Clinical trial results:
A Double-Blind, Randomized, Placebo-Controlled Clinical Trial to Assess the Efficacy and Safety of Oral GKT137831 in Patients with Primary Biliary Cholangitis Receiving Ursodeoxycholic Acid and with Persistently Elevated Alkaline Phosphatase

Summary

EudraCT number	2016-004599-23
Trial protocol	BE GB ES GR DE IT
Global end of trial date	08 April 2019

Results information

Result version number	v1 (current)
This version publication date	01 March 2022
First version publication date	01 March 2022
Summary attachment (see zip file)	Synopsis 07Feb20 (GSN000300_Final Synopsis_07Feb2020.pdf)

Trial information

Trial identification

Sponsor protocol code	GSN000300

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03226067
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Genkyotex SA
Sponsor organisation address	16 Ch des Aulx, Plan-les-Ouates, Switzerland, 1228
Public contact	Richard Philipson, MD (CMO, Calliditas), Genkyotex SA, +46 8 411 3005, richard.philipson@calliditas.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:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	07 February 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 April 2019
Global end of trial reached?	Yes
Global end of trial date	08 April 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of oral GKT137831 in comparison with placebo, in subjects with PBC receiving UDCA and with persistently elevated Alkaline Phosphatase (ALP).

Protection of trial subjects:

Independent safety monitoring board

Background therapy:

UDCA

Evidence for comparator:

N/A

Actual start date of recruitment	15 June 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 6
Country: Number of subjects enrolled	United Kingdom: 16
Country: Number of subjects enrolled	Belgium: 14
Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	Greece: 10
Country: Number of subjects enrolled	Canada: 6
Country: Number of subjects enrolled	Israel: 13
Country: Number of subjects enrolled	Italy: 12
Country: Number of subjects enrolled	United States: 27
Worldwide total number of subjects	111
EEA total number of subjects	65

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)	91
From 65 to 84 years	20
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

First subject enrolled: 06-Sep-2017
Last subject completed: 08-Apr-2019

Pre-assignment

Screening details:

Male or female subjects aged 18-80 years with primary biliary cholangitis receiving a stable dose of UDCA and with persistently elevated ALP, who met all the inclusion criteria and none of the exclusion criteria.

Period 1

Period 1 title	Treatment (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Blinding implementation details:

This is a double-blind study: the Sponsor, subjects, investigator staff, persons performing the assessments and data reviewers and statisticians will remain blinded to the identity of the study treatments. The identity of the study treatments will be concealed by the use of IMPs which are all identical in packaging, labeling, schedule of administration, appearance and odor. Randomization data will be kept strictly confidential, and will be accessible only to authorized personnel.

Arms

Are arms mutually exclusive?	Yes
Arm title	GKT137831 400 mg OD

Arm description:

GKT137831 400 mg once daily dosing

Arm type	Experimental
Investigational medicinal product name	Setanaxib
Investigational medicinal product code	GKT137831
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

70 capsules of 100 mg GKT137831 and/or matching placebo per bottle. Subjects self-administered IMP (4 capsules) twice daily once in the morning and once in the evening (aiming for a period of at least 10 hours between doses) with meals or up to 30 minutes after eating a meal.

Arm title	GKT137831 400 mg BID

Arm description:

GKT137831 400 mg twice daily dosing

Arm type	Experimental
Investigational medicinal product name	Setanaxib
Investigational medicinal product code	GKT137831
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

70 capsules of 100 mg GKT137831 per bottle. Subjects self-administered IMP (4 capsules) twice daily once in the morning and once in the evening (aiming for a period of at least 10 hours between doses) with meals or up to 30 minutes after eating a meal.

Arm title	Placebo

Arm description:

Placebo twice daily administration

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

Dosage and administration details:

70 capsules of placebo per bottle. Subjects self administered placebo (4 capsules) once in the morning and once in the evening (aiming for a period of at least 10 hours between doses) with meals or up to 30 minutes after eating a meal.

Number of subjects in period 1	GKT137831 400 mg OD	GKT137831 400 mg BID	Placebo
Started	38	36	37
Completed	35	32	37
Not completed	3	4	0
Physician decision	1	-	-
Consent withdrawn by subject	-	1	-
Adverse event, non-fatal	-	2	-
Administrative reasons	1	1	-
Change in UDCA dose	1	-	-

Baseline characteristics

Reporting groups	
Reporting group title	GKT137831 400 mg OD
Reporting group description: GKT137831 400 mg once daily dosing	
Reporting group title	GKT137831 400 mg BID
Reporting group description: GKT137831 400 mg twice daily dosing	
Reporting group title	Placebo
Reporting group description: Placebo twice daily administration	

Reporting group values	GKT137831 400 mg OD	GKT137831 400 mg BID	Placebo
Number of subjects	38	36	37
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)	31	30	30
From 65-84 years	7	6	7
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	30	34	35
Male	8	2	2

Reporting group values	Total		
Number of subjects	111		
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)	91		
From 65-84 years	20		
85 years and over	0		

Gender categorical Units: Subjects			
Female	99		
Male	12		

Subject analysis sets

Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The Intent-to-Treat (ITT) population included all subjects randomly allocated to a treatment arm who received at least one dose of setanaxib or placebo. All 111 randomized subjects were included in the ITT population.

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

Subject analysis set description:

The Safety population included all subjects who received at least one dose of setanaxib or placebo, (irrespective of whether they were randomly allocated to a treatment arm) and had at least one safety assessment. All 111 randomized subjects were included in the Safety population.

Reporting group values	ITT	Safety analysis	
Number of subjects	111	111	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	91	91	
From 65-84 years	20	20	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	99	99	
Male	12	12	

End points

End points reporting groups

Reporting group title	GKT137831 400 mg OD
Reporting group description: GKT137831 400 mg once daily dosing	
Reporting group title	GKT137831 400 mg BID
Reporting group description: GKT137831 400 mg twice daily dosing	
Reporting group title	Placebo
Reporting group description: Placebo twice daily administration	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description: The Intent-to-Treat (ITT) population included all subjects randomly allocated to a treatment arm who received at least one dose of setanaxib or placebo. All 111 randomized subjects were included in the ITT population.	
Subject analysis set title	Safety analysis
Subject analysis set type	Safety analysis
Subject analysis set description: The Safety population included all subjects who received at least one dose of setanaxib or placebo, (irrespective of whether they were randomly allocated to a treatment arm) and had at least one safety assessment. All 111 randomized subjects were included in the Safety population.	

Primary: Percent change from baseline to Week 24 in serum GGT

End point title	Percent change from baseline to Week 24 in serum GGT
End point description:	
End point type	Primary
End point timeframe: Week 24	

End point values	GKT137831 400 mg OD	GKT137831 400 mg BID	Placebo	ITT
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	37	30	35	102
Units: U/L				
arithmetic mean (standard deviation)	-4.9 (± 59.58)	-19 (± 28.89)	-8.4 (± 21.45)	-10.2 (± 41.16)

Statistical analyses

Statistical analysis title	Analysis of Percent Change in serum GGT (W24)
Statistical analysis description: Analysis of Percent Change from Baseline to Week 24 Visit in Serum GGT (ITT Population)	
Comparison groups	Placebo v GKT137831 400 mg BID v GKT137831 400 mg OD

Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.04695 [2]
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Confidence interval	
level	95 %
sides	2-sided
Variability estimate	Standard deviation

Notes:

[1] - The % change from baseline to W24 visit in serum GGT will be analyzed using ANCOVA with the allocated treatment & disease severity at baseline as fixed effects & the serum GGT baseline value as a continuous covariate. The LSM estimate of the difference between each dose of GKT137831 and placebo alongside the 95% CI will be calculated. Given 2 doses of GKT137831 are tested versus placebo, the 97.5% CI of the LSM of the difference between each dose of GKT137831 and placebo will also be calculated.

[2] - statistical significance following Hochberg adjustment for multiple testing: the highest p-value is considered statistically significant if it is <0.04695 and the lowest p-value is considered statistically significant if it is <0.023475

Secondary: Absolute and percent change in serum GGT from baseline to each assessment

End point title	Absolute and percent change in serum GGT from baseline to each assessment

End point description:

End point type	Secondary

End point timeframe:

Baseline to Weeks 2, 6, 12, 18, 24

End point values	GKT137831 400 mg OD	GKT137831 400 mg BID	Placebo	ITT
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	38	35	37	110
Units: U/L				
arithmetic mean (standard deviation)				
Absolute change W2	-14.3 (± 112.66)	-48.5 (± 61.83)	-11.2 (± 45.96)	-24.2 (± 80.49)
Absolute change W6	-22.2 (± 76.68)	-53.5 (± 67.57)	-17.9 (± 59.01)	-30.7 (± 69.42)
Absolute change W12	-3.9 (± 115.13)	-50.6 (± 74.7)	-8.6 (± 70.11)	-20.1 (± 91.18)
Absolute change W18	-19.2 (± 134.32)	-37.9 (± 93.88)	-4.5 (± 79.81)	-19.9 (± 105.83)
Absolute change W24	-17.9 (± 117.62)	-43.6 (± 62.22)	-10.7 (± 78.2)	-23 (± 91.05)
Percent change W2	-7 (± 25.08)	-17 (± 17.25)	-6.2 (± 13.04)	-9.9 (± 19.66)
Percent change W6	-11.8 (± 21.59)	-22 (± 23.4)	-7.5 (± 16.89)	-13.6 (± 21.44)
Percent change W12	1.7 (± 66.84)	-18.6 (± 27.44)	-5.5 (± 19.44)	-7.1 (± 44.23)
Percent change W18	-4.5 (± 69.65)	-18.7 (± 28.55)	-5.2 (± 22.79)	-9.1 (± 46.23)

Percent change W24	-4.9 (± 59.58)	-19.0 (± 28.89)	-8.4 (± 21.45)	-10.2 (± 41.16)

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute and percent change in serum ALP from baseline to each assessment

End point title	Absolute and percent change in serum ALP from baseline to each assessment

End point description:

End point type	Secondary

End point timeframe:

Baseline to Weeks 2, 6, 12, 18 and 24

End point values	GKT137831 400 mg OD	GKT137831 400 mg BID	Placebo	ITT
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	38	35	37	110
Units: U/L				
arithmetic mean (standard deviation)				
Absolute change W2	-19.8 (± 35.95)	-45.9 (± 75.75)	-17 (± 44.4)	-27.2 (± 55.19)
Absolute change W6	-27.3 (± 44.13)	-58.6 (± 63.88)	-14.5 (± 59.72)	-32.9 (± 58.74)
Absolute change W12	-15.3 (± 67.79)	-53 (± 66.51)	-7.1 (± 52.75)	-24.3 (± 65.14)
Absolute change W18	-27.6 (± 62.54)	-53.2 (± 80.01)	-6 (± 50.15)	-28 (± 66.90)
Absolute change W24	-32.5 (± 65.3)	-45.2 (± 84.41)	-12.4 (± 53.48)	-29.4 (± 68.60)
Percent change W2	-5.5 (± 10.95)	-13.0 (± 12.71)	-3.6 (± 11.51)	-7.2 (± 12.29)
Percent change W6	-8.6 (± 13.42)	-16.3 (± 13.32)	-1.4 (± 15.19)	-8.6 (± 15.14)
Percent change W12	-3.9 (± 22.17)	-14.6 (± 17.89)	-0.6 (± 16.41)	-6.1 (± 19.77)
Percent change W18	-7.8 (± 21.68)	-15.8 (± 21.42)	-0.5 (± 15.66)	-7.7 (± 20.50)
Percent change W24	-9.7 (± 21.1)	-12.9 (± 19.55)	-3.1 (± 15.99)	-8.4 (± 19.26)

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute and Percent Change in Serum Conjugated Bilirubin from Baseline to Each Assessment

End point title	Absolute and Percent Change in Serum Conjugated Bilirubin from Baseline to Each Assessment

End point description:

End point type	Secondary

End point timeframe:

Baseline to Week 2,6,12,18 and 24

End point values	GKT137831 400 mg OD	GKT137831 400 mg BID	Placebo	ITT
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	32	27	32	91
Units: µmol/L				
arithmetic mean (standard deviation)				
Absolute change W2	0.0 (± 1.32)	0.3 (± 1.61)	-0.1 (± 1.4)	0.1 (± 1.43)
Absolute change W6	-0.3 (± 1.14)	0.5 (± 2.06)	-0.3 (± 1.29)	-0.0 (± 1.56)
Absolute change W12	0.8 (± 1.97)	0.4 (± 1.28)	-0.1 (± 1.55)	0.3 (± 1.66)
Absolute change W18	0.5 (± 2.10)	0.6 (± 1.78)	-0.0 (± 1.91)	0.3 (± 1.94)
Absolute change W24	1.1 (± 3.44)	1.1 (± 1.76)	0.3 (± 2.57)	0.8 (± 2.70)
Percent change W2	0.9 (± 16.81)	5.2 (± 22.79)	1.3 (± 28.11)	2.3 (± 22.91)
Percent change W6	-3.4 (± 18.7)	6.3 (± 29.4)	-3.5 (± 17.99)	-0.4 (± 22.61)
Percent change W12	9.4 (± 27.14)	4.8 (± 18.55)	-0.7 (± 20.81)	4.5 (± 22.76)
Percent change W18	6.0 (± 28.16)	8.9 (± 19.34)	1.8 (± 25.98)	5.2 (± 24.99)
Percent change W24	12.7 (± 36.35)	16.1 (± 24.85)	6.4 (± 32.90)	11.4 (± 31.85)

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute and Percent Change in Serum Total Bilirubin from Baseline to Each Assessment

End point title	Absolute and Percent Change in Serum Total Bilirubin from Baseline to Each Assessment

End point description:

End point type	Secondary

End point timeframe:

Baseline to Week 2,6,12,18,24

End point values	GKT137831 400 mg OD	GKT137831 400 mg BID	Placebo	ITT
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	38	35	37	110
Units: µmol/L				
arithmetic mean (standard deviation)				
Absolute change W2	-0.2 (± 2.51)	0.1 (± 2.76)	-0.4 (± 3.75)	-0.2 (± 3.03)
Absolute change W6	-0.5 (± 2.35)	0.5 (± 3.39)	-0.5 (± 3.29)	-0.1 (± 3.05)
Absolute change W12	0.6 (± 3.35)	0.1 (± 2.69)	0.0 (± 2.21)	0.2 (± 2.79)
Absolute change W18	0.1 (± 3.22)	0.5 (± 2.82)	-0.1 (± 3.81)	0.1 (± 3.30)
Absolute change W24	0.5 (± 3.77)	1.2 (± 2.71)	0.7 (± 3.23)	0.8 (± 3.28)
Percent change W2	-0.6 (± 23.62)	5.3 (± 32.42)	3.3 (± 39.98)	2.6 (± 32.42)
Percent change W6	-1.6 (± 21.94)	8.8 (± 41.19)	0.1 (± 34.6)	2.3 (± 33.38)
Percent change W12	5.7 (± 32.99)	7.7 (± 37.53)	3.1 (± 22.39)	5.5 (± 3.21)
Percent change W18	1.7 (± 28.34)	9.6 (± 32.56)	4.1 (± 29.50)	4.9 (± 29.97)
Percent change W24	5.4 (± 29.77)	14.5 (± 31.60)	10.5 (± 32.27)	9.8 (± 31.10)

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute and Percent Change from Baseline to Week 24 in Liver Stiffness

End point title	Absolute and Percent Change from Baseline to Week 24 in Liver Stiffness

End point description:

End point type	Secondary

End point timeframe:

Week 24

End point values	GKT137831 400 mg OD	GKT137831 400 mg BID	Placebo	ITT
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	33	26	32	91
Units: kPa				
arithmetic mean (standard deviation)				
Absolute change W24	-0.5 (± 5.24)	-0.3 (± 2.65)	0.7 (± 3.63)	-0.0 (± 4.06)
Percent change W24	3.3 (± 34.95)	7.9 (± 43.68)	10.1 (± 33.11)	7.0 (± 36.75)

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute and Percent Change from Baseline to Week 24 in Liver

Stiffness by Subgroup (≥9.6 kPa) of Baseline Liver Stiffness Values

End point title	Absolute and Percent Change from Baseline to Week 24 in Liver Stiffness by Subgroup (≥9.6 kPa) of Baseline Liver Stiffness Values

End point description:

End point type	Secondary

End point timeframe:

Week 24

End point values	GKT137831 400 mg OD	GKT137831 400 mg BID	Placebo	ITT
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	14	9	16	39
Units: kPa				
arithmetic mean (standard deviation)				
Absolute change W24	-1.9 (± 7.49)	-2.1 (± 2.43)	0.4 (± 4.65)	-1.0 (± 5.51)
Percent change W24	-5.3 (± 35.10)	-16.1 (± 20.71)	4.2 (± 30.09)	-3.9 (± 30.54)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Serum Levels of Collagen Fragments Indicative of Collagen Formation and Degradation, from Baseline to Weeks 12 and 24

End point title	Percent Change in Serum Levels of Collagen Fragments Indicative of Collagen Formation and Degradation, from Baseline to Weeks 12 and 24

End point description:

End point type	Secondary

End point timeframe:

Baseline to Week 12 and Week 24

End point values	GKT137831 400 mg OD	GKT137831 400 mg BID	Placebo	ITT
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	38	33	34	105
Units: ng/mL				
arithmetic mean (standard deviation)				
Percent change ProC3 W12	-2.58 (± 21.09)	-1.31 (± 18.23)	3.64 (± 27.86)	-0.16 (± 22.71)
Percent change ProC3 W24	-3.6 (± 22.54)	0.69 (± 18.17)	3.10 (± 20.78)	-0.01 (± 20.70)

Percent change ProC5 W12	1.17 (± 20.56)	-6.65 (± 22.99)	0.35 (± 22.52)	-1.51 (± 22.03)
Percent change ProC5 W24	2.26 (± 30.36)	-3.27 (± 37.35)	-0.51 (± 37.78)	-0.34 (± 34.88)
Percent change C3M W12	-0.63 (± 15.03)	-3.06 (± 17.73)	1.31 (± 20.17)	-0.74 (± 17.58)
Percent change C3M W24	-0.93 (± 15.29)	0.17 (± 30.10)	-1.06 (± 23.88)	-0.65 (± 23.19)
Percent change C4M W12	1.59 (± 15.76)	-4.82 (± 18.97)	3.19 (± 20.80)	0.14 (± 18.64)
Percent C4M W24	-4.43 (± 17.72)	3.33 (± 37.63)	0.73 (± 21.55)	-0.35 (± 26.21)
Percent change BGM W12	-0.13 (± 14.91)	-4.30 (± 18.81)	-0.12 (± 23.07)	-1.41 (± 18.99)
Percent change BGM W24	1.19 (± 17.15)	2.18 (± 29.14)	3.77 (± 25.89)	2.38 (± 24.03)

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute and Percent Change in Pruritis Visual Analogue Scale (VAS) Scores from baseline to weeks 12 and 24

End point title	Absolute and Percent Change in Pruritis Visual Analogue Scale (VAS) Scores from baseline to weeks 12 and 24

End point description:

End point type	Secondary

End point timeframe:

Baseline to Week 12 and week 24

End point values	GKT137831 400 mg OD	GKT137831 400 mg BID	Placebo	ITT
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	38	34	37	109
Units: score				
arithmetic mean (standard deviation)				
Absolute change W12	-0.1 (± 3.1)	0.3 (± 2.33)	0.5 (± 1.79)	0.2 (± 2.47)
Absolute change W24	-1.0 (± 2.32)	0.1 (± 2.3)	0.7 (± 1.83)	-0.1 (± 2.26)
Percent change W12	-35.1 (± 46.13)	-11.7 (± 73.87)	26.1 (± 79.35)	-8.3 (± 70.68)
Percent change W24	-36.9 (± 58.6)	-0.3 (± 92.71)	27.3 (± 72.88)	-5.6 (± 78.38)

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute and Percent Change from Baseline to Weeks 12 and 24 in PBC-

40 Domain Scores

End point title	Absolute and Percent Change from Baseline to Weeks 12 and 24 in PBC-40 Domain Scores

End point description:

End point type	Secondary

End point timeframe:

Baseline to week 12 and week 24

End point values	GKT137831 400 mg OD	GKT137831 400 mg BID	Placebo	ITT
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	38	34	37	109
Units: Score				
arithmetic mean (standard deviation)				
Absolute change Symptoms W12	-0.4 (± 3.34)	-0.9 (± 3.19)	-0.2 (± 3.52)	-0.5 (± 3.34)
Absolute change symptoms W24	0.1 (± 3.46)	-1.4 (± 4.23)	-0.3 (± 3.10)	-0.5 (± 3.6)
Absolute change Itch W12	-0.2 (± 2.61)	0.6 (± 2.69)	0.4 (± 2.79)	0.2 (± 2.69)
Absolute change Itch W24	-0.4 (± 3.22)	0.1 (± 2.83)	0.1 (± 2.85)	-0.1 (± 2.96)
Absolute change Fatigue W12	-1.8 (± 5.76)	-3.2 (± 8.25)	0.6 (± 4.91)	-1.4 (± 6.53)
Absolute change Fatigue W24	-0.8 (± 6.31)	-3.6 (± 7.32)	0.6 (± 5.35)	-1.1 (± 6.47)
Absolute change Cognitive W12	-0.1 (± 5.02)	-2.4 (± 5.68)	1.0 (± 4.35)	-0.4 (± 5.17)
Absolute change cognitive W24	0.8 (± 4.67)	-1.4 (± 5.34)	0.3 (± 3.67)	0.0 (± 4.61)
Absolute change Emotional W12	-0.5 (± 2.09)	-1.8 (± 3.2)	0.4 (± 2.35)	-0.6 (± 2.68)
Absolute change Emotional W24	-0.3 (± 2.6)	-2.0 (± 3.0)	0.4 (± 1.78)	-0.5 (± 2.65)
Absolute change Social W12	0.6 (± 4.69)	-2.1 (± 5.24)	2.0 (± 5.43)	0.2 (± 5.34)
Absolute change Social W24	0.8 (± 5.08)	-2.2 (± 4.93)	1.7 (± 5.01)	0.2 (± 5.22)
Percent change Symptoms W12	-2.8 (± 24.68)	-2.7 (± 24.48)	3.1 (± 37.21)	-0.8 (± 29.34)
Percent change Symptoms W24	1.1 (± 25.27)	-3.7 (± 25.19)	1.1 (± 35.03)	-0.3 (± 28.84)
Percent change Itch W12	-5.6 (± 62.92)	-9.2 (± 43.43)	-2.5 (± 48.47)	-5.5 (± 52.28)
Percent change Itch W24	-11.4 (± 52.75)	-9.5 (± 41.83)	-6.8 (± 40.62)	-9.2 (± 45.18)
Percent change Fatigue W12	-3.4 (± 21.11)	-6.8 (± 26.51)	3.4 (± 20.45)	-2.1 (± 22.91)
Percent change Fatigue W24	0.3 (± 24.89)	-9.9 (± 19.81)	2.4 (± 23.07)	-2.0 (± 23.24)
Percent change Cognitive W12	6.1 (± 56.79)	-9.5 (± 32.14)	11.7 (± 51.28)	3.1 (± 48.71)
Percent change Cognitive W24	16.0 (± 62.27)	-1.9 (± 40.79)	5.2 (± 46.11)	7.0 (± 51.23)
Percent change Emotional W12	-1.2 (± 35.5)	-12.8 (± 33.88)	8.7 (± 45.99)	-1.5 (± 39.53)
Percent change Emotional W24	4.9 (± 54.41)	-16.9 (± 26.85)	8.7 (± 34.49)	-0.1 (± 42.16)
Percent change Social W12	4.8 (± 24.14)	-6.2 (± 21.65)	13.9 (± 40.03)	4.5 (± 30.72)
Percent change Social W24	8.1 (± 27.94)	-7.7 (± 18.38)	9.3 (± 28.53)	3.9 (± 26.59)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From ICF signature until 4 weeks after the last study drug administration.	
Adverse event reporting additional description:	
Treatment-emergent AEs	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups	
Reporting group title	GKT137831 400 mg OD
Reporting group description:	
GKT137831 400 mg once daily dosing	
Reporting group title	GKT137831 400 mg BID
Reporting group description:	
GKT137831 400 mg twice daily dosing	
Reporting group title	Placebo
Reporting group description:	
Placebo twice daily administration	

Serious adverse events	GKT137831 400 mg OD	GKT137831 400 mg BID	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 38 (0.00%)	1 / 36 (2.78%)	1 / 37 (2.70%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Multiple fractures			
subjects affected / exposed	0 / 38 (0.00%)	1 / 36 (2.78%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 38 (0.00%)	0 / 36 (0.00%)	1 / 37 (2.70%)
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 %

Non-serious adverse events	GKT137831 400 mg OD	GKT137831 400 mg BID	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 38 (89.47%)	31 / 36 (86.11%)	31 / 37 (83.78%)
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 38 (0.00%)	0 / 36 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 38 (13.16%)	4 / 36 (11.11%)	5 / 37 (13.51%)
occurrences (all)	8	4	5
Dizziness			
subjects affected / exposed	4 / 38 (10.53%)	2 / 36 (5.56%)	1 / 37 (2.70%)
occurrences (all)	5	2	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 38 (2.63%)	3 / 36 (8.33%)	8 / 37 (21.62%)
occurrences (all)	1	3	8
Pyrexia			
subjects affected / exposed	1 / 38 (2.63%)	2 / 36 (5.56%)	2 / 37 (5.41%)
occurrences (all)	1	2	3
Asthenia			
subjects affected / exposed	0 / 38 (0.00%)	2 / 36 (5.56%)	0 / 37 (0.00%)
occurrences (all)	0	4	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	3 / 38 (7.89%)	6 / 36 (16.67%)	4 / 37 (10.81%)
occurrences (all)	3	7	6
Abdominal pain			
subjects affected / exposed	3 / 38 (7.89%)	3 / 36 (8.33%)	0 / 37 (0.00%)
occurrences (all)	4	3	0
Abdominal pain upper			
subjects affected / exposed	2 / 38 (5.26%)	2 / 36 (5.56%)	2 / 37 (5.41%)
occurrences (all)	2	2	2
Diarrhoea			

subjects affected / exposed	1 / 38 (2.63%)	2 / 36 (5.56%)	3 / 37 (8.11%)
occurrences (all)	1	2	5
Constipation			
subjects affected / exposed	1 / 38 (2.63%)	3 / 36 (8.33%)	1 / 37 (2.70%)
occurrences (all)	1	4	1
Gastrooesophageal reflux disease			
subjects affected / exposed	3 / 38 (7.89%)	1 / 36 (2.78%)	1 / 37 (2.70%)
occurrences (all)	4	1	1
Abdominal discomfort			
subjects affected / exposed	1 / 38 (2.63%)	1 / 36 (2.78%)	2 / 37 (5.41%)
occurrences (all)	1	1	2
Dry mouth			
subjects affected / exposed	2 / 38 (5.26%)	0 / 36 (0.00%)	1 / 37 (2.70%)
occurrences (all)	2	0	1
Abdominal distension			
subjects affected / exposed	0 / 38 (0.00%)	2 / 36 (5.56%)	0 / 37 (0.00%)
occurrences (all)	0	2	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 38 (2.63%)	2 / 36 (5.56%)	1 / 37 (2.70%)
occurrences (all)	1	2	2
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	8 / 38 (21.05%)	8 / 36 (22.22%)	8 / 37 (21.62%)
occurrences (all)	11	10	8
Alopecia			
subjects affected / exposed	0 / 38 (0.00%)	1 / 36 (2.78%)	2 / 37 (5.41%)
occurrences (all)	0	1	2
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 38 (5.26%)	1 / 36 (2.78%)	3 / 37 (8.11%)
occurrences (all)	2	1	3
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	3 / 38 (7.89%)	1 / 36 (2.78%)	3 / 37 (8.11%)
occurrences (all)	3	1	5

Upper respiratory tract infection			
subjects affected / exposed	0 / 38 (0.00%)	2 / 36 (5.56%)	2 / 37 (5.41%)
occurrences (all)	0	2	2
Urinary tract infection			
subjects affected / exposed	0 / 38 (0.00%)	2 / 36 (5.56%)	4 / 37 (10.81%)
occurrences (all)	0	2	5
Oral Herpes			
subjects affected / exposed	0 / 38 (0.00%)	1 / 36 (2.78%)	2 / 37 (5.41%)
occurrences (all)	0	1	2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 May 2017	Amendment 1
09 November 2017	Amendment 2
24 July 2018	Amendment 3

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported