ID: SYR-322-MET-008 Efficacy and Safety of Alogliptin Combined With Metformin in Participants With Type 2 Diabetes Mellitus NCT00286442

Results Preview

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Participant Flow

Recruitment Details	Participants enrolled at 115 investigative sites in Australia, Brazil, Chile, Germany, Guatemala, Hungary, India, Mexico, New Zealand, The Netherlands, Poland, South Africa, Spain, and the United States from 10 March 2006 to 12 June 2007.
Pre-Assignment Details	Participants with a historical diagnosis of type 2 diabetes mellitus who were inadequately controlled while receiving a stable dose of metformin monotherapy were enrolled in one of 3, once-daily (QD) treatment groups.

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**	Total (Not public)
Arm/Group Description	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.	
Period Title: Overall Study				
Started	213	210	104	527
Completed	176	165	72	413
Not Completed	37	45	32	114
Reason Not Completed				
Hyperglycemic Rescue	19	17	25	61
Adverse Event	7	6	1	14
Protocol Violation	2	4	2	8
Lost to Follow-up	5	2	1	8
Physician Decision	1	1	1	3
Administrative Error	1	1	0	2
Withdrawal by Subject	2	14	2	18
(Not Public)	Not Completed = 37 Total from all reasons = 37	Not Completed = 45 Total from all reasons = 45	Not Completed = 32 Total from all reasons = 32	

Baseline Characteristics

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**	**Total**
Arm/Group Description	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.	
Overall Number of Baseline Participants	213	210	104	**527**
Baseline Analysis Population Description	[Not specified]			
Age, Customized **Measure Type: Number** **Units: participants**				
<65 years	173	179	83	435
≥65 years	40	31	21	92
Gender, Male/Female **Measure Type: Number** **Units: participants**				

Female	112	96	54	262
Male	101	114	50	265

Outcome Measures

1. Primary Outcome

Title: Change From Baseline in Glycosylated Hemoglobin (HbA1c) at Week 26.

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 26 or final visit and glycosylated hemoglobin collected at baseline.

Time Frame: Baseline and Week 26.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had an HbA1c measurement at baseline and at Week 26.

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	210	203	103
Least Squares Mean (Standard Error) Units: percentage of Glycosylated Hemoglobin	-0.61 (0.053)	-0.59 (0.054)	-0.10 (0.076)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	Null Hypothesis: No difference between treatment and placebo arms in change from baseline in glycosylated hemoglobin at wk 26. Sample size calculated based on normally distributed means. For comparison of either dose vs. placebo (2-sample t-test), study sample size >=500 participants had 95% power to detect a treatment difference as small as 0.4% in the supportive per protocol analysis set assuming SD=0.8%, 2-sided >0.05 significance level and >=80% of participants meeting per protocol criteria.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	A step-down strategy was used for the primary analysis. First, the 25mg dose was compared to placebo at the 2-sided 0.05 significance level. The 12.5 mg dose was compared to placebo only if the comparison of the 25mg dose to placebo was significant.
	Method	ANCOVA
	Comments	Analysis of covariance (ANCOVA) with treatment and geographic region as class variables and baseline metformin dose and baseline HbA1c as covariates.

Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-0.50
	Confidence Interval	(2-Sided) 95% -0.68 to -0.32
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	Null Hypothesis: No difference between treatment and placebo arms in change from baseline in glycosylated hemoglobin at week 26. Sample size calculated based on normally distributed means. For comparison of either dose vs. placebo (2-sample t-test), study sample size >=500 participants had 95% power to detect a treatment difference as small as 0.4% in the per protocol analysis set assuming SD=0.8%, 2-sided test at 0.05 significance level and >=80% of participants meeting per protocol criteria.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	A step-down strategy was used for the primary analysis. First, the 25mg dose was compared to placebo at the 2-sided 0.05 significance level. The 12.5 mg dose was compared to placebo only if the comparison of the 25mg dose to placebo was significant.
	Method	ANCOVA
	Comments	ANCOVA on change from baseline with treatment and geographic region as class variables and baseline metformin dose and baseline HbA1c as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-0.48
	Confidence Interval	(2-Sided) 95% -0.67 to -0.30
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

2. Secondary Outcome

Title: Change From Baseline in Glycosylated Hemoglobin (Week 4).

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 4 and Glycosylated Hemoglobin collected at baseline.

Time Frame: Baseline and Week 4.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had an HbA1c measurement at baseline and at Week 4. Missing data are imputed using last observation carried forward (LOCF).

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	188	187	91
Least Squares Mean (Standard Error) Units: percentage of Glycosylated Hemoglobin	-0.36 (0.031)	-0.40 (0.031)	-0.10 (0.044)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	ANCOVA on change from baseline with treatment and geographic region as class variables and baseline metformin dose and baseline HbA1c as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-0.26
	Confidence Interval	(2-Sided) 95% -0.37 to -0.16
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority	No

	or Equivalence Analysis?	
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	ANCOVA on change from baseline with treatment and geographic region as class variables and baseline metformin dose and baseline HbA1c as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-0.30
	Confidence Interval	(2-Sided) 95% -0.40 to -0.19
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

3. Secondary Outcome

Title: Change From Baseline in Glycosylated Hemoglobin (Week 8).

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 8 and Glycosylated Hemoglobin collected at baseline.

Time Frame: Baseline and Week 8.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had an HbA1c measurement at baseline and at Week 8.

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	210	201	103
Least Squares Mean (Standard Error) Units: percentage of Glycosylated Hemoglobin	-0.59 (0.041)	-0.59 (0.042)	-0.21 (0.058)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of	**P-Value**	<0.001

Hypothesis	**Comments**	No multiplicity adjustments.
	Method	ANCOVA
	Comments	ANCOVA on change from baseline with treatment and geographic region as class variables and baseline metformin dose and baseline HbA1c as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-0.38
	Confidence Interval	(2-Sided) 95% -0.52 to -0.24
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	ANCOVA on change from baseline with treatment and geographic region as class variables and baseline metformin dose and baseline HbA1c as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-0.38
	Confidence Interval	(2-Sided) 95% -0.52 to -0.24
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

4. Secondary Outcome

Title: Change From Baseline in Glycosylated Hemoglobin (Week 12).

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 and Glycosylated Hemoglobin collected at baseline.

Time Frame: Baseline and Week 12.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had an HbA1c measurement at baseline and at Week 12.

Arm/Group Title	Alogliptin 12.5 mg QD	Alogliptin 25 mg QD	Placebo
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	210	203	103
Least Squares Mean (Standard Error) Units: percentage of Glycosylated Hemoglobin	-0.66 (0.047)	-0.66 (0.048)	-0.16 (0.067)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	ANCOVA on change from baseline with treatment and geographic region as class variables and baseline metformin dose and baseline HbA1c as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-0.50
	Confidence Interval	(2-Sided) 95% -0.66 to -0.34
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority	No

	or Equivalence Analysis?	
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	No multiplicity adjustments
	Method	ANCOVA
	Comments	ANCOVA on change from baseline with treatment and geographic region as class variables and baseline metformin dose and baseline HbA1c as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-0.50
	Confidence Interval	(2-Sided) 95% -0.66 to -0.34
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

5. Secondary Outcome

Title: Change From Baseline in Glycosylated Hemoglobin (Week 16).

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 16 and Glycosylated Hemoglobin collected at baseline.

Time Frame: Baseline and Week 16.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had an HbA1c measurement at baseline and at Week 16.

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	210	203	103
Least Squares Mean (Standard Error) Units: percentage of Glycosylated Hemoglobin	-0.66 (0.050)	-0.64 (0.051)	-0.13 (0.072)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of	**P-Value**	<0.001

Hypothesis	**Comments**	No multiplicity adjustments.
	Method	ANCOVA
	Comments	ANCOVA on change from baseline with treatment and geographic region as class variables and baseline metformin dose and baseline HbA1c as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-0.53
	Confidence Interval	(2-Sided) 95% -0.70 to -0.36
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	ANCOVA on change from baseline with treatment and geographic region as class variables and baseline metformin dose and baseline HbA1c as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-0.51
	Confidence Interval	(2-Sided) 95% -0.69 to -0.34
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

6. Secondary Outcome

Title: Change From Baseline in Glycosylated Hemoglobin (Week 20).

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 20 and Glycosylated Hemoglobin collected at baseline.

Time Frame: Baseline and Week 20.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had an HbA1c measurement at baseline and at Week 20.

Arm/Group Title	Alogliptin 12.5 mg QD	Alogliptin 25 mg QD	Placebo
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	210	203	103
Least Squares Mean (Standard Error) Units: percentage of Glycosylated Hemoglobin	-0.63 (0.051)	-0.63 (0.052)	-0.12 (0.073)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	ANCOVA on change from baseline with treatment and geographic region as class variables and baseline metformin dose and baseline HbA1c as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-0.52
	Confidence Interval	(2-Sided) 95% -0.69 to -0.34
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority	No

	or Equivalence Analysis?	
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	ANCOVA on change from baseline with treatment and geographic region as class variables and baseline metformin dose and baseline HbA1c as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-0.52
	Confidence Interval	(2-Sided) 95% -0.69 to -0.34
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

7. Secondary Outcome

Title: Change From Baseline in Fasting Plasma Glucose (Week 1).

Description: The change between the value of fasting plasma glucose collected at final visit or week 1 and fasting plasma glucose collected at baseline.

Time Frame: Baseline and Week 1.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had a fasting plasma glucose measurement at baseline and at Week 1.

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	193	186	98
Least Squares Mean (Standard Error) Units: mg/dL	-14.3 (2.05)	-12.5 (2.09)	-0.6 (2.88)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	No multiplicity adjustments.
	Method	ANCOVA

	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline FPG as covariates. Missing data imputed with LOCF.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-13.7
	Confidence Interval	(2-Sided) 95% -20.7 to -6.8
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the metformin arm.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline FPG as covariates. Missing data imputed with LOCF.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-11.9
	Confidence Interval	(2-Sided) 95% -18.9 to -4.9
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the metformin arm.

8. Secondary Outcome

Title: Change From Baseline in Fasting Plasma Glucose (Week 2).

Description: The change between the value of fasting plasma glucose collected at week 2 and fasting plasma glucose collected at baseline.

Time Frame: Baseline and Week 2.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had a fasting plasma glucose measurement at baseline and at Week 2.

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.

Number of Participants Analyzed	208	199	104
Least Squares Mean (Standard Error) Units: mg/dL	-17.4 (2.11)	-17.6 (2.16)	-0.7 (2.99)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline FPG as covariates. Missing data imputed with LOCF.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-16.7
	Confidence Interval	(2-Sided) 95% -23.9 to -9.5
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline FPG as covariates. Missing data imputed with LOCF.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-16.8
	Confidence Interval	(2-Sided) 95% -24.1 to -9.6
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

9. Secondary Outcome

Title: Change From Baseline in Fasting Plasma Glucose (Week 4).

Description: The change between the value of fasting plasma glucose collected at week 4 and fasting plasma glucose collected at baseline.

Time Frame: Baseline and Week 4.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had a fasting plasma glucose measurement at baseline and at Week 2. Missing data imputed using last observation carried forward (LOCF).

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	211	204	104
Least Squares Mean (Standard Error) Units: mg/dL	-18.4 (1.98)	-18.1 (2.01)	-0.6 (2.82)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline FPG as covariates.

Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-17.8
	Confidence Interval	(2-Sided) 95% -24.6 to -11.0
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline FPG as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-17.5
	Confidence Interval	(2-Sided) 95% -24.3 to -10.6
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

10. Secondary Outcome

Title: Change From Baseline in Fasting Plasma Glucose (Week 8).

Description: The change between the value of fasting plasma glucose collected at week 8 and fasting plasma glucose collected at baseline.

Time Frame: Baseline and Week 8.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had a fasting plasma glucose measurement at baseline and at Week 8. Missing data are imputed using last observation carried forward (LOCF).

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	211	204	104
Least Squares Mean			

(Standard Error) **Units: mg/dL**	-19.6 (2.30)	-17.2 (2.34)	0.4 (3.29)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline FPG as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-20.1
	Confidence Interval	(2-Sided) 95% -28.0 to -12.2
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline FPG as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-17.6
	Confidence Interval	(2-Sided) 95% -25.6 to -9.7
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

11. Secondary Outcome

Title: Change From Baseline in Fasting Plasma Glucose (Week 12).

Description: The change between the value of fasting plasma glucose collected at week 12 and fasting plasma glucose collected at baseline.

Time Frame: Baseline and Week 12.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had a fasting plasma glucose measurement at baseline and at Week 12. Missing data are imputed using last observation carried forward (LOCF).

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	211	204	104
Least Squares Mean (Standard Error) Units: mg/dL	-16.9 (2.44)	-16.8 (2.47)	0.3 (3.48)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline FPG as covariates.

Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-17.2
	Confidence Interval	(2-Sided) 95% -25.6 to -8.9
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline FPG as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-17.0
	Confidence Interval	(2-Sided) 95% -25.4 to -8.6
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

12. Secondary Outcome

Title: Change From Baseline in Fasting Plasma Glucose (Week 16).

Description: The change between the value of fasting plasma glucose collected at week 16 and fasting plasma glucose collected at baseline.

Time Frame: Baseline and Week 16.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had a fasting plasma glucose measurement at baseline and at Week 16. Missing data are imputed using last observation carried forward (LOCF).

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	211	204	104
Least Squares Mean			

(Standard Error) Units: mg/dL	-17.8 (2.43)	-15.4 (2.46)	1.3 (3.46)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline FPG as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-19.1
	Confidence Interval	(2-Sided) 95% -27.4 to -10.8
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline FPG as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-16.7
	Confidence Interval	(2-Sided) 95% -25.0 to -8.3
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

13. Secondary Outcome

Title: Change From Baseline in Fasting Plasma Glucose (Week 20).

Description: The change between the value of fasting plasma glucose collected at week 20 and fasting plasma glucose collected at baseline.

Time Frame: Baseline and Week 20.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had a fasting plasma glucose measurement at baseline and at Week 20. Missing data are imputed using last observation carried forward (LOCF).

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	211	204	104
Least Squares Mean (Standard Error) Units: mg/dL	-18.1 (2.53)	-15.6 (2.57)	-0.1 (3.61)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline FPG as covariates.

Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-18.1
	Confidence Interval	(2-Sided) 95% -26.7 to -9.4
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline FPG as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-15.5
	Confidence Interval	(2-Sided) 95% -24.2 to -6.8
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

14. Secondary Outcome

Title: Change From Baseline in Fasting Plasma Glucose (Week 26).

Description: The change between the value of fasting plasma glucose collected at week 26 or final visit and fasting plasma glucose collected at baseline.

Time Frame: Baseline and Week 26.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had a fasting plasma glucose measurement at baseline and at Week 26. Missing data are imputed using last observation carried forward (LOCF).

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	211	204	104
Least Squares Mean			

(Standard Error) **Units: mg/dL**	-18.7 (2.49)	-17.4 (2.53)	0.0 (3.55)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline FPG as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-18.7
	Confidence Interval	(2-Sided) 95% -27.3 to -10.2
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline FPG as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-17.4
	Confidence Interval	(2-Sided) 95% -25.9 to -8.8
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

15. Secondary Outcome

Title: Number of Participants With Marked Hyperglycemia (Fasting Plasma Glucose ≥ 200 mg Per dL).

Description: The number of participants with a fasting plasma glucose value greater than or equal to 200 mg per dL during the 26 week study.

Time Frame: 26 Weeks.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had at least 1 fasting plasma glucose measurement after baseline.

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	211	206	104
Measure Type: Number Units: participants	61	65	53

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	no multiplicity adjustments.
	Method	Regression, Logistic
	Comments	Logistic regression model includes effects for treatment, geographic region, baseline metformin dose and baseline HbA1c.

Method of Estimation	**Estimation Parameter**	Odds Ratio (OR)
	Estimated Value	0.372
	Confidence Interval	(2-Sided) 95% 0.213 to 0.650
	Estimation Comments	Odd's Ratio (OR) is alogliptin arm versus placebo. OR <1.0 indicates lower incidence compared to placebo.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.002
	Comments	No multiplicity adjustments.
	Method	Regression, Logistic
	Comments	Logistic regression model includes effects for treatment, geographic region, baseline metformin dose and baseline HbA1c.
Method of Estimation	**Estimation Parameter**	Odds Ratio (OR)
	Estimated Value	0.405
	Confidence Interval	(2-Sided) 95% 0.231 to 0.708
	Estimation Comments	Odd's Ratio (OR) is alogliptin arm versus placebo. OR <1.0 indicates lower incidence compared to placebo.

16. Secondary Outcome

Title: Number of Participants Requiring Rescue.

Description: The number of participants requiring rescue for failing to achieve pre-specified glycemic targets during the 26 week study.

Time Frame: 26 Weeks.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who completed at least 1 study visit after baseline.

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	211	207	104
Measure Type: Number Units: participants	19	17	25

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.002
	Comments	no multiplicity adjustments.
	Method	Regression, Logistic
	Comments	Logistic regression model includes effects for treatment, geographic region, baseline metformin dose and baseline HbA1c.
Method of Estimation	**Estimation Parameter**	Odds Ratio (OR)
	Estimated Value	0.302
	Confidence Interval	(2-Sided) 95% 0.143 to 0.635
	Estimation Comments	Odd's Ratio (OR) is alogliptin arm versus placebo. OR <1.0 indicates lower incidence compared to placebo.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	[Not specified]
	Method	Regression, Logistic
	Comments	Logistic regression model includes effects for treatment, geographic region, baseline metformin dose and baseline HbA1c.
Method of Estimation	**Estimation Parameter**	Odds Ratio (OR)
	Estimated Value	0.236
	Confidence Interval	(2-Sided) 95% 0.109 to 0.510
	Estimation Comments	Odd's Ratio (OR) is alogliptin arm versus placebo. OR <1.0 indicates lower incidence compared to placebo.

17. Secondary Outcome

Title: Change From Baseline in Fasting Proinsulin (Week 4).

Description: The change between the value of fasting proinsulin collected at week 4 and fasting proinsulin collected at baseline.

Time Frame: Baseline and Week 4.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had a fasting plasma glucose measurement at baseline and at Week 4. Missing data are imputed using last observation carried forward (LOCF).

Arm/Group Title	Alogliptin 12.5 mg QD	Alogliptin 25 mg QD	Placebo
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	178	174	90
Least Squares Mean (Standard Error) Units: pmol/L	-1.9 (1.76)	-5.0 (1.77)	-0.5 (2.47)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.634
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline proinsulin as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-1.4
	Confidence Interval	(2-Sided) 95% -7.4 to 4.5
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No

	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.136
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline proinsulin as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-4.5
	Confidence Interval	(2-Sided) 95% -10.5 to 1.4
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

18. Secondary Outcome

Title: Change From Baseline in Fasting Proinsulin (Week 8).

Description: The change between the value of fasting proinsulin collected at week 8 and fasting proinsulin collected at baseline.

Time Frame: Baseline and Week 8.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had a proinsulin measurement at baseline and at Week 8. Missing data are imputed using last observation carried forward (LOCF).

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	201	189	100
Least Squares Mean (Standard Error) Units: pmol/L	-2.9 (1.30)	-5.0 (1.34)	-0.4 (1.85)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.274
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables;

baseline metformin dose and baseline proinsulin as covariates.

Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-2.5
	Confidence Interval	(2-Sided) 95% -6.9 to 2.0
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.046
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	[Not specified]
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-4.6
	Confidence Interval	(2-Sided) 95% -9.1 to -0.1
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

19. Secondary Outcome

Title: Change From Baseline in Fasting Proinsulin (Week 12).

Description: The change between the value of fasting proinsulin collected at week 12 and fasting proinsulin collected at baseline.

Time Frame: Baseline and Week 12.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had a proinsulin measurement at baseline and at Week 12. Missing data are imputed using last observation carried forward (LOCF).

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	201	191	100
Least Squares Mean			

(Standard Error) Units: pmol/L	-2.6 (1.76)	-2.7 (1.8)	-1.3 (2.49)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.655
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline proinsulin as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-1.4
	Confidence Interval	(2-Sided) 95% -7.4 to 4.6
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	**P-Value**	0.645
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline FPG as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-1.4
	Confidence Interval	(2-Sided) 95% -7.4 to 4.6
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

20. Secondary Outcome

Title: Change From Baseline in Fasting Proinsulin (Week 16).

Description: The change between the value of fasting proinsulin collected at week 16 and fasting proinsulin collected at baseline.

Time Frame: Baseline and Week 16.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had a proinsulin measurement at baseline and at Week 16. Missing data are imputed using last observation carried forward (LOCF).

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	201	191	100
Least Squares Mean (Standard Error) Units: pmol/L	-1.4 (1.60)	-2.7 (1.64)	-0.5 (2.26)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.748
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline proinsulin as covariates.

Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-0.9
	Confidence Interval	(2-Sided) 95% -6.3 to 4.6
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.432
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline proinsulin as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-2.2
	Confidence Interval	(2-Sided) 95% -7.7 to 3.3
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

21. Secondary Outcome

Title: Change From Baseline in Fasting Proinsulin (Week 20).

Description: The change between the value of fasting proinsulin collected at week 20 and fasting proinsulin collected at baseline.

Time Frame: Baseline and Week 20.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had a proinsulin measurement at baseline and at Week 20. Missing data are imputed using last observation carried forward (LOCF).

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	201	191	100
Least Squares Mean			

(Standard Error) Units: pmol/L	-4.2 (1.62)	-1.1 (1.66)	-2.0 (2.29)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.427
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline proinsulin as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-2.2
	Confidence Interval	(2-Sided) 95% -7.8 to 3.3
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	**P-Value**	0.746
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline proinsulin as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	0.9
	Confidence Interval	(2-Sided) 95% -4.6 to 6.5
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

22. Secondary Outcome

Title: Change From Baseline in Fasting Proinsulin (Week 26).

Description: The change between the value of fasting proinsulin collected at week 26 or final visit and fasting proinsulin collected at baseline.

Time Frame: Baseline and Week 26.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had a PROINSULIN measurement at baseline and at Week 26. Missing data are imputed using last observation carried forward (LOCF).

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	201	191	100
Least Squares Mean (Standard Error) Units: pmol/L	-2.1 (1.80)	-1.6 (1.84)	-3.2 (2.54)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.727
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline proinsulin as

covariates.

Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	1.1
	Confidence Interval	(2-Sided) 95% -5.0 to 7.2
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	1.6
	Comments	No multiplicity adjustments
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline proinsulin as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	0.601
	Confidence Interval	(2-Sided) 95% -4.5 to 7.8
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

23. Secondary Outcome

Title: Change From Baseline in Insulin (Week 4).

Description: The change between the value of insulin collected at week 4 and insulin collected at baseline.

Time Frame: Baseline and Week 4.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had an insulin measurement at baseline and at Week 4. Missing data are imputed using last observation carried forward (LOCF).

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	177	170	89
Least Squares Mean			

(Standard Error) Units: mcIU/mL	1.11 (0.684)	0.52 (0.695)	-1.07 (0.965)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.066
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline insulin as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	2.19
	Confidence Interval	(2-Sided) 95% -0.15 to 4.52
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	**P-Value**	0.180
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline insulin as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	1.60
	Confidence Interval	(2-Sided) 95% -0.74 to 3.93
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

24. Secondary Outcome

Title: Change From Baseline in Insulin (Week 8).

Description: The change between the value of insulin collected at week 8 and insulin collected at baseline.

Time Frame: Baseline and Week 8.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had a Insulin measurement at baseline and at Week 8. Missing data are imputed using last observation carried forward (LOCF).

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	200	186	99
Least Squares Mean (Standard Error) Units: mcIU/mL	2.50 (1.416)	0.18 (1.466)	2.68 (2.015)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.944
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline insulin as covariates.
Method of	**Estimation Parameter**	Mean Difference (Final Values)

Estimation	**Estimated Value**	-0.17
	Confidence Interval	(2-Sided) 95% -5.02 to 4.68
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.316
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline insulin as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-2.50
	Confidence Interval	(2-Sided) 95% -7.40 to 2.40
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

25. Secondary Outcome

Title: Change From Baseline in Insulin (Week 12).

Description: The change between the value of insulin collected at week 12 and insulin collected at baseline.

Time Frame: Baseline and Week 12.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had a Insulin measurement at baseline and at Week 12. Missing data are imputed using last observation carried forward (LOCF).

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	200	188	99
Least Squares Mean (Standard Error) Units: mcIU/mL	1.6 (1.488)	0.46 (1.532)	1.92 (2.118)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.901
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline insulin as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-0.32
	Confidence Interval	(2-Sided) 95% -5.42 to 4.77
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.578
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline insulin as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-1.45
	Confidence Interval	(2-Sided) 95% -6.59 to 3.68
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

26. Secondary Outcome

Title: Change From Baseline in Insulin (Week 16).

Description: The change between the value of insulin collected at week 16 and insulin collected at baseline.

Time Frame: Baseline and Week 16.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had a Insulin measurement at baseline and at Week 16. Missing data are imputed using last observation carried forward (LOCF).

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	200	188	99
Least Squares Mean (Standard Error) Units: mcIU/mL	1.27 (0.964)	1.53 (0.993)	0.64 (1.372)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.708
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline insulin as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	0.63
	Confidence Interval	(2-Sided) 95% -2.67 to 3.93
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	**P-Value**	0.601
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline insulin as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	0.89
	Confidence Interval	(2-Sided) 95% -2.44 to 4.21
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

27. Secondary Outcome

Title: Change From Baseline in Insulin (Week 20).

Description: The change between the value of insulin collected at week 20 and insulin collected at baseline.

Time Frame: Baseline and Week 20.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had a Insulin measurement at baseline and at Week 20. Missing data are imputed using last observation carried forward (LOCF).

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	200	188	99
Least Squares Mean (Standard Error) Units: mcIU/mL	0.91 (0.760)	0.86 (0.782)	-0.21 (1.081)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.398
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline insulin as covariates.
Method of	**Estimation Parameter**	Mean Difference (Final Values)

Estimation	**Estimated Value**	1.12
	Confidence Interval	(2-Sided) 95% -1.48 to 3.72
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.425
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline insulin as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	1.07
	Confidence Interval	(2-Sided) 95% -1.56 to 3.69
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

28. Secondary Outcome

Title: Change From Baseline in Insulin (Week 26).

Description: The change between the value of insulin collected at week 26 and insulin collected at baseline.

Time Frame: Baseline and Week 26.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had a Insulin measurement at baseline and at Week 26. Missing data are imputed using last observation carried forward (LOCF).

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	200	188	99
Least Squares Mean (Standard Error) Units: mcIU/mL	0.63 (0.690)	-0.01 (0.710)	-2.23 (0.981)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.018
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline insulin as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	2.87
	Confidence Interval	(2-Sided) 95% 0.50 to 5.23
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.067
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline insulin as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	2.22
	Confidence Interval	(2-Sided) 95% -0.15 to 4.60
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

29. Secondary Outcome

Title: Change From Baseline in Proinsulin/Insulin Ratio (Week 4).

Description: The change between the ratio value of proinsulin and insulin collected at week 4 and the ratio value of proinsulin and insulin collected at baseline.

Time Frame: Baseline and Week 4.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had insulin and proinsulin measurements at baseline and at Week 4. Missing data are imputed using last observation carried forward (LOCF).

Arm/Group Title	Alogliptin 12.5 mg QD	Alogliptin 25 mg QD	Placebo
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	177	170	89
Least Squares Mean (Standard Error) Units: ratio	-0.045 (0.0082)	-0.056 (0.0083)	-0.008 (0.0115)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.011
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline proinsulin/insulin ratio as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-0.036
	Confidence Interval	(2-Sided) 95% -0.064 to -0.009
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No

	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline proinsulin/insulin ratio as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-0.047
	Confidence Interval	(2-Sided) 95% -0.075 to -0.019
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

30. Secondary Outcome

Title: Change From Baseline in Proinsulin/Insulin Ratio (Week 8).

Description: The change between the ratio value of proinsulin and insulin collected at week 8 and the ratio value of proinsulin and insulin collected at baseline.

Time Frame: Baseline and Week 8.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had insulin and proinsulin measurements at baseline and at Week 8. Missing data are imputed using last observation carried forward (LOCF.

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	200	186	99
Least Squares Mean (Standard Error) Units: ratio	-0.055 (0.0073)	-0.046 (0.0075)	-0.009 (0.0103)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	No multiplicity adjustments.
	Method	ANCOVA

	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline proinsulin/insulin ratio as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-0.045
	Confidence Interval	(2-Sided) 95% -0.070 to -0.021
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.004
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline proinsulin/insulin ratio as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-0.037
	Confidence Interval	(2-Sided) 95% -0.062 to -0.012
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

31. Secondary Outcome

Title: Change From Baseline in Proinsulin/Insulin Ratio (Week 12).

Description: The change between the ratio value of proinsulin and insulin collected at week 12 and the ratio value of proinsulin and insulin collected at baseline.

Time Frame: Baseline and Week 12.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had insulin and proinsulin measurements at baseline and at Week 12. Missing data are imputed using last observation carried forward (LOCF).

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and	Alogliptin 25 mg, tablets, orally, once daily and	Alogliptin placebo-matching tablets, orally, once daily and

	metformin for up to 26 weeks.	metformin for up to 26 weeks.	metformin for up to 26 weeks.
Number of Participants Analyzed	200	188	99
Least Squares Mean (Standard Error) Units: ratio	-0.044 (0.0083)	-0.042 (0.0085)	-0.005 (0.0118)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.007
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline proinsulin/insulin ratio as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-0.039
	Confidence Interval	(2-Sided) 95% -0.068 to -0.011
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No

	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.011
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline proinsulin/insulin ratio as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-0.037
	Confidence Interval	(2-Sided) 95% -0.066 to -0.008
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm

32. Secondary Outcome

Title: Change From Baseline in Proinsulin/Insulin Ratio (Week 16).

Description: The change between the ratio value of proinsulin and insulin collected at week 16 and the ratio value of proinsulin and insulin collected at baseline.

Time Frame: Baseline and Week 16.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had insulin and proinsulin measurements at baseline and at Week 16. Missing data are imputed using last observation carried forward (LOCF).

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	200	188	99
Least Squares Mean (Standard Error) Units: ratio	-0.051 (0.0082)	-0.043 (0.0085)	0.001 (0.0117)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	No multiplicity adjustments.
	Method	ANCOVA

	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline proinsulin/insulin ratio as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-0.052
	Confidence Interval	(2-Sided) 95% -0.080 to -0.024
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.003
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline proinsulin/insulin ratio as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-0.044
	Confidence Interval	(2-Sided) 95% -0.072 to -0.015
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

33. Secondary Outcome

Title: Change From Baseline in Proinsulin/Insulin Ratio (Week 20).

Description: The change between the ratio value of proinsulin and insulin collected at week 20 and the ratio value of proinsulin and insulin collected at baseline.

Time Frame: Baseline and Week 20.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had insulin and proinsulin measurements at baseline and at Week 20. Missing data are imputed using last observation carried forward (LOCF).

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and	Alogliptin 25 mg, tablets, orally, once daily and	Alogliptin placebo-matching tablets, orally, once daily and

	metformin for up to 26 weeks.	metformin for up to 26 weeks.	metformin for up to 26 weeks.
Number of Participants Analyzed	200	188	99
Least Squares Mean (Standard Error) Units: ratio	-0.53 (0.0150)	-0.011 (0.0155)	-0.007 (0.0213)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.078
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline proinsulin/insulin ratio as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-0.046
	Confidence Interval	(2-Sided) 95% -0.097 to 0.005
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No

	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.860
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline proinsulin/insulin ratio as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-0.005
	Confidence Interval	(2-Sided) 95% -0.056 to 0.047
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

34. Secondary Outcome

Title: Change From Baseline in Proinsulin/Insulin Ratio (Week 26).

Description: The change between the ratio value of proinsulin and insulin collected at week 26 or final visit and the ratio value of proinsulin and insulin collected at baseline.

Time Frame: Baseline and Week 26.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had insulin and proinsulin measurements at baseline and at Week 26. Missing data are imputed using last observation carried forward (LOCF).

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	200	188	99
Least Squares Mean (Standard Error) Units: ratio	-0.049 (0.0154)	0.000 (0.0159)	0.004 (0.0219)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.048
	Comments	No multiplicity adjustments.
	Method	ANCOVA

	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline proinsulin/insulin ratio as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-0.053
	Confidence Interval	(2-Sided) 95% -0.106 to -0.001
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.889
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline proinsulin/insulin ratio as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-0.004
	Confidence Interval	(2-Sided) 95% -0.057 to 0.050
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

35. Secondary Outcome

Title: Change From Baseline in C-peptide (Week 4).

Description: The change between the value of C-peptide collected at week 4 and C-peptide collected at baseline.

Time Frame: Baseline and Week 4.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had C-peptide measurements at baseline and at Week 4. Missing data are imputed using last observation carried forward (LOCF).

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants	186	184	92

Analyzed Least Squares Mean (Standard Error) Units: ng/mL	0.222 (0.0893)	0.190 (0.0897)	-0.114 (0.1273)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.031
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline C-peptide as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	0.336
	Confidence Interval	(2-Sided) 95% 0.030 to 0.642
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	**P-Value**	0.051
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline C-peptide as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	0.304
	Confidence Interval	(2-Sided) 95% -0.002 to 0.611
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

36. Secondary Outcome

Title: Change From Baseline in C-peptide (Week 8).

Description: The change between the value of C-peptide collected at week 8 and C-peptide collected at baseline.

Time Frame: Baseline and Week 8.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had C-peptide measurements at baseline and at Week 8. Missing data are imputed using last observation carried forward (LOCF).

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	210	200	103
Least Squares Mean (Standard Error) Units: ng/mL	0.215 (0.0864)	0.238 (0.0884)	0.127 (0.1236)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.563
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline C-peptide as covariates.

Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	0.088
	Confidence Interval	(2-Sided) 95% -0.209 to 0.384
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.467
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline C-peptide as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	0.111
	Confidence Interval	(2-Sided) 95% -0.188 to 0.410
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

37. Secondary Outcome

Title: Change From Baseline in C-peptide (Week 12).

Description: The change between the value of C-peptide collected at week 12 and C-peptide collected at baseline.

Time Frame: Baseline and Week 12.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had C-peptide measurements at baseline and at Week 12. Missing data are imputed using last observation carried forward (LOCF).

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	210	202	103
Least Squares Mean (Standard Error)	0.154 (0.0915)	0.246 (0.0932)	-0.033 (0.1309)

Units: ng/mL

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.243
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline C-peptide as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	0.187
	Confidence Interval	(2-Sided) 95% -0.127 to 0.501
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	**P-Value**	0.083
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline C-peptide as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	0.279
	Confidence Interval	(2-Sided) 95% -0.037 to 0.595
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

38. Secondary Outcome

Title: Change From Baseline in C-peptide (Week 16).

Description: The change between the value of C-peptide collected at week 16 and C-peptide collected at baseline.

Time Frame: Baseline and Week 16.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had C-peptide measurements at baseline and at Week 16. Missing data are imputed using last observation carried forward (LOCF).

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	210	202	103
Least Squares Mean (Standard Error) Units: ng/mL	0.138 (0.0894)	0.250 (0.0910)	-0.018 (0.1280)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.321
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline C-peptide as covariates.

Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	0.155
	Confidence Interval	(2-Sided) 95% -0.152 to 0.463
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.089
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline C-peptide as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	0.268
	Confidence Interval	(2-Sided) 95% -0.041 to 0.577
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

39. Secondary Outcome

Title: Change From Baseline in C-peptide (Week 20).

Description: The change between the value of C-peptide collected at week 20 and C-peptide collected at baseline.

Time Frame: Baseline and Week 20.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had C-peptide measurements at baseline and at Week 20. Missing data are imputed using last observation carried forward (LOCF).

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	210	202	103
Least Squares Mean (Standard Error)	0.007 (0.0803)	0.054 (0.0818)	-0.137 (0.1149)

Units: ng/mL

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.305
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline C-peptide as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	0.144
	Confidence Interval	(2-Sided) 95% -0.132 to 0.420
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	**P-Value**	0.177
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline C-peptide as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	0.191
	Confidence Interval	(2-Sided) 95% -0.086 to 0.468
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

40. Secondary Outcome

Title: Change From Baseline in C-peptide (Week 26).

Description: The change between the value of C-peptide collected at week 26 or final visit and C-peptide collected at baseline.

Time Frame: Baseline and Week 26.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had C-peptide measurements at baseline and at Week 26. Missing data are imputed using last observation carried forward (LOCF).

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	210	202	103
Least Squares Mean (Standard Error) Units: ng/mL	-0.083 (0.0833)	-0.214 (0.0848)	-0.476 (0.1192)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.007
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline C-peptide as

covariates.

Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	0.394
	Confidence Interval	(2-Sided) 95% 0.107 to 0.680
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.074
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline C-peptide as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	0.263
	Confidence Interval	(2-Sided) 95% -0.025 to 0.550
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

41. Secondary Outcome

Title: Number of Participants With Glycosylated Hemoglobin ≤ 6.5%.

Description: The number of participants with a value for the percentage of glycosylated hemoglobin (the percentage of hemoglobin that is bound to glucose) less than or equal to 6.5% during the 26 week study.

Time Frame: Baseline and Week 26.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set).

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	213	207	104
Measure Type: Number			

Units: participants	42	36	4

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	no multiplicity adjustments.
	Method	Regression, Logistic
	Comments	Logistic regression model includes effects for treatment, geographic region, baseline metformin dose and baseline HbA1c.
Method of Estimation	**Estimation Parameter**	Odds Ratio (OR)
	Estimated Value	6.150
	Confidence Interval	(2-Sided) 95% 2.117 to 17.864
	Estimation Comments	Odd's Ratio (OR) is alogliptin arm versus placebo. OR >1.0 indicates higher incidence of response compared to placebo.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical	**P-Value**	0.002

Test of Hypothesis	**Comments**	No multiplicity adjustments.
	Method	Regression, Logistic
	Comments	Logistic regression model includes effects for treatment, geographic region, baseline metformin dose and baseline HbA1c.
Method of Estimation	**Estimation Parameter**	Odds Ratio (OR)
	Estimated Value	5.322
	Confidence Interval	(2-Sided) 95% 1.820 to 15.564
	Estimation Comments	Odd's Ratio (OR) is alogliptin arm versus placebo. OR >1.0 indicates higher incidence of response compared to placebo.

42. Secondary Outcome

Title: Number of Participants With Glycosylated Hemoglobin ≤ 7.0%.

Description: The number of participants with a value for the percentage of glycosylated hemoglobin (the percentage of hemoglobin that is bound to glucose) less than or equal to 7.0% during the 26 week study.

Time Frame: Baseline and Week 26.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set).

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	213	207	104
Measure Type: Number Units: participants	110	92	19

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	No multiplicity adjustments.
	Method	Regression, Logistic
	Comments	Logistic regression model includes effects for treatment, geographic region, baseline metformin dose and baseline HbA1c.
Method of Estimation	**Estimation Parameter**	Odds Ratio (OR)
	Estimated Value	6.092

	Confidence Interval	(2-Sided) 95% 3.271 to 11.345
	Estimation Comments	Odd's Ratio (OR) compares alogliptin arm versus placebo. OR >1.0 indicates higher incidence of response compared to placebo.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	No multiplicity adjustments.
	Method	Regression, Logistic
	Comments	Logistic regression model includes effects for treatment, geographic region, baseline metformin dose and baseline HbA1c.
Method of Estimation	**Estimation Parameter**	Odds Ratio (OR)
	Estimated Value	4.451
	Confidence Interval	(2-Sided) 95% 2.388 to 8.296
	Estimation Comments	Odd's Ratio (OR) compares alogliptin arm versus placebo. OR >1.0 indicates higher incidence of response compared to placebo.

43. Secondary Outcome

Title: Number of Participants With Glycosylated Hemoglobin ≤ 7.5%.

Description: The number of participants with a value for the percentage of glycosylated hemoglobin (the percentage of hemoglobin that is bound to glucose) less than or equal to 7.5% during the 26 week study.

Time Frame: Baseline and Week 26.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set).

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	213	207	104
Measure Type: Number Units: participants	153	137	47

Statistical Analysis 1

Statistical Analysis	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]

Overview		
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	No multiplicity adjustments.
	Method	Regression, Logistic
	Comments	Logistic regression model includes effects for treatment, geographic region, baseline metformin dose and baseline HbA1c.
Method of Estimation	**Estimation Parameter**	Odds Ratio (OR)
	Estimated Value	4.238
	Confidence Interval	(2-Sided) 95% 2.327 to 7.717
	Estimation Comments	Odd's Ratio (OR) compares alogliptin arm versus placebo. OR >1.0 indicates higher incidence of response compared to placebo.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	[Not specified]
	Method	Regression, Logistic
	Comments	Logistic regression model includes effects for treatment, geographic region, baseline metformin dose and baseline HbA1c.
Method of Estimation	**Estimation Parameter**	Odds Ratio (OR)
	Estimated Value	3.293
	Confidence Interval	(2-Sided) 95% 1.814 to 5.979
	Estimation Comments	Odd's Ratio (OR) compares alogliptin arm versus placebo. OR >1.0 indicates higher incidence of response compared to placebo.

44. Secondary Outcome

Title: Number of Participants With Glycosylated Hemoglobin Decrease From Baseline ≥ 0.5%.

Description: The number of participants with a decrease from baseline in the percentage of glycosylated hemoglobin (the percentage of hemoglobin that is bound to glucose) greater than or equal to 0.5% during the 26 week study.

Time Frame: Baseline and Week 26.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set).

Arm/Group Title	Alogliptin 12.5 mg QD	Alogliptin 25 mg QD	Placebo
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	213	207	104
Measure Type: Number Units: participants	123	122	28

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	No multiplicity adjustments.
	Method	Regression, Logistic
	Comments	Logistic regression model includes effects for treatment, geographic region, baseline metformin dose and baseline HbA1c.
Method of Estimation	**Estimation Parameter**	Odds Ratio (OR)
	Estimated Value	4.103
	Confidence Interval	(2-Sided) 95% 2.428 to 6.934
	Estimation Comments	Odd's Ratio (OR) compares alogliptin arm versus placebo. OR >1.0 indicates higher incidence of response compared to placebo.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	No multiplicity adjustments.
	Method	Regression, Logistic
	Comments	Logistic regression model includes effects for treatment, geographic region, baseline metformin dose and baseline HbA1c.
Method of Estimation	**Estimation Parameter**	Odds Ratio (OR)
	Estimated Value	4.314
	Confidence Interval	(2-Sided) 95% 2.545 to 7.312
	Estimation Comments	Odd's Ratio (OR) compares alogliptin arm versus placebo. OR >1.0 indicates higher incidence of response compared to placebo.

45. Secondary Outcome

Title: Number of Participants With Glycosylated Hemoglobin Decrease From Baseline ≥ 1.0%.

Description: The number of participants with a decrease from baseline in the percentage of glycosylated hemoglobin (the percentage of hemoglobin that is bound to glucose) greater than or equal to 1.0% during the 26 week study.

Time Frame: Baseline and Week 26.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set).

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	213	207	104
Measure Type: Number Units: participants	61	62	9

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	No multiplicity adjustments.
	Method	Regression, Logistic
	Comments	Logistic regression model includes effects for treatment, geographic region, baseline metformin dose and baseline HbA1c.
Method of	**Estimation Parameter**	Odds Ratio (OR)

Estimation	**Estimated Value**	5.601
	Confidence Interval	(2-Sided) 95% 2.554 to 12.282
	Estimation Comments	Odd's Ratio (OR) compares alogliptin arm versus placebo. OR >1.0 indicates higher incidence of response compared to placebo.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	No multiplicity adjustments.
	Method	Regression, Logistic
	Comments	Logistic regression model includes effects for treatment, geographic region, baseline metformin dose and baseline HbA1c.
Method of Estimation	**Estimation Parameter**	Odds Ratio (OR)
	Estimated Value	5.793
	Confidence Interval	(2-Sided) 95% 2.645 to 12.684
	Estimation Comments	Odd's Ratio (OR) compares alogliptin arm versus placebo. OR >1.0 indicates higher incidence of response compared to placebo.

46. Secondary Outcome

Title: Number of Participants With Glycosylated Hemoglobin Decrease From Baseline ≥ 1.5%.

Description: The number of participants with a decrease from baseline in the percentage of glycosylated hemoglobin (the percentage of hemoglobin that is bound to glucose) greater than or equal to 1.5% during the 26 week study.

Time Frame: Baseline and Week 26.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set).

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	213	207	104
Measure Type: Number Units: participants	20	24	6

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.085
	Comments	No multiplicity adjustments.
	Method	Regression, Logistic
	Comments	Logistic regression model includes effects for treatment, geographic region, baseline metformin dose and baseline HbA1c.
Method of Estimation	**Estimation Parameter**	Odds Ratio (OR)
	Estimated Value	2.449
	Confidence Interval	(2-Sided) 95% 0.883 to 6.797
	Estimation Comments	Odd's Ratio (OR) compares alogliptin arm versus placebo. OR >1.0 indicates higher incidence of response compared to placebo.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.034
	Comments	No multiplicity adjustments.
	Method	Regression, Logistic
	Comments	Logistic regression model includes effects for treatment, geographic region, baseline metformin dose and baseline HbA1c.
Method of Estimation	**Estimation Parameter**	Odds Ratio (OR)
	Estimated Value	2.958
	Confidence Interval	(2-Sided) 95% 1.087 to 8.046
	Estimation Comments	Odd's Ratio (OR) compares alogliptin arm versus placebo. OR >1.0 indicates higher incidence of response compared to placebo.

47. Secondary Outcome

Title:	Number of Participants With Glycosylated Hemoglobin Decrease From Baseline ≥ 2.0%.
Description:	The number of participants with a decrease from baseline in the percentage of glycosylated hemoglobin (the percentage of hemoglobin that is bound to glucose) greater than or equal to 2.0% during the 26 week study.
Time Frame:	Baseline and Week 26.
Safety Issue?	No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set).

Arm/Group Title	Alogliptin 12.5 mg QD	Alogliptin 25 mg QD	Placebo
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	213	207	104
Measure Type: Number Units: participants	7	5	4

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.639
	Comments	No multiplicity adjustments.
	Method	Regression, Logistic
	Comments	Logistic regression model includes effects for treatment, geographic region, baseline metformin dose and baseline HbA1c.
Method of Estimation	**Estimation Parameter**	Odds Ratio (OR)
	Estimated Value	1.404
	Confidence Interval	(2-Sided) 95% 0.340 to 5.803
	Estimation Comments	Odd's Ratio (OR) compares alogliptin arm versus placebo. OR >1.0 indicates higher incidence of response compared to placebo.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	**P-Value**	0.956
	Comments	No multiplicity adjustments.
	Method	Regression, Logistic
	Comments	Logistic regression model includes effects for treatment, geographic region, baseline metformin dose and baseline HbA1c.
Method of Estimation	**Estimation Parameter**	Odds Ratio (OR)
	Estimated Value	0.959
	Confidence Interval	(2-Sided) 95% 0.218 to 4.223
	Estimation Comments	Odd's Ratio (OR) compares alogliptin arm versus placebo. OR >1.0 indicates higher incidence of response compared to placebo.

48. Secondary Outcome

Title: Change From Baseline in Body Weight (Week 8).

Description: The change between Body Weight measured at week 8 and Body Weight measured at baseline.

Time Frame: Baseline and Week 8.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had weight measurements at baseline and at Week 8. Missing data are imputed using last observation carried forward (LOCF).

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	198	193	102
Least Squares Mean (Standard Error) Units: kg	-0.30 (0.134)	-0.53 (0.135)	-0.12 (0.186)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.439
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline weight as covariates.
	Estimation Parameter	

Method of Estimation		Mean Difference (Final Values)
	Estimated Value	-0.18
	Confidence Interval	(2-Sided) 95% -0.63 to 0.27
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.075
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline weight as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-0.41
	Confidence Interval	(2-Sided) 95% -0.86 to 0.04
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

49. Secondary Outcome

Title: Change From Baseline in Body Weight (Week 12).

Description: The change between Body Weight measured at week 12 and Body Weight measured at baseline.

Time Frame: Baseline and Week 12.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had weight measurements at baseline and at Week 12. Missing data are imputed using last observation carried forward (LOCF).

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	205	198	103
Least Squares Mean (Standard Error) Units: kg	-0.28 (0.161)	-0.64 (0.164)	-0.57 (0.227)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.305
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline weight as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	0.29
	Confidence Interval	(2-Sided) 95% -0.26 to 0.83
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	**P-Value**	0.788
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline weight as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-0.08
	Confidence Interval	(2-Sided) 95% -0.63 to 0.47
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

50. Secondary Outcome

Title: Change From Baseline in Body Weight (Week 20).

Description: The change between Body Weight measured at week 20 and Body Weight measured at baseline.

Time Frame: Baseline and Week 20.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had weight measurements at baseline and at Week 20. Missing data are imputed using last observation carried forward (LOCF).

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	205	198	103
Least Squares Mean (Standard Error) Units: kg	-0.38 (0.178)	-0.58 (0.182)	-0.40 (0.252)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.930
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline weight as covariates.

Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	0.03
	Confidence Interval	(2-Sided) 95% -0.58 to 0.63
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.559
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline weight as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-0.18
	Confidence Interval	(2-Sided) 95% -0.79 to 0.43
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

51. Secondary Outcome

Title: Change From Baseline in Body Weight (Week 26).

Description: The change between Body Weight measured at week 26 or final visit and Body Weight measured at baseline.

Time Frame: Baseline and Week 26.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least 1 dose of study drug (Full Analysis Set), and who had weight measurements at baseline and at Week 26. Missing data are imputed using last observation carried forward (LOCF).

Arm/Group Title	**Alogliptin 12.5 mg QD**	**Alogliptin 25 mg QD**	**Placebo**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.
Number of Participants Analyzed	206	198	103
Least Squares Mean			

(Standard Error) Units: kg	-0.39 (0.194)	-0.67 (0.198)	-0.39 (0.274)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.996
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline weight as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	0.00
	Confidence Interval	(2-Sided) 95% -0.66 to 0.66
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 mg QD, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	**P-Value**	0.407
	Comments	No multiplicity adjustments.
	Method	ANCOVA
	Comments	Treatment and geographic region as class variables; baseline metformin dose and baseline weight as covariates.
Method of Estimation	**Estimation Parameter**	Mean Difference (Final Values)
	Estimated Value	-0.28
	Confidence Interval	(2-Sided) 95% -0.94 to 0.38
	Estimation Comments	Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm.

Adverse Events

Time Frame	Treatment-emergent adverse events are adverse events that started after the first dose of double-blind study drug and no more than 14 days (or 30 days for a serious adverse event) after the last dose of double-blind study drug.
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 participant or observed by the investigator was recorded, irrespective of the relation to study treatment.
Source Vocabulary Name	MedDRA 10.0
Assessment Type	Systematic Assessment

Arm/Group Title	Alogliptin 12.5 mg QD	Alogliptin 25 mg QD	Placebo
Arm/Group Description	Alogliptin 12.5 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and metformin for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and metformin for up to 26 weeks.

Serious Adverse Events

	Alogliptin 12.5 mg QD Affected / at Risk (%)	**Alogliptin 25 mg QD** Affected / at Risk (%)	**Placebo** Affected / at Risk (%)
Total	6/213 (2.82%)	8/207 (3.86%)	4/104 (3.85%)
Cardiac disorders			
Angina unstable † A	0/213 (0%)	0/207 (0%)	1/104 (0.96%)
Bradycardia † A	1/213 (0.47%)	0/207 (0%)	0/104 (0%)
Cardiac failure congestive † A	0/213 (0%)	1/207 (0.48%)	0/104 (0%)
Hypertensive heart disease † A	1/213 (0.47%)	0/207 (0%)	0/104 (0%)
Congenital, familial and genetic disorders			
Hydrocele † A	0/213 (0%)	0/207 (0%)	1/104 (0.96%)
General disorders			
Non-cardiac chest pain † A	0/213 (0%)	2/207 (0.97%)	0/104 (0%)
Hepatobiliary disorders			
Cholelithiasis † A	0/213 (0%)	1/207 (0.48%)	0/104 (0%)
Infections and infestations			
Appendicitis † A	1/213 (0.47%)	0/207 (0%)	0/104 (0%)
Cellulitis † A	0/213 (0%)	0/207 (0%)	1/104 (0.96%)
Postoperative wound infection † A	0/213 (0%)	1/207 (0.48%)	0/104 (0%)
Pyelonephritis † A	0/213 (0%)	0/207 (0%)	1/104 (0.96%)

Urinary tract infection † A	0/213 (0%)	1/207 (0.48%)	0/104 (0%)
Injury, poisoning and procedural complications			
Burns third degree † A	0/213 (0%)	0/207 (0%)	1/104 (0.96%)
Fall † A	1/213 (0.47%)	0/207 (0%)	0/104 (0%)
Musculoskeletal and connective tissue disorders			
Osteoarthritis † A	0/213 (0%)	1/207 (0.48%)	0/104 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Endometrial cancer † A	1/213 (0.47%)	0/207 (0%)	0/104 (0%)
Non-secretory adenoma of the pituitary † A	1/213 (0.47%)	0/207 (0%)	0/104 (0%)
Prostate cancer † A	1/213 (0.47%)	0/207 (0%)	0/104 (0%)
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism † A	0/213 (0%)	1/207 (0.48%)	0/104 (0%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 10.0

Other (Not Including Serious) Adverse Events

Frequency Threshold for Reporting Other Adverse Events	3%

	Alogliptin 12.5 mg QD Affected / at Risk (%)	**Alogliptin 25 mg QD** Affected / at Risk (%)	**Placebo** Affected / at Risk (%)
Total	62/213 (29.11%)	41/207 (19.81%)	37/104 (35.58%)
Gastrointestinal disorders			
Diarrhoea † A	6/213 (2.82%)	7/207 (3.38%)	6/104 (5.77%)
General disorders			
Pain in extremity † A	5/213 (2.35%)	3/207 (1.45%)	4/104 (3.85%)
Infections and infestations			
Bronchitis † A	9/213 (4.23%)	6/207 (2.9%)	2/104 (1.92%)
Nasopharyngitis † A	12/213 (5.63%)	7/207 (3.38%)	6/104 (5.77%)
Sinusitis † A	5/213 (2.35%)	4/207 (1.93%)	5/104 (4.81%)
Upper respiratory tract infection † A	10/213 (4.69%)	5/207 (2.42%)	7/104 (6.73%)
Urinary tract infection † A	14/213 (6.57%)	5/207 (2.42%)	4/104 (3.85%)
Musculoskeletal and connective tissue disorders			
Arthralgia † A	4/213 (1.88%)	3/207 (1.45%)	5/104 (4.81%)
Nervous system disorders			
Headache † A	8/213 (3.76%)	4/207 (1.93%)	2/104 (1.92%)
Vascular disorders			
Hypertension † A	4/213 (1.88%)	6/207 (2.9%)	5/104 (4.81%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 10.0

Limitations and Caveats

[Not Specified]

More Information

Certain Agreements

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

No publication related to study results will be published prior to publication of a multi-center report submitted for publication within 18 months after conclusion or termination of a study at all study sites. Results publications will be submitted to sponsor for review 60 days in advance of publication. Sponsor can require removal of confidential information unrelated to study results. Sponsor can embargo a proposed publication for another 60 days to preserve intellectual property.

Results Point of Contact

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