A trial of hormone therapy and abemaciclib for early breast cancer

Submission date	Recruitment status No longer recruiting	Prospectively registered		
31/01/2022		Protocol		
Registration date 28/03/2022	Overall study status Ongoing Condition category Cancer	Statistical analysis plan		
		Results		
Last Edited		Individual participant data		
21/10/2025		[X] Record updated in last year		

Plain English summary of protocol

https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-of-hormone-therapy-and-abemaciclib-for-early-breast-cancer-poetic-a

Contact information

Type(s)

Scientific

Contact name

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Additional identifiers

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Integrated Research Application System (IRAS)

271343

ClinicalTrials.gov (NCT)

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Protocol serial number

CRCTSU/2019/10068, IRAS 271343, CPMS 44805

Study information

Scientific Title

POETIC-A: Pre-Operative Endocrine Therapy for Individualised Care with Abemaciclib

Acronym

POETIC-A

Study objectives

To determine the benefit of adding abemaciclib to standard adjuvant endocrine therapy (ET) in a sub-population of ER+/HER2- breast cancer who exhibit early evidence suggestive of sub-optimal endocrine responsiveness and high risk of disease relapse.

Ethics approval required

Ethics approval required

Ethics approval(s)

approved 14/04/2020, London - Chelsea Research Ethics Committee (Skipton House, 80 London Road, London, SE1 6LH, United Kingdom; +44 (0)207 104 8029; chelsea.rec@hra.nhs.uk), ref: 20 /LO/0196

Study design

Phase III multi-centre randomized controlled trial

Primary study design

Interventional

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Operable invasive breast cancer which is ER positive and HER2 negative, with high (20%) 5-year risk of relapse with endocrine therapy (ET) alone in postmenopausal women

Interventions

Current interventions as of 12/01/2024:

The trial has two parts:

1. A registration part

In this part patients receive aromatase inhibitor treatment (either 2.5 mg letrozole daily or 1 mg anastrozole daily) for at least 10 days immediately prior to surgery if they fit the eligibility criteria of the trial.

2. A randomised intervention part:

In this part patients who are eligible by virtue of a centrally assessed high Ki67 at surgery (Ki67S)

will be asked to consent to the randomised part of the study where they will be allocated in a 1:1 ratio. Treatment allocation is by computer-generated random permuted blocks, stratified by age, use of chemotherapy, and time on pre-surgical AI.

They will be randomised to receive either:

- 1. Endocrine therapy alone for 5 years, or
- 2. Endocrine therapy for 5 years + abemaciclib for 2 years

In both groups, endocrine therapy will be prescribed as per standard of care for an expected duration of at least 5 years or until evidence of disease recurrence or other discontinuation criteria are met. The choice of endocrine therapy is as per clinician's decision and may include non-steroidal AI (letrozole or anastrozole), steroidal AI (exemestane) or tamoxifen.

Abemaciclib will be administered at a dose of 150 mg twice daily for 2 years and it is provided as 50 mg tablets. It should be taken with a glass of water, with at least 6 hours separating doses. All patients on both arms of the trial will be followed up to 5 years after Week 1 Day 1.

Previous interventions:

The trial has two parts:

1. A registration part

In this part patients receive aromatase inhibitor treatment (either 2.5 mg letrozole daily or 1 mg anastrozole daily) for at least 10 days immediately prior to surgery if they fit the eligibility criteria of the trial.

2. A randomised intervention part:

In this part patients who are eligible by virtue of a centrally assessed high Ki67 at surgery (Ki67S) will be asked to consent to the randomised part of the study where they will be allocated in a 1:1 ratio. Treatment allocation is by computer-generated random permuted blocks, stratified by age, use of chemotherapy, time on pre-surgical AI and the Aromatase Inhibitor Resistant-CDK4/6 Inhibitor Sensitive (AIR-CIS) signature.

They will be randomised to receive either:

- 1. Endocrine therapy alone for 5 years, or
- 2. Endocrine therapy for 5 years + abemaciclib for 2 years

In both groups, endocrine therapy will be prescribed as per standard of care for an expected duration of at least 5 years or until evidence of disease recurrence or other discontinuation criteria are met. The choice of endocrine therapy is as per clinician's decision and may include non-steroidal AI (letrozole or anastrozole), steroidal AI (exemestane) or tamoxifen.

Abemaciclib will be administered at a dose of 150 mg twice daily for 2 years and it is provided as 50 mg tablets. It should be taken with a glass of water, with at least 6 hours separating doses. All patients on both arms of the trial will be followed up to 5 years post-randomisation.

Intervention Type

Drug

Phase

Phase III

Drug/device/biological/vaccine name(s)

Abemaciclib

Primary outcome(s)

Time to tumour (local or distant disease) recurrence, defined as the time from randomisation to local, regional or distant tumour recurrence or death from breast cancer without prior notification of relapse. Second primary cancers and inter-current deaths will be treated as censoring events. Ongoing follow up through routine data sources via electronic data linkage (from the patients' national medical records) annually until the end of the study.

Key secondary outcome(s))

Current secondary outcome measures as of 12/01/2024:

- 1. Relapse-free survival, defined as the time from randomisation to local, regional or distant tumour recurrence or death from any cause
- 2. Time to distant recurrence, defined as the time from randomisation to distant tumour recurrence. Second primary cancers and inter-current deaths will be treated as censoring events
- 3. Breast cancer-specific survival, defined as time from randomisation to death from breast cancer (with or without prior notification of relapse). Inter-current deaths will be treated as censoring events
- 4. Overall survival, defined as the time from randomisation to death from any cause
- 5. Quality of life: patient-reported quality of life measured using validated questionnaires which will be defined before the commencement of the relevant sub-study
- 6. Grade 3/4 adverse events, serious adverse events (SAEs) and hospitalisations assessed by Common Terminology Criteria for Adverse Events, version 5 (CTCAE v5)
- 7. Treatment-related deaths, defined as death occurring at any time point after randomisation and assessed to be possibly, probably or definitely related to the intervention

Previous secondary outcome measures as of 19/12/2022 to 12/01/2024:

Ongoing follow-up through routine data sources via electronic data linkage (from the patients' national medical records) annually until the end of the study:

- 1. Relapse-free survival, defined as the time from randomisation to local, regional or distant tumour recurrence or death from any cause
- 2. Time to distant recurrence, defined as the time from randomisation to distant tumour recurrence. Second primary cancers and inter-current deaths will be treated as censoring events
- 3. Breast cancer-specific survival, defined as time from randomisation to death from breast cancer (with or without prior notification of relapse). Inter-current deaths will be treated as censoring events
- 4. Overall survival, defined as the time from randomisation to death from any cause
- 5. Quality of life: patient-reported quality of life measured using validated questionnaires which will be defined before the commencement of the relevant sub-study
- 6. Grade 3/4 adverse events, serious adverse events (SAEs) and hospitalisations assessed by Common Terminology Criteria for Adverse Events, version 5 (CTCAE v5)
- 7. Treatment-related deaths, defined as death occurring at any time point after randomisation and assessed to be possibly, probably or definitely related to the intervention

Previous secondary outcome measures:

Ongoing follow up through routine data sources via electronic data linkage (from the patients' national medical records) annually until the end of the study:

1. Relapse-free survival, defined as the time from randomisation to local, regional or distant tumour recurrence or death from any cause

- 2. Time to distant recurrence, defined as the time from randomisation to distant tumour recurrence. Second primary cancers and inter-current deaths will be treated as censoring events
- 3. Breast cancer-specific survival, defined as time from randomisation to death from breast cancer (with or without prior notification of relapse). Inter-current deaths will be treated as censoring events
- 4. Overall survival, defined as the time from randomisation to death from any cause
- 5. Quality of life: patient-reported quality of life measured using validated questionnaires which will be defined before the commencement of the relevant sub-study
- 6. Grade 3/4 adverse events, serious adverse events (SAEs) and hospitalisations assessed by Common Terminology Criteria for Adverse Events, version 5 (CTCAE v5)
- 7. Treatment-related deaths: patient-reported quality of life will be measured using validated questionnaires which will be defined before the commencement of the relevant sub-study

Completion date

21/10/2030

Eligibility

Key inclusion criteria

Current inclusion criteria as of 12/01/2024:

Registration:

- 1. Women determined to be postmenopausal according to established local criteria
- 2. Diagnosed with operable invasive breast cancer with a clinical/radiological tumour size ≥1.0 cm.
- 3. Grade 2 or 3 tumours.
- 4. Preoperative full assessment completed (including bilateral breast examination and imaging with mammogram +/- ultrasound/MRI as performed locally)
- 5. Tumour ER-positive. ER positivity is defined as \geq 1% cells staining positive (or equivalent Allred Score of ER \geq 3 out of 8)
- 6. Tumour HER2 negative or HER2 status unknown. HER2 negativity will be defined as per the 2018 American Society of Clinical Oncology and the College of American Pathologists (ASCO /CAP) updated guidelines. Patients whose HER2 status is pending/unknown at the time of registration will be allowed to register for the trial. However, please note that only patients who are confirmed to be HER2 negative will be eligible to join the randomised part.
- 7. Received or planned to receive 10 days to 6 months of anastrozole or letrozole prior to surgery
- 8. Written informed consent to enter the registration part of the trial and to the donation of tissue
- 9. The patient has given written informed consent prior to any study-specific procedures and is willing and able to make herself available for the duration of the study and amenable and able to follow study schedule during treatment and follow-up and for the use of routinely collected electronic health and related records

Randomisation:

- 1. Patient previously consented and registered for screening component of POETIC-A
- 2. Tumour HER2 negative. HER2 negativity will be defined as per the 2018 ASCO/CAP updated quidelines
- 3. Centrally confirmed Ki67 ≥8% following pre-surgical AI
- 4. Patient is expected by the time of treatment initiation to have undergone definitive surgery for the primary breast tumour with clear radial margins as judged by the multidisciplinary team, and will have completed any adjuvant chemotherapy or radiotherapy (if prescribed)

- 5. Surgical staging of the axilla must have been undertaken by sentinel node biopsy, axillary sampling or dissection
- 6. The patient is randomised in time for treatment to start no later than 3 months after completion of non-endocrine therapy (defined as the final fraction of radiotherapy, Day 1 of the final cycle of chemotherapy or the date of the final surgical procedure)
- 7. The patient is able to swallow oral medications (excluding transient side effects from adjuvant non-endocrine treatment, if randomised before the end of this treatment)
- 8. The patient intends to take adjuvant endocrine therapy for at least 5 years
- 9. The patient has given written informed consent prior to any study-specific procedures (for the randomised intervention part), is willing to donate tissue from diagnostic biopsy, and is willing and able to make herself available for the duration of the study and to follow the study schedule during treatment and follow-up and for the use of routinely collected electronic health and related records

Week 1 Day 1:

- 1. Patient must have undergone definitive surgery for the primary breast tumour with clear radial margins as judged by the multidisciplinary team.
- 2. Adjuvant chemotherapy, if prescribed, must have been completed prior to Week 1 Day 1, and patients must have recovered (Common Terminology Criteria for Adverse Events, version 5 [CTCAE v5] Grade ≤1) from the acute effects of chemotherapy except for residual alopecia or Grade 2 peripheral neuropathy prior to Week 1 Day 1. A washout period of a minimum of 28 days from day 1 of the last cycle of treatment is required.
- 3. Adjuvant radiotherapy, if prescribed, must have been completed prior to Week 1 Day 1, and patients must have recovered (Grade \leq 1) from the acute effects of radiotherapy. A washout period of at least 14 days is required between end of radiotherapy and Week 1 Day 1.
- 4. Week 1 Day 1 is scheduled to take place no later than three months after completion of nonendocrine therapy (defined as the final fraction of radiotherapy, Day 1 of the final cycle of chemotherapy or the date of the final surgical procedure, whichever is latest).
- 5. The patient is able to swallow oral medications.
- 6. The patient has adequate organ function for all of the following criteria defined as:
- 6.1. ANC ≥1.5 × 10(9)/l
- 6.2. Platelets ≥100 × 10(9)/l
- 6.3. Haemoglobin ≥8 g/dl
- 6.4. Total bilirubin \leq 1.5 × upper limit of normal (ULN). Patients with Gilbert's syndrome with total bilirubin \leq 2.0 x ULN and direct bilirubin within normal limits are permitted
- 6.5. ALT and AST ≤3 × ULN

Previous inclusion criteria as of 19/12/2022 to 12/01/2024: Registration:

- 1. Women determined to be postmenopausal according to established local criteria
- 2. Diagnosed with operable invasive breast cancer with a clinical/radiological tumour size ≥1.5 cm. Patients who enter the trial after surgery can do so based on a locally measured Ki67 of ≥8% at surgery (following ≥10 days of pre-surgical AI therapy). They will still be eligible for registration even if their tumour at baseline was <1.5cm, assuming they meet all other eligibility criteria.
- 3. Preoperative full assessment completed (including bilateral breast examination and imaging with mammogram +/- ultrasound/MRI as performed locally)
- 4. Tumour ER-positive. ER positivity is defined as \geq 1% cells staining positive (or equivalent Allred Score of ER \geq 3 out of 8)
- 5. Tumour HER2 negative or HER2 status unknown. HER2 negativity will be defined as per the

2018 American Society of Clinical Oncology and the College of American Pathologists (ASCO /CAP) updated guidelines. Patients whose HER2 status is pending/unknown at the time of registration will be allowed to register for the trial. However, please note that only patients who are confirmed to be HER2 negative will be eligible to join the randomised part.

- 6. Received or planned to receive 10 days to 6 months of anastrozole or letrozole prior to surgery7. Written informed consent to enter the registration part of the trial and to the donation of tissue
- 8. The patient has given written informed consent prior to any study-specific procedures and is willing and able to make herself available for the duration of the study and amenable and able to follow study schedule during treatment and follow-up and for the use of routinely collected electronic health and related records

Randomisation:

- 1. Patient previously consented and registered for screening component of POETIC-A
- 2. Tumour HER2 negative. HER2 negativity will be defined as per the 2018 ASCO/CAP updated quidelines
- 3. Centrally confirmed Ki67 ≥8% following pre-surgical AI
- 4. Aromatase Inhibitor Resistant-CDK4/6 Inhibitor Sensitive (AIR-CIS) signature analysis has been performed by the central laboratory and available result confirmed by ICR-CTSU
- 5. Patient must have undergone definitive surgery for the primary breast tumour with clear radial margins as judged by the multidisciplinary team
- 6. Surgical staging of the axilla must have been undertaken by sentinel node biopsy, axillary sampling or dissection
- 7. Adjuvant chemotherapy, if prescribed, must have been completed prior to randomisation and patients must have recovered (Common Terminology Criteria for Adverse Events, version 5 [CTCAE v5] Grade ≤1) from the acute effects of chemotherapy except for residual alopecia or Grade 2 peripheral neuropathy prior to randomisation. A washout period of a minimum of 28 days from day 1 of the last cycle of treatment is required.
- 8. Adjuvant radiotherapy, if prescribed, must have been completed prior to randomisation, and patients must have recovered (Grade ≤1) from the acute effects of radiotherapy. A washout period of at least 14 days is required between the end of radiotherapy and randomisation.
- 9. The patient should be randomised no later than 3 months after completion of non-endocrine therapy (defined as the final fraction of radiotherapy, Day 1 of the final cycle of chemotherapy or the date of the final surgical procedure)
- 10. The patient is able to swallow oral medications
- 11. The patient has adequate organ function for all of the following criteria defined as:
- 11.1. ANC ≥1.5 × 10(9)/l
- 11.2. Platelets ≥100 × 10(9)/l
- 11.3. Haemoglobin ≥8 g/dl
- 11.4. Total bilirubin \leq 1.5 × upper limit of normal (ULN) patients with Gilbert's syndrome with total bilirubin \leq 2.0 x ULN and direct bilirubin within normal limits are permitted
- 11.5. ALT and AST ≤3 × ULN
- 12. The patient intends to take adjuvant endocrine therapy for at least 5 years
- 13. The patient has given written informed consent prior to any study-specific procedures (for the randomised intervention part), willing to donate tissue from diagnostic biopsy, and is willing and able to make herself available for the duration of the study and to follow the study schedule during treatment and follow-up and for the use of routinely collected electronic health and related records

Previous inclusion criteria:

Registration:

- 1. Postmenopausal women defined at diagnosis as:
- 1.1. A postmenopausal state is defined as no menses for 12 months without an alternative medical cause. A high follicle-stimulating hormone (FSH) level in the postmenopausal range may be used to confirm a post-menopausal state in women not using hormonal contraception or hormonal replacement therapy. However, in the absence of 12 months of amenorrhea, a single FSH measurement is insufficient; OR
- 1.2. Documented bilateral oophorectomy
- 2. Diagnosed operable invasive breast cancer with a clinical/radiological tumour size ≥1.5 cm
- 3. Tumour ER-positive. ER positivity is defined as \geq 1% cells staining positive (or equivalent Allred Score of ER \geq 3 out of 8)
- 4. Tumour HER2 negative or HER2 status unknown. HER2 negativity will be defined as per the 2018 American Society of Clinical Oncology and the College of American Pathologists (ASCO /CAP) updated guidelines. Patients whose HER2 status is pending/unknown at the time of registration will be allowed to register for the trial. However, please note that only patients who are confirmed to be HER2 negative will be eligible to join the randomised part.
- 5. Received or planned to receive 10 days to 6 months of anastrozole or letrozole prior to surgery
- 6. No evidence of metastatic spread by standard assessment according to local guidelines 7. Written informed consent to enter the registration part of the trial and to the donation of tissue
- 8. No medical condition or other factor likely to preclude entry to randomised part of the study if eligible e.g. patient would not be suitable to receive abemaciclib due to concomitant medications or medical history.
- 9. The patient has given written informed consent prior to any study-specific procedures and is willing and able to make herself available for the duration of the study and amenable and able to follow study schedule during treatment and follow-up and for the use of routinely collected electronic health and related records.
- 10. Patients who enter the trial after surgery can do so based on a locally measured Ki67 of ≥8% at surgery (following ≥10 days of pre-surgical AI therapy). They will still be eligible for registration even if their tumour at baseline was <1.5cm, assuming they meet all other eligibility criteria.

Randomisation:

- 1. Patient previously consented and registered for screening component of POETIC-A
- 2. Tumour HER2 negative. HER2 negativity will be defined as per the 2018 ASCO/CAP updated guidelines
- 3. Centrally confirmed Ki67 ≥8% following pre-surgical AI
- 4. Aromatase Inhibitor Resistant-CDK4/6 Inhibitor Sensitive (AIR-CIS) signature analysis has been performed by the central laboratory and available result confirmed by ICR-CTSU
- 5. Patient must have undergone definitive surgery for the primary breast tumour with clear radial margins as judged by the multidisciplinary team
- 6. Surgical staging of the axilla must have been undertaken by sentinel node biopsy, axillary sampling or dissection
- 7. Adjuvant chemotherapy, if prescribed, must have been completed prior to randomisation and patients must have recovered (Common Terminology Criteria for Adverse Events, version 5 [CTCAE v5] Grade ≤1) from the acute effects of chemotherapy except for residual alopecia or Grade 2 peripheral neuropathy prior to randomisation. A washout period of a minimum of 28 days from day 1 of the last cycle of treatment is required.
- 8. Adjuvant radiotherapy, if prescribed, must have been completed prior to randomisation, and patients must have recovered (Grade ≤ 1) from the acute effects of radiotherapy. A washout

period of at least 14 days is required between the end of radiotherapy and randomisation.

- 9. The patient should be randomised no later than 3 months after completion of non-endocrine therapy (defined as the final fraction of radiotherapy, Day 1 of the final cycle of chemotherapy or the date of the final surgical procedure)
- 10. The patient is able to swallow oral medications
- 11. The patient has adequate organ function for all of the following criteria defined as:
- 11.1. ANC* ≥1.5 × 10e9/l
- 11.2. Platelets ≥100 × 10e9/l
- 11.3. Haemoglobin ≥8 g/dl
- 11.4. Total bilirubin \leq 1.5 × upper limit of normal (ULN) patients with Gilbert's syndrome with total bilirubin \leq 2.0 times ULN and direct bilirubin within normal limits are permitted
- 11.5. ALT and AST ≤3 × ULN
- 12. The patient intends to take adjuvant endocrine therapy for at least 5 years
- 13. The patient has given written informed consent prior to any study-specific procedures (for the randomised intervention part), willing to donate tissue from diagnostic biopsy, and is willing and able to make herself available for the duration of the study and to follow the study schedule during treatment and follow-up and for the use of routinely collected electronic health and related records.

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 years

Sex

Female

Key exclusion criteria

Current exclusion criteria as of 12/01/2024:

Registration:

- 1. Men and pre-/peri-menopausal women
- 2. Intended or actual use of HRT or any other oestrogen-containing medication (including vaginal oestrogens) within 4 weeks prior to planned surgery (date when surgical tissue sample being taken). Note: patients with a Mirena coil in situ at the time of registration are not excluded.
- 3. Patients who commenced pre-surgical AI therapy >6 months prior to surgery
- 4. Prior endocrine therapy for breast cancer or breast cancer prevention
- 5. Prior neoadjuvant chemotherapy for breast cancer
- 6. Evidence of metastatic disease
- 7. Locally advanced breast cancer not amenable to surgery
- 8. Bilateral invasive breast cancer (excluding contralateral ductal or lobular carcinoma in situ [DCIS/LCIS])
- 9. Multiple unilateral tumours with different ER and/or HER2 status. Synchronous DCIS/LCIS, as well as multifocal disease with homogenous ER/HER2 status, is allowed if at least one lesion is at least 1.0 cm; the largest lesion should be used for sample collection and CRF completion. If ER

/HER2 status of smaller foci is unknown at time of registration, patients can be registered; however, note that congruity of receptor status will need to be confirmed by the time of randomisation (unless smaller foci are <10mm and receptor status is unknown).

- 10. Previous invasive breast cancer except for ipsilateral DCIS/LCIS treated >5 years previously by locoregional therapy alone or contralateral DCIS/LCIS treated by locoregional therapy at any time
- 11. Any invasive malignancy diagnosed within the previous 5 years (other than non-melanoma skin cancer or cervical carcinoma in situ)
- 12. Any other medical condition likely to exclude the patient from subsequent randomisation part (see Randomisation)

Randomisation:

- 1. Patient has received prior CDK4/6 inhibitor therapy
- 2. Patient is planned to receive adjuvant abemaciclib as standard of care.
- 3. Any patient with a history of VTE (for example, DVT of the leg or arm and/or PE) will be excluded. Note: patients with a history of venous catheter occlusion by thrombus that did NOT surround the catheter, and the lumen could be made patent by appropriate measures (for example, saline or thrombolytic agent), are not excluded
- 4. The patient has a serious/or uncontrolled pre-existing medical condition(s) that, in the judgment of the investigator, is likely to preclude study treatment (such as severe renal impairment, [for example, estimated creatinine clearance <30 ml/min], interstitial lung disease, severe dyspnoea at rest or requiring oxygen therapy, history of major surgical resection involving the stomach or small bowel, or pre-existing Crohn's disease or ulcerative colitis or a pre-existing chronic condition resulting in baseline Grade 2 diarrhoea)
- 5. The patient has a personal history of any of the following conditions: syncope of cardiovascular aetiology, ventricular arrhythmia of pathological origin (including, but not limited to, ventricular tachycardia and ventricular fibrillation), or sudden cardiac arrest. Note: patients with controlled atrial fibrillation diagnosed more than 30 days prior to randomisation are not excluded
- 6. The patient has received an experimental treatment in a clinical trial within the last 30 days or 5 half-lives, whichever is longer, prior to randomisation, or is currently enrolled in any other type of medical research (for example: medical device) judged by the Chief Investigator not to be scientifically or medically compatible with this study
- 7. The patient has any known active systemic bacterial infections (that would be expected to require IV antibiotics at the time of initiating study treatment), systemic fungal infection or detectable viral infection (such as known HIV positivity or with known active hepatitis B or C, e.g. hepatitis B surface antigen-positive), which would be expected to preclude study treatment. Screening is not required for enrolment.
- 8. Evidence of metastatic disease or local recurrence
- 9. Multiple unilateral tumours with different ER and/or HER2 status (DCIS/LCIS are permitted, and confirmation of congruent ER/HER2 status is not necessary for lesions less than 10 mm)

Week 1 Day 1:

- 1. Patient has received any CDK4/6 inhibitor therapy since randomisation.
- 2. Any newly occurring or diagnosed VTE since randomisation (for example, DVT of the leg or arm and/or PE). Note: patients with a history of venous catheter occlusion by thrombus that did NOT surround the catheter, and the lumen could be made patent by appropriate measures (for example, saline or thrombolytic agent), are not excluded.
- 3. Any newly occurring or diagnosed medical conditions since randomisation that, in the judgment of the investigator, would preclude participation in this study (such as severe renal impairment, [for example, estimated creatinine clearance <30 mL/min], interstitial lung disease, severe dyspnoea at rest or requiring oxygen therapy, major surgical resection involving the

stomach or small bowel, or condition resulting in baseline Grade 2 diarrhoea).

- 4. Any newly occurring or diagnosed cardiovascular conditions since randomisation such as: syncope of cardiovascular aetiology, ventricular arrhythmia of pathological origin (including, but not limited to ventricular tachycardia and ventricular fibrillation), or sudden cardiac arrest.
- 5. Major surgery within 14 days prior to Week 1 Day 1.
- 6. The patient has received an experimental treatment in a clinical trial within the last 30 days or 5 half-lives, whichever is longer, prior to Week 1 Day 1, or is currently enrolled in any other type of medical research (for example: medical device) judged by the Chief Investigator not to be scientifically or medically compatible with this study.
- 7. Any active systemic bacterial infections (requiring IV antibiotics at time of Week 1 Day 1), systemic fungal infection or detectable viral infection (such as known HIV positivity or active hepatitis B or C, e.g. hepatitis B surface antigen positive). Screening is not required for initiation of treatment.
- 8. Evidence of metastatic disease or local recurrence

Previous exclusion criteria as of 19/12/2022 to 12/01/2024: Registration:

- 1. Men and pre-/peri-menopausal women
- 2. Grade 1 tumours. For patients who enter the trial after surgery patients with a grade 1 tumour at diagnosis will still be eligible for registration if they have Ki67 ≥8% at surgery (following ≥10 days of pre-surgical AI therapy), as measured at the local site, and meet all other eligibility criteria
- 3. Intended or actual use of HRT or any other oestrogen-containing medication (including vaginal oestrogens) within 4 weeks prior to planned surgery (date when surgical tissue sample being taken). Note: patients with a Mirena coil in situ at the time of registration are not excluded.
- 4. Patients who commenced pre-surgical AI therapy >6 months prior to surgery
- 5. Prior endocrine therapy for breast cancer or breast cancer prevention
- 6. Prior neoadjuvant chemotherapy for breast cancer
- 7. Evidence of metastatic disease
- 8. Locally advanced breast cancer not amenable to surgery
- 9. Bilateral invasive breast cancer (excluding contralateral ductal or lobular carcinoma in situ [DCIS/LCIS])
- 10. Multiple unilateral tumours with different ER and/or HER2 status. Synchronous DCIS/LCIS, as well as multifocal disease with homogenous ER/HER2 status, is allowed if at least one lesion is at least 1.5 cm; the largest lesion should be used for sample collection and CRF completion. If ER /HER2 status of smaller foci is unknown at time of registration, patients can be registered; however, note that congruity of receptor status will need to be confirmed by the time of randomisation.
- 11. Previous invasive breast cancer except for ipsilateral DCIS/LCIS treated >5 years previously by locoregional therapy alone or contralateral DCIS/LCIS treated by locoregional therapy at any time
- 12. Any invasive malignancy diagnosed within the previous 5 years (other than non-melanoma skin cancer or cervical carcinoma in situ)
- 13. Any other medical condition likely to exclude the patient from subsequent randomisation part (see Randomisation)

Randomisation:

- 1. Patient has received prior CDK4/6 inhibitor therapy
- 2. Any patient with a history of VTE (for example, DVT of the leg or arm and/or PE) will be excluded. Note: patients with a history of venous catheter occlusion by thrombus that did NOT

surround the catheter, and the lumen could be made patent by appropriate measures (for example, saline or thrombolytic agent), are not excluded

- 3. The patient has a serious/or uncontrolled pre-existing medical condition(s) that, in the judgment of the investigator, would preclude participation in this study (such as severe renal impairment, [for example, estimated creatinine clearance <30 ml/min], interstitial lung disease, severe dyspnoea at rest or requiring oxygen therapy, history of major surgical resection involving the stomach or small bowel, or pre-existing Crohn's disease or ulcerative colitis or a pre-existing chronic condition resulting in baseline Grade 2 diarrhoea)
- 4. The patient has a personal history of any of the following conditions: syncope of cardiovascular aetiology, ventricular arrhythmia of pathological origin (including, but not limited to, ventricular tachycardia and ventricular fibrillation), or sudden cardiac arrest. Note: patients with controlled atrial fibrillation diagnosed more than 30 days prior to randomisation are not excluded
- 5. The patient has had major surgery within 14 days prior to randomisation
- 6. The patient has received an experimental treatment in a clinical trial within the last 30 days or 5 half-lives, whichever is longer, prior to randomisation, or is currently enrolled in any other type of medical research (for example: medical device) judged by the Chief Investigator not to be scientifically or medically compatible with this study
- 7. The patient has active systemic bacterial infections (requiring IV antibiotics at the time of initiating study treatment), systemic fungal infection or detectable viral infection (such as known HIV positivity or with known active hepatitis B or C (e.g. hepatitis B surface antigen-positive). Screening is not required for enrolment.
- 8. Evidence of metastatic disease
- 9. Multiple unilateral tumours with different ER and/or HER2 status (DCIS/LCIS are permitted, and confirmation of congruent ER/HER2 status is not necessary for lesions less than 10 mm)

Previous exclusion criteria:

Registration:

- 1. Men and pre-/peri-menopausal women
- 2. Grade 1 tumours*
- 3. Intended or actual use of HRT or any other oestrogen-containing medication (including vaginal oestrogens) within 4 weeks prior to planned surgery (date when surgical tissue sample being taken). Note: patients with a Mirena coil in situ at the time of registration are not excluded.
- 4. Patients who commenced pre-surgical AI therapy >6 months prior to surgery
- 5. Prior endocrine therapy for breast cancer or breast cancer prevention
- 6. Prior neoadjuvant chemotherapy for breast cancer
- 7. Evidence of metastatic disease
- 8. Locally advanced breast cancer not amenable to surgery
- 9. Bilateral invasive breast cancer (excluding contralateral ductal carcinoma in situ [DCIS])
- 10. Multiple unilateral tumours with different ER/PgR/HER2 status, grade or type (e.g. ductal vs lobular) i.e. anything that suggests two or more different cancers. Multifocal disease with homogenous ER/PgR/HER2 status, grade and type is allowed if at least one lesion is at least 1.5 cm; the largest lesion should be used for sample collection and CRF completion
- 11. Previous invasive breast cancer except for ipsilateral DCIS/lobular carcinoma in situ (LCIS) treated >5 years previously by locoregional therapy alone or contralateral DCIS/LCIS treated by locoregional therapy at any time
- 12. Any invasive malignancy diagnosed within the previous 5 years (other than non-melanoma skin cancer or cervical carcinoma in situ)
- 13. Any other medical condition likely to exclude the patient from subsequent randomisation part (see Randomisation)

*For patients who enter the trial after surgery - patients with a grade 1 tumour will still be eligible for registration if they have Ki67 ≥8% at surgery (following ≥10 days of pre-surgical AI therapy), as measured at the local site, and meet all other eligibility criteria

Randomisation:

- 1. Patient has received prior CDK4/6 inhibitor therapy
- 2. Any patient with a history of VTE (for example, DVT of the leg or arm and/or PE) will be excluded. Note: patients with a history of venous catheter occlusion by thrombus that did NOT surround the catheter, and the lumen could be made patent by appropriate measures (for example, saline or thrombolytic agent), are not excluded
- 3. The patient has a serious/or uncontrolled pre-existing medical condition(s) that, in the judgment of the investigator, would preclude participation in this study (such as severe renal impairment, [for example, estimated creatinine clearance <30 ml/min], interstitial lung disease, severe dyspnoea at rest or requiring oxygen therapy, history of major surgical resection involving the stomach or small bowel, or pre-existing Crohn's disease or ulcerative colitis or a pre-existing chronic condition resulting in baseline Grade 2 diarrhoea)
- 4. The patient has a personal history of any of the following conditions: syncope of cardiovascular aetiology, ventricular arrhythmia of pathological origin (including, but not limited to, ventricular tachycardia and ventricular fibrillation), or sudden cardiac arrest. Note: patients with controlled atrial fibrillation diagnosed more than 30 days prior to randomisation are not excluded
- 5. The patient has active systemic bacterial infections (requiring IV antibiotics at the time of initiating study treatment), systemic fungal infection or detectable viral infection (such as known HIV positivity or with known active hepatitis B or C (e.g. hepatitis B surface antigen-positive). Screening is not required for enrolment
- 6. Evidence of metastatic disease

Date of first enrolment 23/12/2020

Date of final enrolment 14/10/2025

Locations

Countries of recruitment

United Kingdom

England

Northern Ireland

Scotland

Wales

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

Study participating centre Queen Elizabeth Hospital

Queen Elizabeth Hospital King's Lynn United Kingdom PE30 4ET

Study participating centre Great Western Hospital

Marlborough Road Swindon United Kingdom SN3 6BB

Study participating centre Royal Marsden Hospital

Downs Road Sutton United Kingdom SM2 5NG

Study participating centre Aberdeen Royal Infirmary

Foresterhill Road Aberdeen United Kingdom AB25 2ZN

Study participating centre Royal Albert Edward Infirmary

Wigan Lane, Wigan United Kingdom WN1 2NN

Study participating centre Doncaster Royal Infirmary

Armthorpe Road Doncaster United Kingdom DN2 5LT

Study participating centre Royal Bournemouth Hospital

Castle Lane East Bournemouth United Kingdom BH7 7DW

Study participating centre Poole General Hospital

Longfleet Road Poole United Kingdom BH15 2JB

Study participating centre University College Hospital (London)

250 Euston Road London United Kingdom NW1 2PG

Study participating centre Royal Berkshire Hospital

London Road Reading United Kingdom RG1 5AN

Study participating centre Harrogate District Hospital

Lancaster Park Road Harrogate United Kingdom HG2 7SX

Study participating centre Royal Sussex County Hospital

Eastern Road Brighton United Kingdom BN2 5BE

Study participating centre Charing Cross Hospital

Fulham Palace Road London United Kingdom W6 8RF

Study participating centre Royal Free Hospital

Pond Street London United Kingdom NW3 2QG

Study participating centre East Surrey Hospital

Canada Avenue Redhill United Kingdom RH1 5RH

Study participating centre Ysbyty Gwynedd

Penrhosgarnedd Bangor United Kingdom LL57 2PW

Study participating centre Dumfries and Galloway Royal Infirmary

Garroch Cargenbridge

Dumfries United Kingdom DG2 8RX

Study participating centre Glan Clwyd Hospital

Sarn Lane Rhyl United Kingdom LL18 5UJ

Study participating centre Ninewells Hospital

Dundee Dundee United Kingdom DD1 9SY

Study participating centre Blackpool Victoria Hospital

Whinney Heys Road Blackpool United Kingdom FY3 8NR

Study participating centre Royal Shrewsbury Hospital

Mytton Oak Road Shrewsbury United Kingdom SY3 8XQ

Study participating centre Kingston Hospital

Galsworthy Road Kingston upon Thames United Kingdom KT2 7QB

Study participating centre St James's University Hospital

Beckett Street Leeds United Kingdom LS9 7TF

Study participating centre Royal Devon & Exeter Hospital

Barrack Road Exeter United Kingdom EX2 5DW

Study participating centre Northampton General Hospital

Cliftonville Northampton United Kingdom NN1 5BD

Study participating centre Royal Cornwall Hospitals NHS Trust

Royal Cornwall Hospital Treliske Truro United Kingdom TR1 3LJ

Study participating centre Mid Yorkshire Hospitals NHS Trust

Pinderfields Hospital Aberford Road Wakefield United Kingdom WF1 4DG

Study participating centre Burnley General Hospital

Casterton Avenue Burnley United Kingdom BB10 2PQ

Study participating centre Royal Blackburn Hospital

Haslingden Road Blackburn United Kingdom BB2 3HH

Study participating centre Ipswich Hospital

Heath Road Ipswich United Kingdom IP4 5PD

Study participating centre Western General Hospital

Crewe Road South Edinburgh Lothian United Kingdom EH4 2XU

Study participating centre St John's Hospital

Howden W Road Howden Livingston United Kingdom EH54 6PP

Study participating centre Royal Surrey County Hospital Guildford

Egerton Road Guildford United Kingdom GU2 7XX

Study participating centre Milton Keynes University Hospital NHS Foundation Trust

Standing Way Eaglestone Milton Keynes United Kingdom MK6 5LD

Study participating centre Belfast City Hospital

51 Lisburn Rd Belfast United Kingdom BT9 7AB

Study participating centre Wythenshawe Hospital

Southmoor Road Wythenshawe Manchester United Kingdom M23 9LT

Study participating centre The Christie Clinic

550 Wilmslow Road Manchester United Kingdom M20 4BX

Study participating centre Forth Valley Royal Hospital

Stirling Road Larbert United Kingdom FK5 4WR

Study participating centre Southampton

Southampton General Hospital

Tremona Road Southampton United Kingdom SO16 6YD

Study participating centre Royal United Hospitals Bath NHS Foundation Trust

Combe Park Bath United Kingdom BA1 3NG

Study participating centre North Manchester General Hospital

Delaunays Road Crumpsall Manchester United Kingdom M8 5RB

Study participating centre University Hospitals of North Tees and Hartlepool

Hardwick Road Stockton-on-Tees United Kingdom TS19 8PE

Study participating centre Barnet Hospital

Wellhouse Lane Barnet United Kingdom EN5 3DJ

Study participating centre Chase Farm Hospital

127 the Ridgeway Enfield United Kingdom EN2 8JL

Study participating centre Warwick Hospital

Lakin Road Warwick United Kingdom CV34 5BW

Study participating centre Beatson West of Scotland Cancer Centre

1053 Great Western Road Glasgow United Kingdom G12 0YN

Study participating centre Royal Stoke University Hospital

Newcastle Road Stoke-on-trent United Kingdom ST4 6QG

Study participating centre Llandough Hospital

Penlan Road Llandough Penarth United Kingdom CF64 2XX

Study participating centre St George's University Hospitals

Blackshaw Road, Tooting London United Kingdom SW17 0QT

Study participating centre Calderdale Royal Hospital

Huddersfield Road

Halifax United Kingdom HX3 0PW

Study participating centre Huddersfield Royal Infirmary

Acre Street Huddersfield United Kingdom HD3 3EA

Study participating centre Lincoln County Hospital

Greetwell Road Lincoln United Kingdom LN2 5QY

Study participating centre Pilgrim Hospital

Sibsey Road Boston United Kingdom PE21 9QS

Study participating centre University Hospitals of Morecambe Bay NHS Foundation Trust

Ashton Road Lancaster United Kingdom

LA1 4RP

Study participating centre Borders General Hospital

Huntlyburn Terrace Melrose United Kingdom TD6 9BS

Study participating centre North Tyneside General Hospital

Rake Lane North Shields United Kingdom NE29 8NH

Study participating centre Wansbeck General Hospital

Woodhorn Lane Ashington United Kingdom NE63 9JJ

Study participating centre Kettering General Hospital

Rothwell Road Kettering United Kingdom NN16 8UZ

Study participating centre Musgrove Park Hospital (taunton)

Musgrove Park Hospital Taunton United Kingdom TA1 5DA

Study participating centre Worcestershire Acute Hospitals NHS Trust

Worcestershire Royal Hospital Charles Hastings Way Worcester United Kingdom WR5 1DD

Study participating centre George Eliot Hospital

Lewes House College Street Nuneaton

Study participating centre Maidstone and Tunbridge Wells NHS Trust

The Maidstone Hospital Hermitage Lane Maidstone United Kingdom ME16 9QQ

Sponsor information

Organisation

Institute of Cancer Research

ROR

https://ror.org/043jzw605

Funder(s)

Funder type

Industry

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

Funder Name

Eli Lilly and Company

Alternative Name(s)

Lilly, Eli Lilly & Company, Eli Lilly & Co., Eli Lilly And Co, Eli Lilly & Co

Funding Body Type

Government organisation

Funding Body Subtype

For-profit companies (industry)

Location

United States of America

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study will be available on request from the POETIC-A trial team via poetic-a-icrctsu@icr.ac.uk via completion of a data access request form after such time that the primary analysis publication and any other key analyses have been completed. Optional advanced consent/authorisation for the possible future sharing of information collected about patients will be obtained at study entry.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
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