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# A trial looking at GDC0941 and anastrozole for oestrogen positive breast cancer (OPPORTUNE)

| Submission date | Recruitment status | [_] Prospectively registered |
|---|---|---|
| 18/02/2014 | No longer recruiting | [_] Protocol |
| **Registration date** | **Overall study status** | [_] Statistical analysis plan |
| 18/02/2014 | Completed | [X] Results |
| **Last Edited** | **Condition category** | [_] Individual participant data |
| 01/11/2019 | Cancer | |

**Plain English summary of protocol**
http://www.cancerresearchuk.org/cancer-help/trials/a-trial-looking-gdc0941-anastrozole-oestrogen-positive-breast-cancer-opportune?

## Contact information

**Type(s)**
Scientific

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## Additional identifiers

**Clinical Trials Information System (CTIS)**
2011-003530-13

**Protocol serial number**
11583

## Study information

## Scientific Title
Randomised phase II window study of short term preoperative treatment with the PI3K inhibitor GDC0941 plus Anastrozole versus Anastrozole alone in patients with ER positive primary breast cancer

## Acronym
OPPORTUNE

## Study objectives
This open-label, randomised phase II study of 2-week preoperative treatment with anastrozole alone or in combination with the PI3K-inhibitor GDC-0941 is designed to test the hypothesis that the combination of estrogen deprivation and PI3K-inhibition has synergistic activity in ER-positive, HER2-negative invasive primary breast cancer. The study will also try to characterize the patient population who might benefit from treatment with PI3K inhibitors and to identify surrogate markers of antitumour effects.

Estrogenblocking drugs such as anastrozole (Arimidex) are often prescribed after breast surgery to prevent disease recurrence. Anastrozole is not effective in all women. GDC0941 is an experimental drug that may help overcome this resistance to anastrozole by inhibiting an enzyme (phosphoinositide3kinase) involved in the mechanisms by which cells talk to each other. Before starting large clinical trials we want to confirm the expected short term effects on breast tumour cells and signalling pathways using a modified window of opportunity study. This study will guide the development of GDC0941, as it helps understand which breast cancers are likely to benefit.

Window studies are used at early stages of drug development. A sample of a suspected tumour is stored after the diagnostic biopsy. If surgery is required then an experimental drug can be given in the interval between diagnosis and surgery (typically 24 weeks in the NHS). Another sample of the tumour is taken at surgery and compared to the original baseline sample. Window studies allow the initial assessment of a drug with relatively little intrusion into a womans progress through the care pathway.

## Ethics approval required
Old ethics approval format

## Ethics approval(s)
NRES Committee London - City & East, 17/10/2011, ref: 11/LO/1559

## Study design
Randomised; Interventional; Design type: Treatment

## Primary study design
Interventional

## Study type(s)
Treatment

## Health condition(s) or problem(s) studied
Topic: National Cancer Research Network; Subtopic: Breast Cancer; Disease: Breast

## Interventions

Breast Tumour Biopsy, Before study treatment and after study treatment during surgery; ECG, Before study treatment and after two weeks of study treatment; Informed Consent, Obtained in writing prior to any protocol specific procedures
Study Treatment, Two weeks of either GDC-0941 and anastrozole or anastrozole alone
Venepuncture, Before study treatment and after two weeks of treatment

Follow Up Length: 2 month(s)

Study Entry : Single Randomisation only

Added 28/02/2017:
This is a short-term randomised controlled trial of pre-operative drug therapy in women newly-diagnosed with estrogen-dependent invasive primary breast cancer whose tumours are ≥ 1 cm in diameter. There is no 'usual treatment' arm in this study. Current UK practice is to offer anastrozole as neoadjuvant therapy (i.e. for months rather than weeks), to some women, generally when the tumour is too large to be operated on immediately. The women recruited in the present study are not offered pre-operative anastrozole therapy as their tumours are considered operable.

Participants are randomly allocated to one of the two treatment arms: anastrozole (1 mg/d for about 2 weeks) or anastrozole (1 mg/d) co-prescribed with the investigational drug GDC-0941 (340 mg/d) for about two weeks followed by a one week GDC-0941 washout involving anastrozole alone (1 mg/d). Randomisation is based on a 2:1 allocation in favour of the GDC-0941 /anastrozole combination in order to maximise the information on the safety and tolerability of the investigational drug. There is no attempt to blind the women or the research team to treatment group other than at the level of data analysis.

This is a modified 'window of opportunity' study in which the drugs are given for the approximately 2 week interval between diagnosis and surgery. This approach allows comparison of the effects of these drugs on a) tumour biology using the initial biopsy sample and the tissue removed at subsequent biopsies or surgery and b) plasma biomarkers, using blood samples taken at the time of diagnosis and at surgery. However, as a precaution we will ask those women allocated to the combined therapy to stop taking the GDC-0941 component for a one week washout prior to surgery. This means that their surgery will be delayed by one week although, importantly, will still be completed within the NHS-recommended time.

Participation of women in both groups will involve the following procedures:

· Recruitment and signed informed consent
· Additional small samples of tumour to be taken a) at the time of the diagnostic biopsy and b) from the tissue removed at surgery
· Additional blood samples taken at a) the time of the diagnostic biopsy and b)at the time of surgery
· General monitoring for adverse effects over the two weeks of treatment

Following surgery all women will be given a final clinical assessment. They will continue under the care of their medical team with no further involvement in this specific research project.

## Intervention Type
Drug

## Phase

Phase II

### Drug/device/biological/vaccine name(s)
Anastrazole, GDC0941 (pictilisib)

### Primary outcome(s)
Change in Ki67 content of the tumour biopsies; Timepoint(s): Before and after two weeks of treatment.

Added 28/02/2017:
Change in tumour cell proliferation measured by Ki67 immunohistochemical assessment (%) in biopsy samples taken at diagnosis and day 15.

### Key secondary outcome(s))
1. Change in apoptosis in biopsies, plasma biomarkers; Timepoint(s): After two weeks
2. Clinical objective responses, adverse events and vital signs.; Timepoint(s): After two weeks
3. Genetic states of participants in relation to above changes; Timepoint(s): After two weeks

Added 28/02/2017:
1. Change in apoptosis in biopsies are assessed by changes in the tumour (TUNEL assay) at diagnosis and day 15
2. Tumour cell proliferation after discontinuation of GDC-0941 as measured by Ki67 IHC (%) on day 15 and the day of surger (anastrozole+GDC-0941 arm only)
3. Clinical objective responses, adverse events and vital signs at diagnosis and day 15
4. Pathological response and residual cancer burden

### Completion date
31/12/2017

## Eligibility

### Key inclusion criteria
1. Histologically confirmed breast cancer involving a palpable tumour of any size, or a tumour with an ultrasound assessed diameter of ≥ 1.0 cm
2. Estrogen receptor (ER) positive tumours with ≥1% of tumour cells positive for ER on immunohistochemical staining or an immunhistochemistry score (Allred) of 3 or higher
3. No prior systemic treatment regimens for the new primary breast cancer currently under investigation; prior treatment for previous breast cancer is allowed as long as it was completed at least 1 year prior to inclusion into this trial
4. Postmenopausal, defined as 1) age ≥ 55y and 1y or more of amenorrhea, OR 2) age < 55y and 1y or more of amenorrhea, with an estradiol assay <20 pg/mL, OR 3) age < 55y with prior hysterectomy but intact ovaries with an estradiol level <20 pg/mL,
5. Status after bilateral oophorectomy (≥ 28 days prior to first study treatment)
6. Adequate hematologic function (ANC ≥ 1500 cells/µl + platelet count ≥ 100000/µl)
7. Serum creatinine concentration < 1.5 x ULN¿ AST, ALT, bilirubin level < 1.5 x ULN¿ Fasting plasma glucose level < 7.8 mmol/L
8. ECOG performance status 0-2
9. Written informed consent prior to admission to the study

### Participant type(s)
Patient

### Healthy volunteers allowed
No

### Age group
Adult

### Sex
Female

### Key exclusion criteria
1. Male gender
2. Inflammatory breast cancer
3. HER2 positive tumours with 3+ intensity on IHC staining for HER2 or amplification of the HER2 gene on ISH
4. Evidence of distant metastases
5. Previous systemic or local treatment for the new primary breast cancer currently under investigation (including surgery, radiotherapy, cytotoxic and endocrine treatments); prior treatment for previous breast cancer is allowed as long as it was completed at least 1 year prior to inclusion into this trial
6. Clinically significant pulmonary dysfunction
7. Uncontrolled Type 1 or 2 diabetes mellitus (diabetic patients must have been on a stable regimen of oral antihyperglycemic therapy for at least 3 weeks duration and must have home monitoring levels without fasting blood glucose >8.9 mmol/L or hypoglycemia for one week prior to study entry)
8. Serious intercurrent medical or psychiatric illness, including serious active infection
9. Concurrent treatment with other experimental drugs or participation in another clinical trial with any investigational drug within 30 days prior to study entry
10. Any other disease, metabolic dysfunction, physical examination finding, or clinical laboratory finding that, in the investigators opinion, gives reasonable suspicion of a disease or condition that contraindicates the use of an investigational drug or that may affect the interpretation of the results or render the patient at high risk from treatment complications

### Date of first enrolment
03/01/2012

### Date of final enrolment
31/07/2014

## Locations

### Countries of recruitment
United Kingdom

England

### Study participating centre
### Clinical Investigation and Research Unit
Brighton

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# Sponsor information

### Organisation
Brighton & Sussex University Hospitals NHS Trust (UK)

# Funder(s)

### Funder type
Industry

### Funder Name
Genentech, Inc

# Results and Publications

### Individual participant data (IPD) sharing plan
The current data sharing plans for the current study are unknown and will be made available at a later date

### IPD sharing plan summary
Data sharing statement to be made available at a later date

### Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Results article | results | 10/06/2016 | | Yes | No |
| HRA research summary | | | 28/06/2023 | No | No |