

# 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

<b>Submission date</b> 28/11/2016	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 07/12/2016	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 04/02/2026	<b>Condition category</b> Cancer	<input type="checkbox"/> 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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### Contact details

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## Additional identifiers

### Clinical Trials Information System (CTIS)

2015-003735-36

**ClinicalTrials.gov (NCT)**

NCT03182634

**Protocol serial number**

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

### Study type(s)

Treatment

### 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

## **Primary outcome(s)**

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.

## **Key secondary outcome(s)**

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

## **Completion date**

31/12/2021

## **Eligibility**

### **Key inclusion criteria**

Current inclusion criteria as of 18/01/2019:

1. Female
2. Aged  $\geq 18$  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  $\leq 2$
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  $\geq 18$  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  $\leq 2$

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)  $\geq 1000/\text{mm}^3$  ( $\geq 1.0 \times 10^9/\text{L}$ ) - Platelet count  $\geq 100,000/\text{mm}^3$  ( $\geq 100 \times 10^9/\text{L}$ ) - Haemoglobin  $\geq 9\text{g/dL}$  ( $\geq 90\text{g/L}$ )

14.2. Renal function: - Serum creatinine  $\leq 1.5 \times$  upper limit of normal (ULN) and calculated creatinine clearance more than 30ml/min

14.3. Liver function tests: - Total bilirubin  $\leq 1.5$  ULN - Alanine aminotransferase (ALT)  $\leq 3$  ULN. In the presence of liver metastases ALT  $\leq 5$  ULN. For patients in Cohort B, C and D: aspartate aminotransferase (AST)  $\leq 3$  ULN. In the presence of liver metastases AST  $\leq 5$  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

**Healthy volunteers allowed**

No

**Age group**

Mixed

**Lower age limit**

18 years

**Upper age limit**

99 years

**Sex**

Female

**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  $\geq 1$ . 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**

United Kingdom

England

Scotland

Wales

**Study participating centre**

**The Royal Marsden Hospital**

Fulham Road

Chelsea

London

England

SW3 6JJ

**Study participating centre**

**The Royal Marsden Hospital**

Downs Road

Sutton

England

SM2 5PT

**Study participating centre**

**Western General Hospital**

Crewe Road South

Edinburgh  
Scotland  
EH4 2XU

**Study participating centre**  
**Addenbrooke's Hospital**  
Hills Road  
Cambridge  
England  
CB2 0QQ

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

**Study participating centre**  
**Bristol Haematology and Oncology Centre**  
Horfield Road  
Avon  
Bristol  
England  
BS2 8ED

**Study participating centre**  
**The Christie**  
550 Wilmslow Road  
Withington  
Manchester  
England  
M20 4BX

**Study participating centre**  
**Clatterbridge Cancer Centre**  
Clatterbridge Health Park  
Clatterbridge Road  
Birkenhead



Wirral  
England  
CH63 4JY

**Study participating centre**  
**Derriford Hospital**  
Derriford Road  
Plymouth  
England  
PL6 8DH

**Study participating centre**  
**Kent Oncology Centre**  
Maidstone Hospital  
Hermitage Lane  
Maidstone  
England  
ME16 9QQ

**Study participating centre**  
**Royal Bournemouth Hospital**  
Castle Lane East  
Bournemouth  
England  
BH7 7DW

**Study participating centre**  
**Royal Cornwall Hospital**  
2 Penventinnie Lane  
Treliske  
Truro  
England  
TR1 3LQ

**Study participating centre**  
**Southampton General Hospital**  
Tremona Road  
Southampton  
England  
SO16 6YD

**Study participating centre**  
**St Barts Hospital**  
W Smithfield  
London  
England  
EC1A 7BE

**Study participating centre**  
**University College Hospital**  
250 Euston Road  
London  
England  
NW1 2PG

**Study participating centre**  
**Velindre Hospital**  
Velindre Road  
Whitchurch  
Cardiff  
Wales  
CF14 2TL

**Study participating centre**  
**Weston Park Hospital**  
Whitham Road  
Sheffield  
England  
S10 2SJ

**Study participating centre**  
**Churchill Hospital**  
Old Road  
Oxford  
England  
OX3 7LE

**Study participating centre**  
**Royal Devon and Exeter Hospital**  
Barrack Road

Exeter  
England  
EX2 5DW

## Sponsor information

### Organisation

Institute of Cancer Research

### ROR

<https://ror.org/043jzw605>

### Organisation

Royal Marsden NHS Foundation Trust

### ROR

<https://ror.org/0008wzh48>

## Funder(s)

### Funder type

Charity

### Funder Name

Cancer Research UK

### 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

## Results and Publications

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?
<a href="#">Results article</a>	results	01/10/2020	15/09/2020	Yes	No
<a href="#">Results article</a>		23/04/2021	27/04/2021	Yes	No
<a href="#">Results article</a>	Olaparib and Ceralasertib (AZD6738) in Patients with Triple-Negative Advanced Breast Cancer: Results from Cohort E of the plasmaMATCH Trial (CRUK/15/010)	01/12/2023	04/02/2026	Yes	No
<a href="#">Results article</a>	The Prognostic and Predictive Impact of ctDNA Levels in Patients with Advanced Breast Cancer Enrolled on the plasmaMATCH Trial	06/01/2026	04/02/2026	Yes	No
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Other publications</a>	Commentary	07/05/2022	20/01/2023	Yes	No
<a href="#">Plain English results</a>			09/02/2024	No	Yes