Clinical trial results:
UNTERSUCHUNG DER GENETISCH BEDINGTEN VARIABILITÄT DES OPIOID- UND OPIATBEDARFS IM RAHMEN DES DROGENSUBSTITUTIONSPROGRAMMS und HÄUFIGKEITEN GENETISCHER POLYMORPHISMEN BEI POPULATIONEN MIT UND OHNE OPIOIDABHÄNGIGKEITSERKRANKUNG (STUDIENTEIL B)

Summary

EudraCT number	2008-002714-22
Trial protocol	AT
Global end of trial date	31 December 2020

Results information

Result version number	v1 (current)
This version publication date	18 December 2021
First version publication date	18 December 2021

Trial information

Trial identification

Sponsor protocol code	7108

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Medical University Innsbruck
Sponsor organisation address	Christoph-Probst-Platz 1, Innrain 52, Innsbruck, Austria, 6020
Public contact	Dr.in med. univ. Beate Beer-Sandner, Bezirkshauptmannschaft Kufstein, Bozner Platz 1 6330 Kufstein , +43 5372 606 6144, bh.ku.gesundheitswesen@tirol.gv.at
Scientific contact	Dr.in med. univ. Beate Beer-Sandner, Bezirkshauptmannschaft Kufstein, Bozner Platz 1 6330 Kufstein , +43 5372 606 6144, bh.ku.gesundheitswesen@tirol.gv.at

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	30 April 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 April 2013
Global end of trial reached?	Yes
Global end of trial date	31 December 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The major aim of the present study was to identify genetic polymorphisms contributing to the individual susceptibility to opioid addiction and to replicate earlier findings in this regard, respectively.

Protection of trial subjects:

Only DNA samples were taken. DNA samples of all participants were obtained via buccal swabs.

Background therapy:

There was no background therapy.

Evidence for comparator:

There was no evidence for a comparator.

Actual start date of recruitment	28 August 2008
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	Austria: 284
Worldwide total number of subjects	284
EEA total number of subjects	284

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)	284
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

For the presented candidate gene association study, a total of 148 unrelated opioid dependent individuals undergoing opioid maintenance treatment were recruited at the drug addiction outpatient clinic of the Innsbruck Medical University. In total, 142 of the 148 recruited patients and all 142 healthy control subjects were included in the study.

Pre-assignment

Screening details:

Following inclusion criteria were applied:
written informed consent; opioid dependence according to the DSM-IV criteria; opioid maintenance therapy with either methadone or buprenorphine; history of at least 2 years of daily heroin (and/or morphine) use.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Outpatients

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Buprenorphine hydrochloride
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Sublingual tablet
Routes of administration	Sublingual use

Dosage and administration details:

A total of 142 unrelated opioid dependent individuals undergoing opioid maintenance treatment were enrolled in the study. Each patient was treated individually.

Investigational medicinal product name	Methadone hydrochloride
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral liquid
Routes of administration	Oral use

Dosage and administration details:

A total of 142 unrelated opioid dependent individuals undergoing opioid maintenance treatment were enrolled in the study. Each patient was treated individually.

Arm title	Control

Arm description: -

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Outpatients	Control
Started	142	142
Completed	142	142

Baseline characteristics

Reporting groups	
Reporting group title	Outpatients
Reporting group description: -	
Reporting group title	Control
Reporting group description: -	

Reporting group values	Outpatients	Control	Total
Number of subjects	142	142	284
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	142	142	284
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	31	29	
standard deviation	± 8	± 6	-
Gender categorical Units: Subjects			
Female	45	61	106
Male	97	81	178

End points

End points reporting groups	
Reporting group title	Outpatients
Reporting group description: -	
Reporting group title	Control
Reporting group description: -	

Primary: GAL, rs948854 (GG genotype)	
End point title	GAL, rs948854 (GG genotype)
End point description: Analysis of homozygous carriers of the minor allele (GG genotype) .	
End point type	Primary
End point timeframe: Day 1	

End point values	Outpatients	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	142	142		
Units: number	18	4		

Statistical analyses

Statistical analysis title	GAL, rs948854 (GG genotype)
Comparison groups	Outpatients v Control
Number of subjects included in analysis	284
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.002 [1]
Method	t-test, 2-sided
Parameter estimate	Odds ratio (OR)
Point estimate	5.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.54
upper limit	18

Notes:

[1] - Homozygous carriers of the minor allele (GG genotype) were significantly more prevalent in the patient group ($p = 0.002$, $\chi 2 = 9.657$, $df = 1$).

Primary: OPRD1, rs223686 (TT genotype)	
End point title	OPRD1, rs223686 (TT genotype)

End point description:	
Analysis of homozygous carriers of the minor allele (TT genotype) .	
End point type	Primary
End point timeframe:	
Day 1	

End point values	Outpatients	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	142	142		
Units: number	3	13		

Statistical analyses

Statistical analysis title	OPRD1, rs223686 (TT genotype)
Comparison groups	Outpatients v Control
Number of subjects included in analysis	284
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.018
Method	t-test, 2-sided
Parameter estimate	Odds ratio (OR)
Point estimate	0.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.05
upper limit	0.83

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Day 1

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4.03

Reporting groups

Reporting group title	Outpatients
Reporting group description: -	
Reporting group title	Control
Reporting group description: -	

Serious adverse events	Outpatients	Control	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 142 (0.00%)	0 / 142 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Outpatients	Control	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 142 (0.00%)	0 / 142 (0.00%)	

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: As only a buccal swab was performed, no AEs and SAEs were reported.

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/24086514