ISRCTN17334319 https://doi.org/10.1186/ISRCTN17334319

The ROSETA Optimisation Trial – Investigating strategies to improve medication adherence in women with early-stage breast cancer

Submission date 29/01/2024	**Recruitment status** Recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 02/02/2024	**Overall study status** Ongoing	
Last Edited 21/10/2025	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims
The ROSETA Optimisation trial is testing how well four ways (called interventions) support women with breast cancer in taking hormone therapy (e.g., Tamoxifen, Raloxifene, Anastrozole, Letrozole, Exemestane). The study will test what, if any, is the best combination of the interventions. The interventions being tested comprise SMS text reminders to support taking medication, a leaflet providing information about the medication, a website to provide useful resources for managing the side effects of the medication, and a skills programme known as Acceptance and Commitment Therapy (ACT) which encourages approaching experiences with openness and awareness, and supports you to engage with your values. This is led by a therapist and involves learning and practising skills at home.

Who can participate?
Women aged 18 years old and over who have been diagnosed with breast cancer and prescribed medication to reduce the risk of the cancer returning

What does the study involve?
The study team will:
• Confirm participants' eligibility and ask if they consent to take part.
• Ask them to complete a total of 4 questionnaires over 12 months.
• Ask them if they are willing to be interviewed after around 6 and 12 months, to discuss their experiences of taking part. The interviews are optional, so they can take part in ROSETA without being interviewed.

Participants will be randomly allocated either to one or more of the interventions in addition to your usual care, or to your usual care alone. If they are randomly allocated to the ACT sessions, you will attend a total of 5 remote sessions and will be asked to complete home practice tasks.

What are the possible benefits and risks of participating?
BENEFITS: Although it is not known which intervention, if any, helps women with breast cancer, participants might personally find them useful. They will also be contributing to important

research that may benefit women with breast cancer in the future. They may also enjoy learning more about health research.

RISKS: No risks in taking part are expected. Agreeing to take part in this study will mean giving up some time to complete questionnaires. Some questionnaires ask about how they are feeling, and this may upset some people. Your researcher will provide details of organisations that can be contacted if the research is upsetting in any way.

Where is the study run from?
The trial is centrally coordinated by the Leeds Clinical Trials Research Unit (CTRU) based at the University of Leeds

When is the study starting and how long is it expected to run for?
January 2023 to November 2026

Who is funding the study?
The study is funded by the National Institute of Health Research (NIHR) (https://fundingawards.nihr.ac.uk/award/NIHR300588)

Who is the main contact?
ROSETA@leeds.ac.uk

https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-study-looking-at-supporting-people-with-their-hormone-therapy-for-breast-cancer-roseta

Contact information

Type(s)
Scientific

Contact name
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Type(s)
Public

Contact name
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Contact details

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United Kingdom
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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
328413

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 58021, IRAS 328413

Study information

Scientific Title
Refining and Optimising a behavioural intervention to Support Endocrine Therapy Adherence: The ROSETA Optimisation Trial

Acronym
The ROSETA Optimisation Trial

Study objectives
To determine the most effective intervention package for supporting adjuvant endocrine therapy (AET) adherence at 12 months post-randomisation. This trial will also have an embedded Study Within a Trial (SWAT), a self-contained research study that has been embedded within the host trial to evaluate ways of delivering follow-up trial processes. The overall aim of the SWAT is to understand the impact of SMS pre-notification and reminder messages in the context of clinical trials using online data capture for patient-reported questionnaires.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 25/01/2024, Yorkshire & The Humber - South Yorkshire Research Ethics Committee (NHSBT Newcastle Blood Donor Centre, Holland Drive, Newcastle upon Tyne, NE2 4NQ, United Kingdom; +44 (0)207 104 8021; southyorks.rec@hra.nhs.uk), ref: 23/YH/0250

Study design
Randomized controlled 2^4 factorial optimisation trial with an embedded Study Within a Trial

Primary study design

Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Supporting adjuvant endocrine therapy (AET) adherence in breast cancer

Interventions
This study aims to recruit a total of 512 women with breast cancer from around 25 NHS sites in the UK. Potential participants will be screened according to pre-defined criteria and approached during end of treatment summary meetings, appointments to discuss side effects and/or problems with medication taking, or by post/email.

Potential participants will also be alerted to the trial via the Be Part of Research Volunteer Service (a register open to members of the public interested in research), cancer support groups, social media and charities. Interested patients will be encouraged to access the ROSETA website to read further information about the trial and complete a screening questionnaire. The CTRU will contact patients who self-refer through the website to inform them whether or not they may be suitable to take part, and securely pass on the details of those suitable to the research team at their local NHS site.

The local research team will confirm suitability to take part, take informed consent and collect data from the participant's medical records. The participant will complete the baseline questionnaire.

Following consent and baseline data collection, an automated system will be used to randomly allocate participants to one of 16 groups. A group can be a combination of interventions, one intervention or no interventions. All groups will receive the usual care provided by their hospital. Details of what women will receive when allocated to a group are as follows:
Group 1: usual care, text reminders, information leaflet, ACT, website
Group 2: usual care, text reminders, information leaflet, ACT
Group 3: usual care, text reminders, information leaflet, website
Group 4: usual care, text reminders, information leaflet
Group 5: usual care, text reminders, ACT, website
Group 6: usual care, text reminders, ACT
Group 7: usual care, text reminders, website
Group 8: usual care, text reminders
Group 9: usual care, information leaflet, ACT, website
Group 10: usual care, information leaflet, ACT
Group 11: usual care, information leaflet, website
Group 12: usual care, information leaflet
Group 13: usual care, ACT, website
Group 14: usual care, ACT
Group 15: usual care, website
Group 16: usual care
The four intervention components are:

SMS text reminders:
The content of the SMS reminders has been co-developed with experts in behaviour change and /or medication adherence, and women who have experienced breast cancer. Over 4 months

participants randomised to a group containing this intervention will receive 43 SMS messages. These include 3 opening messages, 36 messages aiming to make medication taking more habitual, a closing message, and 3 messages informing participants they can stop the SMS messages by emailing the trial email address at any time (one per month). The SMS messages are sent by the CTRU and information about the delivery of the SMS messages will be routinely collected.

Information leaflet:
Participants randomised to a group containing this intervention will receive a 6-page patient information leaflet at 1 week post-randomisation. This will be sent to the participant by the local research team. The leaflet aims to target specific adjuvant hormone therapy medication beliefs. The content of this leaflet will include explanations of how adjuvant endocrine therapy (AET) works, supplemented by diagrams, information about the benefits and side effects of AET and answers to common concerns. The leaflet will also indicate that it has been codesigned by researchers and breast cancer survivors, and will include quotes from breast cancer survivors. They can then read this information leaflet as they wish. Participants will self-report whether or not they have received and read the information leaflet in the follow-up questionnaires.

A website:
The website will contain sections on managing side effects, patient stories (including videos) and signposting for further information/places of support. Participants randomised to a group containing this intervention will receive the website address and their unique login details at 1 week post-randomisation. The details will be sent to the participant by the local research team. Data will be collected about each participant's receipt of website details and their website use, including pages visited, whether videos were watched and the percentage of the video viewed on a per participant level. The data collected on a participant’s website registration and usage is collected by google analytics and will be obtained and summarised by the trial team at the CTRU. Only the University of Leeds will have access to the tracking data.

Acceptance and Commitment Therapy (ACT):
The ACT component is a guided self-help program consisting of four modules with home practice tasks. Participants randomised to a group containing this intervention will take part in five remote sessions with a therapist – one introductory session plus four modules, each corresponding to a different ACT-based skill: Mindfulness and unhooking; Following your values; Taking an observer perspective; Recap, reflection, and staying committed. Each module consists of a participant manual containing information about the relevant ACT skill, alongside home practice exercises to complete. All sessions will take place via videoconferencing or telephone, and each session will last 25 minutes. The first session will take place within 6 weeks of randomisation, and the remaining four sessions will occur approximately every two weeks thereafter. It is recommended that all five ACT sessions are delivered within 3 months of the first session. Within these support sessions, the therapist and the patient will discuss the module completed over the past week, their experiences of the home practice exercises, and can discuss and problem solve any difficulties that arose. Session attendance and engagement with home practice tasks will be monitored.

The ACT sessions will be audio-recorded, if the participant gives consent, for the purpose of monitoring the therapist's delivery of ACT and to ensure the trial is being conducted properly. Recordings will be securely stored at the site and at the University of Leeds with access restricted to the trial team and those involved in monitoring therapist delivery of ACT.

Suitably qualified therapists will be identified and will undergo a training programme in the ACT intervention prior to patient recruitment. This will be delivered by the central ACT intervention

lead or delegate, who has expertise in ACT applied to chronic disease. Training will take place over 2-3 half days and will be delivered remotely via videoconferencing. Training will include general teaching about ACT and practice of intervention-specific therapy methods. Therapists will be trained in groups where feasible. Therapists delivering the intervention will be offered fortnightly group supervision (60 minutes), for the duration of the intervention by phone or video call, with the central ACT intervention lead or delegate. The therapist can also access local clinical supervision if they wish, as part of their standard clinical practice.

To help further understand the interventions and how they worked in practice, researchers will interview a sample of participants and therapists, with their consent. This is called a process evaluation. The interviews will take place remotely via videoconferencing software or phone and will last no longer than 60 minutes. Interviews will be audio recorded. Participants will be invited to two interviews: one at 6-7 months post-randomisation and one at 12-13 months post-randomisation (updated 21/10/2025, previously: Participants will be invited to two interviews: one at 4-5 months post-randomisation and one at 12-13 months post-randomisation). Therapists will be invited to one interview 1 month before the end of the intervention delivery period.

Participants will complete further questionnaires at 4, 8, and 12-months after randomisation, and receive a maximum of 4 reminders to complete by text, email and/or phone. They will be completed online via REDCap, a secure web application created by Vanderbilt University, or over the phone with the local research team. The CTRU manage the follow-up questionnaire process and the REDCap database. The trial includes an embedded Study Within A Trial (SWAT) where the participant is randomised to receive a pre-notification (24 hours before questionnaire is sent) at 4- months post-randomisation. Participants will retain their allocation to SMS pre-notification or no pre-notification at 8 and 12-months. Participants who have not returned the questionnaire after 6 days will be randomised again to receive either standard SMS reminder or non-standard reminder.

The local research team will also collect additional data from the participant's medical records at the end of the trial. The CTRU will collect participant prescribing and/or dispensing data at 12-months post-randomisation via central sources of healthcare data such as NHS Digital (a standard NHS patient registry). The CTRU will also explore the possibility of using central sources of healthcare data such as NHS Digital to conduct longer-term follow-up (i.e. post 12-months randomisation) of those participants recruited early to the trial.

Intervention Type
Behavioural

Primary outcome(s)
To determine the most effective intervention package for supporting adjuvant endocrine therapy (AET) adherence by using the Domains of Subjective Extent of Nonadherence (DOSE-Nonadherence) measure – collected at 12 months post-randomisation

Key secondary outcome(s))
Secondary Outcomes (at 12 months post-randomisation):
1. Determine the most effective intervention package for:
1.1. Supporting AET adherence and persistence measured using NHS prescribing and/or dispensing data
1.2. Global quality of life (QoL) using EuroQol 5 Dimensions 5 Levels (EQ-5D-5L) and McGill Quality of Life-Revised (MQoL-R)
1.3. Self-efficacy using Self-Efficacy for Appropriate Medication Use Scale (SEAMS)

1.4. For supporting AET adherence, considering key restraints such as cost using DOSE-Nonadherence
2. Estimate the cost of developing and delivering each intervention component using NHS Reference Costs, Personal Social Services Research Unit (PSSRU) cost data and UK Cancer Costs questionnaire

Secondary Outcomes (at 4- and 8- months post-randomisation):
1. Estimate the main effects and interactions of the intervention components for:
1.1. Supporting AET adherence using DOSE-Nonadherence
1.2. Global quality of life using EuroQol 5 Dimensions 5 Levels (EQ-5D-5L) and McGill Quality of Life-Revised (MQoL-R)
1.3. Self-efficacy using Self-Efficacy for Appropriate Medication Use Scale (SEAMS)
2. Estimate the effect of the (at 4-, 8- and 12-months post randomisation):
2.1. SMS component on habit formation using Self-Report Behavioural Automaticity Index (SRBAI)
2.2. The information leaflet on beliefs about medication using Beliefs about Medicine Questionnaire-Adjuvant Endocrine Therapy (BMQ-AET)
2.3. ACT component on psychological flexibility and distress using Multidimensional Psychological Flexibility Inventory – Short version (MPFI) and Depression, Anxiety and Stress Scale-21 (DASS-21)
2.4. Website component on symptomatic quality of life using European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-C30 (EORTC QLQ-C30), European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-BR45 (EORTC QLQ-BR45) and European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-IL133 (EORTC QLQ-IL133)

SWAT
1. Questionnaire response rate at one month follow-up.
2. Proportion of participants in each SWAT group who submit the questionnaire within 6 days, 11 days of them being sent out.
3. Number of days between the questionnaire being sent to participants and it being submitted by participants.
4. Proportion of non-mandatory questionnaire items missing
5. Proportion of non-mandatory questionnaire measures with complete data
6. Cost of SWAT intervention per participant retained at one-month.

Completion date
30/11/2026

Eligibility

Key inclusion criteria
1. Capacity to provide informed consent
2. Women with early stage (1-3) breast cancer according to the Tumor, Node, Metastasis (TNM) /American Joint Committee on Cancer (AJCC) staging system
Note: Women being treated for a second primary breast cancer or a breast cancer local recurrence are eligible for the trial, providing at least one of the cancers is being treated with AET, and they meet all eligibility criteria. Women with bilateral breast cancer are permitted, providing at least one breast is affected by hormone receptor-positive disease
3. Aged >= 18 years old
4. Have sufficient proficiency in English to be able to adhere to all intervention components and

data collection required
5. Treated with curative intent
6. Completed their hospital-based treatment (e.g., surgery, radiotherapy and/or chemotherapy) for the current breast cancer within the last 24 months. Note: Women are still eligible for the trial if they are being treated with abemaciclib or monoclonal antibody-based therapy such as trastuzumab, kadcyla, pertuzumab, and phesgo; these medications do not have to be completed within the 24 months stipulated within this criterion.
(Updated 21/10/2025, previously: Completed their hospital-based treatment (e.g., surgery, radiotherapy and/or chemotherapy) for the current breast cancer within the last 12 months. Note: Women are still eligible for the trial if they are being treated with abemaciclib or monoclonal antibody-based therapy such as trastuzumab, kadcyla, pertuzumab, and phesgo; these medications do not have to be completed within the 12 months stipulated within this criterion).
7. Currently prescribed oral AET (tamoxifen, raloxifene, anastrozole, letrozole, exemestane)
8. Access to a mobile phone to receive SMS messages*
9. Access to a computer or smart device that can access the internet*

*Source data for these items will be either partially or completely patient self-report.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
Female

Key exclusion criteria
1. Stopped taking AET if it is clinically contraindicated according to clinical recommendation
2. Involved in a similar research trial where medication adherence is a primary outcome*,**
3. Currently attending psychotherapy/psycho-oncology/psychology/counselling services, for any clinical reason*
4. Need for treatment for a severe mental health disorder or crisis, which is likely to interfere with participation (e.g., active psychosis, bipolar disorder, significant issues with addiction or self-harm or expressing active suicidal ideation with active plans and intent*)
5. Auditory problems that would prevent the patient from participating in a telephone or video call, or hearing audio clips*
6. Taken part in the ROSETA Pilot trial.

*Source data for these items will be either partially or completely patient self-report.
**Consented to and the trial is still being delivered.

Participation in another trial will not necessarily exclude a patient from participation. CTRU should be notified of any potential conflicting trials to facilitate a review of the feasibility of co-

enrolment by the CI and Trial Management Group (TMG). The review will consider the methodological impact and participant burden.

Date of first enrolment
30/04/2024

Date of final enrolment
31/03/2026

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Leeds Teaching Hospitals NHS Trust - Lead centre
St. James's University Hospital
Beckett Street
Leeds
United Kingdom
LS9 7TF

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

Study participating centre
Manchester University NHS Foundation Trust
Cobbett House
Oxford Road
Manchester
United Kingdom
M13 9WL

Study participating centre
Northwick Park Hospital
Watford Road
Harrow

United Kingdom
HA1 3UJ

Study participating centre
Croydon University Hospital
London Road
Croydon
United Kingdom
CR7 7YE

Study participating centre
Chesterfield Royal Hospital NHS Foundation Trust
Chesterfield Road
Calow
Chesterfield
United Kingdom
S44 5BL

Study participating centre
Mid and South Essex NHS Foundation Trust
Prittlewell Chase
Westcliff-on-sea
United Kingdom
SS0 0RY

Study participating centre
Watford General Hospital
60 Vicarage Road
Watford
United Kingdom
WD18 0HB

Study participating centre
University Hospital Lewisham
Lewisham High Street
London
United Kingdom
SE13 6LH

Study participating centre
Whiston Hospital
Warrington Road
Prescot
United Kingdom
L35 5DR

Study participating centre
East Surrey Hospital
Canada Avenue
Redhill
United Kingdom
RH1 5RH

Study participating centre
Bradford Royal Infirmary
Duckworth Lane
Bradford
United Kingdom
BD9 6RJ

Study participating centre
Bolton Royal Hospital
Minerva Road
Farnworth
Bolton
United Kingdom
BL4 0JR

Study participating centre
Hull Royal Infirmary
Anlaby Road
Hull
United Kingdom
HU3 2JZ

Study participating centre
St Marys Hospital
Floyd Drive

Warrington
United Kingdom
WA2 8DB

Study participating centre
York Hospital
Wigginton Road
York
United Kingdom
YO31 8HE

Study participating centre
The Princess Alexandra Hospital NHS Trust
Hamstel Road
Harlow
United Kingdom
CM20 1QX

Study participating centre
Queen Elizabeth Hospital
Edgbaston
Birmingham
United Kingdom
B15 2TH

Study participating centre
Bolton Royal Hospital
Minerva Road
Farnworth
Bolton
United Kingdom
BL4 0JR

Study participating centre
St Helens Hospital
Marshalls Cross Road
St. Helens
United Kingdom
WA9 3DA

Study participating centre
Castle Hill Hospital
Entrance 3
Castle Road
Cottingham
United Kingdom
HU16 5JQ

Study participating centre
Ealing Hospital
Uxbridge Road
Southall
United Kingdom
UB1 3HW

Study participating centre
The James Cook University Hospital
Marton Road
Middlesbrough
United Kingdom
TS4 3BW

Study participating centre
Queen Elizabeth Hospital
Woolwich Stadium Road
Woolwich
London
United Kingdom
SE18 4QH

Study participating centre
Pontefract Hospital
Friarwood Lane
Southgate
Pontefract
United Kingdom
WF8 1PL

Study participating centre

Dewsbury & District Hospital
Halifax Road
Dewsbury
United Kingdom
WF13 4HS

Study participating centre
Milton Keynes University Hospital
Milton Keynes Hospital
Standing Way
Eaglestone
Milton Keynes
United Kingdom
MK6 5LD

Study participating centre
Tameside and Glossop Integrated Care NHS Foundation Trust
Tameside General Hospital
Fountain Street
Ashton-under-lyne
United Kingdom
OL6 9RW

Study participating centre
Surrey and Sussex Healthcare NHS Trust
Trust Headquarters
East Surrey Hospital
Canada Avenue
Redhill
United Kingdom
RH1 5RH

Study participating centre
Torbay Hospital
Newton Road
Torquay
United Kingdom
TQ2 7AA

Study participating centre

St Lukes Hospital
Little Horton Lane
Bradford
United Kingdom
BD5 0NA

Study participating centre
St. Bartholomews Hospital
West Smithfield
London
United Kingdom
EC1A 7BE

Study participating centre
Royal Liverpool University Hospital
Prescot Street
Liverpool
United Kingdom
L7 8YE

Study participating centre
Aintree University Hospital
Lower Lane
Liverpool
United Kingdom
L9 7AL

Study participating centre
Queen Elizabeth Hospital
Sheriff Hill
Gateshead
United Kingdom
NE9 6SX

Study participating centre
Homerton University Hospital
Homerton Row
London
United Kingdom
E9 6SR

Study participating centre
North Tyneside Hospital
Rake Lane
North Shields
United Kingdom
NE29 8NH

Study participating centre
Wansbeck Hospital
Woodhorn Lane
Ashington
United Kingdom
NE63 9JJ

Study participating centre
Hexham General Hospital
Corbridge Road
Hexham
United Kingdom
NE46 1QJ

Sponsor information

Organisation
University of Leeds

ROR
https://ror.org/024mrxd33

Funder(s)

Funder type
Government

Funder Name
National Institute for Health and Care Research

Alternative Name(s)

National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
De-identified individual participant data datasets generated and/or analysed during the current study will be available upon request from the Clinical Trials Research Unit, University of Leeds (contact CTRU-DataAccess@leeds.ac.uk in the first instance). Data will be made available at the end of the trial, i.e. usually when all primary and secondary endpoints have been met and all key analyses are complete. Data will remain available from then on for as long as CTRU retains the data.

CTRU makes data available by a 'controlled access' approach. Data will only be released for legitimate secondary research purposes, where the Chief Investigator, Sponsor and CTRU agree that the proposed use has scientific value and will be carried out to a high standard (in terms of scientific rigour and information governance and security) and that there are resources available to satisfy the request. Data will only be released in line with participants' consent, all applicable laws relating to data protection and confidentiality, and any contractual obligations to which the CTRU is subject. No individual participant data will be released before an appropriate agreement is in place setting out the conditions of release. The agreement will govern data retention, usually stipulating that data recipients must delete their copy of the released data at the end of the planned project.

The CTRU encourages a collaborative approach to data sharing and believes it is best practice for researchers who generated datasets to be involved in subsequent uses of those datasets. Recipients of trial data for secondary research will also receive data dictionaries, copies of key trial documents and any other information required to understand and reuse the released datasets.

The conditions of release for aggregate data may differ from those applying to individual participant data. Requests for aggregate data should also be sent to the above email address to discuss and agree on suitable requirements for release.

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

Study website	Study website	11/11/2025	11/11/2025	No	Yes