



## Clinical trial results:

### Comparison of ambulatory glucose profile prior to and during pancreatic enzyme replacement therapy in patients with diabetes and pancreatic exocrine insufficiency: a single-arm phase IV trial

#### Summary

EudraCT number	2017-001227-45
Trial protocol	GB
Global end of trial date	31 May 2019

#### Results information

Result version number	v1 (current)
This version publication date	02 June 2022
First version publication date	02 June 2022

#### Trial information

##### Trial identification

Sponsor protocol code	PHT/2017/20
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##### Additional study identifiers

ISRCTN number	ISRCTN14889127
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

##### Sponsors

Sponsor organisation name	Portsmouth Hospitals NHS Trust
Sponsor organisation address	Queen Alexandra Hospital, Portsmouth, United Kingdom, PO6 3LY
Public contact	Linda Harndahl , Portsmouth Hospitals NHS Trust, 0044 02392286236, research.office@porthosp.nhs.uk
Scientific contact	Michael Cummings , Portsmouth Hospitals NHS Trust, 0044 02392286000, michael.cummings@porthosp.nhs.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	31 May 2019
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	31 May 2019
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To compare glucose variability in patients with diabetes and pancreatic exocrine insufficiency before starting pancreatic enzyme replacement therapy and 6 weeks after starting pancreatic enzyme replacement therapy.

Protection of trial subjects:

The study was conducted in accordance with the Declaration of Helsinki, the International Conference on Harmonisation (ICH) and Good Clinical Practice guidelines. All regulatory, safety and other requirements for patient safety were maintained throughout the study.

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

Actual start date of recruitment	01 June 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 19
Worldwide total number of subjects	19
EEA total number of subjects	19

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)	14

From 65 to 84 years	5
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

19 participants were recruited from study opening (July 2017) until study closure in May 2019. All recruited participants completed the study; no participants withdrew.

### Pre-assignment

Screening details:

Potential participants were screened against eligibility criteria prior to enrolment in the study. There was no screening test or other procedure carried out. Only those meeting all eligibility criteria were approached, consented and recruited and proceeded to undertake study-related activities.

### Period 1

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

### Arms

Are arms mutually exclusive?	No
<b>Arm title</b>	Pre-PERT

Arm description:

To compare glucose variability (represented by mean interquartile range (IQR) over 2 weeks) in patients with diabetes and PEI prior to starting PERT

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

Dosage and administration details:

1–2 capsules, dose to be taken with each meal either taken whole or contents mixed with acidic fluid or soft food (then swallowed immediately without chewing)

<b>Arm title</b>	6 weeks after starting PERT
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Arm description:

To compare glucose variability (represented by mean interquartile range (IQR) over 2 weeks) in patients with diabetes and PEI 6 weeks after starting PERT

Arm type	Active comparator
Investigational medicinal product name	Creon
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1–2 capsules, dose to be taken with each meal either taken whole or contents mixed with acidic fluid or soft food (then swallowed immediately without chewing)

<b>Number of subjects in period 1</b>	Pre-PERT	6 weeks after starting PERT
Started	19	19
Completed	19	19

## Baseline characteristics

### Reporting groups

Reporting group title	study period
Reporting group description: -	

Reporting group values	study period	Total	
Number of subjects	19	19	
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)	18	18	
From 65-84 years	1	1	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	60.83		
standard deviation	± 10.90	-	
Gender categorical			
Units: Subjects			
Female	9	9	
Male	10	10	

### Subject analysis sets

Subject analysis set title	Within participant before and after treatment with PERT
Subject analysis set type	Per protocol

Subject analysis set description:

For the purposes of this study, a decrease in mean 24-hour IQR of 1mmol/l is considered to be clinically significant

Reporting group values	Within participant before and after treatment with PERT		
Number of subjects	19		
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)	18		
From 65-84 years	1		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean	60.83		
standard deviation	± 10.90		
Gender categorical			
Units: Subjects			
Female	9		
Male	10		

## End points

### End points reporting groups

Reporting group title	Pre-PERT
Reporting group description: To compare glucose variability (represented by mean interquartile range (IQR) over 2 weeks) in patients with diabetes and PEI prior to starting PERT	
Reporting group title	6 weeks after starting PERT
Reporting group description: To compare glucose variability (represented by mean interquartile range (IQR) over 2 weeks) in patients with diabetes and PEI 6 weeks after starting PERT	
Subject analysis set title	Within participant before and after treatment with PERT
Subject analysis set type	Per protocol
Subject analysis set description: For the purposes of this study, a decrease in mean 24-hour IQR of 1mmol/l is considered to be clinically significant	

### Primary: Mean glucose interquartile range

End point title	Mean glucose interquartile range
End point description:	
End point type	Primary
End point timeframe: Collected over 14 days using the Freestyle Libre Pro glucose monitoring system prior to and 6 weeks after starting PERT therapy.	

End point values	Pre-PERT	6 weeks after starting PERT	Within participant before and after treatment with PERT	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	19	19	19	
Units: mmol/l				
number (not applicable)	19	19	19	

### Statistical analyses

Statistical analysis title	Comparisons before and after PERT using T-test
Statistical analysis description: Simple descriptive statistical analysis will be undertaken to describe the parameters and groups, and will depend on whether the data is normally distributed or not. Within patient comparisons will either be undertaken using Paired t-test or Wilcoxon signed rank test. Across group comparison will be undertaken using either the Two-sample t-test or Mann-Whitney U test.	
Comparison groups	Pre-PERT v 6 weeks after starting PERT v Within participant before and after treatment with PERT



Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05 <sup>[1]</sup>
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)

Notes:

[1] -  $p < 0.05$  was taken to be significant at the 95% confidence level

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse events were continuously monitored over a 10 week period as per the participant's involvement in the study.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
Dictionary version	21

### Reporting groups

Reporting group title	Non-serious adverse events
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Reporting group description:

A related AE is defined as an AE which is considered, by the Chief Investigator (CI), Principal Investigator (PI) or the Sponsor, to have a reasonable causal relationship with the subject's participation in the study. This includes any AE that would not ordinarily have occurred but for that subject's participation in the research protocol. The expression 'reasonable causal relationship' means to convey, in general, that there is evidence or argument to suggest a causal relationship, namely that the event is 'possibly', 'probably' or 'definitely' caused by the research protocol.

Serious adverse events	Non-serious adverse events		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Non-serious adverse events		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 8 (100.00%)		
Injury, poisoning and procedural complications			
Cracked tooth	Additional description: Tooth cracked and fell out.		
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	8		
Burnt throat on hot food	Additional description: Burnt throat on hot food, patient		
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	8		
Vascular disorders			

Erythema  subjects affected / exposed  occurrences (all)	Additional description: Increasing erythema and discomfort in legs in region of chronic vascular skin changes		
	1 / 8 (12.50%)  8		
Surgical and medical procedures  Planned tooth extraction  subjects affected / exposed  occurrences (all)	Additional description: Attended dentist for planned tooth extraction due to longstanding problem. Simple procedure, quick recovery.		
	1 / 8 (12.50%)  8		
Gastrointestinal disorders  Increased nausea  subjects affected / exposed  occurrences (all)   Gastroenteritis and coryzal illness.  subjects affected / exposed  occurrences (all)	Additional description: Increased nausea, on background of known gastroparesis.		
	1 / 8 (12.50%)  8		
	Additional description: Unwell with gastroenteritis and coryzal illness. Self resolving.		
	1 / 8 (12.50%)  8		
Musculoskeletal and connective tissue disorders  Minor fall  subjects affected / exposed  occurrences (all)	Additional description: Minor fall, resulting in back / shoulder pain on background of pre-existing back pain. Required additional medication from GP.		
	1 / 8 (12.50%)  8		
Infections and infestations  Coryzal symptoms,  subjects affected / exposed  occurrences (all)	Additional description: Coryzal symptoms, sore throat, dry cough, laryngitis, self managed		
	1 / 8 (12.50%)  8		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported