EU Clinical Trials Register

Clinical trial results:
Hydrocortisone vs. pasireotide in preventing pancreatic fistula and other complications after pancreatic resection - a prospective, randomized, controlled trial

Summary

EudraCT number	2016-000212-16
Trial protocol	FI
Global end of trial date	26 October 2024

Results information

Result version number	v1 (current)
This version publication date	06 February 2025
First version publication date	06 February 2025

Trial information

Trial identification

Sponsor protocol code	HYKS-190116

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02775227
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Helsinki University Hospital
Sponsor organisation address	Haartmaninkatu 4, Helsinki, Finland, 00290
Public contact	MEM13, Helsinki University Central Hospital, ville.sallinen@helsinki.fi
Scientific contact	MEM13, Helsinki University Central Hospital, ville.sallinen@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	18 December 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 December 2018
Global end of trial reached?	Yes
Global end of trial date	26 October 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Determine non-inferiority of hydrocortisone compared to pasireotide in preventing pancreatic surgery complications.

Protection of trial subjects:

Both studied drugs have been used to reduce complications after pancreatic surgery. Complications after pancretic surgery are abundant and cause major morbidity and even mortality. The side effects these study drugs have are nausea and elevation of blood sugar levels for pasireotide and symphatic overexcitement for hydrocortisone. These side effects were registered and treated with antiemetics and insulin. Also, if an allergic reaction was noted, the study drug was prematurerly stopped. However, the possible side effects of these study drugs cause far less morbidity than the actual complications after pancreatic surgery.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 May 2016
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy, Scientific research
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Finland: 168
Worldwide total number of subjects	168
EEA total number of subjects	168

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)	75
From 65 to 84 years	93
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited between 19th of May 2016 and 17th of December 2018. All patients were treated in the Helsinki University Hospital, Helsinki Finland. Only patient in a high risk for postoperative pancreatic fistula were recruited. 42 patients out of 168 were excluded due to intraoperative findings indicating a low risk for fistula.

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	168
Number of subjects completed	126

Pre-assignment subject non-completion reasons

Reason: Number of subjects	non eligible: 42

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Data analyst, Subject

Blinding implementation details:

The randomization sequence was generated using a computer algorithm with randomly variable block size (2, 4, and 6). The randomization sequence was concealed in opaque and numbered envelopes.

Arms

Are arms mutually exclusive?	Yes
Arm title	Pasireotide

Arm description:

Patients who received perioperative pasierotide

Arm type	Active comparator
Investigational medicinal product name	pasireotide
Investigational medicinal product code	
Other name	signifor
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

900 micrograms twice a day starting the morning of surgery until the sixth postoperative day. 14 doses in total.

Arm title	Hydrocortisone

Arm description:

Patients who received perioperative hydrocortisone

Arm type	Experimental
Investigational medicinal product name	Hydrocrotisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for dispersion for injection
Routes of administration	Intravenous use

Dosage and administration details:

100 mg, intravenously 3 times a day, starting on the morning of the operation and continuing until the evening dose on postoperative day 2 (9 doses)

Number of subjects in period 1[1]	Pasireotide	Hydrocortisone
Started	63	63
Completed	63	63

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 168 patients enrolled but 42 patients were intraoperatively excluded since they either did not under go a pancreatic resection (i.e. disseminated cancer at laparoscopy) or they were found to have low risk pancreas (i.e. firm pancreas or wide pancreatic duct). All these features are impossible to determine pre operatively but the study drug need to be started preoperatively. Thus some patients are excluded after the randomization.

Baseline characteristics

Reporting groups

Reporting group title	Pasireotide
Reporting group description:	
Patients who received perioperative pasierotide	
Reporting group title	Hydrocortisone
Reporting group description:	
Patients who received perioperative hydrocortisone	

Reporting group values	Pasireotide	Hydrocortisone	Total
Number of subjects	63	63	126
Age categorical			
Units: Subjects			
Adults (18 and over)	63	63	126
Age continuous			
Units: years			
median	64	67	
inter-quartile range (Q1-Q3)	56 to 70	56 to 73	-
Gender categorical			
Units: Subjects			
Female	28	38	66
Male	35	25	60
ASA physical status			
Units: Subjects			
ASA 1	2	2	4
ASA 2	30	29	59
ASA 3	29	29	58
ASA 4	2	3	5
Charslon Comorbidity Index			
Units: Subjects			
Mild (0-2)	45	37	82
Moderate (3-4)	15	18	33
Severe (over 5)	3	8	11
BMI			
Units: kg/m2			
arithmetic mean	27.3	26.8	
standard deviation	± 3.6	± 4.3	-

Subject analysis sets

Subject analysis set title	Baseline characacteristics
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Patients with a high risk for postoperative pancreatic fistula continued the study drug after the operation. 63 patients in each arm (126 in total) continued the study drug. 42 of the 168 randomized patients were excluded intraoperatively since they were found to have a low risk for fistula or no pancreatic resection was made.

Reporting group values	Baseline characaeristics		
Number of subjects	126		
Age categorical			
Units: Subjects			
Adults (18 and over)	126		
Age continuous			
Units: years			
median	66		
inter-quartile range (Q1-Q3)	56 to 72		
Gender categorical			
Units: Subjects			
Female	66		
Male	60		
ASA physical status			
Units: Subjects			
ASA 1	4		
ASA 2	59		
ASA 3	58		
ASA 4	5		
Charslon Comorbidity Index			
Units: Subjects			
Mild (0-2)	82		
Moderate (3-4)	33		
Severe (over 5)	11		
BMI			
Units: kg/m2			
arithmetic mean	27.1		
standard deviation	± 4.0		

End points

End points reporting groups

Reporting group title	Pasireotide
Reporting group description:	
Patients who received perioperative pasierotide	
Reporting group title	Hydrocortisone
Reporting group description:	
Patients who received perioperative hydrocortisone	
Subject analysis set title	Baseline characeristics
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
Patients with a high risk for postoperative pancreatic fistula continued the study drug after the operation. 63 patients in each arm (126 in total) continued the study drug. 42 of the 168 randomized patients were excluded intraoperatively since they were found to have a low risk for fistula or no pancreatic resection was made.	

Primary: Comprehensive complication index

End point title	Comprehensive complication index
End point description:	
End point type	Primary
End point timeframe:	
For the first 30 postoperative days	

End point values	Pasireotide	Hydrocortisone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	63		
Units: CCI				
number (not applicable)	23.94	30.11		

Statistical analyses

Statistical analysis title	CCI
Comparison groups	Pasireotide v Hydrocortisone
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	t-test, 2-sided
Parameter estimate	Odds ratio (OR)

Secondary: CD 2 or more

End point title	CD 2 or more
End point description:	
Clavien-Dindo complication 2 or more	
End point type	Secondary
End point timeframe:	
First 30 PODs	

End point values	Pasireotide	Hydrocortisone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	63		
Units: n				
yes	43	44		
no	20	19		

Statistical analyses

Statistical analysis title	CD 2 or more
Comparison groups	Pasireotide v Hydrocortisone
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.05
Method	Chi-squared

Secondary: POPF

End point title	POPF
End point description:	
Post operative pancreatic fistula	
End point type	Secondary
End point timeframe:	
30 PODs	

End point values	Pasireotide	Hydrocortisone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	63		
Units: n				
yes	34	39		
no	29	24		

Statistical analyses

Statistical analysis title	POPF
Comparison groups	Pasireotide v Hydrocortisone
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.05
Method	Chi-squared

Secondary: DGE

End point title	DGE
End point description:	

End point type	Secondary
End point timeframe:	
30 PODs	

End point values	Pasireotide	Hydrocortisone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	63		
Units: n				
yes	12	19		
no	51	44		

Statistical analyses

Statistical analysis title	dge
Comparison groups	Pasireotide v Hydrocortisone
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.05
Method	Chi-squared

Secondary: PPH

End point title	PPH
End point description:	
End point type	Secondary
End point timeframe:	
30 PODs	

End point values	Pasireotide	Hydrocortisone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	63		
Units: n				
yes	0	7		
no	63	56		

Statistical analyses

Statistical analysis title	pph
Comparison groups	Pasireotide v Hydrocortisone
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.05
Method	Chi-squared

Secondary: LOS

End point title	LOS
End point description:	
End point type	Secondary
End point timeframe:	
Length of stay	

End point values	Pasireotide	Hydrocortisone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	63		
Units: days				
median (inter-quartile range (Q1-Q3))	8 (7 to 13)	10 (6 to 13.5)		

Statistical analyses

Statistical analysis title	LOS
Comparison groups	Pasireotide v Hydrocortisone
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	> 0.05
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Odds ratio (OR)
Confidence interval	
level	95 %
sides	2-sided

Secondary: Adjuvant chemo

End point title	Adjuvant chemo
End point description:	
End point type	Secondary
End point timeframe:	

Adjuvant chemo if needed for cancer patients

End point values	Pasireotide	Hydrocortisone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	24		
Units: n				
yes	20	17		
no	6	7		

Statistical analyses

Statistical analysis title	adjuvant chemo
Comparison groups	Pasireotide v Hydrocortisone

Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.05
Method	Chi-squared

Adverse events

Adverse events information

Timeframe for reporting adverse events:	
First 30 post operative days	
Assessment type	Systematic

Dictionary used

Dictionary name	ICD-10
Dictionary version	2019

Reporting groups

Reporting group title	Pasireotide
Reporting group description:	
Patients who received pasireotide	
Reporting group title	Hydrocortisone
Reporting group description:	
Patients who received hydrocortisone	

Serious adverse events	Pasireotide	Hydrocortisone	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	
number of deaths (all causes)	1	2	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Pasireotide	Hydrocortisone	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 63 (9.52%)	1 / 63 (1.59%)	
Immune system disorders			
Allergic reaction to excipient	Additional description: Allergic reaction to pasierotide		
subjects affected / exposed	1 / 63 (1.59%)	0 / 63 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	5 / 63 (7.94%)	1 / 63 (1.59%)	
occurrences (all)	5	1	

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/32022887