Clinical trial results:
Palatability testing in children of a new paediatric formulation of Racecadotril as oral suspension strawberry-flavored administered via an oral graduated syringe compared to the current formulation (apricot-flavored oral powder in sachet to be diluted).

Summary

EudraCT number	2017-000278-13
Trial protocol	FR
Global end of trial date	07 July 2017

Results information

Result version number	v1 (current)
This version publication date	04 October 2022
First version publication date	04 October 2022

Trial information

Trial identification

Sponsor protocol code	P16-07/BP0.52

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	BIOPROJET Pharma
Sponsor organisation address	9 rue Rameau, Paris, France, 75002
Public contact	Bioprojet clinical departement, BIOPROJET PHARMA, 0033 (0)1 47 03 66 33, contact@bioprojet.com
Scientific contact	Bioprojet clinical departement, BIOPROJET PHARMA, 0033 (0)1 47 03 66 33, contact@bioprojet.com

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 August 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 July 2017
Global end of trial reached?	Yes
Global end of trial date	07 July 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluate the non-inferiority of the palatability of a new paediatric formulation of Racecadotril strawberry-flavored administered as oral suspension via a graduated oral syringe compared to the current formulation (apricot-flavored oral powder pack) in healthy children 7-12 years of age.

Protection of trial subjects:

The study was conducted in accordance with ICH (International Council for Harmonisation) guidelines and GCP (Good Clinical Practices). Using the "swish and spit" methodology, the study drug is not swallowed following administration: the subject keeps it in the mouth for approximately 5 seconds and spits it out. This type of study minimizes the risk of adverse effect.

Background therapy:

N/A

Evidence for comparator: -

Actual start date of recruitment	17 May 2017
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)	38
Adolescents (12-17 years)	2
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Screening session could take place either before or on the day of taste testing. Each pair of subjects (child + his (her) parent) was assigned to the treatments in a random order. The same inclusion number was attributed to the child and his (her) parent.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	Test Product

Arm description:

This arm included 40 couples (one couple is composed of 1 children + 1 parent).
Each formulation was to be evaluated twice according to a randomized cross-over design with 4 sequences:
Control Product – Test Product – Control Product – Test Product
Control Product – Test Product – Test Product – Control Product
Test Product – Control Product – Test Product – Control Product
Test Product – Control Product – Control Product – Test Product

Arm type	Experimental
Investigational medicinal product name	Tiorfan® 4 mg/mL, strawberry-flavored oral suspension (Test)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

The same dose of racecadotril, i.e. 5 mL corresponding to approximately 20 mg, was administered to all subjects (children and parents) whatever their weight, and according to the method "swish and spit".
The administration of 5 mL of each formulation was standardized as:
- Tiorfan® 4 mg/mL, oral suspension administered directly into the mouth via an oral syringe graduated in kg (from 4-13 kg).
- Tiorfan® 30 mg, oral powder packed in sachet, was diluted in 8 mL of water (in order to respect the same concentration as the suspension) and 5 mL transferred in a teaspoon for oral intake.
Each formulation was administered twice resulting in 4 administrations, each separated by a free interval of 15 minutes.

Arm title	Control Product

Arm description:

This arm included 40 couples (one couple is composed of 1 children + 1 parent)
Each formulation was to be evaluated twice according to a randomized cross-over design with 4 sequences:
Control Product – Test Product – Control Product – Test Product
Control Product – Test Product – Test Product – Control Product
Test Product – Control Product – Test Product – Control Product
Test Product – Control Product – Control Product – Test Product

Arm type	Active comparator

Investigational medicinal product name	Tiorfan® 30 mg, apricot-flavored oral powder in sachet (Control)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral solution in sachet
Routes of administration	Oral use

Dosage and administration details:

The same dose of racecadotril, i.e. 5 mL corresponding to approximately 20 mg, was administered to all subjects (children and parents) whatever their weight, and according to the method "swish and spit". The administration of 5 mL of each formulation was standardized as:
- Tiorfan® 4 mg/mL, oral suspension administered directly into the mouth via an oral syringe graduated in kg (from 4-13 kg).
- Tiorfan® 30 mg, oral powder packed in sachet, was diluted in 8 mL of water (in order to respect the same concentration as the suspension) and 5 mL transferred in a teaspoon for oral intake.
Each formulation was administered twice resulting in 4 administrations, each separated by a free interval of 15 minutes.

Number of subjects in period 1	Test Product	Control Product
Started	40	40
Completed	40	40

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	40	40	
Age categorical			
Subjects are composed of children and adults. Subjects are paired as a couple (1 children + 1 parent). The primary objective does not include the adult population.			
Units: Subjects			
Children (2-11 years)	38	38	
Adolescents (12-17 years)	2	2	
Age continuous			
Units: years			
arithmetic mean	9.3		
standard deviation	± 1.4	-	
Gender categorical			
Units: Subjects			
Female	22	22	
Male	18	18	

End points

End points reporting groups

Reporting group title	Test Product

Reporting group description:

This arm included 40 couples (one couple is composed of 1 children + 1 parent).
Each formulation was to be evaluated twice according to a randomized cross-over design with 4 sequences:
Control Product – Test Product – Control Product – Test Product
Control Product – Test Product – Test Product – Control Product
Test Product – Control Product – Test Product – Control Product
Test Product – Control Product – Control Product – Test Product

Reporting group title	Control Product

Reporting group description:

This arm included 40 couples (one couple is composed of 1 children + 1 parent)
Each formulation was to be evaluated twice according to a randomized cross-over design with 4 sequences:
Control Product – Test Product – Control Product – Test Product
Control Product – Test Product – Test Product – Control Product
Test Product – Control Product – Test Product – Control Product
Test Product – Control Product – Control Product – Test Product

Primary: 7-point hedonic facial scale

End point title	7-point hedonic facial scale

End point description:

This is a self-assessment scale representing 7 facial emoticon symbols varying from "super bad" to "super good". Just after each drug administration, the child was asked to choose the emoticon that represented best his/her sensation just after the spit.
This endpoint was only assessed in the Evaluable population (N=40).

End point type	Primary

End point timeframe:

Evaluations were performed just after the spit for children and 2 times for adults, just after the spit and 2 minutes later. The taste assessments for the child and his (her) parent were done simultaneously. Each subject performed 4 assessments.

End point values	Test Product	Control Product		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40[1]	40[2]		
Units: score				
least squares mean (standard error)	6 (± 0.2)	4.5 (± 0.2)		

Notes:

[1] - Subjects analyzed are 40 children.

[2] - Subjects analyzed are 40 children.

Statistical analyses

Statistical analysis title	Primary analysis

Statistical analysis description:

The primary analysis had to test the non-inferiority of the Test product (T), compared to the Control Product (C) using a 95% confidence interval. The difference (LS mean) Control - Test (C - T) was equal to - 1.5 (± 0.2). As the non-inferiority criterion was predefined as a difference of 2 points between

product groups, the statistical analysis showed the non-inferiority of the Control Product compared to the Test product, with a highly statistical significance (p<0.0001).

Comparison groups	Test Product v Control Product
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

The collection period for AEs and SAEs started after signature of the Informed Consent Form and ended after procedures for the last study visit have been completed or after the end of the study if thought to be related to study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Control Product
Reporting group description: -	
Reporting group title	Test Product
Reporting group description: -	

Serious adverse events	Control Product	Test Product	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 40 (0.00%)	0 / 40 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Control Product	Test Product	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 40 (0.00%)	0 / 40 (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: There were no reports of Adverse Events and Serious Adverse Events.

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