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PRIMROSE CSF - Cerebrospinal Fluid Collection in Breast Cancer

Submission date	Recruitment status	[X] Prospectively registered
19/02/2021	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
30/03/2021	Completed	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
06/03/2024	Cancer	[_] Record updated in last year

Plain English summary of protocol

Background and study aims
The PRIMROSE CSF Study aims to study cerebrospinal fluid (CSF) in patients with breast cancer that has spread to the brain (brain metastasis) or the lining surrounding the brain (leptomeningeal disease).
What is CerebroSpinal Fluid (CSF)?
This is the liquid that surrounds and protects the brain and spinal cord. CSF is constantly produced by our body and small amounts removed during extraction procedures are rapidly replaced.
What is a metastasis?
This is when cancer cells break off from the main tumour (in this case – in the breast), enters the blood stream and spreads to another part of the body such as the brain (so called brain metastasis or the thin lining over the brain (so called leptomeningeal disease).
The PRIMROSE CSF Study aims to improve our understanding of breast cancers that spread to the brain/brain lining by collecting and studying the fluid that circulates around the brain and comparing the sample to other cancer samples and blood samples.

Who can participate?
Patients aged 16 years or older, recently diagnosed with breast cancer.

What does the study involve?
After we check there is no reason why participants cannot have a sample taken, we will ask for consent to the following:
Collection of CSF sample: This will occur via one of two procedures - lumbar puncture or aspiration from Ommaya Reservoir (device inserted in the head).
Collection of Blood sample: This will occur immediately before the CSF extraction procedure. A 20ml blood sample will be collected immediately before lumbar puncture or Ommaya Reservoir.
Collection of Tissue: This will occur almost immediately after participants consent to the CSF Study. We will organise for the collection of breast cancer material which has been collected and stored or which will be collected, as part of routine clinical care.
Optional CSF sample: Roughly three months after the initial collection of CSF sample, participants may be asked to undergo a further CSF extraction as part of routine care. We would also like to obtain a blood sample for the study, should this happen.

What are the possible benefits and risks of participating?
Research in brain metastases in breast cancer is rare and limited. If we are able to collect enough samples, we will be able to increase the resources for research. Potential risks and side effects of the procedures include infection (rare), nerve root irritation (rare), backpain(rare) and headache (possibly begins immediately or a few days after procedure and usually lasts less than 1 week). To minimise risk: - lumbar punctures will be performed using appropriate local anaesthesia by clinicians experienced in the procedure. - Where patients are undergoing a neurosurgical procedure, the lumbar puncture will be carried out once patient has been anaesthetised so reducing any side effects. - Patients will be followed up roughly a month post-procedure to understand the side effects if any that occur post procedure.

Where is the study run from?
University of Liverpool (UK)

When is the study starting and how long is it expected to run for?
May 2020 to June 2025

Who is funding the study?
North West Cancer Research Fund incorporating Clatterbridge Cancer Research (UK)

Who is the main contact?
Professor Carlo Palmieri, c.palmieri@liv.ac.uk

https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-study-to-learn-more-about-breast-cancer-that-has-spread-to-the-brain-primrose-study

Study website
https://www.lctc.org.uk

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
286155

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 47541, IRAS 286155

Study information

Scientific Title
PRIMROSE CSF Study: A prospective study of the genomic landscape of central nervous system disease secondary to breast cancer utilising cell-free DNA derived from cerebrospinal fluid (CSF).

Acronym
PRIMROSE CSF

Study objectives
PRIMROSE Cerebrospinal Fluid (CSF) Study aims to collect and investigate CSF samples and related data from patients with central nervous system disease secondary to breast cancer.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 11/01/2021, West Midlands – South Birmingham REC (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, UK; +44 (0)207 104 8388; southbirmingham.rec@hra.nhs.uk), ref: 20/WM/0296

Study design
Interventional non-randomized

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Screening

Participant information sheet
See additional files

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

Interventions
Data Collection: Most of the data should be collected retrospectively sourced from medical records and patient medical notes (Data will be collected on Demographic Information, Clinico-pathological information and Prior Cancer Therapy).

Tissue Collection: Clinical staff will be responsible for tissue collection (i.e. primary breast, cranial metastasis or noncranial metastasis) using sample kits provided and shipment to GCP Laboratories.

First Lumbar Puncture / Ommaya Reservoir Aspiration Visit: Where a patient will be undergoing lumbar puncture or aspiration of an Ommaya Reservoir, they will be appropriately informed of the date and time of the procedure. Immediately before the procedure the delegated clinical staff conducting the procedure should extract 20ml blood sample (10ml EDTA and 10ml Serum). During the procedure Lumbar Puncture or Ommaya Reservoir aspiration should occur using standard procedure (please use atraumatic needles unless discussed with PI and CI) where between 10ml and 15ml CSF sample is required.

The patient will be re-informed following the collection of CSF that the post- procedure questionnaire may take place over the phone or at a routine clinical visit (whichever is earlier or preferred) after around a month.

Post-procedure questionnaire after CSF collection: If there is a routine visit scheduled after the CSF collection, patients will be asked to fill in questionnaire at this visit. If no routine visits are scheduled, the interview will be done over the phone after a month. If over the phone, clinical staff will schedule a time to ring the patient 28 days ± 7 days postprocedure to administer questionnaire.

The questionnaire has been validated by a wider network of researchers, clinicians and lay individuals to make it easy to understand while capturing required data on experiences.

Data collection at Disease Progression/Event driven Follow-up:
If patient comes in for routine visit and there are no changes in disease or treatment, then there is no requirement to update eCRF.
In the event of patient disease progression, treatment changes or in the event of death, the following data will be collected onto eCRF (Disease progression, Treatment changes, Death data (cause and date)).

Second Lumbar Puncture / Ommaya Reservoir Aspiration Visit:
Where there is disease progression or if the patient remains well – after 3 months of the first CSF extraction the patients will be asked to undergo a second lumbar puncture or aspiration of an Ommaya Reservoir (this will be mentioned on the patient information sheet).

The process described in "First Lumbar Puncture / Ommaya Reservoir Aspiration Visit" will be followed.

As described in "Post- procedure questionnaire after CSF collection", a date and time will be organised 28 days ± 7 days post-procedure to administer questionnaire.

The end of the study is defined to be the date on which data for all participants has been analysed.

Intervention Type
Procedure/Surgery

Primary outcome measure
Feasibility outcomes:
1. RECRUITMENT
1.1. Recruitment rate: defined as the total number of patients randomised per month measured using populated REDCAP eCRFs
1.2. Site opening: defined as the time take to open the target number of sites measured using LCTC Portal
2. STUDY PROTOCOL
2.1. Patient adherence to protocol: to determine whether the patient and/or caregivers adhere to the conditions of the protocol, measured via the number of minor or major protocol deviations measured using ...
2.2. Review of the practicality of delivering interventions measured using Monitoring Reports and discussions held at TMG
3. SAMPLE SIZE INFORMATION
3.1. The estimation of quantities required for an accurate sample size calculation, such as the standard deviation of the outcome measure
4. DATA COLLECTION
4.1. The proportion of expected CRFs returned and the rate of missing key data items
5. PATIENT ACCEPTABILITY
5.1. Estimate drop-out rates: We are not anticipating any patient drop-outs
5.2. Participation rates measured as a proportion of those patients recruited

Secondary outcome measures
1. Actionable mutations found in CSF cfDNA that match a specific gene database, namely TARGET (Tumour Alterations Relevant to Genomics Driven Therapy) gene database measured using genome analysis after all samples have been collected
2. Complications post lumbar puncture or aspiration of CSF from an Ommaya reservoir measured using a patient questionnaire and a clinician questionnaire post-procedure (eCRF will be used to record the date, the ease of the procedure complications and the need for intravenous fluid and /or analgesia)

Overall study start date
01/05/2020

Completion date
01/06/2025

Eligibility

Key inclusion criteria
1. Male or female
2. >=16 years of age

3. Any ER, PgR or HER2 status
4. Newly diagnosed with BCBM OR Progressive BCBM following either local or systemic treatment OR Leptomeningeal disease
5. Informed Consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
16 Years

Sex
Both

Target number of participants
Planned Sample Size: 67; UK Sample Size: 67

Key exclusion criteria
1. Unable to comply with study procedures or give informed consent
2. Where the investigator considers it unsafe to undertake a lumbar puncture or perform an aspiration from the Ommaya reservoir
3. Where the investigator considers it not in the best interest of the patient to participate

Date of first enrolment
01/06/2021

Date of final enrolment
01/06/2024

Locations

Countries of recruitment
England

Scotland

United Kingdom

Study participating centre
Addenbrooke's Hospital
Cambridge University Hospitals NHS Foundation Trust
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
Guy's Hospital
Guy's & St Thomas' NHS Foundation Trust
Great Maze Pond
London
United Kingdom
SE1 9RT

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

Study participating centre
Queen Elizabeth Hospital
University Hospitals Birmingham NHS Foundation Trust
Mindelsohn Way
Birmingham
United Kingdom
B15 2TH

Study participating centre
John Radcliffe Hopsital
Oxford University Hospitals NHS Foundation Trust
Headley Way
Oxford
United Kingdom
OX3 9DU

Study participating centre
The Walton Centre NHS Foundation Trust
Lower Lane
Liverpool
United Kingdom
L9 7LJ

Study participating centre
Wolfson Wohl Cancer Research Centre
Garscube Estate
Switchbank Road
Bearsden
United Kingdom
G61 1QH

Study participating centre
St James University Hospital
Leeds Teaching Hospitals NHS Trust
Beckett Street
Leeds
United Kingdom
LS9 7TF

Study participating centre
Northern General Hospital
Sheffield Teaching Hospitals NHS Foundation Trust
Herries Road
Sheffield
United Kingdom
S5 7AU

Study participating centre
Southampton General Hospital
University of Southampton and University Hospital Southampton NHS Foundation Trust
Tremona Road
Southampton
United Kingdom
SO16 6YD

Study participating centre
Royal Liverpool University Hospital
Royal Liverpool University Hospitals NHS Trust
Prescot Street
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L7 8XP

Sponsor information

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Sponsor type
University/education

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

ROR
https://ror.org/04xs57h96

Funder(s)

Funder type
Charity

Funder Name
North West Cancer Research Fund incorporating Clatterbridge Cancer Research; Grant Codes: AR2019.09

Alternative Name(s)
North West Cancer Research Fund, NWCR

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal.

Intention to publish date
01/06/2026

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be 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?
Participant information sheet	version v3.0	02/02/2021	30/03/2021	No	Yes
Participant information sheet	version v2.0	04/01/2021	30/03/2021	No	Yes
Protocol file	version v2	20/10/2020	30/03/2021	No	No
HRA research summary			28/06/2023	No	No