University College London Hospitals NHS
NHS Foundation Trust

NIHR/Wellcome UCLH Clinical Research Facility

Cancer Trials Portfolio

September 2015

NHS National Institute for Health Research

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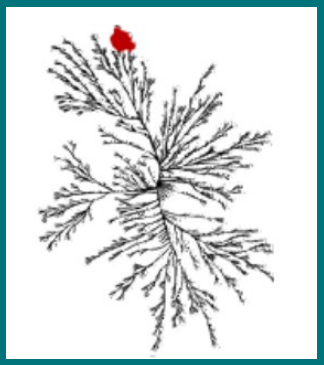
New Trial for Liver Cancer

This month we will open a first-in-man trial of BLU-554, an inhibitor of FGFR4 for advanced hepatocellular cancer and biliary tract cancer.

Hepatocellular cancer is the second most common cause of cancer death worldwide yet only one drug - sorafenib- has been licenced for treatment of advanced disease. There are no predictive biomarkers and genetic analysis of HCC has revealed few tractable targets. However a subset of HCC harbour amplifications of FGF19 leading to increased expression and activation of its receptor FGFR4. Preclinical studies have provided a compelling rational to investigate FGFR4 inhibition in patients and Blueprint Medicines Corporation have developed a potent, highly selective and irreversible inhibitor of FGFR4. UCLH has been selected to undertake the first-in-man dose escalation study which is now open to patients with advanced HCC progressing on, or intolerant to sorafenib.

Once the recommended dose is defined, this drug will be tested in patients with HCC or cholangiocarcinoma with overexpression of FGF19. This will be one of the first HCC trials that is enriched based on target expression.



Professor Tim Meyer
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Principal Investigator
Consultant Medical Oncologist

For further details and eligibility see ClinicalTrials.gov identifier: NCT02508467.

How to refer a patient

By post:

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Contents

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Brain

Drug Class / PI / Status	Description
Focal Adhesion Kinase Inhibitor PI: Dr Paul Mulholland Status: Open to recruitment	A Phase 1 Open label Dose escalation study of the focal adhesion kinase inhibitor, GSK2256098, in subjects with solid tumours

Gastro-Intestinal

Drug Class / PI / Status	Description
Adoptive T-cell therapy: NY-ESO-1 T -cells PI: Prof Daniel Hochhauser and Dr Emma Morris Status: In set-up	NY-ESO-1 Targeted T Cells in Advanced Oesophagogastric Cancer
First in class nucleotide analogue (ProTide) PI: Dr John Bridgewater Status: In set-up	A phase Ib, multi-centre, open-label study of a first-in-class nucleotide analogue Acelarin (NUC-1031) in combination with cisplatin in patients with locally advanced/metastatic biliary tract cancers
Antibody Drug Conjugate (ADC) PI: Dr John Bridgewater Status: Open to recruitment	A Phase 2 Trial of MLN0264 in Previously Treated Patients With Advanced or Metastatic Pancreatic Adenocarcinoma Expressing Guanylyl Cyclase C (GCC)
Anti-VEGF PI: Dr John Bridgewater Status: Open to recruitment	A phase I/II dose finding study evaluating the safety and tolerabilty of Capecitabine and Afilbercept in patients with unresectable metastatic colorectal cancer deemed unsuitable for double/ triplet chemotherapy
Stratified –multi-agent PI: Dr John Bridgewater Status: Open to recruitment	FOCUS-4: Molecular selection of therapy in metastatic colorectal cancer: a molecularly stratified randomised controlled trial programme
Inhibitor of EGFR, ERBB2 and ERBB3 PI: Prof Daniel Hochhauser Status: Open to recruitment	AZD8931, an inhibitor of EGFR, ERBB2 and ERBB3 signalling, in combination with FOLFIRI: A Phase I/II study to determine the importance of schedule and activity in colorectal cancer

Gynaecological

Drug Class / PI / Status	Description
WEE1 Kinase inhibitor PI: Prof Jonathan Ledermann Status: In set-up	A multi-centre, randomised, phase II study of AZD1775 plus chemotherapy versus chemotherapy alone in patients with platinum-resistant TP53-mutated epithelial ovarian, fallopian tube, or primary peritoneal cancer
Synthetic alkylating agent PI: Dr Martin Forster Status: Open to recruitment (relapsed endometrial cancer only)	Phase I Multicenter, Open-label, Clinical and Pharmacokinetic Study of PM01183 in Combination with Doxorubicin in Non-heavily Pretreated Patients with Selected Advanced Solid Tumors

Haematology

Drug Class / PI / Status	Description
Bcl2 inhibitor PI: Dr Rakesh Popat Status: In set-up	Phase I dose-escalation study of oral administration of the selective Bcl2 inhibitor S 55746 in patients with refractory or relapsed Chronic Lymphocytic Leukaemia and B-Cell Non-Hodgkin Lymphoma
P13K inhibitor + proteasome inhibitor PI: Dr Rakesh Popat Status: In set-up	Phase 1B Study of buparlisib with Bortezomib in Defined Genetic Subgroups of Patients with Relapsed or Refractory Multiple Myeloma
SYK inhibitor PI: Dr Rakesh Popat Status: In set-up	An Open-Label, Dose Escalation, Phase 1, First-in-Human Study of TAK-659 in Adult Patients with Advanced Solid Tumor and Lymphoma Malignancies
HDAC inhibitor + proteasome inhibitor PI: Dr Rakesh Popat Status: In set-up	Phase I/II study to determine the maximum tolerated dose and activity of the combination of romidepsin and carfilzomib in relapsed or refractory peripheral T-cell lymphoma
LSD1/ KDM1A inhibitor PI: Dr Rakesh Popat Status: Open to recruitment	A phase I study of the Human Pharmacokinetics and Safety of ORY-1001
P13K and mTOR inhibitor PI: Dr Rakesh Popat Status: Open to recruitment	Phase I study of oral PQR309 in Patients with Relapsed or Refractory Lymphomas

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Haematology *continued*

Drug Class / PI / Status	Description
JAK inhibitor + P13K inhibitor PI: Dr Rakesh Popat Status: Open to recruitment	A phase Ib, open-label, multi-center, two-arm, dose-finding study to assess the safety and efficacy of the oral combination of Ruxolitinib (INC424) and BKM120 in patients with primary myelofibrosis (PMF), postpolycythemia vera-myelofibrosis (PPV-MF), or postessential thrombocythemia-myelofibrosis (PET-MF)
VTD associated with Inhibitor (DACi) PI: Dr Rakesh Popat Status: Open to recruitment	A Phase I/IIa trial of VTD-panobinostat treatment and panobinostat maintenance in relapsed and relapsed/refractory multiple myeloma patients
HDACi PI: Dr Rakesh Popat Status: Open to recruitment	A Phase I/IIa, Dose-Escalation, Study of CHR-3996 in Combination with Tosedostat in Participants with Relapsed, Refractory Multiple Myeloma
Humanized IgG1 antibody drug conjugate (ADC) PI: Dr Rakesh Popat Status: Open to recruitment	A Phase I Open-label, dose escalation study to investigate the safety, pharmocokinetics, pharmacodynamics, immunogenicity and clinical activity of the antibody drug conjugate GSK2857916 in subjects with relapsed/refractory multiple myeloma and other advanced hematologic malignancies expressing BCMA
IL3-receptor PI: Dr Rakesh Popat Status: Open to recruitment	FiM Anti-IL-3Ra (CD123) mAb; fully human IgG1 for patients with previously untreated AML, relapsed/refractory AML, relapsed/refractory MDS or MDS who are not candidates to receive a hypomethylating agent

Head and Neck

Drug Class / PI / Status	Description
P13K inhibitor PI: Dr Martin Forster Status: in set-up	MLN1117: A Phase 1b/Adaptive Phase 2 Study of Docetaxel with or Without MLN1117 in Patients With Locally Advanced or Metastatic Non-small Cell Lung Cancer
PARP-1 inhibitor PI: Dr Martin Forster Status: in set-up	A phase I study of olaparib in addition to cisplatin-based concurrent chemoradiotherapy for patients with high risk locally advanced squamous cell carcinoma of the head and neck (HNSCC)
IgG1 monoclonal antibody PI: Dr Martin Forster Status: Open to recruitment	An open-label, phase 1b safety evaluation of patritumab (u3-1287) in combination with cetuximab plus platinum-containing therapy in subjects with recurrent or metastatic squamous cell carcinoma of the head and neck

Hepatobiliary

Drug Class / PI / Status	Description
FGFR4 inhibitor PI: Prof Tim Meyer Status: In set-up	A Phase 1 Study to Assess the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics, and Preliminary Efficacy of BLU-554 in Patients with Hepatocellular Carcinoma and Cholangiocarcinoma
Small activating RNA (saRNA) PI: Prof Tim Meyer Status: In set-up	Phase 1 clinical study with RNA oligonucleotide drug MTL-CEBPA to investigate its safety and tolerability and to ascertain whether MTL-CEBPA mediated up-regulation of CEBPA gene expression is associated with increase in serum albumin in patients with advanced hepatocellular carcinoma or patients presenting with secondary liver tumours derived from extra hepatic primary cancer types.
HDACi PI: Prof Tim Meyer Status: Open to recruitment	A Phase I/II dose escalation trial of HDAC inhibitor tefinostat (CHR- 2845) for cancer associated inflammation in hepatocellular carcinoma

Neuroendocrine

Drug Class / PI / Status	Description
Receptor Tyrosine Kinase PI: Dr Chrissie Thirlwell Status: Open to recruitment	A phase I trial of vandetanib combined with 131I-mIBG radiotherapy in patients with neuroendocrine tumours, advanced phaeochromocytoma and paraganglioma

Solid Tumours

Drug Class / PI / Status	Description
Synthetic alkylating agent PI: Dr Rebecca Kristeleit Status: In set-up	A multi-centre phase II clinical trial of Lurbinectedin (PM01183) in selected advanced solid tumours
Receptor tyrosine kinase PI: Prof Tim Meyer Status: In set-up	An open-label, phase 2 study of Neratinib in patients with solid tumours with somatic human epidermal growth factor receptor (EGFR, HER2, HER3) mutations or EGFR gene amplification
mTOR kinase inhibitor PI: Dr Martin Forster Status: In set-up	A Phase Ib/IIa study of AZD2014 in combination with Selumetinib in patients with advanced cancers
IgG4 anti-PD-1 monoclonal antibody PI: Prof Tim Meyer Status: In set-up	Non-Comparative, Two-Cohort, Single-Arm, Open-Label, Phase 1/2 Study of Nivolumab (BMS-936558) in Subjects with Virus-Positive and Virus-Negative Solid Tumors

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Solid Tumours *continued*	
Drug Class / PI / Status	**Description**
Immunotherapeutic peptide PI: Dr Rebecca Kristeleit Status: Open to recruitment	A phase I, open-label, multi-centre, multi-dose, dose escalation study of LTX-315 in patients with transdermally accessible tumours
PARP inhibitor (PARP-1, -2, -3) PI: Dr Rebecca Kristeleit Status: Open to recruitment	A Phase I multi-centre trial of the Combination of olaparib (PARP inhibitor) and AZD5363 (AKT inhibitor) in patients with advanced solid tumours
Microtubule inhibitor PI: Dr Rebecca Kristeleit Status: Open to recruitment	An open-label Phase 1/2a study of oral BAL101553 in adult patients with advanced solid tumors
Synthetic alkylating agent PI: Dr Martin Forster Status: Open to recruitment	Phase I multicentre, open-label, clinical and pharmacokinetic study of Lurbinectedin (PM01183) in combination with Cisplatin in patients with advanced solid tumours
IV microtubule inhibitor PI: Dr Rebecca Kristeleit Status: Open to recruitment (Pancreas, gastric, NSCLC, Breast only)	An Open-Label Phase I/IIa Study of Intravenous BAL101553 in Adult Patients with Advanced Solid Tumours
PARPi PI: Dr Rebecca Kristeleit Status: Open to recruitment	An Open-label, Non-randomised, Multicentre, Comparative, Phase I Study to Determine the Pharmacokinetics, Safety and Tolerability of Olaparib following a Single Oral 300 mg Dose to Patients with Advanced Solid Tumours and Normal Hepatic Function or Mild or Moderate Hepatic Impairment
ATR kinase inhibitor PI: Dr Martin Forster Status: Open to recruitment	A Phase I study to assess the tolerability, safety and biological effects of a specific ataxia telangiectasia and Rad3-Related (ATR) inhibitor (AZD6738) as a single agent and in combination with palliative radiation therapy in patients with solid tumours
P13K and mTOR inhibitor + chemotherapy PI: Dr Rebecca Kristeleit Status: Open to recruitment (Triple negative breast, NSCLC and Bladder only)	A Multi-Arm Safety and Tolerability Study of investigational medication in Combination with Other Anti-Tumour Agents
PARPi PI: Dr Rebecca Kristeleit	A Phase I/II, Open-Label, Safety, Pharmacokinetic, and Preliminary Efficacy Study of Oral Rucaparib in Patients with gBRCA Mutation Ovarian Cancer or Other Solid Tumor

Urology	
Drug Class / PI / Status	**Description**
n/a PI: Mr Hashim Ahmed Status: Open to recruitment	A Single Centre, Open Label, Phase IIa Study, Evaluating the Safety and Tolerability of Targeted Intra-prostatic Administration of PRX302 to Treat Men with Histologically Proven, Clinically Significant, Localised, Low to Intermediate Risk Prostate Cancer that is Associated with an MRI Lesion
n/a PI: Mr Hashim Ahmed Status: Open to recruitment	Radiofrequency Ablation Focal Treatment A Prospective Development Study evaluating Focal Therapy using EncageTM coiled bipolar radiofrequency ablation in Men with Localised Prostate Cancer
n/a PI: Mr Hashim Ahmed Status: Open to recruitment	Prostate Cancer Genomic Heterogeneity
n/a PI: Mr Hashim Ahmed Status: Open to recruitment	An evaluation of a novel imaging based complex diagnostic and therapeutic pathway intervention for men who fail radiotherapy for prostate cancer
n/a PI: Prof Mark Emberton Status: Open to recruitment	Focal therapy for localised prostate cancer using Irreversible Electroporation
n/a PI: Prof Mark Emberton Status: Open to recruitment	A Multicentre Prospective Single Arm Intervention Trial Evaluating Focal Therapy using High Intensity Focused Ultrasound (Sonablate 500) for Localised Prostate Cancer
Anti-androgen 10-amino acid peptide PI: Dr Rebecca Kristeleit Status: Open to recruitment (Prostate only)	A Phase I/II, Dose Escalation study to assess the safety and tolerability of VAL201 in patients with locally advanced or metastatic prostate cancer and other advanced solid tumours
n/a PI: Prof Mark Emberton Status: Open to recruitment	Evaluation of Multi-Parametric Magnetic Resonance Imaging in the Diagnosis and Characterisation of Prostate Cancer

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