



Clinical trial results:

Detection of paracetamol concentration in blood-, saline- and urine samples with an electrochemical indicator in healthy volunteers - a validation study for a novel technique.

Summary

EudraCT number	2020-002908-39
Trial protocol	FI
Global end of trial date	06 October 2023

Results information

Result version number	v1 (current)
This version publication date	03 December 2023
First version publication date	03 December 2023
Summary attachment (see zip file)	Introduction of an electrochemical point-of-care assay for quantitative determination of paracetamol in finger-prick capillary whole blood samples (Brit J Clinical Pharma - 2023 - Kujala - Introduction of an electrochemical pointofcare assay for quantitative (1).pdf)

Trial information

Trial identification

Sponsor protocol code	FEPODPara2020-1
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04690673
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Helsinki University Hospital
Sponsor organisation address	Stenbäckinkatu 9, Helsinki, Finland, 00290
Public contact	Johanna Kujala, Helsinki University Hospital, johanna.kujala@helsinki.fi
Scientific contact	Johanna Kujala, Helsinki University Hospital, johanna.kujala@helsinki.fi

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	13 April 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 April 2022
Global end of trial reached?	Yes
Global end of trial date	06 October 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective was to assess whether a novel electrochemical tool is reliable in detecting concentration of paracetamol in fingerprick-, saline-, urine-, and serum samples. We recruited 12 healthy volunteers, ages 18-45. They were delivered 1 g oral paracetamol. Paracetamol concentration was detected from abovementioned samples at timely intervals for 12 hours, analyzed with the novel electrochemical method and compared to gold standard mass-spectrometry analysis.

Protection of trial subjects:

The trial included 12 volunteered adults, who were given one single dose of paracetamol 1 gram. This dose can be considered non-harmful.

Data of the subjects and their privacy was considered carefully during and after the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 November 2020
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	Finland: 12
Worldwide total number of subjects	12
EEA total number of subjects	12

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)	12
From 65 to 84 years	0

85 years and over	0
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Subject disposition

Recruitment

Recruitment details:

The subjects were recruited by announcements in the social media platforms for university students. 15 persons volunteered. 3 persons were excluded from the study due to contraindications (medication or tobacco use). 12 were recruited.

Pre-assignment

Screening details:

Volunteers were recruited in accordance with the WMA Helsinki Declaration's ethical principles. For screening, medical history, laboratory tests including blood count, kidney and liver function and pregnancy tests for women, and physical examination were performed.

Period 1

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

Blinding implementation details:

This was a pharmacokinetic study, no blinding.

Arms

Arm title	Pharmacokinetic study
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Arm description:

All volunteers were introduced to the pharmacokinetic study

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

Dosage and administration details:

The volunteers entered the study premises after overnight fasting. A single dose of oral paracetamol 1 g was administered with 200 ml lukewarm water.

Number of subjects in period 1	Pharmacokinetic study
Started	12
Completed	12

Baseline characteristics

Reporting groups

Reporting group title	Pharmacokinetic measurements
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Reporting group description:

Twelve healthy subjects aged 18–28 years, nine male, three female, European origin, were recruited; BMIs were 21–28 kg/m² (median 23); all completed.

Reporting group values	Pharmacokinetic measurements	Total	
Number of subjects	12	12	
Age categorical			
All subjects were adults.			
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)	12	12	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female	3	3	
Male	9	9	

Subject analysis sets

Subject analysis set title	Pharmacokinetic study
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Subject analysis set type	Per protocol
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Subject analysis set description:

Volunteers ingested 1 g of paracetamol (Para-Tabs® 1 g, Orion Pharma, Finland) with 200 mL of water after overnight fasting. They had standardized meals four and eight hours after the paracetamol.

Paired finger-prick and venous blood samples were collected prior to paracetamol administration, followed by sampling at timepoints 0.5; 1.0; 1.5; 2.0; 3.0; 4.0; 6.0; 8.0 and 12 h.

Venous blood samples were centrifuged to plasma and frozen at -80°C for later HPLC-MS/MS analysis.

Capillary finger-prick samples were collected for fast electrochemical POC analysis, and duplicate capillary blood samples with the VAMS Mitra® Cartridge Blood Sampling Device (Neoteryx, CA, USA) for later HPLC-MS/MS analysis.

Reporting group values	Pharmacokinetic study		
Number of subjects	12		
Age categorical			
All subjects were adults.			
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)	12		
From 65-84 years	0		
85 years and over	0		
Gender categorical			
Units: Subjects			
Female	3		
Male	9		

End points

End points reporting groups

Reporting group title	Pharmacokinetic study
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Reporting group description:

All volunteers were introduced to the pharmacokinetic study

Subject analysis set title	Pharmacokinetic study
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Subject analysis set type	Per protocol
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Subject analysis set description:

Volunteers ingested 1 g of paracetamol (Para-Tabs® 1 g, Orion Pharma, Finland) with 200 mL of water after overnight fasting. They had standardized meals four and eight hours after the paracetamol. Paired finger-prick and venous blood samples were collected prior to paracetamol administration, followed by sampling at timepoints 0.5; 1.0; 1.5; 2.0; 3.0; 4.0; 6.0; 8.0 and 12 h. Venous blood samples were centrifuged to plasma and frozen at -80°C for later HPLC-MS/MS analysis. Capillary finger-prick samples were collected for fast electrochemical POC analysis, and duplicate capillary blood samples with the VAMS Mitra® Cartridge Blood Sampling Device (Neoteryx, CA, USA) for later HPLC-MS/MS analysis.

Primary: Cmax POC Capillary

End point title	Cmax POC Capillary ^[1]
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End point description:

Pharmacokinetic parameters of paracetamol from capillary whole blood samples with the novel electrochemical point-of-care (POC) method

End point type	Primary
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End point timeframe:

0- 12 hours.

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 is a concentration measurement. Data were presented as geometric means with geometric coefficients of variation as percentage.

End point values	Pharmacokinetic study			
Subject group type	Subject analysis set			
Number of subjects analysed	12			
Units: mmol/l				
geometric mean (geometric coefficient of variation)	101.73 (± 21)			

Statistical analyses

No statistical analyses for this end point

Primary: Tmax POC Capillary

End point title	Tmax POC Capillary ^[2]
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End point description:

Pharmacokinetic parameters of paracetamol from capillary whole blood samples with the novel electrochemical point-of-care (POC) method

End point type	Primary
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End point timeframe:

0-12 h

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: This is a concentration measurement. Data were presented as geometric means with geometric coefficients of variation as percentage.

End point values	Pharmacokinetic study			
Subject group type	Subject analysis set			
Number of subjects analysed	12			
Units: hour				
median (full range (min-max))	0.5 (0.5 to 2)			

Statistical analyses

No statistical analyses for this end point

Primary: AUC 0-last POC Capillary

End point title AUC 0-last POC Capillary^[3]

End point description:

Pharmacokinetic parameters of paracetamol from capillary whole blood samples with the novel electrochemical point-of-care (POC) method

End point type Primary

End point timeframe:

0-12 h

Notes:

[3] - 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 is a concentration measurement. Data were presented as geometric means with geometric coefficients of variation as percentage.

End point values	Pharmacokinetic study			
Subject group type	Subject analysis set			
Number of subjects analysed	12			
Units: h µmol/l				
geometric mean (geometric coefficient of variation)	330.60 (± 29)			

Statistical analyses

No statistical analyses for this end point

Primary: Cmax HPLC-MS/MS venous plasma

End point title Cmax HPLC-MS/MS venous plasma^[4]

End point description:

Pharmacokinetic parameters of paracetamol from venous plasma samples measured with HPLC-MS/MS.

End point type Primary

End point timeframe:

0-12 h

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: This is a concentration measurement. Data were presented as geometric means with geometric coefficients of variation as percentage.

End point values	Pharmacokinetic study			
Subject group type	Subject analysis set			
Number of subjects analysed	12			
Units: µM				
geometric mean (geometric coefficient of variation)	65.61 (± 27)			

Statistical analyses

No statistical analyses for this end point

Primary: Tmax HPLC-MS/MS venous plasma

End point title	Tmax HPLC-MS/MS venous plasma ^[5]
End point description: Pharmacokinetic parameters of paracetamol from venous plasma samples measured with HPLC-MS/MS.	
End point type	Primary
End point timeframe: 0-12 h	

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: This is a concentration measurement. Data were presented as geometric means with geometric coefficients of variation as percentage.

End point values	Pharmacokinetic study			
Subject group type	Subject analysis set			
Number of subjects analysed	12			
Units: hour				
median (full range (min-max))	1.0 (0.5 to 2.0)			

Statistical analyses

No statistical analyses for this end point

Primary: AUC 0-last HPLC-MS/MS venous plasma

End point title	AUC 0-last HPLC-MS/MS venous plasma ^[6]
End point description: Pharmacokinetic parameters of paracetamol from venous plasma samples measured with HPLC-MS/MS.	
End point type	Primary

End point timeframe:

0-12 h

Notes:

[6] - 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 is a concentration measurement. Data were presented as geometric means with geometric coefficients of variation as percentage.

End point values	Pharmacokinetic study			
Subject group type	Subject analysis set			
Number of subjects analysed	12			
Units: h µmol/L				
geometric mean (geometric coefficient of variation)	262.21 (± 26)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax HPLC-MS/MS capillary

End point title	Cmax HPLC-MS/MS capillary
End point description: Pharmacokinetic parameters of paracetamol from capillary whole blood samples measured with HPLC-MS/MS.	
End point type	Secondary
End point timeframe: 0-12 h	

End point values	Pharmacokinetic study			
Subject group type	Subject analysis set			
Number of subjects analysed	12			
Units: µM				
geometric mean (geometric coefficient of variation)	98.67 (± 31)			

Statistical analyses

No statistical analyses for this end point

Secondary: Tmax HPLC-MS/MS capillary

End point title	Tmax HPLC-MS/MS capillary
End point description: Pharmacokinetic parameters of paracetamol from capillary whole blood samples measured with HPLC-MS/MS.	
End point type	Secondary

End point timeframe:

0-12 h

End point values	Pharmacokinetic study			
Subject group type	Subject analysis set			
Number of subjects analysed	12			
Units: hour				
median (full range (min-max))	0.5 (0.5 to 2.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: AUC 0-last HPLC-MS/MS from capillary

End point title	AUC 0-last HPLC-MS/MS from capillary
End point description: Pharmacokinetic parameters of paracetamol from capillary whole blood samples measured with HPLC-MS/MS.	
End point type	Secondary
End point timeframe: 0-12 h	

End point values	Pharmacokinetic study			
Subject group type	Subject analysis set			
Number of subjects analysed	12			
Units: h µmol/L				
geometric mean (geometric coefficient of variation)	283.41 (± 30)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

24 h

Adverse event reporting additional description:

The subjects received a standard 1g dose of paracetamol. The samples were collected within 12 hours from paracetamol intake. No adverse effects were reported.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	26.1
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Frequency threshold for reporting non-serious adverse events: 1 %

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: The volunteers were provided with 1 g of paracetamol with no adverse effects noticed from the drug. Venous and capillary blood samples were collected during 12 hours. No noticeable adverse effects occurred during sample collection.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/37218304>