Clinical trial results:
An open-label, randomised, phase 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.

Summary

EudraCT number	2017-004780-13
Trial protocol	GB
Global end of trial date	23 May 2023

Results information

Result version number	v1 (current)
This version publication date	12 April 2025
First version publication date	12 April 2025

Trial information

Trial identification

Sponsor protocol code	CeNturIOn-2016

Additional study identifiers

ISRCTN number	ISRCTN10490346
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	NHS Greater Glasgow & Clyde
Sponsor organisation address	Research & Innovation Department, Admin Building, Level 2, Gartnavel Royal Hospital, Glagsow, United Kingdom, G12 0XH
Public contact	Karen Allan, Glasgow Oncology Clinical Trials Unit, 0141 3017959, karen.allan.3@glasgow.ac.uk
Scientific contact	Karen Allan, Glasgow Oncology Clinical Trials Unit, 0141 3017959, karen.allan.3@glasgow.ac.uk
Sponsor organisation name	University of Glasgow
Sponsor organisation address	Wolfson Medical School Building, University Avenue, University of Glasgow, Glasgow, United Kingdom, G12 8QQ
Public contact	Karen Allan, University of Glasgow, 0141 3017959, karen.allan.3@glasgow.ac.uk
Scientific contact	Karen Allan, University of Glasgow, 0141 3017959, karen.allan.3@glasgow.ac.uk

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No	No

1901/2006 apply to this trial?	

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 May 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 October 2022
Global end of trial reached?	Yes
Global end of trial date	23 May 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To compare the length of remission from ovarian, primary peritoneal and fallopian tube cancer for patients taking rucaparib alone with patients on combinations of rucaparib with nivolumab or nivolumab and ipilimumab. This will be assessed using scan changes to show cancer shrinkage. Only patients with cancer that has come back and whose cancer is likely to respond to rucaparib (based on testing of their cancer tissue) will be recruited.

Protection of trial subjects:

Trial participants were closely monitored while receiving trial treatment, attending clinic appointments fortnightly for the initial 6 weeks then 6-weekly appointments to be assessed by their clinician. For each treatment visit, participants had blood testes taken to make sure their blood count, kidney and liver functions were good enough so that it was safe from them to receive treatment. They were also assessed to make sure they were not having any problems with the trial drugs.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 May 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 15
Worldwide total number of subjects	15
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	8
From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Patients were registered for screening to the safety run-in phase before any screening procedures took place, these included blood test, pregnancy test for women of child bearing potential, CT/MRI scan, physical examination, vital signs and ECG. Following this, patients were then registered for trial treatment if all eligibility criteria were met.

Period 1

Period 1 title	Safety Run-in (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1

Arm description:

Rucaparib 600mg orally twice a day continuously starting on day 1 and Nivolumab 240mg intravenously (IV) on day 1 and repeated every 14 days and Ipilimumab 1mg/kg IV on day 1 and repeated every 42 days. Each cycle was 42 days. Treatment continued until progression, and to a maximum of one year for nivolumab and ipilimumab.

Arm type	Experimental
Investigational medicinal product name	rucaparib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Rucaparib 600mg orally twice a day continuously until progression or unacceptable toxicity. Each cycle is repeated every 6 weeks from cycle 2 onwards. For the first cycle, patients received two-weekly dispensing to ensure tolerability.

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Nivolumab 240mg IV infusion over approximately 30 minutes, administered every 14 days, starting on day 1 (i.e. given on day 1, day 15 and day 29 of each 42 day cycle). On day 1 of each cycle, nivolumab is administered prior to ipilimumab.

Investigational medicinal product name	Ipilimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ipilimumab 1mg/kg IV infusion over approximately 30 minutes, administered every 42 days, starting on day 1 (i.e. given on day 1 of each 42 day cycle). On day 1 of each cycle, nivolumab is administered prior to ipilimumab.

Arm title	Cohort 2

Arm description:

Rucaparib 600mg orally twice a day continuously starting on day 1 and Nivolumab 240mg intravenously (IV) on day 1 and repeated every 14 days and Ipilimumab 1mg/kg IV on day 1 and repeated every 42 days. Each cycle was 42 days. Treatment continued until progression, and to a maximum of one year for nivolumab and ipilimumab.

Please note: After recruitment of 4 patients (3 evaluable) to this second safety cohort, the starting dose of rucaparib was reduced to 400mg orally twice a day. In addition, the maximum number of cycles of ipilimumab was capped at four cycles.

Arm type	Experimental
Investigational medicinal product name	rucaparib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Rucaparib 600mg orally twice a day continuously until progression or unacceptable toxicity. Each cycle is repeated every 6 weeks from cycle 2 onwards. For the first cycle, patients received two-weekly dispensing to ensure tolerability.

Please note: the starting dose of rucaparib was subsequently reduced to 400mg orally twice a day.

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Nivolumab 240mg IV infusion over approximately 30 minutes, administered every 14 days, starting on day 1 (i.e. given on day 1, day 15 and day 29 of each 42 day cycle). On day 1 of each cycle, nivolumab is administered prior to ipilimumab.

Investigational medicinal product name	Ipilimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ipilimumab 1mg/kg IV infusion over approximately 30 minutes, administered every 42 days, starting on day 1 (i.e. given on day 1 of each 42 day cycle). On day 1 of each cycle, nivolumab is administered prior to ipilimumab.

Number of subjects in period 1	Cohort 1	Cohort 2
Started	7	8
Completed	6	6
Not completed	1	2
Unevaluable for DLTs	1	2

Baseline characteristics

Reporting groups

Reporting group title	Cohort 1

Reporting group description:

Rucaparib 600mg orally twice a day continuously starting on day 1 and Nivolumab 240mg intravenously (IV) on day 1 and repeated every 14 days and Ipilimumab 1mg/kg IV on day 1 and repeated every 42 days. Each cycle was 42 days. Treatment continued until progression, and to a maximum of one year for nivolumab and ipilimumab.

Reporting group title	Cohort 2

Reporting group description:

Rucaparib 600mg orally twice a day continuously starting on day 1 and Nivolumab 240mg intravenously (IV) on day 1 and repeated every 14 days and Ipilimumab 1mg/kg IV on day 1 and repeated every 42 days. Each cycle was 42 days. Treatment continued until progression, and to a maximum of one year for nivolumab and ipilimumab.

Please note: After recruitment of 4 patients (3 evaluable) to this second safety cohort, the starting dose of rucaparib was reduced to 400mg orally twice a day. In addition, the maximum number of cycles of ipilimumab was capped at four cycles.

Reporting group values	Cohort 1	Cohort 2	Total
Number of subjects	7	8	15
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
Newborns (0-27 days)			0
Infants and toddlers (28 days-23 months)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
median	67	59.5	
inter-quartile range (Q1-Q3)	64 to 72	56 to 65	-
Gender categorical Units: Subjects			
Female	7	8	15
Male	0	0	0

Subject analysis sets

Subject analysis set title	All Patients
Subject analysis set type	Full analysis

Subject analysis set description:

All patients registered on to the study

Subject analysis set title	Evaluable Population

Subject analysis set type	Sub-group analysis

Subject analysis set description:

Evaluable for DLT assessment period

Reporting group values	All Patients	Evaluable Population	
Number of subjects	15	13	
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous Units: years			
median	64	64	
inter-quartile range (Q1-Q3)	58 to 68	58 to 68	
Gender categorical Units: Subjects			
Female	15	13	
Male	0	0	

End points

End points reporting groups

Reporting group title	Cohort 1

Reporting group description:

Rucaparib 600mg orally twice a day continuously starting on day 1 and Nivolumab 240mg intravenously (IV) on day 1 and repeated every 14 days and Ipilimumab 1mg/kg IV on day 1 and repeated every 42 days. Each cycle was 42 days. Treatment continued until progression, and to a maximum of one year for nivolumab and ipilimumab.

Reporting group title	Cohort 2

Reporting group description:

Rucaparib 600mg orally twice a day continuously starting on day 1 and Nivolumab 240mg intravenously (IV) on day 1 and repeated every 14 days and Ipilimumab 1mg/kg IV on day 1 and repeated every 42 days. Each cycle was 42 days. Treatment continued until progression, and to a maximum of one year for nivolumab and ipilimumab.

Please note: After recruitment of 4 patients (3 evaluable) to this second safety cohort, the starting dose of rucaparib was reduced to 400mg orally twice a day. In addition, the maximum number of cycles of ipilimumab was capped at four cycles.

Subject analysis set title	All Patients
Subject analysis set type	Full analysis

Subject analysis set description:

All patients registered on to the study

Subject analysis set title	Evaluable Population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Evaluable for DLT assessment period

Primary: Dose Limiting Toxicities

End point title	Dose Limiting Toxicities[1]

End point description:

Drug-related DLTs (CTCAE v5) during first 6 weeks of treatment:
- G≥3 haematologic toxicity persistent for >14 consecutive days despite stopping rucaparib
- Persistent G3 AST/ALT with <2.5 x ULN bilirubin and /or alkaline phosphatase < 3 x ULN for >14 days despite stopping rucaparib / nivolumab / ipilimumab
- Any > G2 AST/ALT with > 2.5 x ULN bilirubin and / or alkaline phosphatase >3 x ULN persisting beyond >14 days after stopping all trial medication
- Grade 4 AST/ALT
- Any G3-4 non-haematologic / non-hepatic toxicity not present prior to treatment which, in the opinion of the investigator, in consultation with the SRC, is associated with trial treatment

Patients starting treatment were evaluable if they:
- Completed 6 weeks of protocol therapy with the ipilimumab infusion, 2/3 scheduled nivolumab infusions and 60% rucaparib during this period without a DLT
- Experience a DLT regardless of the amount of protocol therapy delivered

End point type	Primary

End point timeframe:

6 weeks

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This was a safety run-in with no planned statistical analysis.

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6[2]	6[3]		
Units: Patients				
DLT Experienced	0	1		
No DLT Experienced	6	5		

Notes:

[2] - One patient was unevaluable

[3] - 2 patients were unevaluable

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Timeframe for AE

Adverse event reporting additional description:

AE additional description

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Cohort 1

Reporting group description: -

Reporting group title	Cohort 2

Reporting group description: -

Serious adverse events	Cohort 1	Cohort 2	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 7 (85.71%)	6 / 8 (75.00%)	
number of deaths (all causes)	5	2	
number of deaths resulting from adverse events	5	2	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasms benign malignant and unspecified (incl cysts and polyps) - Other specify	Additional description: Neoplasms benign malignant and unspecified (incl cysts and polyps) - Other specify		
subjects affected / exposed	4 / 7 (57.14%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	4 / 4	0 / 0	
deaths causally related to treatment / all	4 / 4	0 / 0	
Vascular disorders			
Hypertension	Additional description: Hypertension		
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pain	Additional description: Pain		
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Non-cardiac chest pain	Additional description: Non-cardiac chest pain		
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions - Other specify	Additional description: General disorders and administration site conditions - Other specify		
subjects affected / exposed	0 / 7 (0.00%)	5 / 8 (62.50%)	
occurrences causally related to treatment / all	0 / 0	6 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fever	Additional description: Fever		
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death NOS	Additional description: Death NOS		
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Respiratory, thoracic and mediastinal disorders			
Pneumothorax	Additional description: Pneumothorax		
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion	Additional description: Pleural effusion		
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Psychosis	Additional description: Psychosis		
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Platelet count decreased	Additional description: Platelet count decreased		

subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutrophil count decreased	Additional description: Neutrophil count decreased		
subjects affected / exposed	0 / 7 (0.00%)	2 / 8 (25.00%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Creatinine increased	Additional description: Creatinine increased		
subjects affected / exposed	1 / 7 (14.29%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Ventricular tachycardia	Additional description: Ventricular tachycardia		
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocarditis	Additional description: Myocarditis		
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation	Additional description: Atrial fibrillation		
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anemia	Additional description: Anemia		
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia	Additional description: Febrile neutropenia		
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			

Colonic obstruction	Additional description: Colonic obstruction		
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Ascites	Additional description: Ascites		
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis	Additional description: Colitis		
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain	Additional description: Abdominal pain		
subjects affected / exposed	0 / 7 (0.00%)	2 / 8 (25.00%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhea	Additional description: Diarrhea		
subjects affected / exposed	1 / 7 (14.29%)	4 / 8 (50.00%)	
occurrences causally related to treatment / all	1 / 1	9 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatic failure	Additional description: Hepatic failure		
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders - Other specify	Additional description: Hepatobiliary disorders - Other specify		
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury	Additional description: Acute kidney injury		
subjects affected / exposed	2 / 7 (28.57%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	4 / 4	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infections and infestations			
Urinary tract infection	Additional description: Urinary tract infection		
subjects affected / exposed	1 / 7 (14.29%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis infectious	Additional description: Enterocolitis infectious		
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations - Other specify	Additional description: Infections and infestations - Other specify		
subjects affected / exposed	1 / 7 (14.29%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Sepsis	Additional description: Sepsis		
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin infection	Additional description: Skin infection		
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Anorexia	Additional description: Anorexia		
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Cohort 1	Cohort 2	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 7 (100.00%)	8 / 8 (100.00%)	
Vascular disorders			

Hypertension	Additional description: Hypertension		
subjects affected / exposed	4 / 7 (57.14%)	2 / 8 (25.00%)	
occurrences (all)	11	3	
General disorders and administration site conditions			
General disorders and administration site conditions - Other specify	Additional description: General disorders and administration site conditions - Other specify		
subjects affected / exposed	6 / 7 (85.71%)	8 / 8 (100.00%)	
occurrences (all)	23	30	
Malaise	Additional description: Malaise		
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Non-cardiac chest pain	Additional description: Non-cardiac chest pain		
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Pain	Additional description: Pain		
subjects affected / exposed	1 / 7 (14.29%)	2 / 8 (25.00%)	
occurrences (all)	4	2	
Respiratory, thoracic and mediastinal disorders			
Dyspnea	Additional description: Dyspnea		
subjects affected / exposed	6 / 7 (85.71%)	7 / 8 (87.50%)	
occurrences (all)	14	20	
Cough	Additional description: Cough		
subjects affected / exposed	5 / 7 (71.43%)	2 / 8 (25.00%)	
occurrences (all)	9	11	
Psychiatric disorders			
Insomnia	Additional description: Insomnia		
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Investigations			
Platelet count decreased	Additional description: Platelet count decreased		
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Creatinine increased	Additional description: Creatinine increased		
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			

Peripheral sensory neuropathy	Additional description: Peripheral sensory neuropathy		
subjects affected / exposed	4 / 7 (57.14%)	5 / 8 (62.50%)	
occurrences (all)	13	9	
Dysgeusia	Additional description: Dysgeusia		
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Blood and lymphatic system disorders			
Anemia	Additional description: Anemia		
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Eye disorders			
Eye pain	Additional description: Eye pain		
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Dry eye	Additional description: Dry eye		
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal disorders			
Abdominal pain	Additional description: Abdominal pain		
subjects affected / exposed	3 / 7 (42.86%)	4 / 8 (50.00%)	
occurrences (all)	8	5	
Vomiting	Additional description: Vomiting		
subjects affected / exposed	5 / 7 (71.43%)	4 / 8 (50.00%)	
occurrences (all)	8	5	
Colitis	Additional description: Colitis		
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Nausea	Additional description: Nausea		
subjects affected / exposed	6 / 7 (85.71%)	8 / 8 (100.00%)	
occurrences (all)	15	16	
Gastric fistula	Additional description: Gastric fistula		
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Dry mouth	Additional description: Dry mouth		
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Diarrhea	Additional description: Diarrhea		

subjects affected / exposed	3 / 7 (42.86%)	7 / 8 (87.50%)	
occurrences (all)	11	15	
Constipation	Additional description: Constipation		
subjects affected / exposed	3 / 7 (42.86%)	1 / 8 (12.50%)	
occurrences (all)	6	3	
Small intestinal obstruction	Additional description: Small intestinal obstruction		
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Hepatobiliary disorders			
Hepatobiliary disorders - Other specify	Additional description: Hepatobiliary disorders - Other specify		
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Pruritus	Additional description: Pruritus		
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	3	0	
Skin ulceration	Additional description: Skin ulceration		
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Palmar-plantar erythrodysesthesia syndrome	Additional description: Palmar-plantar erythrodysesthesia syndrome		
subjects affected / exposed	1 / 7 (14.29%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
Dry skin	Additional description: Dry skin		
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Renal and urinary disorders			
Acute kidney injury	Additional description: Acute kidney injury		
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia	Additional description: Arthralgia		
subjects affected / exposed	2 / 7 (28.57%)	0 / 8 (0.00%)	
occurrences (all)	4	0	
Infections and infestations			

Mucosal infection	Additional description: Mucosal infection		
subjects affected / exposed	2 / 7 (28.57%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Urinary tract infection	Additional description: Urinary tract infection		
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Anorexia	Additional description: Anorexia		
subjects affected / exposed	6 / 7 (85.71%)	7 / 8 (87.50%)	
occurrences (all)	15	14	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 August 2018	The protocol was updated following comments from the initial grounds for non-acceptance from the MHRA.
13 February 2019	The main update to the protocol was to remove the doublet safety run-in cohort for the combination of nivolumab and rucaparib, therefore the trial will start with the triplet combination safety run-in cohort. The other substantial change was to amend the eligibility criteria to allow the inclusion of patients previously treated with a PARP inhibitor and/or immunotherapy (but not when received in combination).
20 December 2019	The main updates to the protocol were to include a pre-screening blood sample for phase II patients, to update the advice given on managing dose reductions of rucaparib, and to allow patients with disease progression on initial RECIST assessments who are continuing to derive clinical benefit to continue on trial treatment to the next imaging time-point.
05 March 2020	The main update to the protocol was to include a second safety run-in cohort of 6 additional patients as the Independent Data Monitoring Committee could not agree to move forward to Phase II as it was judged that patients in the initial safety run-in cohort did not receive sufficient rucaparib. The second safety run-in cohort of patients recruited, must receive ≥60% rucaparib dose across the DLT period of 6 weeks to be evaluable. The eligibility for the additional patients was updated to ensure they have no more than 3 prior lines of therapy (in line with the phase II patients). The dose limiting toxicity criteria with regards to the grade 3 or 4 non-haematologic / non-hepatic toxicity not present prior to treatment commencing was updated.
19 October 2020	To notify of a temporary halt to recruitment, during which the starting dose of IMP Rucaparib was to be evaluated, following the observation of rucapraib-related toxicities in patients recruited to the safety run-in cohort.
14 December 2020	The reason for the amendment was to restart the trial, following a temporary halt to recruitment, during which the starting dose of IMP Rucaparib had been reduced, following the observation of rucapraib-related toxicities in patients recruited to the safety run-in cohort.
21 October 2021	The purpose of this amendment was to implement protocol Version 8 and the following updates: Correction of an inconsistency in the previous protocol version (V7.0) regarding the method of calculating rucaparib compliance in the safety cohorts. The amendment also introduces updates to the Adverse Events of Special Interest (AESIs), and their reporting requirements. The amendment also adds details of remote monitoring. Following a Sponsor risk assessment of the Covid-19 vaccine against the Centurion IMPs, a Covid-19 Vaccine patient letter was introduced to advise that participation in the trial does not impact on the vaccine safety for patients on trial treatment. Ahead of the end of the Brexit transition period, notification of a change in QP oversight for Nivolumab and Ipilimumab supplies imported to GB from January 2022 were provided.
25 May 2022	The amendment was to inform the MHRA and REC that recruitment to the trial had prematurely ended due to the withdrawal of support from Bristol Myers-Squibb (BMS), one of the pharmaceutical companies involved in the trial. The trial would no longer proceed to Phase II.

25 January 2023	The amendment was to update the protocol with details of the close down period for the trial and to confirm the trial would not be moving to phase II.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
19 October 2020	Temporary halt to recruitment, during which the starting dose of IMP Rucaparib was to be evaluated, following the observation of rucapraib-related toxicities in patients recruited to the safety run-in cohort.	14 December 2020
25 May 2022	Recruitment to the trial was prematurely ended due to the withdrawal of support from Bristol Myers-Squibb (BMS), one of the pharmaceutical companies involved in the trial. Recruitment to the trial had previously paused following the completion of the safety run-in phase in August 2021, while waiting for Phase II to open to recruitment. Therefore, no sites were actively recruiting to the trial at the time of this decision. The trial would no longer proceed to Phase II.	-

Notes:

Limitations and caveats

None reported