PORTFOLIO NEWSLETTER

MARCH 2021

NIHR University College London Hospital Clinical Research Facility Cancer Trials

INSIDE THIS ISSUE:

COVID-19 and Early Phase Cancer Trials at UCLH

During this difficult time we are trying to keep the early phase cancer trials program open to enrolment. The CRF is a geographically distinct unit to the main hospital and patients are treated in individual rooms as much as possible to minimize infection risk.

We therefore continue to welcome referrals; however due to the pressures at the front line, we are running at limited capacity and may not be able to take your patient immediately. Please liaise with the PI of the study you are considering referring to.

This newsletter provides you with details of the current ongoing cancer trials.

Dr. Rakesh Popat, Consultant Haematologist

Cancer Lead NIHR UCLH Clinical Research Facility

Spotlight on Research

Consultant Medical Oncologist & Associate Professor of Oncology UCL

This month we will highlight research conducted by Dr Mark Linch.
Mark Linch is an Associate Professor of Oncology at University College London (UCL) Cancer Institute where he leads the Urological Cancer Biology Group (UCBG). His work is focused on immunotherapy resistance in prostate and bladder cancers and how this can be overcome by manipulation of the tumour immune microenvironment.

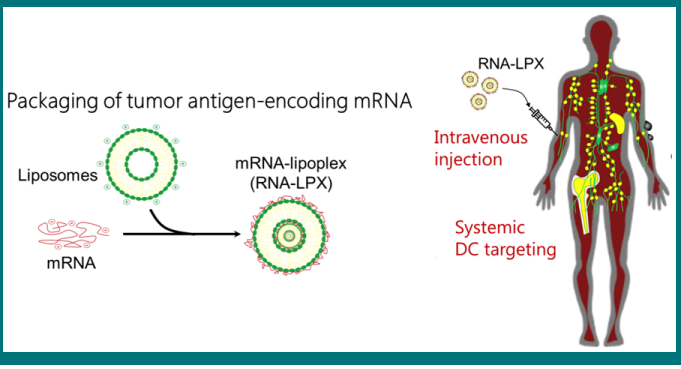
Immunotherapy has led to a step change in the management of many cancers, but the majority of patients with prostate and bladder cancer still don't respond. Tumours can evade the immune system by a multiplicity of mechanisms including physical and chemical barriers, decoy signals, and downregulating distinctive cancer markers (antigens). Dr Linch is exploring a number ways to circumvent this resistance including the use of vaccines, something that we are all becoming more familiar with given the current COVID-19 pandemic. Cancer vaccines prime the immune system to look for cancer antigens, attack the cancer cells and because the immune system has special cells for memory, hopefully continue to work long after the vaccine is given.

Pro-MERIT

This is a first in human multi-stage trial of BNT112, a prostate cancer antigen encoding mRNA vaccine, to evaluate the safety and preliminary efficacy (see Fig 1). The UCL/UCLH Cancer Research Facility is the global lead site for this study. In the first part, patients with metastatic castrate resistant prostate cancer that had received at least 1 previous therapy were given the prostate cancer vaccine, on a weekly basis for the first 6 doses and then 3-weekly. Following successful completion of this first part, we have just opened part 2. In part 2, we are testing the safety and efficacy of BNT112 in two additional scenarios 1) In combination with cemiplimab, a PD-1 inhibitor that helps to stimulate T-cells and 2) In patients with localised prostate cancer prior to undergoing prostatectomy (removal of the prostate). BNT112 was developed by BioNTech and following the start of the COVID-19 pandemic was modified, in collaboration with Pfizer, to generate BNT162b2 their hugely successful COVID-19 vaccine.

S-488210/S-488211

This was a single centre first in human study of a peptide cancer vaccine against antigens found on a number of cancers including bladder cancer. Patients were eligible if they had exhausted conventional treatment options. Patients received a subcutaneous injection on a weekly basis for the first 5-doses and then bi-weekly dosing up to 9 doses in total. S-488210/S-488211 was developed by Shionogi Ltd who are also testing a similar peptide vaccine in a late-stage clinical trial for COVID-19. Following the recent completion of the S-488210/S-488211 vaccine trial, UCL have secured a grant from Shionogi and AstraZeneca to run the DURANCE study, a UK multi-centre phase 2 trial of S-488210/S-488211 in combination with durvalumab (PD-L1 inhibitor that stimulates T-cells) in patients with non-muscle invasive localised bladder cancer who have previously failed BCG treatment. It is anticipated that this study will open to recruitment in June 2021.



For more information on research being led by Dr Mark Linch please see: https://www.ucl.ac.uk/cancer/research/department-oncology/urological-cancer-biology-group

Figure 1.
Packaging and delivery of the BNT112 prostate cancer mRNA vaccine. The mRNA that encodes 5 separate prostate cancer antigens are mixed with lipid spheres called liposomes and this mixture is injected into patients where is gets taken up by immune cells (Dendritic cell [DC]) and migrates to lymphoid organs (depicted in yellow). Here the prostate antigens are expressed on the surface of dendritic cells presenting them to T-cells, stimulating them and expanding a population of T-cells capable of killing the prostate cancer.

Latest News

UCLH CRF Fellows presented at European Conferences

We are pleased to highlight our UCLH Clinical Research Facility fellows presented at international conferences in March 2021. The project looked at the safety and efficacy of immune checkpoint inhibitors in cancer patients with pre-existing autoimmune disease.

Dr. Grisma Patel presented the findings as an e-poster at the ESMO Targeted Anticancer Therapies Congress (TAT 2021). The conference is known to offer a glimpse of the future of Phase I in oncology. Dr. Paramvir Sawhney presented an e-poster at the European Lung Cancer Virtual Congress (ELCC 2021). The abstract/e-poster looked at a subset of participants, investigating the safety and efficacy of immune checkpoint inhibitors in NSCLC patients with pre-existing autoimmune disease.

We would like to congratulate our fellows on their achievement. Dr. Sawhney's abstract can be viewed at ELCC and Dr. Patel's e-poster is available online at ESMO TAT.

How to refer a patient

By Post:
NIHR UCLH Clinical Research Facility,
University College London Hospitals NHS Foundation Trust, 4th Floor, 170 Tottenham Court Road,
London, W1T 7HA

By Telephone:
Reception: 020344 72929/72930
Reception Fax: 020344 72994

By Email*:
*When referring patients, ensure you use nhs.net emails. Patient identifiable data *should not* be sent to/via non-NHS email accounts.

Principal Investigator

Prof. John Bridgewater

Dr. Martin Forster

Prof. Daniel Hochhauser

Prof. Sam Janes

Dr. Mark Linch

Prof. Tim Meyer

Dr. Rowan Miller

Dr. Jenny O'Nions

Dr. Dionysis Papadatos-Pastos

Dr. Rakesh Popat

Dr. Rebecca Roylance

Dr. Beatrice Seddon

Dr. Heather Shaw

Dr. Sandra Strauss

Dr. William Townsend

Contents

As it appears in alphabetical order

UCLH Find a Study

To find more information on UCLH CRF Early Phase Cancer Clinical Trials visit the UCLH Find a Study database:

https://findastudy.uclh.nhs.uk/#/trial

Using the 'Study Name' and/or 'Local Project Reference' (LRP).

NIHR UCLH Clinical Research Facility
Cancer Trials Open to Recruitment

For more information on a trial, including eligibility criteria click the hyperlinked **Local Project Reference (LRP)** ID.

Breast

Study Acronym/ Full Title	LPR	PI	Drug Class/ Tumour Target
B-PRECISE-01 (MEN1611-01) Open-label, Multicentre, Phase Ib Dose-escalation Study of MENI6I 1, a P13K Inhibitor Combined with Trastuzumab ± Fulvestrant, in Subjects with PIK3CA Mutated HER2-positive Locally Recurrent Unresectable (advanced) or Metastatic Breast Cancer Progressed to Anti-HER2 Based Therapy.	120910	Dr. Rebecca Roylance	**P13K Inhibitor** PIK3CA Mutated HER2-positive Locally Recurrent Unresectable (advanced) or Metastatic Breast Cancer

Gynaecological

Study Acronym/ Full Title	LPR	PI	Drug Class/ Tumour Target
GCT1015-05 ENGOT innovaTV 205: A Phase 1b/2 Open-Label Trial of Tisotumab Vedotin (HuMax-TF-ADC) in Combination with Other Agents in Subjects with Recurrent or Stage IVB Cervical Cancer.	113569	Dr. Rowan Miller	**Antibody-Drug Conjugate (ADC) Targeting Tissue Factor (TF)** Recurrent or Stage IVB Cervical Cancer

Haematology

Study Acronym/ Full Title	LRP	PI	Drug Class/ Tumour Target
AML1001 A Phase 1, First in Human (FIH), Dose Escalation Study of JNJ -74856665 (dihydroorotate dehydrogenase [DHODH] Inhibitor) in Participants with Acute Myeloid Leukemia (AML) or Myelodysplastic Syndrome (MDS)	135994	Dr. Jenny O'Nions	**Dihydroorotate Dehydrogenase (DHODH) Inhibitor** Acute Myeloid Leukemia (AML) or Myelodysplastic Syndrome (MDS)
ASTX660 Phase 1-2 Study of the Safety, Pharmacokinetics, and Preliminary Activity of ASTX660 in Subjects with Advanced Solid Tumors and Lymphomas.	106548	Dr. William Townsend	**Dual Antagonist of Cellular Inhibitor of Apoptosis cIAP & XIAP** Relapsed T-Cell Lymphomas
BP41072 An Open-Label, Phase I Study To Evaluate The Safety, Pharmacokinetics And Preliminary Antitumor Activity Of Ro7227166 (A Cd19 Targeted 4-1bb Ligand) In Combination With Obinutuzumab And Incombination With Ro7082859 (Cd20-Tcb) Following A Pre-Treatment Dose Of Obinutuzumab Administered In Participants With Relapsed/ Refractory B-Cell Non-Hodgkin's Lymphoma.	129333	Dr. William Townsend	**Ro7227166 (CD19-directed 41BB ligand) + Obinutuzumab (anti-CD20 Monoclonal Antibody) or Glofitamab (CD3-CD20 T-Cell Bispecific Antibody)** Relapsed/Refractory B-Cell Non-Hodgkin's Lymphoma

Haematology (II)

Study Acronym/ Full Title	LRP	PI	Drug Class/ Tumour Target
CC-220-MM-001 A Phase 1B/2A Multicenter, Open-Label, Dose-Escalation Study to Determine the Maximum Tolerated Dose, Assess the Safety and Tolerability, Pharmacokinetics and Preliminary Efficacy of CC-220 Monotherapy and in Combination with Dexamethasone in Subjects with Relapsed and Refractory Multiple Myeloma.	16/0336	Dr. Rakesh Popat	**Cereblon E3 Ligase Modulator** Relapsed and Refractory Multiple Myeloma
CC-92480-MM-001 A Phase 1 Multicenter, Open-Label Study to Assess The Safety, Pharmacokinetics And Preliminary Efficacy of CC-92480 in Combination With Dexamethasone in Subjects With Relapsed And Refractory Multiple Myeloma.	18/0040	Dr. Rakesh Popat	**Cereblon E3 Ligase Modulator** Relapsed and Refractory Multiple Myeloma
CL1-65487-003 Phase I / II, open label, dose escalation part (phase I) followed by non-comparative expansion part (phase II), multicentre study, evaluating safety, pharmacokinetics and efficacy of S65487, a Bcl2 inhibitor combined with azacitidine in adult patients with previously untreated acute myeloid leukemia not eligible for intensive treatment.	136715	Dr. Jenny O'Nions	**BCL-2 Inhibitor** Previously Untreated Acute Myeloid Leukaemia, not eligible for Intensive Treatment
CO41942 Ph1b study of bispecifics with lenalidomide in relapsed/ refractory FL.	130416	Dr. William Townsend	**CD3-CD20 Bispecific Antibody** Relapsed or Refractory Follicular Lymphoma
DREAMM-6 A Phase I/II, Open-label, Dose Escalation and Expansion Study to Evaluate Safety, Tolerability, and Clinical Activity of the Antibody-Drug Conjugate GSK2857916 Administered in Combination with Lenalidomide Plus Dexamethasone (Treatment Arm A), or Bortezomib Plus Dexamethasone (Treatment Arm B) in Participants with Relapsed or Refractory Multiple Myeloma.	18/0571	Dr. Rakesh Popat	**Humanised Monoclonal Antibody (anti-BCMA)** Relapsed or Refractory Multiple Myeloma
EP0042-101 A Modular, Multipart, Multi-arm, Open-label, Phase I/IIa Study to Evaluate theSafety and Tolerability of EP0042 Alone and in Combination with Anti-cancerTreatments in Patients with Advanced Malignancies.	134892	Dr. Jenny O'Nions	**FLT3 inhibitor & Aurora Kinase Inhibitor** Acute Myeloid Leukaemia (AML) or Myelodysplastic Syndromes (MDS)
NVG111-101 NVG111-101: An open-label, phase 1/2, first in human study investigating the safety, tolerability, pharmacokinetics and efficacy of NVG-111 in subjects with relapsed/refractory chronic lymphocytic leukaemia and mantle cell lymphoma.	135715	Dr. William Townsend	**Receptor Tyrosine Kinase Like Orphan Like Receptor 1 (ROR1) Bispecific antibody** Relapsed or Refractory Multiple Myeloma
Teclistamab in Relapsed or Refractory Multiple Myeloma A Phase 1/2b, First-in-Human, Open-Label, Dose Escalation Study of Teclistamab, a Humanised BCMA x CD3 Bispecific Antibody, in Subjects with Relapsed or Refractory Multiple Myeloma.	134949	Dr. Rakesh Popat	**Humanised Bispecific Antibody (BCMA & CD3)** Relapsed or Refractory Multiple Myeloma

Hepatobiliary

Study Acronym/ Full Title	LPR	PI	Drug Class/ Target
ADP-0033-001 A Phase I Open Label Clinical Trial Evaluating the Safety and Anti-Tumor Activity of Autologous T Cells Expressing Enhanced TCRs Specific for Alpha Fetoprotein (AFP^{c332}T) in HLA -A2 Positive Subjects With Advanced Hepatocellular Carcinoma (HCC) or Other AFP Expressing Tumor Types.	17/0093	Prof. Tim Meyer	**T-Cell Therapy** Advanced Hepatocellular Carcinoma (HCC) or Other AFP Expressing Tumour Types

Lung

Study Acronym/ Full Title	LPR	PI	Drug Class/ Target
TACTICAL Targeted Stromal Cells Expressing TRAIL as a therapy for lung cancer.	14/0453	Prof. Sam Janes	**MSC-TRAIL with chemo-immunotherapy as first line therapy** Advanced Lung Cancer

Sarcoma

Study Acronym/ Full Title	LPR	PI	Drug Class/ Target
Afatinib in Chordoma A phase 2, single arm, European multi-center trial evaluating the efficacy of afatinib as first-line or later-line treatment in advanced Chordoma.	17/0146	Dr. Sandra Strauss	**EGFR Small Molecule Inhibitor** Advanced Chordoma
DCC-3014 A Multicenter Phase 1, Open-Label Study of DCC-3014 to Assess the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics in Patients with Advanced Tumors.	128373	Dr. Beatrice Seddon	**Tyrosine Kinase Inhibitor.** Cohort B only (Expansion Phase) — Tenosynovial Giant Cell Tumour (DTGCT)

Solid Tumours

Study Acronym/ Full Title	LPR	PI	Drug Class/ Target
AGI-134 A phase I/IIa, multicentre, open label study designed to evaluate the safety and tolerability of AGI-134 as monotherapy and in combination with pembrolizumab, in unresectable metastatic solid tumours.	104916	Dr. Martin Forster	**Anti-αGal** Unresectable Superficial Metastatic Melanoma or Squamous Cell Cancers
BLU-667 A Phase 1 Study of the Highly-selective RET Inhibitor, BLU-667, in Patients with Thyroid Cancer, Non-Small Cell Lung Cancer (NSCLC) and Other Advanced Solid Tumors.	17/0783	Dr. Martin Forster	**RET Inhibitor** Thyroid Cancer, NSCLC, Other RET-driven Advanced Solid Tumours
BT1718 A Cancer Research UK Phase I/IIa trial of BT1718, (A Bicycle drug conjugate), given intravenously in patients with advanced solid tumours.	100211	Dr Dionysios Papadatos-Pastos	**Bicycle Drug Conjugate** Advanced Solid Tumours

Solid Tumours (II)

Study Acronym/ Full Title	LRP	PI	Drug Class/ Target
Cancer Peptide Vaccine Open-label, phase 1 study of S-488210/S-488211 to evaluate the safety and tolerability in patients with unresectable re-current and/or metastatic solid tumor.	119614	Dr. Mark Linch	**5-peptide cancer vaccine** Unresectable recurrent and/or Metastatic Solid Tumour
D9170C00001 A Phase I/IIa, Open-Label Study to Assess the Safety, Tolera-bility, Pharmacokinetics and Preliminary Efficacy of Ascend-ing Doses of AZD7648 Monotherapy or in Combination with either Cytotoxic Chemotherapies or Novel Anti-Cancer Agents in Patients with Advanced Malignancies	18/0580	Dr. Rowan Miller	**DNA-PK Inhibitor** Advanced Malignancies
FIGHT-207 A Phase 2, Open-Label, Single-Arm, Multicenter Study to Evaluate the Efficacy and Safety of Pemigatinib in Partici-pants With Previously Treated Locally Advanced/Metastatic or Surgically Unresectable Solid Tumor Malignancies Harbor-ing Activating FGFR Mutations or Translocations.	124183	Prof. John Bridgewater	**FGFR Inhibitor** Advanced/Metastatic or Surgically Unrespectable Solid Tumour Malignancies Harbouring Activating FGFR Mutations or Translocations
Garnet A Phase 1 Dose Escalation and Cohort Expansion Study of TSR-042, an anti-PD-1 Monoclonal Antibody, in Patients with Advanced Solid Tumors.	16/0355	Dr. Rowan Miller	**Anti PD-L1 Monoclonal Antibody** Cohorts Open: *Part 2B: Cohort A1* dMMR/MSI-H en-dometrial cancer *Part 2B: Cohort F* non-endometrial dMMR/MSI-H & POLE-Mut cancers
LOXO-TRK-15002 (Navigate) LOXO-TRK-15002: A Phase II Basket Study of the Oral TRK Inhibitor LOXO-101 in Subjects with NTRK Fusion-Positive Tumors.	16/0077	Dr. Martin Forster	**TRK Inhibitor** NTRK Fusion-Positive Tumours
MOv18 A Cancer Research UK Phase I study of MOv18 IgE, a first in class chimeric IgE antibody against folate receptor-α, in pa-tients with advanced solid tumours.	17/0121	Dr. Rowan Miller	**IgE Antibody against Folate Receptor-α** Advanced solid tumours
Starpharma CTX A phase 1/2 dose-escalation study to evaluate the safety, tolerability, pharmacokinetics and preliminary efficacy of CTX-SPL9111 (a cabazitaxel (CTX)-dendrimer conjugate) in patients with advanced solid tumours.	18/0016	Dr. Martin Forster	**Drug-Dendrimer Conjugate** Advanced solid tumours
Starpharma DTX A phase 1/2 dose-escalation study to evaluate the safety, tolerability, pharmacokinetics and preliminary efficacy of DTX-SPL8783 (a docetaxel (DTX)-dendrimer conjugate) as monotherapy in patients with advanced solid tumours or in combination with nintedanib in patients with non-small cell lung cancer (NSCLC).	17/0585	Dr. Martin Forster	**Drug-Dendrimer Conjugate (Tubulin Polymerase Inhibitor)** Advanced solid tumours Or non-small cell lung cancer (NSCLC)

Solid Tumours (III)

Study Acronym/ Full Title	LRP	PI	Drug Class/ Target
TACTI-002 (Two ACTive Immunotherapeutics): A multicenter, open label, phase II study in patients with previously untreated unresectable or metastatic non-small cell lung cancer (NSCLC), or recurrent PD-X refractory NSCLC or with recurrent or metastatic squamous head and neck cancer (HNSCC) receiving the soluble LAG-3 fusion protein eftilagimod alpha (IMP321) in combination with pembrolizumab (PD-1 antagonist).	18/0560	Dr. Martin Forster	**APC Activator & Anti-PD-1 Monoclonal Antibody** Previously untreated unresectable or metastatic non-small cell lung cancer (NSCLC), Or recurrent PD-X refractory NSCLC Or with recurrent or metastatic squamous head and neck cancer (HNSCC)

Urology

Study Acronym/ Full Title	LRP	PI	Drug Class/ Target
BXCL701 A Phase 1b/2 Study of BXCL701, a Small Molecule Inhibitor of Dipeptidyl Peptidases (DPP), Administered in Combination with the Anti-Programmed Cell Death 1(PD-1) Monoclonal Antibody Pembrolizumab (PEMBRO; Keytruda®) in Patients with Small Cell Neuroendocrine Prostate Cancer (SCNC; NEPC).	113103	Dr. Mark Linch	**Dipeptidyl Peptidases (DPP) Inhibit & Anti-PD-1 Monoclonal Antibody** Small Cell Neuroendocrine Prostate Cancer (SCNC; NEPC)
CORT125281 Phase 1/2 Dose-Escalation and Expansion Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of CORT125281 with Enzalutamide in Patients with Metastatic Castration-Resistant Prostate Cancer.	18/0135	Dr. Mark Linch	**Glucocorticoid Receptor (GR) Antagonist** Metastatic Castration-Resistant Prostate Cancer
FIDES-02 An open-label multi-cohort Phase 1/2 study of derazantinib and atezolizumab in patients with urothelial cancer expressing activating molecular FGFR aberrations (FIDES-02)	124615	Dr. Mark Linch	**FGFR Inhibitor & Anti PD-L1 Monoclonal Antibody** Advanced Urothelial cancer expressing FGFR genetic aberrations. *Substudy 4:* Urothelial progression - FGFR-inhibitor resistant (>12 weeks) & previous chemo and CPI
PRO-MERIT (Prostate Cancer Messenger RNA Immunotherapy): A first-in-human, dose titration and expansion trial to evaluate safety, immunogenicity and preliminary efficacy of W_pro1 in patients with metastatic castration resistant prostate cancer and W_pro1 in combination with cemiplimab and/or goserelin acetate in patients with high-risk, localized prostate cancer.	122815	Dr. Mark Linch	**W_pro1 mRNA Cancer Vaccine** *Group 1:* mCRPC that have exhausted conventional treatment *Group 2:* High-risk, Localized Prostate Cancer prior to Prostatectomy