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PARTNER: Platinum and PARP inhibitor for neoadjuvant treatment of triple-negative and /or BRCA-positive breast cancer

Submission date 16/07/2018	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol
Registration date 20/11/2018	**Overall study status** Ongoing	[_] Statistical analysis plan [_] Results
Last Edited 05/12/2023	**Condition category** Cancer	[_] Individual participant data [_] Record updated in last year

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-olaparib-with-chemotherapy-for-early-breast-cancer-partner

Contact information

Type(s)
Scientific

Contact name
Dr Study Team

Contact details
Cambridge Cancer Trials Centre (S4)
Box 279
Addenbrooke's Hospital
Cambridge Biomedical Campus
Hills Road
Cambridge
United Kingdom
CB2 0QQ
None provided
cuh.partner@nhs.net

Additional identifiers

ClinicalTrials.gov (NCT)
NCT03150576

Clinical Trials Information System (CTIS)

2015-002811-13

Integrated Research Application System (IRAS)
178681

Protocol serial number
30433

Study information

Scientific Title
Randomised, phase II
/III, 3 stage trial to evaluate the safety and efficacy of the addition of olaparib to platinum-based neoadjuvant chemotherapy in breast cancer patients with TNBC and/or gBRCA

Acronym
PARTNER

Study objectives
This trial investigates whether introducing olaparib at an earlier stage of breast cancer might produce more shrinkage of the breast cancer before surgery, which may allow a better chance of avoiding mastectomy and may lead to a better chance of avoiding recurrence of the breast cancer.

Ethics approval required
Old ethics approval format

Ethics approval(s)
North West - Haydock Research Ethics Committee, 05/01/2016, ref: 15/NW/0926

Primary study design
Interventional

Study design
Randomized; Interventional; Design type: Treatment, Drug

Study type(s)
Treatment

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

Interventions
Patients are randomised using a web-based system. Eligible patients will be randomly assigned to either the control arm (chemotherapy alone) or one of the two research arms (chemotherapy with olaparib at different timings) using minimisation method in a 1:1:1 ratio in Stage 1 and Stage 2. At the end of stage 2, one of the research treatments will be dropped using the ‘pick the winner’ method. In Stage 3, patients will be randomly assigned with a 1:1 ratio to either control or the selected research arm.

Control arm: 4 cycles of: Paclitaxel 80mg/m2 Day 1, 8 & 15, every 3 weeks, Carboplatin AUC5, Day 1, every 3 weeks.
Research arm 1: 4 cycles of: Paclitaxel 80mg/m2 on Days 1, 8 & 15 every 3 weeks, Carboplatin AUC 5 Day 1, every 3 weeks, Olaparib oral 150mg twice daily, D-2 to D10 every 3 weeks
Research arm 2: 4 cycles of: Paclitaxel 80mg/m2 on Days 1, 8 & 15 every 3 weeks, Carboplatin AUC 5 Day 1, every 3 weeks, Olaparib oral 150mg twice daily, D3 to D14 every 3 weeks. 3 cycles of anthracycline-based chemotherapy.

Intervention Type
Drug

Phase
Phase II/III

Drug/device/biological/vaccine name(s)
Paclitaxel, carboplatin, olaparib

Primary outcome(s)
1. Safety of the addition of olaparib to three weekly carboplatin / weekly paclitaxel chemotherapy
2. pCR in each of the two research arms. At the end of stage 2, one of the research treatments will be dropped using the 'pick the winner' method
3. pCR at surgery after neoadjuvant treatment
4. pCR rates after neoadjuvant chemotherapy +/- olaparib, defined as no residual invasive carcinoma within the breast (Ductal Carcinoma in situ permitted) AND no evidence of metastatic disease within the lymph nodes
Timepoint(s): Stage I Safety, Stage II pCR, Stage III pCR

Key secondary outcome(s)
1. pCR at surgery, assessed by central pathology review of the diagnosis and surgery slides. Time Frame: Up to 2 years after last patient randomised
2. Relapse-Free Survival (RFS), calculated from date of randomisation to date of first relapse or date of death from all causes, whichever occurs first. Time Frame: Up to 10 years after last patient is randomised
3. Breast cancer specific survival (BCSS), calculated from date of randomisation to date of death from breast cancer. Time Frame: Up to 10 years after last patient is randomised
4. Distant disease-free survival, calculated from date of randomisation to date of the first distant disease relapse or date of death from all causes, whichever occurs first. Time Frame: Up to 10 years after last patient is randomised
5. Local recurrence-free survival, calculated from date of randomisation to date of the first local recurrence or date of death from all causes, whichever occurs first. Time Frame: Up to 10 years after last patient is randomised
6. Overall survival (OS), calculated from date of randomisation to date of death from all causes. Time Frame: Up to 10 years after last patient is randomised
7. Time to second cancer (TTSC), calculated from the date of randomisation to the date of diagnosis of second cancer. Time Frame: Up to 10 years after last patient is randomised
8. pCR in breast alone. Time Frame: Up to 2 years after last patient is randomised
9. Residual Cancer Burden (RCB) I-III will be assessed by central pathology review. Time Frame: Up to 10 years after last patient is randomised
10. Radiological response, assessed by radiological response criteria as per RECIST v1.1 after 4th and final cycles. Time Frame: Up to 2 years after last patient is randomised

11. Treatment related toxicities, assessed by CTCAE v4.03. Time Frame: Up to 10 years after last patient is randomised
12. Quality of life (sub-study). Time Frame: Up to 10 years after last patient is randomised

Other pre-specified outcome measures:
Discovery and validation of prognostic, pharmacogenetic and pharmacogenomic markers that can be correlated with outcomes (pCR and RFS) in patients randomised to receive olaparib compared with those who are not. Time Frame: Up to 15 years after last patient is randomised

Completion date
30/01/2034

Eligibility

Key inclusion criteria
Current inclusion criteria as of 13/01/2022:
1. Aged between 16 and 70 at time of Informed Consent
2. Written informed consent, willing and able to comply with the Protocol for the duration of the trial including undergoing treatment and scheduled visits and examinations
3. Histologically confirmed invasive breast cancer
4. ER-negative, and HER2-negative breast cancer (TNBC, non-BRCA). Patients will be eligible with any PR status but PR expression must be scored.
OR
Germline BRCA (gBRCA) mutation positive, HER2 negative, and PgR/ER of any status
Note: mutation in BRCA1 or BRCA2 must be documented and predicted to be detrimental/lead to loss of function.
5. T1c, T2 or T3 tumours (>10 mm diameter)
OR
T4 tumour of any size with direct extension to (a) chest wall or (b) skin
OR
Inflammatory carcinoma with tumour of any size
OR
Other locally advanced disease:
- Involvement of ipsilateral large or fixed axillary lymph nodes, or infra or supraclavicular nodes (>10mm diameter or clinical N2 or N3) and primary breast tumour of any diameter
- Involvement of ipsilateral large or fixed axillary lymph nodes, or infra or supraclavicular nodes (>10mm diameter, or clinical N2 or N3), without a primary breast tumour identified, the presence of breast cancer in a Lymph Node (LN) must be histopathologically confirmed by LN biopsy
OR
Multifocal tumour:
- with at least one tumour with a size >10 mm
- Non-BRCA patients with multifocal disease are eligible to enter the trial provided that these foci are TNBC and one of them meets the size criteria above. If a patient is thought to have unifocal disease at diagnosis and then is later found to be multifocal they may remain within the trial as long as no new foci are HER2 positive
6. Patients with bilateral disease are eligible to enter the trial provided they are either BRCA positive or that both breast diseases are HER2 negative and one of them meets the size criteria above and is TNBC
7. Be fit to receive the trial chemotherapy regimen in the opinion of the responsible clinician:
- Adequate bone marrow, hepatic, and renal function
- ECOG performance status of 0, or 1

8. Treatment should be commenced within 6 weeks of the diagnostic biopsy. In uncommon circumstances, where medically acceptable, treatment is permitted to start within a maximum of 9 weeks of the diagnostic biopsy
9. Availability of the Tumour Infiltrating Lymphocytes score is required
10. Availability of CK5/6 and/or EGFR +/- Androgen Receptor IHC score if the patient is non-BRCA TNBC
11. Availability of slides and paraffin-embedded tissue blocks from pre-treatment core biopsy and from primary surgical resection is required
12. Women of child-bearing potential (WCBP), defined as not surgically sterilized or not post-menopausal for at least 24 consecutive months if age ≤55 years or 12 months if age >55 years, must have a negative serum pregnancy test within 14 days prior to randomisation. Once a negative pregnancy test is received the patient must be informed that they must use adequate contraception for at least 6 months after the last dose of the trial treatment.
13. All WCBP and all sexually active male patients, as well as their partners, must be aware that they should not conceive during the treatment period and therefore must use effective forms of contraception, throughout their participation in the trial and for at least 6 months after the last dose of trial treatment.

Previous inclusion criteria:
1. Aged between 16 and 70 at time of Informed Consent
2. Written informed consent, willing and able to comply with the Protocol for the duration of the trial including undergoing treatment and scheduled visits and examinations
3. Histologically confirmed invasive breast cancer
4. ER-negative, and HER2-negative breast cancer (TNBC). Patients will be eligible with any PR status but PR expression must be scored
OR
Germline BRCA (gBRCA) mutation positive, HER2 negative, and PgR/ER of any status
Note: mutation in BRCA1 or BRCA2 must be documented and predicted to be detrimental/lead to loss of function
5. T1, T2 or T3 tumours (>10mm diameter)
OR
T4 tumour of any size with direct extension to (a) chest wall or (b) skin.
OR
Inflammatory carcinoma with tumour of any size.
OR
Other locally advanced disease:
- Involvement of ipsilateral large or fixed axillary lymph nodes, or infra or supraclavicular nodes (>10mm diameter or clinical N2 or N3, see Appendix 5) and primary breast tumour of any diameter
- Involvement of ipsilateral large or fixed axillary lymph nodes, or infra or supraclavicular nodes (>10mm diameter, or clinical N2 or N3, see Appendix 5), without a primary breast tumour identified, the presence of breast cancer in a Lymph Node (LN) must be histopathologically confirmed by LN biopsy
OR
Multifocal tumour:
- with at least one tumour with a size >10mm
- Patients with multifocal disease are eligible to enter the trial provided that these foci are TNBC and one of them meets the size criteria above. If a patient is thought to have unifocal disease at diagnosis and then is later found to be multifocal they may remain within the trial as long as no new foci are HER2 positive
6. Patients with bilateral disease are eligible to enter the trial provided they are either BRCA positive or that both breast diseases are TNBC and one of them meets the size criteria above

7. Be fit to receive the trial chemotherapy regimen in the opinion of the responsible clinician:
- Adequate bone marrow, hepatic, and renal function
- ECOG performance status of 0, or 1
8. Treatment should be commenced within 6 weeks of the diagnostic biopsy. In uncommon circumstances, where medically acceptable, treatment is permitted to start within a maximum of 9 weeks of the diagnostic biopsy
9. Availability of the Tumour Infiltrating Lymphocytes score is required
10. Availability of CK5/6 and/or EGFR +/- Androgen Receptor IHC score if patient is TNBC
11. Availability of slides and paraffin embedded tissue blocks from pre-treatment core biopsy and from primary surgical resection is required
12. Women of child-bearing potential (WCBP), defined as not surgically sterilized or not post-menopausal for at least 24 consecutive months if age ≤55 year or 12 months if age >55 years, must have a negative serum pregnancy test within 14 days prior to randomisation. Once a negative pregnancy test is received the patient must be informed that they must use adequate contraception for at least 6 months after the last dose of the trial treatment
13. All WCBP and all sexually active male patients as well as their partners must be aware that they should not conceive during the treatment period and therefore should routinely use effective forms of contraception, throughout their participation in the trial and for at least 6 months after the last dose of trial treatment

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
16 Years

Upper age limit
70 Years

Sex
All

Key exclusion criteria
Current exclusion criteria as of 13/01/2022:
1. T0 tumour in absence of axillary node >10 mm
2. TNBC with a non-basal phenotype and over-expressing Androgen Receptor
3. Triple-negative subtypes such as adenoid cystic, apocrine, metaplastic, low grade adenosquamous or secretory carcinoma
4. Patients diagnosed with ipsilateral synchronous ER-positive (Allred Score >3) breast cancer tumours (known at inclusion) in absence of germline BRCA mutation
5. Previous or concomitant chemotherapy or biological agents used for the treatment of cancer in the last 5 years
6. Malignancy within the last 5 years except: adequately treated non-melanoma skin cancer; curatively treated in situ cancer of the cervix; ductal carcinoma in situ (DCIS); Stage 1, grade 1 endometrial carcinoma; or other solid tumours including lymphomas (without bone marrow

involvement) curatively treated with no evidence of disease for ≥5 years.
7. Patients with myelodysplastic syndrome/acute myeloid leukaemia
8. Previous history of allogeneic marrow transplant
9. Evidence of distant metastasis apparent prior to randomisation
10. Patients with uncontrolled seizures. Pre-existing sensory or motor neuropathy of CTCAE v4. 03, grade ≥2, There are some possible exceptions in cases of severe pre-existing disability.
11. Concomitant use of known potent CYP3A4 inhibitors and inducers. There is consideration for wash-out periods.
12. Pregnant or breastfeeding women
13. Not suitable for neoadjuvant chemotherapy in the opinion of the responsible clinician
14. Major surgery within 14 days prior to starting trial treatment and patients must have recovered from any effects of any major surgery
15. Any evidence of other disease or any concomitant medical or psychiatric problems which in the opinion of the Investigator would prevent completion of treatment or follow-up. For example:
- Evidence of severe or uncontrolled cardiac disease
- Uncontrolled ventricular arrhythmia
- Recent myocardial infarction (within 12 months)
- Active infection including Hepatitis B, Hepatitis C and Human Immunodeficiency Virus (HIV). Screening for chronic conditions is not required.
16. Patients unable to swallow orally administered medication and patients with gastrointestinal disorders likely to interfere with absorption of the trial medication. This includes but is not limited to refractory nausea and vomiting, chronic gastrointestinal diseases or previous significant bowel resection
17. Known hypersensitivity to olaparib, carboplatin, paclitaxel or their excipients (including cremophor)
18. Whole blood transfusions in the last 120 days prior to blood sampling for the BRCA test as it may interfere with the results (packed red blood cells and platelet transfusions are acceptable)

Previous exclusion criteria:
1. T0 tumour in absence of axillary node >10 mm
2. TNBC with a non-basal phenotype and over-expressing Androgen Receptor
3. Not suitable for neoadjuvant chemotherapy
4. Distant metastases apparent prior to randomisation
5. Prior history of invasive breast cancer within the last 5 years
6. Previous PARP inhibitor use or any previous chemotherapy or targeted agent.
7. Any previous chemotherapy or agent used for the treatment of cancer within the last 5 years

Date of first enrolment
30/05/2016

Date of final enrolment
31/12/2024

Locations

Countries of recruitment
United Kingdom

England

Scotland

Wales

Study participating centre
University Hospital Crosshouse
Kilmarnock Road
Kilmarnock
United Kingdom
KA2 0BE

Study participating centre
University Hospital Ayr
Dalmellington Road
Ayr
United Kingdom
KA6 6DX

Study participating centre
Addenbrooke's Hospital
Hill's Road
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
Southampton General Hospital
Tremona Road
Southampton
United Kingdom
SO16 6YD

Study participating centre
West Suffolk Hospital
Hardwick Lane
Bury Saint Edmunds
United Kingdom
IP33 2QZ

Study participating centre
Colchester General Hospital
Turner Road
Colchester
United Kingdom
CO4 5JL

Study participating centre
Nottingham City Hospital
Hucknall Road
Nottingham
United Kingdom
NG5 1PB

Study participating centre
Royal Bournemouth Hospital
Castle Lane East
Bournemouth
United Kingdom
BH7 7DW

Study participating centre
Peterborough City Hospital
Bretton Gate
Peterborough
United Kingdom
PE3 9GZ

Study participating centre
Basingstoke and North Hampshire Hospital
Aldermaston Road
Basingstoke
United Kingdom
RG24 9NA

Study participating centre
Royal Hampshire County Hospital
Romsey Road
Winchester
United Kingdom
SO22 5DG

Study participating centre
Velindre Cancer Centre
Velindre Road
Cardiff
United Kingdom
CF14 2TL

Study participating centre
University College London Hospital
Euston Road
London
United Kingdom
NW1 2PG

Study participating centre
Bristol Haematology & Cancer Centre
Horfield Road
Bristol
United Kingdom
BS2 8ED

Study participating centre
Worcestershire Royal Hospital
Charles Hastings Way
Worcester
United Kingdom
WR5 1DD

Study participating centre
Kidderminster General Hospital
Bewdley Road
Kidderminster
United Kingdom
DY11 6RJ

Study participating centre
The Alexandra Hospital
Woodrow Drive

Redditch
United Kingdom
B98 7UB

Study participating centre
Bedford General Hospital
Kempston Road
Bedford
United Kingdom
MK42 9DJ

Study participating centre
Churchill Hospital
Old Road
Oxford
United Kingdom
OX3 7LE

Study participating centre
Queen's Hospital
Rom Valley Way
Romford
United Kingdom
RM7 OAG

Study participating centre
Royal Free Hospital
Pond Street
London
United Kingdom
NW3 2QG

Study participating centre
Russells Hall Hospital
Pensnett Road
Dudley
United Kingdom
DY1 2HQ

Study participating centre
Pinderfields General Hospital
Aberford Road
Wakefield
United Kingdom
WF1 4DG

Study participating centre
Burton Hospitals NHS Foundation Trust
Queen's Hospital
Belvedere Road
Burton-on-trent
United Kingdom
DE13 0RB

Study participating centre
The Christie NHS Foundation Trust
550 Wilmslow Road
Withington
Manchester
United Kingdom
M20 4BX

Study participating centre
University Hospitals Dorset NHS Foundation Trust
Management Offices
Poole Hospital
Longfleet Road
Poole
United Kingdom
BH15 2JB

Study participating centre
Ipswich Hospital
Heath Road
Ipswich
United Kingdom
IP4 5PD

Study participating centre

Singleton Hospital
Sketty Lane
Sketty
Swansea
United Kingdom
SA2 8QA

Study participating centre
Hinchingbrooke Hospital
Hinchingbrooke Park
Huntingdon
United Kingdom
PE29 6NT

Study participating centre
Mount Vernon Hospital
Rickmansworth Road
Northwood
United Kingdom
HA6 2RN

Sponsor information

Organisation
Cambridge University Hospitals NHS Foundation Trust

ROR
https://ror.org/04v54gj93

Funder(s)

Funder type
Industry

Funder Name
AstraZeneca

Alternative Name(s)
AstraZeneca PLC, Pearl Therapeutics, AZ

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 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?
HRA research summary			28/06/2023	No	No