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Lapatinib plus capecitabine versus continued trastuzumab plus capecitabine after local therapy in patients with ErbB2-positive metastatic breast cancer developing brain metastasis/es

Submission date 20/10/2010	**Recruitment status** Stopped	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data [_] Record updated in last year
Registration date 25/03/2011	**Overall study status** Stopped	
Last Edited 25/10/2022	**Condition category** Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-%20trial-lapatinib-trastuzumab-alongside-capecitabine-breast-cancer-spread-brain-lantern

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
CO10/9344

Study information

Scientific Title
A randomised phase II screening trial with functional imaging and patient reported toxicity sub-studies comparing Lapatinib plus capecitabine versus continued Trastuzumab plus capecitabine after local therapy in patients with ErbB2-positive metastatic breast cancer developing brain metastasis/es

Acronym
LANTERN

Study objectives
Patients with HER-2 positive metastatic breast cancer commonly develop brain metastases. This causes profound morbidity. Current treatment is to continue trastuzumab and offer brain radiotherapy and capecitabine chemotherapy. Lapatinib may be a better option compared to trastuzumab and we wish to explore this in a randomised phase II study.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Leeds East Research Ethics Committee pending approval as of 21/10/2010 (meeting scheduled for 02/11/2010)

Study design
Randomised multicentre prospective controlled open-label parallel-group phase II screening trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Breast cancer, developing brain metastasis/es

Interventions
1. Participants will be randomised on an equal basis to either:
1.1. Lapatinib (1250 mg daily) on days 1 - 14 plus capecitabine (1000 mg/m^2 twice daily) on days 1 - 14 of 21 day cycles until disease progression or unacceptable toxicity
1.2. Trastuzumab (6 mg/kg 3-weekly) on day 1 plus capecitabine (1000 mg/m^2 twice daily) on days 1 - 14 of 21 day cycles until disease progression or unacceptable toxicity
2. Participants will receive treatment until disease progression. Patients will be followed up within the trial until the 24 week post-randomisation clinical review with the exception of SAEs which will continue to be collected until 30 days after trial treatment has stopped.

Intervention Type
Drug

Phase

Phase II

Drug/device/biological/vaccine name(s)
1. Lapatinib 2. Capecitabine 3. Trastuzumab

Primary outcome(s)
Time to progression of central nervous system (CNS) metastases defined as time from randomisation to the date of diagnosis of CNS disease progression as measured by Response Evaluation Criteria in Solid Tumours (RECIST) on reviewed magnetic resonance imaging (MRI) scans

Key secondary outcome(s))
1. Progression-free survival (CNS or non-CNS): time from randomisation to first documented evidence of disease progression or death from any cause -
1.1. CNS progression will be assessed by RECIST of MRI-scans
1.2. Non-CNS disease progression will be measured and reported as per local standard clinical practice (i.e. clinical or radiological evidence of disease progression)
2. Overall survival defined as time from randomisation to date of death from any cause
3. CNS overall response rate (CR or PR) is defined as complete or partial response (CR or PR) as measured by RECIST and based on reviewed MRI scans
4. CNS clinical benefit response rate (confirmed CR or PR at any time or SD at the 24-week time-point) as measured by RECIST and based on reviewed MRI scans
5. Total days of steroid use for palliation of CNS symptoms will be measured every 3 weeks by research nurse-elicitation from the participants regarding their steroid use
6. General and neurological quality of life as measured by the patient self-reported EORTC QLQ-C30 and BN20 questionnaires and patient self-reported symptoms and side-effects assessments at baseline and at 12 and 24 weeks
7. Patient self-reported symptoms and side-effects assessments will also be completed every 3 weeks post-randomisation to correspond with clinically-assessed toxicity reporting according to NCI CTC-AE grading criteria
8. Delay/stabilisation of CNS symptoms will be measured using the patient self-reported EORTC QLQ-C30 and BN20 questionnaires at baseline and at 12 and 24 weeks. Patient self-reported symptoms and side-effects assessments will also be completed every 3 weeks post-randomisation to correspond with clinically-assessed toxicity reporting according to NCI CTC-AE grading criteria
9. Qualitative and quantitative toxicities: Patient self-reported symptoms and side-effects assessments will also be completed at baseline and every 3 weeks post-randomisation to correspond with clinically-assessed toxicity reporting according to NCI CTC-AE grading criteria
10. Feasibility of recruitment into a phase III trial

Completion date
28/02/2013

Reason abandoned (if study stopped)
Participant recruitment issue

Eligibility

Key inclusion criteria
1. Male or female aged greater than or equal to 18 years
2. Eastern Cooperative Oncology Group (ECOG) performance status 0 - 2

3. Given written informed consent prior to any trial specific procedures
4. Expected survival greater than or equal to 12 weeks
5. Histologically or cytologically confirmed invasive breast cancer, with stage IV disease including newly diagnosed central nervous system (CNS) metastasis/es
6. ErbB2 overexpression in the invasive component of the primary or metastatic lesion as locally defined by:
7.1. 3+ staining by immunohistochemistry (IHC)
7.2. 2+ staining by IHC in conjunction with ErbB2 gene amplification by FISH
7.3. ErbB2 gene amplification by FISH
8. Participants with a negative or equivocal overall result are not eligible for inclusion in the trial
9. Evidence of metastatic brain disease. To be considered evaluable for the primary endpoint and the CNS response rates endpoints, participants must have at least one measurable brain lesion that can be accurately measured in at least one dimension (shortest dimension to be recorded) as greater than 20 mm with conventional techniques or as greater than 10 mm with spiral computed tomography (CT) scan. Participants with leptomeningeal disease are not eligible for participation in the trial due to the lack of measurable disease.
10. Treated previously with taxanes or anthracyclines in the adjuvant or metastatic setting. All treatment related adverse events must be less than or equal to grade 1 at the time of randomisation.
11. Prior treatment with trastuzumab is required and all treatment related adverse events must be less than or equal to Grade 1 at the time of randomisation
12. Completed local cranial therapy (stereotactic radio surgery or whole brain radiotherapy)
13. Able to swallow and retain oral medication
14. Normal organ and bone marrow function as defined below:
15.1. Leukocytes greater than 3,000/µL
15.2. Absolute neutrophil count greater than 1,500/µL
15.3. Platelets greater than 100,000/µL
15.4. Total bilirubin within normal institutional limits
15.5. Aspartate aminotransferase (AST) (serum glutamic oxaloacetic transaminase [SGOT]) /alanine aminotransferase (ALT) (serum glutamic pyruvic transaminase [SGPT]) less than or equal to 2.5 x institutional upper limits of normal
15.6. Creatinine within normal institutional limits or creatinine clearance greater than or equal to 60 ml/min/1.73 m^2 for participants with creatinine levels above institutional normal
16. Cardiac ejection fraction greater than or equal to 50% or within the institutional limit as measured by echocardiogram scan. Note that the baseline and on treatment scan should be performed using the same modality and preferably the same institution.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
30

Key exclusion criteria
1. Prior therapy with lapatinib or an ErbB2 inhibitor other than trastuzumab
2. Prior treatment with capecitabine
3. Concurrent chemotherapy, radiation therapy, immunotherapy, biologic therapy (including an ErbB1 and/or ErbB2 inhibitor), or hormonal therapy for treatment of cancer
4. Known dihydropyrimidine dehydrogenase (DPD) deficiency
5. Current active hepatic or biliary disease (with exception of participants with Gilbert's syndrome, asymptomatic gallstones, liver metastases or stable chronic liver disease per investigator assessment)
6. Pregnant or lactating females. Women of child-bearing potential and men must agree to use adequate contraception (hormonal or barrier method of birth control or abstinence) prior to trial entry and for the duration of the trial participation.
7. History of significant non-breast malignancy (aside from non-melanomatous skin cancer, carcinoma in situ of the uterine cervix, superficial bladder cancer treated with curative intent)
8. History of allergic reactions attributed to compounds of a similar chemical or biological composition as to lapatinib
9. Uncontrolled inter-current illness including, but not limited to:
9.1. Ongoing or active infection
9.2. Symptomatic congestive heart failure
9.3. Unstable angina pectoris
9.4. Cardiac arrhythmia
9.5. Psychiatric illness/social situations that would limit compliance with trial requirements
10. Gastrointestinal (GI) tract disease resulting in an inability to take oral medication, malabsorption syndrome, a requirement for intravenous (IV) alimentation, prior surgical procedures affecting absorption, uncontrolled inflammatory GI disease (e.g., Crohn's, ulcerative colitis)
11. Renal function as measured by creatinine clearance less than 30 ml/min (ratio to norm less than 0.1)
12. Not recovered from adverse events due to agents administered more than 4 weeks earlier with the exception of adverse events less than or equal to grade 1 after previous chemotherapy
13. Prior treatment with epidermal growth factor receptor (EGFR) targeting therapies
14. Active cardiac disease, defined as:
14.1. History of uncontrolled angina
14.2. History of arrhythmias requiring medications, or clinically significant, with the exception of asymptomatic atrial fibrillation requiring anticoagulation
14.3. Myocardial infarction less than 6 months from trial entry
14.4. Uncontrolled or symptomatic congestive heart failure
14.5. Ejection fraction below 50% or the institutional lower normal limit
14.6. Any other cardiac condition, which in the opinion of the treating investigator, would make this protocol unreasonably hazardous for the participant
15. Any concomitant medications or substances forming part of the part of normal ongoing care locally known to affect, or have the potential to affect, the activity or pharmacokinetics of lapatinib

Date of first enrolment
01/03/2011

Date of final enrolment

28/02/2013

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University of Leeds
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Sponsor information

Organisation
Leeds Teaching Hospitals NHS Trust (UK)

ROR
https://ror.org/00v4dac24

Funder(s)

Funder type
Industry

Funder Name
GlaxoSmithKline (UK)

Alternative Name(s)
GlaxoSmithKline plc., GSK plc., GlaxoSmithKline plc, GSK

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

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?
Results article	results	01/10/2020	22/07/2020	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Plain English results			25/10/2022	No	Yes