



Clinical trial results:

The CAPER study: A Phase Ib clinical trial of Cyclophosphamide And PEmbrolizumab in metastatic Renal cell carcinoma (CAPER Trial)

Summary

EudraCT number	2018-004314-17
Trial protocol	GB
Global end of trial date	28 April 2023

Results information

Result version number	v1
This version publication date	30 June 2024
First version publication date	30 June 2024
Summary attachment (see zip file)	CAPER Statistical Analysis Report Version 1.0 (CAPER Final Analysis Report V1.0 20240501.pdf)

Trial information

Trial identification

Sponsor protocol code	CFTSp148
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Additional study identifiers

ISRCTN number	ISRCTN95900287
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	The Christie NHS Foundation Trust
Sponsor organisation address	550 Wilmslow Road, Manchester, United Kingdom, M20 4BX
Public contact	Dr Clare Griffin, Research Integrity and Governance Manager, The Christie NHS Foundation Trust, clare.griffin1@nhs.net
Scientific contact	Dr Clare Griffin, Research Integrity and Governance Manager, The Christie NHS Foundation Trust, clare.griffin1@nhs.net

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 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 May 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 April 2023
Global end of trial reached?	Yes
Global end of trial date	28 April 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate whether the combination of oral metronomic (low doses of drug taken more often) cyclophosphamide and pembrolizumab will lead to objective tumour responses (a measurable shrinking of the tumour) in metastatic clear cell renal carcinoma (cancer of kidney cells that have spread to other parts of the body) patients who have previously progressed on immuno-oncology therapy (therapy that stimulates the immune system to fight cancer).

Protection of trial subjects:

Central and site monitoring is conducted to ensure protection of patients participating in the trial, and that trial procedures, trial intervention administration, and laboratory and data collection processes are of high quality and meet sponsor and, when appropriate, regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 January 2021
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: 9
Worldwide total number of subjects	9
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 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	4
From 65 to 84 years	5

85 years and over	0
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Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Start of screening is defined as when a patient has been provided with the PIS and ICF and has had a discussion with their clinical care team regarding their treatment and the possibility of entry into a trial requiring additional tests.

Period 1

Period 1 title	Main Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Cyclophosphamide and Pembrolizumab
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Arm description:

Cyclophosphamide

- Oral tablet
- 50mg once daily (OD) dosing (metronomic schedule)
- 21-day run-in period prior to commencing pembrolizumab
- Continuous dosing in 21-day cycles throughout (Q3W)

Pembrolizumab

- IV infusion
- 200mg flat dosing Q3W
- Commenced at C2D1 (following cyclophosphamide run-in)
- Continuous dosing Q3W throughout

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

Dosage and administration details:

- Oral tablet
- 50mg once daily (OD) dosing (metronomic schedule)
- 21-day run-in period prior to commencing pembrolizumab
- Continuous dosing in 21-day cycles throughout (Q3W)

Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

- IV infusion
- 200mg flat dosing Q3W
- Commenced at C2D1 (following cyclophosphamide run-in)
- Continuous dosing Q3W throughout

Number of subjects in period 1	Cyclophosphamide and Pembrolizumab
Started	9
Completed	0
Not completed	9
Disease Progression	9

Baseline characteristics

Reporting groups

Reporting group title	Main Trial
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Reporting group description: -

Reporting group values	Main Trial	Total	
Number of subjects	9	9	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	4	4	
From 65-84 years	5	5	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	64.1		
standard deviation	± 9	-	
Gender categorical			
Units: Subjects			
Female	2	2	
Male	7	7	
Ethnicity			
Units: Subjects			
White British	7	7	
Any other white background	1	1	
Asian or Asian British: Indian	1	1	
Smoking Status			
Units: Subjects			
Current Smoker	1	1	
Ex-smoker	6	6	
Never Smoked	2	2	
Alcohol status			
Units: Subjects			
Regular	2	2	
Sporadic	4	4	
None	3	3	
ECOG performance			
Units: Subjects			
Zero	6	6	
One	3	3	
Protein			

Units: Subjects			
Negative	9	9	
Glucose			
Units: Subjects			
Negative	6	6	
Positive	3	3	
Blood			
Units: Subjects			
Negative	4	4	
Trace	4	4	
Positive	1	1	
Presence of sarcomatoid component			
Units: Subjects			
Yes	1	1	
No	7	7	
Missing	1	1	
Current TNM Stage			
Units: Subjects			
TX/NX/M1	1	1	
TX/N0/M1	2	2	
TX/N1/M1	2	2	
T1/N0/M1	1	1	
T3/NX/M1	1	1	
T4/N0/M1	1	1	
T4/N1/M1	1	1	
Fuhrman Grade			
Units: Subjects			
Two	1	1	
Three	3	3	
Four	4	4	
Missing	1	1	
IMDC prognostic group classification			
Units: Subjects			
Zero	2	2	
One	2	2	
Two	4	4	
Three	1	1	
Surgery for RCC			
Units: Subjects			
Yes	7	7	
No	2	2	
Radiotherapy for RCC			
Units: Subjects			
Yes	1	1	
No	8	8	
Systemic therapy for RCC			
Units: Subjects			
Yes	9	9	
Nitrites			
Units: Subjects			
Negative	9	9	

Number of years smoking			
This is only for the seven people that smoked.			
Units: Years			
arithmetic mean	21.1		
standard deviation	± 14.2	-	
Number of cigarettes per day			
This is for the seven smokers			
Units: Cigarettes			
arithmetic mean	12.4		
standard deviation	± 9.9	-	
Height			
Units: cm			
arithmetic mean	169.8		
standard deviation	± 9.8	-	
Weight			
Units: kg			
arithmetic mean	84.5		
standard deviation	± 19.2	-	
Systolic Blood Pressure			
Units: mmHg			
arithmetic mean	132.7		
standard deviation	± 8	-	
Diastolic blood pressure			
Units: mmHg			
arithmetic mean	75.1		
standard deviation	± 5.8	-	
Temperature			
Units: degrees Celsius			
arithmetic mean	36.5		
standard deviation	± 0.5	-	
Respiratory rate			
Units: breaths per minute			
arithmetic mean	15.9		
standard deviation	± 2.3	-	
Pulse rate			
Units: beats per minute			
arithmetic mean	81		
standard deviation	± 9.8	-	
Oxygen saturation			
Units: percentage			
arithmetic mean	97.3		
standard deviation	± 1.5	-	
Haemoglobin			
Units: g/L			
arithmetic mean	135.3		
standard deviation	± 7.5	-	
White blood cell count			
Units: x10 ⁹ /L			
arithmetic mean	9.5		
standard deviation	± 1.5	-	
Platelets			
Units: x10 ⁹ /L			

arithmetic mean standard deviation	295.4 ± 79.3	-	
Red blood cell count Units: x10 ⁹ /L arithmetic mean standard deviation	4.9 ± 0.4	-	
Haematocrit Units: L/L arithmetic mean standard deviation	0.4 ± 0	-	
Prothrombin time Units: seconds arithmetic mean standard deviation	11.7 ± 0.9	-	
Absolute neutrophil count Units: x10 ⁹ /L arithmetic mean standard deviation	6.8 ± 1.4	-	
Eosinophils Units: x10 ⁹ /L arithmetic mean standard deviation	0.2 ± 0.1	-	
Basophils Units: x10 ⁹ /L arithmetic mean standard deviation	0 ± 0	-	
Lymphocytes Units: x10 ⁹ /L arithmetic mean standard deviation	1.8 ± 0.4	-	
Monocyte levels Units: x10 ⁹ /L arithmetic mean standard deviation	0.5 ± 0.2	-	
INR Units: INR arithmetic mean standard deviation	1.0 ± 0.1	-	
Sodium Units: mmol/L arithmetic mean standard deviation	136.9 ± 2	-	
Potassium Units: mmol/L arithmetic mean standard deviation	4.6 ± 0.4	-	
Urea Units: mmol/L arithmetic mean standard deviation	6.5 ± 3	-	
Creatinine Units: µmol/L			

arithmetic mean standard deviation	98.4 ± 22.7	-	
GFR Units: ml/min arithmetic mean standard deviation	68 ± 21.5	-	
Alkaline phosphatase Units: IU/L arithmetic mean standard deviation	98.9 ± 23.4	-	
Bilirubin Units: µmol/L arithmetic mean standard deviation	7.4 ± 4	-	
Calcium – unadjusted Units: mmol/L arithmetic mean standard deviation	2.4 ± 0.2	-	
Magnesium Units: mmol/L arithmetic mean standard deviation	0.8 ± 0.1	-	
Phosphate Units: mmol/L arithmetic mean standard deviation	1.1 ± 0.2	-	
Alanine aminotransferase Units: ul/L arithmetic mean standard deviation	25.2 ± 17.6	-	
Lactate dehydrogenase Units: IU/L arithmetic mean standard deviation	183.1 ± 31.9	-	
Total protein Units: g/L arithmetic mean standard deviation	70.1 ± 3.1	-	
Albumin Units: g/L arithmetic mean standard deviation	42.2 ± 3.6	-	
Glucose Units: mmol/L arithmetic mean standard deviation	9.2 ± 5.8	-	
Free T4 Units: mmol/L arithmetic mean standard deviation	16.4 ± 3.1	-	
Thyroid stimulating hormone Units: mIU/L			

arithmetic mean standard deviation	2.6 ± 1.4	-	
Specific gravity Units: Specific gravity arithmetic mean standard deviation	114.2 ± 339.7	-	
pH Units: pH arithmetic mean standard deviation	6 ± 0.6	-	
Time from initial diagnosis to registration Units: days arithmetic mean standard deviation	2589.6 ± 1630.3	-	
Time from metastatic disease confirmation to registration Units: days arithmetic mean standard deviation	1728.9 ± 1344.8	-	
Sum of lesion diameter Units: mm arithmetic mean standard deviation	94.7 ± 58.5	-	
Activated Partial Thromboplastin Time Units: Seconds arithmetic mean standard deviation	26.9 ± 3.5	-	

End points

End points reporting groups

Reporting group title	Cyclophosphamide and Pembrolizumab
Reporting group description:	
Cyclophosphamide	
<ul style="list-style-type: none">• Oral tablet• 50mg once daily (OD) dosing (metronomic schedule)• 21-day run-in period prior to commencing pembrolizumab• Continuous dosing in 21-day cycles throughout (Q3W)	
Pembrolizumab	
<ul style="list-style-type: none">• IV infusion• 200mg flat dosing Q3W• Commenced at C2D1 (following cyclophosphamide run-in)• Continuous dosing Q3W throughout	

Primary: Object response as per RECIST

End point title	Object response as per RECIST ^[1]
End point description:	

End point type	Primary
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End point timeframe:

The primary endpoint of the trial is ORR according to RECIST version 1.1 from baseline until end of study or death, and will be calculated using the best response achieved during study treatment for each participant.

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: Due to the trial being stopped early, there was no statistical analyses conducted.

End point values	Cyclophosphamide and Pembrolizumab			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Participants				
Progressive Disease	3			
Stable Disease	6			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression free survival

End point title	Progression free survival
End point description:	

End point type	Secondary
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End point timeframe:

PFS, measured from the time of first treatment to the time of first documented progression or the

End point values	Cyclophosphamide and Pembrolizumab			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Months				
median (confidence interval 95%)	3.9 (1.2 to 8.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

End point title	Overall survival
End point description: 12 month survival probability is reported as the median survival time could not be calculated.	
End point type	Secondary
End point timeframe: OS, defined as the time from first treatment to death by any cause in months	

End point values	Cyclophosphamide and Pembrolizumab			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Probability				
number (confidence interval 95%)	0.9 (0.4 to 1.0)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Safety and tolerability of the combination of cyclophosphamide and pembrolizumab, reported following the CTCAE version 5 guidelines

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	24
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Reporting groups

Reporting group title	Safety
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Reporting group description:

Participants had to have had at least once dose of medication.

Serious adverse events	Safety		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 9 (22.22%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events	0		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Safety		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 9 (100.00%)		
Investigations			
Biopsy			

subjects affected / exposed occurrences (all)	2 / 9 (22.22%) 2		
Injury, poisoning and procedural complications Procedural pain subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 2		
Nervous system disorders Hemiparesis subjects affected / exposed occurrences (all) Neuralgia subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1 1 / 9 (11.11%) 1		
General disorders and administration site conditions Chest discomfort subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all) Mucosal inflammation subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1 4 / 9 (44.44%) 5 1 / 9 (11.11%) 1		
Gastrointestinal disorders Abdominal distension subjects affected / exposed occurrences (all) Frequent bowel movements subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 2 1 / 9 (11.11%) 1 4 / 9 (44.44%) 5		
Respiratory, thoracic and mediastinal disorders			

Cough subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 2		
Epistaxis subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Haemoptysis subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Nasal congestion subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 2		
Rash subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Psychiatric disorders Affect lability subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Insomnia subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Irritability subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Back pain subjects affected / exposed occurrences (all)	2 / 9 (22.22%) 2		

Musculoskelatal pain subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Neck pain subjects affected / exposed occurrences (all)	2 / 9 (22.22%) 2		
Infections and infestations			
Abscess limb subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 2		
COVID-19 subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Infection subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Lower respiratory tract infection subjects affected / exposed occurrences (all)	2 / 9 (22.22%) 2		
Onychomycosis subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Urinary tract infection subjects affected / exposed occurrences (all)	2 / 9 (22.22%) 2		
Tooth abscess subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	2 / 9 (22.22%) 2		
Hypercalcaemia subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Hypocalcaemia			

subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 July 2021	<p>This version was no approved by the MHRA</p> <p>Main changes were:</p> <ul style="list-style-type: none">- Clarification on End of Trial Definition in line with LCTC protocol template- Update to inclusion criterion 12: male participants contraception/abstinence timeframe from 180 days to 210 days; and inclusion criterion 13: female participants contraception/abstinence timeframe from 180 days to 150 days- Update to Exclusion criterion 14 with inclusion of interstitial lung disease to align with MSD protocol template- Update to male participants contraception/abstinence timeframe from 180 days to 210 days; and female participants contraception/abstinence timeframe from 180 days to 150 days- Update to dose modification guidance for pembrolizumab for immune-related AEs to align with MSD protocol template- Update to dose modification & toxicity management table for pembrolizumab for immune-related AEs to align with MSD protocol- Update to table to clarify what constitutes an SAE in line with regulatory definitions and funder AESI- Clarification on archiving responsibilities of sites and organisations involved in the study
17 November 2021	<ul style="list-style-type: none">- Update to inclusion criterion 13: female participants contraception/abstinence timeframe from 150 days to 180 days- Update to female participants contraception/abstinence timeframe from 150 days to 180 days
16 December 2021	<p>Main changes were -</p> <ul style="list-style-type: none">- Update to inclusion criterion 3: clarification on previous IO therapies patients can have received- Update to exclusion criterion 1: clarification on previous IO therapies patients can have received- Update on exclusion criterion 3: clarification to allow prior use of pembrolizumab for the CAPER study as per inclusion criterion 3- Clarification that investigator can perform physical examinations if clinically indicated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
28 April 2023	The sponsor and CI have taken the decision to terminate the trial early due to poor recruitment and lack of funding.	-

Notes:

Limitations and caveats

None reported