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plasmaMATCH: A clinical trial aiming to assess the safety and activity of targeted treatments in patients with advanced breast cancer where the targetable mutation is identified through circulating tumour DNA screening

Submission date 28/11/2016	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol
Registration date 07/12/2016	**Overall study status** Completed	[_] Statistical analysis plan [X] Results
Last Edited 09/02/2024	**Condition category** Cancer	[_] Individual participant data

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-using-a-blood-test-to-find-certain-gene-changes-and-decide-treatment-for-advanced-breast

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2015-003735-36

IRAS number

ClinicalTrials.gov number
NCT03182634

Secondary identifying numbers
31608

Study information

Scientific Title
The UK plasma based Molecular profiling of Advanced breast cancer to inform Therapeutic Choices (plasmaMATCH) Trial: A multiple parallel cohort, open-label, multi-centre phase IIa clinical trial aiming to provide proof of principle efficacy for designated targeted therapies in patients with advanced breast cancer where the targetable mutation is identified through ctDNA screening

Acronym
plasmaMATCH

Study objectives
Current hypothesis as of 18/01/2019:
plasmaMATCH aims to assess whether ctDNA screening can be used to detect patient subgroups who will be sensitive to targeted therapies, and will also assess the safety and efficacy of these targeted treatments.

Previous hypothesis:
plasmaMATCH aims to assess whether ctDNA screening can be used to detect patients with targetable mutations, and will assess the safety and activity of the targeted treatments in patients with targetable mutations identified at ctDNA screening.

Ethics approval required
Old ethics approval format

Ethics approval(s)
South Central - Oxford C Research Ethics Committee, 20/07/2016, ref: 16/SC/0271

Study design
Randomised; Both; Design type: Treatment, Screening, Drug, Cohort study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)

Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

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

Interventions
Cohort A: ESR1 mutation identified in ctDNA screening treated with extended-dose fulvestrant.
500mg fulvestrant to be administered intramuscularly (IM) on Cycle 1 Days 1, 8 and 15 and Cycle 2 onwards Days 1 and 15.

Cohort B: HER2 mutation identified in ctDNA screening in patients with estrogen receptor (ER) positive breast cancer treated with neratinib plus fulvestrant, or in patients with ER negative breast cancer treated with neratinib only.
240mg neratinib to be administered on a continuous schedule starting on Cycle 1 Day 1.
In ER positive breast cancer, 500mg fulvestrant to be administered IM on Cycle 1 Days 1 and 15 and Cycle 2 onwards Day 1.

Cohort C: AKT1 mutation identified in ctDNA screening in patients with ER positive breast cancer treated with AZD5363 and fulvestrant.
400mg AZD5363 to be administered twice daily on a 7 day schedule of 4 days on treatment followed by 3 days off treatment.
500mg fulvestrant IM Cycle 1 Days 1 and 15 and Cycle 2 onwards Day 1.

Cohort D: AKT activation basket with mutations of AKT1 in patients with ER negative breast cancer or AKT2/3 E17K, PIK3R1 or PTEN mutations or homozygous deletion of PTEN in both ER positive and ER negative breast cancer identified in ctDNA screening or in prior tumour sequencing conducted outside of plasmaMATCH, treated with AZD5363.
480mg AZD5363 to be administered twice daily on a 7 day schedule of 4 days on treatment followed by 3 days off treatment.

Cohort E: Patients with triple negative breast cancer (TNBC) on their most recent tumour biopsy who do not have a targetable mutation identified by ctDNA screening or tumour sequencing that would allow entry into Cohorts A to D, or who have an actionable mutation identified but are not otherwise eligible for Cohorts A to D, will be invited to enter Cohort E and consenting patients will receive 160mg AZD6738 to be administered once daily on Days 1–7 of each cycle and 300mg olaparib to be administered twice daily on a continuous schedule starting on Cycle 1 Day 1.

For each cohort a cycle consists of 28 days.

Treatment will continue until disease progression according to RECIST v1.1. Patients will be assessed by CT scan every 8 weeks with assessment of response by RECIST v1.1. After 32 weeks patients will be assessed by CT scan every 12 weeks.

Intervention Type
Other

Phase
Phase II

Primary outcome measure
Confirmed objective response rate as defined by RECIST v1.1 for each cohort separately. A patient will be said to have had an objective response if they have a complete/partial response at any point during trial treatment.

Secondary outcome measures
1. Clinical benefit rate and progression free survival (PFS), defined as complete/partial response or stable disease as defined by RECIST v1.1 lasting at least 24 weeks. PFS will be measured from the date of entry into the treatment cohort until first date of either confirmed progressive disease according to RECIST criteria or death.
2. Safety and tolerability of therapies will be assessed throughout the treatment period using the NCI CTCAE v4.0
3. Duration of response is measured from the time of first documentation of RECIST complete /partial response (whichever status is recorded first) until the first date that recurrence or progressive disease is objectively documented
4. Frequency of mutations identified in ctDNA screening and the proportion of patients with a targetable mutation who enter the therapeutic component
5. Agreement between ctDNA mutation status and tissue mutation status for patients entering the therapeutic component
6. Pharmacokinetics in Cohort A assessed at Cycle 2-4 Day 1 and Cohort B assessed Cycle 1-4 Day 1

Overall study start date
01/09/2015

Completion date
31/12/2021

Eligibility

Key inclusion criteria
Current inclusion criteria as of 18/01/2019:
1. Female
2. Aged ≥ 18 years old
3. Histologically confirmed invasive breast carcinoma
4. Metastatic or recurrent locally advanced breast cancer that is not suitable for treatment with radical or curative intent
5. Demonstrated progression of disease by radiological assessment or by clinical assessment within the last 6 weeks
6. Measurable disease by RECIST v1.1
7. Patients must have completed at least one prior line of treatment for advanced breast cancer and/or relapse within 12 months of completing (neo)adjuvant chemotherapy. Patients with HER2 positive breast cancer must have been treated with at least two courses of HER2 targeted therapy in the advanced setting (or one course if no further courses of HER2 targeted therapy are available locally)
8. Patient must either be suitable for a baseline biopsy of recurrent disease or have an archival biopsy of recurrent disease available. Patients are requested to consent to a baseline biopsy but if deemed unsafe by the Investigator, an archival biopsy of recurrent disease can be used

instead. If it is deemed unsafe to proceed with baseline biopsy, and no archival recurrent disease biopsy is available, the patient will not be eligible for entry into the treatment cohort
9. ECOG performance status ≤ 2
10. Life expectancy >3 months in Cohorts A-D and >16 weeks in Cohort E
11. Patients must be a) surgically sterile; b) have a sterilised sole partner; or c) be postmenopausal; or d) must agree to practice true abstinence; or e) use effective contraception during the period of trial treatment and be willing to do so for 6 months following the end of trial treatment
12. Patients of childbearing potential should have a negative serum pregnancy test within 14 days prior to initiation of trial treatment.
13. At least 4 weeks washout period after the end of trial treatment on a different cohort within plasmaMATCH
14. Adequate haematological, renal and hepatic function as defined by cohort-specific criteria in the protocol
15. For patients with ER positive breast cancer in Cohorts A, B and C: EITHER postmenopausal, as defined by at least one of the following criteria:
15.1. Age >60 years
15.2. Age <60 years and cessation of regular menses for at least 12 consecutive months with no alternative pathological or physiological cause; and serum estradiol and follicle stimulating hormone (FSH) level within the laboratory's reference range for postmenopausal females
15.3. Documented bilateral oophorectomy; medically confirmed ovarian failure.
OR Pre-/peri-menopausal (i.e. not meeting the criteria for being postmenopausal) if being treated with an LHRH agonist that was commenced at least 4 weeks prior to Cycle 1 Day 1, and continues on the LHRH agonist throughout the trial period.
NB. Additional eligibility criteria apply for entry into each treatment cohort.

Previous inclusion criteria:
1. Female
2. Aged ≥ 18 years old
3. Histologically confirmed invasive breast carcinoma
4. Metastatic or recurrent locally advanced breast cancer that is not suitable for treatment with radical or curative intent
5. Demonstrated progression of disease by radiological assessment or by clinical assessment within the last 6 weeks
6. Measurable disease by RECIST v1.1
7. Patients must have completed at least one prior line of treatment for advanced breast cancer and/or relapse within 12 months of completing (neo)adjuvant chemotherapy. Patients with HER2 positive breast cancer must have been treated with at least two courses of HER2 targeted therapy in the advanced setting (or one course if no further courses of HER2 targeted therapy are available locally)
8. Patient must either be suitable for a baseline biopsy of recurrent disease or have an archival biopsy of recurrent disease available. Patients are requested to consent to a baseline biopsy but if deemed unsafe by the Investigator, an archival biopsy of recurrent disease can be used instead. If it is deemed unsafe to proceed with baseline biopsy, and no archival recurrent disease biopsy is available, the patient will not be eligible for entry into the treatment cohort
9. ECOG performance status ≤ 2
10. Life expectancy >3 months
11. Patients must be surgically sterile, be postmenopausal or must agree to use effective contraception during the period of trial treatment and be willing to do so for 6 months following the end of trial treatment. Effective contraception is defined as double barrier contraception (e.g. condom plus spermicide in combination with a diaphragm, cervical cap or intrauterine device). Ovarian suppression with an LHRH agonist is not a method of contraception

12. Patients of childbearing potential should have a negative serum pregnancy test within 14 days prior to initiation of trial treatment.
13. At least 4 weeks washout period after the end of trial treatment on a different cohort within plasmaMATCH
14. Adequate haematological, renal and hepatic function as defined by:
14.1. Haematology: - Absolute neutrophil count (ANC) ≥1000/mm3 (≥1.0 x 109/L) - Platelet count ≥100,000/mm3 (≥100 x 109/L) - Haemoglobin ≥9g/dL (≥90g/L)
14.2. Renal function: - Serum creatinine ≤1.5 x upper limit of normal (ULN) and calculated creatinine clearance more than 30ml/min
14.3. Liver function tests: - Total bilirubin ≤1.5 ULN - Alanine aminotransferase (ALT) ≤3 ULN. In the presence of liver metastases ALT ≤5 ULN. For patients in Cohort B, C and D: aspartate aminotransferase (AST) ≤3 ULN. In the presence of liver metastases AST ≤5 ULN.
15. For patients with ER positive breast cancer in Cohorts A, B and C: EITHER postmenopausal, as defined by at least one of the following criteria:
15.1. Age >60 years
15.2. Age <60 years and cessation of regular menses for at least 12 consecutive months with no alternative pathological or physiological cause; and serum estradiol and follicle stimulating hormone (FSH) level within the laboratory's reference range for postmenopausal females
15.3. Documented bilateral oophorectomy; medically confirmed ovarian failure.
OR Pre-/peri-menopausal (i.e. not meeting the criteria for being postmenopausal) if being treated with an LHRH agonist that was commenced at least 4 weeks prior to Cycle 1 Day 1, and continues on the LHRH agonist throughout the trial period.
NB. Additional eligibility criteria apply for entry into each treatment cohort.

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Female

Target number of participants
Planned Sample Size: 1150; UK Sample Size: 1150

Total final enrolment
1051

Key exclusion criteria
1. Prior treatment with radiotherapy (except for palliative reasons), endocrine therapy, immunotherapy, chemotherapy or IMPs during the previous 4 weeks (6 weeks for nitrosoureas, Mitomycin-C) before trial treatment, except for hormonal therapy with LHRH analogues, which are permitted, and bisphosphonates or RANK ligand antibodies that are permitted for the management of bone metastases
2. Uncontrolled CNS disease (brain metastases or leptomeningeal disease). Patients with prior diagnosis of CNS metastases must be stable by clinical assessment having ceased steroids after prior treatment

3. History of clinically significant or uncontrolled cardiac disease, including congestive heart failure, angina, myocardial infarction within the last 6 months or ventricular arrhythmia. Patients with a history of any of the above listed cardiac conditions judged not to be clinically significant by the local investigator must be notified to the trial team at the ICR-CTSU for approval by the CI and/or Cohort Lead
4. Ongoing toxic manifestations of previous treatments Grade ≥1. Exceptions to this are alopecia or toxicities which in the opinion of the Investigator should not exclude the patient. Such cases should be clearly documented in the patient's notes by the Investigator
5. Major surgery (excluding minor procedures, e.g. placement of vascular access) within 4 weeks of the first dose of trial treatment
6. Pregnant or breastfeeding
7. Any condition that according to the treating physician may compromise the patient's safety or the conduct of the trial
8. Current malignancies of other types, with the exception of adequately treated in situ carcinoma of the cervix and basal or squamous cell carcinoma of the skin. Cancer survivors, who have undergone potentially curative therapy for a prior malignancy and have no evidence of the disease for 3 years or more are eligible for the trial. NB. Additional eligibility criteria apply for entry into each treatment cohort.

NB. Additional eligibility criteria apply for entry into each treatment cohort

Date of first enrolment
15/12/2016

Date of final enrolment
30/06/2019

Locations

Countries of recruitment
England

Scotland

United Kingdom

Wales

Study participating centre
The Royal Marsden Hospital
Fulham Road
Chelsea
London
United Kingdom
SW3 6JJ

Study participating centre

The Royal Marsden Hospital
Downs Road
Sutton
United Kingdom
SM2 5PT

Study participating centre
Western General Hospital
Crewe Road South
Edinburgh
United Kingdom
EH4 2XU

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

Study participating centre
Beatson West of Scotland Cancer Centre
1053 Great Western Road
Glasgow
United Kingdom
G12 0YN

Study participating centre
Bristol Haematology and Oncology Centre
Horfield Road
Avon
Bristol
United Kingdom
BS2 8ED

Study participating centre
The Christie
550 Wilmslow Road
Withington

Manchester
United Kingdom
M20 4BX

Study participating centre
Clatterbridge Cancer Centre
Clatterbridge Health Park
Clatterbridge Road
Birkenhead
Wirral
United Kingdom
CH63 4JY

Study participating centre
Derriford Hospital
Derriford Road
Plymouth
United Kingdom
PL6 8DH

Study participating centre
Kent Oncology Centre
Maidstone Hospital
Hermitage Lane
Maidstone
United Kingdom
ME16 9QQ

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

Study participating centre
Royal Cornwall Hospital
2 Penventinnie Lane
Treliske

Truro
United Kingdom
TR1 3LQ

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

Study participating centre
St Barts Hospital
W Smithfield
London
United Kingdom
EC1A 7BE

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

Study participating centre
Velindre Hospital
Velindre Road
Whitchurch
Cardiff
United Kingdom
CF14 2TL

Study participating centre
Weston Park Hospital
Whitham Road
Sheffield
United Kingdom
S10 2SJ

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

Study participating centre
Royal Devon and Exeter Hospital
Barrack Road
Exeter
United Kingdom
EX2 5DW

Sponsor information

Organisation
Institute of Cancer Research

Sponsor details
Royal Cancer Hospital
123 Old Brompton Road
London
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United Kingdom
SW7 3RP
+44 20 8722 4152
plasmamatch-icrctsu@icr.ac.uk

Sponsor type
Research organisation

Website
http://www.icr.ac.uk/

ROR
https://ror.org/043jzw605

Organisation
Royal Marsden NHS Foundation Trust

Sponsor details

Fulham Road
London
England
United Kingdom
SW3 6JJ
+44 20 8722 4152
plasmamatch-icrctsu@icr.ac.uk

Sponsor type
Hospital/treatment centre

Website
http://www.royalmarsden.nhs.uk/pages/home.aspx

ROR
https://ror.org/0008wzh48

Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK

Alternative Name(s)
CR_UK, Cancer Research UK - London, CRUK

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Publication and dissemination plan
The main trial results for each treatment cohort will be published either separately or together in a peer-reviewed journal, on behalf of all collaborators. The results of the screening component, individual cohorts and translational research may be published together or individually.

Intention to publish date
31/12/2022

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from plasmaMATCH-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	results	01/10/2020	15/09/2020	Yes	No
Results article	Commentary	23/04/2021	27/04/2021	Yes	No
Other publications		07/05/2022	20/01/2023	Yes	No
HRA research summary			28/06/2023	No	No
Plain English results			09/02/2024	No	Yes