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Diet-driven gut microbiome and outcome in patients with early-stage triple-negative breast cancer undergoing neoadjuvant chemotherapy and immunotherapy

Submission date
23/10/2025

Recruitment status
Recruiting

Registration date
04/11/2025

Overall study status
Ongoing

Last Edited
04/11/2025

Condition category
Cancer

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Triple-negative breast cancer (TNBC) accounts for approximately 20% of all breast cancers. TNBC is associated with shorter overall survival than other breast cancer subtypes, despite the use of curative-intent anthracycline- and taxane–based systemic chemotherapy. Neoadjuvant chemotherapy (NACT) is the current standard of care for patients with early disease. The addition of the immune checkpoint inhibitor (ICI) pembrolizumab to NACT regimens has recently been shown to substantially improve the outcome of patients with stage II or III TNBC. The gut microbiome (GM) refers to the genetic makeup of all microbes that exist within the human gastrointestinal tract. Constituents of the GM have been shown to interact with one another and the host immune system in ways that influence physiological homeostasis and the development of diseases. Multiple translational studies suggest the potential influence of the GM in modulating the efficacy of ICI-based therapies. The role of the GM appears far more complex than previously thought, extending beyond specific species and functions present in responders and non-responders, and suggests the existence of a unique, multi-mechanistic interplay of biological factors, which may be reflected in the faecal microbiome signatures, offering the potential for therapeutic and diagnostic exploitation. An exciting prospect of researching the role of the GM is the therapeutic potential to improve patient outcomes by manipulating the GM. It is well recognised that a change in diet can alter the composition of the GM, with evidence showing significant microbial shifts as early as 5 days of commencing dietary interventions. Dietary interventions, therefore, have the potential to affect outcomes of patients undergoing ICI therapy and might be utilised as a safe, cost-efficient, and readily accessible therapeutic intervention. It remains to be shown whether the association between specific microbiota and improved outcomes with ICI therapies is merely a reflection of a pre-existing immune response that is amplified by ICI or could instead be the result of a more complex and dynamic interaction between different systems. This prospective longitudinal study aims to investigate the complex interactions between the GM, the tumour biology of early-stage TNBCs, the efficacy and tolerability of NACT/ICI therapy (including the possible impact on cognitive function), and the long-term outcome. A specific focus will be to study the association of the GM and the risk of

breast cancer recurrence in the high-risk group of patients with residual disease after NACT. The study will furthermore assess dynamic changes in both the GM and the tumour biology, and their association with long-term outcome. Furthermore, the association of nutritional input and the GM will be studied. Results of this trial might be the basis for future interventional studies that might stratify treatment modalities based on the GM or attempt to modulate treatment outcomes through targeting the GM.

Who can participate?
Female Patients ≥ 18 years of age undergoing either neoadjuvant chemotherapy plus immunotherapy or neoadjuvant chemotherapy alone will be recruited from within the NHS setting.

What does the study involve?
As part of the trial, stool samples for the analysis of the GM will be collected before the start of neoadjuvant treatment and at the end of the neoadjuvant treatment. Formalin-fixed paraffin-embedded (FFPE) core tumour biopsies will be collected at baseline. In patients with residual invasive cancer, a FFPE sample of the residual tumour will also be collected. In a subset of patients (optional), additional snap-frozen tumour samples may be collected at baseline and at the time of surgery. Nutritional input and cognitive function will be assessed at baseline, end of chemotherapy and during follow-up, using validated questionnaires. All data will be correlated with clinical outcome data.

What are the possible benefits and risks of participating?
The tests performed on patient samples are not established medical tests, and results will not be used to direct their medical care. The analysis performed in this study is for research purposes only, and as such, it is unlikely that patients will directly benefit from taking part in the study. However, we hope that the information we gain in the study will benefit individuals who may develop cancer in the future.

The study poses very little risk for research participants; blood samples and faecal samples are routinely performed in hospitals.
Blood sampling: Risk associated with drawing blood from the participants, including mild discomfort, bruising, light-headedness and on rare occasions infection. When participants are approached regarding the study, especially during a visit to an outpatient clinic, they may feel obliged to take part in the study. To address this issue, we emphasise that participation is voluntary. Participants are provided with ample time to consider participation and provide informed consent. It is also emphasised that declining to take part in the study will have no impact on their future care.

Where is the study run from?
Sampling, treatment and follow-up visits will all be conducted at selected NHS Hospital sites. The study will be coordinated at the Coordinating Centre, Centre for Experimental Cancer Medicine, Barts Cancer Institute, Queen Mary University of London, UK.

When is the study starting and how long is it expected to run for?
October 2025 to November 2032

Who is the Funder?
Barts Charity, UK

Who is the main contact?
Coordinating Team and study PI: Dr Melissa Phillips, bci-captivate@qmul.ac.uk

Contact information

Type(s)
Public, Scientific, Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
342769

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 64916

Study information

Scientific Title
Diet-driven gut microbiome and outcome in patients with early-stage triple-negative breast cancer undergoing neoadjuvant chemotherapy and immunotherapy (CAPTIVATE)

Acronym
CAPTIVATE

Study objectives
Primary Objectives: To investigate the association of the gut microbiome and investigator-assessed pathologic complete response (pCR) following neoadjuvant chemotherapy +/- immunotherapy. To evaluate the association of the pre- and end-of-treatment gut microbiome and event-free survival.

Secondary Objectives: To investigate the association of the gut microbiome and the occurrence and severity of immune-related adverse events (irAEs). To investigate the association of the gut

microbiome, the tumour mutational burden and the pre- and post-treatment immune-phenotype of the tumour. To investigate the association of nutritional input and the gut microbiome. To investigate the association of the gut microbiome and cognitive function.

Ethics approval required
Ethics approval required

Ethics approval(s)
notYetSubmitted 01/11/2025, Ethics committee name not provided (Address not provided, City not provided, Zip/postal code not provided; Telephone number not provided; not@available.com), ref: Reference number not provided

Study design
This multi-centre, translational phase II trial aims to investigate the impact of the GM on treatment outcomes in women with untreated, stage I-III TNBC undergoing neoadjuvant treatment with and without ICI.

Primary study design
Observational

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Stage I-III Triple Negative Breast Cancer

Interventions
This multi-centre, translational phase II trial aims to investigate the impact of the gut microbiome (GM) on treatment outcomes in women with untreated, stage I-III TNBC undergoing neoadjuvant treatment with and without ICI.

This study investigates the complex interactions between the GM, the tumour biology of early-stage TNBCs, and the efficacy and tolerability of chemotherapy/chemoimmunotherapy. A specific focus will be to study the association of the GM and the risk of breast cancer recurrence in the high-risk group of patients with residual disease after NACT. The study will furthermore assess dynamic changes in both the GM and the tumour biology, and their association with long-term outcome.

As part of the trial, stool samples for the analysis of the GM will be collected before the start of neoadjuvant treatment and at the end of the neoadjuvant treatment. Formalin-fixed paraffin-embedded (FFPE) core tumour biopsies will be collected at baseline. In patients with residual invasive cancer, a FFPE sample of the residual tumour will also be collected. In a subset of patients (optional), additional snap-frozen tumour samples may be collected at baseline and at the time of surgery. Nutritional input and cognitive function will be assessed at baseline, end of chemotherapy and during follow-up, using validated questionnaires. All data will be correlated with clinical outcome data (pathologic complete response (pCR), event-free survival (EFS) and immune-related adverse events (irAEs)).

Intervention Type
Other

Primary outcome(s)
1. Association between gut microbiome composition and investigator-assessed pathologic complete response following neoadjuvant chemotherapy ± immunotherapy, measured using microbiome analysis and clinical assessment post-treatment
2. Association between pre- and end-of-treatment gut microbiome composition and event-free survival, measured using microbiome analysis and clinical follow-up at pre-treatment, end-of-treatment, and post-treatment timepoints.

Key secondary outcome(s))
1. Association between gut microbiome composition and occurrence and severity of immune-related adverse events, measured using microbiome analysis and clinical assessment during treatment
2. Association between gut microbiome composition, tumour mutational burden, and pre- and post-treatment immune-phenotype of the tumour, measured using microbiome analysis and tumour profiling at pre- and post-treatment timepoints
3. Association between nutritional input and gut microbiome composition, measured via dietary assessment using the Cancer Council Victoria Dietary Questionnaire for Epidemiological Studies (DQES v3.2) and microbiome analysis during treatment
4. Association between gut microbiome composition and cognitive function, measured using microbiome analysis and cognitive assessment using the PROMIS Perceived Cognitive Function Concerns (PCF) short form questionnaire during treatment

Completion date
01/11/2032

Eligibility

Key inclusion criteria
1. Willing and able to provide written informed consent before study entry
2. Female > 18 years of age
3. Histologically confirmed operable primary breast cancer with a tumour size of >1 cm
4. Triple-Negative disease
4.1. Defined as tumours with <10% of tumour cells positive for ER and PR1 on IHC staining or an IHC score (Allred) of £3
4.2. HER2-negative tumours, defined as 0, 1+ or 2+ intensity on IHC and no evidence of amplification of the HER2 gene on ISH.
5. Patient planned to undergo neoadjuvant chemotherapy (as per institutional standard) with /without immunotherapy
6. Representative FFPE breast tumour samples with an associated pathology report that are determined to be available and sufficient for central testing OR tumour accessible for biopsy.
7. Ability to comply with the protocol, including but not limited to completion of the patient-reported outcome questionnaires.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group

Adult

Lower age limit
18 years

Sex
Female

Key exclusion criteria
1. Previous systemic or local treatment for the new primary breast cancer currently under investigation (including surgery, radiotherapy, cytotoxic and endocrine treatments) over the last five years.
2. Received therapeutic oral or intravenous antibiotics within 14 days prior to randomisation.
3. Known distant metastases

Date of first enrolment
01/11/2025

Date of final enrolment
01/11/2032

Locations

Countries of recruitment
United Kingdom

England

Northern Ireland

Scotland

Study participating centre
St Bartholomew's Hospital
W Smithfield
Barts Health NHS Trust
London
United Kingdom
EC1A 7BE

Study participating centre
Belfast City Hospital
51 Lisburn Rd
Belfast
United Kingdom
BT9 7AB

Study participating centre
Greater Glasgow and Clyde
Gartnavel Royal Hospital
1055 Great Western Road
Glasgow
United Kingdom
G12 0XH

Study participating centre
NHS Lothian
Waverley Gate
2-4 Waterloo Place
Edinburgh
United Kingdom
EH1 3EG

Study participating centre
Oxford University Hospitals
John Radcliffe Hospital
Headley Way
Headington
Oxford
United Kingdom
OX3 9DU

Study participating centre
Imperial College Healthcare NHS Trust
The Bays
St Marys Hospital
South Wharf Road
London
United Kingdom
W2 1BL

Sponsor information

Organisation
Barts Health NHS Trust

ROR

https://ror.org/00b31g692

Funder(s)

Funder type
Charity

Funder Name
Barts Charity

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
All study data shall be the property of Barts Health NHS Trust. CAPTIVATE Protocol v1.0 05Oct2025 Page 41 of 46. If research misconduct or data integrity concerns have been raised, the sponsor, with senior management of the affected organisation in discussion with the CI, reserves the right to review, request a hold on publication submission, or refuse permission to publish. Responsibility for ensuring the accuracy of any publication from this study is delegated to the CI. All results will be available on the research summary section of the HRA website, as well as clinicaltrials.gov.

• The name and email address of the investigator/body who should be contacted for access to the datasets: Dr Mays Jawad, Governance Operations Manager, Joint Research Management Office, Research Services, Dept. W, 69-89 Mile End Road. London E1 4UJ
• The type of data that will be shared: Not avainable
• Timing for availability: The full study report will be accessible via the HRA website or other suitable public website within one year of the End of the Trial Notification.
• Whether consent from participants was required and obtained: Yes, this will be the case
• Comments on data anonymization: Not available
• Any ethical or legal restrictions: Not available
• Any additional comments: Data sharing statement to be made available at a later date

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes