Clinical trial results:
The effect of tapentadol on the human pain system: A study based on advanced neurophysiology and imaging techniques to illustrate the mechanism of tapentadol and oxycodone in the central, autonomic and enteric nervous systems

Summary

EudraCT number	2017-000141-52
Trial protocol	DK
Global end of trial date	09 May 2019

Results information

Result version number	v1 (current)
This version publication date	03 December 2020
First version publication date	03 December 2020
Summary attachment (see zip file)	Landscaping_2017 summary (Landscaping_2017 summary.pdf)

Trial information

Trial identification

Sponsor protocol code	Landscaping_2017

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Mech-Sense
Sponsor organisation address	Dept. Gastroenterology & Hepatology , Aalborg, Denmark, 9000
Public contact	Asbjørn Mohr Drewes, Mech-Sense Dept. Gastroenterology & Hepatology Aalborg University Hospital, +45 97663524, amd@rn.dk
Scientific contact	Rasmus Bach Nedergaard, Mech-Sense Dept. Gastroenterology & Hepatology Aalborg University Hospital, +45 97663524, r.nedergaard@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	23 December 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 May 2019
Global end of trial reached?	Yes
Global end of trial date	09 May 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objectives are to investigate the effect of tapentadol on the central, the autonomic and the enteric nervous systems.

Protection of trial subjects:

After each ended drug administration a subjective opiate withdrawal scale (SOWS) for grading opioid withdrawal symptoms was filled in by the subject. In cases where any subject had what was classified above mild withdrawal (a total score of 11 or above) the subject was contacted and followed till they were in a mild withdrawal classification. No subjects reproted a score of 11 or above in any of the the treatment arms.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 April 2017
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	Denmark: 22
Worldwide total number of subjects	22
EEA total number of subjects	22

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)	22

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment started at 16/02/2018 and ended 22/01/2019.

Pre-assignment

Screening details:

The inclusion criteria were: Male, between 20 and 45 years of age and of Scandinavian descent. The subjects were deemed to be healthy by a physician and the subjects had to be opioid naïve. There was a wash out period of 7 days between treatmet arms.

Period 1

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

Blinding implementation details:

The medication was handled, packed and delivered by the Hospital Pharmacy, Central Denmark Region, Denmark who also performed the randomization of the study.

Arms

Are arms mutually exclusive?	No
Arm title	Placebo

Arm description:

Placebo tablets were administered orally on day 1 (after baseline measurements) and day 14 (in the morning) once, and twice a day on day 2-13 (morning and evening). In total 26 doses were administered per treatment arm.

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

Dosage and administration details:

Placebo tablets were administered orally on day 1 (after baseline measurements) and day 14 (in the morning) once, and twice a day on day 2-13 (morning and evening). In total 26 doses were administered per treatment arm.

Arm title	Tapentadol

Arm description:

Tapentadol (Palexia®, extended release 50 mg) tablets were administered orally on day 1 (after baseline measurements) and day 14 (in the morning) once, and twice a day on day 2-13 (morning and evening). In total 26 doses were administered per treatment arm.

Arm type	Experimental
Investigational medicinal product name	Palexia
Investigational medicinal product code	EMEA-000018-PIP01-07-M14
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

extended release 50 mg administered orally on day 1 (after baseline measurements) and day 14 (in the morning) once, and twice a day on day 2-13 (morning and evening). In total 26 doses

Arm title	Oxycodone

Arm description:

Oxycodone (OxyContin®, extended release 10 mg) tablets were administered orally on day 1 (after baseline measurements) and day 14 (in the morning) once, and twice a day on day 2-13 (morning and evening). In total 26 doses were administered per treatment arm.

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

Dosage and administration details:

extended release 10 mg administered orally on day 1 (after baseline measurements) and day 14 (in the morning) once, and twice a day on day 2-13 (morning and evening). In total 26 doses

Number of subjects in period 1	Placebo	Tapentadol	Oxycodone
Started	22	22	22
Completed	21	21	21
Not completed	1	1	1
one subject was excluded	1	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall period

Reporting group description: -

Reporting group values	Overall period	Total	
Number of subjects	22	22	
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	24.9		
standard deviation	± 2.7	-	
Gender categorical Units: Subjects			
Female	0	0	
Male	22	22	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Placebo tablets were administered orally on day 1 (after baseline measurements) and day 14 (in the morning) once, and twice a day on day 2-13 (morning and evening). In total 26 doses were administered per treatment arm.	
Reporting group title	Tapentadol
Reporting group description:	
Tapentadol (Palexia®, extended release 50 mg) tablets were administered orally on day 1 (after baseline measurements) and day 14 (in the morning) once, and twice a day on day 2-13 (morning and evening). In total 26 doses were administered per treatment arm.	
Reporting group title	Oxycodone
Reporting group description:	
Oxycodone (OxyContin®, extended release 10 mg) tablets were administered orally on day 1 (after baseline measurements) and day 14 (in the morning) once, and twice a day on day 2-13 (morning and evening). In total 26 doses were administered per treatment arm.	

Primary: Nociceptive withdrawal reflex

End point title	Nociceptive withdrawal reflex[1]
End point description:	
Visual analogue scale (VAS) measured at 2 times the electrical nociceptive withdrawal reflex of the foot.	
End point type	Primary
End point timeframe:	
Baseline and end of treatment for each treatment arm	
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: The data analysis is not completed, and has not been published.	

End point values	Placebo	Tapentadol	Oxycodone	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	20	20	
Units: VAS				
arithmetic mean (standard deviation)	2.71 (± 2.12)	2.2 (± 1.4)	2.7 (± 2)	

Statistical analyses

No statistical analyses for this end point

Primary: Ice water pain perception

End point title	Ice water pain perception[2]
End point description:	
VAS after submerging the hand in ice chilled water for 120 seconds	
End point type	Primary

End point timeframe:

Baseline to end of trial

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: The data analysis is not completed, and has not been published.

End point values	Placebo	Tapentadol	Oxycodone	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	21	21	
Units: VAS				
arithmetic mean (standard deviation)	5.86 (± 1.8)	5.9 (± 1.81)	5.62 (± 1.94)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 16/02/2018 to 26/04/2019	
Assessment type	Systematic

Dictionary used	
Dictionary name	Questionnaire
Dictionary version	1

Reporting groups	
Reporting group title	Placebo
Reporting group description: Placebo tablets were administered orally on day 1 (after baseline measurements) and day 14 (in the morning) once, and twice a day on day 2-13 (morning and evening). In total 26 doses were administered per treatment arm.	
Reporting group title	Tapentadol
Reporting group description: Tapentadol (Palexia®, extended release 50 mg) tablets were administered orally on day 1 (after baseline measurements) and day 14 (in the morning) once, and twice a day on day 2-13 (morning and evening). In total 26 doses were administered per treatment arm.	
Reporting group title	Oxycodone
Reporting group description: Oxycodone (OxyContin®, extended release 10 mg) tablets were administered orally on day 1 (after baseline measurements) and day 14 (in the morning) once, and twice a day on day 2-13 (morning and evening). In total 26 doses were administered per treatment arm.	

Serious adverse events	Placebo	Tapentadol	Oxycodone
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	0 / 21 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Placebo	Tapentadol	Oxycodone
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 21 (80.95%)	18 / 21 (85.71%)	21 / 21 (100.00%)
Nervous system disorders			
Discomfort			
subjects affected / exposed	3 / 21 (14.29%)	4 / 21 (19.05%)	10 / 21 (47.62%)
occurrences (all)	3	4	10
Dizzy			

subjects affected / exposed	4 / 21 (19.05%)	5 / 21 (23.81%)	12 / 21 (57.14%)
occurrences (all)	4	5	12
Headache			
subjects affected / exposed	4 / 21 (19.05%)	5 / 21 (23.81%)	9 / 21 (42.86%)
occurrences (all)	4	5	9
Nausea			
subjects affected / exposed	1 / 21 (4.76%)	2 / 21 (9.52%)	9 / 21 (42.86%)
occurrences (all)	1	2	9
Tired/drowsy			
subjects affected / exposed	9 / 21 (42.86%)	9 / 21 (42.86%)	18 / 21 (85.71%)
occurrences (all)	9	9	18
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 21 (19.05%)	1 / 21 (4.76%)	3 / 21 (14.29%)
occurrences (all)	4	1	3
Acid reflux			
subjects affected / exposed	1 / 21 (4.76%)	2 / 21 (9.52%)	3 / 21 (14.29%)
occurrences (all)	1	2	3
Constipation			
subjects affected / exposed	6 / 21 (28.57%)	6 / 21 (28.57%)	15 / 21 (71.43%)
occurrences (all)	6	6	15
Difficulty swallowing			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	2 / 21 (9.52%)
occurrences (all)	0	0	2
Dry mouth			
subjects affected / exposed	3 / 21 (14.29%)	6 / 21 (28.57%)	8 / 21 (38.10%)
occurrences (all)	3	6	8
Heartburn			
subjects affected / exposed	1 / 21 (4.76%)	0 / 21 (0.00%)	3 / 21 (14.29%)
occurrences (all)	1	0	3
Hunger pain			
subjects affected / exposed	4 / 21 (19.05%)	4 / 21 (19.05%)	5 / 21 (23.81%)
occurrences (all)	4	4	5
Reduced appetite			
subjects affected / exposed	2 / 21 (9.52%)	3 / 21 (14.29%)	11 / 21 (52.38%)
occurrences (all)	2	3	11

Straining during defecation subjects affected / exposed occurrences (all)	11 / 21 (52.38%) 11	8 / 21 (38.10%) 8	17 / 21 (80.95%) 17
Skin and subcutaneous tissue disorders Skin irritation subjects affected / exposed occurrences (all)	3 / 21 (14.29%) 3	3 / 21 (14.29%) 3	6 / 21 (28.57%) 6

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