



Clinical trial results:

A Phase 2 Randomized, Placebo-Controlled, Double-Blind Parallel-Group, Multicenter Study to Evaluate the Glycemic Effects and Safety of Fasiglifam 25 mg Twice Daily and 50 mg Once Daily on Glycemic Control in Subjects with Type 2 Diabetes

Summary

EudraCT number	2013-000886-35
Trial protocol	SK
Global end of trial date	31 January 2014

Results information

Result version number	v1 (current)
This version publication date	04 March 2016
First version publication date	06 August 2015

Trial information

Trial identification

Sponsor protocol code	TAK-875_203
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01982253
WHO universal trial number (UTN)	U1111-1146-1263

Notes:

Sponsors

Sponsor organisation name	Takeda
Sponsor organisation address	61 Aldwych, London, United Kingdom, WC2B 4AE
Public contact	Program Manager, Takeda Development Centre Europe Ltd., 0044 0203116 8000, clinicaloperations@tgrd.com
Scientific contact	Program Manager, Takeda Development Centre Europe Ltd., 0044 0203116 8000, clinicaloperations@tgrd.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	28 August 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 January 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of fasiglifam 25 mg BID and fasiglifam 50 mg QD on glycemic control over a 12-week treatment period in subjects with type 2 diabetes mellitus (T2DM) who are inadequately controlled on diet and exercise alone.

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	21 October 2013
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	United States: 10
Worldwide total number of subjects	10
EEA total number of subjects	0

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)	9
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects took part in the study at 5 investigative sites in the United States from 21 October 2013 to 31 January 2014.

Pre-assignment

Screening details:

Subjects with a historical diagnosis of T2DM and inadequate glycemic control on diet and exercise alone were enrolled in 1 of 3 treatment groups, placebo, fasiglifam 25 milligram (mg) twice daily (BID) and fasiglifam 50 mg once daily (QD).

Period 1

Period 1 title	Overall Trial (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
Arm title	Placebo

Arm description:

Fasiglifam placebo-matching tablets, orally, twice daily for up to Day 47.

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

Dosage and administration details:

Fasiglifam placebo-matching tablets, orally, twice daily for up to Day 47.

Arm title	Fasiglifam 25 mg BID
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Arm description:

Fasiglifam 25 mg, tablets, orally, twice daily for up to Day 47.

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

Dosage and administration details:

Fasiglifam 25 mg tablets, orally, twice daily for up to Day 47.

Arm title	Fasiglifam 50 mg QD
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Arm description:

Fasiglifam 50 mg, tablet, orally, once daily and fasiglifam- placebo matching tablet, orally, once daily for up to Day 47.

Arm type	Experimental
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Investigational medicinal product name	Fasiglifam
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Fasiglifam 50 mg tablet, orally, once daily for up to Day 47.	
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Fasiglifam placebo-matching tablet, orally, once daily for up to Day 47.	

Number of subjects in period 1	Placebo	Fasiglifam 25 mg BID	Fasiglifam 50 mg QD
Started	2	4	4
Completed	0	0	0
Not completed	2	4	4
Consent withdrawn by subject	1	-	-
Study terminated by sponsor	1	4	4

Baseline characteristics

Reporting groups

Reporting group title	Placebo
Reporting group description: Fasiglifam placebo-matching tablets, orally, twice daily for up to Day 47.	
Reporting group title	Fasiglifam 25 mg BID
Reporting group description: Fasiglifam 25 mg, tablets, orally, twice daily for up to Day 47.	
Reporting group title	Fasiglifam 50 mg QD
Reporting group description: Fasiglifam 50 mg, tablet, orally, once daily and fasiglifam- placebo matching tablet, orally, once daily for up to Day 47.	

Reporting group values	Placebo	Fasiglifam 25 mg BID	Fasiglifam 50 mg QD
Number of subjects	2	4	4
Age categorical Units: Subjects			
18 to 64 years	1	4	4
65 to 84 years	1	0	0
Gender categorical Units: Subjects			
Female	1	3	2
Male	1	1	2
Race/Ethnicity, Customized Units: Subjects			
Black or African American	1	0	1
White	1	4	3
Race/Ethnicity, Customized Units: Subjects			
Hispanic or Latino	1	3	1
Not Hispanic or Latino	1	1	3
Glycosylated Haemoglobin (HbA1c) Units: Subjects			
Less than (<) 8.5 percent (%)	2	2	3
Greater than or equal to (≥) 8.5 percent (%)	0	2	1

Reporting group values	Total		
Number of subjects	10		
Age categorical Units: Subjects			
18 to 64 years	9		
65 to 84 years	1		
Gender categorical Units: Subjects			
Female	6		
Male	4		

Race/Ethnicity, Customized Units: Subjects			
Black or African American	2		
White	8		
Race/Ethnicity, Customized Units: Subjects			
Hispanic or Latino	5		
Not Hispanic or Latino	5		
Glycosylated Haemoglobin (HbA1c) Units: Subjects			
Less than (<) 8.5 percent (%)	7		
Greater than or equal to (≥) 8.5 percent (%)	3		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Fasiglifam placebo-matching tablets, orally, twice daily for up to Day 47.	
Reporting group title	Fasiglifam 25 mg BID
Reporting group description: Fasiglifam 25 mg, tablets, orally, twice daily for up to Day 47.	
Reporting group title	Fasiglifam 50 mg QD
Reporting group description: Fasiglifam 50 mg, tablet, orally, once daily and fasiglifam- placebo matching tablet, orally, once daily for up to Day 47.	

Primary: Change From Baseline in HbA1c at Week 12

End point title	Change From Baseline in HbA1c at Week 12 ^[1]
End point description: The change in the value of glycosylated hemoglobin (the concentration of glucose bound to hemoglobin as a percent of the absolute maximum that can be bound) collected at week 12 or final visit relative to baseline. In accordance with the Statistical Analysis Plan (SAP), due to the limited enrollment at the time of study termination, the summaries and statistical analyses of primary and secondary efficacy parameters originally intended and described in the protocol were not produced.	
End point type	Primary
End point timeframe: Baseline and Week 12	

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: In accordance with the SAP, due to the limited enrollment at the time of study termination, the summaries and statistical analyses of primary and secondary efficacy parameters originally intended and described in the protocol were not produced.

End point values	Placebo	Fasiglifam 25 mg BID	Fasiglifam 50 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 ^[2]	0 ^[3]	0 ^[4]	
Units: percentage of glycosylated hemoglobin				
least squares mean (standard error)	()	()	()	

Notes:

[2] - Limited enrollment at the time of study termination.

[3] - Limited enrollment at the time of study termination.

[4] - Limited enrollment at the time of study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Fasting Plasma Glucose (FPG) at Week 12

End point title	Change From Baseline in Fasting Plasma Glucose (FPG) at Week 12
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End point description:

The change between the FPG value collected at week 12 or final visit relative to baseline. In accordance with the SAP, due to the limited enrollment at the time of study termination, the summaries and statistical analyses of primary and secondary efficacy parameters originally intended and described in the protocol were not produced.

End point type	Secondary
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End point timeframe:

Baseline and Week 12

End point values	Placebo	Fasiglifam 25 mg BID	Fasiglifam 50 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 ^[5]	0 ^[6]	0 ^[7]	
Units: millimole per liter (mmol/L)				
least squares mean (standard error)	()	()	()	

Notes:

[5] - Limited enrollment at the time of study termination.

[6] - Limited enrollment at the time of study termination.

[7] - Limited enrollment at the time of study termination.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events are adverse events that started after the first dose of double-blind study drug and no more than 30 days after the last dose of double-blind study drug.

Adverse event reporting additional description:

At each visit the investigator had to document any occurrence of adverse events and abnormal laboratory findings. Any event spontaneously reported by the subject or observed by the investigator was recorded, irrespective of the relation to study treatment.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.1
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Reporting groups

Reporting group title	Placebo
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Reporting group description:

Fasiglifam placebo-matching tablets, orally, twice daily for up to Day 47.

Reporting group title	Fasiglifam 25 mg BID
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Reporting group description:

Fasiglifam 25 mg, tablets, orally, twice daily for up to Day 47.

Reporting group title	Fasiglifam 50 mg QD
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Reporting group description:

Fasiglifam 50 mg, tablet, orally, once daily and fasiglifam- placebo matching tablet, orally, once daily for up to Day 47.

Serious adverse events	Placebo	Fasiglifam 25 mg BID	Fasiglifam 50 mg QD
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	Placebo	Fasiglifam 25 mg BID	Fasiglifam 50 mg QD
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 2 (50.00%)	1 / 4 (25.00%)	2 / 4 (50.00%)
General disorders and administration site conditions			
Abdominal distension			
subjects affected / exposed	1 / 2 (50.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0

Abdominal hernia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Bronchitis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	1 / 2 (50.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Skin fissures			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	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? Yes

Date	Interruption	Restart date
26 December 2013	Due to specific liver--related safety signals that emerged in the phase 3 program, Takeda concluded that based on all available information, the benefits of treating subjects with fasiglifam do not outweigh the potential risks, thus Takeda decided voluntarily to terminate all development activities for fasiglifam based on liver safety concerns.	-

Notes:

Limitations and caveats

None reported