ECMC Trials

The ECMCs trials listed below are looking for help in speeding up patient recruitment through referrals and/or opening at additional sites.
Please contact the Centre directly if you can help.
Please note that the trial information detailed below has been provided by ECMCs and to the best of our knowledge was up to date when this document was produced.
If you would like to have a trial included in this list please contact the ECMC Secretariat: ecmcadmin@cancer.org.uk

Study name and Contact	Cancer type	Inclusion and Exclusion summary	# of patients needed	Sites
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 Dr Martin Forster UCL **m.forster@ucl.ac.uk**	Solid Tumours	Inclusion Criteria: 1. Diagnosis of histologically or cytologically documented solid tumour refractory to conventional treatment, or for which no conventional therapy exists or is declined by the patient 2. Parts B and C only: documented disease progression prior to study entry and measurable disease by RECIST 1.1 within 4 weeks of study entry 3. p53 pathway abnormality defined on analysis of tumour material (for part B only). 4. Evidence of measurable or evaluable disease by RECIST 1.1 5. All acute toxic effects of any prior chemotherapy or surgical procedures must have resolved to Common Terminology Criteria for Adverse Events (CTCAE, Version 4) Grade ≤1. Surgery must have occurred at least 14 days prior to study enrolment. 6. Age must be 18 years or over. 7. ECOG performance status 0-1 (part A); 0-2 (parts B and C) 8. Life expectancy of at least 3 months. 9. Patients must have normal organ and bone marrow function measured within 7 days prior to administration of study treatment as defined below: • Haemoglobin ≥9.0 g/dL • Absolute neutrophil count (ANC) ≥ 1.5 x 10^9/L • White blood cells (WBC) > 3x10^9/L • Platelet count ≥ 100 x 10^9/L	3-42 (Part A) 12- 36 (Part B) 72 (Part C)	Royal Marsden Chelsea and Sutton, University College London Hospitals, Guys and St Thomas's

Study name and Contact	Cancer type	Inclusion and Exclusion summary	# of patients needed	Sites

- Albumin >30g/L
- AST and ALT <3 times ULN
- Total bilirubin <1.5 times ULN
-
- PT/APTT (<1.5 x upper limit of normal)
- INR < 1.5 and no other evidence of impaired hepatic synthetic function
- Glomerular filtration rate (GFR) >50mL/min, as assessed using the standard methodology at the investigating centre (i.e. Cockroft-Gault, MDRD or CKD-EPI formulae, EDTA clearance or 24 hour urine collection)
- Serum creatinine <1.5 times ULN
- Negative serum pregnancy test for females of childbearing potential

10. Signed informed consent indicating that the subject is aware of the neoplastic nature of their disease and have been informed of the procedures to be followed, the experimental nature of the therapy, alternatives, potential benefits, side effects, risks, and discomforts.
11. Willing and able to comply with scheduled visits, tissue sampling, treatment plan, and laboratory tests.
12. Able to swallow, absorb and retain oral medication.

Part B only: archival tumour material available for analysis; tumour site amenable to fresh biopsy (clinical or radiologically-guided)

Exclusion Criteria:

1. Therapy with any other investigational medical product (IMP) concurrently or within 28 days prior to signing of consent.
2. Investigational medicinal products, endocrine therapy, immunotherapy or chemotherapy during the previous four weeks (six weeks for nitrosoureas, mitomycin-C) before treatment.
3. Receiving, or having received, concomitant medications, herbal supplements

Study name and Contact	Cancer type	Inclusion and Exclusion summary	# of patients needed	Sites
		and/or foods that significantly modulate CYP3A4 or P-gp activity (wash out periods of two weeks, but three weeks for St. John's Wort). Note these include common azole antifungals, macrolide antibiotics and other medications listed in 7.6.1 and 7.6.2. 4. Pregnant or breast-feeding women. 5. Ability to become pregnant (or already pregnant or lactating). However, those female patients who have a negative serum or urine pregnancy test before enrolment and agree to use two highly effective forms of contraception (oral, injected or implanted hormonal contraception and condom, have an intra-uterine device and condom, diaphragm with spermicidal gel and condom) for four weeks before entering the trial, during the trial and for six months afterwards are considered eligible. Non-child-bearing potential is confirmed by fulfilling one of the following criteria at screening: a. Post-menopausal (defined as aged more than 50 years and amenorrhoeic for at least 12 months following cessation of all exogenous hormonal treatments) b. Documentation of irreversible surgical sterilisation by hysterectomy, bilateral oophorectomy or bilateral salpingectomy but not tubal ligation c. Amenorrhoeic for 12 months and serum follicle-stimulating hormone (FSH), luteinizing hormone (LH) and plasma oestradiol levels in the postmenopausal range for the institution 6. Male patients with partners of child-bearing potential (unless they agree to take measures not to father children by using one form of highly effective contraception [condom plus spermicide] during the trial and for six months afterwards). Men with pregnant or lactating partners should be advised to use barrier method contraception (for example, condom plus spermicidal gel) to prevent exposure to the foetus or neonate 7. Clinically significant cardiac disease including: a. pre-existing arrhythmia,		

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i. Mean resting QTc >470 msec obtained from 3 electrocardiograms (ECGs) in 24 hours
ii. Clinically important abnormalities in rhythm, conduction or morphology of resting ECG (including complete left bundle-branch block, third degree heart block

b. Any factor increasing the risk of QTc prolongation or arrhythmia
i. Hypokalaemia
ii. Congenital long QT syndrome
iii. Immediate family history of long QT syndrome or unexplained sudden death below the age of 40 years

c. uncontrolled angina pectoris
d. myocardial infarction 1 year prior to study entry
e. unstable cardiac arrhythmias
f. Cardiac failure
i. reduced LVEF <50%
ii. New York Heart Association (NYHA) grade 2-4 cardiac failure

8. Known HIV positive or active hepatitis B or C infection
9. Uncontrolled active infection
10. Symptomatic and progressive or steroid-requiring brain metastases or leptomeningeal disease involvement.
11. Uncontrolled hypertension requiring clinical intervention, hypertension requiring 2 or more antihypertensive agents
12. Relative hypotension (<100/60mmHg) or clinically relevant orthostatic hypotension, including a fall in blood pressure of >20mmHg
13. Haematuria: +++ on microscopy or dipstick
14. Hepatic or renal function that, in the opinion of the investigator, is unstable or worsening
15. Dementia or altered mental status that would prohibit informed consent.
16. A known hypersensitivity to AZD6738 or any excipient of the product.
17. Other severe, acute, or chronic medical or psychiatric condition or laboratory

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		abnormality that may increase the risk associated with study participation or study drug administration or may interfere with the interpretation of study results and, in the judgment of the Principal Investigator, would make the subject inappropriate for this study. **Patient Selection criteria for Part C** **Inclusion criteria Part C** 1. As for Parts A and B 2. Symptomatic disease or disease that (in the judgment of the clinician) is likely to cause symptoms within a short period of time such that palliative radiotherapy is indicated or justified. 3. Disease suitable for localised short-course palliative radiotherapy. **Exclusion criteria Part C** 1. As for Parts A and B. 2. Prior radiotherapy to the treatment site.		
VIBRaNT A phase I trial of Vandetanib combined with 131I-m**IB**G **Ra**diotherapy in patients with Neuroendocrine **T**umours, advanced phaeochromocytoma and paraganglioma Rubina Begum Trials Coordinator Cancer Research UK & UCL Cancer Trials Centre Tel: 020 7679 9514	Neuroendocrine Tumours – Phaeochromocytoma and Paraganglioma	**Main Inclusion Criteria:** 1. Histopathological or cytological diagnosis of advanced phaeo/PG defined as patients with local or metastatic disease not amenable to surgical resection, or R1 resection post original surgical debulking 2. Positive ^{123}I-mIBG diagnostic scan 3. Stable blood pressure (<140/90 mmHg), if appropriate, on anti-hypertensive therapy 4. No previous systemic therapy for advanced or metastatic disease 5. Measurable disease (according to RECIST v1.1) 6. WHO performance status 0 or 1 7. Age ≥ 18 8. Estimated life expectancy > 3 months 9. Adequate bone marrow, liver and renal function:	10-18	University College London Hospital NHS Foundation Trust Guy's and St Thomas' NHS Foundation Trust The Christie NHS Foundation Trust (no additional

Study name and Contact	Cancer type	Inclusion and Exclusion summary	# of patients needed	Sites
Email: ctc.vibrant@ucl.ac.uk		10. Electrolytes: § Potassium ≥ 4.0 mmol/L and ≤ 5.5 mmol/L § Magnesium ≥ LLN and ≤ 1.23 mmol/L § Corrected calcium within institution normal range 11. Patients should be able to swallow oral medication e.g. capsules or tablets **Main Exclusion Criteria:** 1. Patients undergoing current treatment with curative intent 2. Previous or current malignancies of other histological types within the last 5 years, with the exception of: § Tumours associated with MEN-2a, MEN-2b, VHL and NF1; § In-situ carcinoma of the cervix, and; § Adequately treated basal cell or squamous cell carcinoma of the skin 3. Any prior exposure to VEGF, EGFR, or RET inhibitors or history of hypersensitivity to vandetanib, or any excipient agents 4. Evidence of active uncontrolled infection (patients on antibiotics are eligible) 5. Chronic gastrointestinal disease (e.g. inflammatory bowel disease), or significant bowel resection that would preclude adequate absorption 6. Cardiac conditions that could be exacerbated by vandetanib. 7. Any psychiatric or other disorder likely to impact on informed consent or ability to manage isolation 8. Major surgery within 28 days prior to registration 9. Brain metastases or spinal cord compression, unless treated at least four weeks before the first vandetanib dose and stable without steroid treatment for 10 days 10. Any concomitant medications that may affect QTc, or induce CYP3A4 function (with the exception of somatostatin or somatostatin analogue) and/or prohibited medications 11. Women who are pregnant or lactating		sites required)
CAPITAL A phase I/II dose finding study evaluating the safety and tolerability of CAPecitabine and afllbercept in patients with unresectable metasTAtic colorectaL cancer	Colorectal Cancer	Inclusion Criteria • Histologically confirmed colorectal cancer with evidence of metastatic disease • Adequate medical fitness to undergo fluoropyrimidine-based chemotherapy. • No known dihydropyrimidine dehydrogenase deficiency. • Adequate bone marrow function with platelets > 100 x 109/l; WBC > 3 x 109/l;	Phase I (including expansion cohort at MTD) - maximum of	UCLH

Study name and Contact	Cancer type	Inclusion and Exclusion summary	# of patients needed	Sites
deemed unsuitable for doublet/ triplet chemotherapy Patricia Danaswamy Oncology Research Nurse Clinical Research Facility NIHR/Wellcome Trust University College London Hospital Tel: 020 3447 6008 **Patricia.Danaswamy@uclh.nhs.uk**		neutrophils > 1.5 x 109/l; Hb > 9 g/dl • Serum bilirubin < 1.5 x upper limit of institutional normal range (ULN), alkaline phosphatase < 5 x ULN and transaminases < 3 x ULN unless liver metastasis then < 5 x ULN. • Serum creatinine ≤ 1.5 x ULN or creatinine clearance > 50ml/min • Proteinuria < 2+ (dipstick urinalysis) or ≤ 1g/24hour. • For female patients of childbearing potential, negative serum pregnancy test within 1 week (7 days) prior of starting study treatment, • Female patients must commit to using reliable and appropriate methods of contraception until at least three months after the end of study treatment (when applicable). Male patients with a partner of childbearing potential must agree to use contraception in addition to having their partner use another contraceptive method during the trial. • Recovery from any treatment related grade 3/4 non-haematological toxicity (except alopecia and fatigue) to baseline or ≤ grade 1 • Absence of pre-existing liver dysfunction of Childs-Pugh B or worse • Life expectancy > 3 months • Age ≥ 18 years *Phase I study specific criteria* • WHO performance status 0 – 1 • Progressive disease after at least first line chemotherapy treatment • Previous fluoropyrimidine therapy has not required dose reduction of greater than 25%, significant delay (≥ 7 days) or stopped treatment due to fluoropyrimidine toxicity • Phase II study specific criteria • WHO performance status 0 – 2 • Patients not deemed suitable for doublet/triplet combination chemotherapy. This will be defined as 3 or more comorbidities or 1 or more on CIRS-G and/or MMSE of 26 or below and or IADL impairment in more than 1 category and or physical function difficulty from physical function section of EORTC QLQC30. • No previous treatment for mCRC. <u>Exclusion Criteria</u> • Known evidence of brain metastases	16. Phase 2- maximum of 32	

Study name and Contact	Cancer type	Inclusion and Exclusion summary	# of patients needed	Sites
		• Liver-only metastatic disease deemed to be resectable • LVEF <50% • Patients who did not previously tolerate IV 5-FU or capecitabine (required dose reduction, significant delay (≥ 7days) or stopped treatment due to fluoropyrimidine toxicity • Any of the following within 3 months prior to inclusion: grade 3-4 gastrointestinal bleeding/haemorrhage (unless due to resected tumour), treatment resistant peptic ulcer disease, erosive oesophagitis or gastritis, infectious or inflammatory bowel disease, diverticulitis, pulmonary embolism or other uncontrolled thrombo-embolic event. • Any of the following within 6 months prior to inclusion: myocardial infarction, acute coronary syndrome, unstable angina pectoris, coronary revascularisation (PCI or CABG), NYHA class III or IV congestive heart failure, stroke or transient ischaemic attack. • Any patient who has undergone major surgery <1month prior to trial entry. • Uncontrolled hypertension (grade 3 /4) • Significant proteinuria (≥2+ on dipstick or ≥1g/24hour) • Significant bleeding diathesis or significant underlying coagulopathy (INR>1.5) in the absence of vitamin K antagonist therapy. • Intolerance to loperamide • Previous history of gastrointestinal fistula or perforation • Evidence of bowel obstruction • Clinically relevant history of drug or alcohol abuse • Serious uncontrolled inter current illness including poorly controlled diabetes mellitus • HIV, HBV or HCV infection. • Pregnancy or lactation. Men and women of child-bearing potential must use adequate contraception • Any psychological, familial, sociological or geographic condition potentially hampering compliance with the study protocol and follow-up schedule.		
SarCaBON: A randomised double-blind phase II trial of saracatinib versus placebo for cancer-induced bone pain Hannah McMellon Clinical Trial Practitioner	All tumour types with metastatic bone disease or myeloma	Cytologically or histologically confirmed solid tumours or multiple myeloma with painful bone metastases and poor control of bone pain in spite of pain medication including opioids. Prostate cancer patients without histology or cytology can be recruited if their prostate specific antigen (PSA) was >100 ng/mL at diagnosis and they have a bone scan confirming skeletal metastases. WHO performance status ≤ 2; Baseline pain score for pain on average ≥ 4 and ≤ 9 on a 0-10 numerical scale; No previous or planned radiotherapy at site of pain within one month of first dose.	62	Sheffield

Study name and Contact	Cancer type	Inclusion and Exclusion summary	# of patients needed	Sites
Department of Oncology University of Sheffield **h.mcmellon@sheffield.ac.uk** 0114 226 5721				
TRAcking non-small cell lung Cancer Evolution through therapy (Rx): **TRACERx**. Professor Charles Swanton. Chief Investigator. charles.swanton@cancer.org.uk 020 7269 3463	All histological subtypes of non-small cell lung cancer (NSCLC)	**Inclusion criteria:** - Written Informed consent - Patients ≥18 years of age, with early stage I-IIIA disease who are eligible for primary surgery (including stage IA; and stage IIIA considered unsuitable for chemoradiation) - Histopathologically confirmed NSCLC, or a strong suspicion of cancer on lung imaging necessitating surgery (e.g. diagnosis determined from frozen section in theatre) - Primary surgery in keeping with NICE guidelines planned - Agreement to be followed up in a specialist centre - Performance status 0 or 1 **Exclusion criteria:** - Any other current malignancy or malignancy diagnosed or relapsed within the past 5 years (other than nonmelanomatous skin cancer and in situ cervical cancer) - Psychological condition that would preclude informed consent - Adjuvant regimen other than platinum-based therapy (if a patient is deemed suitable for adjuvant therapy) - Patients infected with blood borne viruses Hepatitis C, Hepatitis B and/or HIV	850	Six recruiting sites: London, Leicester, Manchester, Aberdeen, Birmingham, and Cardiff
ENDCaP-C Enhanced Neoplasia Detection and Cancer Prevention in Chronic Colitis (ENDCaP-C) . A Multicentre test accuracy study Trial coordinator: Dr Steve Johnson. Email: **ENDCAP-c@trials.bham.ac.uk** Tel:0121 415 9103	Colorectal cancer prevention	**Inclusion criteria** • Diagnosis of chronic ulcerative colitis of over 10 years duration • **AND** disease beyond the splenic flexure • **OR** known Primary Sclerosing Cholangitis • Scheduled for surveillance colonoscopy during study period • Willing to accept the possibility of an additional colonoscopy after 6 months • No previous history of colorectal cancer • Aged 18 years or over • Be able and willing to provide written informed consent for the study • **Exclusion criteria** • Patients with fulminant colitis • Bowel obstruction	1000	New Queen Elizabeth Hospital (Birmingham); Russells Hall Hospital (Dudley); City Hospital (Birmingham); Birmingham Heartlands Hospital (Birmingham); New Cross Hospital,

Study name and Contact	Cancer type	Inclusion and Exclusion summary	# of patients needed	Sites
		• Patients in whom it is not possible to do complete colonoscopies • Patients with proctitis only • Crohns colitis patients • Patients with unclassified IBD • Patients with microscopic colitis • Unable to give written informed consent • Less than 18 years of age		(Wolverhampton); Manor Hospital, (Walsall); Northwick Park Hospital, (Harrow); Worcestershire Royal Hospital, (Worcester); Glasgow Royal Infirmary (Glasgow); John Radcliffe Hospital, (Oxford)
AZD0424 A Cancer Research UK Phase I study to determine the maximum tolerated dose of the oral Src/ABL inhibitor AZD0424, and to identify tolerable and effective AZD0424 combination regimens for the treatment of advanced solid tumours. Karen Dyer Clinical Study Manager Centre for Drug Development Cancer Research UK Tel: 020 3469 6953 **Karen.Dyer@cancer.org.uk**	Solid tumour	**Inclusion criteria:** • Histologically or cytologically proven solid tumour, refractory to conventional treatment, or for which no conventional therapy exists or is declined by the patient or for whom there is the prospect of clinical benefit • Life expectancy of at least 12 weeks • World Health Organisation (WHO) performance status of 0-2 • Haematological and biochemical indices within the ranges shown below. These measurements must be performed within one week (Day -7 to Day 1) before the patient receives AZD0424 ○	26-66	Belfast City Hospital Edinburgh Western General The Churchill Hospital (Oxford)

Study name and Contact	Cancer type	Inclusion and Exclusion summary	# of patients needed	Sites

Laboratory Test	Value required
Haemoglobin (Hb)	≥ 9.0 g/dL
Absolute neutrophil count (ANC)	≥ 1.5 x 10^9/L
Platelet count	≥ 100 x 10^9/L
Serum bilirubin	≤ 1.5 x upper limit of normal (ULN)
Alanine aminotransferase (ALT) and aspartate aminotransferase (AST)	≤ 2.5 x (ULN)
Either: Calculated creatinine clearance Or Isotope Clearance measurement	 ≥ 50 mL/min Or ≥ 50 mL/min (uncorrected)

- 18 years or over
- Written (signed and dated) informed consent and be capable of co-operating with treatment and follow-up
- **MTD Expansion cohorts only:** A tumour which is safely accessible for biopsy (single and combination)
- **Single Agent Expansion cohort only:** Patient must either fulfil inclusion criterion number 7, or patient must be willing and capable to have Fluorodeoxyglucose ([18F]FDG) positron emission tomography (PET)–CT imaging performed within two weeks of first AZD0424 administration and again two weeks after first AZD0424 administration.

Additional inclusion criteria for combination part of study

AZD0424 in Combination
MTOR

- Adequate lung function indicated by a resting oxygen saturation level (on air) ≥ 94%, a CO-transfer factor > 60%

Exclusion criteria:

- Radiotherapy (except for palliative reasons), endocrine therapy, immunotherapy or chemotherapy during the previous four weeks (six weeks for nitrosoureas, Mitomycin-C and four weeks for investigational medicinal products) before

Study name and Contact	Cancer type	Inclusion and Exclusion summary	# of patients needed	Sites
		treatment. Patients with prostate cancer may continue to receive endocrine therapy to maintain castrate levels of androgens. • Ongoing toxic manifestations of previous treatments. Exceptions to this are alopecia or certain Grade 1 toxicities, which in the opinion of the Investigator and the DDO should not exclude the patient. • Symptomatic brain metastases (if brain metastases are present they must have been stable for > 3 months). • Patients with evidence of interstitial lung disease (bilateral, diffuse, parenchymal lung disease). • Patients with a peanut allergy will be excluded. • Ability to become pregnant (or already pregnant or lactating). However, those female patients who have a negative serum or urine pregnancy test before enrolment and agree to use two highly effective forms of contraception (oral, injected or implanted hormonal contraception and condom, have a intra-uterine device and condom, diaphragm with spermicidal gel and condom) for four weeks before entering the trial, during the trial and for six months afterwards are considered eligible. • Male patients with partners of child-bearing potential (unless they agree to take measures not to father children by using one form of highly effective contraception [condom plus spermicide] during the trial and for six months afterwards). Men with pregnant or lactating partners should be advised to use barrier method contraception (for example, condom plus spermicidal gel) to prevent exposure to the foetus or neonate. • Major thoracic or abdominal surgery from which the patient has not yet recovered. • At high medical risk because of non-malignant systemic disease including active uncontrolled infection. • Known to be serologically positive for hepatitis B, hepatitis C or human immunodeficiency virus (HIV). • Resting ECG with measurable QTc interval of >480 msec (mean value) of at least 3 time points within a 24 hour period. The Fridericia method of calculation is preferred for QTc monitoring in this study. • Concurrent hypotension defined as a baseline supine blood pressure (BP) systolic < 90 mmHg. • Concurrent congestive heart failure, prior history of class III/ IV cardiac disease (New York Heart Association [NYHA] - refer to Appendix 4), prior history of cardiac ischaemia or prior history of cardiac arrhythmia within 6 months. Coronary		

Study name and Contact	Cancer type	Inclusion and Exclusion summary	# of patients needed	Sites
		angioplasty or stenting in the previous 12 months. • Is a participant or plans to participate in another interventional clinical trial, whilst taking part in this Phase Ia/Ib study of AZD0424 single agent and in combination. Participation in an observational, counselling or psychological trial would be acceptable. • Patients receiving trazodone (from three days prior to starting AZD0424 up to Cycle 2 Day 3 of the single agent, or Cycle 2 Day 1 of the combination agent portion of the study). • Any other condition which in the Investigator's opinion would not make the patient a good candidate for the clinical trial.		
[^{124}I]*m*IBG A Cancer Research UK Phase I/II study to compare [^{124}I]*meta*-Iodobenzylguanidine (*m*IBG) positron emission tomography/computerised tomography (PET/CT) to [^{123}I]*m*IBG imaging in patients with metastatic neuroblastoma. Jane Peters Senior Clinical Study Manager Centre for Drug Development Cancer Research UK Tel: 020 3469 6972 **Jane.Peters@cancer.org.uk**	Metastatic neuroblastoma	**Inclusion criteria:** 1. Histologically proven Stage 4 neuroblastoma as defined by the International Neuroblastoma Staging System (INSS). 2. Aged ≥ 1 year at the time that written informed consent is given. 3. Planned to undergo conventional [^{123}I]*m*IBG planar scintigraphy for routine clinical care of neuroblastoma. 4. Life expectancy of at least 12 weeks. 5. World Health Organisation (WHO) performance status of 0, 1 or 2 (Appendix 2) for patients aged > 12 years old or Lansky play scale score of ≥ 50% (Appendix 3) for patients aged ≤ 12 years old. 6. Written (signed and dated) informed consent from patient ≥ 16 years old and/or parent or legal guardian for patients <16 years old and the patient be capable of co-operating with scanning requirements. (N.B. Written or verbal assent as appropriate should be sought from all patients who are under 16 years old). **Additional Inclusion Criteria for Biokinetic sub-study:** 1. Aged ≤ 16 years at the time that written informed consent is given. 2. No requirement for general anaesthesia to undergo PET/CT scanning. 3. Written (signed and dated) informed consent for the sub-study from patients aged 16 years or from the patient's parent or guardian for patients aged <16 years. Capable of co-operating with the additional study PET/CT scans. (N.B. Written or verbal assent as appropriate should be sought from all patients who are under 16 years old.)	A minimum of 25	The Royal Marsden Hospital – Sutton, Surrey University College London Hospitals

Study name and Contact	Cancer type	Inclusion and Exclusion summary	# of patients needed	Sites
		Additional Inclusion Criteria for PET/MRI sub-study: 1. No requirement for general anaesthesia to undergo hybrid PET/MRI scanning. 2. No previous experience of claustrophobia. 3. Written (signed and dated) informed consent for the sub-study from patients aged 16 years or from the patient's parent or guardian for patients aged <16 years. Capable of co-operating with the additional study PET/MRI scans. (N.B. Written or verbal assent as appropriate should be sought from all patients who are under 16 years old.) **Exclusion criteria:** 1. Treatment with any medications contra-indicated with mIBG scanning as listed in Appendix 4. For example, decongestants containing pseudoephedrine, phenylpropalomine and phenylephrine, sympathomimetics, cocaine, antihypertensives, tricyclic antidepressants. These drugs should be stopped before administration as indicated in this list (usually for four biological half-lives to allow almost complete wash-out but refer to list). 2. Stage 4S neuroblastoma as defined by the INSS. 3. Any anti-cancer treatment planned between the routine [^{123}I]*m*IBG imaging and the [^{124}I]*m*IBG PET/CT scan on Day 2. Anti-cancer treatments can be started only after the Off-Study assessment on Day 3 to Day 7, see schedule of assessments in Section 7. N.B. Patients should not be enrolled in the study if their participation will delay their subsequent treatment for neuroblastoma. 4. Female patients who are pregnant or lactating. 5. At high medical risk because of non-malignant systemic disease including active uncontrolled infection. 6. Known to be serologically positive for Hepatitis B, Hepatitis C or Human Immunodeficiency Virus (HIV). 7. Patients with known hypersensitivity to *m*IBG. 8. Any other condition which in the Investigator's opinion would not make the patient a good candidate for the clinical study.		
OPARATIC (Olaparib) A Cancer Research UK Phase I trial of olaparib (AZD2281), an oral	Glioblastoma	**Inclusion criteria:** 1. Histologically proven glioblastoma (World Health Organisation [WHO] Grade 4).	Stage 1: cohort of up to 6 patients	The Beatson West of Scotland Cancer Centre

Study name and Contact	Cancer type	Inclusion and Exclusion summary	# of patients needed	Sites
PARP Inhibitor, in combination with extended low-dose oral temozolomide in patients with relapsed glioblastoma. Jane Peters Senior Clinical Study Manager Centre for Drug Development Cancer Research UK Tel: 020 3469 6972 Jane.Peters@cancer.org.uk		2. Radiological diagnosis of recurrent or progressive disease according to RANO criteria, which is suitable for palliative resection. 3. Patients who will undergo palliative resection should have enough resectable tumour tissue for sampling requirements in the opinion of the neurosurgeon. Patients who will not undergo palliative resection should have measurable disease according to RANO criteria. 4. Prior 1st line treatment with radical radiotherapy, or chemoradiation followed by adjuvant chemotherapy. 5. Aged between 18 and 70 years at the time the patient provides informed consent. 6. Life expectancy > 12 weeks. 7. WHO performance status of 0-2 (Appendix 1). 8. Haematological and biochemical indices within the ranges shown below measured on Day -7 to pre-dose on Cycle 0 Day 1 (first administration of olaparib). **Laboratory Test** / **Value required** Haemoglobin (Hb) / ≥ 9.0 g/dL Absolute neutrophil count (ANC) / ≥ 1.5 x 10^9/L Platelet count / ≥ 100 x 10^9/L Bilirubin / ≤ 1.5 x upper limit of normal (ULN) Alanine aminotransferase (ALT) or aspartate aminotransferase (AST) / ≤ 2.5 x ULN Calculated creatinine clearance or Isotope clearance measurement / ≥ 50 mL/min or ≥ 50 mL/min (uncorrected) 9. Ability to swallow and retain oral medications. 10. Written (signed and dated) informed consent and be capable of co-operating with treatment, scans and follow-up. **Exclusion criteria:** 1. Radiotherapy, endocrine therapy or immunotherapy during the previous 12 weeks before Day 1, or chemotherapy or biological therapy during the 4 weeks before Day 1. Any previous chemotherapy for recurrent disease. 2. Any previous treatment with a PARP inhibitor, including olaparib 3. Ongoing toxic manifestations of previous treatments. Exceptions to this are alopecia, lymphopenia, or Grade 1 toxicities, which in the opinion of the	Stage 2: 16-28 patients	Southern General Hospital (Glasgow) The Christie Hospital (Manchester) Royal Marsden Hospital (Surrey) Queen Elizabeth Hospital (Birmingham) Addenbrooke's Hospital (Cambridge) Western General Hospital (Edinburgh) Bristol Haematology and Oncology Centre

Study name and Contact	Cancer type	Inclusion and Exclusion summary	# of patients needed	Sites
		Investigator and the Centre for Drug Development (CDD) should not exclude the patient. Patients with lymphocyte count below 0.5 x 10^9/L (Grade 3 or 4) should receive prophylaxis with co-trimoxazole according to the guidance in Section 4.7. 4. Change to systemic steroids dose between Day -5 and Day -1 (i.e. must be on a stable dose prior to olaparib administration on Day 1). 5. Female patients who are able to become pregnant (or already pregnant or lactating). However, those female patients who have a negative serum or urine pregnancy test before enrolment and agree to use two highly effective forms of contraception (oral, injected or implanted hormonal contraception and condom, have an intra-uterine device and condom, diaphragm with spermicidal gel and condom) effective at the first administration of either IMP, throughout the trial, and for six months afterwards, are considered eligible. 6. Male patients with partners of child-bearing potential (unless they agree to take measures not to father children by using one form of highly effective contraception [condom plus spermicide] effective at the first administration of IMP, throughout the trial, and for six months afterwards). Men with pregnant or lactating partners should be advised to use barrier method contraception (for example, condom plus spermicidal gel) to prevent exposure to the foetus or neonate. 7. Major thoracic or abdominal surgery from which the patient has not yet recovered. 8. At high medical risk because of non-malignant systemic disease including active uncontrolled infection. 9. Known to be serologically positive for hepatitis B, hepatitis C or human immunodeficiency virus (HIV). 10. Concurrent congestive heart failure, prior history of class III/ IV cardiac disease (New York Heart Association [NYHA] - refer to Appendix 3), prior history of cardiac ischaemia or prior history of cardiac arrhythmia within the previous 12 months. 11. Patients with pacemakers, a history of previous heart surgery, any major surgery in the preceding six weeks, metal fragments in their eyes, shrapnel or bullet injuries are excluded (on the basis of their unsuitability to undergo MRI scans). Patients with metal implants or tattoos should be discussed with MRI staff. 12. Grand mal seizures occurring ≥ 3 times per week in any of the previous four weeks. 13. Patients with gastrointestinal disorders likely to interfere with absorption of the study medication. 14. Patients taking drugs known to be potent inhibitors or inducers of CYP3A4 including phenytoin, carbamazepine and phenobarbitone which cannot be stopped		

Study name and Contact	Cancer type	Inclusion and Exclusion summary	# of patients needed	Sites
		for the duration of the trial. 15. Immunisations with live vaccines received within the four weeks before Day 1 (or expected to receive during the trial and up to at least six months after receiving last study treatment). Including BCG and yellow fever. 16. Known hypersensitivity to any of the components of olaparib 17. Stage 2 only - Known hypersensitivity to temozolomide (TMZ), any of its components, or to dacarbazine (DTIC). 18. Stage 2 only - Known lactose intolerance. 19. Is a participant or plans to participate in another interventional clinical study, whilst taking part in this Phase I study. Participation in an observational study would be acceptable. 20. Any other condition which in the Investigator's opinion would not make the patient a good candidate for the clinical trial.		
VanSel-1 A Cancer Research UK Phase I dose escalation trial of oral VEGFR and EGFR inhibitor, Vandetanib in combination with the oral MEK inhibitor, Selumetinib (VanSel-1) in solid tumours (dose escalation) and NSCLC (expansion cohort) Susan Wan Clinical Study Manager Centre for Drug Development Cancer Research UK Tel: 020 3469 6913 **Susan.Wan@cancer.org.uk**	Dose escalation phase – Any Solid Tumour Expansion cohort – Non Small Cell Lung Carcinoma (NSCLC)	**Inclusion criteria:** 1. **(Dose escalation cohorts)** Histologically or cytologically proven solid tumour for which no conventional therapy exists or is declined by the patient 2. **(Expansion cohort only)** Histologically or cytologically confirmed NSCLC patients only, for which no conventional therapy exists or is declined by the patient • If only cytologically confirmed, baseline biopsy is mandatory for a patient to be eligible. • For NSCLC patients to be eligible for the expansion cohort they must have received: o One prior line of chemotherapy o Previous platinum based chemotherapy o Previous EGFR inhibitor 3. **(Expansion cohort only)** Measurable disease according to RECIST criteria Version 1.0 4. Life expectancy of at least 12 weeks 5. World Health Organisation (WHO) performance status of 0-1 (Appendix 1) 6. Baseline LVEF $\geq$ 50% 7. Haematological and biochemical indices within the ranges shown below. These measurements must be performed within one week (Day -7 to Day -1) before the	Dose escalation phase: 9-45 Expansion cohort: up to 30	Addenbrooke's Hosptial (Cambridge) The Christie Hospital (Manchester) The Churchill Hospital (Oxford)

Study name and Contact	Cancer type	Inclusion and Exclusion summary	# of patients needed	Sites

patient goes on study.

Laboratory Test	Value required
Haemoglobin (Hb)	≥9.0 g/dL
Absolute neutrophil count	≥1.5 x 10^9/L
Platelet count	≥100 x 10^9/L
Normal serum calcium (adjusted)*	2.15-2.55 mmol/L
Normal serum magnesium*	0.60-1.0 mmol/L
Normal serum potassium	≥4.0 mmol/L
Either: Serum bilirubin	≤1.5 x upper limit of normal (ULN) This does not apply to patients with Gilbert's disease.
Or: Alanine amino-transferase (ALT) or aspartate amino-transferase (AST) and alkaline phosphatase (ALP)	≤ 2.5 x ULN unless raised due to liver metastases in which case up to 5 x ULN is permissible
Either: Calculated creatinine clearance (using the Wright or C&G formula)	> 50 mL/min
Or: Isotope clearance measurement**	≥ 50 mL/min (uncorrected)
INR or aPTT***	< 1.5 x ULN

*or normal range according to the local laboratory

** Isotope clearance result to be used to confirm eligibility if calculated C&G/Wright method results in GFR of = 50 mL/min.

*** Therapeutic INR values (2.0-3.0) are acceptable to confirm eligibility for patients who are taking concomitant warfarin.

8. 18 years or over
9. Ability to swallow and retain oral medications.
10. Written (signed and dated) informed consent and be capable of co-operating with treatment, and follow-up

Exclusion criteria:

1. Radiotherapy (except for palliative reasons), endocrine therapy, immunotherapy or chemotherapy during the previous 4 weeks (6 weeks for investigational medicinal products) before treatment.
2. Patients who have been withdrawn from treatment with agents that target EGFR because of unacceptable toxicity (prior treatment with these agents is allowed) and

Study name and Contact	Cancer type	Inclusion and Exclusion summary	# of patients needed	Sites
		those patients who have had EGFR dose reductions. 3. **Expansion cohort only:** Prior treatment with any agent that targets MEK or VEGFR or VEGF 4. Any prior exposure to RAS or RAF inhibitors 5. Ongoing toxic manifestations of previous treatments. Exceptions to this are alopecia or certain Grade 1 toxicities, which in the opinion of the Investigator and the Centre for Drug Development (CDD) should not exclude the patient. 6. Symptomatic brain metastases (patients must be stable for >3 months post RT treatment) or spinal cord compression. 7. Patients with interstitial lung disease. 8. Pregnant or lactating women are excluded. Female patients with the ability to become pregnant who have a negative serum or urine pregnancy test before enrolment and agree to use two of the following three highly effective forms of combined contraception (oral, injected or implanted hormonal contraception and condom, have a intra-uterine device and condom, diaphragm with spermicidal gel and condom) for four weeks before entering the trial, during the trial and for six months afterwards are considered eligible. 9. Male patients with partners of child-bearing potential (unless they agree to take measures not to father children by using one form of highly effective contraception [condom plus spermicide] during the trial and for six months afterwards). Men with pregnant or lactating partners should be advised to use barrier method contraception (e.g. condom plus spermicidal gel) to prevent exposure to the foetus or neonate. 10. Major surgery from which the patient has not yet recovered. 11. At high medical risk because of non-malignant systemic disease including active uncontrolled infection. 12. Known to be serologically positive for Hepatitis B, Hepatitis C or Human Immunodeficiency Virus (HIV). 13. Cardiac conditions as follows: • Clinically significant cardiovascular event within 3 months prior to entry to include: ○ Myocardial infarction ○ Angina requiring use of nitrates more than once weekly ○ Superior vena cava syndrome ○ Class II/III/IV cardiac disease (New York Heart Association [NYHA]) (Appendix 4) ○ Presence of cardiac disease that in the opinion of the		

Study name and Contact	Cancer type	Inclusion and Exclusion summary	# of patients needed	Sites

Investigator increases the risk of ventricular arrhythmia.

- History of arrhythmia which is symptomatic or requires treatment (CTCAE 4.02), symptomatic or uncontrolled atrial fibrillation despite treatment or asymptomatic sustained ventricular tachycardia. Patients with atrial fibrillation controlled by medication are permitted.
- Uncontrolled hypertension (BP ≥ 160/100 despite optimal therapy)
- Prior or current cardiomyopathy
- Atrial fibrillation with heart rate >100 bpm
- QTcB (Bazett's formula) ≥ 450 msec on screening ECG (Note: If a patient has a QTcB interval ≥ 450 msec on screening ECG, the screen ECG may be repeated twice [at least 24 hours apart]. The average QTcB from the three screening ECGs must be < 450 msec in order for the subject to be eligible for the study.)
- History of congenital long QT syndrome
- History of Torsade de Pointes (or any concurrent medication with a known risk of inducing Torsades de Pointes. See Appendix 16.8)

14. Concomitant medications that are potent inducers of CYP3A4 function i.e. rifampicin, rifabutin, phenytoin, carbamazepine, Phenobarbital and St John's Wort.
15. Any other condition which in the Investigator's opinion would not make the patient a good candidate for the clinical trial (e.g. evidence of severe or uncontrolled systemic disease or concurrent condition or that may affect ability to absorb oral agents).
16. Current malignancies of other types, with the exception of adequately treated cone-biopsied in situ carcinoma of the cervix uteri and basal or squamous cell carcinoma of the skin. Cancer survivors, who have undergone potentially curative therapy for a prior malignancy, have no evidence of that disease for five years or more and are deemed at negligible risk for recurrence, are eligible for the trial.
17. If a participant plans to participate in another interventional clinical study, whilst taking part in this Phase I study. Participation in an observational study would be acceptable.
18. **(Expansion cohort only)** If the patient is unsuitable for administration of DCE-MRI contrast material because of hypersensitivity or impaired renal function.

Study name and Contact	Cancer type	Inclusion and Exclusion summary	# of patients needed	Sites
AdUP A Phase I Clinical Trial of a replication defective type 5 adenovirus vector expressing nitroreductase and GMCSF (AdNRGM) given via trans-perineal, template-guided, intra-prostatic injection, followed by intravenous CB1954, in patients with locally relapsed Prostate Cancer. Anna Rowe Trial Coordinator, Early Drug Development Team 0121 414 4032 a.l.rowe@bham.ac.uk	Locally Recurrent Prostate Cancer	**Inclusion Criteria** • Patients who present with biopsy-proven local recurrence of prostate cancer following radical radiotherapy and a rising PSA with or without androgen suppression with antiandrogens or LHRH agonist/antagonist therapy or after bilateral orchidectomy. A rising PSA is defined as 2 increases over 3 or 4 readings over a minimum period of 6 weeks, with time-points separated by at least 2 weeks. If the patient is on antiandrogens or LHRH agonist/antagonist therapy, this therapy should be continued • Life expectancy greater than 3 months. • Aged at least 18 years. • Written informed consent. • WHO performance status of 0-1. • PSA value ≥ 2 and ≤ 100 ng/ml at study entry. • Adequate hepatic function (i.e. bilirubin, AST, ALT all < 1.5 x upper limit of normal for Institution). • Normal renal function (<1.25 x upper normal limit for the Institution). • Adequate haematological function (i.e. haemoglobin > 10g/dl, WCC > 3x109/l, platelets > 150x109/l) and normal clotting (INR and APTT <1.2). • Patients must agree not to father a child within 12 months following AdNRGM administration, and must use at least two methods of contraception, one of which is barrier, starting from the time of AdNRGM administration for at least 12 months. • No known immuno-incompetence. **Exclusion Criteria** • Patients with a prostate or abnormal focus which is deemed clinically unsuitable for trans-perineal template-guided injection. • Patients who have previously been treated with prostate brachytherapy. • Patients who have previously been treated with AdNRGM and CB1954; or who have been administered any other human adenovirus type 5 vector within the last 5 years. • Patients who have received chemotherapy, radiotherapy or immunotherapy within 28 days of study entry. • Acute active infection (viral, bacterial, or fungal) which requires specific therapy. • Chronic hepatitis B or C infection, HIV positive patients. (Patients will be tested for HBV/HCV, but not HIV). • Concurrent severe medical illnesses incompatible with the treatment including psychiatric pathology likely to affect protocol compliance.	15-30 (2 recruited)	Queen Elizabeth Hospital, Birmingham

Study name and Contact	Cancer type	Inclusion and Exclusion summary	# of patients needed	Sites
		• Tumours of other organs or tissues of high malignant potential still active or treated radically less than 3 years before (except that successfully treated, non-metastatic skin cancers or non-muscle invasive bladder cancers are not an exclusion criterion). • Concurrent corticosteroids, or any medication known to have significant immunosuppressive action. • Patients unable to travel for regular hospital assessments. • Evidence of adenovirus infection and/or shedding at baseline. • Clinical judgement by the Investigator that the patient should not participate in the study.		
RAvVA Louise Dudley Trial Coordinator - Haematology Team 0121 371 4365 l.m.dudley@bham.ac.uk	Acute myeloid leukaemia or high risk myelodysplastic syndromes	Inclusion Criteria: • Adults with AML (except Acute Promyelocytic Leukaemia (APL)) as defined by the World Health Organisation (WHO) Classification or patients with high risk MDS categorised as INT-2 or high risk according to the International Prognostic Scoring System (IPSS) who are deemed ineligible for intensive chemotherapy on the grounds of age or co-morbidities with **ONE** of the following disease status: i) Newly diagnosed **OR** ii) Relapsed Disease: patients must have achieved a previous morphological CR and show evidence of recurrent disease **OR** iii) Refractory Disease: patients who have failed to achieve a morphological CR with previous therapy • Patients are able to receive treatment as an out-patient • Adequate renal and hepatic function • Patients have given written informed consent • Eastern Cooperative Oncology Group (ECOG) performance status ≤2 - Exclusion Criteria: • Patients with greater than class III of the New York Heart Association (NYHA) cardiac impairment - • Blastic transformation of Chronic Myeloid Leukaemia (CML) • Any concurrent active malignancy • Prior allogeneic haematopoietic stem cell transplant (HSCT) • Pregnant or lactating women (women of childbearing potential must have a negative urine or serum pregnancy test within 7 days prior to the start of treatment) • Adults of reproductive potential not willing to use appropriate, effective, contraception during the trial and for specified amount of time afterwards. • Patients who have received prior histone deacetylase inhibitor (HDACi) treatment as	260	Queen Elizabeth Hospital (Birmingham), The Christie Hospital (Manchester), The Churchill Hospital (Oxford), Royal Liverpool University Hospital (Liverpool), St Bartholomew's Hospital (London), Southampton General Hospital (Southampton), St James University Hospital (Leeds) University Hospital of Wales (Cardiff) The Beatson

Study name and Contact	Cancer type	Inclusion and Exclusion summary	# of patients needed	Sites
		anti-tumour therapy. (Patients who have received HDACi treatment for other indications e.g valproic acid for epilepsy may enrol after a 30-day washout period). • Previous anti-tumour therapies, including prior experimental agents or approved anti-tumour small molecules and biologics, within 30 days before the start of protocol treatment. (Patients receiving anti-tumour therapies to control blood counts) may enrol into the trial and receive trial treatment simultaneously). • Patients who have received prior treatment with demethylating agents such as 5-azacitidine or decitabine. • Patients with contraindications to receiving azacitidine or vorinostat such as hypersensitivity, patients unable to have a subcutaneous injection or swallow oral capsules. • Active symptomatic fungal, bacterial, and/or viral infection including known active HIV or known viral (A, B, or C) hepatitis. • Any co-morbidity that could limit compliance with the trial (see section 4 of the protocol)		West of Scotland Cancer Centre (Glasgow) Belfast City Hospital (Belfast), Hammersmith Hospital (London), King's College Hospital (London), University Hospital of North Staffordshire (Stoke-on-trent), Nottingham University Hospital City Campus (Nottingham) Hereford County Hospital (Hereford) Ysbyty Gwynedd (Bangor) Aberdeen Royal Infirmary (Aberdeen) Croyden University Hospital

Study name and Contact	Cancer type	Inclusion and Exclusion summary	# of patients needed	Sites
Axi-STS A clinico-pathological phase II study of axitinib in patients with advanced angiosarcoma & other soft tissue sarcomas Ana Hughes Senior Trial Coordinator 0121 4143793 Axi-STS@trials.bham.ac.uk	Angiosarcoma Synovial sarcoma	Inclusion Criteria: • Age ≥ 16 • Pathologically confirmed angiosarcoma, leiomyosarcoma, synovial sarcoma. • Locally advanced or metastatic disease incurable by surgery or radiotherapy. • Measurable disease according to RECIST criteria. • Evidence of objective disease progression in the past 6 months, without anticancer treatment since progression. • Patients ineligible for chemotherapy (e.g. through age, clinical condition or patient refusal) or who have received no more than two prior chemotherapy regimens. • At least 4 weeks from prior anticancer treatment (surgery, radiotherapy and systemic therapies) and full recovery from all their adverse effects). • WHO performance status 0, 1 or 2. Exclusion Criteria: • Known central nervous system metastases. • Previous malignancies (except curatively treated non-melanoma skin cancer or carcinoma in situ of the cervix or breast) within the past 3 years. • Uncontrolled or poorly controlled hypertension. • Heart failure ≥ NYHA class II. • Thromboembolic events (arterial or venous thrombosis, myocardial infarction, unstable angina, cardiac angioplasty or stenting) within the past 12 months. • Therapeutic dose warfarin. • History of malabsorption or major gastrointestinal tract resection likely to affect trial drug absorption. • Patients with cavitating lung metastases or any metatstasis abutting or invading a major pulmonary blood vessel on baseline CT or MRI scan. • History of bleeding diathesis or coagulopathy within 12 months of study entry • History of haemoptysis > 2.5 ml (½ teaspoonful) of blood in any 24-hour period within 6 months of enrolment. • Regular treatment with antiplatelet medication, including aspirin >325 mg/day or NSAIDs..	• 10 Angiosarcoma • 7 Synovial Sarcoma	Edinburgh, Leeds, London, Manchester, Oxford, Sheffield, Southampton, Nottingham, Aberdeen, Bristol, Wirral, Dundee

Study name and Contact	Cancer type	Inclusion and Exclusion summary	# of patients needed	Sites
RTL Advanced - GI159 Liz Anne Lewsley Project Manager 0141 301 7193 Liz-Anne.Lewsley@glasgow.ac.uk	Gastro-oesophageal	Inclusion Criteria: • Histologically or cytologically confirmed locally advanced or metastatic gastric, gastro-oesophageal junction, or oesophageal adenocarcinoma. • Patients who are due to start chemotherapy with either the ECX/ECF (epirubicin, cisplatin and capecitabine/5-FU) or EOX/EOF (epirubicin, oxaliplatin and capecitabine/5-FU) regimens. Additionally, patients randomised in the NCRN REAL-3 study to receive EOX + panitumumab will also be eligible. • Written informed consent. • At least one lesion which is uni-dimensionally measurable by RECIST (5) Age >18 years. • Able to comply with study protocol. Exclusion Criteria: • Any evidence of any medical or psychiatric disorders that would be a contra-indication to venesection. • Women who are pregnant or lactating • Patients who have had systemic anti-cancer therapy or radiotherapy within the previous 6 weeks. • Life expectancy < 3 months.	330	Aberdeen Royal Infirmary, Airedale General Hospital, Beatson WoS Cancer Centre, Calderdale & Huddersfield NHS Trust, Castle Hill Hospital, Furness General & Royal Lancaster, Musgrove Park Hospital, Russells Hall Hospital, St James's University Hospital, Western General Hospital and Weston Park Hospital. Study can be opened at other sites
RTL Peri-operative - GI160 Liz Anne Lewsley Project Manager 0141 301 7193 Liz-Anne.Lewsley@glasgow.ac.uk	Gastro-oesophageal	Inclusion Criteria: • Histologically or cytologically confirmed gastric or gastro-oesophageal junction (including Type I lower oesophageal) • adenocarcinoma. • Patients who are considered to have operable disease as determined by the MDT (Multi-Disciplinary Team) and who are candidates for peri-operative chemotherapy with either the ECF/EOF or ECX/EOX (epirubicin, Cisplatin/oxaliplatin and capecitabine/5-FU) regimens. Additionally, patients randomised in the NCRN STO3	306	Aberdeen Royal Infirmary, Airedale General Hospital, Beatson WoS Cancer Centre, Belfast City Hospital,

Study name and Contact	Cancer type	Inclusion and Exclusion summary	# of patients needed	Sites
		study to receive ECX + bevacizumab will also be eligible. • Written informed consent. • Age >18 years. • Able to comply with study protocol. Exclusion Criteria: • Any evidence of any medical or psychiatric disorders that would be a contra-indication to venesection. • Women who are pregnant or lactating • Patients who have had systemic anti-cancer therapy or radiotherapy within the previous 6 weeks. • Life expectancy < 3 months.		Calderdale & Huddersfield NHS Trust, Castle Hill Hospital, Furness General & Royal Lancaster, Musgrove Park Hospital, Russells Hall Hospital, Weston Park Hospital Study can be opened at other sites
CUFOX study A phase I/IIa study combining curcumin (Curcumin C3-Complex, Sabinsa) with standard care FOLFOX chemotherapy in patients with inoperable colorectal cancer Prof Will Steward Prof of Medical Oncology Osborne Building, Leicester Royal Infirmary, LE1 5WW 0116 258 7597 wps1@le.ac.uk	Colorectal cancer (Metastatic, inoperable)	Inclusion Criteria: • Metastatic colorectal cancer • Measurable by RECIST 1.1 • ECOG Performance status 0/1 • ≥ Age 18 • Life expectancy > 12 weeks Exclusion Criteria: • Contraindication to FOLFOX chemotherapy • Previous cancer <5 years (except colorectal, basal cell carcinoma, in-situ cervical) • Serious concurrent medical condition • Major surgery within 4 weeks	Phase I: 9 – 18 Phase IIa: 33	Leicester Royal Infirmary (University Hospitals of Leicester NHS Trust)
RADICAL Study A single arm phase IIa study (with combination safety run-in) to assess the safety and efficacy of AZD4547 in combination with anastrozle or letozole in ER positive breast	Breast cancer with documented positive oestrogen receptor status (ER+) of primary or metastatic	Inclusion Criteria: • Written informed consent and ability to comply with study protocol • Aged ≥ 25 years of age • Post menopausal women with histological confirmation of breast cancer with documented positive oestrogen receptor status (ER+) of primary or metastatic tumour	Safety run-in: Recruitment complete Phase IIa: 50	Charing Cross Hospital, London Addenbrooke's Hospital, Cambridge Freeman

Study name and Contact	Cancer type	Inclusion and Exclusion summary	# of patients needed	Sites
cancer patients who have progressed on treatment with anastrozole or letrozole Philip D Badman Clinical Trial Co-ordinator Imperial Clinical Trials Unit - Cancer Department of Surgery and Cancer Imperial College London 1st Floor, Medical Oncology Charing Cross Hospital Fulham Palace Road, London W6 8RF Tel: 020 3311 5203 E-mail: radical@imperial.ac.uk	tumour tissue	tissue • ECOG performance status 0-1 and minimum life expectancy of 12 weeks • Fulfils criteria for previous treatment of breast cancer: a. **Safety run-in**: Relapse during a single regimen of adjuvant endocrine therapy with either anastrozole or letrozole **OR** b. Progression during first line endocrine therapy with anastrozole or letrozole for advanced breast cancer c. **Phase IIa**: Progressing or progression at some point during breast cancer treatment on endocrine therapy with a non-steroidal AI* d. Co-administration of a targeted agent with the non-steroidal AI is permitted providing all toxicities have recovered to CTCAE Grade 1 or below. e. Prior chemotherapy in the advanced and adjuvant setting is permitted. f. Prior treatment with exemestane with or without everolimus is permitted. *anastrozole or letrozole does not have to be the most recent line therapy • **Safety run-in**: At least 1 lesion (measurable/non measurable) that can be accurately assessed by CT/MRI/plain x-ray at baseline and follow-up • **Phase IIa**: At least 1 measurable lesion ≥ 10mm in longest diameter (or ≥ 15mm in the short axis for nodal disease) at baseline that can be accurately assessed by CT/MRI at baseline and follow up. Patients with bone only metastatic cancer must have a lytic or mixed lytic-blastic lesion that can be accurately assessed by CT or MRI. • Adequate haematological, hepatic and renal function • **Phase IIa:** Mandatory provision of tumour biopsy for assessment of FGFR1 status by FISH • **Safety run-in**: Study entry must be preceded by a minimum of 21 days of anastrozole or letrozole treatment • **Phase IIa:** No set duration of anastrozole or letrozole treatment prior to study entry		Hospital, Newcastle Beatson West of Scotland Cancer Centre, Glasgow **Up to 10 new sites**
DI-B4 anti-CD19 Zoe Backholer Clinical Study Manager Centre for Drug Development	B-Cell Lymphoma and Chronic Lymphocytic Leukaemia	**Inclusion Criteria:** 1. Relapsed or refractory indolent B-cell lymphoma or chronic lymphocytic leukaemia patients who have received at least one line of previous therapy. 2. CD19 positive malignancy by immunohistochemistry or flow cytometry 3. Life expectancy of at least 12 weeks	16 -40	Southampton General Hospital The Christie Hospital (Manchester)

Study name and Contact	Cancer type	Inclusion and Exclusion summary	# of patients needed	Sites
Cancer Research UK Tel: 020 3469 6992 zoe.backholer@cancer.org.uk		4. World Health Organisation (WHO) performance status of 0-1 5. Haematological and biochemical indices within the ranges shown below. Haemoglobin (Hb) ≥ 9.0 g/dL (red cell support is permissible), Absolute neutrophil count (ANC) ≥1.0 x 10^9/L (or ≥0.5 x 10^9/L if bone marrow involvement), Platelet count ≥75 x 10^9/L (or ≥50 x 10^9/L if bone marrow involvement), Serum bilirubin ≤1.5 x upper limit of normal (ULN) unless raised by Gilbert's syndrome in which case up to 3 x ULN is acceptable, Alanine amino-transferase (ALT) and/or aspartate amino-transferase (AST) ≤ 2.5 x (ULN) unless raised due to hepatic involvement in which case up to 5 x ULN is permissible Calculated creatinine clearance (Cockroft-Gault formula) ≥30 ml/min (uncorrected value) 6. 18 years or over 7. Written (signed and dated) informed consent and be capable of co-operating with treatment and follow-up 8 Indolent B-cell lymphoma patients only: Patient has either at least one measurable lesion by CT scan (defined as >1.5 cm in one axis) or in the case of Waldenström's macroglobulinemia, disease must be assessable by the criteria stated in the protocol. **Exclusion Criteria:** 1. Radiotherapy (except for palliative reasons), endocrine therapy, immunotherapy, chemotherapy or investigational medicinal products during the previous 4 weeks before treatment. 2. Ongoing toxic manifestations of previous treatments. Exceptions to this are alopecia or certain Grade 1 toxicities, which in the opinion of the Investigator and the Sponsor should not exclude the patient. 3. Known to be serologically positive for hepatitis B (unless due to vaccination), hepatitis C or human immunodeficiency virus (HIV). 4. Patients with clinically active leptomeningeal or central nervous system lymphoma/leukaemia. 5. Patients with transformed lymphoma from a pre-existing indolent lymphoma. Patients with a previous history of transformation, but on this disease episode have a biopsy proven indolent recurrence may be included. 6. Patients receiving corticosteroids, except where the patient has been on a stable dose for the preceding seven days. Doses of prednisolone or equivalent >10 mg daily are not permitted whilst on the study. 7. Concurrent congestive heart failure, prior history of class III/ IV cardiac disease NYHA, prior history of cardiac ischaemia or prior history of cardiac arrhythmia.		The Royal Liverpool University Hospital The Churchill Hospital (Oxford) Derriford Hospital (Plymouth)

Study name and Contact	Cancer type	Inclusion and Exclusion summary	# of patients needed	Sites
		8. Ability to become pregnant (or already pregnant or lactating). However, those female patients who have a negative serum or urine pregnancy test before enrolment and agree to use two highly effective forms of contraception during the trial and for six months afterwards are considered eligible. 9. Male patients with partners of child-bearing potential (unless they agree to take measures not to father children by using one form of highly effective contraception during the trial and for six months afterwards). Men with pregnant or lactating partners should be advised to use barrier method contraception to prevent exposure to the foetus or neonate. 10. Major thoracic or abdominal surgery from which the patient has not yet recovered. 11. At high medical risk because of non-malignant systemic disease including active uncontrolled infection. 12. Is a participant or plans to participate in another interventional clinical trial, whilst taking part in this Phase I study of DI-B4. Participation in an observational trial would be acceptable. 13. Any other condition which in the Investigator's opinion would not make the patient a good candidate for the clinical trial.		
Short Title: CEDAR **Title:** A Phase II, randomised, open-label study of Gemcitabine/Carboplatin first-line chemotherapy in combination with or without the antisense oligonucleotide OGX-427 in advanced squamous cell lung cancers **Contact:** CEDAR Coordinator - 0207 882 8490 **Email:** CEDAR@qmcr.qmul.ac.uk	non small cell lung cancers	**INCLUSION:** 1. Written informed consent prior to admission to this study 2. Histologically confirmed squamous cell lung cancer; patients with adenosquamous or mixed histology are not eligible for this study 3. Stage IIIB disease that is unsuitable to radio-chemotherapy or Stage IV disease or recurrent NSCLC; recurrent disease must not be amenable to resection or radical radiotherapy with curative intent. 4 Patients must have: • at least one lesion, not previously irradiated, that can be measured accurately at baseline as ≥10 mm in the longest diameter (except lymph nodes which must have short axis ≥15 mm) with computed tomography (CT) or magnetic resonance imaging (MRI) which is suitable for accurate repeated measurements OR • lytic or mixed (lytic + sclerotic) bone lesions in the absence of measurable disease as defined above; NOTE: patients with sclerotic/osteoblastic bone lesions only in the absence of measurable disease are not eligible 5 Willing to donate archival diagnostic tissue for translational research, if available. 6 Haematologic and biochemical indices within the ranges shown below. These	140	The Christie NHS Foundation Trust; Royal Surrey County Hospital NHS Foundation Trust; Royal Berkshire NHS Foundation Trust; University College Hospitals NHS Foundation Trust; Barts and the London NHS Foundation Trust; Colchester Hospital

Study name and Contact	Cancer type	Inclusion and Exclusion summary	# of patients needed	Sites
		measurements must be performed within one week prior to randomisation • ANC ≥1.5 x 109/L;, platelet count ≥100 x 109/L, • Serum creatinine < 1.5 times the upper limit of normal (ULN) • Bilirubin level < 1.5 X ULN • AST or ALT <3.0 X ULN or <5 X ULN in the presence of liver metastases 7 ECOG performance status 0-2 8 Non-childbearing potential (i.e., physiologically incapable of becoming pregnant), including any female who has had a hysterectomy, bilateral oophorectomy, bilateral tubular ligation or is post-menopausal (total cessation of menses for ≥ 1 year; if the patient is of childbearing potential, she must have a negative serum pregnancy test within 2 weeks prior to the first dose of study treatment, preferably as close to the first dose as possible, and agrees to use adequate contraception (for example, intrauterine device [IUD], birth control pills unless clinically contraindicated, or barrier device) beginning 2 weeks before the first dose of investigational product and for 28 days after the final dose of investigational product. 9 Male or Female aged ≥18 years **EXCLUSION:** 1 Symptomatic CNS involvement or CNS involvement requiring steroid therapy; patients with treated brain metastases that are asymptomatic and have been clinically stable for 1 month will be eligible for protocol participation 2 Previous systemic treatment for lung cancer (exception for patients with recurrent disease: adjuvant chemotherapy is allowed as long as this was finished at least 1 year prior to enrolment and did not contain gemcitabine) 3 Known tumour EGFR mutation, unless contraindication to EGFR-directed therapy 4 Known tumour ALK rearrangements, unless contraindication to Alk-directed therapy or Alk-directed therapy not available 1 5 Pre-existing sensory or motor polyneuropathy ≥ Grade 2 according to NCI CTCAE 6 Significant cardiovascular disease, such as • History of myocardial infarction, acute coronary syndromes (including unstable angina), or history of coronary angioplasty/stenting/bypass grafting within past 6 months. • History of symptomatic congestive heart failure (CHF) New York Heart Association (NYHA) Classes III-IV or LVEF <50% by either ECHO or MUGA within past 6 months. • Severe cardiac arrhythmia requiring medication or severe conduction abnormalities • Poorly controlled hypertension (resting diastolic blood pressure >115 mmHg)		University NHS Foundation Trust; Sandwell and West Birmingham Hospitals NHS Trust; Velindre NHS Trust; Nottingham University Hospitals NHS Trust; Betsi Cadwaladr University Health Board – Glan Clwyd Hospital; Heart of England NHS Foundation Trust; Abertawe Bro Morgannwg Uni Health Board – Singleton Hospital; Betsi Cadwaladr University Health Board – Wrexham Maelor Hospital; University Hospital Birmingham NHS Foundation Trust; Yeovil District Hospital NHS Foundation

Study name and Contact	Cancer type	Inclusion and Exclusion summary	# of patients needed	Sites
		• Clinically significant valvular disease, cardiomegaly, ventricular hypertrophy, or cardiomyopathy 7 Active second malignancy (except non-melanomatous skin cancer): active secondary malignancy is defined as a current need for cancer therapy or a high possibility (>30%) of recurrence during the study. 8 Concurrent treatment with other experimental drugs or participation in another clinical trial with any investigational drug within 30 days prior to study entry. 9 Any other disease, metabolic dysfunction, physical examination finding, or clinical laboratory finding that, in the investigator's opinion, gives reasonable suspicion of a disease or condition that contraindicates the use of an investigational drug, may affect the interpretation of the results, render the patient at high risk from treatment complications or interferes with obtaining informed consent. 10 Psychological, familial, sociological or geographical conditions that do not permit compliance with the study protocol. 11 Pregnant or nursing women 12 Male or Female aged <18 years		Trust; Royal Free London NHS Foundation Trust; Hinchingbrooke Health Care NHS Trust; Belfast Health and Social Care Trust; Royal United Hospital Bath Trust; Royal Cornwall Hospitals NHS Trust; Lewisham and Greenwich NHS Trust; University's Hospitals of Leicester NHS Trust; Western Area Health NHS Trust; Royal Devon and Exeter NHS Foundation Trust
ComPAKT: A Phase I multi-centre trial of the Combination of olaparib (PARP inhibitor) and AZD5363 (AKT inhibitor) in patients with advanced solid tumours **Contact:** Dr Timothy Yap, Drug Development Unit, Sycamore House, The Institute of Cancer	Advanced solid tumours enriched for BRCA1/2 mutant cancers, triple negative breast cancer (TNBC), castration-resistant prostate cancer (CRPC) and high	**Inclusion criteria** 1. **Escalation phase**: Patients with histologically or cytologically confirmed malignant advanced solid tumours refractory to standard therapy or for which no suitable effective standard therapy exists, including, but not limited to patients with: *BRCA1/2* mutant cancers (including those previously exposed to PARP inhibitors), TNBC, CRPC and HGSOC, and those with somatic mutations or other aberrations known to result in a hyperactivated PI3K-AKT pathway. **Expansion phase**: **(1) BRCA1/2 mutation cohort:** Patients with advanced germline *BRCA1/2* mutant solid tumours including those previously exposed to PARP	58	ICR/RMH, Newcastle, Hammersmith

Study name and Contact	Cancer type	Inclusion and Exclusion summary	# of patients needed	Sites
Research and Royal Marsden Hospital, Downs Road, Sutton SM2 5PT. **timothy.yap@icr.ac.uk**	grade serous ovarian cancer (HGSOC), and those with somatic mutations or other aberrations known to result in a hyperactivated phosphatidylinositol-3-kinase (PI3K)-AKT pathway	inhibitors; **(2) Sporadic cancers cohort:** This cohort will include advanced sporadic cancers that are not known to harbour germline *BRCA1/2* mutations, but which may harbour homologous recombination (HR) defects, e.g. advanced TNBC, CRPC and HGSOC, and those with somatic mutations or other aberrations known to result in a hyperactivated PI3K-AKT pathway. 2. ECOG performance status of 0-1 3. Evaluable or measurable disease as assessed by RECIST 1.1 4. Haematological and biochemical indices within the ranges shown below.		

Laboratory Test	
Haemoglobin (Hb)	**Value required**
Absolute neutrophil count	≥ 10.0 g/dL (and no blood transfusions in the preceding 28 days)
Platelet count	≥ 1.5 x 10^9/L
Serum bilirubin	≥ 100 x 10^9/L
Alanine aminotransferase (ALT) and aspartate aminotransferase (AST)	≤ 1.5 x upper limit of normal (ULN) except for patients with documented Gilburt's disease
Creatinine	≤ 2.5 x (ULN) unless raised due to tumour in which case up to 5 x ULN is permissible

Exclusion criteria

1. Radiotherapy (except for palliative reasons), endocrine therapy, immunotherapy or chemotherapy during the previous four weeks (six weeks for nitrosoureas, Mitomycin-C) and 4 weeks for investigational medicinal products before treatment, except for hormonal therapy with luteinizing hormone-releasing hormone (LHRH) analogues for medical castration in patients with CRPC, which are permitted.
2. Ongoing toxic manifestations of previous treatments. Exceptions to this are Grade 1 toxicities, which in the opinion of the Investigator should not exclude the patient.
3. Ability to become pregnant (or already pregnant or lactating). However, those female patients who have a negative serum or urine pregnancy test before enrolment and agree to use two highly effective forms of contraception (oral, injected or implanted hormonal contraception and condom, have an intra-uterine device and condom, diaphragm with spermicidal gel and condom) for four weeks

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		before entering the trial, during the trial and for six months afterwards are considered eligible. 4. Male patients with partners of child-bearing potential (unless they agree to take measures not to father children by using one form of highly effective contraception [condom plus spermicide] during the trial and for six months afterwards). Men with pregnant or lactating partners should be advised to use barrier method contraception (for example, condom plus spermicidal gel) to prevent exposure to the foetus or neonate. 5. Major surgery (excluding minor procedures, e.g. placement of vascular access) within 4 weeks of the first dose of study treatment. 6. At high medical risk because of severe or uncontrolled systemic disease including active bleeding diathesis or active infection including hepatitis B, hepatitis C and human immunodeficiency virus (HIV). Screening for chronic conditions is not required. 7. Clinically significant abnormalities of glucose metabolism as defined by any of the following: • Diagnosis of diabetes mellitus type I or II (irrespective of management). • Glycosylated haemoglobin (HbA1C) ≥ 8.0% at screening (64 mmol/mol) (conversion equation for HbA1C [IFCC-HbA1C (mmol/mol)] = [DCCT-HbA1C (%) – 2.15] x 10.929) • Fasting Plasma Glucose ≥ 8.9mmol/L at screening. Fasting is defined as no caloric intake for at least 8 hours. 8. Proteinuria 3+ on dipstick analysis or >500mg/24 hours. 9. For Part B (sporadic cancers arm) of dose expansion cohort only: Previous treatment with a PARP inhibitor or PI3K/AKT inhibitor 10. Treatment with potent inhibitors or inducers or substrates of CYP3A4 or substrates of CYP2D6 within 2 weeks before the first dose of study treatment (3 weeks for St John's Wort). 11. Spinal cord compression or brain metastases unless asymptomatic, treated and stable and not requiring steroids for at least 4 weeks prior to start of study treatment 12. Any of the following cardiac criteria: • Mean resting corrected QT interval (QTc) > 470 msec obtained from 3 consecutive electrocardiograms (ECGs) • Any clinically significant abnormalities in rhythm, conduction or		

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		morphology of resting ECG, e.g. complete left bundle branch block, third degree heart block • Any factors that increase the risk of QTc prolongation or risk of arrhythmic events, such as heart failure, hypokalaemia, congenital long QT syndrome, family history of long QT syndrome or unexplained sudden death under 40 years of age or any concomitant medication known to prolong the QT interval • Experience of any of the following procedures or conditions in the preceding 6 months: coronary artery bypass graft, angioplasty, vascular stent, myocardial infarction, angina pectoris, congestive heart failure New York Heart Association [NYHA0 Grade 2 (refer to Appendix 4) • Uncontrolled hypotension – Systolic BP <90mmHg and/or diastolic BP <50mmHg Left ventricular ejection fraction (LVEF) below institutional lower limit of normal. 13. Refractory nausea and vomiting, chronic gastrointestinal diseases, inability to swallow the formulated product or previous significant bowel resection that would preclude adequate absorption of olaparib and AZD5363. 14. History of hypersensitivity to active or inactive excipients of AZD5363 or olaparib or drugs with a similar chemical structure or class to AZD5363 and olaparib. 15. Is a participant or plans to participate in another interventional clinical trial, whilst taking part in this Phase I study. Participation in an observational trial would be acceptable. 16. Any other condition which in the Investigator's opinion would not make the patient a good candidate for the clinical trial. **17.** Patients with myelodysplastic syndrome or acute myeloid leukaemia		
COAST Cisplatin Ototoxicity attenuated by ASpirin Trial Chief Investigator: Dr Emma King Clinical Trials Manager: Karen Martin	Head and Neck, Germ Cell, Bladder-carcinoma and thoracic patient groups will make up the majority of enrolled patients,	<u>Inclusion Criteria</u> 1. Written informed consent 2. Any patient deemed fit for chemotherapy according to sites own local defined cancer network protocol for chemotherapy regimes, and offered a cumulative dose $\geq$200mg/m^2 cisplatin as a single agent or as combination chemotherapy for malignancy with planned treatment of a maximum of two consecutive days cisplatin per cycle. 3. Over 18 years of age.	88	<u>Open sites</u> Southampton General Hospital Royal Marsden Hospital (Chelsea/Sutton & William Rous Unit Kingston)

Study name and Contact	Cancer type	Inclusion and Exclusion summary	# of patients needed	Sites
Clinical Trials Coordinator: Julia Abab University of Southampton Clinical Trials Unit MP131 Southampton General Hospital Tremona Road Southampton SO16 6YD Tel: 02381 205154 Fax: 0844 7740621 **Email**: coast@soton.ac.uk	however all patients, irrespective of tumour site will be eligible to enroll with the exception of Nasopharyngeal carcinoma patients who will be excluded from the Trial.	Exclusion Criteria 1. Previous cisplatin treatment. 2. Patients with a diagnosis of nasopharyngeal (or skull base) carcinoma. (Patients with other head and neck tumours being treated with radiotherapy are eligible). 3. Patients where planned cisplatin is to be given as a split dose regimen on days 1 to 5 or on days 1 and 8. 4. Patients receiving therapeutic aspirin defined as >75mg per day. 5. Previous Haemorrhagic stroke. 6. Inflammatory bowel disease. 7. Patients with absolute contraindications to aspirin, PPIs or their excipients i.e. allergies, ulcers, renal impairment or use of oral anticoagulants. 8. Haematological or clotting disorders. 9. Patients with symptomatically overt hearing loss which the Principal Investigator (PI) considers should exclude the use of cisplatin. 10. Pregnant or breast-feeding patients. Women of childbearing potential must have a negative pregnancy test performed within 7 days prior to the start of trial drug. Both men and women enrolled in this Trial must use adequate birth control. Patients enrolled or who plan to enrol in IMP or Surgical Interventional Clinical Trial during the trial period.		St James Hospital, Leeds Queen Elizabeth Hospital, Birmingham Royal Bournemouth Hospital Poole Hospital Beatson West of Scotland Cancer Centre Closed to recruitment Velindre Hospital, Cardiff
ProCAID An open label phase I/randomised, double blind phase II study in metastatic castration resistant Prostate Cancer of AZD5363 In combination with Docetaxel and prednisolone chemotherapy Karen Martin: Clinical Trial Manager Nicky Downs: Clinical Trial Coordinator University of Southampton Clinical Trials Unit MP131 Southampton General Hospital	Prostate	**INCLUSION CRITERIA** Patients will be required to meet the following criteria in full: 1.Histologically or cytologically proven mCRPC with documented metastases (measurable or evaluable disease is acceptable) now eligible for treatment with docetaxel chemotherapy 2. Disease progression since the last change in therapy defined by one or more of the following according to the Prostate Cancer Working Group (PCWG2) criteria (Scher et al. 2008 J Clin Oncol. 26; 1148): i. PSA progression as defined by the prostate cancer working group 2 (PCWG2) criteria (Scher et al. 2008 J Clin Oncol. 26; 1148). This must be based on a series of at least 3 readings at least 7 days apart demonstrating rising PSA. The 3rd reading must be ≥ 2ng/ml. In the event where an intermediate reading is lower than a previous reading, then the patient will still be eligible (i.e. the 3 readings do not need to be consecutive). The first	Phase I: 9-18 Phase II: 150	Phase I currently in progress Southampton General Hospital, Beatson WoS Cancer Centre, Royal Marsden Hospital (London)

Study name and Contact	Cancer type	Inclusion and Exclusion summary	# of patients needed	Sites
Tremona Road Southampton SO16 6YD Tel: 02381 205302 Fax: 0844 7740621 **Email**: procaid@soton.ac.uk		of the three readings must have been obtained after commencing the previous systemic therapy, or, in the case of androgen receptor antagonists, after discontinuing. ii. Radiographic progression of nodal or visceral metastases as defined by RECIST version 1.1 (See Appendix 5) iii. The appearance of two or more new bony metastases 3. Serum testosterone <1.7 nmol/L (ongoing LHRH analogue or antagonist therapy is permitted to maintain a castrate state) 4. Discontinuation of prior therapies for prostate cancer ≥ 4 weeks prior to commencing study treatment (with the exception of an LHRH agonist or antagonist where required for ongoing testosterone suppression) 5. No anti-androgen withdrawal response. Consistent with PCWG2 guidelines, investigators should evaluate patients to exclude withdrawal response for 6 weeks after stopping anti-androgen therapy. Investigators need not wait to assess for withdrawal response in patients who did not respond, or who showed a PSA decline for ≤ 3 months, after an anti-androgen was administered as a second-line or later intervention 6. ECOG performance status 0 or 1 7.Hb ≥ 9g/dL; platelets ≥ 100 x 109/L; neutrophils ≥ 1.5 x109/L 8. Bilirubin ≤ ULN ; ALT and AST ≤ 1.5 x ULN. 9. Sodium and potassium within the normal range for the treating institution 10. Able to swallow oral study drugs (without crushing/opening in the case of AZD5363) 11. Life expectancy > 3 months 12. Aged 18 years or over 13. Provision of written informed consent **EXCLUSION CRITERIA** Patients with any of the following are ineligible for this study: 1. Previous treatment with cytotoxic chemotherapy (patients may have received previous or ongoing bisphosphonates or denosumab). There are no restrictions on		

Study name and Contact	Cancer type	Inclusion and Exclusion summary	# of patients needed	Sites
		prior use of second generation hormonal therapies e.g. abiraterone, enzalutamide 2. Prior malignancy with an estimated ≥ 30% chance of relapse within 2 years 3. Previously identified brain metastases, or spinal cord compression unless treated with full functional recovery 4. Prior radiotherapy to > 30% of bone marrow 5. Administration of an investigational agent within 30 days of first dose of study medication 6. Type I or II diabetes mellitus requiring either insulin or oral hypoglycaemics for routine management. Patients with type II diabetes mellitus that is well controlled by dietary measures alone are eligible to participate. Patients found to have a fasting glucose ≥7 mmol/L (≥126 mg/dL) or glycosylated haemoglobin >8% (64 mmol/mol) at screening should be assessed for appropriate management according to local policy. 7. Malabsorption syndrome, previous gastrointestinal surgery, or other gastrointestinal condition that may affect drug absorption 8. Coronary artery bypass graft, angioplasty, vascular stent, myocardial infarction, angina pectoris or congestive heart failure (NYHA ≥ grade 2) within the last 6 months 9. Abnormal echocardiogram (LVEF <LLN) 10. Uncontrolled hypotension (systolic blood pressure <90 mmHg and/or diastolic blood pressure <50 mmHg) 11. QTc interval of >480 msec at two or more time points within a 24 hour period 12. Proteinuria (either 3+ on dipstick analysis or >500 mg/24 hours) or creatinine >1.5 x ULN concurrent with creatinine clearance <50 mL/min (assessed as per local practice e.g. by Cockcroft and Gault estimation) 13. Exposure to potent inhibitors or inducers of CYP3A4 or CYP2D6 or substrates of CYP3A4 within 2 weeks before the first dose of study treatment (3 weeks for St John's Wort) 14. Unresolved toxicity ≥ grade 2 (except alopecia) from previous cancer therapy 15. Patients with a partner of child-bearing potential who are not using a highly effective method of contraception, who are unwilling to use condoms during the		

Study name and Contact	Cancer type	Inclusion and Exclusion summary	# of patients needed	Sites
		study and for 30 days after the last dose of study drug 16. Known hypersensitivity to AZD5363, its excipients, or drugs in its class 17. Previous exposure to agents with the following mechanisms of action: • inhibition of AKT (e.g., MK2206, GDC0068, GSK2110183, GSK2141795) any inhibitor with PI3K pharmacology (e.g., GDC0941, XL147, BKM120, PX866, BYL719, AMG319, GDC0032, INK1117, INK119) • any compound with mixed PI3K and mammalian target of rapamycin (mTOR) kinase pharmacology (e.g., BEZ235, GDC0980, PF04691502, PF05212384, GSK2126458, XL765) • or any mTOR kinase inhibitor (e.g., AZD8055, AZD2014, OSI027, INK128)		
A phase I open-label, dose escalation study of **GSK2816126** (EZH2 inhibitor) in subjects with relapsed/refractory diffuse large B cell and transformed follicular lymphoma Contacts: Dr Tim Yap at timothy.yap@icr.ac.uk (Royal Marsden Hospital Drug Development Unit, Sutton) or Professor Peter Johnson at johnsonp@soton.ac.uk (Southampton Cancer Research UK Centre)	Relapsed/refractory diffuse large B cell and transformed follicular lymphoma	**Inclusion Criteria** Subjects eligible for enrollment in the study must meet all of the following criteria: 1. Provided signed written informed consent 2. Males and females ≥18 years of age (at the time consent is obtained). 3. Tumor type criteria: relapsed/refractory NHL that meets one of the following criteria: • GCB-DLBCL or transformed FL relapsed after or refractory to at least one prior chemotherapy regimen (e.g., rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone [R-CHOP]) AND not a candidate for standard salvage regimens or autologous stem cell transplant (eg due to age, comorbid conditions or failure to respond to salvage chemotherapy) • GCB-DLBCL or transformed FL relapsed after or refractory to at least two prior chemotherapy regimens 4. Must have a pre-existing central venous access such as a port, Hickmann catheter or a peripherally inserted central catheter (PICC line) or be willing and able to have one inserted 5. Availability of archival tissue, or willingness to undergo fresh biopsy for: prospective confirmation of GCB-DLBCL status (DLBCL subjects); and retrospective central testing of EZH2 mutation status (all subjects). 6. ECOG Performance Status of 0 or 1 7. Adequate organ system function.	100 worldwide	Southampton and ICR/RMH, Sutton (UK sites)

Study name and Contact	Cancer type	Inclusion and Exclusion summary	# of patients needed	Sites

Exclusion Criteria

1. Currently receiving cancer therapy (chemotherapy, radiation therapy, immunotherapy or biologic therapy) (permitting corticosteroids to control systemic or
local symptoms, up to a dose of 10 mg prednisolone or equivalent daily and stable for at least 2 weeks prior to enrollment).
2. Received an investigational anti-cancer drug within 4 weeks, or within 5 half-lives (whichever is shorter) of the first dose of study drug(s). At least 14 days must have passed between the last dose of prior investigational agent and the first dose of study drug.
3. Known HIV, Hepatitis B (positive HBsAg), or Hepatitis C infection. Subjects
Who are negative for HBsAg, but HBcAB positive, a HB DNA test will be performed and if positive will be excluded. Subjects with positive serology but negative HCV RNA test results are eligible.
4. Current use of therapeutic warfarin. Therapeutic dosing of warfarin is defined as resulting in an INR >1.3. Low molecular weight heparin is permitted.
5. Any major surgery, radiotherapy or immunotherapy within the 4 weeks prior to first dose of study drug, or palliative radiotherapy to a single symptomatic lesion within the 2 weeks prior to first dose of study drugs.
6. Subjects who have previously received an autologous stem cell transplant are allowed if a minimum of 100 days has elapsed from the time of transplant (T0) and the subject has recovered from transplant-associated toxicities prior to the first dose of GSK2816126.
7. Chemotherapy regimens with delayed toxicity within the 3 weeks prior to first dose of study drug(s). Chemotherapy regimens given continuously or on a weekly basis with limited potential for delayed toxicity within 2 weeks prior to first dose of study drug(s).
8. Unresolved toxicity greater than NCI-CTCAE version 4 (Grade 1 if marrow is clear, Grad 2 if not) from previous anti-cancer therapy, with the exception of alopecia and lymphopenia [NCI-CTCAE, 2009].
9. Psychological, familial, sociological or geographical conditions that do not permit

Study name and Contact	Cancer type	Inclusion and Exclusion summary	# of patients needed	Sites
		compliance with the protocol. 10. Cardiac exclusion criteria: • History of acute coronary syndromes (including myocardial infarction and unstable angina), coronary angioplasty, or stenting within the past 6 months prior to first dose of study drug(s). • QTc interval > 480msec • Uncontrolled arrhythmias. Subjects with controlled atrial fibrillation for > 1 month prior to first dose of study drug may be eligible. • Class II, III or IV heart failure as defined by the New York Heart Association (NYHA) functional classification system. 11. Known immediate or delayed hypersensitivity reaction or idiosyncrasy to drugs chemically related to the study drug or their excipients. 12. Pregnant or lactating female. 13. Unwillingness or inability to follow the procedures outlined in the protocol. 14. Uncontrolled diabetes or other medical condition that may interfere with assessment of toxicity.		
AT13148 A Cancer Research UK Phase I first in man study of the novel AGC kinase inhibitor AT13148 given orally in patients with advanced solid tumours Zoe Backholer Clinical Study Manager Centre for Drug Development Cancer Research UK Tel: 020 3469 6992 **Zoe.Backholer@cancer.org.uk**	Solid tumour	**Inclusion criteria:** • Histologically proven advanced solid tumours, refractory to conventional treatment, or for which no conventional therapy exists or is declined by the patient. Paraffin-embedded tumour tissue must be available for genetic mutation status testing. • Life expectancy of at least 12 weeks • World Health Organisation (WHO) performance status of 0, 1 or 2 • Haematological and biochemical indices within the ranges shown below. These measurements must be performed within 7 days before their first dose of AT13148 taken between Day -7 to -4. ○	40	The Royal Marsden Hospital, Sutton, Surrey

Study name and Contact	Cancer type	Inclusion and Exclusion summary	# of patients needed	Sites

Laboratory Test	Value required
Haemoglobin (Hb)	≥ 9.0 g/dL
Absolute neutrophil count	≥ 1.5 x 10^9/L
Platelet count	≥ 100 x 10^9/L
Fasting glucose	≤ 7 mmol/L
Either: Serum bilirubin Or: Alanine aminotransferase (ALT) and aspartate aminotransferase (AST)	≤ 1.5 x upper limit of normal (ULN) ≤ 2.5 x (ULN) unless raised due to tumour in which case up to 5 x ULN is permissible
Either: Calculated creatinine clearance Or: Isotope clearance measurement	≥ 50 mL/min ≥ 50mL/min (uncorrected)

- Adequate lung function indicated by a resting oxygen saturation level (on air) ≥ 94%, a CO-transfer factor > 60%
- 18 years or over
- Written (signed and dated) informed consent and be capable of co-operating with treatment and follow-up

Exclusion criteria:

- Radiotherapy (except for palliative reasons), endocrine therapy (except luteinizing hormone releasing hormone (LHRH) agonists for prostate cancer), immunotherapy or chemotherapy during the previous four weeks (six weeks for nitrosoureas, Mitomycin-C) and 4 weeks for investigational medicinal products) before treatment.
- Ongoing toxic manifestations of previous treatments. Exceptions to this are alopecia or certain Grade 1 toxicities, which in the opinion of the Investigator and the Centre for Drug Development (CDD) should not exclude the patient.
- Symptomatic brain metastases (if present they must have been stable for > 3 months).
- Ability to become pregnant (or already pregnant or lactating). However, those female patients who have a negative serum or urine pregnancy test before enrolment and agree to use two highly effective forms of contraception (oral, injected or implanted hormonal contraception and condom, have a intra-uterine device and condom, diaphragm with spermicidal gel and condom) during the study and for six months afterwards are considered eligible.
- Male patients with partners of child-bearing potential (unless they agree to take measures not to father children by using one form of highly effective contraception [condom plus spermicide] during the study and for six months afterwards). Men

Study name and Contact	Cancer type	Inclusion and Exclusion summary	# of patients needed	Sites
		with pregnant or lactating partners should be advised to use barrier method contraception (e.g. condom plus spermicidal gel) to prevent exposure to the foetus or neonate. • Major thoracic or abdominal surgery from which the patient has not yet recovered. • At high medical risk because of non-malignant systemic disease including active uncontrolled infection. • Known to be serologically positive for Hepatitis B, Hepatitis C or Human Immunodeficiency Virus (HIV). • History of severe auto-immune disease or known allergy to peanuts. • Concurrent hypotension defined as a baseline supine blood pressure (BP) systolic < 90 mmHg. • Patients receiving anti-hypertensive treatment or treatment with beta-blockers or rate-limiting calcium agents. A washout period of 5 x half-life of the drug should be applied following withdrawal of any of these treatments. • Concurrent congestive heart failure, prior history of class III/ IV cardiac disease (New York Heart Association [NYHA]) see Appendix 4, prior history of cardiac ischaemia or prior history of cardiac arrhythmia. Coronary angioplasty or stenting in the previous 12 months. • Patients with a known left ventricular ejection fraction (LVEF) < 50%. A multi-gated acquisition (MUGA) scan or echocardiogram (ECHO) must be performed in all patients. • Concurrent diabetes requiring treatment (diet-controlled diabetes would be acceptable). • Prior bone marrow transplant or have had extensive radiotherapy to greater than 25% of bone marrow within eight weeks. • A history of or underlying interstitial lung disease. • Any other condition which in the Investigator's opinion would not make the patient a good candidate for the clinical study. • Is a participant or plans to participate in another interventional clinical study whilst taking part in this study. Participation in an observational study would be acceptable.		
AZD3965 A Cancer Research UK Phase I trial of AZD3965, a monocarboxylate transporter 1 inhibitor (MCT1) in	Advanced solid tumour or lymphoma	**Inclusion criteria:** 1. Part 1 • Histologically or cytologically proven advanced solid tumour or lymphoma,	63-81	Newcastle Freeman Hospital The Royal

Study name and Contact	Cancer type	Inclusion and Exclusion summary	# of patients needed	Sites
patients with advanced cancer Jane Peters Senior Clinical Study Manager Centre for Drug Development Cancer Research UK Tel: 020 3469 6972 **Jane.Peters@cancer.org.uk**		refractory to conventional treatment or for which no conventional therapy exists (if the diagnosis is confirmed by cytology and no follow-up historical tumour sample has been obtained, the patient will not be eligible). • Available archived tumour samples. Part 2: • Histologically proven castration resistant prostate cancer, diffuse large B-cell lymphoma or gastric cancer, which is refractory to conventional treatment or for which no conventional therapy exists or has been refused by the patient. • Available archived tumour samples. • Measurable disease according to RECIST criteria version 1.1 or documented rising prostate specific antigen (PSA) for prostate cancer. 2. Life expectancy of at least 12 weeks 3. World Health Organisation (WHO) performance status of 0 or 1 (Appendix 1) 4. Haematological and biochemical indices within the ranges shown below. These measurements should be performed within one week (Day -14 to Day -7) before the patient receives their first dose of AZD3965. Measurements performed before Day -14 may be accepted by the DDO to demonstrate eligibility if repeat testing is logistically difficult for the patient and is not considered medically important in the opinion of the Investigator or DDO.		Marsden Hospital – Sutton, Surrey

Laboratory Test	Value required
Haemoglobin (Hb)	≥ 9.0 g/dL or ≥10.0 g/dL if transfusion wit last 4 weeks
Absolute neutrophil count (ANC)	≥ 1.5 x 10^9/L
Platelet count	≥ 100 x 10^9/L
Serum bilirubin	≤ 1.5 x upper limit of normal (ULN)
Alanine amino-transferase (ALT), aspartate amino-transferase (AST) and alkaline phosphatase (ALP)	≤ 2.5 x ULN or ≤ 5 x ULN in presence liver metastases (ALP ≤ 5 x ULN presence of bone metastases)
GFR Either: Calculated creatinine clearance	≥ 50 mL/min

Or: Isotope clearance measurement (uncorrected)	
Prothrombin time (PT)	<1.5 x ULN
Glucose (fasting)	< 7.8 mmol/L

5. LVEF>50%
6. 18 years or over
7. Written (signed and dated) informed consent and be capable of co-operating with treatment and follow-up

Exclusion criteria:

1. Radiotherapy (except for palliative reasons), endocrine therapy, immunotherapy or chemotherapy during the previous four weeks (six weeks for nitrosoureas, Mitomycin-C and 4 weeks for investigational medicinal products) before treatment.[1] Part 2 gastric patients only: received more than two lines of chemotherapy for advanced disease
2. Ongoing toxic manifestations of previous treatments greater than NCI CTCAE Grade 1 at the time of starting study treatment. Exceptions to this are alopecia or certain Grade 2 toxicities, which in the opinion of the Investigator and the DDO should not exclude the patient.
3. Known brain or leptomeningeal metastases.
4. Patients with known retinal disease or macular degeneration affecting visual acuity as assessed by ophthalmologic tests.
5. Ability to become pregnant (or already pregnant or lactating). However, those female patients who have a negative serum or urine pregnancy test before enrolment and agree to use two highly effective forms of contraception (oral, injected or implanted hormonal contraception and condom, have a intra-uterine device and condom, diaphragm with spermicidal gel and condom) during the trial and for six months afterwards are considered eligible.
6. Male patients with partners of child-bearing potential (unless they agree to take measures not to father children by using one form of highly effective contraception [condom plus spermicide] during the trial and for six months afterwards). Men

Study name and Contact	Cancer type	Inclusion and Exclusion summary	# of patients needed	Sites

with pregnant or lactating partners should be advised to use barrier method contraception (for example, condom plus spermicidal gel) to prevent exposure to the foetus or neonate.

7. Any major surgery in the preceding eight weeks prior to the start of treatment or major thoracic or abdominal surgery from which the patient has not yet recovered
8. Patients who are unable to swallow oral medication.
9. Alterations to corticosteroid dose within 2 weeks prior to first dose of AZD3965.
10. Gastrointestinal disorders likely to interfere with absorption of the study drug (e.g. partial bowel obstruction or malabsorption).
11. At high medical risk because of non-malignant systemic disease including active uncontrolled infection.
12. Known to be serologically positive for hepatitis B, hepatitis C or human immunodeficiency virus (HIV). (N.B. Mandatory testing not required).
13. History of serious allergy or auto-immune disease.
14. Diabetes mellitus (patients with diet controlled diabetes may be included with fasting glucose < 7.8 mmol/l and normal HbA1c)
15. Cardiac conditions as follows:
    - Clinically significant cardiovascular event within 6 months prior to study entry to include:
      a) Acute coronary syndrome (myocardial infarction or unstable angina)
      b) congestive heart failure requiring therapy;
    - Severe valvular heart disease (as defined by British Society of Echocardiography – see Appendices 6)
    - Presence of an atrial or ventricular arrhythmia, other than atrial fibrillation with well controlled ventricular rate, for which treatment is indicated (anti-arrhythmic drugs or implantable cardioverter defibrillator)[2]
    - First, second or third degree heart block with or without symptoms unless functioning pacemaker[7]
    - QTc > 450 msec in adult male and > 460 msec in adult females (QTc to be verified manually (QTc F correction))
    - History of congenital long QT syndrome
    - History of Torsade de Pointes (or any concurrent medication with a known risk of QT prolongation) – See Appendix 4 for further details
    - Uncontrolled hypertension (BP ≥ 160/100mmHg despite medical therapy)

Study name and Contact	Cancer type	Inclusion and Exclusion summary	# of patients needed	Sites
		16. Prior allogeneic bone marrow transplant or have had extensive radiotherapy to greater than 25% of bone marrow within 8 weeks. Prior autologous bone marrow transplant will not exclude a patient 17. Is a participant, or plans to participate in another interventional clinical trial, whilst taking part in this Phase I study of AZD3965. Participation in an observational trial would be acceptable. 18. Any other condition which in the Investigator's opinion would not make the patient a good candidate for the clinical trial. 19. <u>For Part 2 only:</u> Current malignancies of other types, with the exception of adequately treated cone-biopsied *in situ* carcinoma of the cervix uteri and basal or squamous cell carcinoma of the skin.		