Clinical trial results:
A Phase II Pilot Trial Of Paclitaxel Protein Bound Plus Cisplatin Plus Gemcitabine and the Addition Of Paricalcitol Upon Disease Progression in Patients With Previously Untreated Metastatic Pancreatic Ductal Adenocarcinoma

Summary

EudraCT number	2017-004467-13
Trial protocol	GB
Global end of trial date	19 September 2023
Results information	
Result version number	v1 (current)
This version publication date	02 May 2025
First version publication date	02 May 2025
Summary attachment (see zip file)	Abstract CT214: Proceedings of the American Association for Cancer Research Annual Meeting 2024 (Abstract CT214 Paricalcitol addition to chemotherapy in patients with previously untreated metastat.pdf)

Trial information

Trial identification	
Sponsor protocol code	012255
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04054362
WHO universal trial number (UTN)	-

Notes:

Sponsors	
Sponsor organisation name	Barts Health NHS Trust
Sponsor organisation address	Joint Research and Management Office, 5 Walden Street, London, United Kingdom, E1 2EF
Public contact	Dr David Propper, Barts Health NHS Trust, 44 2034655051, bci-pinball@qmul.ac.uk
Scientific contact	Dr David Propper, Barts Health NHS Trust, 44 2034655051, bci-pinball@qmul.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 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 September 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 September 2022
Global end of trial reached?	Yes
Global end of trial date	19 September 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the clinical benefit of adding paricalcitol to the regimen of paclitaxel protein bound plus cisplatin plus gemcitabine for patients with progressive metastatic pancreatic ductal adenocarcinoma.

Protection of trial subjects:

Pancreatic cancer patients require new treatments that are better tolerated and with fewer associated toxicities. This combination has demonstrated anti-tumour activity previously.
The sequence of drug administration for patients receiving the standard two drug combination was paclitaxel protein bound followed by gemcitabine. For patients receiving the triple regimen, paclitaxel protein bound was given first, then after adequate hydration, cisplatin was given. Gemcitabine was given last because paclitaxel protein bound decreases cytidine deaminase which potentiates gemcitabine activity (less degradation of gemcitabine by the enzyme). When paricalcitol was added to the regimens it was e given last as in previously published studies (NCT02930902, NCT02754726).

Patients were treated with the two or three drug chemotherapy combination alone until upon reassessment they have stable or progressive disease. It was a decision by the Principal Investigator (PI) which of the two chemotherapy regimens were given. At this point the participants were given Paricalcitol with a paired biopsy.

Background therapy: -
Evidence for comparator: -

Actual start date of recruitment	02 April 2018
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: 13
Worldwide total number of subjects	13
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)	13
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 26 participants were enrolled at Barts Health NHS Trust in the UK.

Of these, 13 participants started paricalcitol, therefore making them evaluable. The following analyses are limited to these 13 participants.

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	13
Intermediate milestone: Number of subjects	Started Paricalcitol: 13
Number of subjects completed	13

Period 1

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

Arms

Arm title	Paricalcitol addition to chemotherapy

Arm description:

Evalulable patients were patients that met the eligibility criteria and have received at least 1 dose of paricalcitol.

Arm type	Experimental
Investigational medicinal product name	Paricalcitol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Solution for injection

Dosage and administration details:

Fixed dose of 25 mcg over 5 minutes as slow push

Number of subjects in period 1	Paricalcitol addition to chemotherapy
Started	13
Completed	13

Baseline characteristics

Reporting groups	
Reporting group title	Paricalcitol

Reporting group description: -

Reporting group values	Paricalcitol	Total	
Number of subjects	13	13	
Age categorical Units: Subjects			
Adults (18-64 years)	11	11	
From 65-84 years	2	2	
85 years and over	0	0	
Age continuous Units: years			
median	59		
full range (min-max)	43 to 73	-	
Gender categorical Units: Subjects			
Female	6	6	
Male	7	7	

End points

End points reporting groups

Reporting group title	Paricalcitol addition to chemotherapy

Reporting group description:

Evalulable patients were patients that met the eligibility criteria and have received at least 1 dose of paricalcitol.

Primary: Objective Response Rate

End point title	Objective Response Rate[1]

End point description:

End point type	Primary

End point timeframe:

Objective response rate after addition of paricalcitol

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: Single arm study result. Of 12 evaluable participants, 5 (41.7%) achieved ORR (15.2–72.3%). No p-value or CI available for this result.

End point values	Paricalcitol addition to chemotherapy			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: percentage ORR	5			

Statistical analyses

No statistical analyses for this end point

Primary: Disease control rate

End point title	Disease control rate[2]

End point description:

Of 11 participants evaluable at 9 weeks, 2 (18.2%) achieved DCR (2.3–51.8%).

End point type	Primary

End point timeframe:

From starting paricalcitol to 9 weeks.

Notes:

[2] - 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: Single arm study result. Of 11 participants evaluable at 9 weeks, 10 (90.9%) achieved DCR (58.7–99.8%).

End point values	Paricalcitol addition to chemotherapy			
Subject group type	Reporting group			
Number of subjects analysed	11[3]			
Units: number of patients	2			

Notes:

[3] - 2 patients did not have post paricalcitol scans.

Statistical analyses

No statistical analyses for this end point

Primary: Time to disease progression after paricalcitol

End point title	Time to disease progression after paricalcitol[4]

End point description:

PFS is defined as the interval from the date of the addition of paricalcitol to the earliest date of documented evidence of recurrent or progressive disease, or the date of death due to any cause, whichever occurs.

End point type	Primary

End point timeframe:

Time from starting paricalcitol to disease progression

Notes:

[4] - 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: Single arm study result. 13 participants had disease progression or died after starting paricalcitol. Median (95% CI) time from starting paricalcitol to progression was 1.6 (1.1—2.4) months.

End point values	Paricalcitol addition to chemotherapy			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: month				
number (confidence interval 95%)	1.6 (1.1 to 2.4)			

Statistical analyses

No statistical analyses for this end point

Primary: Overall Survival

End point title	Overall Survival[5]

End point description:

End point type	Primary

End point timeframe:

Overall survival was measured from the addition of paricalcitol to the date of death due to any cause, or the date of last contact (censored observations).

Notes:

[5] - 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: Single arm study result. 13 patients died after starting paricalcitol. Median (95% CI) time

from starting paricalcitol to death was 4.6 (2.2—10.4) months.

End point values	Paricalcitol addition to chemotherapy			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: month				
number (confidence interval 95%)	4.6 (2.2 to 10.4)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From informed consent until safety visit post treatment.	
Adverse event reporting additional description:	
Only AE's during paricalcitol treatment reported here.	
Assessment type	Systematic

Dictionary used	
Dictionary name	CTCAE
Dictionary version	4.03

Reporting groups	
Reporting group title	Paricalcitol addition to chemotherapy
Reporting group description:	
Evalulable patients were patients that met the eligibility criteria and have received at least 1 dose of paricalcitol.	

Serious adverse events	Paricalcitol addition to chemotherapy		
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 13 (61.54%)		
number of deaths (all causes)	13		
number of deaths resulting from adverse events	0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	3 / 13 (23.08%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Ascites			

subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pleural Effusion			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Paricalcitol addition to chemotherapy		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 13 (23.08%)		
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Shortness of Breath			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 August 2019	Change in treatment options, change in CI & Barts PI, administrative changes throughout protocol and PIS. Updated docs included: protocol, PIS, GP letter, patient card
28 May 2020	Change in treatment, to allow patients to enter directly into the study at the add on paricalcitol stage. Updated docs: Protocol and PIS.
16 March 2021	Updated SmPC's (all four updated). PIS' updated to incorporate RSI updates. Updates to the inclusion/exclusion criteria (Cr cl range updated and history of hearing impairment for those without cisplatin). Minor administrative changes to the PIS and protocol. Extend end of study to 30Sep22.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Monitoring activities were severely limited during the COVID-19 pandemic, and an extension to data cleaning was requested following the end of trial date of 30th September 2022, to 12th May 2023.

Notes: