ISRCTN00549973 https://doi.org/10.1186/ISRCTN00549973

Cediranib maleate with or without gefitinib in treating patients with recurrent or progressive glioblastoma

Submission date 27/05/2011	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 27/05/2011	**Overall study status** Completed	
Last Edited 20/01/2022	**Condition category** Cancer	

Plain English summary of protocol
http://cancerhelp.cancerresearchuk.org/trials/a-study-looking-cediranib-with-without-gefitinib-for-type-brain-tumour-glioblastoma-doric

Contact information

Type(s)
Scientific

Contact name
Dr Fiona Dungey

Contact details
Cancer Research UK & UCL Cancer Trials Centre
90 Tottenham Court Road
London
United Kingdom
W1T 4TJ

Additional identifiers

EudraCT/CTIS number
2010-021531-13

IRAS number

ClinicalTrials.gov number
NCT01310855

Secondary identifying numbers

9563

Study information

Scientific Title
Multi-centre, randomised, double-blind phase II study comparing cediranib (AZD2171) plus gefitinib (Iressa, ZD1839) with cediranib plus placebo in subjects with recurrent/progressive glioblastoma (DORIC Trial)

Acronym
DORIC

Study objectives
This is a phase II, randomised, double-blind placebo-controlled study in patients with recurrent or progressive glioblastoma (WHO grade IV). Patients are to receive cediranib in combination with gefitinib or cediranib with placebo. The primary endpoint is Progression Free Survival.

Ethics approval required
Old ethics approval format

Ethics approval(s)
First MREC approval on 17/02/2011, ref:10/H0715/77

Study design
Randomised interventional trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format

Health condition(s) or problem(s) studied
Brain Tumour

Interventions
This is a randomised double blind multicentre phase II trial of daily cediranib +/- gefitinib for patients with recurrent/progression Glioblastoma. Patients will continue treatment until confirmed progression, patient decision or the development of unacceptable toxicity. Follow up for the trial is continuous unless the patient requests otherwise. A translational component will examine the roles of potential biomarkers and stratify the results based on known indicators of

prognosis such as MGMT methylation and IDH 1 and 2. Doses: Cediranib 30mg daily, Gefitinib 500mg or matching placebo daily

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Cediranib, gefitinib

Primary outcome measure
1. Progression free survival
2. Timepoint(s): throughout trial

Secondary outcome measures
1. Overall survival, timepoint(s): date of death
2. Overall survival rate at 12 months, timepoint(s): 12 months
3. Progression free survival at 6 months, timepoint(s): 6 months
4. Radiographic response rate, timepoint(s): at each MRI scan (6 weekly)
5. Safety and tolerability, timepoint(s): throughout trial
6. Steroid use, timepoint(s): thoughout trial
7. Time to deterioration of neurological status or death, timepoint(s): throughout trial, death
8. Time to sustained increase in steroid dosage, timepoint(s): throughout trial

Overall study start date
24/05/2011

Completion date
24/11/2012

Eligibility

Key inclusion criteria
1. Provision of informed consent
2. Age ≥18 years
3. Life expectancy ≥ 12 weeks
4. Histological/cytological confirmation of glioblastoma (WHO grade IV)
5. Patients with measurable disease (contrast-enhancing tumour ≥10 mm by shortest diameter on 2 axial slices) by MRI imaging within 7 days prior to enrolment. (If patients have recently had a routine MRI scan, this should be assessed before deciding whether or not to screen the patient, and booking the screening/baseline MRI.)
6. Patients must have been on no steroids or a stable dose of steroids (dexamethasone) for at least 5 days before the baseline MRI
7. Patients must have completed standard first-line treatment for glioblastoma including surgery (with exception, if patient does not receive surgery as part of first-line treatment due to anatomical location, based on neurosurgeon's assessment), cranial radiotherapy and chemotherapy with concomitant temozolomide
7.1. It is not essential that the entire Stupp regimen of 6 cycles of adjuvant temozolomide

following chemoradiotherapy has been completed
7.2. The last dose of temozolomide must be more than 28 days from enrolment
7.3. Gliadel® wafers are permitted, as it is part of local treatment
7.4. No other previous treatment for glioblastoma is permitted (other than steroids)
8. Patients must have a Karnofsky Performance Score of 70 or above
9. Patients must have a mini-mental status examination score of 15 or greater
10. Patients who require either oral anticoagulants (coumadin, warfarin) or low molecular weight heparin are eligible provided there is increased vigilance with respect to monitoring INR.
11. For inclusion in the genetic research, patients must fulfil the following criterion:
11.1. Provision of informed consent for genetic research (separate consent required for tumour biopsy, blood sample, and post mortem donations)
11.2. If a patient declines to participate in any of the genetic research, there will be no penalty or loss of benefit to the patient
11.3. The patient will not be excluded from other aspects of the study described in this Clinical Study Protocol, so long as they consent to the main study

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
UK Sample Size: 112

Total final enrolment
38

Key exclusion criteria
1. Patients on enzyme-inducing anti-epileptic drugs within 2 weeks prior to study enrolment
Note: Patients are eligible if they switched to non-enzyme inducing agents and discontinued enzyme-inducing agents for more than or equal to 2 weeks prior to randomisation
2. Inadequate bone marrow reserve as demonstrated by an absolute neutrophil count ≤1.5 x 109 /L or platelet count ≤100 x 109 /L or requiring regular blood transfusions to maintain haemoglobin >9g/dL
3. Serum bilirubin ≥1.5 x ULRR (except for patients with known documented cases of Gilberts Syndrome)
4. ALT or AST ≥5 x ULRR
5. Serum creatinine >1.5 x ULRR or a creatinine clearance of ≤50mL/min calculated by Cockcroft-Gault
6. Greater than +1 proteinuria on two consecutive dipsticks taken no less than 1 week apart unless urinary protein <1.5g in a 24 hr period or UPC (Urine Protein: Creatinine) ratio <1.5
7. History of significant gastrointestinal impairment, as judged by the investigator, that would significantly affect the absorption of cediranib or gefitinib, including the ability to swallow the tablet whole

8. Patients with a history of poorly controlled hypertension with resting blood pressure >150 /100mmHg in the presence or absence of a stable regimen of anti-hypertensive therapy, or patients who are requiring maximal doses of calcium channel blockers to stabilise blood pressure
9. Any evidence of severe or uncontrolled diseases (e.g. unstable or uncompensated respiratory, cardiac, hepatic or renal disease)
10. Unresolved toxicity >CTC AE grade 1 from previous anti-cancer therapy (including radiotherapy) except alopecia (if applicable)
11. Mean QTc with Bazetts correction >470msec in screening ECG or history of familial, long QT syndrome
12. Cardiac ventricular arrhythmias requiring anti-arrhythmic therapy
13. Significant haemorrhage (>30mL bleeding/episode in previous 3 months) or haemoptysis (>5mL fresh blood in previous 4 weeks)
14. Recent (<14 days) major surgery or brain biopsy
15. Recent craniotomy (<28 days) prior to first dose, or a surgical incision that is not fully healed
16. Pregnant or breast-feeding women or women of childbearing potential with a positive pregnancy test prior to receiving study medication
17. Known hypersensitivity to cediranib, gefitinib or any of its excipients
18. History of other malignancies (except for adequately treated basal or squamous cell carcinoma or carcinoma in situ) within 5 years, unless the patient has been disease free for 2 years and they have tissue diagnosis of the target lesion
19. Known infection with hepatitis B or C or HIV
20. Involvement in the planning and conduct of the study (applies to both UCL CTC, AstraZeneca staff and staff at the study site)
21. Past medical history of interstitial lung disease, idiopathic pulmonary fibrosis, drug-induced interstitial disease, radiation pneumonitis which required steroid treatment or any evidence of clinically active interstitial lung disease
22. Previous enrolment as part of the present study
23. Treatment with an investigational drug within 30 days prior to the first dose of cediranib /gefitinib
24. Other concomitant anti-cancer therapy except steroids (dexamethasone only)
25. Previous anti-angiogenesis (e.g. bevacizumab, sorafenib, sunitinib) therapy
26. Previous anti-EGFR treatments (e.g. cetuximab, panitumumab or small molecule tyrosine kinase inhibitors etc.) or downstream targets e.g. mTOR inhibitors
27. Patients with evidence of any intratumoural or peritumoural haemorrhage deemed significant by the treating physician
28. Patients who have received any form of cranial radiation within 3 months prior to study entry (excluding imaging)
29. Patients who have progressed within 3 months of completion of standard cranial radiation
30. Patients that have received radiosurgery or brachytherapy
31. Patients on >8mg/day dexamethasone or equivalent steroids on any day of the 2 weeks prior to randomisation

Date of first enrolment
24/05/2011

Date of final enrolment
08/08/2012

Locations

Countries of recruitment

England

United Kingdom

Study participating centre
Cancer Research UK & UCL Cancer Trials Centre
London
United Kingdom
W1T 4TJ

Sponsor information

Organisation
University College London (UK)

Sponsor details
Gower Street
London
England
United Kingdom
WC1E 6BT

Sponsor type
University/education

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Industry

Funder Name
AstraZeneca (UK)

Alternative Name(s)
AstraZeneca PLC, Pearl Therapeutics

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

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

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	27/05/2016		Yes	No
Basic results			20/05/2019	No	No
Plain English results			20/01/2022	No	Yes
HRA research summary			28/06/2023	No	No