Clinical trial results:
Effects of a peripherally acting -opioid receptor antagonist on recurrent acute pancreatitis: An investigator-initiated, randomized, placebo-controlled, double-blind clinical trial

Summary

EudraCT number	2021-000069-34
Trial protocol	DK
Global end of trial date	03 June 2024

Results information

Result version number	v1 (current)
This version publication date	20 July 2025
First version publication date	20 July 2025

Trial information

Trial identification

Sponsor protocol code	PAMORA_2020_RAP

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04966559
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Mech-Sense, Aalborg University Hospital
Sponsor organisation address	Mølleparkvej 4, Aalborg, Denmark, 9320
Public contact	Mathias Ellgaard Cook, Mech-Sense, Aalborg University Hospital, +45 97663520, m.cook@rn.dk
Scientific contact	Mathias Ellgaard Cook, Mech-Sense, Aalborg University Hospital, +45 97663520, m.cook@rn.dk

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	02 September 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 June 2024
Global end of trial reached?	Yes
Global end of trial date	03 June 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

In outpatients with recurrent acute pancreatitis it will be investigated whether 12 months treatment with oral naldemedine will significantly reduce the number of pancreatitis attacks as compared to placebo.

Protection of trial subjects:

The safety and well-being of all participants are prioritized throughout the trial in accordance with Good Clinical Practice (GCP) and applicable regulatory requirements. Adverse events and safety concerns are continuously monitored, assessed, and reported as required to relevant authorities and ethics committees. Appropriate follow-up is conducted to ensure resolution or stabilization of any safety issues. All trial procedures are designed to minimize risk and ensure participant protection at every stage.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 September 2021
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	Denmark: 74
Worldwide total number of subjects	74
EEA total number of subjects	74

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)	65
From 65 to 84 years	9
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Inclusion started at the Aalborg site 12-01-2022, Bispebjerg 19-04-2022, Hvidovre 27-04-2022 and Odense 23-06-2022. Recruitment ended on all sites October 30, 2023.

Pre-assignment

Screening details:

Patient with a history of recurrent acute pancreatitis were approach either after acute admissions or from outpatient clinics. In total 88 patients were assessed for eligibility and 14 were excluded since they did not meeting the exact inclusion criteria (7), or did not want to participate (7).

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	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

The randomization and intervention allocation procedures were handled by pharmacists at Aalborg University Hospital, who were not affiliated with the trial. Participants were randomized to active treatment (tablet naldemedine 0.2 mg) or placebo in a 1:1 ratio using the web-based tool provided by www.sealedenvelope.com with random block size.

Arms

Are arms mutually exclusive?	Yes
Arm title	Active, Naldemedine

Arm description:

Active, Naldemedine

Arm type	Experimental
Investigational medicinal product name	Naldemedine 0.2mg Film-coated Tablet
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

0.2mg per day.

Arm title	Placebo

Arm description:

Placebo

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

otherwise identical to the IMP

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet

Routes of administration	Oral use

Dosage and administration details:

Otherwise identical to the IMP

Number of subjects in period 1	Active, Naldemedine	Placebo
Started	36	38
Completed	34	32
Not completed	2	6
Adverse event, non-fatal	1	3
Lost to follow-up	1	3

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	74	74	
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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
arithmetic mean	45.7		
standard deviation	± 14.8	-	
Gender categorical Units: Subjects			
Female	30	30	
Male	44	44	

End points

End points reporting groups

Reporting group title	Active, Naldemedine
Reporting group description: Active, Naldemedine	
Reporting group title	Placebo
Reporting group description: Placebo	

Primary: Individual difference in number of AP attacks verified by the Atlanta criteria between the naldemedine group and the placebo group during the 12-month treatment period

End point title	Individual difference in number of AP attacks verified by the Atlanta criteria between the naldemedine group and the placebo group during the 12-month treatment period
End point description:	
End point type	Primary
End point timeframe: After 12 months	

End point values	Active, Naldemedine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	38		
Units: Number of events	19	35		

Statistical analyses

Statistical analysis title	Primary outcome
Statistical analysis description: The Anderson-Gill method for recurrent event analysis	
Comparison groups	Active, Naldemedine v Placebo
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.054
Method	Anderson-Gill
Parameter estimate	Hazard ratio (HR)
Point estimate	0.54

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.29
upper limit	1.01

Secondary: Difference in number and severity (assessed by questionnaires) of pain attacks (without fulfilling AP criteria) between subgroups during the 12-month treatment period

End point title	Difference in number and severity (assessed by questionnaires) of pain attacks (without fulfilling AP criteria) between subgroups during the 12-month treatment period

End point description:

End point type	Secondary

End point timeframe:

After 12 months

End point values	Active, Naldemedine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	38		
Units: Number of events	56	59		

Statistical analyses

No statistical analyses for this end point

Secondary: Difference in gut function assessed with the Bristol Stool Form Scale between subgroups from baseline to 12 months follow-up

End point title	Difference in gut function assessed with the Bristol Stool Form Scale between subgroups from baseline to 12 months follow-up

End point description:

End point type	Secondary

End point timeframe:

After 12 months

End point values	Active, Naldemedine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	38		
Units: Score				
arithmetic mean (standard deviation)	0.4 (± 0.45)	-0.4 (± 0.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Difference in exocrine pancreas function between subgroups, assessed by new-onset EPI, from baseline to 12 months follow-up

End point title	Difference in exocrine pancreas function between subgroups, assessed by new-onset EPI, from baseline to 12 months follow-up

End point description:

End point type	Secondary

End point timeframe:

After 12 months

End point values	Active, Naldemedine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	38		
Units: Number of events	1	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Difference in gut function assessed with the Gastrointestinal Symptom Rating Scale between subgroups from baseline to 12 months follow-up

End point title	Difference in gut function assessed with the Gastrointestinal Symptom Rating Scale between subgroups from baseline to 12 months follow-up

End point description:

End point type	Secondary

End point timeframe:

After 12 months

End point values	Active, Naldemedine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	38		
Units: Score				
arithmetic mean (standard deviation)	-0.1 (± 0.13)	-0.3 (± 0.15)		

Statistical analyses

No statistical analyses for this end point

Secondary: Difference in endocrine pancreas function between subgroups, assessed by new-onset diabetes, from baseline to 12 months follow-up

End point title	Difference in endocrine pancreas function between subgroups, assessed by new-onset diabetes, from baseline to 12 months follow-up

End point description:

End point type	Secondary

End point timeframe:

After 12 months

End point values	Active, Naldemedine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	38		
Units: Number of events	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Difference between subgroups in quality of life, assessed by questionnaires, from baseline to 12 months follow-up

End point title	Difference between subgroups in quality of life, assessed by questionnaires, from baseline to 12 months follow-up

End point description:

End point type	Secondary

End point timeframe:

After 12 months

End point values	Active, Naldemedine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	38		
Units: Score				
arithmetic mean (standard deviation)	1.0 (± 3.7)	3.9 (± 4.8)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
After 12 months	
Adverse event reporting additional description:	
Monthly phonecalls and visits at study end.	
Assessment type	Systematic

Dictionary used	
Dictionary name	None
Dictionary version	0

Reporting groups	
Reporting group title	Active, Naldemedine
Reporting group description:	
Active, Naldemedine	
Reporting group title	Placebo
Reporting group description:	
Placebo	

Serious adverse events	Active, Naldemedine	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 36 (36.11%)	19 / 38 (50.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Gastrointestinal disorders			
Pancreatitis acute			
subjects affected / exposed	13 / 36 (36.11%)	19 / 38 (50.00%)	
occurrences causally related to treatment / all	0 / 19	0 / 35	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Active, Naldemedine	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 36 (41.67%)	16 / 38 (42.11%)	
Gastrointestinal disorders			
Diarrhea			
subjects affected / exposed	7 / 36 (19.44%)	10 / 38 (26.32%)	
occurrences (all)	7	10	
Abdominal pain			

subjects affected / exposed occurrences (all)	15 / 36 (41.67%) 15	15 / 38 (39.47%) 15	

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