Clinical trial results:
A Phase 3, Multicenter Study to Assess the Long Term Safety and Tolerability of ALKS 3831 in Subjects with Schizophrenia

Summary

EudraCT number	2015-003880-13
Trial protocol	SK HU BG
Global end of trial date	18 June 2018

Results information

Result version number	v1 (current)
This version publication date	04 July 2019
First version publication date	04 July 2019

Trial information

Trial identification

Sponsor protocol code	ALK3831-A306

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02669758
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Alkermes
Sponsor organisation address	852 Winter Street, Waltham, United States, 02451
Public contact	Eva Stroynowski, Alkermes Inc, ++1 718609-7000, eva.stroynowski@alkermes.com
Scientific contact	Eva Stroynowski, Alkermes Inc, ++1 718609-7000, eva.stroynowski@alkermes.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	12 February 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 June 2018
Global end of trial reached?	Yes
Global end of trial date	18 June 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the long term safety and tolerability of ALKS 3831 in subjects with schizophrenia.

Protection of trial subjects:

This trial was conducted in compliance with Good Clinical Practice (GCP) guidelines for conducting clinical trials. The informed consent form (ICF), protocol, and amendments were reviewed and approved by the institutional review board (IRB) or independent ethics committee (IEC) for each clinical trial site.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 January 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	Bulgaria: 100
Country: Number of subjects enrolled	United States: 75
Country: Number of subjects enrolled	Ukraine: 69
Country: Number of subjects enrolled	Serbia: 33
Worldwide total number of subjects	277
EEA total number of subjects	100

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)	273

From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects who completed the 4-week treatment period of the antecedent study, ALK3831-A305, were eligible to be enrolled in Study ALK3831-A306 within 7 days of their last study visit in ALK3831-A305.

Pre-assignment

Screening details:

A total of 4 subjects enrolled but were not dosed. Three subjects were lost-to-follow-up prior to receiving study drug, and one subject was not compliant with study drug. A total of 277 patients were administered at least one dose of ALKS 3831 and were included in the safety population.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	ALKS 3831

Arm description:

Olanzapine + samidorphan; administered as a coated bilayer tablet

Arm type	Experimental
Investigational medicinal product name	ALKS 3831
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Tablets were administered for daily dosing

Number of subjects in period 1	ALKS 3831
Started	277
Completed	183
Not completed	94
Consent withdrawn by subject	43
Non-Compliance with Study Drug	8
Adverse event, non-fatal	16
Pregnancy	1
Study non-compliance	1
Lost to follow-up	19
Lack of efficacy	5
Protocol deviation	1

Baseline characteristics

Reporting groups

Reporting group title	Overall Study

Reporting group description: -

Reporting group values	Overall Study	Total	
Number of subjects	277	277	
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			
arithmetic mean	41.4		
standard deviation	± 11.31	-	
Gender categorical Units: Subjects			
Female	116	116	
Male	161	161	

Subject analysis sets

Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety Population includes all subjects who received at least one dose of study drug.

Reporting group values	Safety Population		
Number of subjects	277		
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			

From 65-84 years 85 years and over			

Age continuous Units: years arithmetic mean standard deviation	 41.4 ± 11.31		
Gender categorical Units: Subjects			
Female Male			

End points

End points reporting groups

Reporting group title	ALKS 3831
Reporting group description:	
Olanzapine + samidorphan; administered as a coated bilayer tablet	
Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis
Subject analysis set description:	
The Safety Population includes all subjects who received at least one dose of study drug.	

Primary: Incidence of Adverse Events

End point title	Incidence of Adverse Events[1]
End point description:	
Safety population includes all subjects who received at least one dose of study drug.	
End point type	Primary
End point timeframe:	
Up to 52 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: Summary statistics were conducted for the primary endpoint, and have been included.

End point values	ALKS 3831			
Subject group type	Reporting group			
Number of subjects analysed	277			
Units: Participants	136			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to 52 weeks	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.0
Reporting groups	
Reporting group title	ALKS 3831
Reporting group description:	
Administered as a coated bilayer tablet; ALKS 3831: Daily dosing	

Serious adverse events	ALKS 3831		
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 277 (2.89%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Fibula fracture			
subjects affected / exposed	1 / 277 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intentional overdose			
subjects affected / exposed	1 / 277 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tibia fracture			
subjects affected / exposed	1 / 277 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Schizophrenia			
subjects affected / exposed	5 / 277 (1.81%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		

Suicide attempt			
subjects affected / exposed	1 / 277 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Gastroenteritis viral			
subjects affected / exposed	1 / 277 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	ALKS 3831		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	102 / 277 (36.82%)		
Investigations			
Blood insulin increased			
subjects affected / exposed	6 / 277 (2.17%)		
occurrences (all)	6		
Blood prolactin increased			
subjects affected / exposed	6 / 277 (2.17%)		
occurrences (all)	6		
Weight decreased			
subjects affected / exposed	6 / 277 (2.17%)		
occurrences (all)	6		
Weight increased			
subjects affected / exposed	37 / 277 (13.36%)		
occurrences (all)	40		
Injury, poisoning and procedural complications			
Extra dose administered	Additional description: Resulted from the errors made by the subjects or caregivers while taking the study medication		
subjects affected / exposed	9 / 277 (3.25%)		
occurrences (all)	11		
Nervous system disorders			
Headache			
subjects affected / exposed	11 / 277 (3.97%)		
occurrences (all)	13		

Somnolence			
subjects affected / exposed	23 / 277 (8.30%)		
occurrences (all)	27		
Social circumstances			
Social stay hospitalisation	Additional description: Per protocol social stay hospitalisations were not considered Serious Adverse Events, and were recorded as AEs		
subjects affected / exposed	7 / 277 (2.53%)		
occurrences (all)	7		
Gastrointestinal disorders			
Dry mouth			
subjects affected / exposed	7 / 277 (2.53%)		
occurrences (all)	9		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	7 / 277 (2.53%)		
occurrences (all)	7		
Insomnia			
subjects affected / exposed	6 / 277 (2.17%)		
occurrences (all)	6		
Schizophrenia			
subjects affected / exposed	6 / 277 (2.17%)		
occurrences (all)	6		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	11 / 277 (3.97%)		
occurrences (all)	11		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 March 2016	Updated laboratory parameters, and added clarification lanauge
25 April 2017	Clarification language added surrounding end of study visits; dosage and administration details were updated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported