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Effect of Peri-operative anti-HER2 therapy On early breast cancer Study - Biological phase

Submission date 23/02/2009	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 19/03/2009	**Overall study status** Completed	
Last Edited 27/11/2025	**Condition category** Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-effect-having-trastuzumab-or-lapatinib-before-surgery-early-breast-cancer-ephos-b

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Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2008-005466-30

Integrated Research Application System (IRAS)
6930

ClinicalTrials.gov (NCT)
NCT01104571

Protocol serial number
ICR-CTSU/2008/10017, IRAS 6930

Study information

Scientific Title
Effect of peri-operative anti-HER2 therapy on early breast cancer: a randomised phase III open-label multicentre clinical trial

Acronym
EPHOS-B

Study objectives
The EPHOS-B study will test the hypothesis that peri-operative anti-HER2 therapy causes a significant increase in tumour apoptosis and a significant decrease in tumour cell proliferation.

Please note that as of 19/02/10 this record has been updated. All updates can be found in the relevant field with the above update date. Please also note that the start and end dates of this trial have been updated from 01/06/2009 and 01/12/2009 to 01/04/2010 and 01/11/2021 respectively. This includes the follow up period.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 12/01/2010, West Midlands Research Ethics Committee (1st Floor, NHSBT Newcastle Blood Donor Centre, Holland Drive, Newcastle Upon Tyne, NE2 4NQ, United Kingdom; +44 (0) 2071048357; edgbaston.rec@hra.nhs.uk), ref: 09/H1208/52

Study design
Randomized phase III open-label multicentre clinical trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Early breast cancer

Interventions
Current information as of 19/02/10:
Group I: control (i.e. no peri-operative treatment)
Group II: trastuzumab 6 mg/kg intravenous (iv) given on days 1 and 8 pre-surgery, and 2 mg/kg iv on day 15 post-operatively
Group III: Lapatinib 1500mg/day p.o. continuously for 28 days, starting 11 days (± 1 day) pre-surgery.

Initial information at time of registration:
Group I: control (i.e. no peri-operative treatment)
Group II: trastuzumab 6 mg/kg intravenous (iv) given on days 1 and 8 pre-surgery, and 2 mg/kg iv on days 15 and 22 post-operatively
Group III: lapatinib 1500 mg/day orally (p.o.) for approximately 6 weeks, starting 11 days (± 1 day) pre-operatively and continued for 4 weeks post-operatively

Patients should be followed-up 28 days after surgery and then every 6 months until the end of year 2. Patients will then be followed up annually for at least 10 years after completion of recruitment.

Added 27/11/2025:
Additional Data Linkage Information:
Participants from this trial will also be included in the INTERACT project which will link to their data held by NHS England. For more information, please see the INTERACT website: https://www.icr.ac.uk/interact.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Trastuzumab, lapatinib

Primary outcome(s)
1. Increase in apoptosis: change in the tumour (morphological apoptosis and activated caspase 3) measured at diagnosis and at surgery
2. Fall in proliferation between diagnosis and surgery: change in proliferation measured by Ki67 immunohistochemical assessment (%) at diagnosis and at surgery

Key secondary outcome(s))

1. Changes in the angiogenic serum markers vascular endothelial growth factor A (VEGF-A), VEGF-R1 and CD105, measured at diagnosis, surgery (plus also tumour CD31) and 28 days post-surgery
2. To establish if the expression of molecular markers (epidermal growth factor receptor [EGFR], Her-3, insulin-like growth factor 1 receptor [IGF1R], c-myc, Akt, p-ERK, pS6 Kinase, activated Src, or truncated p95HER-2 expression) predict increases in apoptosis or decreases in proliferation in response to therapy

Completion date
19/12/2022

Eligibility

Key inclusion criteria
1. Women aged greater than or equal to 18 years old
2. HER2 (3+ on immunohistochemistry [IHC] or amplification proven by fluorescent in-situ hybridisation [FISH]) positive operable invasive breast cancer diagnosed by core biopsy
3. Planned surgery within one month of diagnosis
4. Serum creatinine and bilirubin less than 2 times the upper limits of normal for the institution, or creatinine clearance greater than 30 mg/dL (Marginally
abnormal test results should be repeated)
5. Eastern Cooperative Oncology Group (ECOG) performance status 0,1, or 2 (Karnofsky greater than or equal to 60%)
6. Non-pregnant and non-lactating with no intention of pregnancy during study treatment
7. Written informed consent obtained for trial and to donation of tissue and blood samples

Added 19/02/10:
8. Patients must be candidates for and willing to undergo adjuvant chemotherapy and trastuzumab post surgery

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
100 years

Sex
Female

Total final enrolment
257

Key exclusion criteria

Current information as of 19/02/10:
1. HER2 negative cancers and those with unknown HER2 status
2. Inoperable breast cancer (T4 category) or suspicion of distant metastases
3. Diagnosis of inflammatory breast cancer
4. Clinical evidence of metastatic disease
5. Prior herceptin therapy within the last 3 months or local (radiotherapy) cancer treatments
6. Previous cancer at any other site that has been treated within the last 6 months (except previous basal cell carcinoma and cervical carcinoma in situ)
7. Have current active hepatic or biliary disease (with exception of patients with Gilbert's syndrome, asymptomatic gallstones, liver metastases or stable chronic liver disease per investigator assessment)
8. Impaired gastro-intestinal function thought sufficient to reduce lapatinib absorption
9. Contra-indicated to receive adjuvant chemotherapy and/or trastuzumab (ECOG >2)
10. Known immediate or delayed hypersensitivity, reaction to drugs chemically related to trastuzumab or lapatinib
11. Other concomitant investigational agents or concurrent anti-cancer therapy
12. Regular use of systemic steroids or other agents that could influence study endpoints (inhaled steroids are allowed)
13. Any altered mental state that would preclude obtaining written informed consent
14. Patients who have clinically significant cardiac abnormalities or uncontrolled hypertension
15. Previous myocardial infarction, heart failure, or significant angina. Cardiac function should be assessed by physical examination, ECG, and baseline LVEF should be ≥55% as measured by echocardiography or MUGA.

Initial information at time of registration:
1. HER2 negative cancers and those with unknown HER2 status
2. Inoperable breast cancer (T4 category) or suspicion of distant metastases
3. Diagnosis of inflammatory breast cancer
4. Clinical evidence of metastatic disease
5. No prior systemic (i.e. chemotherapy) or local (radiotherapy) cancer treatments
6. Previous cancer at any other site (except previous basal cell carcinoma and cervical carcinoma in situ)
7. Abnormal renal function
8. Abnormal liver function tests
9. Have current active hepatic or biliary disease (with exception of patients with Gilbert's syndrome, asymptomatic gallstones, liver metastases or stable chronic liver disease per investigator assessment)
10. Impaired gastro-intestinal function thought sufficient to reduce lapatinib absorption
11. Contra-indication to receive adjuvant chemotherapy and/or trastuzumab (ECOG greater than 2)
12. Known immediate or delayed hypersensitivity, reaction to drugs chemically related to trastuzumab or lapatinib
13. Other concomitant investigational agents or concurrent anti-cancer therapy. In addition all herbal (alternative) therapies are prohibited.
14. Regular use of systemic steroids or other agents that could influence study endpoints
15. Patient must not have clinically significant cardiac abnormalities or uncontrolled hypertension
16. No previous myocardial infarction, heart failure, or significant angina. Cardiac function

should be assessed by physical examination, electrocardiogram (ECG), and baseline left ventricular ejection fraction (LVEF) should be greater than or equal to 50% as measured by echocardiography or multiple-gated acquisition (MUGA) scan.

Date of first enrolment
01/04/2010

Date of final enrolment
30/09/2015

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University of Manchester
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Sponsor information

Organisation
University of Manchester (UK)

ROR
https://ror.org/027m9bs27

Organisation
Manchester University NHS Foundation Trust

ROR
https://ror.org/00he80998

Organisation
Institute of Cancer Research

ROR
https://ror.org/043jzw605

Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK (CRUK) (UK) (ref: C7525/A8965)

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

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

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.
EPHOS-B-icrctsu@icr.ac.uk

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		01/04/2022	09/03/2023	Yes	No
Abstract results		01/03/2016	09/03/2023	No	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Plain English results			17/07/2023	No	Yes
Poster results	version 2	07/12/2021	09/03/2023	No	No
Protocol file	version 8.0	04/09/2019	21/12/2023	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes