



Clinical trial results:

An open-label study to investigate the local tolerability and acceptability of Lipovir® Gel (Acyclovir 5%) compared to Zovirax® Cream (Acyclovir 5%) on patients with Recurrent Herpes Labialis

Summary

EudraCT number	2017-000549-38
Trial protocol	PT
Global end of trial date	09 August 2018

Results information

Result version number	v1 (current)
This version publication date	05 August 2021
First version publication date	05 August 2021
Summary attachment (see zip file)	Synopsis (LIP-01-01-Synopsis.pdf)

Trial information

Trial identification

Sponsor protocol code	LIP-01-01
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Laboratorios Ojer Pharma, S.L.
Sponsor organisation address	Calle Sancho el Mayor Nº 2, 1º Izquierda, Pamplona, Spain, 31002
Public contact	Laboratorios Ojer Pharma, S.L., Laboratorios Ojer Pharma, S.L., +34 948 281 776, pojer@ojerpharma.com
Scientific contact	Blueclinical Lda, Blueclinical - Investigação e Desenvolvimento em Saúde, Lda, +351 220 995 159, regulatory@blueclinical.pt

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 2018
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	09 August 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the local tolerability and acceptability of Lipovir® Gel compared to Zovirax® Cream in patients with RHL, according to participants' self-report.

Protection of trial subjects:

This is a Phase IV study with products already approved, therefore there are no additional risks that required additional safety measures. Nevertheless, the safety of the participants was ensured during the whole study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 February 2018
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	Portugal: 60
Worldwide total number of subjects	60
EEA total number of subjects	60

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)	60
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The selection of participants for this trial will be made from the population of patients who go to the Institutions where the three sites are located.

Pre-assignment

Screening details:

Screening visit comprises medical history, physical examination, vital signs, 12-lead electrocardiogram and clinical laboratory safety tests. Screening results were valid for 28 days.

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?	Yes
Arm title	Lipovir

Arm description:

acyclovir 5% Gel

Arm type	Experimental
Investigational medicinal product name	Lipovir® gel
Investigational medicinal product code	
Other name	Lavirk®
Pharmaceutical forms	Gel
Routes of administration	Topical

Dosage and administration details:

5 times daily (every 4 hours, avoiding sleep hours) up to a maximum of 10 days

Arm title	Zovirax
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Arm description:

acyclovir 5% Cream (comparator)

Arm type	Active comparator
Investigational medicinal product name	Zovirax® Cream
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical

Dosage and administration details:

5 times daily (every 4 hours, avoiding sleep hours) up to a maximum of 10 days

Number of subjects in period 1	Lipovir	Zovirax
Started	30	30
Completed	30	29
Not completed	0	1
Lost to follow-up	-	1

Baseline characteristics

Reporting groups

Reporting group title	Lipovir
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Reporting group description:

acyclovir 5% Gel

Reporting group title	Zovirax
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Reporting group description:

acyclovir 5% Cream (comparator)

Reporting group values	Lipovir	Zovirax	Total
Number of subjects	30	30	60
Age categorical			
Units: Subjects			
Adults (18-64 years)	30	30	60
Gender categorical			
Units: Subjects			
Male	8	9	17
Female	22	21	43
Time since first symptoms			
Units: hours			
median	16.13	18.48	
standard deviation	± 10.14	± 10.96	-

End points

End points reporting groups

Reporting group title	Lipovir
Reporting group description:	
acyclovir 5% Gel	
Reporting group title	Zovirax
Reporting group description:	
acyclovir 5% Cream (comparator)	

Primary: Bleeding (Products' local tolerability self-reported by the participant)

End point title	Bleeding (Products' local tolerability self-reported by the participant)
End point description:	
Local tolerability was assessed at every treatment day by asking the subjects whether they experienced RHL lesions related symptoms	
End point type	Primary
End point timeframe:	
From the first product administration (day 1) until the end of the study (Day 10)	

End point values	Lipovir	Zovirax		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	29		
Units: Number of Symptoms	28	41		

Statistical analyses

Statistical analysis title	Mann-Whitney Utests
Comparison groups	Lipovir v Zovirax
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.04166
Method	Wilcoxon (Mann-Whitney)

Primary: Burning (Products' local tolerability self-reported by the participant)

End point title	Burning (Products' local tolerability self-reported by the participant)
End point description:	
Local tolerability was assessed at every treatment day by asking the subjects whether they experienced RHL lesions related symptoms	

End point type	Primary
End point timeframe:	
From the first product administration (day 1) until the end of the study (Day 10)	

End point values	Lipovir	Zovirax		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	29		
Units: Number of Symptoms	50	87		

Statistical analyses

Statistical analysis title	Effectiveness
Comparison groups	Lipovir v Zovirax
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.00009
Method	Wilcoxon (Mann-Whitney)

Primary: Drying (Products' local tolerability self-reported by the participant)

End point title	Drying (Products' local tolerability self-reported by the participant)
End point description:	
Local tolerability was assessed at every treatment day by asking the subjects whether they experienced RHL lesions related symptoms	
End point type	Primary
End point timeframe:	
From the first product administration (day 1) until the end of the study (Day 10)	

End point values	Lipovir	Zovirax		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	29		
Units: Number of Symptoms	116	151		

Statistical analyses

Statistical analysis title	Effectiveness
Comparison groups	Lipovir v Zovirax

Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.00009
Method	Wilcoxon (Mann-Whitney)

Primary: Itching (Products' local tolerability self-reported by the participant)

End point title	Itching (Products' local tolerability self-reported by the participant)
End point description: Local tolerability was assessed at every treatment day by asking the subjects whether they experienced RHL lesions related symptoms	
End point type	Primary
End point timeframe: From the first product administration (day 1) until the end of the study (Day 10)	

End point values	Lipovir	Zovirax		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	29		
Units: Number of Symptoms	50	84		

Statistical analyses

Statistical analysis title	Effectiveness
Comparison groups	Lipovir v Zovirax
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.00016
Method	Wilcoxon (Mann-Whitney)

Primary: Pain (Products' local tolerability self-reported by the participant)

End point title	Pain (Products' local tolerability self-reported by the participant)
End point description: Local tolerability was assessed at every treatment day by asking the subjects whether they experienced RHL lesions related symptoms	
End point type	Primary
End point timeframe: From the first product administration (day 1) until the end of the study (Day 10)	

End point values	Lipovir	Zovirax		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	29		
Units: Number of Symptoms	34	43		

Statistical analyses

Statistical analysis title	Effectiveness
Comparison groups	Lipovir v Zovirax
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.10012
Method	Wilcoxon (Mann-Whitney)

Primary: Redness (Products' local tolerability self-reported by the participant)

End point title	Redness (Products' local tolerability self-reported by the participant)
End point description:	
End point type	Primary
End point timeframe:	From the first product administration (day 1) until the end of the study (Day 10)

End point values	Lipovir	Zovirax		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	29		
Units: Number of Symptoms	127	148		

Statistical analyses

Statistical analysis title	Effectiveness
Comparison groups	Lipovir v Zovirax

Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.00371
Method	Wilcoxon (Mann-Whitney)

Primary: Stinging (Products' local tolerability self-reported by the participant)

End point title	Stinging (Products' local tolerability self-reported by the participant)
End point description:	Local tolerability was assessed at every treatment day by asking the subjects whether they experienced RHL lesions related symptoms
End point type	Primary
End point timeframe:	From the first product administration (day 1) until the end of the study (Day 10)

End point values	Lipovir	Zovirax		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	29		
Units: Number of Symptoms	35	46		

Statistical analyses

Statistical analysis title	Effectiveness
Comparison groups	Lipovir v Zovirax
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.07185
Method	Wilcoxon (Mann-Whitney)

Primary: Swelling (Products' local tolerability self-reported by the participant)

End point title	Swelling (Products' local tolerability self-reported by the participant)
End point description:	Local tolerability was assessed at every treatment day by asking the subjects whether they experienced RHL lesions related symptoms
End point type	Primary
End point timeframe:	From the first product administration (day 1) until the end of the study (Day 10)

End point values	Lipovir	Zovirax		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	29		
Units: Number of Symptoms	80	100		

Statistical analyses

Statistical analysis title	Effectiveness
Comparison groups	Lipovir v Zovirax
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.01546
Method	Wilcoxon (Mann-Whitney)

Primary: Tingling (Products' local tolerability self-reported by the participant)

End point title	Tingling (Products' local tolerability self-reported by the participant)
End point description: Local tolerability was assessed at every treatment day by asking the subjects whether they experienced RHL lesions related symptoms	
End point type	Primary
End point timeframe: From the first product administration (day 1) until the end of the study (Day 10)	

End point values	Lipovir	Zovirax		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	29		
Units: Number of Symptoms	39	58		

Statistical analyses

Statistical analysis title	Effectiveness
Comparison groups	Lipovir v Zovirax

Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.01597
Method	Wilcoxon (Mann-Whitney)

Primary: Spread well on the skin (Product's Acceptability as assessed by the participant)

End point title	Spread well on the skin (Product's Acceptability as assessed by the participant)
End point description: Subjects were asked to answer questions about the product's acceptability using a 4-point scale: Totally Agree, Agree, Disagree, Totally Disagree	
End point type	Primary
End point timeframe: At the end of study	

End point values	Lipovir	Zovirax		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	29		
Units: Number of Subjects				
Totally Agree	28	22		
Agree	2	7		
Disagree	0	0		
Totally Disagree	0	0		

Statistical analyses

Statistical analysis title	Effectiveness
Comparison groups	Lipovir v Zovirax
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.03304
Method	Wilcoxon (Mann-Whitney)

Primary: Pleasant texture (Product's Acceptability as assessed by the participant)

End point title	Pleasant texture (Product's Acceptability as assessed by the participant)
End point description: Subjects were asked to answer questions about the product's acceptability using a 4-point scale: Totally Agree, Agree, Disagree, Totally Disagree	

End point type	Primary
End point timeframe:	
At the end of study	

End point values	Lipovir	Zovirax		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	29		
Units: Number of Subjects				
Totally Agree	27	17		
Agree	3	11		
Disagree	0	1		
Totally Disagree	0	0		

Statistical analyses

Statistical analysis title	Effectiveness
Comparison groups	Lipovir v Zovirax
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.00292
Method	Wilcoxon (Mann-Whitney)

Primary: Embarrassment social anxiety (Product's Acceptability as assessed by the participant)

End point title	Embarrassment social anxiety (Product's Acceptability as assessed by the participant)
End point description:	
Subjects were asked to answer questions about the product's acceptability using a 4-point scale: Totally Agree, Agree, Disagree, Totally Disagree	
End point type	Primary
End point timeframe:	
At the end of study	

End point values	Lipovir	Zovirax		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	29		
Units: Number of Subjects				
Totally Agree	1	1		
Agree	0	2		
Disagree	4	11		

Totally Disagree	25	15		
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Statistical analyses

Statistical analysis title	Effectiveness
Comparison groups	Lipovir v Zovirax
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.00579
Method	Wilcoxon (Mann-Whitney)

Primary: Non-compliance due to aesthetic reasons (Product's Acceptability as assessed by the participant)

End point title	Non-compliance due to aesthetic reasons (Product's Acceptability as assessed by the participant)
End point description:	Subjects were asked to answer questions about the product's acceptability using a 4-point scale: Totally Agree, Agree, Disagree, Totally Disagree
End point type	Primary
End point timeframe:	At the end of study

End point values	Lipovir	Zovirax		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	29		
Units: Number of Subjects				
Totally Agree	1	0		
Agree	1	1		
Disagree	6	8		
Totally Disagree	22	20		

Statistical analyses

Statistical analysis title	Effectiveness
Comparison groups	Lipovir v Zovirax

Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.40164
Method	Wilcoxon (Mann-Whitney)

Primary: Smaller herpes lesion (Product's Acceptability as assessed by the participant)

End point title	Smaller herpes lesion (Product's Acceptability as assessed by the participant)
End point description:	Subjects were asked to answer questions about the product's acceptability using a 4-point scale: Totally Agree, Agree, Disagree, Totally Disagree
End point type	Primary
End point timeframe:	At the end of study

End point values	Lipovir	Zovirax		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	29		
Units: Number of Subjects				
Totally Agree	9	6		
Agree	12	12		
Disagree	2	4		
Totally Disagree	7	6		

Statistical analyses

Statistical analysis title	Effectiveness
Comparison groups	Lipovir v Zovirax
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.29131
Method	Wilcoxon (Mann-Whitney)

Primary: Faster healing (Product's Acceptability as assessed by the participant)

End point title	Faster healing (Product's Acceptability as assessed by the participant)
End point description:	Subjects were asked to answer questions about the product's acceptability using a 4-point scale: Totally Agree, Agree, Disagree, Totally Disagree

End point type	Primary
End point timeframe:	
At the end of study	

End point values	Lipovir	Zovirax		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	29		
Units: Number of Subjects				
Totally Agree	15	6		
Agree	9	16		
Disagree	3	4		
Totally Disagree	3	3		

Statistical analyses

Statistical analysis title	Effectiveness
Comparison groups	Lipovir v Zovirax
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.03875
Method	Wilcoxon (Mann-Whitney)

Primary: Less Itching, burning and tingling (Product's Acceptability as assessed by the participant)

End point title	Less Itching, burning and tingling (Product's Acceptability as assessed by the participant)
End point description:	
Subjects were asked to answer questions about the product's acceptability using a 4-point scale: Totally Agree, Agree, Disagree, Totally Disagree	
End point type	Primary
End point timeframe:	
At the end of study	

End point values	Lipovir	Zovirax		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	29		
Units: Number of Subjects				
Totally Agree	17	8		
Agree	9	11		
Disagree	2	8		

Totally Disagree	2	2		
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Statistical analyses

Statistical analysis title	Effectiveness
Comparison groups	Lipovir v Zovirax
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.01041
Method	Wilcoxon (Mann-Whitney)

Primary: Comfort Sensation (Product's Acceptability as assessed by the participant)

End point title	Comfort Sensation (Product's Acceptability as assessed by the participant)
End point description:	Subjects were asked to answer questions about the product's acceptability using a 4-point scale: Totally Agree, Agree, Disagree, Totally Disagree
End point type	Primary
End point timeframe:	At the end of study

End point values	Lipovir	Zovirax		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	29		
Units: Number of Subjects				
Totally Agree	20	5		
Agree	9	23		
Disagree	1	1		
Totally Disagree	0	0		

Statistical analyses

Statistical analysis title	Effectiveness
Comparison groups	Lipovir v Zovirax

Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.00016
Method	Wilcoxon (Mann-Whitney)

Primary: Refreshing sensation (Product's Acceptability as assessed by the participant)

End point title	Refreshing sensation (Product's Acceptability as assessed by the participant)
End point description: Subjects were asked to answer questions about the product's acceptability using a 4-point scale: Totally Agree, Agree, Disagree, Totally Disagree	
End point type	Primary
End point timeframe: At the end of study	

End point values	Lipovir	Zovirax		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	29		
Units: Number of Subjects				
Totally Agree	18	3		
Agree	10	13		
Disagree	2	12		
Totally Disagree	0	1		

Statistical analyses

Statistical analysis title	Effectiveness
Comparison groups	Lipovir v Zovirax
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.00001
Method	Wilcoxon (Mann-Whitney)

Primary: Skin around herpes lesion less dehydrated than usual (Product's Acceptability as assessed by the participant)

End point title	Skin around herpes lesion less dehydrated than usual (Product's Acceptability as assessed by the participant)
End point description: Subjects were asked to answer questions about the product's acceptability using a 4-point scale: Totally	

Agree, Agree, Disagree, Totally Disagree

End point type	Primary
End point timeframe:	
At the end of study	

End point values	Lipovir	Zovirax		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	29		
Units: Number of Subjects				
Totally Agree	9	4		
Agree	14	12		
Disagree	3	10		
Totally Disagree	4	3		

Statistical analyses

Statistical analysis title	Effectiveness
Comparison groups	Lipovir v Zovirax
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.04827
Method	Wilcoxon (Mann-Whitney)

Primary: Repairing effect (Product's Acceptability as assessed by the participant)

End point title	Repairing effect (Product's Acceptability as assessed by the participant)
End point description:	
Subjects were asked to answer questions about the product's acceptability using a 4-point scale: Totally Agree, Agree, Disagree, Totally Disagree	
End point type	Primary
End point timeframe:	
At the end of study	

End point values	Lipovir	Zovirax		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	29		
Units: Number of Subjects				
Totally Agree	9	3		
Agree	18	20		
Disagree	3	6		

Totally Disagree	0	0		
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Statistical analyses

Statistical analysis title	Effectiveness
Comparison groups	Lipovir v Zovirax
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.02581
Method	Wilcoxon (Mann-Whitney)

Primary: Good Tolerance (Product's Acceptability as assessed by the participant)

End point title	Good Tolerance (Product's Acceptability as assessed by the participant)
End point description:	Subjects were asked to answer questions about the product's acceptability using a 4-point scale: Totally Agree, Agree, Disagree, Totally Disagree
End point type	Primary
End point timeframe:	At the end of study

End point values	Lipovir	Zovirax		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	29		
Units: Number of Subjects				
Totally Agree	27	18		
Agree	3	11		
Disagree	0	0		
Totally Disagree	0	0		

Statistical analyses

Statistical analysis title	Effectiveness
Comparison groups	Lipovir v Zovirax

Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0064
Method	Wilcoxon (Mann-Whitney)

Adverse events

Adverse events information

Timeframe for reporting adverse events:

24-FEB-2018 to 09-AUG-2018

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.0
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Reporting groups

Reporting group title	Lipovir
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Reporting group description: -

Reporting group title	Zovirax
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Reporting group description: -

Serious adverse events	Lipovir	Zovirax	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 30 (0.00%)	0 / 29 (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	Lipovir	Zovirax	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 30 (0.00%)	1 / 29 (3.45%)	
General disorders and administration site conditions			
Application site dryness			
subjects affected / exposed	0 / 30 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	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

None reported