



## Clinical trial results:

### Effects of intranasal administrations of oxytocin on behavioural troubles, hyperphagia and social skills in children with Prader-Willi syndrome aged from 3 to 12 years.

#### Summary

EudraCT number	2016-003273-18
Trial protocol	FR
Global end of trial date	11 January 2019

#### Results information

Result version number	v1 (current)
This version publication date	14 June 2024
First version publication date	14 June 2024

#### Trial information

##### Trial identification

Sponsor protocol code	RC31-15-7837
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03114371
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	CHU de Toulouse
Sponsor organisation address	2 rue de Viguerie, Toulouse, France, 31059
Public contact	Nadège ALGANS, University Hospital of Toulouse, +33 0561777204, algans.n@chu-toulouse.fr
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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	11 January 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 January 2019
Global end of trial reached?	Yes
Global end of trial date	11 January 2019
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

Study the effect of the administration intranasale of oxytocin (OXT) during 12 weeks on the behavior disorders by comparison with a placebo

Protection of trial subjects:

An Independent Monitoring Committee (IMC) was formed to review the study data and to assess the safety of the OXYJEUNE study based on Serious and Non-Serious Events, in particular their potential relationship to the investigational drug.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 November 2016
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	France: 40
Worldwide total number of subjects	40
EEA total number of subjects	40

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)	35
Adolescents (12-17 years)	5
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Patients with Prader-Willi Syndrome will be recruited by the PWS Reference Center of the Toulouse University Hospital from the active file of patients followed.

### Pre-assignment

Screening details:

Patients with PWS aged from 3 to 12 years

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	OXYTOCIN

Arm description:

Daily intranasal administrations of oxytocin for 12 weeks. Oxytocin dose will be 8 International Unit for patients aged from 3 to 6 years and 16 International Unit for patients aged from 7 to 12 years.

Arm type	Experimental
Investigational medicinal product name	Syntocinon PR1
Investigational medicinal product code	H01BB02
Other name	
Pharmaceutical forms	Nasal spray
Routes of administration	Nasal use

Dosage and administration details:

The dosage of OXT will be 8 IU for patients aged 3-6 years and 16 IU for patients aged 7-12 years at inclusion.

<b>Arm title</b>	PLACEBO
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Arm description:

Daily intranasal administrations of placebo for 12 weeks. Oxytocin dose will be International Unit for patients aged from 3 to 6 years and 16 International Unit for patients aged from 7 to 12 years.

Arm type	Placebo
Investigational medicinal product name	Syntocinon PR1
Investigational medicinal product code	H01BB02
Other name	
Pharmaceutical forms	Nasal spray
Routes of administration	Nasal use

Dosage and administration details:

The dosage of OXT will be 8 IU for patients aged 3-6 years and 16 IU for patients aged 7-12 years at inclusion.

Number of subjects in period 1	OXYTOCIN	PLACEBO
Started	20	20
Completed	20	20

## Period 2

Period 2 title	OT vs Placebo
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

## Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	OXYTOCIN

Arm description:

Oxytocin treatment 8 unit for patients aged from 3 to 6 years and 16 units for patients aged from 7 to 12.

Arm type	Experimental
Investigational medicinal product name	Syntocinon PR1
Investigational medicinal product code	H01BB02
Other name	
Pharmaceutical forms	Nasal spray
Routes of administration	Nasal use

Dosage and administration details:

The dosage of OXT will be 8 IU for patients aged 3-6 years and 16 IU for patients aged 7-12 years at inclusion.

<b>Arm title</b>	Placebo
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Arm description:

2 spray for patients aged from 3 to 6 years

4 spray for patients aged from 7 to 12 years

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use

Dosage and administration details:

2 spray for patients aged from 3 to 6 years

4 spray for patients aged from 7 to 12 years

Number of subjects in period 2	OXYTOCIN	Placebo
Started	20	20
Completed	19	20
Not completed	1	0
Consent withdrawn by subject	1	-

### Period 3

Period 3 title	open label period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

### Arms

<b>Arm title</b>	Oxytocin
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Arm description:

8 UI (2 spray) for patients aged from 3 to 6 years

16 UI (4 spray) for patients aged from 7 to 12 years

Arm type	Experimental
Investigational medicinal product name	Syntocinon
Investigational medicinal product code	HB01BB02
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use

Dosage and administration details:

8 UI (2 spray) for patients aged from 3 to 6 years

16 UI (4 spray) for patients aged from 3 to 6 years

Number of subjects in period 3	Oxytocin
Started	39
Completed	38
Not completed	1
Consent withdrawn by subject	1

## Baseline characteristics

### Reporting groups

Reporting group title	OXYTOCIN
Reporting group description:	
Daily intranasal administrations of oxytocin for 12 weeks. Oxytocin dose will be 8 International Unit for patients aged from 3 to 6 years and 16 International Unit for patients aged from 7 to 12 years.	
Reporting group title	PLACEBO
Reporting group description:	
Daily intranasal administrations of placebo for 12 weeks. Oxytocin dose will be International Unit for patients aged from 3 to 6 years and 16 International Unit for patients aged from 7 to 12 years.	

Reporting group values	OXYTOCIN	PLACEBO	Total
Number of subjects	20	20	40
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)	18	17	35
Adolescents (12-17 years)	2	3	5
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	6.7	7.2	
standard deviation	± 2.9	± 3.05	-
Gender categorical			
Among all the children participating in the study, in the oxytocin (OTX) study arm there are 4 boys and 6 girls (3 and 6 years), and 5 boys and 5 girls (7/12 years). In the placebo arm there are 4 girls and 6 boys (3/6 years) and 2 boys and 8 girls (7/12 years).			
Units: Subjects			
Female	11	12	23
Male	9	8	17
age category			
Units: Subjects			
Age 3-6 years	10	10	20
Age 7-12 years	10	10	20

## End points

### End points reporting groups

Reporting group title	OXYTOCIN
Reporting group description: Daily intranasal administrations of oxytocin for 12 weeks. Oxytocin dose will be 8 International Unit for patients aged from 3 to 6 years and 16 International Unit for patients aged from 7 to 12 years.	
Reporting group title	PLACEBO
Reporting group description: Daily intranasal administrations of placebo for 12 weeks. Oxytocin dose will be International Unit for patients aged from 3 to 6 years and 16 International Unit for patients aged from 7 to 12 years.	
Reporting group title	OXYTOCIN
Reporting group description: Oxytocin treatment 8 unit for patients aged from 3 to 6 years and 16 units for patients aged from 7 to 12.	
Reporting group title	Placebo
Reporting group description: 2 spray for patients aged from 3 to 6 years 4 spray for patients aged from 7 to 12 years	
Reporting group title	Oxytocin
Reporting group description: 8 UI (2 spray) for patients aged from 3 to 6 years 16 UI (4 spray) for patients aged from 7 to 12 years	

### Primary: Behavioural troubles (Child Behavior Check List Questionnaire)

End point title	Behavioural troubles (Child Behavior Check List Questionnaire)
End point description: Change from baseline at week 12 of CBCL Total problems T score	
End point type	Primary
End point timeframe: week 12	

End point values	OXYTOCIN	PLACEBO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	20		
Units: score	19	20		

### Statistical analyses

Statistical analysis title	Total problems score
Statistical analysis description: Change from baseline at Week 12 in Total Problems score	
Comparison groups	OXYTOCIN v PLACEBO

Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	ANCOVA

## Secondary: Hyperphagia

End point title	Hyperphagia
End point description: Responder analysis on the global score of Dykens Hyperphagia questionnaire: among the patients who had an abnormal score at baseline, number of patients with normal score at week 12	
End point type	Secondary
End point timeframe: week 12	

End point values	OXYTOCIN	PLACEBO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	20		
Units: score	19	20		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Social skills

End point title	Social skills
End point description: Responder analysis on social skills after 12 weeks of oxytocin/placebo treatment: the social skills were assessed by the PSA questionnaire in children aged from 3 to 6 years and by the SRS questionnaire for children aged from 7 to 12 years.Among the patients who had an abnormal score at baseline, number of patients with normal score at week 12	
End point type	Secondary
End point timeframe: week 12	

End point values	OXYTOCIN	PLACEBO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	20		
Units: score	19	20		



## Statistical analyses

No statistical analyses for this end point

## Secondary: Evaluation of auto- and hetero-aggressive behaviour

End point title	Evaluation of auto- and hetero-aggressive behaviour
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End point description:

Responder analysis on ECAA questionnaire item 5 after 12 weeks of oxytocin/placebo treatment: among the patients who had an abnormal score at baseline, number of patients with normal score at week 12

End point type	Secondary
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End point timeframe:

week 12

End point values	OXYTOCIN	PLACEBO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	20		
Units: score	19	20		

## Statistical analyses

No statistical analyses for this end point

## Secondary: the effect of oxytocin (OXT) vs. placebo on psychopathology

End point title	the effect of oxytocin (OXT) vs. placebo on psychopathology
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End point description:

Different scores are obtained: T scores from 50 to 64 are normal; T scores from 65 to 69 are borderline; beyond 69, we are in the pathological.

End point type	Secondary
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End point timeframe:

Evaluation based on the variation of each of the sub-scores obtained on the CBCL questionnaire between J0 and S12.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Evaluation of Global Clinical Status After 12 Weeks of Oxytocin/Placebo Treatment

End point title	Evaluation of Global Clinical Status After 12 Weeks of Oxytocin/Placebo Treatment
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End point description:

It is improvement of the patient's overall clinical condition after 12 weeks of treatment with oxytocin/placebo. It's assessed by the Clinical Global Impression Scale's score.

responder analysis: responders were defined as patients with a score of +1, +2 or +3

End point type	Secondary
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End point timeframe:

week 12

End point values	OXYTOCIN	PLACEBO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	20		
Units: Score	19	20		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Evaluation of acyl and desacyl ghrelin plasma levels after 12 weeks of oxytocin/placebo treatment

End point title	Evaluation of acyl and desacyl ghrelin plasma levels after 12 weeks of oxytocin/placebo treatment
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End point description:

It is evolution of circulating levels of acylated and deacylated ghrelin will be the variations of these rates and the variation of the relationships between day 0 and week 12.

End point type	Secondary
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End point timeframe:

between day 0 and week 12

<b>End point values</b>	OXYTOCIN	PLACEBO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	20		
Units: score	1	19		

### Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

The adverse events (serious or not) are reported during all the study.

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.0
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### Reporting groups

Reporting group title	oxytocin group
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Reporting group description:

Daily intranasal administrations of oxytocin for 12 weeks, followed by an open-label period of 12 weeks of oxytocin. Oxytocin dose will be 8 International Unit for patients aged from 3 to 6 years and 16 International Unit for patients aged from 7 to 12 years.

Reporting group title	Placebo group
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Reporting group description:

Daily intranasal administrations of placebo for 12 weeks, followed by an open-label period of 12 weeks of oxytocin. Oxytocin dose will be International Unit for patients aged from 3 to 6 years and 16 International Unit for patients aged from 7 to 12 years.

Serious adverse events	oxytocin group	Placebo group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (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: 0 %

Non-serious adverse events	oxytocin group	Placebo group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 20 (95.00%)	18 / 20 (90.00%)	
Nervous system disorders			
Nervous system disorders			
subjects affected / exposed	6 / 20 (30.00%)	3 / 20 (15.00%)	
occurrences (all)	6	3	
General disorders and administration site conditions			
pyrexia and site administration disorder			

subjects affected / exposed occurrences (all)	3 / 20 (15.00%) 3	4 / 20 (20.00%) 4	
Gastrointestinal disorders Gastrointestinal disorder subjects affected / exposed occurrences (all)	4 / 20 (20.00%) 4	5 / 20 (25.00%) 5	
Psychiatric disorders Psychiatric disorders subjects affected / exposed occurrences (all)	4 / 20 (20.00%) 4	1 / 20 (5.00%) 1	
Musculoskeletal and connective tissue disorders Musculoskeletal and connective tissue disorders subjects affected / exposed occurrences (all)	3 / 20 (15.00%) 3	3 / 20 (15.00%) 3	
Infections and infestations infections and infestations subjects affected / exposed occurrences (all)	9 / 20 (45.00%) 9	11 / 20 (55.00%) 11	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 April 2017	The method of randomization has changed: <ul style="list-style-type: none"><li>- Patients now have a unique subject number that will correspond to the sequence number and then the first letter of the last and first names.</li><li>- The pre-selection visit has been modified: the investigating physician is responsible for obtaining the signed informed consent form.</li><li>- Change in sampling times and the timing of the ECG was requested in order to avoid duplication of blood sampling and to simplify patient management.</li><li>- The addition of the appendix 11 corresponding to the grid the global evolution of the patient in the different times between D0 and S12 and between J0 and S24.</li></ul>
23 April 2018	Modification of a secondary endpoint for the analysis of data from the Dykens Questionnaire; modification of a secondary endpoint for the assessment of the evolution of the patient's clinical condition; extension of the duration of inclusions; modification of the dosage of oxytocin treatment
26 November 2018	Addition of an Independent Monitoring Committee (IMC).
11 January 2019	<ul style="list-style-type: none"><li>- Collaboration with CROs for statistical analysis design (Excelsus) and statistical analysis (Atlanstat).</li><li>- Modification of secondary objectives: Circulating levels of OXT are measured to verify whether OXT accumulates or remains stable as a function of administered doses.</li><li>- Modification of primary endpoint: Some children changed age groups during the study, so the questionnaire used is clarified.</li></ul>

Notes:

### 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.

NA

Notes: