ISRCTN10490346 https://doi.org/10.1186/ISRCTN10490346

# An investigation of whether rucaparib is safe and more effective when combined with either one or two immunotherapy drugs (nivolumab and ipilimumab), when compared to rucaparib on its own

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|---|---|---|
| **Submission date**<br>02/02/2018 | **Recruitment status**<br>No longer recruiting | [X] Prospectively registered<br>[_] Protocol |
| **Registration date**<br>14/02/2018 | **Overall study status**<br>Completed | [_] Statistical analysis plan<br>[_] Results |
| **Last Edited**<br>08/04/2025 | **Condition category**<br>Cancer | [_] Individual participant data<br>[X] Record updated in last year |

**Plain English summary of protocol**
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-adding-immunotherapy-to-rucaparib-for-ovarian-cancer-that-has-come-back-centurion

## Contact information

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# Additional identifiers

**Clinical Trials Information System (CTIS)**
2017-004780-13

**Integrated Research Application System (IRAS)**
233151

**ClinicalTrials.gov (NCT)**
Nil known

**Protocol serial number**
IRAS 233151

# Study information

**Scientific Title**
An open-label, randomised, phase I/II trial of ruCaparib combined with Nivolumab +/- Ipilimumab to augment response in homologous repair deficient patients with relapsed Ovarian, primary peritoneal and fallopian tube cancer (CeNturIOn)

**Acronym**
CeNturIOn

**Study objectives**
The addition of nivolumab with or without ipilimumab will improve clinical efficacy as compared to rucaparib monotherapy in patients with homologous recombination deficient relapsed high grade serous ovarian (fallopian tube, primary peritoneal) carcinoma.

**Ethics approval required**
Old ethics approval format

**Ethics approval(s)**

Approved 22/08/2018, London - Harrow Research Ethics Committee (Level 3, Block B, Whitefriars, Lewins Mead, Bristol, BS1 2NT; Tel: +44 (0)207 104 8241; Email: nrescommittee.london-harrow@nhs.net), ref: 18/LO/1022

## Study design
Phase I/II open-label randomized multicentre trial

## Primary study design
Interventional

## Study type(s)
Treatment

## Health condition(s) or problem(s) studied
Relapsed high grade serous ovarian (fallopian tube, primary peritoneal) carcinoma

## Interventions
After an initial safety run-in phase, part randomised (to the phase II part of the trial) to one of the three trial treatment arms by a computer which decides randomly which treatment the patient will receive, like tossing a coin or rolling a die.

Treatment Arm 1: Rucaparib alone (R) participants begin by taking oral rucaparib tablets twice a day (approximately 12 h apart) continuously for each 42-day cycle. This dose may be reduced if the participant has side effects.

Treatment Arm 2: Rucaparib with nivolumab (RN) participants begin by taking oral rucaparib tablets twice a day (approximately 12 h apart) continuously for each 42-day cycle. Participants also have a drip of nivolumab (taking approximately 60 min) every 2 weeks. The dose of rucaparib may be reduced if the patient has side effects relating to this drug.

Treatment Arm 3: Rucaparib with nivolumab and ipilimumab (RNI) participants begin by taking rucaparib tablets twice a day (approximately 12 h apart) continuously for each 42-day cycle. Participants also have a drip of nivolumab (taking approximately 60 min) every 2 weeks and a 30-min drip of ipilimumab every 6 weeks. The dose of rucaparib may be reduced if the patient has side effects relating to this drug.

## Intervention Type
Drug

## Phase
Phase I/II

## Drug/device/biological/vaccine name(s)
Rucaparib, nivolumab, ipilimumab

## Primary outcome(s)
Progression-Free Survival (PFS) is measured using the RECIST v 1.1. with CT scans performed every 8 weeks for the first year and then every 16 weeks until disease progression. PFS is defined as the time from randomisation to confirmed progression or death form any cause (whichever occurs first).

### Key secondary outcome(s))
1. Overall response is measured using RECIST 1.1 and separately on combined RECIST / GCIG CA125 criteria using CT scans performed every 8 weeks for the first year and then every 16 weeks until disease progression
2. Duration of response
3. Overall survival measured using date of death. Overall survival is defined as the time from the date of randomisation until death from any cause.
4. Safety and tolerability is assessed using the based on toxicities coded using NCI-CTCAE v4.03. Toxicities are reviewed before treatment, Days 1/15/28/42 for all cycles, and at the end of treatment
5. Quality of life is assessed using the EQ-5D-5L questionnaire at baseline, before each cycle of treatment and at the end of treatment
6. resource use for health economic assessment prior to each cycle of treatment and at the end of treatment

### Completion date
23/05/2023

## Eligibility

### Key inclusion criteria
1. Age ≥ 16 years
2. Written informed consent prior to participating in the trial and any trial related procedures being performed
3. Histologically confirmed high-grade serous or Grade 3 endometrioid epithelial ovarian, fallopian tube, or primary peritoneal cancer
3.1. If mixed histology, > 50% of the primary tumour must be confirmed to be high-grade serous or endometrioid upon review by local pathology, with < 50% being 'other', e.g. carcinosarcoma – please contact CTU for advice if uncertain. The high-grade serous / endometrioid sections should be used for FM and translational blocks.
3.2. Patients with high grade ovarian cancer histology of other than serous or endometrioid are also eligible if they are already known to harbour a deleterious germline or somatic BRCA1/2 mutation
NB patients who have an original diagnosis based on cytology only will not be eligible for entry into the trial unless a biopsy confirming criteria above is performed.
4. Received ≥ 1 prior platinum containing chemotherapy regimen(s). Patients can have had up to 3 prior lines (including primary therapy) of therapy for ovarian cancer. Agents administered in the maintenance setting will not be counted as a separate regimen but these must have been stopped at least 28 days prior to trial treatment. Hormonal agents (e.g. tamoxifen, letrozole etc.), anti-angiogenic agents (e.g. bevacizumab, pazopanib, cediranib etc.), and other non-chemotherapy agents will not be counted as a chemotherapy regimen but must have been stopped at least 28 days prior to trial treatment. No previous PARP inhibitor, anti-PD-1 or anti-PDL-1 or CTLA4 therapy.
5. Has documented treatment-free interval of ≥ 3 - < 12 months following the last chemotherapy regimen received. These time points are defined as time between Day 1 last cycle (this does not have to be a platinum but could be single agent liposomal doxorubicin or weekly taxol) and RECIST evaluable disease progression.
6. Has documented platinum free interval of > 3 - <12 months from last platinum containing regimen. These time points are defined as time between Day 1 last cycle and RECIST evaluable disease progression.
7. RECIST evaluable disease (by RECIST criteria v1.1). Patients with CA125 progression in the

absence of RECIST evaluable disease will NOT be eligible.
8. Already known to have a deleterious germline or somatic BRCA1/2 mutation (proof required from local testing) OR be gBRCAwt LoHHIGH or BRCA 1/2 mutant as confirmed by the central laboratory (Foundation Medicine).
Note: Tissue from BRCA mutant patients already identified locally will be required for confirmation. Sufficient archival formalin-fixed paraffin-embedded (FFPE) tumour tissue of adequate quality (see below) must be available for the central laboratory testing. Cytospin blocks from ascites are not acceptable. To be acceptable for Foundation Medicine testing, tumour tissue must be the most recently obtained specimen with at least 30% tumour content, and a minimum of 80% nucleated cellular content. If it is a mixed tumour, the majority of the specimen sent for central testing and translational work should be the high-grade component, e. g. not the carcinosarcoma / clear cell features. In the event that archival tumour tissue is not available a screening biopsy sample must be collected and provided to the central laboratory.
9. Willingness to undergo mandatory biopsy pre cycle 1 day 1, where safe and technically feasible. RECIST target lesions should be avoided if possible. A further biopsy is optional at the end of trial treatment. Patients who do not have disease amenable to biopsy are exempt from the biopsy, provided all other inclusion criteria are met, however they must have archival tumour tissue available for central laboratory (Foundation Medicine) testing.
10. Adequate haematological and biochemical function as indicated below, performed within 14 days prior to randomisation:
10.1. Absolute neutrophil count >1.5 x 109/L
10.2. Platelet count >100 x 109/L
10.3. Haemoglobin >90 g/L (blood / platelet transfusions within 2 weeks prior to randomisation or patients requiring regular haematopoetic support factors or blood transfusions, e.g. 2 or more times in the 4 weeks prior to first dose of trial drug, are not eligible).
10.4. Serum creatinine <1.5 times ULN or creatinine clearance ≥45 mL/min (measured or calculated by Cockcroft and Gault equation/Wright formula); confirmation of creatinine clearance is only required when serum creatinine is >1.5 times the ULN
10.5. Total bilirubin <1.5 times ULN. In cases of Gilbert's syndrome, bilirubin < 2 x ULN is allowed
10.6. Alanine aminotransferase (ALT) or aspartate aminotransferase (AST) <3 times ULN if no demonstrable liver metastases or <5 times ULN in the presence of liver metastases
10.7. Alkaline phosphatase <5 x ULN
10.8. Albumin > 25 g/L
11. Willingness to comply with scheduled visits, treatment plans and laboratory tests and other trial procedures.
12. Evidence of non-childbearing status. For women of childbearing potential:
12.1. negative serum pregnancy test within 7 days of trial treatment
12.2. (Post-menopausal defined as aged more than 50 years and amenorrhoeic for at least 12 months following cessation of all exogenous hormonal treatments, or, women under 50 years old who have been amenorrhoeic for at least 12 months following cessation of all exogenous hormonal treatments and have serum follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels in the post-menopausal range for the institution
OR
12.3. Documentation of irreversible surgical sterilisation by hysterectomy, bilateral oophorectomy or bilateral salpingectomy but not tubal ligation.
13. Patients with synchronous tumours e.g. ovarian and endometrial or history of prior malignancy are eligible provided that there is biopsy evidence that the disease measurable (by RECIST version 1.1, on CT / MRI is ovarian in origin and of appropriate histological types (see above).
14. Ability to swallow oral medication
15. Life expectancy of at least 12 weeks
16. ECOG Performance Status of 0,1

## Participant type(s)
Patient

## Healthy volunteers allowed
No

## Age group
Adult

## Lower age limit
16 years

## Sex
Female

## Total final enrolment
15

## Key exclusion criteria
1. Prior chemotherapy, biological therapy, radiation therapy, hormonal anti-cancer therapy, immunotherapy, other anticancer agents within 28 days of starting trial treatment (not including palliative radiotherapy at focal, non-RECIST target sites). Treatment with any investigational agent within the preceding 4 weeks or within 5 half-lives of the investigational agent, whichever is longer.
2. Any prior PARP inhibitor, anti PD-1 or anti PD-L1, anti-PD-L2, anti-CD137, or cytotoxic T lymphocyte-associated antigen 4 (CTLA4) antibody (including ipilimumab, tremelimumab or any other antibody or drug specifically targeting T-cell co-stimulation or immune checkpoint pathways)
3. Pregnant or lactating women
4. Women of childbearing age and reproductive potential who are not willing, or their male partners are not willing, to use two highly effective forms of contraception. In addition, patients will be excluded if they are not willing to use contraception for the duration of the trial and for 6 months following the last dose of trial treatment.
5. With the exception of alopecia and stable peripheral neuropathy from previous taxanes, any unresolved toxicities from prior chemotherapy should be no greater than CTCAE (Version 4.03) Grade 1 at the time of starting trial treatment
6. Major surgery within 3 weeks or minor surgery within 5 days of trial entry (excluding placement of vascular access devices)
7. Spinal cord compression, known leptomeningeal involvement or brain metastases, unless treated and stable either on physiological doses of steroids (eg <10mg prednisolone) or off steroids altogether for at least 4 weeks prior to randomisation
8. Oral anticoagulants such as warfarin are not permitted. Anticoagulation with low molecular weight heparin and anti-Factor X is allowed. Patients who have a new diagnosis of deep vein thrombosis or pulmonary embolism within 2 weeks of randomisation are permitted if clinically stable on a therapeutic dose of LMWH or anti-Factor X.
9. Any haemopoietic growth factors (e.g., G-CSF, GM-CSF) and blood / platelet transfusions within 2 weeks prior to randomization or patients requiring regular blood transfusions (e.g. 2 or more times in the 4 weeks prior to first dose of trial drug), granulocyte colony-stimulating factor, or platelet transfusions
10. Hospitalization for bowel obstruction within 3 months prior to randomization

11. Any gastrointestinal disorder or defect that would, in the opinion of the Investigator, interfere with absorption of rucaparib
12. Has a known diagnosis of immunodeficiency, active infection including hepatitis B, hepatitis C, and human immunodeficiency virus (screening for these is not required). Receiving systemic steroid therapy or any other form of immunosuppressive therapy within 7 days prior to the first dose of trial treatment. Includes prior organ transplantation including allogenic stem-cell transplant. The following are exceptions to this exclusion criterion:
12.1. Intranasal, inhaled, topical steroids, or local steroid injections (e.g. intra-articular injection)
12.2. Systemic corticosteroids at physiologic doses not to exceed 10 mg/day of prednisone or equivalent
12.3. Steroids as premedication for hypersensitivity reactions (e.g. CT scan premedication)
13. Has a known history of active TB (Bacillus Tuberculosis)
14. Previous additional malignancy that is progressing or has required active treatment in the last 2 years. Please discuss with the CTU if further clarification is required. Exceptions include:
14.1. Non-melanomatous skin cancer (if adequately treated or not requiring treatment)
14.2. Previous DCIS or breast cancer > 5 years as long as adequately treated
14.3. In situ or early (up to stage 1B1) cervical cancer (if adequately treated)
14.4 VIN or vulval cancer (if adequately treated)
14.5. Prior or synchronous endometrial cancer (if adequately treated), provided all of the following criteria are met: G1 or G2, no LVSI and FIGO (2010) stage IA only
15. Has active autoimmune disease that has required systemic treatment in the past 2 years (i.e. with use of disease modifying agents, corticosteroids or immunosuppressive drugs). Replacement therapy (e.g. thyroxine, insulin, or physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency etc.) is not considered a form of systemic treatment. Patients with diabetes type I, vitiligo, psoriasis, hypo- or hyperthyroid disease not requiring immunosuppressive treatment are eligible.
16. Has received a live vaccine within 30 days of planned start of trial therapy. Seasonal influenza vaccines for injection are generally inactivated flu vaccines and are allowed; however intranasal influenza vaccines (e.g. Flu-Mist®) are live attenuated vaccines, and are not allowed.
17. As judged by the Investigator, any evidence of severe or uncontrolled systemic diseases (e.g. severe hepatic impairment, interstitial lung disease [bilateral, diffuse, parenchymal lung disease], uncontrolled chronic renal diseases [glomerulonephritis, nephritic syndrome or renal tubular acidosis], current unstable or uncompensated respiratory or cardiac conditions, uncontrolled hypertension, active bleeding diatheses or active infection, Torsades de Pointes within 12 months of trial entry, known psychiatric or substance abuse disorders that would interfere with cooperation with the requirements of the trial[includes patients with known alcohol or drug abuse])
18. Unsuitable to participate in the trial because the patient is unlikely to comply with trial procedures, restrictions and requirements
19. Hypersensitivity to rucaparib, nivolumab or ipilimumab or any of the excipients

### Date of first enrolment
01/05/2019

### Date of final enrolment
01/06/2022

## Locations

### Countries of recruitment
United Kingdom

England

Northern Ireland

Scotland

Wales

**Study participating centre**
**Mount Vernon Cancer Centre**
Rickmansworth Road
Northwood
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HA6 2RN

**Study participating centre**
**The Beatson West of Scotland Cancer Centre**
1053 Great Western Road
Glasgow
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G12 0YN

**Study participating centre**
**Royal Surrey County Hospital**
Egerton Road
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GU2 7XX

**Study participating centre**
**Western General Hospital, Edinburgh**
Crewe Rd S
Edinburgh
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EH4 2XU

**Study participating centre**
**Churchill Hospital**
Old Road
Headington
Oxford

United Kingdom
OX3 7LE

**Study participating centre**
**Clatterbridge Centre for Oncology**
Clatterbridge Road
Birkenhead
United Kingdom
CH63 4JY

**Study participating centre**
**The Christie**
Wilmslow Road
Manchester
United Kingdom
M20 4BX

**Study participating centre**
**The Royal Marsden**
The Royal Marsden Hospital
203 Fulham Road
Chelsea
London
United Kingdom
SW3 6JJ

**Study participating centre**
**St Bartholomew's Hospital**
W Smithfield
London
United Kingdom
EC1A 7BE

**Study participating centre**
**Worthing Hospital**
Lyndhurst Road
Worthing
United Kingdom
BN11 2DH

**Study participating centre**
**Royal Berkshire Hospital**
Craven Road
Reading
United Kingdom
RG1 5AN

**Study participating centre**
**St James' University Hospital**
Beckett Street
Leeds
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LS9 7TF

**Study participating centre**
**Southampton General Hospital**
Tremona Road
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SO16 6YD

**Study participating centre**
**Kent and Canterbury Hospital**
Ethelbert Road
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CT1 3NG

**Study participating centre**
**Leicester General Hospital**
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LE5 4PW

**Study participating centre**
**Royal United Hospital**
Combe Park

Bath
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BA1 3NG

**Study participating centre**
**Queen Elizabeth Hospital**
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Birmingham
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B15 2WB

**Study participating centre**
**Velindre Cancer Centre**
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CF14 2TL

**Study participating centre**
**Addenbrookes Hospital**
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CB2 0QQ

**Study participating centre**
**Guys and St Thomas Hospitals**
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**Study participating centre**
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NR4 7UY

**Study participating centre**
**Gloucestershire Royal Hospital**
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GL1 3NN

**Study participating centre**
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**Study participating centre**
**Belfast City Hospital**
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BT9 7AB

# Sponsor information

**Organisation**
NHS Greater Glasgow and Clyde

**ROR**

https://ror.org/05kdz4d87

**Organisation**
University of Glasgow

**ROR**
https://ror.org/00vtgdb53

# Funder(s)

**Funder type**
Industry

**Funder Name**
Bristol-Myers Squibb

**Alternative Name(s)**
Bristol-Myers Squibb Company, Bristol Myers Squibb, Bristol-Myers Company, BMS

**Funding Body Type**
Government organisation

**Funding Body Subtype**
For-profit companies (industry)

**Location**
United States of America

**Funder Name**
Clovis Oncology

# Results and Publications

**Individual participant data (IPD) sharing plan**
The datasets generated during and/or analysed during the current study will be stored in a non-publically available repository.

**IPD sharing plan summary**

**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 |