ISRCTN69481429 https://doi.org/10.1186/ISRCTN69481429

Dose escalation trial of oral Vascular Endothelial Growth Factor Receptor (VEGFR) and Epidermal Growth Factor Receptor (EGFR) inhibitor, Vandetanib in combination with the oral Mitogen Activated Kinase (MEK) inhibitor, Selumetinib (VanSel-1) in solid tumours (dose escalation) and NSCLC (expansion cohort)

Submission date
07/11/2011

Recruitment status
No longer recruiting

Registration date
07/11/2011

Overall study status
Completed

Last Edited
05/08/2022

Condition category
Cancer

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol
http://cancerhelp.cancerresearchuk.org/trials/a-trial-of-vandetanib-and-selumetinib-for-solid-tumours-including-nsclc-vansel-1

Contact information

Type(s)
Scientific

Contact name
Ms Susan Wan

Contact details
Drug Development Office
Angel Building
407 St. John Street
London
United Kingdom
EC1V 4AD
+44 20 3469 6913
susan.wan@cancer.org.uk

Additional identifiers

Clinical Trials Information System (CTIS)
2011-000627-33

Protocol serial number
11219

Study information

Scientific Title
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)

Acronym
VanSel1: A Phase I trial of Vandetanib and Selumetinib

Study objectives
The purpose of this Phase I study is to establish a safety and toxicity profile of combining two study drugs; vandetanib, a Vascular Endothelial Growth Factor Receptor (VEGFR) and Epidermal Growth Factor Receptor (EGFR) inhibitor, with selumetinib a Mitogen Activated Kinase (MEK) inhibitor.

Ethics approval required
Old ethics approval format

Ethics approval(s)
South Central Oxford A ethics committee. Date of approval 21st October 2011, ref: 11/SC/0409

Study design
Non-randomised; Interventional; Design type: Treatment

Primary study design
Interventional

Study type(s)
Screening

Health condition(s) or problem(s) studied
Topic: National Cancer Research Network; Subtopic: Lung Cancer; Disease: Lung (non-small cell)

Interventions
Biopsy: Optional: bronchoscopies to obtain biopsy samples.

Disease assessment: Radiological disease assessment to include CT/MRI/X-ray/bone scans as applicable.

Laboratory assessments: Blood sampling for haematology and biochemstry parameters

Research blood sampling: For pharmacokinetic and pharmacodynamic analysis.

Research imaging, Optional fluorodeoxyglucose positron emission tomography FDG PET and DCE-MRI imaging

Treatment: Drug administration of two oral drugs. All patients will receive the same combination of vandetanib and selumetinib.
Cycle 1 consists of 4 days at 300mg vandetanib (once daily), 10 days of 100mg vandetanib (once daily) followed by 28 days of combination therapy to consist of vandetanib (100mg once daily) and selumetinib (25 or 50 or 75 mg twice daily.)
Cycle 2 onwards will consist of 28 day cycles of the combination treatment i.e. vandetanib (100mg once daily) and selumetinib (25 or 50 or 75 mg twice daily.)

Total duration of treatment: If a patient is benefiting from treatment with vandetanib & selumetinib (i.e. has stable or responding disease as measured by RECIST) after 6 cycles of combination treatment, then the Principal Investigator can ask the Sponsor by a formal written request if the patient can continue with treatment. The Sponsor will provide a written response based on the review of the full toxicity profile of that patient (approval or refusal). All other patients coming off the study will go on standard care.

Follow up: All patients will be followed up for survival at one year.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Vandetanib, selumetinib

Primary outcome(s)
Identification of toxicity and establish safety profile; Timepoint(s): Throughout study

Key secondary outcome(s))
Determine maximum tolerated dose for patients and recommend Phase II dose; Timepoint(s): During and end of study

Completion date
12/12/2014

Eligibility

Key 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 Non-small cell lung cancer (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:
2.1. One prior line of chemotherapy

2.2. Previous platinum based chemotherapy
Also eligible are those patients who:
2.3. Are erlotinib resistant
2.4. Are untreated with erlotinib
2.5. Have been treated with docetaxel
3. (Expansion cohort only) Measurable disease according to Response Evaluation Criteria In Solid Tumors (RECIST) criteria Version 1.0
4. Life expectancy of at least 12 weeks
5. World Health Organisation (WHO) performance status of 0-1
6. Baseline left ventricular ejection fraction (LVEF) > or = 50%
7. Haematological and biochemical indices as follows:
7.1. Haemoglobin > or = 9.0g/dL
7.2. Absolute neutrophil count > or = 1.5 x 10^9/L
7.3. Platelet count > or = 100 x10^9/L
7.4. Normal serum calcium (adjusted) 2.15-2.55 mmol/L
7.5. Normal serum magnesium 0.60-1.0 mmol/L
7.6. Normal serum potassium > or = 4.0mmol/L
7.7. Either: Serum bilirubin < or = 1.5 x upper limit of normal (ULN)
This does not apply to patients with Gilberts disease or
7.8. Alanine amino-transferase (ALT) or aspartate amino-transferase (AST) and alkaline phosphatase (ALP) < or = 2.5 x ULN unless raised due to liver metastases in which case up to 5 x ULN is permissible
7.9. Either: Calculated creatinine clearance (using the Wright formula) > or = 50mL/min. Isotope clearance measurement > or = 50mL/min(uncorrected)
7.10. International Normalized Ratio (INR) or activated partial thromboplastin time (aPTT) < 1.5 x ULN
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.; Target Gender: Male & Female ; Lower Age Limit 18 years

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
58

Key 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 those patients who have had EGFR dose reductions
3. Prior treatment with any agent that targets MEK or VEGFR
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 Drug Development Office (DDO) 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 three highly effective forms of combined contraception 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 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 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:
13.1. Clinically significant cardiovascular event within 3 months prior to entry to include:
13.1.1. Myocardial infarction
13.1.2. Angina requiring use of nitrates more than once weekly
13.1.3. Superior vena cava syndrome
13.1.4. Class II/III/IV cardiac disease (New York Heart Association [NYHA])
13.1.5. Presence of cardiac disease that in the opinion of the Investigator increases the risk of ventricular arrhythmia.
13.1.6. History of arrhythmia which is symptomatic or requires treatment[Common Terminology Criteria for Adverse Events v3.0 (CTCAE 3)], symptomatic or uncontrolled atrial fibrillation despite treatment or asymptomatic sustained ventricular tachycardia. Patients with atrial fibrillation controlled by medication are permitted.
13.2. Uncontrolled hypertension (BP > 160/100 despite optimal therapy)
13.3. Prior or current cardiomyopathy
13.4. Atrial fibrillation with heart rate >100 bpm
13.5. QTcB > 450 msec on screening electrocardiogram (ECG)
13.6. History of congenital long QT syndrome
13.7. History of Torsade de Pointes (or any concurrent medication with a known risk of inducing Torsades de Pointes.
14. Concomitant medications that are potent inducers of CYP3A4 function i.e. rifampicin, rifabutin, phenytoin, carbamazepine, Phenobarbital and St Johns Wort.
15. Any other condition which in the Investigators 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 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 Dynamic contrast enhanced-magnetic resonance imaging (DCE-MRI) contrast material because of hypersensitivity or impaired renal function

Date of first enrolment
12/12/2011

Date of final enrolment
12/12/2014

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Drug Development Office
London
United Kingdom
EC1V 4AD

Sponsor information

Organisation
Cancer Research UK (CRUK) (UK)

ROR
https://ror.org/054225q67

Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK (CRUK) (UK)

Alternative Name(s)
CR_UK, Cancer Research UK - London, Cancer Research UK (CRUK), CRUK

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Plain English results			05/08/2022	No	Yes