PORTFOLIO NEWSLETTER

OCTOBER 2021

NIHR University College London Hospital Clinical Research Facility Cancer Trials

INSIDE THIS ISSUE:

COVID-19 and Early Phase Cancer Trials at UCLH

Whilst COVID-19 restrictions have eased across the country, we're very much aware that some cancer patients remain vulnerable to COVID-19 even if they have been vaccinated.

As a result we are continuing to take full precautions for the safety of our patients and staff. Our early phase clinical trials programme is fully open and we are happy to take referrals, please contact the PI for the study of interest to gauge timelines for enrolment. The pandemic has led to delays in a number of trials opening; however over the next few months we hope to open a significant number of new cancer trials.

Thank you for your patience and support in performing local blood/ COVID tests during this exceptional time. We're looking forward to getting back to having a full portfolio of studies open.

Dr. Rakesh Popat, Consultant Haematologist

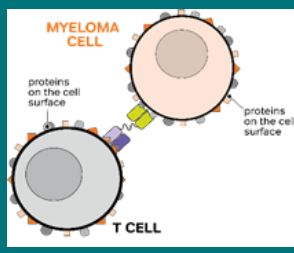
Cancer Lead NIHR UCLH Clinical Research Facility

Spotlight on Research

Consultant Haematologist

This month we will highlight research conducted by Dr. Rakesh Popat.
Rakesh Popat is a consultant haematologist at UCLH and honorary associate professor at University College London with specialist expertise in multiple myeloma. He is the Cancer Lead at the NIHR UCLH Clinical Research Facility.

Myeloma Early Phase Clinical Trials



There continues to be substantial progress with new therapies for patients with relapsed myeloma. Immunotherapies appear to make a significant impact, resulting in high response and MRD negativity rates. T-Cell engagers are antibodies that link T-Cells (via CD3) to a myeloma antigen leading to cell death. Their mechanism is like CAR-T cells in that they direct T-Cells to myeloma cells. However these are "off-the-shelf" products without a need for bridging therapy whilst awaiting manufacturing. Additionally, the toxicity profile of cytokine release syndrome and neurotoxicity is generally more predictable and better tolerated due to the short T-Cell activations.
Although as a result, these agents need to be given regularly in order to maintain a response.
We currently have 2 T-Cell engager trials open, targeting BCMA or GPRC5D. This allows us to offer a more personalised choice of treatment according to the patient's previous history.

MMY1004: MajesTec 2
This is a Phase I trial of Teclistamab (T-Cell engager targeting BCMA) in combination with SoC regimens. The current recruiting cohorts are below, but other cohorts may open in the future:
Cohort B2: Teclistamab plus Daratumumab, Lenalidomide and Bortezomib for patients that have had 1-2 prior lines.
Cohort E: Teclistamab plus Daratumumab and Lenalidomide for patients that have had 1-3 prior lines including a PI and IMiD.

BP42233 (GRACE):
This is a First-in-Human trial of a T-Cell engager against GPR5CD, and therefore provides an alternative target to BCMA. This trial is in the dose finding phase; however response have already been observed. The main adverse events are CRS, neurotoxicity, skin rashes and nail changes due to the expression pattern of GPRC5D.

In the Pipeline:

Magnetismm-9
This is a Phase I trial investigating different step-up doses to minimise adverse events with Elranatamab (a BCMA targeting T-Cell engager) for patients that are triple class (PI, IMiD and CD38 Mab) refractory. Prior BCMA therapy is permitted.

ProMMise
This is a Phase I UK Myeloma Research Alliance NIHR portfolio study of Belantamab Mafodotin (BCMA Antibody Drug Conjugate) as monotherapy, in combination with Cyclophosphamide plus Dexamethasone or with Ixazomib, Cyclophosphamide and Dexamethasone for patients with relapsed Myeloma that have had 1-3 prior lines.

How to Refer:

You can refer a patient by email or by letter as per normal routes. However, as these are Phase I trials, there will be a short delay in getting pa-tients on. This is as we need to request a slot from the Sponsor for safety purposes, as well as ensuring that we have capacity locally to deliver these complex treatments. I therefore advocate an early referral so enrolment can be planned.
In general patients will need to have a measurable paraprotein or serum free light chains, have reasonable bone marrow function (not transfusion dependent or requiring GCSF to support neutrophils) and have a GFR of at least 30ml/min. Autoimmune and CNS disorders are typically excluded for T-Cell engager trials.

Latest News

New CRF Early Phase Cancer Trial Consultants

The have been three new consultant appointments in Thoracic Oncology, Gastro-intestinal Oncology and Uro-Oncology.
These consultants will have dedicated sessions for early phase cancer trials and we look forward to them expanding their respective therapeutic areas in the next few months.

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 Investigators

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. Elisavet Papadimitraki

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

Gastro-Intestinal

Study Acronym/ Full Title	LPR	PI	Drug Class/ Tumour Target
FIDES-03 (DZB-CS-202) A Phase 1b/2 study of derazantinib as monotherapy and combination therapy with paclitaxel, ramucirumab or atezolizumab in patients with HER2-negative gastric adenocarcinoma harboring FGFR genetic aberrations (FIDES-03)	133317	Prof. John Bridgewater	**FGFR Inhibitor** Stomach or Gastro-esophageal Adenocarcinoma harbouring FGFR2 genetic aberrations

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)
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
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

Haematology (II)

Study Acronym/ Full Title	LRP	PI	Drug Class/ Tumour Target
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
CCS1477-02 An open-label Phase I/IIa study to evaluate the safety and efficacy of CCS1477 as monotherapy in patients with advanced haematological malignancies	121140	Dr. Jenny O'Nions	**P300/CBP Inhibitor** Advanced Haematological Malignancies
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)
GRACE (BP42233) An Open-Label, Multicenter, Phase I Study Evaluating The Safety And Pharmacokinetics Of Escalating Doses Of RO7425781 In Participants With Relapsed Or Refractory Multiple Myeloma	137532	Dr. Rakesh Popat	**T-Cell Engager against GPR5CD** Relapsed or Refractory Multiple Myeloma
MajesTEC-2 (64007957MMY1004) A Multi-arm Phase 1b Study of Teclistamab With Other Anti-cancer Therapies in Participants with Multiple Myeloma	137973	Dr. Rakesh Popat	**T-Cell Engager targeting BCMA** Multiple Myeloma
NP40126 A Phase 1b Study Evaluating Ro7082859 In Combination With Rituximab (R) Or Obinutuzumab (G) Plus Cyclophosphamide, Doxorubicin, Vincristine, And Prednisone (CHOP) In Participants With Relapsed Refractory Follicular Lymphoma (R/R Fl) Or In Participants With Untreated Diffuse Large B-Cell Lymphoma	17/0859	Dr. William Townsend	**Glofitamab (CD3-CD20 T-Cell Bispecific Antibody)** Relapsed Refractory Follicular Lymphoma Or Untreated Diffuse Large B-Cell Lymphoma

Haematology (III)

Study Acronym/ Full Title	LRP	PI	Drug Class/ Tumour Target
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 Chronic Lymphocytic Leukaemia & Mantle Cell Lymphoma
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
TAS-120 A Dose Finding Phase I Study of TAS-120 in Patients with Advanced Solid Tumors With or Without Fibroblast Growth Factor/Receptor (FGF/FGFR)-Related Abnormalities Followed by a Phase 2 Study in Patients With Advanced Solid Tumors FGF/FGFR-Related Abnormalities	17/0474	Prof. John Bridgewater	**FGFR2 Inhibitor** Cholangiocarcinoma harbouring FGFR2 Gene Fusion

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
ImmunoSARC2(GEIS-52) Phase I - II trial of sunitinib plus nivolumab after standard treatment in advanced soft tissue and bone sarcomas	119516	Dr. Sandra Strauss	**PD-1 inhibiting IgG4 Monoclonal Antibody and RTK Inhibitor** Advanced Soft Tissue & Bone Sarcomas

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
BICYCLE Study: BT171/8 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
D9170C00001 A Phase I/IIa, Open-Label Study to Assess the Safety, Tolerability, Pharmacokinetics and Preliminary Efficacy of Ascending 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
IMC-F106C-101 A Phase 1/2 First-in-Human Study of the Safety and Efficacy of IMC-F106C as a Single Agent and in Combination with Checkpoint Inhibitors in HLA-A*02:01-Positive Participants with Advanced PRAME-Positive Cancers	130728	Dr. Heather Shaw	**PRAME Immune-Mobilizing T-Cell Receptor against Cancer** HLA-A*02:01-Positive Participants with Advanced PRAME-Positive Cancers
LOXO-TRK-15002 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 patients with advanced solid tumours.	17/0121	Dr. Rowan Miller	**IgE Antibody against Folate Receptor-α** Advanced Solid Tumours
MULTI-31 An open-label, Phase II, platform trial evaluating safety and efficacy of multiple BI 754091 anti-PD-1 based combination regimens in PD-(L)1 naïve and PD-(L)1 pretreated patient populations with advanced and/or metastatic solid tumours who have had at least one line of systemic therapy	123071	Dr. Martin Forster	**Anti-PD-L1 Based Combination Regime** PD-(L)1 naïve & PD-(L)1 pre-treated patients with advanced and/or metastatic solid tumours, had at least one line of systemic therapy.
PATRIOT A Phase I Study to assess the Tolerability, Safety and Biological Effects of a Specific Ataxia Telangiectasia and Rad3Related (ATR) Inhibitor (AZD6738) as a Single Agent and in Combination with Palliative Radiation Therapy in Patients with Solid Tumours	14/0342	Dr. Martin Forster	**ATR Serine/Threonine Protein Kinase Inhibitor** Solid Tumours

Solid Tumours (II)

Study Acronym/ Full Title	LPR	PI	Drug Class/ Target
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)
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)
FIDES-02 (DZB-CS-201) 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 Anti-body** 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