Clinical trial results:
Pramipexole augmentation to target anhedonia in depression - a pilot study

Summary

EudraCT number	2019-001907-19
Trial protocol	SE
Global end of trial date	18 March 2021

Results information

Result version number	v1 (current)
This version publication date	06 July 2022
First version publication date	06 July 2022
Summary attachment (see zip file)	Text appendix (Text appendix.docx)

Trial information

Trial identification

Sponsor protocol code	PILOT-PRAXOL

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04121091
WHO universal trial number (UTN)	-
Other trial identifiers	Swedish Ethical Review Authority: 2019-02843

Notes:

Sponsors

Sponsor organisation name	Region Skåne
Sponsor organisation address	Baravägen 1, Lund, Sweden, 22185
Public contact	Vuxenpsykiatri Lund, Region Skåne, daniel.lindqvist@med.lu.se
Scientific contact	Vuxenpsykiatri Lund, Region Skåne, 46 173885, daniel.lindqvist@med.lu.se

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	31 October 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 March 2021
Global end of trial reached?	Yes
Global end of trial date	18 March 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective is to test the efficacy of add-on pramipexole in treating anhedonia in patients with depression.

Protection of trial subjects:

- Blood samples including eGFR, liver transaminases, hemoglobin and beta-hCG were taken before baseline visit to ensure treatment safety and exclude potential subject if pregnant.
- All trial subjects were asked about history of cardiovascular or pulmonary disease.
- All trial subjects were screened with Young Mania Rating Scale and Questionnaire for Impulsive-Compulsive Disorders (QUIP) at screening visit and every other week during participation.
- All trial subjects were informed about the mechanisms of Pramipexole and the importance of adjusting the dosage in steps.

Background therapy:

All trial subjects had a stable ongoing antidepressant medication at least four weeks prior to enrollment. Trial subjects with bipolar disorder also had stable medications with mood stabilizers.

Evidence for comparator:

No comparators. All trial subjects received pramipexole.

Actual start date of recruitment	02 September 2019
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	Sweden: 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

Subject disposition

Recruitment

Recruitment details:

The first trial subject was enrolled 04-Nov-2019 and the last trial subject 05-Oct-2020. All patients were recruited from Scania, Sweden.

Pre-assignment

Screening details:

Test subjects with diagnosis of depression were recruited through self-referral and through referral from primary care and psychiatric clinics in Scania. If the test subject had an ongoing treatment with antipsychotics, a wash-out period of at least four weeks was applied (if it was assessed as appropriate by the test subjects doctor).

Period 1

Period 1 title	Treatment with pramipexole baseline
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Treatment pramipexole baseline

Arm description:

Treatment with pramipexole, baseline at week 0

Arm type	Baseline
Investigational medicinal product name	Pramipexole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Prolonged-release tablet
Routes of administration	Oral use

Dosage and administration details:

Pramipexole titrated to highest tolerable dose (doses in salt):
Week 1: 1 tablet 0.375 mg
Week 2: 1 tablet 0.75 mg
Week 3: 1 tablet 1.5 mg
Week 4: 1 tablet 1.5 mg + 1 tablet 0.75 mg (total dose: 2.25 mg)
Week 5: 1 tablet 3 mg

The increase in dosage was paused if the trial subject had limiting side effects or displayed at least 50% improvement regarding depressive symptoms.

Number of subjects in period 1	Treatment pramipexole baseline
Started	12
Completed	12

Period 2

Period 2 title	Treatment with pramipexole endpoint
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Treatment with pramipexole endpoint

Arm description:

After 10 weeks of treatment with pramipexole

Arm type	Endpoint
Investigational medicinal product name	Pramipexole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Prolonged-release tablet
Routes of administration	Oral use

Dosage and administration details:

Pramipexole titrated to highest tolerable dose (doses in salt):
Week 1: 1 tablet 0.375 mg
Week 2: 1 tablet 0.75 mg
Week 3: 1 tablet 1.5 mg
Week 4: 1 tablet 1.5 mg + 1 tablet 0.75 mg (total dose: 2.25 mg)
Week 5: 1 tablet 3 mg

The increase in dosage was paused if the trial subject had limiting side effects or displayed at least 50% improvement regarding depressive symptoms.

Number of subjects in period 2	Treatment with pramipexole endpoint
Started	12
Completed	12

Baseline characteristics

Reporting groups	
Reporting group title	Treatment with pramipexole baseline

Reporting group description: -

Reporting group values	Treatment with pramipexole baseline	Total	
Number of subjects	12	12	
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			
median	45.2		
standard deviation	± 15.7	-	
Gender categorical			
Units: Subjects			
Female	8	8	
Male	4	4	
SSRI users			
Users of selective serotonine reuptake inhibitors			
Units: Subjects			
Yes	5	5	
No	7	7	
SNRI users			
Users of serotonine norepinephrine reuptake inhibitors			
Units: Subjects			
Yes	6	6	
No	6	6	
NDRI users			
Users of norepinephrine dopamine reuptake inhibitors			
Units: Subjects			
Yes	2	2	
No	10	10	
Antipsychotic users			
Users of antipsychotics			
Units: Subjects			
Yes	0	0	

No	12	12	
Mood stabilizers users			
Users of mood stabilizers			
Units: Subjects			
Yes	2	2	
No	10	10	
Previously ECT			
Previously received electroconvulsive therapy			
Units: Subjects			
Yes	4	4	
No	8	8	
Anxiety comorbidity			
Anxiety disorder diagnosis			
Units: Subjects			
Yes	6	6	
No	6	6	
BMI			
Mean Body Mass Index			
Units: kg/m2			
arithmetic mean	30.2		
standard deviation	± 5.2	-	
CRP			
C-reactive peptide levels			
Units: ng/L			
arithmetic mean	3.8		
standard deviation	± 4.7	-	
Previous antidepressant treatment			
Median number of previous antidepressant treatments			
Units: treatments			
median	5		
full range (min-max)	2 to 14	-	

End points

End points reporting groups	
Reporting group title	Treatment pramipexole baseline
Reporting group description: Treatment with pramipexole, baseline at week 0	
Reporting group title	Treatment with pramipexole endpoint
Reporting group description: After 10 weeks of treatment with pramipexole	

Primary: Responder MADRS	
End point title	Responder MADRS
End point description: >50% decrease on MADRS	
End point type	Primary
End point timeframe: Nov 2019 - Mar 2021	

End point values	Treatment pramipexole baseline	Treatment with pramipexole endpoint		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: 12				
Yes	4	4		
No	8	8		

Attachments (see zip file)	Figure1A.png

Statistical analyses

Statistical analysis title	Comparison of means
Statistical analysis description: Mean baseline value was compared to endpoint value using Wilcoxon signed ranks test. This was performed for MADRS, SHAPS and DARS, as well as CRP. See attached file for more information.	
Comparison groups	Treatment pramipexole baseline v Treatment with pramipexole endpoint
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Mean difference (final values)

Confidence interval	
level	95 %
sides	1-sided
Variability estimate	Standard deviation

Secondary: Responder SHAPS	
End point title	Responder SHAPS
End point description:	
>50% decrease on Snaith Hamilton Pleasure scale	
End point type	Secondary
End point timeframe:	
Nov 2019 - Mar 2021	

Attachments (see zip file)	Figure1A.png

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Endpoint pramipexole dose	
End point title	Endpoint pramipexole dose
End point description:	
Mean dose of pramipexole (mg salt/day) at week 10	
End point type	Other pre-specified
End point timeframe:	
Nov 2019 - Mar 2021	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Endpoint CRP	
End point title	Endpoint CRP
End point description: Mean level of hs-CRP (ng/L) at week 10	
End point type	Other pre-specified
End point timeframe: Nov 2019 - Mar 2021	

Attachments (see zip file)	Figure 2.png

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Nov 2019 - Mar 2021	
Adverse event reporting additional description:	
Weekly report from trial subjects through a diary	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	25

Reporting groups	
Reporting group title	Treatment
Reporting group description:	
Treatment with pramipexole (all enrolled subjects)	

Serious adverse events	Treatment		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Treatment		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 12 (100.00%)		
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
General disorders and administration site conditions			
Headache			
subjects affected / exposed	10 / 12 (83.33%)		
occurrences (all)	10		
Nausea			

subjects affected / exposed	9 / 12 (75.00%)		
occurrences (all)	9		
Fatigue			
subjects affected / exposed	3 / 12 (25.00%)		
occurrences (all)	3		
Appetite disorder	Additional description: Loss of appetite		
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Eating disorder	Additional description: Overeating, temporarily.		
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Psychiatric disorders			
Depressed mood			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Agitation	Additional description: Mild agitation		
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

This is a small pilot study, to examine the applicability of pramipexole in this patient group.

Notes: