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A randomised phase II double blind placebo controlled trial of Whole Brain RadioTherapy (WBRT) and Tarceva (OSI-774, erlotinib) in patients with advanced Non-Small Cell Lung Cancer (NSCLC) with multiple brain metastases

Submission date 15/08/2007	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol
Registration date 21/09/2007	**Overall study status** Completed	[_] Statistical analysis plan [X] Results
Last Edited 19/03/2020	**Condition category** Cancer	[_] Individual participant data

Plain English summary of protocol
http://www.cancerhelp.org.uk/trials/a-trial-looking-at-radiotherapy-with-tarceva-for-lung-cancer-that-has-spread-to-the-brain

Contact information

Type(s)
Scientific

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT00554775

Clinical Trials Information System (CTIS)
2006-000113-38

Protocol serial number
BRD/05/177

Study information

Scientific Title
A randomised phase II double blind placebo controlled trial of Whole Brain RadioTherapy (WBRT) and Tarceva (OSI-774, erlotinib) in patients with advanced Non-Small Cell Lung Cancer (NSCLC) with multiple brain metastases

Acronym
TACTIC

Study objectives
Tarceva has been found to have significant activity against primary brain tumours. A promising property of EGFR inhibitors is that they significantly increase the therapeutic selectivity of ionizing radiation with no increase of toxicity. It is reasonable to speculate that this property can be exploited to treat NSCLC patients with multiple cerebral metastases conventionally treated with WBRT since Tarceva can be combined with WBRT in an attempt to exploit its anti-tumour activity on brain metastases and at the same time harness its radiation-sensitising property when combined with WBRT and its beneficial systemic activity.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Hammersmith and Queen Charlotte's and Chelsea Research Ethics Committee, 07/03/2007, ref: 06/Q0406/141

Primary study design
Interventional

Study design
Randomised controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Non-Small Cell Lung Cancer (NSCLC) with brain metastases

Interventions
Interventions:
Patients are randomised 1:1 to one of two treatment arms. Each arm will receive five 4.0 Gy fractions (to isocentre), one fraction per day, over 5 days (excluding weekends) to a total dose of 20 Gy.

Arm 1: Tarceva (OSI-774, erlotinib) PO (by mouth) 100 mg daily during WBRT, increasing to 150 mg daily after WBRT for up to 24 months.
Arm 2: WBRT plus matched placebo for the same schedule and duration as above.

Patients will be assessed 2 weekly for the first 8 weeks from Day 1 and thereafter monthly while on study drug. After stopping study drug, they will be assessed 2 monthly. The end of trial is the date the last patient completes 2 months of treatment but all patients will be followed until death.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Erlotinib

Primary outcome(s)
Current primary outcome measures as of 22/02/2008:
To estimate the effect on neurological progression-free survival at 2 months of WBRT with concomitant Tarceva compared to WBRT alone in patients with advanced NSCLC with multiple brain metastases.

Previous primary outcome measures:
To estimate the effect on neurological progression-free survival at 2 months of WBRT with concomitant Tarceva compared to WBRT alone in patients with advanced NSCLC with multiple brain metastases assessed using RECIST.

Key secondary outcome(s)
Current secondary outcome measures as of 22/02/2008:
1. Toxicity
2. Response rate. Response will be measured by CT/MRI scan and whole body scan at baseline, 2 months and at progression.
3. Quality of life assessed by EuroQol EQ-5D, completed monthly for the first 12 months and at 18 and 24 months from Day 1
4. Change in Performance Status, to investigate the time to and duration of relief of baseline symptoms, as well as tolerance of therapy
5. Steroid dosing
6. Sites of progression (cranial or extracranial) will also be recorded

Previous secondary outcome measures:
1. Toxicity
2. Response rate. Response will be measured by CT/MRI scan and whole body scan at baseline, 2 months and at progression
3. Quality of life assessed by the European Organisation for Research and Treatment of Cancer (EORTC) Questionnaires Q29 and Q30 and EuroQol EQ-5D, completed monthly for the first 12 months and at 18 and 24 months from Day 1
4. Change in Performance Status, to investigate the time to and duration of relief of baseline

symptoms, as well as tolerance of therapy
5. Steroid dosing over the 2 weeks of WBRT
6. Sites of progression (cranial or extracranial) will also be recorded

Completion date
31/12/2009

Eligibility

Key inclusion criteria
1. Histologically or cytologically confirmed NSCLC. A biopsy of metastatic disease in the brain is not required for study enrolment
2. Relapsed patients with newly diagnosed multiple brain metastases
3. Diagnosis of brain metastases must be confirmed on contrast Computerised Tomography (CT) or Magnetic Resonance Imaging (MRI) scan. Subjects with post-craniotomy incomplete resection will be eligible
4. No prior cranial radiotherapy
5. >= 28 days since last chemotherapy for relapsed patients originally treated with chemotherapy
6. Clinician certain of the role of WBRT
7. Karnofsky performance status >= 70
8. The Radiation Therapy Oncology Group Recursive Partitioning Analysis (RTOG RPA) class I and II
9. Symptoms attributable to brain tumour
10. Maximum of three sites (organ systems) of extracranial metastases
11. Age >18 years
12. Able to take oral medication
13. Using effective contraception if of reproductive potential (women of childbearing potential must have a negative pregnancy test performed by a healthcare professional prior to randomisation)
14. Willing and able to give informed consent
15. Carer able and willing to participate
16. Patient and carer with access to telephone and willing to respond to telephone interview

Added as of 15/09/2008:
17. Patients with brain metastases at first presentation, not suitable for first-line chemotherapy

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
1. Chemo-naïve patients with brain metastases who are considered suitable for first-line chemotherapy treatment
2. Presence of a solitary brain metastasis
3. Clinician certain that WBRT will not be of benefit
4. Clinician uncertain of the role of WBRT
5. Previous treatment with any EGFR anti-cancer therapy (e.g. Tarceva, Iressa or Cetuximab)
6. Previous treatment for brain metastases (radiosurgery, radiotherapy or chemotherapy); however, prior radiation therapy to the primary tumour and/or systemic treatment to metastatic sites of disease is acceptable
7. Pregnant or lactating women
8. Evidence of other significant laboratory finding or concurrent uncontrolled medical illness which in the opinion of the investigator would interfere with protocol treatment or results comparison or render the subject at high risk from treatment complications. For example:
8.1. Severe uncontrolled infection
8.2. Cardiovascular - unstable angina, myocardial infarction within 1 month
8.3. Gastro-intestinal - uncontrolled inflammatory bowel disease (e.g. Crohn's or ulcerative colitis)
8.4. Hepatic - serum bilirubin >= 2x upper limit of normal (ULN)
8.5. Serum transaminases >= 2 x ULN in the absence of liver metastases or >= 5 x ULN with liver metastases
8.6. Renal - acute renal failure
9. Other previous or current malignant disease likely to interfere with protocol treatment or comparisons
10. Current treatment with Cox II inhibitor

Please note that, as of 15/09/2008, the exclusion criterion "MRI evidence of solitary brain metastases for resection, radiosurgery or stereotactic radiotherapy" has been replaced with "Presence of a solitary brain metastasis" (see exclusion criterion 2)

Date of first enrolment
04/01/2008

Date of final enrolment
31/12/2009

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University College London Hospital (UCLH)
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Sponsor information

Organisation
University College London (UK)

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK (UK) (ref: C1438/A6406)

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

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	16/07/2014	28/02/2019	Yes	No
Plain English results				No	Yes