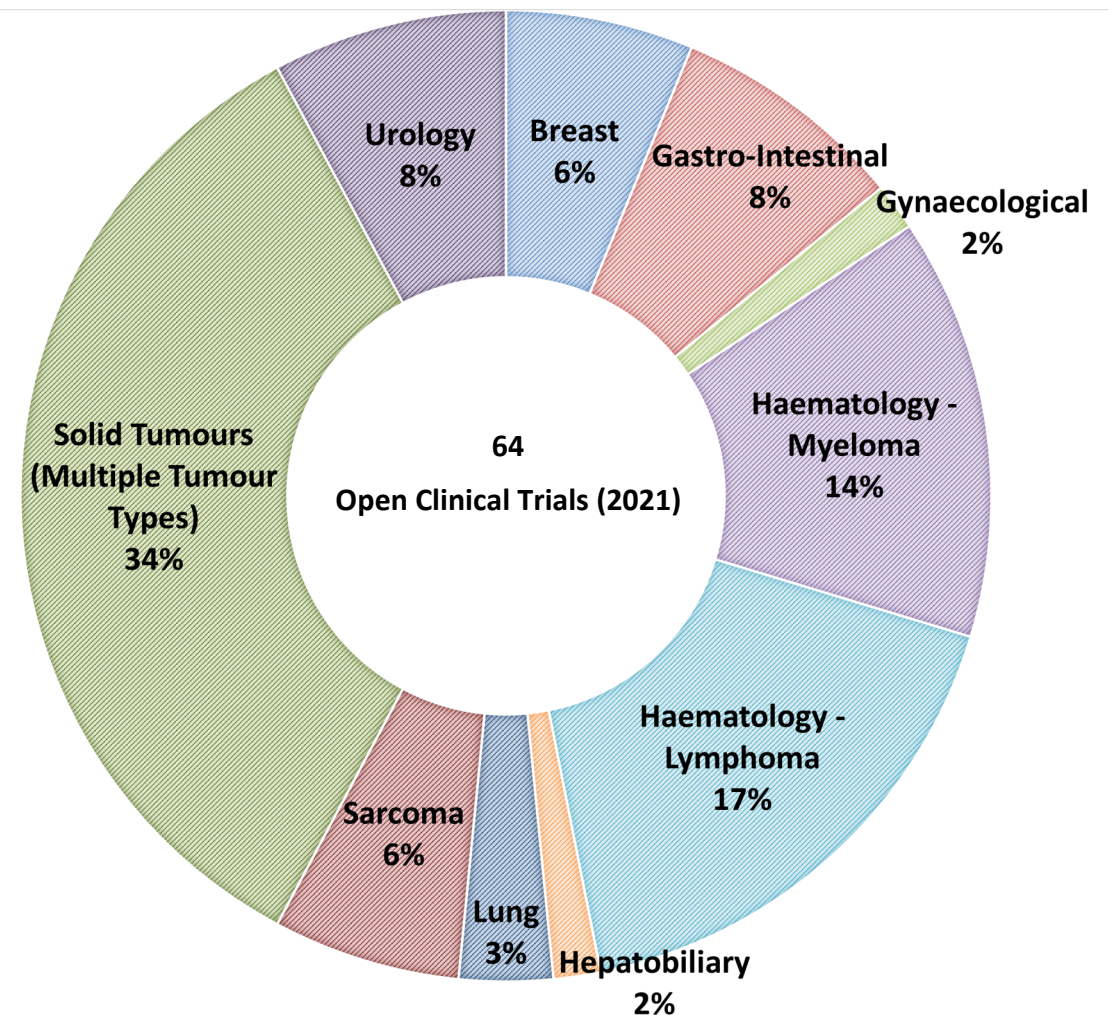


A STORY OF EARLY PHASE CANCER CLINICAL TRIALS IN NUMBERS - 2021 REVIEW

Our 2021 Cancer Trials Portfolio



In 2021 our Cancer clinical trials portfolio per tumour group looked like this:



DIVERSITY IN ENROLMENT TO CLINICAL TRIALS

In the NIHR UCLH Clinical Research Facility (CRF) we are determined to improve diversity and access to research.

There are several reasons why it is so important to include under-represented groups in clinical research, most importantly because we live in a broad, diverse population and failing to include a broad range of participants means that clinical trial results may not be generalisable to the population.

Importantly different groups may respond differently to an intervention, especially with complex conditions such as cancer. Above all, we have a principle to ensure that research is offered to all individuals, including under-represented groups.

During the year, we sought to investigate the diversity of participants enrolled into Multiple Myeloma (MM) clinical trials within the UCLH NHS service. This was a collaboration between the UCLH CRF Haematology Clinical Research Fellows, the UCLH Myeloma team and the UCLH Cancer Clinical Trials Unit (CCTU) Haematology clinical research team.

The study, led by Dr. Rakesh Popat, Consultant Haematologist and CRF Cancer Lead, with the CRF Haematology fellows Dr. Samir Asher & Dr. Aikaterini Kazantzi, looked at enrolment into MM clinical trials from 2014–2017.

The ethnic diversity of this population was assessed against the known diversity of the UK population and Multiple Myeloma incidence.

MM is a cancer of the bone marrow which comprises 2% of all cancers, but the incidence varies with ethnicity. Those from a Black ethnic group are approximately twice as likely to develop MM to White patients or Asian patients. Despite this, a lower proportion of Black patients have been reported to be enrolled into clinical trials.

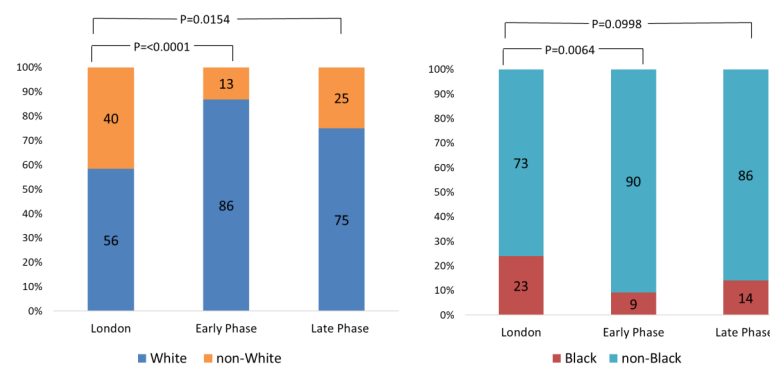
An abstract of the results was presented during the European Haematology Association (EHA) 2021 Virtual Congress. You can read the full abstract on the [EHA website](#).

Within the NIHR UCLH Clinical Research Facility, as part of our commitment to equitable access to clinical trials for all, we are investigating ethnic diversity across all tumour groups, for patients enrolled into our early phase cancer trials.

In our study we investigated 182 patients across 25 Multiple Myeloma clinical trials at UCLH.

The proportion of ethnic minorities enrolled into MM clinical trials was lower than expected compared to the incidence of MM in the UK. This was particularly apparent in early phase (Phase I/II) clinical trials where patients are referred from a wider geographical area.

We also observed a lower proportions of ethnic minorities enrolled into clinical trials compared to MM cases in London (as shown by the diagram below):



This has led to further work being performed in MM across the UK investigating the impact of ethnicity into trial enrolment, access to treatments and survival outcomes.

WHY WE NEED TO DO BETTER - A PATIENT'S PERSPECTIVE ON INEQUALITIES IN CLINICAL TRIALS

By *Edwin Ammisah Carr*

The importance of increasing the diversity of people participating in Phase I clinical trials and particularly those from Black and minority ethnic backgrounds must not be underestimated.

The reason for this is simple, its about reducing health inequalities that have existed without suitable intervention. However, the reason for the reticence for people of Black and minority ethnic groups being underrepresented is not a simple one. There are current and historic reasons that have led to the under representation in the various trial phases today.

It is not enough for health professionals to simply want to encourage increased participation, the reasons behind such need to be acknowledged, understood, and addressed in order to reach the longer term aims.

Discussions about Race and Inequality aren't easy or straightforward but if progress is sought then such dialogue is essential. I speak as a patient with no medical training, but I do know my own body and can often feel when something isn't right.

There have been occasions when I have sought medical intervention only to feel that my concerns have been heard but not listened to. I've felt that I have been dismissed and not afforded the level of care deserved. I accept that this does not only happen to those who have Black or Brown skin but when it does, it does so against a backdrop of historic inequality which adds to it being more readily perceived as prejudice.

A person in such a position often has a base impulse of fight or flight that is exhibited as verbally challenging the physician who holds a position of hierarchy or simply retreating.

A patient in fight or flight mode is maybe less likely to be viewed as 'positively engaging' and opportunities to discuss medical trials available are reduced.

Trust and respect are fundamental when discussing early phase trials within a patient and doctor scenario as without such, any active participation in trials is severely hindered.

As current understanding and development of future therapeutics seem destined to rely far more on genetics it's becoming more important to include participants from underrepresented ethnic groups.

It is accepted that ethnicity can be an important factor in successful medical trials as therapeutics need to be developed taking more diverse factors into account.

People of Black and minority ethnic groups need to be part of early phase research in order to help bring about a more equitable tomorrow in which Health Inequality is greatly reduced.

TRAINING OUR FUTURE RESEARCHERS – A PERSPECTIVE FROM OUR CLINICAL FELLOWS

DR. SAMIR ASHER

Myeloma Clinical Research Fellow
UCL Cancer Institute



Working in the NIHR UCLH Clinical Research Facility (CRF) provides an excellent opportunity for those who are keen to broaden their experience in clinical research and develop key skills to further a career within Haemato-Oncology.

As a Senior Haematology Specialist Registrar, I had limited clinical trial experience. This opportunity allowed me to gain a detailed

insight into the design and set-up of early phase clinical trials whilst working closely alongside a dedicated research team including research nurses, trial coordinators, and data managers. I quickly gained an understanding of both the challenges and constraints of commercially sponsored trials when delivering experimental treatments to an often clinically challenging cohort of haematology patients. The role provides the opportunity to engage directly with global teams of each clinical trial from site-initiation visits, dose-escalation, and investigator safety meetings as well as internal multi-disciplinary team (MDT) discussions allowing further development of key communication and presentation skills.

During my time in the CRF I was able to further engage in other clinical research opportunities such as participating in the Experimental Cancer Medicine Centre (ECMC) Junior Investigator Network Group (JING) meeting and designing and presenting my own early phase trial to a panel of clinical experts, trial statisticians and patient liaison group. I received a UK Myeloma Forum (UKMF) and Sanofi bursary for my European Haematology Association (EHA) abstract and poster presentation for work on ethnic diversity in myeloma clinical trials which I later presented in a UKMF conference.

The opportunities in the UCLH CRF have meant I have been able to meet with other members of the wider UCLH Myeloma team and, utilising the experiences and skills I have gained within the CRF, am now working as a Myeloma research fellow in the University College London Cancer Institute.

DR. SARAH BENAFIF

Consultant Medical Oncologist in Lung & Early Phase Trials
University College London Hospitals



The UCLH CRF provides a unique clinical research experience for oncology trainees as well as junior doctors interested in training in oncology to gain an in-depth insight into all aspects of early phase interventional oncology trials. Having worked in the unit as a junior trainee in my first year of medical oncology training, I was keen to build on my PhD research and clinical trials experience by learning about early phase trials set-up and management.

Working as a Clinical Research Fellow in the CRF provided this. With the rapid progress in precision oncology and translational research, novel drugs are increasingly targeted to specific alterations and in turn early phase trials are also more complex, and often aiming to target a specific patient population. Excellent communication skills are developed through the consultations carried out in this setting where the nuances of these trials need to be explained to patients. Alongside communication skills, the clinical fellow role ensures the development of excellent organisation and management skills when navigating trial protocols and interacting with trial sponsors and representatives.

Depending on the stages the trials are at, there are often opportunities to be involved in the preparation of conference abstracts presenting data for a trial that we have worked on. Attending the Experimental Cancer Medicine Centres (ECMC) annual Junior Investigator Meeting was a very valuable experience to learn from the experience of investigators, statisticians and patient representatives about the challenges involved in developing novel treatment approaches into a clinical trial.

I am now very excited to continue my oncology career in a consultant role that will allow me to move into the role of a Principal Investigator in early phase trials. I was successful in being appointed to a role at UCLH in Medical Lung Oncology and early phase trials, and I am looking forward to contributing to the continued development of the CRF and leading my own trials.

LATEST NEWS & PUBLICATIONS



Early Phase Cancer Trials Website in Development

We are happy to announce the development of the Early Phase Cancer Trials Programme at UCL & UCLH website.

The Early Phase Cancer Trials Programme brings scientists and clinicians together to deliver ground-breaking therapies for the treatment of cancer through clinical trials, with patients being at the heart of its research. The website will act as the central hub of information for clinicians, researchers, collaborators, patients, and the public. Our goal is to highlight our comprehensive list of early phase cancer trials open to recruitment and provide essential information on these trials. The website will be updated with helpful information alongside the latest news and events from the programme.

We are reviewing the beta-launch of the website and hope for a public launch in Q1 of 2022.

ORCA-2 Trial Presented at a Leading Medical Oncology Conference

We are pleased to highlight a presentation led by Dr. Martin Forster, Associate Professor at UCL and Consultant Medical Oncologist at UCLH, as lead author.

The e-poster was given at the European Society for Medical Oncology (ESMO) Congress on the 16th September 2021, looking at the ORCA-2 trial (A Phase I study of Olaparib in addition to Cisplatin-based concurrent chemo-radiotherapy for patients with high risk locally advanced Squamous Cell Carcinoma of the Head and Neck).

Dr. Forster conducted the study as Chief Investigator, with UCL as responsible party and sponsor, funded through the Cancer Research UK ECMC/ AstraZeneca Combinations Alliance. The trial incorporated a novel modified CRM design and began in September 2015, closing to recruitment in December 2019 having enrolled 16 patients from 3 UK hospitals.

The results show promising anti-tumour activity, but due to the excess acute toxicity seen this combination will not be proposed for future studies. The study does highlight the ability and success of academic lead industry collaborations, including complex studies with radical radiotherapy.

We would like to congratulate Dr. Forster on the achievement and all the team at UCLH & UCL who worked on this trial. The abstract can be viewed at the [ESMO Congress 2021 page](#).

Drug Developed at UCL Gains FDA Accelerated Approval

We are pleased to announce Zynlonta (Loncastuximab Tesirine) has received FDA Accelerated approval in the USA for the treatment of patients with refractory or relapsed Diffuse large B-Cell Lymphoma (DLBCL).

The drug, developed by Switzerland-based ADC Therapeutics (ADCT), was partially developed at University College London in the laboratory of Professor John Hartley, Professor of Cancer Studies at the UCL Cancer Institute, and his team. The approval came from data on the Phase I trial ADCT-402-101 (#NCT02669017) and the Phase II ADCT-402 (#NCT03589469).

The Phase I ADCT-402-101 trial was conducted at the UCLH CRF, with Dr. Kirit Ardeshta as Principal Investigator, and CRF Consultant Dr. William Townsend as Co-Investigator on the study. The trial at UCLH recruited an impressive 18 participants, making it one of the highest recruiting centres internationally. The Phase II study was later conducted at the UCLH Cancer Clinical Trials Unit (CCTU).

We would like to congratulate Professor John Hartley, Dr. Kirit Ardeshta, Dr. William Townsend and the teams at UCL Cancer Institute, UCLH Clinical Research Facility and the UCLH CCTU for all their work and this incredible achievement highlighting the bed-to-bedside approach of research.

You can read more about this announcement in the [CRUK news feature](#).