ISRCTN71165034 https://doi.org/10.1186/ISRCTN71165034

Lapatinib Pre-surgical Phase II Study in Patients with Primary Breast Cancer

Submission date 08/05/2006	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 16/06/2006	**Overall study status** Completed	
Last Edited 26/10/2018	**Condition category** Cancer	

Plain English summary of protocol
http://www.cancerhelp.org.uk/trials/a-trial-looking-at-lapatinib-before-surgery-for-breast-cancer

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2006-001055-36

Protocol serial number
LAP106974

Study information

Scientific Title
Lapatinib Pre-surgical Phase II Study in Patients with Primary Breast Cancer

Acronym
PSL

Study objectives
Response to treatment with lapatinib before surgery will depend on oestrogen receptor (ER) phenotype.

Ethics approval required
Old ethics approval format

Ethics approval(s)
MREC for Wales, 01/08/2006, ref: 06/MRE09/30

Study design
Open-label phase II sequential trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Breast cancer

Interventions
Women will be allocated to two groups (according to whether oestrogen positive or negative) and will then receive lapatinib 1500 mg daily for 4 - 6 weeks until definitive surgery.

Intervention Type
Drug

Phase
Phase II

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

Primary outcome(s)
Response evaluation criteria in solid tumours (RECIST) by ultrasound measurement in the two treatment groups (ER+/ER-).

Key secondary outcome(s))
1. Change in the following biomarkers: Ki67 antibody, phosphorylated epidermal growth factor receptor (p-EGFR), phosphorylated c-erbB2 (P-c-erbB2), phosphorylated estrogen receptor (P-ER), insulin-like growth factor receptor 1 (IGFR-1), P13 kinase pathway, presence of P13 kinase mutations, expression of forkhead proteins, expression of protein kinase B (AKT), phosphorylated AKT (P-AKT), tumor suppressor Pten, cell cycle-related proteins, cyclins, cyclin-dependent kinase (CDK), apoptotic-related proteins such as caspase 3 and Bim
2. Adverse events

3. Response rates in each of the groups defined by immunostaining for EGFR as judged by the following antibody makers:
3.1. DAKO
3.2. Zymed
3.3. Biogenix
3.4. Novocastra
4. Serum markers
5. Change in c-erbB2 extracellular domain (ECD)
6. Change in EGFR ECD

Completion date
31/08/2008

Eligibility

Key inclusion criteria
1. Patients must have histologically or cytologically confirmed breast cancer
2. Patient can be ER positive or ER negative, and must be epidermal growth factor receptor (EGFR)-positive as defined by positive immuno-staining with cell signalling antibody #2232
3. Patients must have measurable breast cancer, defined as at least one lesion that can be accurately measured in at least one dimension (longest diameter to be recorded) as greater than or equal to 20 mm with the conventional techniques or as greater than or equal to 10 mm with ultrasound
4. No prior systemic therapy for breast cancer is permissible
5. Aged greater than or equal to 18 years. No dosing or adverse event data are currently available on the use of lapatinib in patients less than 18 years of age; children are therefore excluded from the study
6. Life expectancy of greater than 12 weeks
7. Eastern Cooperative Oncology Group (ECOG) performance status 2 (Karnofsky greater than or equal to 60%)
8. Patients must have normal organ and marrow function as defined by:
8.1. Leukocytes greater than or equal to 3,000/µl
8.2. Absolute neutrophil count greater than or equal to 1,500/µl
8.3. Platelets greater than or equal to 100,000/µl
8.4. Total bilirubin within normal institutional limits
8.5. Serum glutamic-oxaloacetic transaminase (SGOT)/aspartate aminotransferase (AST) or serum glutamic pyruvic transaminase (SGPT)/alanine aminotransferase (ALT) less than or equal to 2.5 times institutional upper limit of normal
8.6. Creatinine within normal institutional limits or creatinine clearance greater than or equal to 60 ml/min/1.73 m^2 for patients with creatinine levels above institutional normal limit
9. Cardiac ejection fraction within the institutional range of normal as measured by echocardiogram. Note that baseline and on treatment scans should be performed at the same institution.
10. Eligibility of patients receiving medications or substances known to affect, or with the potential to affect the activity or pharmacokinetics of lapatinib will be determined following review of their use by the principal investigator
11. The effect of lapatinib on the developing human foetus at the recommended therapeutic dose is unknown. For this reason, women of child-bearing potential and men must agree to use adequate contraception (hormonal or barrier method of birth control or abstinence) prior to study entry and for the duration of study participation. Should a woman become pregnant or suspect she is pregnant while participating in this study she should inform her treating physician

immediately.
12. Ability to understand and willingness to sign a written informed consent document
13. Able to swallow and retain oral medication

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
Female

Key exclusion criteria
1. Patients who have had any chemotherapy, radiotherapy or endocrine therapy
2. Patients who have had prior treatment with EGFR-targeting therapies
3. Patients may not be receiving any other investigational concurrent anticancer therapy. In addition, all herbal (alternative) medicines are excluded.
4. Patients with metastatic disease
5. Patients with c-erbB2+++ (or c-erb++ provided confirmed by fluorescence in situ hybridization test [FISH])
6. Patients not willing, or for whom it is planned, to resect the primary breast cancer 4-6 weeks after the start of the study
7. Patients with rapidly progressive disease, or local disease that, in the opinion of the investigator, is not amenable to surgical resection
8. Patients with known brain metastases should be excluded from this clinical trial because of their poor prognosis, and because they often develop progressive neurologic dysfunction that would confound the evaluation of neurologic and other adverse events
9. History of allergic reactions attributed to compounds of similar chemical or biologic composition to lapatinib
10. Uncontrolled inter-current illness including, but not limited to, ongoing or active infection, symptomatic congestive heart failure, unstable angina pectoris, cardiac arrhythmia, or psychiatric illness or social situations that would limit compliance with study requirements
11. Pregnant women are excluded from this study because lapatinib is member of the 4-anilinoquinazoline class of kinase inhibitors with the potential for teratogenic or abortifacient effects. There is an unknown but potential risk of adverse events in nursing infants secondary to treatment of the mother with lapatinib; breastfeeding should be discontinued if the mother is treated with lapatinib
12. Human immunodeficiency virus (HIV)-positive patients receiving combination anti-retroviral therapy are excluded from the study because of possible pharmacokinetic interactions with lapatinib. Appropriate studies will be undertaken in patients receiving combination anti-retroviral therapy when indicated.
13. Patients with 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 or

ulcerative colitis)
14. Concomitant requirement for medication classified as CYP3A4 inducers or inhibitors
15. Any concomitant severe skin disorder
16. Hormone replacement therapy (HRT) must have been discontinued at least 2 weeks prior to the start of trial medication
17. Clinical or ultrasound assessment of the breast mass may, therefore, have to be repeated prior to the start of trial medication in this case, and only patients who show no evidence of any degree of regression following discontinuation of the HRT will be entered on the study

Date of first enrolment
01/09/2006

Date of final enrolment
31/08/2008

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
8th Floor Cycotron Building
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Sponsor information

Organisation
Imperial College London (UK)

ROR
https://ror.org/041kmwe10

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

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/07/2012		Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Plain English results				No	Yes