Clinical trial results:
A Comparative, Randomized, Open-Label, Multi-Center, Single Dose Pharmacokinetic, Pharmacodynamic and Safety Study of Alogliptin (12.5 mg and 25 mg) Between Children, Adolescents, and Adults with Type 2 (Non-Insulin Dependent) Diabetes Mellitus

Summary

EudraCT number	2009-011221-13
Trial protocol	Outside EU/EEA
Global end of trial date	22 November 2013

Results information

Result version number	v1 (current)
This version publication date	04 March 2016
First version publication date	29 May 2015

Trial information

Trial identification

Sponsor protocol code	SYR-322_104

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00957268
WHO universal trial number (UTN)	U1111-1111-7810

Notes:

Sponsors

Sponsor organisation name	Takeda Development Center Americas, Inc.
Sponsor organisation address	One Takeda Parkway, Deerfield, United States, 60015
Public contact	Study Registration Call Centre, Takeda Global Research & Development Center, Inc., 001 800 778-2860, medicalinformation@tpna.com
Scientific contact	Study Registration Call Centre, Takeda Global Research & Development Center, Inc., 001 800 778-2860, medicalinformation@tpna.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000496-PIP01-08
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	22 November 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 November 2013
Global end of trial reached?	Yes
Global end of trial date	22 November 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to determine the pharmacokinetic and safety profile of alogliptin in children, adolescents, and adults with type 2 diabetes mellitus.

Protection of trial subjects:

All participants signed an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 September 2009
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: 46
Worldwide total number of subjects	46
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)	2
Adolescents (12-17 years)	22
Adults (18-64 years)	21
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants took part in the study at 6 investigative sites in the United States from 17 Sep 2009 to 22 Nov 2013.

Pre-assignment

Screening details:

Participants aged 10 to 65 with a diagnosis of type 2 diabetes mellitus were enrolled in 1 of 5 treatment groups and received 12.5 or 25 mg alogliptin once.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Alogliptin 12.5 mg (age 10 to < 14 years)

Arm description:

Alogliptin 12.5 mg, tablets, orally, 1 dose only.

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

Dosage and administration details:

Alogliptin tablets

Arm title	Alogliptin 25 mg (Age 10 to < 14 Years)

Arm description:

Alogliptin 25 mg, tablets, orally, 1 dose only.

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

Dosage and administration details:

Alogliptin tablets

Arm title	Alogliptin 12.5 mg (Age 14 to < 18 Years)

Arm description:

Alogliptin 12.5 mg, tablets, orally, 1 dose only.

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

Dosage and administration details:
Alogliptin tablets

Arm title	Alogliptin 25 mg (Age 14 to < 18 Years)
Arm description: Alogliptin 25 mg, tablets, orally, 1 dose only.	
Arm type	Experimental
Investigational medicinal product name	Alogliptin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:
Alogliptin tablets

Arm title	Alogliptin 25 mg (Age 18 to 65 Years)
Arm description: Alogliptin 25 mg, tablets, orally, 1 dose only.	
Arm type	Experimental
Investigational medicinal product name	Alogliptin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:
Alogliptin tablets

Number of subjects in period 1	Alogliptin 12.5 mg (age 10 to < 14 years)	Alogliptin 25 mg (Age 10 to < 14 Years)	Alogliptin 12.5 mg (Age 14 to < 18 Years)
Started	5	4	8
Completed	5	4	7
Not completed	0	0	1
'Voluntary Withdrawl '	-	-	1

Number of subjects in period 1	Alogliptin 25 mg (Age 14 to < 18 Years)	Alogliptin 25 mg (Age 18 to 65 Years)
Started	7	22
Completed	7	22
Not completed	0	0
'Voluntary Withdrawl '	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Alogliptin 12.5 mg (age 10 to < 14 years)
Reporting group description:	
Alogliptin 12.5 mg, tablets, orally, 1 dose only.	
Reporting group title	Alogliptin 25 mg (Age 10 to < 14 Years)
Reporting group description:	
Alogliptin 25 mg, tablets, orally, 1 dose only.	
Reporting group title	Alogliptin 12.5 mg (Age 14 to < 18 Years)
Reporting group description:	
Alogliptin 12.5 mg, tablets, orally, 1 dose only.	
Reporting group title	Alogliptin 25 mg (Age 14 to < 18 Years)
Reporting group description:	
Alogliptin 25 mg, tablets, orally, 1 dose only.	
Reporting group title	Alogliptin 25 mg (Age 18 to 65 Years)
Reporting group description:	
Alogliptin 25 mg, tablets, orally, 1 dose only.	

Reporting group values	Alogliptin 12.5 mg (age 10 to < 14 years)	Alogliptin 25 mg (Age 10 to < 14 Years)	Alogliptin 12.5 mg (Age 14 to < 18 Years)
Number of subjects	5	4	8
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	12.4	12	15.4
standard deviation	± 0.89	± 0.82	± 0.92
Gender categorical			
Units: Subjects			
Female	4	3	6
Male	1	1	2
Race/Ethnicity, Customized			
Units: Subjects			
Hispanic or Latino	0	1	1
Non-Hispanic or Latina	5	3	7
Race/Ethnicity			
Units: Subjects			

Asian Black or African American	5	3	4
White	0	1	4
Smoking Status Units: Subjects			
Never Smoked	5	4	8
Current Smoker	0	0	0
Ex-Smoker	0	0	0
Height Units: cm			
arithmetic mean	162.4	165.8	168.6
standard deviation	± 8.56	± 8.88	± 5.71
Weight Units: kg			
arithmetic mean	86.62	98.9	116.28
standard deviation	± 13.979	± 11.957	± 33.163
Body Mass Index (BMI) Units: kg/m^2			
arithmetic mean	32.22	36.16	40.92
standard deviation	± 4.621	± 3.422	± 9.19

Reporting group values	Alogliptin 25 mg (Age 14 to < 18 Years)	Alogliptin 25 mg (Age 18 to 65 Years)	Total
Number of subjects	7	22	46
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	15.1	51.3	
standard deviation	± 0.69	± 8.24	-
Gender categorical Units: Subjects			
Female	5	16	34
Male	2	6	12
Race/Ethnicity, Customized Units: Subjects			
Hispanic or Latino	1	4	7
Non-Hispanic or Latina	6	18	39
Race/Ethnicity Units: Subjects			
Asian Black or African American	5	15	32
White	2	7	14

Smoking Status Units: Subjects			
Never Smoked	7	14	38
Current Smoker	0	0	0
Ex-Smoker	0	8	8
Height Units: cm			
arithmetic mean	168.9	167.5	
standard deviation	± 9.03	± 9.81	-
Weight Units: kg			
arithmetic mean	103.71	92.25	
standard deviation	± 17.103	± 16.454	-
Body Mass Index (BMI) Units: kg/m^2			
arithmetic mean	36.46	32.84	
standard deviation	± 6.764	± 4.49	-

End points

End points reporting groups

Reporting group title	Alogliptin 12.5 mg (age 10 to < 14 years)
Reporting group description: Alogliptin 12.5 mg, tablets, orally, 1 dose only.	
Reporting group title	Alogliptin 25 mg (Age 10 to < 14 Years)
Reporting group description: Alogliptin 25 mg, tablets, orally, 1 dose only.	
Reporting group title	Alogliptin 12.5 mg (Age 14 to < 18 Years)
Reporting group description: Alogliptin 12.5 mg, tablets, orally, 1 dose only.	
Reporting group title	Alogliptin 25 mg (Age 14 to < 18 Years)
Reporting group description: Alogliptin 25 mg, tablets, orally, 1 dose only.	
Reporting group title	Alogliptin 25 mg (Age 18 to 65 Years)
Reporting group description: Alogliptin 25 mg, tablets, orally, 1 dose only.	
Subject analysis set title	Safety set
Subject analysis set type	Safety analysis
Subject analysis set description: Subject who received at least one dose of study drug	

Primary: Cmax: Maximum Observed Plasma Concentration for Alogliptin

End point title	Cmax: Maximum Observed Plasma Concentration for
End point description: Maximum observed plasma concentration (Cmax) is the peak plasma concentration of a drug after administration, obtained directly from the plasma concentration-time curve.	
End point type	Primary
End point timeframe: 1 hour pre-dose and 1, 2, 4, 8, 12, 16, 24, 48, and 72 hours post-dose	

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: The analysis was only descriptive.

End point values	Alogliptin 12.5 mg (age 10 to < 14 years)	Alogliptin 25 mg (Age 10 to < 14 Years)	Alogliptin 12.5 mg (Age 14 to < 18 Years)	Alogliptin 25 mg (Age 14 to < 18 Years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	4	7[2]	7
Units: ng/mL				
arithmetic mean (standard deviation)	57.82 (± 31.5546)	101.38 (± 23.4277)	44.24 (± 16.7907)	96.74 (± 28.3818)

Notes:

[2] - 1 Participant did not have data available for analysis.

End point values	Alogliptin 25 mg (Age 18 to 65 Years)			

Subject group type	Reporting group			
Number of subjects analysed	22			
Units: ng/mL				
arithmetic mean (standard deviation)	135.5 (± 34.2169)			

Statistical analyses

No statistical analyses for this end point

Primary: Tmax: Time to Reach the Maximum Plasma Concentration (Cmax) for Alogliptin

End point title	Tmax: Time to Reach the Maximum Plasma Concentration (Cmax) for Alogliptin[3]

End point description:

Tmax: Time to reach the maximum plasma concentration (Cmax), equal to time (hours) to Cmax.

End point type	Primary

End point timeframe:

1 hour pre-dose and 1, 2, 4, 8, 12, 16, 24, 48, and 72 hours post-dose

Notes:

[3] - 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: The analysis was only descriptive.

End point values	Alogliptin 12.5 mg (age 10 to < 14 years)	Alogliptin 25 mg (Age 10 to < 14 Years)	Alogliptin 12.5 mg (Age 14 to < 18 Years)	Alogliptin 25 mg (Age 14 to < 18 Years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	4	7[4]	7
Units: hour				
arithmetic mean (standard deviation)	3.24 (± 1.106)	2.04 (± 0.0462)	5.58 (± 8.2052)	2.86 (± 1.4707)

Notes:

[4] - 1 Participant did not have data available for analysis.

End point values	Alogliptin 25 mg (Age 18 to 65 Years)			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: hour				
arithmetic mean (standard deviation)	2.09 (± 1.1566)			

Statistical analyses

No statistical analyses for this end point

Primary: AUC(0-inf): Area Under the Plasma Concentration-time Curve From Time 0

to Infinity for Alogliptin

End point title	AUC(0-inf): Area Under the Plasma Concentration-time Curve From Time 0 to Infinity for Alogliptin[5]

End point description:

AUC(0-inf) is measure of area under the curve over the dosing interval (tau) (AUC(0-tau]), where tau is the length of the dosing interval in this study).

End point type	Primary

End point timeframe:

1 hour pre-dose and 1, 2, 4, 8, 12, 16, 24, 48, and 72 hours post-dose

Notes:

[5] - 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: The analysis was only descriptive.

End point values	Alogliptin 12.5 mg (age 10 to < 14 years)	Alogliptin 25 mg (Age 10 to < 14 Years)	Alogliptin 12.5 mg (Age 14 to < 18 Years)	Alogliptin 25 mg (Age 14 to < 18 Years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	4	7[6]	7
Units: ng•hr/mL				
arithmetic mean (standard deviation)	789.29 (± 144.0995)	1221.96 (± 128.0268)	688.63 (± 188.7887)	1318.41 (± 123.6279)

Notes:

[6] - 1 Participant did not have data available for analysis.

End point values	Alogliptin 25 mg (Age 18 to 65 Years)			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: ng•hr/mL				
arithmetic mean (standard deviation)	1704.02 (± 270.6604)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Effect-Time Curve From Time 0 to 24 Hours Post-dose (AUEC[0-24]) of Dipeptidyl Peptidase-4 (DPP-4) Inhibition

End point title	Area Under the Plasma Effect-Time Curve From Time 0 to 24 Hours Post-dose (AUEC[0-24]) of Dipeptidyl Peptidase-4 (DPP-4) Inhibition

End point description:

The area under the plasma effect-time curve from time 0 to 24 hours post-dose (AUEC[0-24]) of dipeptidyl peptidase-4 (DPP-4) inhibition was determined from the inhibition-time curve.

End point type	Secondary

End point timeframe:

1 hour pre-dose and 2, 4, 8, 12, and 24 hours post-dose

End point values	Alogliptin 12.5 mg (age 10 to < 14 years)	Alogliptin 25 mg (Age 10 to < 14 Years)	Alogliptin 12.5 mg (Age 14 to < 18 Years)	Alogliptin 25 mg (Age 14 to < 18 Years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	4	7[7]	7
Units: Percentage inhibition•hr				
arithmetic mean (standard deviation)	1569.633 (± 115.9662)	1698.852 (± 74.1622)	1557.788 (± 179.517)	1854.391 (± 63.7486)

Notes:

[7] - 1 Participant did not have data available for analysis.

End point values	Alogliptin 25 mg (Age 18 to 65 Years)			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: Percentage inhibition•hr				
arithmetic mean (standard deviation)	1890.012 (± 71.4549)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Effect (Emax) of Dipeptidyl Peptidase-4 (DPP-4) Inhibition

End point title	Maximum Observed Effect (Emax) of Dipeptidyl Peptidase-4 (DPP-4) Inhibition

End point description:

The maximum observed effect (Emax) of dipeptidyl peptidase-4 (DPP-4) inhibition was determined from the inhibition-time curve.

End point type	Secondary

End point timeframe:

1 hour pre-dose and 2, 4, 8, 12, and 24 hours post-dose

End point values	Alogliptin 12.5 mg (age 10 to < 14 years)	Alogliptin 25 mg (Age 10 to < 14 Years)	Alogliptin 12.5 mg (Age 14 to < 18 Years)	Alogliptin 25 mg (Age 14 to < 18 Years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	4	7[8]	7
Units: Percantage inhibition				
arithmetic mean (standard deviation)	83.66 (± 4.1446)	89.3 (± 2.642)	81.643 (± 5.9267)	90.429 (± 1.7327)

Notes:

[8] - 1 Participant did not have data available for analysis.

End point values	Alogliptin 25 mg (Age 18 to 65 Years)			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: Percantage inhibition				
arithmetic mean (standard deviation)	92.65 (± 2.0068)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach the Maximum Observed Effect of Dipeptidyl Peptidase-4 (DPP-4) Inhibition

End point title	Time to Reach the Maximum Observed Effect of Dipeptidyl Peptidase-4 (DPP-4) Inhibition

End point description:

The time to reach the maximum observed effect of dipeptidyl peptidase-4 (DPP-4) inhibition was determined from the inhibition-time curve.

End point type	Secondary

End point timeframe:

1 hour pre-dose and 2, 4, 8, 12, and 24 hours post-dose

End point values	Alogliptin 12.5 mg (age 10 to < 14 years)	Alogliptin 25 mg (Age 10 to < 14 Years)	Alogliptin 12.5 mg (Age 14 to < 18 Years)	Alogliptin 25 mg (Age 14 to < 18 Years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	4	7[9]	7
Units: hour				
median (full range (min-max))	4.05 (2 to 4.08)	2.08 (2 to 4)	4 (2 to 4.03)	4 (3.97 to 4.12)

Notes:

[9] - 1 Participant did not have data available for analysis.

End point values	Alogliptin 25 mg (Age 18 to 65 Years)			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: hour				
median (full range (min-max))	2 (2 to 4.07)			

Statistical analyses

No statistical analyses for this end point

Secondary: Observed Effect at 24 Hours Post-dose (E24) of Dipeptidyl Peptidase-4 (DPP-4) Inhibition

End point title	Observed Effect at 24 Hours Post-dose (E24) of Dipeptidyl Peptidase-4 (DPP-4) Inhibition

End point description:

The observed effect at 24 hours post-dose (E24) of dipeptidyl peptidase-4 (DPP-4) inhibition was determined from the inhibition-time curve.

End point type	Secondary

End point timeframe:

1 hour pre-dose and 2, 4, 8, 12, and 24 hours post-dose

End point values	Alogliptin 12.5 mg (age 10 to < 14 years)	Alogliptin 25 mg (Age 10 to < 14 Years)	Alogliptin 12.5 mg (Age 14 to < 18 Years)	Alogliptin 25 mg (Age 14 to < 18 Years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	4	7[10]	7
Units: Percentge inhibition				
arithmetic mean (standard deviation)	52 (± 10.2976)	57.375 (± 5.1292)	55.4 (± 9.0239)	70.4 (± 5.766)

Notes:

[10] - 1 Participant did not have data available for analysis.

End point values	Alogliptin 25 mg (Age 18 to 65 Years)			
Subject group type	Reporting group			
Number of subjects analysed	21[11]			
Units: Percentge inhibition				
arithmetic mean (standard deviation)	72.843 (± 5.2949)			

Notes:

[11] - 1 Participant did not have data available for analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Effect-Time Curve From Time 0 to 24 Hours Post-dose (AUEC[0-24]) of the Baseline-corrected Glucagon-like Peptide-1 (GLP-1) Concentration

End point title	Area Under the Plasma Effect-Time Curve From Time 0 to 24 Hours Post-dose (AUEC[0-24]) of the Baseline-corrected Glucagon-like Peptide-1 (GLP-1) Concentration

End point description:

The area under the plasma effect-time curve from time 0 to 24 hours post-dose (AUEC[0-24]) of baseline-corrected glucagon-like peptide-1 was determined from the concentration-time curve. Baseline-corrected glucagon-like peptide-1 concentrations were calculated as the post-dose concentration at each post-dose time point minus the baseline (pre-dose) concentration.

End point type	Secondary

End point timeframe:

1 hour pre-dose and 2, 4, 8, 12, and 24 hours post-dose

End point values	Alogliptin 12.5 mg (age 10 to < 14 years)	Alogliptin 25 mg (Age 10 to < 14 Years)	Alogliptin 12.5 mg (Age 14 to < 18 Years)	Alogliptin 25 mg (Age 14 to < 18 Years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	4	7[12]	7
Units: pmol•hr/L				
arithmetic mean (standard deviation)	117.842 (± 92.8964)	120.055 (± 60.6825)	168.099 (± 116.283)	122.948 (± 98.3822)

Notes:

[12] - 1 Participant did not have data available for analysis.

End point values	Alogliptin 25 mg (Age 18 to 65 Years)			
Subject group type	Reporting group			
Number of subjects analysed	21[13]			
Units: pmol•hr/L				
arithmetic mean (standard deviation)	278.669 (± 102.3304)			

Notes:

[13] - 1 Participant did not have data available for analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Effect (Emax) of the Baseline-corrected Glucagon-like Peptide-1 (GLP-1) Concentration

End point title	Maximum Observed Effect (Emax) of the Baseline-corrected Glucagon-like Peptide-1 (GLP-1) Concentration

End point description:

The maximum observed effect (Emax) of baseline-corrected glucagon-like peptide-1 was determined from the concentration-time curve. Baseline-corrected glucagon-like peptide-1 concentrations were calculated as the post-dose concentration at each post-dose time point minus the baseline (pre-dose) concentration.

End point type	Secondary

End point timeframe:

1 hour pre-dose and 2, 4, 8, 12, and 24 hours post-dose

End point values	Alogliptin 12.5 mg (age 10 to < 14 years)	Alogliptin 25 mg (Age 10 to < 14 Years)	Alogliptin 12.5 mg (Age 14 to < 18 Years)	Alogliptin 25 mg (Age 14 to < 18 Years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	4	7[14]	7
Units: pmol/L				
arithmetic mean (standard deviation)	11.7 (± 4.6357)	7.475 (± 3.8767)	16.5 (± 15.0423)	9.129 (± 6.6668)

Notes:

[14] - 1 Participant did not have data available for analysis.

End point values	Alogliptin 25 mg (Age 18 to 65 Years)			
Subject group type	Reporting group			
Number of subjects analysed	21[15]			
Units: pmol/L				
arithmetic mean (standard deviation)	23.843 (± 12.1143)			

Notes:

[15] - 1 Participant did not have data available for analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach the Maximum Observed Effect of the Baseline-corrected Glucagon-like Peptide-1 (GLP-1) Concentration

End point title	Time to Reach the Maximum Observed Effect of the Baseline-corrected Glucagon-like Peptide-1 (GLP-1) Concentration

End point description:

The time to reach the maximum observed effect of baseline-corrected glucagon-like peptide-1 was determined from the concentration-time curve. Baseline-corrected glucagon-like peptide-1 concentrations were calculated as the post-dose concentration at each post-dose time point minus the baseline (pre-dose) concentration.

End point type	Secondary

End point timeframe:

1 hour pre-dose and 2, 4, 8, 12, and 24 hours post-dose

End point values	Alogliptin 12.5 mg (age 10 to < 14 years)	Alogliptin 25 mg (Age 10 to < 14 Years)	Alogliptin 12.5 mg (Age 14 to < 18 Years)	Alogliptin 25 mg (Age 14 to < 18 Years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	4	7[16]	7
Units: hour				
median (full range (min-max))	8.17 (8.03 to 12)	11.985 (8 to 12)	11.92 (8 to 12)	8.02 (4 to 24)

Notes:

[16] - 1 Participant did not have data available for analysis.

End point values	Alogliptin 25 mg (Age 18 to			

	65 Years)			
Subject group type	Reporting group			
Number of subjects analysed	21[17]			
Units: hour				
median (full range (min-max))	12 (2.33 to 24.02)			

Notes:

[17] - 1 Participant did not have data available for analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Observed Effect at 24 Hours Post-dose (E24) of the Baseline-corrected Glucagon-like Peptide-1 (GLP-1) Concentration

End point title	Observed Effect at 24 Hours Post-dose (E24) of the Baseline-corrected Glucagon-like Peptide-1 (GLP-1) Concentration

End point description:

The observed effect at 24 hours post-dose (E24) of baseline-corrected glucagon-like peptide-1 was determined from the concentration-time curve. Baseline-corrected glucagon-like peptide-1 concentrations were calculated as the post-dose concentration at each post-dose time point minus the baseline (pre-dose) concentration.

End point type	Secondary

End point timeframe:

1 hour pre-dose and 2, 4, 8, 12, and 24 hours post-dose

End point values	Alogliptin 12.5 mg (age 10 to < 14 years)	Alogliptin 25 mg (Age 10 to < 14 Years)	Alogliptin 12.5 mg (Age 14 to < 18 Years)	Alogliptin 25 mg (Age 14 to < 18 Years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	4	7[18]	7
Units: pmol/L				
arithmetic mean (standard deviation)	2.5 (± 5.3282)	4.575 (± 3.6372)	4.214 (± 5.2737)	4.329 (± 6.2203)

Notes:

[18] - 1 Participant did not have data available for analysis.

End point values	Alogliptin 25 mg (Age 18 to 65 Years)			
Subject group type	Reporting group			
Number of subjects analysed	21[19]			
Units: pmol/L				
arithmetic mean (standard deviation)	5.419 (± 6.2064)			

Notes:

[19] - 1 participants did not have data available for analysis.

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 study drug and no more than 30 days after the last dose of study drug (Up to 31 days).

Adverse event reporting additional description:

Safety set: All enrolled participants who received at least 1 dose of study drug.
At each visit the investigator had to document any occurrence of adverse events and abnormal laboratory findings. Any event spontaneously reported by the participant or observed by the investigator was recorded, irrespective of the relation to study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.1

Reporting groups

Reporting group title	Alogliptin 12.5 mg (age 10 to < 14 years)
Reporting group description:	
Alogliptin 12.5 mg, tablets, orally, 1 dose only.	
Reporting group title	Alogliptin 25 mg (Age 10 to < 14 Years)
Reporting group description:	
Alogliptin 25 mg, tablets, orally, 1 dose only.	
Reporting group title	Alogliptin 12.5 mg (Age 14 to < 18 Years)
Reporting group description:	
Alogliptin 12.5 mg, tablets, orally, 1 dose only.	
Reporting group title	Alogliptin 25 mg (Age 14 to < 18 Years)
Reporting group description:	
Alogliptin 25 mg, tablets, orally, 1 dose only.	
Reporting group title	Alogliptin 25 mg (Age 18 to 65 Years)
Reporting group description:	
Alogliptin 25 mg, tablets, orally, 1 dose only.	

Serious adverse events	Alogliptin 12.5 mg (age 10 to < 14 years)	Alogliptin 25 mg (Age 10 to < 14 Years)	Alogliptin 12.5 mg (Age 14 to < 18 Years)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 8 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Alogliptin 25 mg (Age 14 to < 18 Years)	Alogliptin 25 mg (Age 18 to 65 Years)	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 7 (0.00%)	0 / 22 (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: 5 %

Non-serious adverse events	Alogliptin 12.5 mg (age 10 to < 14 years)	Alogliptin 25 mg (Age 10 to < 14 Years)	Alogliptin 12.5 mg (Age 14 to < 18 Years)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 5 (60.00%)	1 / 4 (25.00%)	5 / 8 (62.50%)
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Haematocrit decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Haemoglobin decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Abdominal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	2 / 8 (25.00%)
occurrences (all)	0	0	2
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Presyncope			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Dysgeusia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Tremor			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Nodule			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Tenderness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Gastritis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Rash papular			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Ecchymosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Erythema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Joint swelling			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Viral infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	2
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Alogliptin 25 mg (Age 14 to < 18 Years)	Alogliptin 25 mg (Age 18 to 65 Years)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 7 (28.57%)	9 / 22 (40.91%)	
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Haematocrit decreased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Haemoglobin decreased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Neutrophil count decreased			

subjects affected / exposed	0 / 7 (0.00%)	0 / 22 (0.00%)	
occurrences (all)	0	0	
Vascular disorders			
Abdominal pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 22 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 7 (0.00%)	4 / 22 (18.18%)	
occurrences (all)	0	4	
Presyncope			
subjects affected / exposed	0 / 7 (0.00%)	0 / 22 (0.00%)	
occurrences (all)	0	0	
Dysgeusia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Tremor			
subjects affected / exposed	0 / 7 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 7 (0.00%)	2 / 22 (9.09%)	
occurrences (all)	0	2	
Pyrexia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 22 (0.00%)	
occurrences (all)	0	0	
Nodule			
subjects affected / exposed	0 / 7 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Tenderness			
subjects affected / exposed	0 / 7 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 7 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	

Gastritis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 22 (0.00%)	
occurrences (all)	0	0	
Nausea			
subjects affected / exposed	0 / 7 (0.00%)	2 / 22 (9.09%)	
occurrences (all)	0	3	
Vomiting			
subjects affected / exposed	0 / 7 (0.00%)	0 / 22 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Rash papular			
subjects affected / exposed	0 / 7 (0.00%)	0 / 22 (0.00%)	
occurrences (all)	0	0	
Ecchymosis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Erythema			
subjects affected / exposed	0 / 7 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Joint swelling			
subjects affected / exposed	0 / 7 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Pain in extremity			
subjects affected / exposed	0 / 7 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Infections and infestations			
Viral infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 22 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 7 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Hypoglycaemia			

subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 22 (4.55%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 May 2009	A substantial amendment was written that included revision to the study design to increase the number of study subjects, revision of inclusion criteria, revision of the exclusion criteria, inclusion of an additional regimen of alogliptin, clarification of Informed Consent Requirements, analysis of additional safety points, inclusion of updated safety information, revision of labs and blood volume, clarification of study procedures, and an update of the adverse event list.
06 July 2009	A substantial amendment was written that included revision of safety labs, revision of inclusion criteria, clarification of dosing, and updated methods of contraception.
03 August 2009	A substantial amendment was written that included revision of inclusion criteria, revision of exclusion criteria, revision of overdose criteria, revision of safety labs, and the addition of a follow-up phone call.
17 November 2009	A substantial amendment was written that included revision of inclusion criteria and safety labs.
13 April 2010	A substantial amendment was written that included revision of inclusion criteria and safety labs.
13 July 2010	A substantial amendment was written that included the deletion of 3 pharmacokinetic samples, reduction of total blood volume, revision of contraception information, and review and approval of all medications by the Investigator and the Takeda Medical Monitor due to changes in the exclusionary medication criteria.
07 December 2011	A substantial amendment was written that included revision of inclusion criteria, reduction of the sample size from 72 to 48 participants, and revision of safety labs.
12 March 2012	A substantial amendment was written that included clarification of study procedures, addition of a fasting insulin test to establish a baseline, and inclusion of a summary of plasma glucose and fasting insulin as part of the pharmacodynamic paramenters.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported