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ROCkeTS GEN V2 Study. Refining Ovarian Cancer Test Accuracy Scores: A test accuracy study to validate new risk scores in postmenopausal women with symptoms of suspected ovarian cancer

Submission date
08/12/2025

Recruitment status
Recruiting

Registration date
02/02/2026

Overall study status
Ongoing

Last Edited
02/02/2026

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
We know that lots of women have symptoms such as bloating and abdominal discomfort. It is also very common to have cysts (balloon-like swellings) on women's ovaries, picked up by ultrasound. In addition, some women have higher levels of a blood marker called CA125. This blood test can be abnormal in many conditions, including menstruation, fibroids, appendicitis, etc. A very small number of women with ovarian cysts or abnormal CA125 levels will be diagnosed with ovarian cancer.
The purpose of this study is to identify better tests for women with ovarian cysts or abnormal blood test results so we can detect ovarian cancer earlier. This will also reduce unnecessary tests, hospital visits, and distress for women who don't have cancer.

Who can participate?
Postmenopausal women referred to secondary care with symptoms of suspected ovarian cancer and blood test indicating raised levels of CA125.

Women referred with symptoms of suspected OC (typical referral symptoms are defined in section 2.5 of the protocol). Only postmenopausal women are included. Menopause is defined as more than 12 months without menstruation. Those no longer menstruating for more than 12 months for reasons such as contraception or hysterectomy should have their menopausal status categorised according to age. In addition, women must have test results from one of the following: a raised CA125 test result (even if imaging has not been done yet), abnormal imaging result showing a lesion (even if CA125 test is not raised), or both a raised CA125 test and an abnormal imaging result showing a lesion. Patients must be able to provide informed consent.

What does the study involve?
Answering a few questions about symptoms, donating a blood sample (about two tablespoons –

30 ml), and providing a few blood spots from a finger (around 3–6 drops, equivalent to 0.1–0.2 ml). If surgery is advised, a small tissue sample will be collected.

What are the possible benefits and risks of participating?
Participating in the study may help doctors determine the best tests and treatments for other women in the future who have similar symptoms. At this time, we don't know how accurate the new tests are. We are going to check how accurate these tests are on the samples we will collect. The side effects from donating a blood sample – about the volume of two tablespoonfuls, about 30 ml – are usually minimal. Occasionally, some patients may experience some bruising at the site, which typically settles within a day or two.

Where is the study run from?
The study is coordinated from The University of Birmingham, who is a Sponsor.

When is the study starting and how long is it expected to run for?
The study is now in the preparation stage and we hope to open sites in February 2026. We expect two years of recruitment, 12 months follow-up and an additional year for data analysis – expected finish is 2029.

Who is funding the study?
The study is funded by the grant from Cancer Research UK.

Who is the main contact?
All queries about the study can be sent to rocketsgenv2@contact.bham.ac.uk
Project Coordinator: Dr Sandra Davies, s.margielewska@bham.ac.uk
Chief Investigator: Prof Sudha Sundar, s.s.sundar@bham.ac.uk

Contact information

Type(s)
Public, Scientific, Principal investigator

Contact name
Prof Sudha Sundar

ORCID ID
https://orcid.org/0000-0002-5843-3015

Contact details
Department of Cancer and Genomic Sciences
University of Birmingham
Edgbaston
Birmingham
United Kingdom
B15 2TT
+44 121 414 44021
s.s.sundar@bham.ac.uk

Additional identifiers

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354933

Study information

Scientific Title
Refining Ovarian Cancer Test Accuracy Scores: A test accuracy study to validate new risk scores in postmenopausal women with symptoms of suspected ovarian cancer. ROCkeTS GEN V2

Acronym
ROCkeTS GEN V2

Study objectives
1. Evaluate Plasma ctDNA Diagnostic Performance:
To evaluate plasma circulating tumour DNA (ctDNA) as a diagnostic test with increased sensitivity and specificity compared to serum CA125 for earlier diagnosis of ovarian cancer in postmenopausal women.
2. Establish Translational Research Resource:
To collect representative blocks from resected tumour tissue to establish a translational resource for future early detection research.
3. Develop Improved Diagnostic Tests:
To collect dried blood spots and serum for analysis of circulating biomarkers and blood ctDNA in cohorts of women at high risk of ovarian cancer, to establish improved diagnostic test for postmenopausal women.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 11/09/2025, East Midlands – Derby Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +442071048255; derby.rec@hra.nhs.uk), ref: 25/EM/0200

Primary study design
Observational

Secondary study design
Cohort study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Ovarian cancer

Interventions

ROCkeTS GEN V2 study is a prospective single-arm cohort diagnostic accuracy study where all patients receive all tests, and accuracy of tests is evaluated against a gold standard of histology or 12-month outcome. A test accuracy study compares measurements obtained by index tests with those obtained by a reference standard. In this way, the accuracy of index tests can be estimated. A reference standard is a test (or combination of tests) that confirms or refutes the presence or absence of disease beyond reasonable doubt.

Here, the reference standard will be histology or cytology of tissues taken from patients who proceed to surgery or biopsy, or in patients who do not undergo surgery or biopsy, assessment of cancer/non-cancer outcomes determined from hospital records at 12 months. The diagnostic performance of the index test will be compared against that of the comparator test – the existing standard risk prediction score RMI 1. RMI combines CA125 and limited ultrasound features to provide a score that is used to determine patient management.

The aim of the study is to deliver a new early diagnostic test for ovarian cancer for postmenopausal women. The study is designed to recruit a significant cohort of women (500) at low or unknown genetic risk of ovarian cancer across multiple NHS sites in the UK.

Recruited women will have the following tests and follow-up recorded:

CA125 (if not performed already as part of standard care)

IOTA transvaginal ultrasound and additional abdominal scan if performed as part of standard care

Histology result where biopsy or surgery is clinically indicated

12-month follow-up status ascertained by research nurses using hospital records

Women entering ROCkeTS GEN V2 will donate dried blood spots and blood samples for plasma and serum analysis at recruitment. Women undergoing surgery for ovarian pathology will also be consented to donate tissue blocks of representative tissue for research.

Representative tissue blocks and slides will be retrieved from pathology labs for patients proceeding to surgery as part of standard care. These blocks will first undergo specialist pathology review by an expert gynaecological pathologist. DNA will then be extracted from cancer tissues for additional analyses, including shallow whole genome sequencing.

In ROCkeTS GEN V2, the index tests (ctDNA analysis) will be externally validated at the end of the study. Therefore, we will collect dried blood spots, serum, and plasma in the study to be analysed and validated at the end of the study. Our project will focus on analysis of circulating tumour DNA (ctDNA) from patient blood, aiming to identify changes and mutations related to cancer, which will allow for early detection of the disease. We also want to analyse proteins and other biomarkers to establish a novel diagnostic test.

Intervention Type

Other

Primary outcome(s)

1. Sensitivity of ctDNA for detecting early-stage (stage I/II) high-grade serous ovarian cancer is measured using ctDNA analysis at baseline
2. Specificity of ctDNA for detecting early-stage (stage I/II) high-grade serous ovarian cancer is measured using ctDNA analysis at baseline
3. Sensitivity of RMI 1 for detecting early-stage (stage I/II) high-grade serous ovarian cancer is measured using RMI 1 score at baseline
4. Specificity of RMI 1 for detecting early-stage (stage I/II) high-grade serous ovarian cancer is measured using RMI 1 score at baseline
5. Histology or cytology confirmation of ovarian cancer status is measured using pathology review at surgery or biopsy
6. Cancer or non-cancer outcome status is measured using hospital records at 12 months

Key secondary outcome(s))
There are no secondary outcome measures

Completion date
01/10/2029

Eligibility

Key inclusion criteria
1. Post menopausal, symptomatic women presenting to primary care with suspected ovarian cancer who are tested for the biomarker CA125 according to current standards of care for investigation of CA125 in the primary care setting.
2. Women referred with symptoms of suspected OC (typical referral symptoms are defined in section 2.5 of the protocol).
3. Only postmenopausal women are included.
Menopause is defined as > 12 months without menstruation. Those no longer menstruating > 12 months for reasons such as contraception or hysterectomy should have their menopausal status categorised according to age; < 50 years premenopausal, 51+ years postmenopausal.
4. In addition, women must have test results from one of the following:
4.1. A raised Ca125 test result (even if imaging has not been done yet)
4.2. Abnormal imaging result showing a lesion (even if CA125 test is not raised).
4.3. Both a raised CA125 test and an abnormal imaging result showing a lesion
5. Patients able to provide informed consent.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
Female

Total final enrolment
0

Key exclusion criteria
1. Premenopausal women
2. USG reveals simple ovarian cysts < 5cm in size (very low risk of malignancy) and patient does not have a raised CA125.
3. Previous ovarian malignancy.
4. Active non-ovarian malignancy – Women with a past history of cancer are only eligible if there are no documented persistent or recurrent disease and they have not received treatment for this in the last 12 months. This exclusion does not apply to patients with premalignant disease e. g. cervical intra-epithelial neoplasia or patients receiving Tamoxifen/other drugs to prevent breast cancer recurrence.

Date of first enrolment
01/02/2026

Date of final enrolment
01/02/2028

Locations

Countries of recruitment
United Kingdom

Study participating centre
City Hospital
Dudley Road
Birmingham
England
B18 7QH

Sponsor information

Organisation
University of Birmingham

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Government

Funder Name
Cancer Research UK

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Data sharing statement to be made available at a later date