



## Clinical trial results:

### Phase 2 Assessment of the Relationship between Serotonin and Efficacy in Ulcerative Colitis: A Multi-Center Randomized, Double Blind, Placebo-Controlled, Pilot Study to Evaluate Safety and Preliminary Efficacy of Orally Administered LX1606 in Subjects with Acute, Mild to Moderate Ulcerative Colitis

#### Summary

EudraCT number	2011-003532-32
Trial protocol	SK LT
Global end of trial date	03 September 2013

#### Results information

Result version number	v1 (current)
This version publication date	13 June 2019
First version publication date	13 June 2019

#### Trial information

##### Trial identification

Sponsor protocol code	LX1606.1-204-UC
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01456052
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	Lexicon Pharmaceuticals, Inc.
Sponsor organisation address	8800 Technology Forest Place, The Woodlands, United States, TX 77381
Public contact	Shanna Jackson, Lexicon Pharmaceuticals, Inc., 001 281 863 3484, sjackson@lexpharma.com
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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:

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**Results analysis stage**

Analysis stage	Final
Date of interim/final analysis	03 September 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 September 2013
Was the trial ended prematurely?	No

Notes:

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**General information about the trial**

Main objective of the trial:

The primary objective of this study is to evaluate the safety and tolerability of orally administered telotristat etiprate (LX1606) after 8 weeks in a cohort of subjects with acute, mild to moderate ulcerative colitis.

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 January 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

Country: Number of subjects enrolled	Poland: 24
Country: Number of subjects enrolled	Slovakia: 6
Country: Number of subjects enrolled	Lithuania: 13
Country: Number of subjects enrolled	United States: 16
Worldwide total number of subjects	59
EEA total number of subjects	43

Notes:

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**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)	57
From 65 to 84 years	2

85 years and over	0
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## Subject disposition

### Recruitment

Recruitment details:

Up to 60 subjects were enrolled and treated in the blinded Treatment period across 24 US and international sites. The recruitment period lasted approximately 10 months.

### Pre-assignment

Screening details:

The study consisted of an approximately 15 days Screening period prior to the blinded Treatment period.

### Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

### Arms

Are arms mutually exclusive?	Yes
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<b>Arm title</b>	Placebo
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Arm description:

Matching placebo administered orally.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Matching placebo administered orally.

<b>Arm title</b>	Low Dose Telotristat Etiprate
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Arm description:

500 mg telotristat etiprate (LX1606) administered orally once daily (QD).

Arm type	Experimental
Investigational medicinal product name	Telotristat etiprate
Investigational medicinal product code	LX1606
Other name	LX1606 Hippurate
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Telotristat etiprate was administered orally as 250 mg capsules at doses of 500 mg (2 x 250 mg capsules) QD.

<b>Arm title</b>	High Dose Telotristat Etiprate
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Arm description:

500 mg telotristat etiprate (LX1606) administered orally three times daily (TID).

Arm type	Experimental
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Investigational medicinal product name	Telotristat etiprate
Investigational medicinal product code	LX1606
Other name	LX1606 Hippurate
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Telotristat etiprate was administered orally as 250 mg capsules at doses of 500 mg (2 x 250 mg capsules) TID.

<b>Number of subjects in period 1</b>	Placebo	Low Dose Telotristat Etiprate	High Dose Telotristat Etiprate
Started	10	25	24
Completed	8	20	19
Not completed	2	5	5
Physician Decision	1	-	1
Adverse Event	1	1	2
Treatment Failure	-	1	1
Protocol Violation	-	1	-
Consent withdrawn	-	2	1

## Baseline characteristics

### Reporting groups

Reporting group title	Placebo
Reporting group description: Matching placebo administered orally.	
Reporting group title	Low Dose Telotristat Etiprate
Reporting group description: 500 mg telotristat etiprate (LX1606) administered orally once daily (QD).	
Reporting group title	High Dose Telotristat Etiprate
Reporting group description: 500 mg telotristat etiprate (LX1606) administered orally three times daily (TID).	

Reporting group values	Placebo	Low Dose Telotristat Etiprate	High Dose Telotristat Etiprate
Number of subjects	10	25	24
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)	9	24	24
From 65-84 years	1	1	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	39.2	45.9	41.7
standard deviation	± 16.16	± 12.38	± 12.69
Gender categorical Units: Subjects			
Female	4	13	7
Male	6	12	17
Race Units: Subjects			
Asian	0	0	1
Black or African American	0	0	1
White	10	25	22

Reporting group values	Total		
Number of subjects	59		
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)	57		
From 65-84 years	2		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	24		
Male	35		
Race			
Units: Subjects			
Asian	1		
Black or African American	1		
White	57		

## End points

### End points reporting groups

Reporting group title	Placebo
Reporting group description: Matching placebo administered orally.	
Reporting group title	Low Dose Telotristat Etiprate
Reporting group description: 500 mg telotristat etiprate (LX1606) administered orally once daily (QD).	
Reporting group title	High Dose Telotristat Etiprate
Reporting group description: 500 mg telotristat etiprate (LX1606) administered orally three times daily (TID).	

### Primary: Number of Subjects Experiencing a Treatment Emergent Adverse Event

End point title	Number of Subjects Experiencing a Treatment Emergent Adverse Event <sup>[1]</sup>
End point description:	
End point type	Primary
End point timeframe: 8 weeks	
Notes: [1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: Statistical analyses were not planned for this endpoint.	

End point values	Placebo	Low Dose Telotristat Etiprate	High Dose Telotristat Etiprate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	24	24	
Units: Subjects	3	9	10	

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects Achieving Clinical Response

End point title	Number of Subjects Achieving Clinical Response
End point description: Clinical response is defined as a decrease in the total modified Mayo score from baseline of $\geq 3$ or a $\geq 30\%$ decrease in the total modified Mayo score from baseline, along with a decrease in the rectal bleeding score $\geq 1$ or an absolute rectal bleeding score $\leq 1$ at Week 8.	
End point type	Secondary
End point timeframe: Baseline to 8 weeks	



End point values	Placebo	Low Dose Telotristat Etiprate	High Dose Telotristat Etiprate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	25	24	
Units: Subjects	4	8	8	

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects Achieving Clinical Remission

End point title	Number of Subjects Achieving Clinical Remission
End point description:	Clinical remission is defined as a total modified Mayo score $\leq 2$ with no individual score $> 1$ at Week 8.
End point type	Secondary
End point timeframe:	Baseline to 8 weeks

End point values	Placebo	Low Dose Telotristat Etiprate	High Dose Telotristat Etiprate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	25	24	
Units: Subjects	2	2	3	

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline in Total Modified Mayo Score

End point title	Change From Baseline in Total Modified Mayo Score
End point description:	A modified Mayo score was used to evaluate disease activity using 4 components, including stool frequency, rectal bleeding, endoscopy, and physician assessment. Components = Stool frequency score 0-3 (normal- $> 4$ stools/day more than normal), rectal bleeding score 0-3 (none-passing blood alone), mucosal appearance at endoscopy 0-3 (normal-severe disease), physician rating of disease activity 0-3 (normal-severe). The total Modified Mayo score ranges from 0 to 12, with higher scores indicating greater disease severity. "n" is the number of subjects with evaluable data at the given time-point.
End point type	Secondary
End point timeframe:	Baseline to 8 weeks

<b>End point values</b>	Placebo	Low Dose Telotristat Etiprate	High Dose Telotristat Etiprate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	19	19	
Units: Score on a scale				
arithmetic mean (standard deviation)	-2.38 (± 2.973)	-1.89 (± 2.865)	-2.53 (± 2.389)	

### Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

10 weeks

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	14.1
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### Reporting groups

Reporting group title	Placebo
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Reporting group description:

Placebo: Matching placebo administered orally

Reporting group title	Low Dose Telotristat Etiprate
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Reporting group description:

500 mg telotristat etiprate (LX1606) administered orally once daily.

Reporting group title	High Dose Telotristat Etiprate
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Reporting group description:

500 mg telotristat etiprate (LX1606) administered orally three times daily.

Serious adverse events	Placebo	Low Dose Telotristat Etiprate	High Dose Telotristat Etiprate
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 10 (10.00%)	3 / 24 (12.50%)	2 / 24 (8.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Blood and lymphatic system disorders			
Iron deficiency anemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 24 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	1 / 10 (10.00%)	3 / 24 (12.50%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			

subjects affected / exposed	0 / 10 (0.00%)	0 / 24 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

<b>Non-serious adverse events</b>	Placebo	Low Dose Telotristat Etiprate	High Dose Telotristat Etiprate
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 10 (30.00%)	9 / 24 (37.50%)	2 / 24 (8.33%)
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 10 (10.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Memory impairment			
subjects affected / exposed	1 / 10 (10.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	1 / 10 (10.00%)	2 / 24 (8.33%)	1 / 24 (4.17%)
occurrences (all)	1	2	1
Abdominal pain			
subjects affected / exposed	0 / 10 (0.00%)	2 / 24 (8.33%)	0 / 24 (0.00%)
occurrences (all)	0	2	0
Diarrhoea			
subjects affected / exposed	0 / 10 (0.00%)	2 / 24 (8.33%)	0 / 24 (0.00%)
occurrences (all)	0	2	0
Dyspepsia			
subjects affected / exposed	0 / 10 (0.00%)	2 / 24 (8.33%)	0 / 24 (0.00%)
occurrences (all)	0	2	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 24 (0.00%)	1 / 24 (4.17%)
occurrences (all)	1	0	1
Sinusitis			
subjects affected / exposed	0 / 10 (0.00%)	2 / 24 (8.33%)	0 / 24 (0.00%)
occurrences (all)	0	2	0

Influenza			
subjects affected / exposed	1 / 10 (10.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 March 2012	Amendment 1: 1. The week 8 visit could occur over multiple days, if needed, to provide flexibility in scheduling the endoscopic evaluation. The original protocol permitted Screening to occur over multiple days, if needed, for the same reason. 2. The list of defined SAEs was clarified, in alignment with ICH E2A reporting conventions, to include important medical events and omitted text that suggested these events had to be considered related to study medication, by the Investigator, to be reported. 3. Cross-referenced text regarding the procedure for withdrawal was updated in Section 6.2.1 to the identical language already in Section 7.11.3 regarding prohibited medications. 4. Schedule of events table in the original protocol included some inadvertent omissions or notations, which were revised under this amendment.

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported