ID: 01-05-TL-322OPI-001 | Efficacy and Safety of Alogliptin Combined With Pioglitazone in Treating Subjects With Type 2 Diabetes Mellitus. | NCT00328627

Results Preview

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Participant Flow

Recruitment Details: Participants took part in the study at 327 investigative sites in 20 countries from 31 May 2006 to 17 March 2008.
Pre-Assignment Details: Participants with a diagnosis of type 2 diabetes who were inadequately controlled on a regimen of metformin alone were equally randomized to 1 of 12 double-blind treatment groups.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45	Total (Not public)
Arm/Group Description	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	
Period Title: Overall Study													
Started	129	128	129	130	130	130	129	130	130	129	130	130	1554
Safety Set	129 [1]	128	129	129	130	130	129	130	130	129	130	130	1553
Completed	70	97	101	93	115	110	94	116	113	97	112	114	1232
Not Completed	59	31	28	37	15	20	35	14	17	32	18	16	322
Reason Not Completed													
Hyperglycemic Rescue	41	18	16	13	6	5	19	6	6	11	3	2	146
Adverse Event	3	1	2	3	1	2	1	2	0	7	5	4	31
Protocol Violation	2	2	2	8	5	5	6	2	1	4	6	2	45
Lost to Follow-up	4	2	2	4	0	2	3	0	3	2	0	1	23
Withdrawal by Subject	5	4	5	6	2	5	4	4	4	5	2	7	53
Pregnancy	0	1	0	0	0	0	0	0	0	0	0	0	1
Physician Decision	4	3	1	2	1	1	1	0	3	2	1	0	19
Other	0	0	0	1	0	0	1	0	0	1	1	0	4
NOTE : "Other" is not sufficiently descriptive for "Other" Reason Not Completed. Please provide a more descriptive label. (Not Public)	Not Completed = 59 Total from all reasons = 59	Not Completed = 31 Total from all reasons = 31	Not Completed = 28 Total from all reasons = 28	Not Completed = 37 Total from all reasons = 37	Not Completed = 15 Total from all reasons = 15	Not Completed = 20 Total from all reasons = 20	Not Completed = 35 Total from all reasons = 35	Not Completed = 14 Total from all reasons = 14	Not Completed = 17 Total from all reasons = 17	Not Completed = 32 Total from all reasons = 32	Not Completed = 18 Total from all reasons = 18	Not Completed = 16 Total from all reasons = 16	

[1] All patients who took at least 1 dose of double-blind study drug.

Baseline Characteristics

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45	Total
Arm/Group Description	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	
Overall Number of Baseline Participants	129	128	129	130	130	130	129	130	130	129	130	130	**1554**
Baseline Analysis Population Description [Not specified]													
Age, Continuous Mean (Standard Deviation) Units: years	55.2 (9.89)	53.1 (9.59)	53.7 (9.31)	54.1 (9.54)	53.6 (9.91)	54.9 (9.18)	56.1 (9.43)	55.0 (9.07)	54.4 (9.69)	54.5 (9.70)	54.0 (9.82)	54.2 (8.86)	54.4 (9.50)
Age, Customized Measure Type: Number Units: participants													
<65 years	106	116	112	113	109	112	101	111	107	112	111	112	1322
≥65 years	23	12	17	17	21	18	28	19	23	17	19	18	232
Gender, Male/Female Measure Type: Number Units: participants													
Female	68	61	79	69	70	69	66	76	75	76	70	78	857
Male	61	67	50	61	60	61	63	54	55	53	60	52	697
Ethnicity (NIH/OMB) Measure Type: Number Units: Participants													
Hispanic or Latino	63	60	63	63	55	57	67	66	62	61	63	65	745
Not Hispanic or Latino	66	68	66	67	75	73	62	64	68	68	67	65	809
Unknown or Not Reported	0	0	0	0	0	0	0	0	0	0	0	0	0
Race (NIH/OMB) Measure Type: Number Units: participants													
American Indian or Alaska Native	0	0	0	0	2	2	0	1	0	0	0	0	5
Asian	5	14	15	11	9	7	10	5	12	12	8	12	120
Native Hawaiian or Other Pacific Islander	0	0	0	0	0	0	0	0	0	0	0	0	0
Black or African American	8	6	5	8	4	3	6	2	5	9	9	3	68
White	93	89	80	85	95	96	96	107	85	85	92	93	1096
More than one race	0	0	0	0	0	0	0	0	0	0	0	0	0
Unknown or Not Reported	23	19	29	26	20	22	17	15	28	23	21	22	265
Weight Mean (Standard Deviation) Units: kg	83.38 (18.378)	84.63 (19.378)	83.25 (18.326)	84.68 (18.634)	85.95 (18.498)	82.90 (16.570)	85.86 (20.347)	83.68 (18.340)	85.77 (18.844)	82.10 (17.019)	85.01 (18.536)	82.79 (18.768)	84.17 (18.470)
Height Mean (Standard Deviation) Units: cm	164.48 (10.157)	164.61 (10.614)	162.38 (9.790)	164.25 (11.007)	164.59 (10.841)	163.74 (10.456)	164.59 (9.724)	163.63 (11.036)	163.64 (9.548)	163.14 (10.961)	163.82 (10.708)	163.73 (11.432)	163.88 (10.522)
Body Mass Index (BMI) Mean (Standard Deviation) Units: kg/m^2	30.59 (4.808)	30.96 (5.133)	31.48 (5.733)	31.25 (5.280)	31.53 (4.979)	30.78 (4.723)	31.41 (5.391)	31.09 (5.054)	31.86 (5.585)	30.69 (4.721)	31.51 (5.206)	30.62 (4.751)	31.15 (5.122)
Diabetes Duration Mean (Standard Deviation) Units: years	6.01 (4.958)	6.17 (5.614)	5.55 (4.879)	5.70 (4.767)	6.08 (5.485)	6.86 (5.489)	7.63 (7.069)	5.81 (5.054)	6.63 (6.005)	5.68 (4.232)	6.59 (5.273)	6.22 (5.014)	6.24 (5.375)
Baseline metformin dose Mean (Standard Deviation) Units: mg	1936.8 (428.41)	1902.0 (450.17)	1851.2 (413.85)	1892.6 (410.70)	1909.6 (418.98)	1880.0 (413.65)	1853.5 (435.72)	1822.3 (444.22)	1867.1 (455.48)	1918.6 (417.91)	1919.6 (421.22)	1884.6 (439.47)	1886.5 (429.08)

Outcome Measures

1. Primary Outcome

Title: Change From Baseline to Week 26 in Glycosylated Hemoglobin (HbA1c) (Grouped Analysis)
Description: The change from Baseline to Week 26 in HbA1c (the concentration of glucose bound to hemoglobin as a percent of the absolute maximum that can be bound).
The primary analysis compared the groupings (combinations of individual treatment groups) of participants who received the combination of pioglitazone with each dose of alogliptin with the grouping of participants who received pioglitazone alone (Pioglitazone Alone).
Time Frame: Baseline and Week 26
Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Pioglitazone Alone	Alogliptin 12.5 + Pioglitazone	Alogliptin 25 + Pioglitazone
Arm/Group Description:	Alogliptin placebo plus all active pioglitazone groups (15, 30, and 45 mg). This combination group includes participants from the following three treatment arms:	Alogliptin 12.5 mg plus all active pioglitazone (15, 30, and 45 mg). This combination group includes participants from the following three treatment arms:	Alogliptin 25 mg plus all active pioglitazone (15, 30, and 45 mg). This combination group includes participants from the following three treatment arms:

	1. Placebo + Pioglitazone 15 mg 2. Placebo + Pioglitazone 30 mg 3. Placebo + Pioglitazone 45 mg	1. Alogliptin 12.5 mg + Pioglitazone 15 mg 2. Alogliptin 12.5 mg + Pioglitazone 30 mg 3. Alogliptin 12.5 mg + Pioglitazone 45 mg	1. Alogliptin 25 mg + Pioglitazone 15 mg 2. Alogliptin 25 mg + Pioglitazone 30 mg 3. Alogliptin 25 mg + Pioglitazone 45 mg
Number of Participants Analyzed	376	385	377
Least Squares Mean (Standard Error) **Units: percentage of glycosylated hemoglobin**	-0.89 (0.046)	-1.43 (0.046)	-1.42 (0.046)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Pioglitazone Alone, Alogliptin 12.5 + Pioglitazone
	Comments	The null hypothesis was that the doses of alogliptin do not have any additive effect on glycemic control (HbA1c) in addition to the effect produced by pioglitazone alone. The alternative hypothesis was that at least the higher dose of alogliptin would have an additive effect on glycemic control (HbA1c) in addition to the effect produced by pioglitazone alone.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	For the primary analysis, the overall average HbA1c response of the Alogliptin/pioglitazone combination groups was compared with that of the pioglitazone alone groups at the 2-sided 0.05 significance level with no adjustment for multiple comparisons.
	Method	ANCOVA
	Comments	ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline HbA1c as continuous covariates.
Method of Estimation	**Estimation Parameter**	Other[LS Mean Difference]
	Estimated Value	-0.54
	Confidence Interval	(2-Sided) 95% -0.67 to -0.41
	Estimation Comments	[Not specified]

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Pioglitazone Alone, Alogliptin 25 + Pioglitazone
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	[Not specified]
	Method	ANCOVA
	Comments	ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline HbA1c as continuous covariates.
Method of Estimation	**Estimation Parameter**	Other[LS Mean Difference]
	Estimated Value	-0.53
	Confidence Interval	(2-Sided) 95% -0.66 to -0.41
	Estimation Comments	[Not specified]

2. Primary Outcome

Title: Change From Baseline to Week 26 in HbA1c

Description: The change from Baseline to Week 26 in HbA1c (the concentration of glucose bound to hemoglobin as a percent of the absolute maximum that can be bound).

Time Frame: Baseline and Week 26

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Placebo**	**Alogliptin 12.5 + Placebo**	**Alogliptin 25 + Placebo**	**Placebo + Pioglitazone 15**	**Alogliptin 12.5 + Pioglitazone 15**	**Alogliptin 25 + Pioglitazone 15**	**Placebo + Pioglitazone 30**	**Alogliptin 12.5 + Pioglitazone 30**	**Alogliptin 25 + Pioglitazone 30**	**Placebo + Pioglitazone 45**	**Alogliptin 12.5 + Pioglitazone 45**	**Alogliptin 25 + Pioglitazone 45**
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	126	122	123	127	130	127	123	128	124	126	127	126
Least Squares Mean (Standard Error) **Units: percentage of glycosylated hemoglobin**	-0.13 (0.080)	-0.64 (0.081)	-0.90 (0.081)	-0.75 (0.079)	-1.34 (0.078)	-1.27 (0.079)	-0.92 (0.081)	-1.39 (0.079)	-1.39 (0.080)	-1.00 (0.080)	-1.55 (0.079)	-1.60 (0.080)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 + Placebo, Alogliptin 12.5 + Pioglitazone 15
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	As a supportive analysis, each of the individual combination treatment groups was compared with the component treatment groups receiving aloliptin alone and pioglitazone alone at the 2-sided 0.05 significance level with no multiplicity adjustment.
	Method	ANCOVA
	Comments	ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline HbA1c as continuous covariates.
Method of Estimation	**Estimation Parameter**	Other[LS Mean Difference]
	Estimated Value	-0.70
	Confidence Interval	(2-Sided) 95% -0.93 to -0.48
	Estimation Comments	[Not specified]

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Placebo + Pioglitazone 15, Alogliptin 12.5 + Pioglitazone 15
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	[Not specified]
	Method	ANCOVA
	Comments	ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline HbA1c as continuous covariates.
Method of Estimation	**Estimation Parameter**	Other[LS Mean Difference]
	Estimated Value	-0.59
	Confidence Interval	(2-Sided) 95% -0.81 to -0.38
	Estimation Comments	[Not specified]

Statistical Analysis 3

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 + Placebo, Alogliptin 25 + Pioglitazone 15
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	0.001
	Comments	[Not specified]
	Method	ANCOVA
	Comments	ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline HbA1c as continuous covariates.
Method of Estimation	**Estimation Parameter**	Other[LS Mean Difference]
	Estimated Value	-0.37
	Confidence Interval	(2-Sided) 95% -0.59 to -0.15
	Estimation Comments	[Not specified]

Statistical Analysis 4

Statistical Analysis Overview	**Comparison Groups**	Placebo + Pioglitazone 15, Alogliptin 25 + Pioglitazone 15
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	[Not specified]
	Method	ANCOVA
	Comments	ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline HbA1c as continuous covariates.
Method of Estimation	**Estimation Parameter**	Other[LS Mean Difference]
	Estimated Value	-0.52
	Confidence Interval	(2-Sided) 95% -0.74 to -0.30
	Estimation Comments	[Not specified]

Statistical Analysis 5

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 + Placebo, Alogliptin 12.5 + Pioglitazone 30
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	[Not specified]
	Method	ANCOVA
	Comments	ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline HbA1c as continuous covariates.
Method of Estimation	**Estimation Parameter**	Other[LS Mean Difference]
	Estimated Value	-0.76
	Confidence Interval	(2-Sided) 95% -0.98 to -0.53
	Estimation Comments	[Not specified]

Statistical Analysis 6

Statistical Analysis Overview	**Comparison Groups**	Placebo + Pioglitazone 30, Alogliptin 12.5 + Pioglitazone 30
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	[Not specified]
	Method	ANCOVA
	Comments	ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline HbA1c as continuous covariates.
Method of Estimation	**Estimation Parameter**	Other[LS Mean Difference]
	Estimated Value	-0.47
	Confidence Interval	(2-Sided) 95% -0.70 to -0.25
	Estimation Comments	[Not specified]

Statistical Analysis 7

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 + Placebo, Alogliptin 25 + Pioglitazone 30
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No

	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	[Not specified]
	Method	ANCOVA
	Comments	ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline HbA1c as continuous covariates.
Method of Estimation	**Estimation Parameter**	Other[LS Mean Difference]
	Estimated Value	-0.49
	Confidence Interval	(2-Sided) 95% -0.71 to -0.27
	Estimation Comments	[Not specified]

Statistical Analysis 8

Statistical Analysis Overview	**Comparison Groups**	Placebo + Pioglitazone 30, Alogliptin 25 + Pioglitazone 30
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	[Not specified]
	Method	ANCOVA
	Comments	ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline HbA1c as continuous covariates.
Method of Estimation	**Estimation Parameter**	Other[LS Mean Difference]
	Estimated Value	-0.47
	Confidence Interval	(2-Sided) 95% -0.70 to -0.25
	Estimation Comments	[Not specified]

Statistical Analysis 9

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 12.5 + Placebo, Alogliptin 12.5 + Pioglitazone 45
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	[Not specified]
	Method	ANCOVA
	Comments	ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline HbA1c as continuous covariates.
Method of Estimation	**Estimation Parameter**	Other[LS Mean Difference]
	Estimated Value	-0.91
	Confidence Interval	(2-Sided) 95% -1.13 to -0.68
	Estimation Comments	[Not specified]

Statistical Analysis 10

Statistical Analysis Overview	**Comparison Groups**	Placebo + Pioglitazone 45, Alogliptin 12.5 + Pioglitazone 45
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	[Not specified]
	Method	ANCOVA
	Comments	ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline HbA1c as continuous covariates.
Method of Estimation	**Estimation Parameter**	Other[LS Mean Difference]
	Estimated Value	-0.55
	Confidence Interval	(2-Sided) 95% -0.77 to -0.33
	Estimation Comments	[Not specified]

Statistical Analysis 11

Statistical Analysis Overview	**Comparison Groups**	Alogliptin 25 + Placebo, Alogliptin 25 + Pioglitazone 45
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	[Not specified]
	Method	ANCOVA
	Comments	ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline HbA1c as continuous covariates.
Method of Estimation	**Estimation Parameter**	Other[LS Mean Difference]
	Estimated Value	-0.70
	Confidence Interval	(2-Sided) 95% -0.92 to -0.48
	Estimation Comments	[Not specified]

Statistical Analysis 12

Statistical Analysis Overview	**Comparison Groups**	Placebo + Pioglitazone 45, Alogliptin 25 + Pioglitazone 45
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	[Not specified]

Method		ANCOVA
Comments		ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline HbA1c as continuous covariates.
Method of Estimation	**Estimation Parameter**	Other[LS Mean Difference]
	Estimated Value	-0.61
	Confidence Interval	(2-Sided) 95% -0.83 to -0.39
	Estimation Comments	[Not specified]

3. Secondary Outcome

Title: Change From Baseline in HbA1c Over Time (Grouped Analysis)

Description: The change from Baseline to Weeks 4, 8, 12, 16 and 20 in HbA1c (the concentration of glucose bound to hemoglobin as a percent of the absolute maximum that can be bound).
This analysis compared the groupings of participants who received the combination of pioglitazone with each dose of alogliptin with the grouping of participants who received pioglitazone alone. Least squares means are from an analysis of covariance (ANCOVA) model with treatment and geographic region as class variables, and baseline metformin dose and HbA1c as continuous covariates.

Time Frame: Baseline and Weeks 4, 8, 12, 16 and 20.

Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Pioglitazone Alone**	**Alogliptin 12.5 + Pioglitazone**	**Alogliptin 25 + Pioglitazone**
Arm/Group Description:	Alogliptin placebo plus all active pioglitazone groups (15, 30, and 45 mg).	Alogliptin 12.5 mg plus all active pioglitazone (15, 30, and 45 mg).	Alogliptin 25 mg plus all active pioglitazone (15, 30, and 45 mg).
Number of Participants Analyzed	387	390	390
Least Squares Mean (Standard Error) Units: percentage of glycosylated hemoglobin			
Week 4 (n=345, 359, 346)	-0.32 (0.023)	-0.57 (0.023)	-0.61 (0.023)
Week 8 (n=376, 385, 377)	-0.61 (0.034)	-1.06 (0.033)	-1.09 (0.034)
Week 12 (n=376, 385, 377)	-0.81 (0.039)	-1.29 (0.039)	-1.38 (0.039)
Week 16 (n=376, 385, 377)	-0.92 (0.041)	-1.44 (0.041)	-1.49 (0.041)
Week 20 (n=376, 385, 377)	-0.92 (0.043)	-1.46 (0.042)	-1.51 (0.043)

4. Secondary Outcome

Title: Change From Baseline to Week 4 in HbA1c

Description: The change from Baseline in HbA1c (the concentration of glucose bound to hemoglobin as a percent of the absolute maximum that can be bound) at week 4. Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline HbA1c as continuous covariates.

Time Frame: Baseline and Week 4

Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Placebo**	**Alogliptin 12.5 + Placebo**	**Alogliptin 25 + Placebo**	**Placebo + Pioglitazone 15**	**Alogliptin 12.5 + Pioglitazone 15**	**Alogliptin 25 + Pioglitazone 15**	**Placebo + Pioglitazone 30**	**Alogliptin 12.5 + Pioglitazone 30**	**Alogliptin 25 + Pioglitazone 30**	**Placebo + Pioglitazone 45**	**Alogliptin 12.5 + Pioglitazone 45**	**Alogliptin 25 + Pioglitazone 45**
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	120	114	110	114	120	116	116	122	118	115	117	112
Least Squares Mean (Standard Error) **Units: percentage of glycosylated hemoglobin**	-0.22 (0.039)	-0.46 (0.040)	-0.51 (0.041)	-0.32 (0.040)	-0.53 (0.039)	-0.61 (0.040)	-0.24 (0.040)	-0.60 (0.039)	-0.60 (0.039)	-0.40 (0.040)	-0.58 (0.040)	-0.63 (0.040)

5. Secondary Outcome

Title: Change From Baseline to Week 8 in HbA1c

Description: The change from Baseline in HbA1c (the concentration of glucose bound to hemoglobin as a percent of the absolute maximum that can be bound) at week 8. Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline HbA1c as continuous covariates.

Time Frame: Baseline and Week 8

Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Placebo**	**Alogliptin 12.5 + Placebo**	**Alogliptin 25 + Placebo**	**Placebo + Pioglitazone 15**	**Alogliptin 12.5 + Pioglitazone 15**	**Alogliptin 25 + Pioglitazone 15**	**Placebo + Pioglitazone 30**	**Alogliptin 12.5 mg + Pioglitazone 30 mg**	**Alogliptin 25 + Pioglitazone 30**	**Placebo + Pioglitazone 45 mg**	**Alogliptin 12.5 + Pioglitazone 45**	**Alogliptin 25 + Pioglitazone 45**
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	126	122	123	127	130	127	123	128	124	126	127	126
Least Squares Mean (Standard Error) **Units: percentage of glycosylated hemoglobin**	-0.30 (0.058)	-0.75 (0.059)	-0.80 (0.059)	-0.50 (0.058)	-1.01 (0.058)	-1.04 (0.058)	-0.57 (0.059)	-1.05 (0.058)	-1.02 (0.059)	-0.76 (0.058)	-1.11 (0.058)	-1.20 (0.058)

6. Secondary Outcome

Title: Change From Baseline to Week 12 in HbA1c

Description: The change from Baseline in HbA1c (the concentration of glucose bound to hemoglobin as a percent of the absolute maximum that can be bound) at week 12.
Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline HbA1c as continuous covariates.

Time Frame: Baseline and Week 12

Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Placebo**	**Alogliptin 12.5 + Placebo**	**Alogliptin 25 + Placebo**	**Placebo + Pioglitazone 15**	**Alogliptin 12.5 + Pioglitazone 15**	**Alogliptin 25 + Pioglitazone 15**	**Placebo + Pioglitazone 30**	**Alogliptin 12.5 mg + Pioglitazone 30 mg**	**Alogliptin 25 + Pioglitazone 30**	**Placebo + Pioglitazone 45 mg**	**Alogliptin 12.5 + Pioglitazone 45**	**Alogliptin 25 + Pioglitazone 45**
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	126	122	123	127	130	127	123	128	124	126	127	126
Least Squares Mean (Standard Error) **Units: percentage of glycosylated hemoglobin**	-0.28 (0.067)	-0.84 (0.069)	-0.92 (0.068)	-0.65 (0.067)	-1.24 (0.066)	-1.26 (0.067)	-0.77 (0.068)	-1.29 (0.067)	-1.33 (0.068)	-1.02 (0.067)	-1.34 (0.067)	-1.53 (0.067)

7. Secondary Outcome

Title: Change From Baseline to Week 16 in HbA1c

Description: The change from Baseline in HbA1c (the concentration of glucose bound to hemoglobin as a percent of the absolute maximum that can be bound) at week 16. Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline HbA1c as continuous covariates.

Time Frame: Baseline and Week 16

Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward (LOCF) imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 mg + Pioglitazone 30 mg	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45 mg	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	126	122	123	127	130	127	123	128	124	126	127	126
Least Squares Mean (Standard Error)	-0.27 (0.071)	-0.82 (0.072)	-1.03 (0.072)	-0.74 (0.071)	-1.36 (0.070)	-1.36 (0.071)	-0.91 (0.072)	-1.42 (0.071)	-1.45 (0.072)	-1.12 (0.071)	-1.53 (0.071)	-1.66 (0.071)
Units: percentage of glycosylated hemoglobin												

8. Secondary Outcome

Title: Change From Baseline to Week 20 in HbA1c

Description: The change from Baseline in HbA1c (the concentration of glucose bound to hemoglobin as a percent of the absolute maximum that can be bound) at week 20.
Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline HbA1c as continuous covariates.

Time Frame: Baseline and Week 20

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 mg + Pioglitazone 30 mg	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45 mg	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	126	122	123	127	130	127	123	128	124	126	127	126
Least Squares Mean (Standard Error)	-0.24 (0.074)	-0.75 (0.075)	-0.99 (0.075)	-0.75 (0.074)	-1.39 (0.073)	-1.37 (0.074)	-0.90 (0.075)	-1.43 (0.074)	-1.49 (0.075)	-1.10 (0.074)	-1.57 (0.074)	-1.66 (0.074)
Units: percentage of glycosylated hemoglobin												

9. Secondary Outcome

Title: Change From Baseline in Fasting Plasma Glucose Over Time (Grouped Analysis)

Description: The change from Baseline in fasting plasma glucose was assessed at weeks 1, 2, 4, 8, 12, 16, 20 and 26.
This analysis compared the groupings of participants who received the combination of pioglitazone with each dose of alogliptin with the grouping of participants who received pioglitazone alone. Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline fasting plasma glucose as covariates.

Time Frame: Baseline and Weeks 1, 2, 4, 8, 12, 16, 20 and 26.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Pioglitazone Alone	Alogliptin 12.5 + Pioglitazone	Alogliptin 25 + Pioglitazone
Arm/Group Description:	Alogliptin placebo plus all active pioglitazone groups (15, 30, and 45 mg).	Alogliptin 12.5 mg plus all active pioglitazone (15, 30, and 45 mg).	Alogliptin 25 mg plus all active pioglitazone (15, 30, and 45 mg).
Number of Participants Analyzed	387	390	390
Least Squares Mean (Standard Error)			
Units: mg/dL			
Week 1 (n=358, 355, 354)	-4.1 (1.56)	-22.6 (1.57)	-23.1 (1.57)
Week 2 (n=379, 383, 381)	-11.3 (1.62)	-30.3 (1.61)	-31.6 (1.62)
Week 4 (n=381, 386, 383)	-19.9 (1.67)	-36.8 (1.66)	-39.8 (1.67)
Week 8 (n=381, 386, 383)	-27.3 (1.77)	-42.3 (1.76)	-45.2 (1.77)
Week 12 (n=381, 386, 383)	-30.3 (1.84)	-45.0 (1.83)	-47.6 (1.83)
Week 16 (n=381, 386, 383)	-27.9 (1.86)	-43.7 (1.85)	-45.4 (1.86)
Week 20 (n=381, 386, 383)	-28.1 (2.00)	-43.6 (1.99)	-45.0 (1.99)
Week 26 (n=381, 386, 383)	-28.3 (2.03)	-45.2 (2.02)	-44.2 (2.03)

10. Secondary Outcome

Title: Change From Baseline to Week 1 in Fasting Plasma Glucose

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline fasting plasma glucose as covariates.

Time Frame: Baseline and Week 1

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	123	114	117	120	121	123	117	119	118	121	115	113
Least Squares Mean (Standard Error)	1.8 (2.67)	-14.5 (2.77)	-18.6 (2.73)	-6.1 (2.70)	-21.3 (2.69)	-20.9 (2.66)	0.4 (2.73)	-23.2 (2.71)	-23.2 (2.72)	-6.7 (2.69)	-23.2 (2.76)	-25.0 (2.78)
Units: mg/dL												

11. Secondary Outcome

Title: Change From Baseline to Week 2 in Fasting Plasma Glucose

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline fasting plasma glucose as covariates.

Time Frame: Baseline and Week 2

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.

	weeks.	weeks.	weeks.									
Number of Participants Analyzed	129	120	125	127	127	129	124	128	126	128	128	126
Least Squares Mean (Standard Error) Units: mg/dL	4.8 (2.78)	-21.9 (2.88)	-18.9 (2.82)	-10.4 (2.80)	-30.1 (2.80)	-31.7 (2.78)	-4.3 (2.83)	-30.0 (2.79)	-31.3 (2.81)	-19.3 (2.79)	-30.8 (2.79)	-31.7 (2.81)

12. Secondary Outcome

Title: Change From Baseline to Week 4 in Fasting Plasma Glucose

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline fasting plasma glucose as covariates.

Time Frame: Baseline and Week 4

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Placebo**	**Alogliptin 12.5 + Placebo**	**Alogliptin 25 + Placebo**	**Placebo + Pioglitazone 15**	**Alogliptin 12.5 + Pioglitazone 15**	**Alogliptin 25 + Pioglitazone 15**	**Placebo + Pioglitazone 30**	**Alogliptin 12.5 + Pioglitazone 30**	**Alogliptin 25 + Pioglitazone 30**	**Placebo + Pioglitazone 45**	**Alogliptin 12.5 + Pioglitazone 45**	**Alogliptin 25 + Pioglitazone 45**
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	129	122	125	127	129	130	125	129	126	129	128	127
Least Squares Mean (Standard Error) Units: mg/dL	3.8 (2.87)	-20.4 (2.95)	-22.8 (2.92)	-20.2 (2.90)	-35.3 (2.87)	-37.3 (2.86)	-13.4 (2.92)	-37.4 (2.88)	-36.0 (2.91)	-26.1 (2.87)	-37.8 (2.89)	-46.2 (2.89)

13. Secondary Outcome

Title: Change From Baseline to Week 8 in Fasting Plasma Glucose

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline fasting plasma glucose as covariates.

Time Frame: Baseline and Week 8

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Placebo**	**Alogliptin 12.5 + Placebo**	**Alogliptin 25 + Placebo**	**Placebo + Pioglitazone 15**	**Alogliptin 12.5 + Pioglitazone 15**	**Alogliptin 25 + Pioglitazone 15**	**Placebo + Pioglitazone 30**	**Alogliptin 12.5 + Pioglitazone 30**	**Alogliptin 25 + Pioglitazone 30**	**Placebo + Pioglitazone 45**	**Alogliptin 12.5 + Pioglitazone 45**	**Alogliptin 25 + Pioglitazone 45**
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	129	122	126	127	129	130	125	129	126	129	128	127
Least Squares Mean (Standard Error) Units: mg/dL	5.7 (3.05)	-19.5 (3.14)	-19.3 (3.09)	-22.2 (3.07)	-42.3 (3.05)	-39.3 (3.04)	-24.0 (3.10)	-40.5 (3.05)	-44.1 (3.08)	-35.6 (3.05)	-44.0 (3.06)	-52.3 (3.07)

14. Secondary Outcome

Title: Change From Baseline to Week 12 in Fasting Plasma Glucose

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline fasting plasma glucose as covariates.

Time Frame: Baseline and Week 12

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Placebo**	**Alogliptin 12.5 + Placebo**	**Alogliptin 25 + Placebo**	**Placebo + Pioglitazone 15**	**Alogliptin 12.5 + Pioglitazone 15**	**Alogliptin 25 + Pioglitazone 15**	**Placebo + Pioglitazone 30**	**Alogliptin 12.5 + Pioglitazone 30**	**Alogliptin 25 + Pioglitazone 30**	**Placebo + Pioglitazone 45**	**Alogliptin 12.5 + Pioglitazone 45**	**Alogliptin 25 + Pioglitazone 45**
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	129	122	126	127	129	130	125	129	126	129	128	127
Least Squares Mean (Standard Error) Units: mg/dL	3.4 (3.16)	-19.3 (3.25)	-23.3 (3.19)	-23.0 (3.18)	-42.9 (3.16)	-42.5 (3.14)	-26.6 (3.21)	-42.8 (3.16)	-49.0 (3.19)	-41.3 (3.16)	-49.2 (3.17)	-51.4 (3.18)

15. Secondary Outcome

Title: Change From Baseline to Week 16 in Fasting Plasma Glucose

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline fasting plasma glucose as covariates.

Time Frame: Baseline and Week 16

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Placebo**	**Alogliptin 12.5 + Placebo**	**Alogliptin 25 + Placebo**	**Placebo + Pioglitazone 15**	**Alogliptin 12.5 + Pioglitazone 15**	**Alogliptin 25 + Pioglitazone 15**	**Placebo + Pioglitazone 30**	**Alogliptin 12.5 + Pioglitazone 30**	**Alogliptin 25 + Pioglitazone 30**	**Placebo + Pioglitazone 45**	**Alogliptin 12.5 + Pioglitazone 45**	**Alogliptin 25 + Pioglitazone 45**
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	129	122	126	127	129	130	125	129	126	129	128	127
Least Squares Mean (Standard Error) Units: mg/dL	1.4 (3.20)	-16.2 (3.29)	-22.6 (3.24)	-21.2 (3.22)	-41.6 (3.20)	-39.1 (3.19)	-26.3 (3.25)	-41.5 (3.20)	-43.4 (3.24)	-36.3 (3.20)	-47.9 (3.21)	-53.8 (3.22)

16. Secondary Outcome

Title: Change From Baseline to Week 20 in Fasting Plasma Glucose

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline fasting plasma glucose as covariates.

Time Frame: Baseline and Week 20

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	129	122	126	127	129	130	125	129	126	129	128	127
Least Squares Mean (Standard Error) Units: mg/dL	6.7 (3.43)	-8.7 (3.53)	-23.5 (3.48)	-22.4 (3.46)	-43.0 (3.43)	-39.3 (3.42)	-26.3 (3.49)	-41.1 (3.44)	-43.1 (3.47)	-35.7 (3.43)	-46.8 (3.45)	-52.4 (3.46)

17. Secondary Outcome

Title: Change From Baseline to Week 26 in Fasting Plasma Glucose

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline fasting plasma glucose as covariates.

Time Frame: Baseline and Week 26

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	129	122	126	127	129	130	125	129	126	129	128	127
Least Squares Mean (Standard Error) Units: mg/dL	6.5 (3.50)	-13.2 (3.59)	-18.6 (3.54)	-23.6 (3.52)	-42.0 (3.50)	-38.0 (3.48)	-28.8 (3.55)	-42.2 (3.50)	-41.7 (3.54)	-32.4 (3.49)	-51.3 (3.51)	-52.7 (3.52)

18. Secondary Outcome

Title: Percentage of Participants With Marked Hyperglycemia (Grouped Analysis)

Description: Marked hyperglycemia is defined as fasting plasma glucose greater than or equal to 200 mg/dL (11.10 mmol/L). This analysis compared the groupings of participants who received the combination of pioglitazone with each dose of alogliptin with the grouping of participants who received pioglitazone alone.

Time Frame: From Week 1 to Week 26

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set including patients with at least one non-missing fasting plasma glucose result in each treatment group.

Arm/Group Title	Pioglitazone Alone	Alogliptin 12.5 + Pioglitazone	Alogliptin 25 + Pioglitazone
Arm/Group Description:	Alogliptin placebo plus all active pioglitazone groups (15, 30, and 45 mg).	Alogliptin 12.5 mg plus all active pioglitazone (15, 30, and 45 mg).	Alogliptin 25 mg plus all active pioglitazone (15, 30, and 45 mg).
Number of Participants Analyzed	381	386	384
Measure Type: Number Units: percentage of participants	39.4	24.6	22.1

19. Secondary Outcome

Title: Percentage of Participants With Marked Hyperglycemia

Description: Marked hyperglycemia is defined as fasting plasma glucose greater than or equal to 200 mg/dL (11.10 mmol/L).

Time Frame: From Week 1 to Week 26

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set including patients with at least one non-missing fasting plasma glucose result in each treatment group.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	129	122	126	127	129	130	125	129	127	129	128	127
Measure Type: Number Units: percentage of participants	60.5	42.6	39.7	37.8	27.1	22.3	39.2	26.4	23.6	41.1	20.3	20.5

20. Secondary Outcome

Title: Percentage of Participants Meeting Rescue Criteria (Grouped Analysis)

Rescue was defined as meeting 1 of the following criteria, confirmed by a 2nd sample drawn within 5 days of the first and analyzed by the central laboratory:

Description:
1. After the Week 1 Visit but prior to the Week 4 Visit: a single fasting plasma glucose ≥300 mg/dL;
2. From the Week 4 Visit but prior to the Week 8 Visit: a single fasting plasma glucose ≥275 mg/dL;
3. From the Week 8 Visit but prior to the Week 12 Visit: a single fasting plasma glucose ≥250 mg/dL;
4. From the Week 12 Visit through the End-of-Treatment Visit: HbA1c ≥8.5% and ≤0.5% reduction in HbA1c as compared with Baseline HbA1c.

Time Frame: From Week 1 to Week 26.
Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set including patients with at least 1 postbaseline visit. This analysis compared the groupings of participants who received the combination of pioglitazone with each dose of alogliptin with the grouping of participants who received pioglitazone alone.

Arm/Group Title	Pioglitazone Alone	Alogliptin 12.5 + Pioglitazone	Alogliptin 25 + Pioglitazone
Arm/Group Description:	Alogliptin placebo plus all active pioglitazone groups (15, 30, and 45 mg).	Alogliptin 12.5 mg plus all active pioglitazone (15, 30, and 45 mg).	Alogliptin 25 mg plus all active pioglitazone (15, 30, and 45 mg).
Number of Participants Analyzed	376	382	377
Measure Type: Number			
Units: percentage of participants	11.4	3.9	3.4

21. Secondary Outcome

Title: Percentage of Participants Meeting Rescue Criteria
Rescue was defined as meeting 1 of the following criteria, confirmed by a 2nd sample drawn within 5 days of the first and analyzed by the central laboratory:

Description:
1. After the Week 1 Visit but prior to the Week 4 Visit: a single fasting plasma glucose ≥300 mg/dL;
2. From the Week 4 Visit but prior to the Week 8 Visit: a single fasting plasma glucose ≥275 mg/dL;
3. From the Week 8 Visit but prior to the Week 12 Visit: a single fasting plasma glucose ≥250 mg/dL;
4. From the Week 12 Visit through the End-of-Treatment Visit: HbA1c ≥8.5% and ≤0.5% reduction in HbA1c as compared with Baseline HbA1c.

Time Frame: From Week 1 to Week 26
Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set including patients with at least 1 postbaseline visit.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	125	124	125	127	129	129	123	126	123	126	127	125
Measure Type: Number												
Units: percentage of participants	32.8	14.5	12.8	10.2	4.7	3.9	15.4	4.8	4.9	8.7	2.4	1.6

22. Secondary Outcome

Title: Percentage of Participants With Glycosylated Hemoglobin ≤ 6.5% (Grouped Analysis)
Description: Clinical response at Week 26 was assessed by the percentage of participants with HbA1c less than or equal to 6.5%.
This analysis compared the groupings of participants who received the combination of pioglitazone with each dose of alogliptin with the grouping of participants who received pioglitazone alone.
Time Frame: Week 26
Safety Issue? No

Outcome Measure Data

Analysis Population Description
The full analysis set. Patients who did not complete the scheduled Week 26 visit were assessed based on their response at the time of discontinuation.

Arm/Group Title	Pioglitazone Alone	Alogliptin 12.5 + Pioglitazone	Alogliptin 25 + Pioglitazone
Arm/Group Description:	Alogliptin placebo plus all active pioglitazone groups (15, 30, and 45 mg).	Alogliptin 12.5 mg plus all active pioglitazone (15, 30, and 45 mg).	Alogliptin 25 mg plus all active pioglitazone (15, 30, and 45 mg).
Number of Participants Analyzed	387	390	390
Measure Type: Number			
Units: percentage of participants	12.4	27.9	29.2

23. Secondary Outcome

Title: Percentage of Participants With Glycosylated Hemoglobin ≤ 6.5%
Description: Clinical response at Week 26 was assessed by the percentage of participants with HbA1c less than or equal to 6.5%.
Time Frame: Week 26
Safety Issue? No

Outcome Measure Data

Analysis Population Description
The full analysis set. Patients who did not complete the scheduled Week 26 visit were assessed based on their response at the time of discontinuation.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	129	128	129	129	130	130	129	130	130	129	130	130
Measure Type: Number												
Units: percentage of participants	0.8	8.6	12.4	6.2	21.5	24.6	11.6	30.0	30.0	19.4	32.3	33.1

24. Secondary Outcome

Title: Percentage of Participants With Glycosylated Hemoglobin ≤ 7.0% (Grouped Analysis)
Description: Clinical response at Week 26 was assessed by the percentage of participants with HbA1c less than or equal to 7%.
This analysis compared the groupings of participants who received the combination of pioglitazone with each dose of alogliptin with the grouping of participants who received pioglitazone alone.
Time Frame: Week 26
Safety Issue? No

Outcome Measure Data

Analysis Population Description
The full analysis set. Patients who did not complete the scheduled Week 26 visit were assessed based on their response at the time of discontinuation.

Arm/Group Title	Pioglitazone Alone	Alogliptin 12.5 + Pioglitazone	Alogliptin 25 + Pioglitazone
Arm/Group Description:	Alogliptin placebo plus all active pioglitazone groups (15, 30, and 45 mg).	Alogliptin 12.5 mg plus all active pioglitazone (15, 30, and 45 mg).	Alogliptin 25 mg plus all active pioglitazone (15, 30, and 45 mg).
Number of Participants Analyzed	387	390	390
Measure Type: Number			
Units: percentage of participants	30.5	54.6	55.9

25. Secondary Outcome

Title: Percentage of Participants With Glycosylated Hemoglobin ≤ 7%

Description: Clinical response at Week 26 was assessed by the percentage of participants with HbA1c less than or equal to 7%.
Time Frame: Week 26
Safety Issue? No

Outcome Measure Data

Analysis Population Description
The full analysis set. Patients who did not complete the scheduled Week 26 visit were assessed based on their response at the time of discontinuation.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	129	128	129	129	130	130	129	130	130	129	130	130
Measure Type: Number												
Units: percentage of participants	6.2	22.7	27.1	25.6	49.2	54.6	29.5	53.1	53.1	36.4	61.5	60.0

26. Secondary Outcome

Title: Percentage of Participants With Glycosylated Hemoglobin ≤ 7.5% (Grouped Analysis)
Description: Clinical response at Week 26 was assessed by the percentage of participants with HbA1c less than or equal to 7.5%.
This analysis compared the groupings of participants who received the combination of pioglitazone with each dose of alogliptin with the grouping of participants who received pioglitazone alone.
Time Frame: Week 26
Safety Issue? No

Outcome Measure Data

Analysis Population Description
The full analysis set. Patients who did not complete the scheduled Week 26 visit were assessed based on their response at the time of discontinuation.

Arm/Group Title	Pioglitazone Alone	Alogliptin 12.5 + Pioglitazone	Alogliptin 25 + Pioglitazone
Arm/Group Description:	Alogliptin placebo plus all active pioglitazone groups (15, 30, and 45 mg).	Alogliptin 12.5 mg plus all active pioglitazone (15, 30, and 45 mg).	Alogliptin 25 mg plus all active pioglitazone (15, 30, and 45 mg).
Number of Participants Analyzed	387	390	390
Measure Type: Number			
Units: percentage of participants	54.8	77.4	74.1

27. Secondary Outcome

Title: Percentage of Participants With Glycosylated Hemoglobin ≤ 7.5%
Description: Clinical response at Week 26 was assessed by the percentage of participants with HbA1c less than or equal to 7.5%.
Time Frame: Week 26
Safety Issue? No

Outcome Measure Data

Analysis Population Description
The full analysis set. Patients who did not complete the scheduled Week 26 visit were assessed based on their response at the time of discontinuation.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	129	128	129	129	130	130	129	130	130	129	130	130
Measure Type: Number												
Units: percentage of participants	24.8	38.3	55.0	51.9	77.7	71.5	55.8	73.8	72.3	56.6	80.8	78.5

28. Secondary Outcome

Title: Percentage of Participants With a Decrease in Glycosylated Hemoglobin ≥ 0.5% (Grouped Analysis)
Description: Clinical response at Week 26 was assessed by the percentage of participants with a decrease from Baseline in HbA1c of greater than or equal to 0.5%.
This analysis compared the groupings of participants who received the combination of pioglitazone with each dose of alogliptin with the grouping of participants who received pioglitazone alone.
Time Frame: Baseline and Week 26
Safety Issue? No

Outcome Measure Data

Analysis Population Description
The full analysis set. Patients who did not complete the scheduled Week 26 visit were assessed based on their response at the time of discontinuation.

Arm/Group Title	Pioglitazone Alone	Alogliptin 12.5 + Pioglitazone	Alogliptin 25 + Pioglitazone
Arm/Group Description:	Alogliptin placebo plus all active pioglitazone groups (15, 30, and 45 mg).	Alogliptin 12.5 mg plus all active pioglitazone (15, 30, and 45 mg).	Alogliptin 25 mg plus all active pioglitazone (15, 30, and 45 mg).
Number of Participants Analyzed	387	390	390
Measure Type: Number			
Units: percentage of participants	67.2	85.6	83.3

29. Secondary Outcome

Title: Percentage of Participants With a Decrease in Glycosylated Hemoglobin ≥ 0.5%
Description: Clinical response at Week 26 was assessed by the percentage of participants with a decrease from Baseline in HbA1c of greater than or equal to 0.5%.
Time Frame: Baseline and Week 26
Safety Issue? No

Outcome Measure Data

Analysis Population Description
The full analysis set. Patients who did not complete the scheduled Week 26 visit were assessed based on their response at the time of discontinuation.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	129	128	129	129	130	130	129	130	130	129	130	130
Measure Type: Number												
Units: percentage of participants	31.8	57.8	66.7	61.2	86.2	79.2	68.2	86.9	83.8	72.1	83.8	86.9

30. Secondary Outcome

Title: Percentage of Participants With a Decrease in Glycosylated Hemoglobin ≥ 1% (Grouped Analysis)
Description: Clinical response at Week 26 was assessed by the percentage of participants with a decrease from Baseline in HbA1c of greater than or equal to 1%.
This analysis compared the groupings of participants who received the combination of pioglitazone with each dose of alogliptin with the grouping of participants who received pioglitazone alone.
Time Frame: Baseline and Week 26
Safety Issue? No

Outcome Measure Data

Analysis Population Description
The full analysis set. Patients who did not complete the scheduled Week 26 visit were assessed based on their response at the time of discontinuation.

Arm/Group Title	Pioglitazone Alone	Alogliptin 12.5 + Pioglitazone	Alogliptin 25 + Pioglitazone
Arm/Group Description:	Alogliptin placebo plus all active pioglitazone groups (15, 30, and 45 mg).	Alogliptin 12.5 mg plus all active pioglitazone (15, 30, and 45 mg).	Alogliptin 25 mg plus all active pioglitazone (15, 30, and 45 mg).
Number of Participants Analyzed	387	390	390
Measure Type: Number			
Units: percentage of participants	45.7	71.8	69.5

31. Secondary Outcome

Title: Percentage of Participants With a Decrease in Glycosylated Hemoglobin ≥ 1%
Description: Clinical response at Week 26 was assessed by the percentage of participants with a decrease from Baseline in HbA1c of greater than or equal to 1%.
Time Frame: Baseline and Week 26
Safety Issue? No

Outcome Measure Data

Analysis Population Description
The full analysis set. Patients who did not complete the scheduled Week 26 visit were assessed based on their response at the time of discontinuation.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	129	128	129	129	130	130	129	130	130	129	130	130
Measure Type: Number												
Units: percentage of participants	16.3	33.6	47.3	36.4	69.2	66.9	46.5	73.1	69.2	54.3	73.1	72.3

32. Secondary Outcome

Title: Percentage of Participants With a Decrease in Glycosylated Hemoglobin ≥ 1.5% (Grouped Analysis)
Description: Clinical response at Week 26 was assessed by the percentage of participants with a decrease from Baseline in HbA1c of greater than or equal to 1.5%.
This analysis compared the groupings of participants who received the combination of pioglitazone with each dose of alogliptin with the grouping of participants who received pioglitazone alone.
Time Frame: Baseline and Week 26
Safety Issue? No

Outcome Measure Data

Analysis Population Description
The full analysis set. Patients who did not complete the scheduled Week 26 visit were assessed based on their response at the time of discontinuation.

Arm/Group Title	Pioglitazone Alone	Alogliptin 12.5 + Pioglitazone	Alogliptin 25 + Pioglitazone
Arm/Group Description:	Alogliptin placebo plus all active pioglitazone groups (15, 30, and 45 mg).	Alogliptin 12.5 mg plus all active pioglitazone (15, 30, and 45 mg).	Alogliptin 25 mg plus all active pioglitazone (15, 30, and 45 mg).
Number of Participants Analyzed	387	390	390
Measure Type: Number			
Units: percentage of participants	27.6	45.9	50.3

33. Secondary Outcome

Title: Percentage of Participants With a Decrease in Glycosylated Hemoglobin ≥ 1.5%
Description: Clinical response at Week 26 was assessed by the percentage of participants with a decrease from Baseline in HbA1c of greater than or equal to 1.5%.
Time Frame: Baseline and Week 26
Safety Issue? No

Outcome Measure Data

Analysis Population Description
The full analysis set. Patients who did not complete the scheduled Week 26 visit were assessed based on their response at the time of discontinuation.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	129	128	129	129	130	130	129	130	130	129	130	130
Measure Type: Number												
Units: percentage of participants	5.4	15.6	28.7	21.7	41.5	46.2	27.1	45.4	46.2	34.1	50.8	58.5

34. Secondary Outcome

Title: Percentage of Participants With a Decrease in Glycosylated Hemoglobin ≥ 2.0% (Grouped Analysis)
Description: Clinical response at Week 26 was assessed by the percentage of participants with a decrease from Baseline in HbA1c of greater than or equal to 2.0%.
This analysis compared the groupings of participants who received the combination of pioglitazone with each dose of alogliptin with the grouping of participants who received pioglitazone alone.
Time Frame: Baseline and Week 26.
Safety Issue? No

Outcome Measure Data

Analysis Population Description
The full analysis set. Patients who did not complete the scheduled Week 26 visit were assessed based on their response at the time of discontinuation.

Arm/Group Title	Pioglitazone Alone	Alogliptin 12.5 + Pioglitazone	Alogliptin 25 + Pioglitazone
Arm/Group Description:	Alogliptin placebo plus all active pioglitazone groups (15, 30, and 45 mg).	Alogliptin 12.5 mg plus all active pioglitazone (15, 30, and 45 mg).	Alogliptin 25 mg plus all active pioglitazone (15, 30, and 45 mg).
Number of Participants Analyzed	387	390	390
Measure Type: Number			
Units: percentage of participants	11.1	25.4	27.7

35. Secondary Outcome

Title: Percentage of Participants With a Decrease in Glycosylated Hemoglobin ≥ 2%
Description: Clinical response at Week 26 was assessed by the percentage of participants with a decrease from Baseline in HbA1c of greater than or equal to 2%.
Time Frame: Baseline and Week 26
Safety Issue? No

Outcome Measure Data

Analysis Population Description
The full analysis set. Patients who did not complete the scheduled Week 26 visit were assessed based on their response at the time of discontinuation.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	129	128	129	129	130	130	129	130	130	129	130	130
Measure Type: Number **Units: percentage of participants**	1.6	7.8	11.6	7.0	23.1	21.5	9.3	22.3	26.2	17.1	30.8	35.4

36. Secondary Outcome

Title: Change From Baseline in Fasting Proinsulin Over Time (Grouped Analysis)

Description: Proinsulin is a precursor to insulin, and was measured as an indicator of pancreatic function. The change from Baseline in fasting proinsulin was assessed at Weeks 4, 8, 12, 16, 20 and 26.
This analysis compared the groupings of participants who received the combination of pioglitazone with each dose of alogliptin with the grouping of participants who received pioglitazone alone. Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and proinsulin as continuous covariates.

Time Frame: Baseline and Weeks 4, 8, 12, 16, 20 and 26.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Pioglitazone Alone	Alogliptin 12.5 + Pioglitazone	Alogliptin 25 + Pioglitazone
Arm/Group Description:	Alogliptin placebo plus all active pioglitazone groups (15, 30, and 45 mg).	Alogliptin 12.5 mg plus all active pioglitazone (15, 30, and 45 mg).	Alogliptin 25 mg plus all active pioglitazone (15, 30, and 45 mg).
Number of Participants Analyzed	387	390	390
Least Squares Mean (Standard Error) Units: pmol/L			
Week 4 (n=328, 319, 327)	-6.2 (0.81)	-10.3 (0.82)	-10.1 (0.81)
Week 8 (n=357, 347, 358)	-7.2 (0.87)	-11.3 (0.88)	-11.3 (0.87)
Week 12 (n=357, 347, 358)	-8.2 (0.91)	-11.6 (0.93)	-11.6 (0.91)
Week 16 (n=358, 348, 358)	-7.2 (0.92)	-12.2 (0.94)	-11.3 (0.92)
Week 20 (n=358, 349, 359)	-6.6 (1.08)	-10.4 (1.09)	-10.7 (1.08)
Week 26 (n=358, 349, 359)	-5.3 (1.09)	-10.6 (1.11)	-9.5 (1.09)

37. Secondary Outcome

Title: Change From Baseline to Week 4 in Fasting Proinsulin

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline proinsulin as continuous covariates.

Time Frame: Baseline and Week 4

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	116	111	109	107	109	109	110	105	114	111	105	104
Least Squares Mean (Standard Error) **Units: pmol/L**	-0.1 (1.36)	-4.7 (1.39)	-2.3 (1.41)	-4.8 (1.42)	-9.9 (1.41)	-8.9 (1.41)	-6.7 (1.40)	-9.6 (1.43)	-9.5 (1.37)	-7.2 (1.39)	-11.3 (1.43)	-11.7 (1.44)

38. Secondary Outcome

Title: Change From Baseline to Week 8 in Fasting Proinsulin

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline proinsulin as continuous covariates.

Time Frame: Baseline and Week 8

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	122	120	123	121	119	120	116	113	119	120	115	119
Least Squares Mean (Standard Error) **Units: pmol/L**	0.7 (1.48)	0.2 (1.50)	-2.6 (1.48)	-3.8 (1.49)	-11.1 (1.50)	-10.7 (1.50)	-8.8 (1.52)	-11.8 (1.54)	-9.4 (1.50)	-9.0 (1.50)	-11.0 (1.53)	-13.8 (1.50)

39. Secondary Outcome

Title: Change From Baseline to Week 12 in Fasting Proinsulin

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline proinsulin as continuous covariates.

Time Frame: Baseline and Week 12

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	122	120	123	121	119	120	116	113	119	120	115	119
Least Squares Mean (Standard Error)	-1.0 (1.56)	-0.7 (1.57)	-2.3 (1.56)	-5.3 (1.57)	-10.1 (1.58)	-8.8 (1.58)	-11.2 (1.60)	-12.1 (1.63)	-12.7 (1.58)	-8.1 (1.58)	-12.7 (1.61)	-13.2 (1.58)

Units: pmol/L

40. Secondary Outcome

Title: Change From Baseline to Week 16 in Fasting Proinsulin

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline proinsulin as continuous covariates.

Time Frame: Baseline and Week 16

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	122	120	123	121	120	120	117	113	119	120	115	119
Least Squares Mean (Standard Error) Units: pmol/L	-3.0 (1.58)	0.0 (1.60)	-2.3 (1.58)	-3.7 (1.59)	-11.0 (1.60)	-8.4 (1.60)	-10.0 (1.62)	-12.6 (1.65)	-11.2 (1.60)	-8.0 (1.60)	-13.0 (1.63)	-14.4 (1.60)

41. Secondary Outcome

Title: Change From Baseline to Week 20 in Fasting Proinsulin

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline proinsulin as continuous covariates.

Time Frame: Baseline and Week 20

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	122	120	123	121	121	121	117	113	119	120	115	119
Least Squares Mean (Standard Error) Units: pmol/L	-0.9 (1.85)	1.5 (1.86)	-3.0 (1.84)	-3.4 (1.86)	-11.2 (1.86)	-8.7 (1.86)	-9.3 (1.89)	-10.0 (1.92)	-10.7 (1.87)	-7.1 (1.86)	-10.2 (1.90)	-12.5 (1.87)

42. Secondary Outcome

Title: Change From Baseline to Week 26 in Fasting Proinsulin

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline proinsulin as continuous covariates.

Time Frame: Baseline and Week 26

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	122	120	123	121	121	121	117	113	119	120	115	119
Least Squares Mean (Standard Error) Units: pmol/L	1.2 (1.87)	0.7 (1.88)	-3.3 (1.86)	-3.5 (1.88)	-10.9 (1.88)	-7.2 (1.88)	-8.4 (1.91)	-8.9 (1.95)	-8.8 (1.89)	-4.1 (1.89)	-12.1 (1.93)	-12.6 (1.89)

43. Secondary Outcome

Title: Change From Baseline in Insulin Over Time (Grouped Analysis)

Description: The change from Baseline in fasting insulin was assessed at Weeks 4, 8, 12, 16, 20 and 26. This analysis compared the groupings of participants who received the combination of pioglitazone with each dose of alogliptin with the grouping of participants who received pioglitazone alone. Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline insulin as continuous covariates.

Time Frame: Baseline and Weeks 4, 8, 12, 16, 20 and 26.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Pioglitazone Alone	Alogliptin 12.5 + Pioglitazone	Alogliptin 25 + Pioglitazone
Arm/Group Description:	Alogliptin placebo plus all active pioglitazone groups (15, 30, and 45 mg).	Alogliptin 12.5 mg plus all active pioglitazone (15, 30, and 45 mg).	Alogliptin 25 mg plus all active pioglitazone (15, 30, and 45 mg).
Number of Participants Analyzed	387	390	390
Least Squares Mean (Standard Error) Units: µIU/mL			
Week 4 (n=325, 318, 326)	-2.29 (0.440)	-2.11 (0.445)	-2.19 (0.440)
Week 8 (n=355, 346, 356)	-2.35 (0.535)	-2.44 (0.542)	-2.36 (0.534)
Week 12 (n=355, 347, 356)	-2.62 (0.498)	-1.73 (0.503)	-2.62 (0.497)
Week 16 (n=356, 348, 356)	-2.19 (0.488)	-2.60 (0.494)	-2.48 (0.488)
Week 20 (n=356, 349, 357)	-2.35 (0.511)	-1.91 (0.516)	-2.06 (0.510)

Week 26 (n=356, 349, 357)	-1.74 (1.212)			-2.05 (1.225)					-1.66 (1.210)			

44. Secondary Outcome

Title: Change From Baseline to Week 4 in Insulin Levels

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline insulin as continuous covariates.

Time Frame: Baseline and Week 4

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Placebo**	**Alogliptin 12.5 + Placebo**	**Alogliptin 25 + Placebo**	**Placebo + Pioglitazone 15**	**Alogliptin 12.5 + Pioglitazone 15**	**Alogliptin 25 + Pioglitazone 15**	**Placebo + Pioglitazone 30**	**Alogliptin 12.5 + Pioglitazone 30**	**Alogliptin 25 + Pioglitazone 30**	**Placebo + Pioglitazone 45**	**Alogliptin 12.5 + Pioglitazone 45**	**Alogliptin 25 + Pioglitazone 45**
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	116	110	106	107	109	108	109	104	114	109	105	104
Least Squares Mean (Standard Error) **Units: µIU/mL**	1.06 (0.737)	-0.33 (0.756)	2.31 (0.771)	-1.68 (0.767)	-3.03 (0.760)	-1.86 (0.763)	-2.43 (0.760)	-1.45 (0.779)	-2.05 (0.743)	-2.76 (0.760)	-1.85 (0.774)	-2.65 (0.778)

45. Secondary Outcome

Title: Change From Baseline to Week 8 in Insulin Levels

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline insulin as continuous covariates.

Time Frame: Baseline and Week 8

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Placebo**	**Alogliptin 12.5 + Placebo**	**Alogliptin 25 + Placebo**	**Placebo + Pioglitazone 15**	**Alogliptin 12.5 + Pioglitazone 15**	**Alogliptin 25 + Pioglitazone 15**	**Placebo + Pioglitazone 30**	**Alogliptin 12.5 + Pioglitazone 30**	**Alogliptin 25 + Pioglitazone 30**	**Placebo + Pioglitazone 45**	**Alogliptin 12.5 + Pioglitazone 45**	**Alogliptin 25 + Pioglitazone 45**
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	122	119	123	121	119	119	116	112	118	118	115	119
Least Squares Mean (Standard Error) **Units: µIU/mL**	-0.46 (0.912)	1.80 (0.923)	1.69 (0.909)	-1.47 (0.916)	-2.21 (0.923)	-2.78 (0.923)	-2.74 (0.935)	-3.15 (0.953)	-1.20 (0.927)	-2.83 (0.927)	-1.96 (0.939)	-3.09 (0.924)

46. Secondary Outcome

Title: Change From Baseline to Week 12 in Insulin Levels

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline insulin as continuous covariates.

Time Frame: Baseline and Week 12

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Placebo**	**Alogliptin 12.5 + Placebo**	**Alogliptin 25 + Placebo**	**Placebo + Pioglitazone 15**	**Alogliptin 12.5 + Pioglitazone 15**	**Alogliptin 25 + Pioglitazone 15**	**Placebo + Pioglitazone 30**	**Alogliptin 12.5 + Pioglitazone 30**	**Alogliptin 25 + Pioglitazone 30**	**Placebo + Pioglitazone 45**	**Alogliptin 12.5 + Pioglitazone 45**	**Alogliptin 25 + Pioglitazone 45**
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	122	119	123	121	119	119	116	113	118	118	115	119
Least Squares Mean (Standard Error) **Units: µIU/mL**	0.06 (0.849)	1.79 (0.859)	1.93 (0.846)	-1.29 (0.852)	-1.47 (0.859)	-2.01 (0.859)	-3.61 (0.870)	-1.36 (0.882)	-2.83 (0.863)	-2.95 (0.863)	-2.35 (0.874)	-3.01 (0.859)

47. Secondary Outcome

Title: Change From Baseline to Week 16 in Insulin Levels

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline insulin as continuous covariates.

Time Frame: Baseline and Week 16

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Placebo**	**Alogliptin 12.5 + Placebo**	**Alogliptin 25 + Placebo**	**Placebo + Pioglitazone 15**	**Alogliptin 12.5 + Pioglitazone 15**	**Alogliptin 25 + Pioglitazone 15**	**Placebo + Pioglitazone 30**	**Alogliptin 12.5 + Pioglitazone 30**	**Alogliptin 25 + Pioglitazone 30**	**Placebo + Pioglitazone 45**	**Alogliptin 12.5 + Pioglitazone 45**	**Alogliptin 25 + Pioglitazone 45**
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	122	119	123	121	120	119	117	113	118	118	115	119
Least Squares Mean (Standard Error)	0.34 (0.833)	1.22 (0.843)	1.83 (0.830)	-0.63 (0.836)	-2.28 (0.840)	-1.11 (0.843)	-3.46 (0.851)	-2.50 (0.866)	-2.82 (0.847)	-2.48 (0.847)	-3.00 (0.858)	-3.52 (0.844)

Units: µIU/mL

48. Secondary Outcome

Title: Change From Baseline to Week 20 in Insulin Levels

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline insulin as continuous covariates.

Time Frame: Baseline and Week 20

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	122	119	123	121	121	120	117	113	118	118	115	119
Least Squares Mean (Standard Error) **Units: µIU/mL**	0.18 (0.873)	2.03 (0.883)	0.76 (0.869)	-0.66 (0.876)	-2.35 (0.876)	-0.90 (0.880)	-3.29 (0.891)	-2.20 (0.907)	-2.29 (0.887)	-3.12 (0.887)	-1.16 (0.899)	-3.01 (0.884)

49. Secondary Outcome

Title: Change From Baseline to Week 26 in Insulin Levels

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline insulin as continuous covariates.

Time Frame: Baseline and Week 26

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	122	119	123	121	121	120	117	113	118	118	115	119
Least Squares Mean (Standard Error) **Units: µIU/mL**	6.78 (2.071)	1.33 (2.096)	1.43 (2.063)	-0.78 (2.078)	-3.05 (2.078)	-0.76 (2.087)	-2.56 (2.114)	-0.76 (2.152)	-1.42 (2.105)	-1.88 (2.105)	-2.33 (2.132)	-2.79 (2.096)

50. Secondary Outcome

Title: Change From Baseline in Proinsulin/Insulin Ratio Over Time (Grouped Analysis)

Description: The ratio of proinsulin to insulin was calculated as proinsulin (pmol/L) / insulin (µIU/mL) at weeks 4, 8, 12, 16, 20 and 26 relative to the Baseline value.
This analysis compared the groupings of participants who received the combination of pioglitazone with each dose of alogliptin with the grouping of participants who received pioglitazone alone. Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline proinsulin/insulin ratio as continuous covariates.

Time Frame: Baseline and Weeks 4, 8, 12, 16, 20 and 26.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Pioglitazone Alone	Alogliptin 12.5 + Pioglitazone	Alogliptin 25 + Pioglitazone
Arm/Group Description:	Alogliptin placebo plus all active pioglitazone groups (15, 30, and 45 mg).	Alogliptin 12.5 mg plus all active pioglitazone (15, 30, and 45 mg).	Alogliptin 25 mg plus all active pioglitazone (15, 30, and 45 mg).
Number of Participants Analyzed	387	390	390
Least Squares Mean (Standard Error) Units: ratio			
Week 4 (n=325, 315, 326)	-0.021 (0.0088)	-0.078 (0.0089)	-0.057 (0.0088)
Week 8 (n=355, 344, 356)	-0.019 (0.0084)	-0.079 (0.0086)	-0.081 (0.0084)
Week 12 (n=355, 345, 356)	-0.042 (0.0083)	-0.086 (0.0084)	-0.082 (0.0083)
Week 16 (n=356, 346, 356)	-0.033 (0.0077)	-0.091 (0.0078)	-0.077 (0.0077)
Week 20 (n=356, 347, 357)	-0.034 (0.0076)	-0.088 (0.0077)	-0.078 (0.0076)
Week 26 (n=356, 347, 357)	-0.027 (0.0088)	-0.087 (0.0090)	-0.076 (0.0088)

51. Secondary Outcome

Title: Change From Baseline to Week 4 in Proinsulin/Insulin Ratio

Description: The ratio of proinsulin to insulin was calculated as proinsulin (pmol/L) / insulin (µIU/mL).
Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline proinsulin/insulin ratio as continuous covariates.

Time Frame: Baseline and Week 4

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	116	110	106	107	108	108	109	102	114	109	105	104

Least Squares Mean (Standard Error) **Units: ratio**	-0.015 (0.0147)	-0.039 (0.0151)	-0.058 (0.0154)	-0.029 (0.0153)	-0.054 (0.0153)	-0.054 (0.0153)	-0.023 (0.0152)	-0.068 (0.0157)	-0.045 (0.0149)	-0.009 (0.0152)	-0.111 (0.0155)	-0.072 (0.0156)

52. Secondary Outcome

Title: Change From Baseline to Week 8 in Proinsulin/Insulin Ratio

Description: The ratio of proinsulin to insulin was calculated as proinsulin (pmol/L) / insulin (µIU/mL).
Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline proinsulin/insulin ratio as continuous covariates.

Time Frame: Baseline and Week 8

Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Placebo**	**Alogliptin 12.5 + Placebo**	**Alogliptin 25 + Placebo**	**Placebo + Pioglitazone 15**	**Alogliptin 12.5 + Pioglitazone 15**	**Alogliptin 25 + Pioglitazone 15**	**Placebo + Pioglitazone 30**	**Alogliptin 12.5 + Pioglitazone 30**	**Alogliptin 25 + Pioglitazone 30**	**Placebo + Pioglitazone 45**	**Alogliptin 12.5 + Pioglitazone 45**	**Alogliptin 25 + Pioglitazone 45**
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	122	119	123	121	119	119	116	110	118	118	115	119
Least Squares Mean (Standard Error) **Units: ratio**	0.005 (0.0144)	-0.025 (0.0146)	-0.045 (0.0143)	-0.007 (0.0144)	-0.086 (0.0146)	-0.077 (0.0146)	-0.036 (0.0148)	-0.054 (0.0152)	-0.072 (0.0146)	-0.013 (0.0146)	-0.098 (0.0148)	-0.093 (0.0146)

53. Secondary Outcome

Title: Change From Baseline to Week 12 in Proinsulin/Insulin Ratio

Description: The ratio of proinsulin to insulin was calculated as proinsulin (pmol/L) / insulin (µIU/mL).
Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline proinsulin/insulin ratio as continuous covariates.

Time Frame: Baseline and Week 12

Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Placebo**	**Alogliptin 12.5 + Placebo**	**Alogliptin 25 + Placebo**	**Placebo + Pioglitazone 15**	**Alogliptin 12.5 + Pioglitazone 15**	**Alogliptin 25 + Pioglitazone 15**	**Placebo + Pioglitazone 30**	**Alogliptin 12.5 + Pioglitazone 30**	**Alogliptin 25 + Pioglitazone 30**	**Placebo + Pioglitazone 45**	**Alogliptin 12.5 + Pioglitazone 45**	**Alogliptin 25 + Pioglitazone 45**
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	122	119	123	121	119	119	116	111	118	118	115	119
Least Squares Mean (Standard Error) **Units: ratio**	-0.006 (0.0142)	-0.024 (0.0144)	-0.041 (0.0141)	-0.041 (0.0142)	-0.073 (0.0144)	-0.056 (0.0144)	-0.063 (0.0146)	-0.072 (0.0149)	-0.088 (0.0144)	-0.021 (0.0144)	-0.112 (0.0146)	-0.101 (0.0144)

54. Secondary Outcome

Title: Change From Baseline to Week 16 in Proinsulin/Insulin Ratio

Description: The ratio of proinsulin to insulin was calculated as proinsulin (pmol/L) / insulin (µIU/mL).
Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline proinsulin/insulin ratio as continuous covariates.

Time Frame: Baseline and Week 16

Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Placebo**	**Alogliptin 12.5 + Placebo**	**Alogliptin 25 + Placebo**	**Placebo + Pioglitazone 15**	**Alogliptin 12.5 + Pioglitazone 15**	**Alogliptin 25 + Pioglitazone 15**	**Placebo + Pioglitazone 30**	**Alogliptin 12.5 + Pioglitazone 30**	**Alogliptin 25 + Pioglitazone 30**	**Placebo + Pioglitazone 45**	**Alogliptin 12.5 + Pioglitazone 45**	**Alogliptin 25 + Pioglitazone 45**
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	122	119	123	121	120	119	117	111	118	118	115	119
Least Squares Mean (Standard Error) **Units: ratio**	-0.026 (0.0132)	-0.036 (0.0133)	-0.046 (0.0131)	-0.035 (0.0132)	-0.078 (0.0133)	-0.066 (0.0134)	-0.035 (0.0135)	-0.094 (0.0138)	-0.061 (0.0134)	-0.030 (0.0134)	-0.102 (0.0136)	-0.104 (0.0133)

55. Secondary Outcome

Title: Change From Baseline to Week 20 in Proinsulin/Insulin Ratio

Description: The ratio of proinsulin to insulin was calculated as proinsulin (pmol/L) / insulin (µIU/mL).
Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline proinsulin/insulin ratio as continuous covariates.

Time Frame: Baseline and Week 20

Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Placebo**	**Alogliptin 12.5 + Placebo**	**Alogliptin 25 + Placebo**	**Placebo + Pioglitazone 15**	**Alogliptin 12.5 + Pioglitazone 15**	**Alogliptin 25 + Pioglitazone 15**	**Placebo + Pioglitazone 30**	**Alogliptin 12.5 + Pioglitazone 30**	**Alogliptin 25 + Pioglitazone 30**	**Placebo + Pioglitazone 45**	**Alogliptin 12.5 + Pioglitazone 45**	**Alogliptin 25 + Pioglitazone 45**
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	122	119	123	121	121	120	117	111	118	118	115	119

Least Squares Mean (Standard Error) **Units: ratio**	-0.007 (0.0131)	-0.014 (0.0132)	-0.046 (0.0130)	-0.039 (0.0131)	-0.081 (0.0131)	-0.065 (0.0132)	-0.042 (0.0133)	-0.085 (0.0137)	-0.077 (0.0133)	-0.020 (0.0133)	-0.099 (0.0134)	-0.092 (0.0132)

56. Secondary Outcome

Title: Change From Baseline to Week 26 in Proinsulin/Insulin Ratio

Description: The ratio of proinsulin to insulin was calculated as proinsulin (pmol/L) / insulin (µIU/mL).
Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline proinsulin/insulin ratio as continuous covariates.

Time Frame: Baseline and Week 26

Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Placebo**	**Alogliptin 12.5 + Placebo**	**Alogliptin 25 + Placebo**	**Placebo + Pioglitazone 15**	**Alogliptin 12.5 + Pioglitazone 15**	**Alogliptin 25 + Pioglitazone 15**	**Placebo + Pioglitazone 30**	**Alogliptin 12.5 + Pioglitazone 30**	**Alogliptin 25 + Pioglitazone 30**	**Placebo + Pioglitazone 45**	**Alogliptin 12.5 + Pioglitazone 45**	**Alogliptin 25 + Pioglitazone 45**
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	122	119	123	121	121	120	117	111	118	118	115	119
Least Squares Mean (Standard Error) **Units: ratio**	-0.007 (0.0151)	-0.001 (0.0153)	-0.064 (0.0151)	-0.038 (0.0152)	-0.071 (0.0152)	-0.063 (0.0152)	-0.030 (0.0154)	-0.081 (0.0159)	-0.072 (0.0154)	-0.014 (0.0154)	-0.109 (0.0156)	-0.092 (0.0153)

57. Secondary Outcome

Title: Change From Baseline in C-peptide Over Time (Grouped Analysis)

Description: C-peptide is a byproduct created when the hormone insulin is produced and is measured by a blood test. Change from Baseline was assessed at Weeks 4, 8, 12, 16, 20 and 26.
This analysis compared the groupings of participants who received the combination of pioglitazone with each dose of alogliptin with the grouping of participants who received pioglitazone alone. Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline C-peptide as continuous covariates.

Time Frame: Baseline and Weeks 4, 8, 12, 16, 20 and 26.

Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Pioglitazone Alone**	**Alogliptin 12.5 + Pioglitazone**	**Alogliptin 25 + Pioglitazone**
Arm/Group Description:	Alogliptin placebo plus all active pioglitazone groups (15, 30, and 45 mg).	Alogliptin 12.5 mg plus all active pioglitazone (15, 30, and 45 mg).	Alogliptin 25 mg plus all active pioglitazone (15, 30, and 45 mg).
Number of Participants Analyzed	387	390	390
Least Squares Mean (Standard Error) Units: ng/mL			
Week 4 (n=335, 335, 336)	-0.292 (0.0417)	-0.255 (0.0417)	-0.282 (0.0416)
Week 8 (n=367, 366, 371)	-0.356 (0.0464)	-0.327 (0.0464)	-0.311 (0.0461)
Week 12 (n=367, 369, 374)	-0.268 (0.0781)	-0.249 (0.0779)	-0.334 (0.0774)
Week 16 (n=369, 374, 374)	-0.352 (0.0456)	-0.343 (0.0453)	-0.333 (0.0453)
Week 20 (n=369, 375, 375)	-0.360 (0.0465)	-0.350 (0.0461)	-0.293 (0.0461)
Week 26 (n=371, 378, 375)	-0.341 (0.0460)	-0.346 (0.0456)	-0.326 (0.0457)

58. Secondary Outcome

Title: Change From Baseline to Week 4 in C-peptide Levels

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline C-peptide as continuous covariates.

Time Frame: Baseline and Week 4

Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Placebo**	**Alogliptin 12.5 + Placebo**	**Alogliptin 25 + Placebo**	**Placebo + Pioglitazone 15**	**Alogliptin 12.5 + Pioglitazone 15**	**Alogliptin 25 + Pioglitazone 15**	**Placebo + Pioglitazone 30**	**Alogliptin 12.5 + Pioglitazone 30**	**Alogliptin 25 + Pioglitazone 30**	**Placebo + Pioglitazone 45**	**Alogliptin 12.5 + Pioglitazone 45**	**Alogliptin 25 + Pioglitazone 45**
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	117	110	108	109	114	112	112	113	117	114	108	107
Least Squares Mean (Standard Error) **Units: ng/mL**	0.002 (0.0705)	-0.032 (0.0727)	0.076 (0.0734)	-0.246 (0.0730)	-0.248 (0.0714)	-0.238 (0.0720)	-0.232 (0.0721)	-0.259 (0.0718)	-0.268 (0.0705)	-0.393 (0.0714)	-0.252 (0.0734)	-0.337 (0.0738)

59. Secondary Outcome

Title: Change From Baseline to Week 8 in C-peptide Levels

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline C-peptide as continuous covariates.

Time Frame: Baseline and Week 8

Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Placebo**	**Alogliptin 12.5 + Placebo**	**Alogliptin 25 + Placebo**	**Placebo + Pioglitazone 15**	**Alogliptin 12.5 + Pioglitazone 15**	**Alogliptin 25 + Pioglitazone 15**	**Placebo + Pioglitazone 30**	**Alogliptin 12.5 + Pioglitazone 30**	**Alogliptin 25 + Pioglitazone 30**	**Placebo + Pioglitazone 45**	**Alogliptin 12.5 + Pioglitazone 45**	**Alogliptin 25 + Pioglitazone 45**
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	124	121	123	124	124	123	119	123	124	124	119	124

Least Squares Mean (Standard Error) **Units: ng/mL**	-0.044 (0.0798)	0.114 (0.0807)	0.108 (0.0801)	-0.221 (0.0798)	-0.315 (0.0798)	-0.261 (0.0801)	-0.380 (0.0814)	-0.365 (0.0802)	-0.207 (0.0797)	-0.467 (0.0798)	-0.300 (0.0814)	-0.464 (0.0798)

60. Secondary Outcome

Title: Change From Baseline to Week 12 in C-peptide Levels

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline C-peptide as continuous covariates.

Time Frame: Baseline and Week 12

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Placebo**	**Alogliptin 12.5 + Placebo**	**Alogliptin 25 + Placebo**	**Placebo + Pioglitazone 15**	**Alogliptin 12.5 + Pioglitazone 15**	**Alogliptin 25 + Pioglitazone 15**	**Placebo + Pioglitazone 30**	**Alogliptin 12.5 + Pioglitazone 30**	**Alogliptin 25 + Pioglitazone 30**	**Placebo + Pioglitazone 45**	**Alogliptin 12.5 + Pioglitazone 45**	**Alogliptin 25 + Pioglitazone 45**
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	125	121	123	124	124	125	119	124	124	124	121	125
Least Squares Mean (Standard Error) **Units: ng/mL**	-0.055 (0.1338)	0.083 (0.1360)	0.140 (0.1349)	0.116 (0.1344)	-0.155 (0.1344)	-0.215 (0.1338)	-0.439 (0.1372)	-0.212 (0.1345)	-0.326 (0.1343)	-0.483 (0.1344)	-0.381 (0.1360)	-0.464 (0.1339)

61. Secondary Outcome

Title: Change From Baseline to Week 16 in C-peptide Levels

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline C-peptide as continuous covariates.

Time Frame: Baseline and Week 16

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Placebo**	**Alogliptin 12.5 + Placebo**	**Alogliptin 25 + Placebo**	**Placebo + Pioglitazone 15**	**Alogliptin 12.5 + Pioglitazone 15**	**Alogliptin 25 + Pioglitazone 15**	**Placebo + Pioglitazone 30**	**Alogliptin 12.5 + Pioglitazone 30**	**Alogliptin 25 + Pioglitazone 30**	**Placebo + Pioglitazone 45**	**Alogliptin 12.5 + Pioglitazone 45**	**Alogliptin 25 + Pioglitazone 45**
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	125	121	123	124	126	125	121	125	124	124	123	125
Least Squares Mean (Standard Error) **Units: ng/mL**	-0.076 (0.0783)	0.032 (0.0796)	0.101 (0.0789)	-0.242 (0.0786)	-0.282 (0.0780)	-0.184 (0.0783)	-0.410 (0.0796)	-0.318 (0.0783)	-0.306 (0.0786)	-0.404 (0.0786)	-0.431 (0.0789)	-0.510 (0.0783)

62. Secondary Outcome

Title: Change From Baseline to Week 20 in C-peptide Levels

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline C-peptide as continuous covariates.

Time Frame: Baseline and Week 20

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Placebo**	**Alogliptin 12.5 + Placebo**	**Alogliptin 25 + Placebo**	**Placebo + Pioglitazone 15**	**Alogliptin 12.5 + Pioglitazone 15**	**Alogliptin 25 + Pioglitazone 15**	**Placebo + Pioglitazone 30**	**Alogliptin 12.5 + Pioglitazone 30**	**Alogliptin 25 + Pioglitazone 30**	**Placebo + Pioglitazone 45**	**Alogliptin 12.5 + Pioglitazone 45**	**Alogliptin 25 + Pioglitazone 45**
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	125	121	123	124	127	126	121	125	124	124	123	125
Least Squares Mean (Standard Error) **Units: ng/mL**	-0.046 (0.0799)	0.114 (0.0812)	0.019 (0.0805)	-0.193 (0.0802)	-0.377 (0.0792)	-0.184 (0.0795)	-0.380 (0.0812)	-0.343 (0.0799)	-0.266 (0.0802)	-0.506 (0.0802)	-0.329 (0.0805)	-0.430 (0.0799)

63. Secondary Outcome

Title: Change From Baseline to Week 26 in C-peptide Levels

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline C-peptide as continuous covariates.

Time Frame: Baseline and Week 26

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Placebo**	**Alogliptin 12.5 + Placebo**	**Alogliptin 25 + Placebo**	**Placebo + Pioglitazone 15**	**Alogliptin 12.5 + Pioglitazone 15**	**Alogliptin 25 + Pioglitazone 15**	**Placebo + Pioglitazone 30**	**Alogliptin 12.5 + Pioglitazone 30**	**Alogliptin 25 + Pioglitazone 30**	**Placebo + Pioglitazone 45**	**Alogliptin 12.5 + Pioglitazone 45**	**Alogliptin 25 + Pioglitazone 45**
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	125	122	123	125	128	126	121	126	124	125	124	125
Least Squares Mean (Standard Error) **Units: ng/mL**	-0.011 (0.0793)	0.000 (0.0802)	0.059 (0.0799)	-0.239 (0.0792)	-0.380 (0.0783)	-0.204 (0.0789)	-0.353 (0.0805)	-0.235 (0.0790)	-0.300 (0.0795)	-0.429 (0.0793)	-0.421 (0.0796)	-0.474 (0.0793)

64. Secondary Outcome

Title: Change From Baseline in Total Cholesterol Over Time (Grouped Analysis)

Description: Change from Baseline in total cholesterol was assessed at Weeks 4, 8, 12, 16, 20 and 26. This analysis compared the groupings of participants who received the combination of pioglitazone with each dose of alogliptin with the grouping of participants who received pioglitazone alone. Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline total cholesterol as continuous covariates.

Time Frame: Baseline and Weeks 4, 8, 12, 16, 20 and 26.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Pioglitazone Alone	Alogliptin 12.5 + Pioglitazone	Alogliptin 25 + Pioglitazone
Arm/Group Description:	Alogliptin placebo plus all active pioglitazone groups (15, 30, and 45 mg).	Alogliptin 12.5 mg plus all active pioglitazone (15, 30, and 45 mg).	Alogliptin 25 mg plus all active pioglitazone (15, 30, and 45 mg).
Number of Participants Analyzed	387	390	390
Least Squares Mean (Standard Error) Units: mg/dL			
Week 4 (n=345, 354, 348)	1.6 (1.41)	-4.3 (1.39)	-6.5 (1.40)
Week 8 (n=374, 380, 376)	4.8 (1.42)	-1.8 (1.41)	-3.3 (1.42)
Week 12 (n=374, 380, 376)	6.6 (1.47)	1.3 (1.46)	-1.7 (1.46)
Week 16 (n=374, 380, 376)	6.5 (1.52)	1.2 (1.51)	0.1 (1.51)
Week 20 (n=374, 380, 376)	5.9 (1.56)	3.0 (1.55)	1.5 (1.56)
Week 26 (n=374, 380, 376)	8.0 (1.63)	4.4 (1.61)	3.9 (1.62)

65. Secondary Outcome

Title: Change From Baseline to Week 4 in Total Cholesterol Levels

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline total cholesterol as continuous covariates.

Time Frame: Baseline and Week 4

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	119	112	111	112	117	118	117	121	118	116	116	112
Least Squares Mean (Standard Error) Units: mg/dL	1.3 (2.40)	-3.8 (2.47)	-3.7 (2.48)	2.1 (2.47)	-2.3 (2.42)	-10.2 (2.41)	3.7 (2.42)	-7.2 (2.38)	-2.7 (2.41)	-1.2 (2.43)	-3.6 (2.43)	-6.7 (2.47)

66. Secondary Outcome

Title: Change From Baseline to Week 8 in Total Cholesterol Levels

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline total cholesterol as continuous covariates.

Time Frame: Baseline and Week 8

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	125	121	123	125	128	127	123	127	124	126	125	125
Least Squares Mean (Standard Error) Units: mg/dL	10.9 (2.46)	-1.4 (2.50)	-0.3 (2.48)	7.3 (2.46)	-2.3 (2.43)	-4.1 (2.44)	6.6 (2.48)	0.1 (2.45)	0.3 (2.47)	0.3 (2.45)	-3.1 (2.46)	-6.2 (2.46)

67. Secondary Outcome

Title: Change From Baseline to Week 12 in Total Cholesterol Levels

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline total cholesterol as continuous covariates.

Time Frame: Baseline and Week 12

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	125	122	123	125	128	127	123	127	124	126	125	125
Least Squares Mean (Standard Error)	7.8 (2.54)	0.4 (2.57)	0.1 (2.56)	8.7 (2.54)	1.9 (2.51)	-0.2 (2.52)	7.3 (2.56)	0.3 (2.52)	-1.0 (2.55)	3.7 (2.53)	1.7 (2.54)	-3.9 (2.54)

Units: mg/dL

68. Secondary Outcome

Title: Change From Baseline to Week 16 in Total Cholesterol Levels

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline total cholesterol as continuous covariates.

Time Frame: Baseline and Week 16

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	125	122	123	125	128	127	123	127	124	126	125	125
Least Squares Mean (Standard Error) Units: mg/dL	5.0 (2.62)	-0.5 (2.66)	-2.9 (2.65)	7.2 (2.62)	-0.4 (2.59)	3.2 (2.60)	10.0 (2.65)	0.9 (2.61)	-1.2 (2.63)	2.3 (2.61)	2.9 (2.62)	-1.8 (2.62)

69. Secondary Outcome

Title: Change From Baseline to Week 20 in Total Cholesterol Levels

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline total cholesterol as continuous covariates.

Time Frame: Baseline and Week 20

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	125	122	123	125	128	127	123	127	124	126	125	125
Least Squares Mean (Standard Error) Units: mg/dL	6.7 (2.70)	1.8 (2.74)	-1.9 (2.73)	6.3 (2.70)	4.0 (2.67)	1.4 (2.68)	7.0 (2.73)	1.1 (2.68)	3.4 (2.71)	4.6 (2.69)	4.0 (2.70)	-0.3 (2.70)

70. Secondary Outcome

Title: Change From Baseline to Week 26 in Total Cholesterol Levels

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline total cholesterol as continuous covariates.

Time Frame: Baseline and Week 26

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	125	122	123	125	128	127	123	127	124	126	125	125
Least Squares Mean (Standard Error) Units: mg/dL	4.4 (2.82)	2.2 (2.85)	0.9 (2.84)	5.8 (2.81)	4.3 (2.78)	3.5 (2.79)	8.8 (2.84)	2.8 (2.80)	3.2 (2.83)	9.5 (2.80)	6.0 (2.81)	5.1 (2.81)

71. Secondary Outcome

Title: Change From Baseline in Low-Density Lipoprotein Cholesterol Over Time (Grouped Analysis)

Description: Change from Baseline in low-density lipoprotein cholesterol (LDL-C) was assessed at Weeks 4, 8, 12, 16, 20 and 26. This analysis compared the groupings of participants who received the combination of pioglitazone with each dose of alogliptin with the grouping of participants who received pioglitazone alone. Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline LDL cholesterol as continuous covariates.

Time Frame: Baseline and Weeks 4, 8, 12, 16, 20 and 26.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Pioglitazone Alone	Alogliptin 12.5 + Pioglitazone	Alogliptin 25 + Pioglitazone
Arm/Group Description:	Alogliptin placebo plus all active pioglitazone groups (15, 30, and 45 mg).	Alogliptin 12.5 mg plus all active pioglitazone (15, 30, and 45 mg).	Alogliptin 25 mg plus all active pioglitazone (15, 30, and 45 mg).
Number of Participants Analyzed	387	390	390
Least Squares Mean (Standard Error) Units: mg/dL			
Week 4 (n=330, 336, 338)	3.1 (1.23)	-0.5 (1.22)	-1.9 (1.22)
Week 8 (n=365, 365, 365)	5.9 (1.28)	1.3 (1.28)	0.1 (1.28)
Week 12 (n=365, 367, 366)	6.9 (1.29)	3.3 (1.29)	1.5 (1.29)
Week 16 (n=365, 368, 366)	6.1 (1.29)	3.3 (1.29)	2.4 (1.29)
Week 20 (n=365, 368, 366)	6.9 (1.37)	4.2 (1.36)	3.0 (1.37)

Week 26 (n=365, 368, 366)	7.4 (1.39)			5.2 (1.39)				5.6 (1.39)				

72. Secondary Outcome

Title: Change From Baseline to Week 4 in Low-Density Lipoprotein Cholesterol

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline LDL cholesterol as continuous covariates.

Time Frame: Baseline and Week 4

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Placebo**	**Alogliptin 12.5 + Placebo**	**Alogliptin 25 + Placebo**	**Placebo + Pioglitazone 15**	**Alogliptin 12.5 + Pioglitazone 15**	**Alogliptin 25 + Pioglitazone 15**	**Placebo + Pioglitazone 30**	**Alogliptin 12.5 + Pioglitazone 30**	**Alogliptin 25 + Pioglitazone 30**	**Placebo + Pioglitazone 45**	**Alogliptin 12.5 + Pioglitazone 45**	**Alogliptin 25 + Pioglitazone 45**
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	113	102	105	107	112	113	112	115	114	111	109	111
Least Squares Mean (Standard Error) **Units: mg/dL**	2.1 (2.11)	-2.4 (2.22)	1.4 (2.19)	2.6 (2.16)	1.6 (2.12)	-2.7 (2.11)	3.2 (2.12)	-2.8 (2.09)	0.4 (2.10)	3.4 (2.13)	-0.3 (2.15)	-3.4 (2.13)

73. Secondary Outcome

Title: Change From Baseline to Week 8 in Low-Density Lipoprotein Cholesterol

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline LDL cholesterol as continuous covariates.

Time Frame: Baseline and Week 8

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Placebo**	**Alogliptin 12.5 + Placebo**	**Alogliptin 25 + Placebo**	**Placebo + Pioglitazone 15**	**Alogliptin 12.5 + Pioglitazone 15**	**Alogliptin 25 + Pioglitazone 15**	**Placebo + Pioglitazone 30**	**Alogliptin 12.5 + Pioglitazone 30**	**Alogliptin 25 + Pioglitazone 30**	**Placebo + Pioglitazone 45**	**Alogliptin 12.5 + Pioglitazone 45**	**Alogliptin 25 + Pioglitazone 45**
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	119	113	119	122	123	122	120	123	119	123	119	124
Least Squares Mean (Standard Error) **Units: mg/dL**	9.4 (2.24)	2.1 (2.30)	3.4 (2.24)	7.3 (2.21)	-0.4 (2.21)	1.0 (2.21)	5.4 (2.24)	2.4 (2.21)	2.7 (2.24)	4.8 (2.21)	2.0 (2.24)	-3.2 (2.20)

74. Secondary Outcome

Title: Change From Baseline to Week 12 in Low-Density Lipoprotein Cholesterol

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline LDL cholesterol as continuous covariates.

Time Frame: Baseline and Week 12

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Placebo**	**Alogliptin 12.5 + Placebo**	**Alogliptin 25 + Placebo**	**Placebo + Pioglitazone 15**	**Alogliptin 12.5 + Pioglitazone 15**	**Alogliptin 25 + Pioglitazone 15**	**Placebo + Pioglitazone 30**	**Alogliptin 12.5 + Pioglitazone 30**	**Alogliptin 25 + Pioglitazone 30**	**Placebo + Pioglitazone 45**	**Alogliptin 12.5 + Pioglitazone 45**	**Alogliptin 25 + Pioglitazone 45**
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	120	115	119	122	125	122	120	123	120	123	119	124
Least Squares Mean (Standard Error) **Units: mg/dL**	6.5 (2.26)	1.9 (2.30)	3.7 (2.26)	8.9 (2.24)	3.3 (2.21)	3.8 (2.24)	6.1 (2.26)	1.9 (2.23)	0.9 (2.25)	5.7 (2.23)	4.9 (2.26)	-0.3 (2.22)

75. Secondary Outcome

Title: Change From Baseline to Week 16 in Low-Density Lipoprotein Cholesterol

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline LDL cholesterol as continuous covariates.

Time Frame: Baseline and Week 16

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Placebo**	**Alogliptin 12.5 + Placebo**	**Alogliptin 25 + Placebo**	**Placebo + Pioglitazone 15**	**Alogliptin 12.5 + Pioglitazone 15**	**Alogliptin 25 + Pioglitazone 15**	**Placebo + Pioglitazone 30**	**Alogliptin 12.5 + Pioglitazone 30**	**Alogliptin 25 + Pioglitazone 30**	**Placebo + Pioglitazone 45**	**Alogliptin 12.5 + Pioglitazone 45**	**Alogliptin 25 + Pioglitazone 45**
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	120	116	119	122	125	122	120	123	120	123	120	124
Least Squares Mean (Standard Error)	4.2 (2.25)	1.3 (2.29)	0.9 (2.26)	7.1 (2.23)	2.9 (2.21)	4.6 (2.23)	7.1 (2.25)	2.1 (2.23)	0.8 (2.25)	4.1 (2.22)	4.9 (2.25)	1.8 (2.21)

Units: mg/dL

76. Secondary Outcome

Title: Change From Baseline to Week 20 in Low-Density Lipoprotein Cholesterol

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline LDL cholesterol as continuous covariates.

Time Frame: Baseline and Week 20

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	120	116	119	122	125	122	120	123	120	123	120	124
Least Squares Mean (Standard Error) Units: mg/dL	6.9 (2.39)	2.9 (2.43)	1.9 (2.40)	7.7 (2.37)	4.3 (2.34)	3.0 (2.37)	6.6 (2.39)	2.3 (2.36)	4.1 (2.39)	6.3 (2.36)	6.1 (2.39)	1.9 (2.35)

77. Secondary Outcome

Title: Change From Baseline to Week 26 in Low-Density Lipoprotein Cholesterol

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline LDL cholesterol as continuous covariates.

Time Frame: Baseline and Week 26

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	120	116	119	122	125	122	120	123	120	123	120	124
Least Squares Mean (Standard Error) Units: mg/dL	3.6 (2.43)	2.8 (2.47)	3.6 (2.44)	7.9 (2.41)	3.7 (2.38)	6.1 (2.41)	6.2 (2.43)	2.9 (2.40)	3.0 (2.43)	8.1 (2.40)	9.1 (2.43)	7.7 (2.39)

78. Secondary Outcome

Title: Change From Baseline in High-Density Lipoprotein Cholesterol Over Time (Grouped Analysis)

Description: Change from Baseline in high-density lipoprotein cholesterol (HDL-C) was assessed at Weeks 4, 8, 12, 16, 20 and 26. This analysis compared the groupings of participants who received the combination of pioglitazone with each dose of alogliptin with the grouping of participants who received pioglitazone alone. Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline HDL cholesterol as continuous covariates.

Time Frame: Baseline and Weeks 4, 8, 12, 16, 20 and 26.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Pioglitazone Alone	Alogliptin 12.5 + Pioglitazone	Alogliptin 25 + Pioglitazone
Arm/Group Description:	Alogliptin placebo plus all active pioglitazone groups (15, 30, and 45 mg).	Alogliptin 12.5 mg plus all active pioglitazone (15, 30, and 45 mg).	Alogliptin 25 mg plus all active pioglitazone (15, 30, and 45 mg).
Number of Participants Analyzed	387	390	390
Least Squares Mean (Standard Error) Units: mg/dL			
Week 4 (n=345, 353, 348)	3.0 (0.33)	2.7 (0.33)	3.4 (0.33)
Week 8 (n=374, 380, 376)	4.0 (0.35)	4.1 (0.34)	4.6 (0.35)
Week 12 (n=374, 380, 376)	5.4 (0.37)	5.3 (0.37)	5.1 (0.37)
Week 16 (n=374, 380, 376)	5.2 (0.39)	5.2 (0.38)	5.0 (0.38)
Week 20 (n=374, 380, 376)	5.2 (0.40)	5.7 (0.40)	5.2 (0.40)
Week 26 (n=374, 380, 376)	5.1 (0.41)	5.5 (0.41)	5.0 (0.41)

79. Secondary Outcome

Title: Change From Baseline to Week 4 in High-Density Lipoprotein Cholesterol

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline HDL cholesterol as continuous covariates.

Time Frame: Baseline and Week 4

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	119	112	111	112	116	118	117	121	118	116	116	112
Least Squares Mean (Standard Error)	-0.4 (0.57)	-0.6 (0.59)	-0.5 (0.59)	2.5 (0.59)	1.6 (0.58)	1.6 (0.57)	3.2 (0.57)	2.3 (0.56)	3.5 (0.57)	3.3 (0.58)	4.2 (0.58)	5.1 (0.59)

Units: mg/dL

80. Secondary Outcome

Title: Change From Baseline to Week 8 in High-Density Lipoprotein Cholesterol

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline HDL cholesterol as continuous covariates.

Time Frame: Baseline and Week 8

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	125	121	123	125	128	127	123	127	124	126	125	125
Least Squares Mean (Standard Error) Units: mg/dL	-0.5 (0.60)	-0.1 (0.61)	0.6 (0.61)	2.8 (0.60)	2.3 (0.59)	2.9 (0.60)	4.8 (0.61)	4.2 (0.60)	4.6 (0.60)	4.5 (0.60)	5.7 (0.60)	6.3 (0.60)

81. Secondary Outcome

Title: Change From Baseline to Week 12 in High-Density Lipoprotein Cholesterol

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline HDL cholesterol as continuous covariates.

Time Frame: Baseline and Week 12

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	125	122	123	125	128	127	123	127	124	126	125	125
Least Squares Mean (Standard Error) Units: mg/dL	-0.2 (0.64)	0.0 (0.65)	0.3 (0.64)	3.8 (0.64)	3.7 (0.63)	3.7 (0.63)	6.3 (0.64)	5.8 (0.63)	5.3 (0.64)	6.1 (0.63)	6.3 (0.64)	6.4 (0.64)

82. Secondary Outcome

Title: Change From Baseline to Week 16 in High-Density Lipoprotein Cholesterol

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline HDL cholesterol as continuous covariates.

Time Frame: Baseline and Week 16

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	125	122	123	125	128	127	123	127	124	126	125	125
Least Squares Mean (Standard Error) Units: mg/dL	-0.3 (0.67)	0.4 (0.68)	0.7 (0.67)	3.9 (0.67)	4.2 (0.66)	4.0 (0.66)	5.7 (0.67)	5.5 (0.66)	4.3 (0.67)	5.9 (0.66)	6.1 (0.67)	6.7 (0.67)

83. Secondary Outcome

Title: Change From Baseline to Week 20 in High-Density Lipoprotein Cholesterol

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline HDL cholesterol as continuous covariates.

Time Frame: Baseline and Week 20

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	125	122	123	125	128	127	123	127	124	126	125	125
Least Squares Mean (Standard Error) Units: mg/dL	0.6 (0.70)	0.9 (0.71)	0.5 (0.70)	3.8 (0.70)	4.3 (0.69)	3.9 (0.69)	5.9 (0.70)	5.7 (0.69)	5.3 (0.70)	5.9 (0.70)	7.1 (0.70)	6.5 (0.70)

84. Secondary Outcome

Title: Change From Baseline to Week 26 in High-Density Lipoprotein Cholesterol

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline HDL cholesterol as continuous covariates.

Time Frame: Baseline and Week 26

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	125	122	123	125	128	127	123	127	124	126	125	125
Least Squares Mean (Standard Error) Units: mg/dL	0.5 (0.71)	0.6 (0.72)	1.3 (0.71)	3.8 (0.71)	4.2 (0.70)	4.1 (0.70)	5.5 (0.71)	6.0 (0.70)	5.0 (0.71)	6.1 (0.70)	6.2 (0.71)	6.0 (0.71)

85. Secondary Outcome

Title: Change From Baseline in Triglycerides Over Time (Grouped Analysis)

Description: Change from Baseline in triglycerides was assessed at Weeks 4, 8, 12, 16, 20 and 26. This analysis compared the groupings of participants who received the combination of pioglitazone with each dose of alogliptin with the grouping of participants who received pioglitazone alone. Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline triglycerides as continuous covariates.

Time Frame: Baseline and Weeks 4, 8, 12, 16, 20 and 26.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Pioglitazone Alone	Alogliptin 12.5 + Pioglitazone	Alogliptin 25 + Pioglitazone
Arm/Group Description:	Alogliptin placebo plus all active pioglitazone groups (15, 30, and 45 mg).	Alogliptin 12.5 mg plus all active pioglitazone (15, 30, and 45 mg).	Alogliptin 25 mg plus all active pioglitazone (15, 30, and 45 mg).
Number of Participants Analyzed	387	390	390
Least Squares Mean (Standard Error) Units: mg/dL			
Week 4 (n=345, 354, 348)	-31.5 (4.07)	-38.9 (4.02)	-48.0 (4.06)
Week 8 (n=374, 380, 376)	-34.7 (4.37)	-44.4 (4.34)	-47.9 (4.36)
Week 12 (n=374, 380, 376)	-34.5 (4.25)	-47.5 (4.21)	-49.4 (4.24)
Week 16 (n=374, 380, 376)	-29.4 (4.43)	-49.3 (4.39)	-46.3 (4.42)
Week 20 (n=374, 380, 376)	-34.9 (4.30)	-43.6 (4.27)	-42.7 (4.29)
Week 26 (n=374, 380, 376)	-29.6 (4.42)	-41.4 (4.39)	-40.7 (4.41)

86. Secondary Outcome

Title: Change From Baseline to Week 4 in Triglyceride Levels

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline triglycerides as continuous covariates.

Time Frame: Baseline and Week 4

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	119	112	111	112	117	118	117	121	118	116	116	112
Least Squares Mean (Standard Error) Units: mg/dL	-2.4 (6.93)	-2.2 (7.15)	-25.0 (7.18)	-21.5 (7.14)	-35.8 (6.99)	-51.1 (6.96)	-26.7 (6.99)	-42.2 (6.88)	-44.4 (6.96)	-47.1 (7.02)	-39.2 (7.03)	-49.1 (7.15)

87. Secondary Outcome

Title: Change From Baseline to Week 8 in Triglyceride Levels

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline triglycerides as continuous covariates.

Time Frame: Baseline and Week 8

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	125	121	123	125	128	127	123	127	124	126	125	125
Least Squares Mean (Standard Error)	26.3 (7.56)	-16.4 (7.69)	-23.0 (7.62)	-20.5 (7.56)	-30.1 (7.47)	-46.4 (7.50)	-30.3 (7.62)	-43.1 (7.51)	-44.5 (7.60)	-53.1 (7.53)	-60.1 (7.57)	-52.7 (7.56)

Units: mg/dL

88. Secondary Outcome

Title: Change From Baseline to Week 12 in Triglyceride Levels

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline triglycerides as continuous covariates.

Time Frame: Baseline and Week 12

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	125	122	123	125	128	127	123	127	124	126	125	125
Least Squares Mean (Standard Error) Units: mg/dL	18.9 (7.35)	-4.3 (7.44)	-18.1 (7.41)	-24.1 (7.34)	-37.4 (7.26)	-44.0 (7.29)	-37.4 (7.40)	-47.9 (7.29)	-46.8 (7.38)	-42.1 (7.31)	-57.1 (7.35)	-57.4 (7.35)

89. Secondary Outcome

Title: Change From Baseline to Week 16 in Triglyceride Levels

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline triglycerides as continuous covariates.

Time Frame: Baseline and Week 16

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	125	122	123	125	128	127	123	127	124	126	125	125
Least Squares Mean (Standard Error) Units: mg/dL	10.6 (7.66)	-7.5 (7.75)	-26.8 (7.72)	-10.5 (7.66)	-53.0 (7.57)	-33.8 (7.60)	-28.2 (7.72)	-44.2 (7.60)	-45.9 (7.69)	-49.4 (7.63)	-50.7 (7.66)	-59.1 (7.66)

90. Secondary Outcome

Title: Change From Baseline to Week 20 in Triglyceride Levels

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline triglycerides as continuous covariates.

Time Frame: Baseline and Week 20

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	125	122	123	125	128	127	123	127	124	126	125	125
Least Squares Mean (Standard Error) Units: mg/dL	5.7 (7.44)	-7.0 (7.53)	-23.7 (7.50)	-18.0 (7.44)	-41.2 (7.35)	-34.6 (7.38)	-37.5 (7.50)	-43.1 (7.39)	-42.4 (7.47)	-49.3 (7.41)	-46.4 (7.44)	-51.2 (7.44)

91. Secondary Outcome

Title: Change From Baseline to Week 26 in Triglyceride Levels

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline triglycerides as continuous covariates.

Time Frame: Baseline and Week 26

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	125	122	123	125	128	127	123	127	124	126	125	125
Least Squares Mean (Standard Error) Units: mg/dL	3.7 (7.65)	-1.1 (7.74)	-15.2 (7.71)	-29.5 (7.65)	-37.7 (7.56)	-38.5 (7.59)	-27.0 (7.71)	-37.3 (7.59)	-33.5 (7.68)	-32.4 (7.62)	-49.3 (7.65)	-50.1 (7.65)

92. Secondary Outcome

Title: Change From Baseline in Free Fatty Acids Over Time (Grouped Analysis)

Description: Change from Baseline in free fatty acids (FFA) was assessed at Weeks 12 and 26. This analysis compared the groupings of participants who received the combination of pioglitazone with each dose of alogliptin with the grouping of participants who received pioglitazone alone. Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline free fatty acid as continuous covariates.

Time Frame: Baseline and Weeks 12 and 26.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Pioglitazone Alone	Alogliptin 12.5 + Pioglitazone	Alogliptin 25 + Pioglitazone
Arm/Group Description:	Alogliptin placebo plus all active pioglitazone groups (15, 30, and 45 mg).	Alogliptin 12.5 mg plus all active pioglitazone (15, 30, and 45 mg).	Alogliptin 25 mg plus all active pioglitazone (15, 30, and 45 mg).
Number of Participants Analyzed	387	390	390
Least Squares Mean (Standard Error) Units: mmol/L			
Week 12 (n=339, 356, 352)	-0.0707 (0.01483)	-0.1306 (0.01447)	-0.1273 (0.01455)
Week 26 (n=353, 368, 363)	-0.0676 (0.01050)	-0.0945 (0.01029)	-0.1144 (0.01036)

93. Secondary Outcome

Title: Change From Baseline to Week 12 in Free Fatty Acids

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline free fatty acid as continuous covariates.

Time Frame: Baseline and Week 12

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	120	116	116	115	119	118	111	118	116	113	119	118
Least Squares Mean (Standard Error) Units: mmol/L	0.0067 (0.02493)	-0.0149 (0.02535)	-0.0769 (0.02535)	-0.0879 (0.02547)	-0.1305 (0.02502)	-0.1291 (0.02512)	-0.0395 (0.02592)	-0.1167 (0.02515)	-0.1126 (0.02534)	-0.0848 (0.02567)	-0.1447 (0.02503)	-0.1401 (0.02514)

94. Secondary Outcome

Title: Change From Baseline to Week 26 in Free Fatty Acids

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline free fatty acid as continuous covariates.

Time Frame: Baseline and Week 26

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	122	120	122	117	124	121	118	122	120	118	122	122
Least Squares Mean (Standard Error) Units: mmol/L	-0.0387 (0.01788)	-0.0427 (0.01802)	-0.0386 (0.01787)	-0.0561 (0.01825)	-0.0752 (0.01772)	-0.0972 (0.01793)	-0.0737 (0.01817)	-0.0956 (0.01788)	-0.1232 (0.01801)	-0.0730 (0.01816)	-0.1125 (0.01787)	-0.1228 (0.01787)

95. Secondary Outcome

Title: Change From Baseline in Plasminogen Activator Inhibitor-1 Over Time (Grouped Analysis)

Description: Change from Baseline in plasminogen activator inhibitor-1 (PAI-1) was assessed at Weeks 12 and 26. This analysis compared the groupings of participants who received the combination of pioglitazone with each dose of alogliptin with the grouping of participants who received pioglitazone alone. Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline PAI-1 as continuous covariates.

Time Frame: Baseline and Weeks 12 and 26.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Pioglitazone Alone	Alogliptin 12.5 + Pioglitazone	Alogliptin 25 + Pioglitazone
Arm/Group Description:	Alogliptin placebo plus all active pioglitazone groups (15, 30, and 45 mg).	Alogliptin 12.5 mg plus all active pioglitazone (15, 30, and 45 mg).	Alogliptin 25 mg plus all active pioglitazone (15, 30, and 45 mg).
Number of Participants Analyzed	387	390	390
Least Squares Mean (Standard Error) Units: ng/mL			
Week 12 (n=311, 333, 328)	-4.14 (1.970)	-8.76 (1.900)	-8.57 (1.914)
Week 26 (n=341, 354, 348)	-4.56 (2.049)	-2.69 (2.010)	-9.25 (2.027)

96. Secondary Outcome

Title: Change From Baseline to Week 12 in Plasminogen Activator Inhibitor-1

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline PAI-1 as continuous covariates.
Time Frame: Baseline and Week 12
Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	106	107	107	108	113	109	107	108	109	96	112	110
Least Squares Mean (Standard Error) Units: ng/mL	-4.55 (3.367)	3.54 (3.350)	-1.80 (3.353)	-5.32 (3.340)	-6.28 (3.260)	-10.94 (3.320)	-8.53 (3.353)	-10.47 (3.336)	-1.71 (3.321)	1.85 (3.539)	-9.13 (3.277)	-12.63 (3.306)

97. Secondary Outcome

Title: Change From Baseline to Week 26 in Plasminogen Activator Inhibitor-1
Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline PAI-1 as continuous covariates.
Time Frame: Baseline and Week 26
Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	115	114	118	115	119	116	117	116	115	109	119	117
Least Squares Mean (Standard Error) Units: ng/mL	-3.00 (3.526)	0.57 (3.540)	-3.29 (3.481)	-5.43 (3.529)	-4.75 (3.465)	-9.62 (3.510)	-5.24 (3.495)	1.89 (3.511)	-6.66 (3.525)	-3.02 (3.622)	-5.22 (3.466)	-11.48 (3.496)

98. Secondary Outcome

Title: Change From Baseline in High-sensitivity C-Reactive Protein Over Time (Grouped Analysis)
Description: Change from Baseline in high-sensitivity C-Reactive Protein (hsCRP) was assessed at Weeks 12 and 26.
This analysis compared the groupings of participants who received the combination of pioglitazone with each dose of alogliptin with the grouping of participants who received pioglitazone alone. Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline hsCRP as continuous covariates.
Time Frame: Baseline and Weeks 12 and 26.
Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Pioglitazone Alone	Alogliptin 12.5 + Pioglitazone	Alogliptin 25 + Pioglitazone
Arm/Group Description:	Alogliptin placebo plus all active pioglitazone groups (15, 30, and 45 mg).	Alogliptin 12.5 mg plus all active pioglitazone (15, 30, and 45 mg).	Alogliptin 25 mg plus all active pioglitazone (15, 30, and 45 mg).
Number of Participants Analyzed	387	390	390
Least Squares Mean (Standard Error) Units: mg/L			
Week 12 (n=346, 356, 355)	-2.0274 (0.32717)	-2.4653 (0.32225)	-1.9208 (0.32253)
Week 26 (n=359, 369, 363)	-0.8889 (0.46384)	-1.7716 (0.45715)	-0.9977 (0.46059)

99. Secondary Outcome

Title: Change From Baseline to Week 12 in High-sensitivity C-Reactive Protein
Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline hsCRP as continuous covariates.
Time Frame: Baseline and Week 12
Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	120	114	118	114	119	118	118	119	116	114	118	121
Least Squares Mean (Standard Error) Units: mg/L	-1.1053 (0.55528)	-1.0730 (0.56942)	0.3516 (0.55954)	-0.9166 (0.56902)	-2.2362 (0.55706)	-2.4217 (0.55929)	-2.7023 (0.55971)	-2.2143 (0.55757)	-1.0006 (0.56412)	-2.4212 (0.57137)	-2.9032 (0.55979)	-2.2978 (0.55243)

100. Secondary Outcome

Title: Change From Baseline to Week 26 in High-sensitivity C-Reactive Protein
Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline hsCRP as continuous covariates.
Time Frame: Baseline and Week 26
Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	121	120	122	119	124	122	121	123	119	119	122	122
Least Squares Mean (Standard Error) Units: mg/L	-0.0550 (0.79868)	-0.6606 (0.80145)	0.2618 (0.79488)	0.2375 (0.80439)	-1.2490 (0.78817)	-0.9438 (0.79442)	-1.0480 (0.79805)	-1.1725 (0.79206)	0.1697 (0.80434)	-1.8562 (0.80771)	-2.8933 (0.79515)	-2.2191 (0.79450)

101. Secondary Outcome

Title: Change From Baseline in Adiponectin Over Time (Grouped Analysis)
Description: Change from Baseline in adiponectin was assessed at Weeks 12 and 26. This analysis compared the groupings of participants who received the combination of pioglitazone with each dose of alogliptin with the grouping of participants who received pioglitazone alone. Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline adiponectin as continuous covariates.
Time Frame: Baseline and Weeks 12 and 26.
Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Pioglitazone Alone	Alogliptin 12.5 + Pioglitazone	Alogliptin 25 + Pioglitazone
Arm/Group Description:	Alogliptin placebo plus all active pioglitazone groups (15, 30, and 45 mg).	Alogliptin 12.5 mg plus all active pioglitazone (15, 30, and 45 mg).	Alogliptin 25 mg plus all active pioglitazone (15, 30, and 45 mg).
Number of Participants Analyzed	387	390	390
Least Squares Mean (Standard Error) Units: µg/mL			
Week 12 (n=339, 357, 348)	6.03 (0.353)	6.51 (0.344)	6.51 (0.348)
Week 26 (n=356, 369, 361)	5.98 (0.396)	6.43 (0.388)	6.46 (0.393)

102. Secondary Outcome

Title: Change From Baseline to Week 12 in Adiponectin
Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline adiponectin as continuous covariates.
Time Frame: Baseline and Week 12
Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	120	114	115	116	121	117	111	118	114	112	118	117
Least Squares Mean (Standard Error) Units: µg/mL	0.02 (0.593)	0.44 (0.609)	0.22 (0.606)	3.54 (0.604)	3.78 (0.591)	2.91 (0.601)	6.07 (0.617)	6.31 (0.599)	7.13 (0.609)	8.47 (0.614)	9.42 (0.598)	9.46 (0.601)

103. Secondary Outcome

Title: Change From Baseline to Week 26 in Adiponectin
Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline adiponectin as continuous covariates.
Time Frame: Baseline and Week 26
Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	122	120	121	119	126	121	118	122	119	119	121	121
Least Squares Mean (Standard Error) Units: µg/mL	0.43 (0.676)	0.48 (0.681)	0.26 (0.678)	3.30 (0.685)	4.80 (0.664)	2.93 (0.678)	5.90 (0.687)	6.30 (0.676)	6.87 (0.684)	8.75 (0.684)	8.18 (0.678)	9.59 (0.678)

104. Secondary Outcome

Title: Change From Baseline in Body Weight Over Time (Grouped Analysis)
Description: Change from Baseline in body weight was assessed at Weeks 8, 12, 20 and 26. This analysis compared the groupings of participants who received the combination of pioglitazone with each dose of alogliptin with the grouping of participants who received pioglitazone alone. Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline weight as continuous covariates.
Time Frame: Baseline and Weeks 8, 12, 20 and 26.
Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Pioglitazone Alone	Alogliptin 12.5 + Pioglitazone	Alogliptin 25 + Pioglitazone
Arm/Group Description:	Alogliptin placebo plus all active pioglitazone groups (15, 30, and 45 mg).	Alogliptin 12.5 mg plus all active pioglitazone (15, 30, and 45 mg).	Alogliptin 25 mg plus all active pioglitazone (15, 30, and 45 mg).
Number of Participants Analyzed	387	390	390
Least Squares Mean (Standard Error) Units: kg			
Week 8 (n=361, 372, 367)	0.45 (0.103)	0.34 (0.101)	0.63 (0.102)
Week 12 (n=368, 374, 373)	0.56 (0.125)	0.57 (0.124)	0.82 (0.124)
Week 20 (n=368, 374, 373)	1.21 (0.152)	1.45 (0.151)	1.46 (0.151)
Week 26 (n=368, 374, 373)	1.49 (0.168)	1.81 (0.167)	1.87 (0.167)

105. Secondary Outcome

Title: Change From Baseline to Week 8 in Body Weight
Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline weight as continuous covariates.
Time Frame: Baseline and Week 8
Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	123	119	120	121	126	122	121	125	121	119	121	124
Least Squares Mean (Standard Error) Units: kg	-0.13 (0.176)	-0.05 (0.179)	-0.45 (0.178)	0.32 (0.177)	0.09 (0.174)	0.22 (0.176)	0.57 (0.177)	0.49 (0.174)	0.74 (0.177)	0.46 (0.179)	0.43 (0.177)	0.93 (0.175)

106. Secondary Outcome

Title: Change From Baseline to Week 12 in Body Weight

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline weight as continuous covariates.

Time Frame: Baseline and Week 12

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	123	122	123	122	127	124	122	125	123	124	122	126
Least Squares Mean (Standard Error) **Units: kg**	-0.46 (0.216)	-0.14 (0.217)	-0.56 (0.216)	0.39 (0.217)	0.22 (0.213)	0.39 (0.215)	0.75 (0.217)	0.60 (0.215)	0.98 (0.216)	0.55 (0.216)	0.88 (0.217)	1.08 (0.214)

107. Secondary Outcome

Title: Change From Baseline to Week 20 in Body Weight

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline weight as continuous covariates.

Time Frame: Baseline and Week 20

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	123	122	123	122	127	124	122	125	123	124	122	126
Least Squares Mean (Standard Error) **Units: kg**	-0.55 (0.263)	-0.08 (0.264)	-0.48 (0.263)	0.76 (0.264)	0.96 (0.259)	0.85 (0.262)	1.51 (0.264)	1.45 (0.261)	1.76 (0.263)	1.35 (0.262)	1.93 (0.264)	1.76 (0.260)

108. Secondary Outcome

Title: Change From Baseline to Week 26 in Body Weight

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline weight as continuous covariates.

Time Frame: Baseline and Week 26

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	123	122	123	122	127	124	122	125	123	124	122	126
Least Squares Mean (Standard Error) **Units: kg**	-0.66 (0.291)	-0.02 (0.292)	-0.67 (0.291)	0.94 (0.292)	1.25 (0.287)	1.27 (0.290)	1.88 (0.292)	1.89 (0.289)	2.10 (0.291)	1.65 (0.290)	2.30 (0.292)	2.25 (0.288)

109. Secondary Outcome

Title: Change From Baseline in Calculated Homeostatic Model Assessment Insulin Resistance (HOMA IR) (Grouped Analysis)

Description: HOMA IR measures insulin resistance based on fasting glucose and insulin measurements:
HOMA IR = fasting plasma insulin (µIU/mL) * fasting plasma glucose (mmol/L) / 22.5.
A higher number indicates a greater insulin resistance. This analysis compared the groupings of participants who received the combination of pioglitazone with each dose of alogliptin with the grouping of participants who received pioglitazone alone.
Least Squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and HOMA-IR as continuous covariates.

Time Frame: Baseline and Weeks 12 and 26.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Pioglitazone Alone	Alogliptin 12.5 + Pioglitazone	Alogliptin 25 + Pioglitazone
Arm/Group Description:	Alogliptin placebo plus all active pioglitazone groups (15, 30, and 45 mg).	Alogliptin 12.5 mg plus all active pioglitazone (15, 30, and 45 mg).	Alogliptin 25 mg plus all active pioglitazone (15, 30, and 45 mg).
Number of Participants Analyzed	387	390	390
Least Squares Mean (Standard Error) Units: insulin resistance			
Week 12 (n=347, 344, 351)	-1.832 (0.3122)	-1.966 (0.3136)	-2.572 (0.3104)
Week 26 (n=348, 346, 352)	-1.571 (0.3501)	-2.209 (0.3512)	-1.711 (0.3481)

110. Secondary Outcome

Title: Change From Baseline to Week 12 in Calculated HOMA Insulin Resistance

Description: The Homeostasis Model Assessment of insulin resistance (HOMA IR) measures insulin resistance based on fasting glucose and insulin measurements:
HOMA IR = fasting plasma insulin (µIU/mL) * fasting plasma glucose (mmol/L) / 22.5.
A higher number indicates a greater degree of insulin resistance. Least Squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and HOMA-IR as continuous covariates.

Time Frame: Baseline and Week 12

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	119	117	122	119	117	118	114	113	116	114	114	117
Least Squares Mean (Standard Error) **Units: insulin resistance**	0.337 (0.5333)	0.063 (0.5375)	0.041 (0.5270)	-1.012 (0.5330)	-1.819 (0.5376)	-2.305 (0.5352)	-2.278 (0.5446)	-1.457 (0.5473)	-2.665 (0.5400)	-2.202 (0.5447)	-2.615 (0.5446)	-2.742 (0.5377)

111. Secondary Outcome

Title: Change From Baseline to Week 26 in Calculated HOMA Insulin Resistance

Description: The Homeostasis Model Assessment of insulin resistance (HOMA IR) measures insulin resistance based on fasting glucose and insulin measurements:
HOMA IR = fasting plasma insulin (µIU/mL) * fasting plasma glucose (mmol/L) / 22.5.
A higher number indicates a greater degree of insulin resistance. Least Squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and HOMA-IR as continuous covariates.

Time Frame: Baseline and Week 26

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	119	117	122	119	119	119	115	113	116	114	114	117
Least Squares Mean (Standard Error) **Units: insulin resistance**	0.464 (0.5988)	0.311 (0.6036)	-0.179 (0.5918)	-0.864 (0.5985)	-2.300 (0.5986)	-0.223 (0.5985)	-2.061 (0.6089)	-1.871 (0.6147)	-2.056 (0.6064)	-1.789 (0.6117)	-2.456 (0.6116)	-2.854 (0.6038)

112. Secondary Outcome

Title: Change From Baseline in Homeostatic Model Assessment Beta Cell Function (Grouped Analysis)

Description: The homeostatic model assessment estimates steady state beta cell function as a percentage of a normal reference population (%B).
HOMA %B = 20 * insulin (µIU/mL) / fasting plasma glucose (mmol/L) - 3.5.
This analysis compared the groupings of participants who received the combination of pioglitazone with each dose of alogliptin with the grouping of participants who received pioglitazone alone. Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline HOMA beta cell function as continuous covariates.

Time Frame: Baseline and Weeks 12 and 26

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Pioglitazone Alone	Alogliptin 12.5 + Pioglitazone	Alogliptin 25 + Pioglitazone
Arm/Group Description:	Alogliptin placebo plus all active pioglitazone groups (15, 30, and 45 mg).	Alogliptin 12.5 mg plus all active pioglitazone (15, 30, and 45 mg).	Alogliptin 25 mg plus all active pioglitazone (15, 30, and 45 mg).
Number of Participants Analyzed	387	390	390
Least Squares Mean (Standard Error) Units: percentage beta cell function			
Week 12 (n=347, 344, 350)	2.591 (3.7892)	23.799 (3.8017)	19.477 (3.7685)
Week 26 (n=348, 346, 351)	5.060 (3.0460)	18.173 (3.0522)	22.182 (3.0297)

113. Secondary Outcome

Title: Change From Baseline to Week 12 in Calculated HOMA Beta-cell Function

Description: The Homeostasis Model Assessment (HOMA) estimates steady state beta cell function (%B) as a percentage of a normal reference population.
HOMA %B = 20 * insulin (µIU/mL) / fasting plasma glucose (mmol/L) - 3.5. Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline HOMA beta cell function as continuous covariates.

Time Frame: Baseline and Week 12

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	118	117	122	119	117	118	114	113	116	114	114	116
Least Squares Mean (Standard Error) **Units: percentage beta cell function**	-3.027 (6.4915)	16.304 (6.5165)	22.996 (6.3854)	2.565 (6.4614)	30.346 (6.5157)	19.887 (6.4916)	1.118 (6.6030)	21.045 (6.6358)	19.935 (6.5444)	4.023 (6.6240)	19.938 (6.6025)	18.541 (6.5456)

114. Secondary Outcome

Title: Change From Baseline to Week 26 in Calculated HOMA Beta-cell Function

Description: The Homeostasis Model Assessment (HOMA) estimates steady state beta cell function (%B) as a percentage of a normal reference population.
HOMA %B = 20 * insulin (µIU/mL) / fasting plasma glucose (mmol/L) - 3.5. Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline HOMA beta cell function as continuous covariates.

Time Frame: Baseline and Week 26

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	118	117	122	119	119	119	115	113	116	114	114	116

Least Squares Mean (Standard Error) **Units: percentage beta cell function**	-0.924 (5.2260)	11.812 (5.2462)	17.814 (5.1407)	2.770 (5.2018)	10.977 (5.2010)	19.320 (5.2044)	8.983 (5.2921)	22.474 (5.3423)	23.475 (5.2687)	3.427 (5.3327)	21.068 (5.3154)	23.752 (5.2696)

115. Secondary Outcome

Title: Change From Baseline in Apolipoprotein A1 Over Time (Grouped Analysis)

Description: Change from Baseline in Apolipoprotein A1 was assessed at Weeks 12 and 26. This analysis compared the groupings of participants who received the combination of pioglitazone with each dose of alogliptin with the grouping of participants who received pioglitazone alone. Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline apolipoprotein A1 as continuous covariates.

Time Frame: Baseline and Weeks 12 and 26.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Pioglitazone Alone**	**Alogliptin 12.5 + Pioglitazone**	**Alogliptin 25 + Pioglitazone**
Arm/Group Description:	Alogliptin placebo plus all active pioglitazone groups (15, 30, and 45 mg).	Alogliptin 12.5 mg plus all active pioglitazone (15, 30, and 45 mg).	Alogliptin 25 mg plus all active pioglitazone (15, 30, and 45 mg).
Number of Participants Analyzed	387	390	390
Least Squares Mean (Standard Error) Units: mg/dL			
Week 12 (n=339, 354, 346)	1.4 (1.00)	0.2 (0.98)	0.3 (0.99)
Week 26 (n=354, 367, 356)	-1.6 (1.09)	-1.5 (1.08)	-2.8 (1.09)

116. Secondary Outcome

Title: Change From Baseline to Week 12 in Apolipoprotein A1

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline apolipoprotein A1 as continuous covariates.

Time Frame: Baseline and Week 12

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Placebo**	**Alogliptin 12.5 + Placebo**	**Alogliptin 25 + Placebo**	**Placebo + Pioglitazone 15**	**Alogliptin 12.5 + Pioglitazone 15**	**Alogliptin 25 + Pioglitazone 15**	**Placebo + Pioglitazone 30**	**Alogliptin 12.5 + Pioglitazone 30**	**Alogliptin 25 + Pioglitazone 30**	**Placebo + Pioglitazone 45**	**Alogliptin 12.5 + Pioglitazone 45**	**Alogliptin 25 + Pioglitazone 45**
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	117	114	112	113	119	114	114	119	118	112	116	114
Least Squares Mean (Standard Error) **Units: mg/dL**	-1.9 (1.70)	-4.4 (1.73)	-3.0 (1.74)	0.8 (1.73)	-1.3 (1.69)	1.7 (1.72)	3.5 (1.72)	0.7 (1.69)	0.4 (1.69)	-0.1 (1.74)	1.1 (1.71)	-1.2 (1.72)

117. Secondary Outcome

Title: Change From Baseline to Week 26 in Apolipoprotein A1

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline apolipoprotein A1 as continuous covariates.

Time Frame: Baseline and Week 26

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Placebo**	**Alogliptin 12.5 + Placebo**	**Alogliptin 25 + Placebo**	**Placebo + Pioglitazone 15**	**Alogliptin 12.5 + Pioglitazone 15**	**Alogliptin 25 + Pioglitazone 15**	**Placebo + Pioglitazone 30**	**Alogliptin 12.5 + Pioglitazone 30**	**Alogliptin 25 + Pioglitazone 30**	**Placebo + Pioglitazone 45**	**Alogliptin 12.5 + Pioglitazone 45**	**Alogliptin 25 + Pioglitazone 45**
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	120	118	119	117	125	116	119	122	121	118	120	119
Least Squares Mean (Standard Error) **Units: mg/dL**	-4.9 (1.88)	-3.0 (1.90)	-4.2 (1.89)	-3.3 (1.90)	-3.5 (1.84)	-2.9 (1.91)	-0.2 (1.89)	-0.1 (1.86)	-3.2 (1.87)	-1.4 (1.89)	-1.0 (1.88)	-2.2 (1.89)

118. Secondary Outcome

Title: Change From Baseline in Apolipoprotein A2 Over Time (Grouped Analysis)

Description: Change from Baseline in Apolipoprotein A2 was assessed at Weeks 12 and 26. This analysis compared the groupings of participants who received the combination of pioglitazone with each dose of alogliptin with the grouping of participants who received pioglitazone alone. Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline apolipoprotein A2 as continuous covariates.

Time Frame: Baseline and Weeks 12 and 26

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Pioglitazone Alone**	**Alogliptin 12.5 + Pioglitazone**	**Alogliptin 25 + Pioglitazone**
Arm/Group Description:	Alogliptin placebo plus all active pioglitazone groups (15, 30, and 45 mg).	Alogliptin 12.5 mg plus all active pioglitazone (15, 30, and 45 mg).	Alogliptin 25 mg plus all active pioglitazone (15, 30, and 45 mg).
Number of Participants Analyzed	387	390	390
Least Squares Mean (Standard Error) Units: mg/dL			
Week 12 (n=339, 354, 345)	3.1 (0.26)	2.5 (0.26)	2.3 (0.26)
Week 26 (n=354, 367, 355)	2.4 (0.28)	2.1 (0.27)	1.8 (0.28)

119. Secondary Outcome

Title: Change From Baseline to Week 12 in Apolipoprotein A2

Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline apolipoprotein A2 as continuous covariates.
Time Frame: Baseline and Week 12
Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	117	114	112	113	119	114	114	119	117	112	116	114
Least Squares Mean (Standard Error) **Units: mg/dL**	0.4 (0.44)	0.1 (0.45)	0.4 (0.45)	2.4 (0.45)	1.4 (0.44)	1.9 (0.45)	3.7 (0.45)	2.5 (0.44)	1.8 (0.44)	3.0 (0.45)	3.7 (0.45)	3.2 (0.45)

120. Secondary Outcome

Title: Change From Baseline to Week 26 in Apolipoprotein A2
Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline apolipoprotein A2 as continuous covariates.
Time Frame: Baseline and Week 26
Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	120	118	119	117	125	116	119	122	120	118	120	119
Least Squares Mean (Standard Error) **Units: mg/dL**	0.1 (0.47)	0.2 (0.48)	0.4 (0.48)	1.9 (0.48)	1.2 (0.47)	1.0 (0.48)	2.7 (0.48)	2.1 (0.47)	1.6 (0.47)	2.8 (0.48)	3.1 (0.47)	2.7 (0.48)

121. Secondary Outcome

Title: Change From Baseline in Apolipoprotein B Over Time (Grouped Analysis)
Description: Change from Baseline in Apolipoprotein B was assessed at Weeks 12 and 26. This analysis compared the groupings of participants who received the combination of pioglitazone with each dose of alogliptin with the grouping of participants who received pioglitazone alone. Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline apolipoprotein B as continuous covariates.
Time Frame: Baseline and Weeks 12 and 26
Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Pioglitazone Alone	Alogliptin 12.5 + Pioglitazone	Alogliptin 25 + Pioglitazone
Arm/Group Description:	Alogliptin placebo plus all active pioglitazone groups (15, 30, and 45 mg).	Alogliptin 12.5 mg plus all active pioglitazone (15, 30, and 45 mg).	Alogliptin 25 mg plus all active pioglitazone (15, 30, and 45 mg).
Number of Participants Analyzed	387	390	390
Least Squares Mean (Standard Error) Units: mg/dL			
Week 12 (n=338, 354, 346)	-3.0 (1.09)	-7.9 (1.06)	-10.0 (1.07)
Week 26 (n=354, 367, 356)	-2.8 (1.16)	-6.4 (1.14)	-6.4 (1.15)

122. Secondary Outcome

Title: Change From Baseline to Week 12 in Apolipoprotein B
Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline apolipoprotein B as continuous covariates.
Time Frame: Baseline and Week 12
Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	117	114	112	113	119	114	114	119	118	111	116	114
Least Squares Mean (Standard Error) **Units: mg/dL**	5.0 (1.85)	-2.3 (1.87)	-3.6 (1.89)	-0.3 (1.88)	-7.2 (1.83)	-6.1 (1.87)	-2.1 (1.88)	-8.4 (1.83)	-12.2 (1.84)	-6.6 (1.90)	-8.0 (1.86)	-11.7 (1.87)

123. Secondary Outcome

Title: Change From Baseline to Week 26 in Apolipoprotein B
Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline apolipoprotein B as continuous covariates.
Time Frame: Baseline and Week 26
Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	120	118	119	117	125	116	119	122	121	118	120	119
Least Squares Mean (Standard Error) **Units: mg/dL**	0.6 (1.99)	-0.6 (2.00)	-3.7 (2.00)	-1.5 (2.01)	-6.0 (1.95)	-4.8 (2.02)	-3.2 (2.00)	-7.2 (1.97)	-8.8 (1.98)	-3.6 (2.00)	-6.1 (1.99)	-5.5 (2.00)

124. Secondary Outcome

Title: Change From Baseline in Apolipoprotein C-III Over Time (Grouped Analysis)
Description: Change from Baseline in apolipoprotein C-III was assessed at Weeks 12 and 26. This analysis compared the groupings of participants who received the combination of pioglitazone with each dose of alogliptin with the grouping of participants who received pioglitazone alone. Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline apolipoprotein C-III as continuous covariates.
Time Frame: Baseline and Weeks 12 and 26
Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Pioglitazone Alone	Alogliptin 12.5 + Pioglitazone	Alogliptin 25 + Pioglitazone
Arm/Group Description:	Alogliptin placebo plus all active pioglitazone groups (15, 30, and 45 mg).	Alogliptin 12.5 mg plus all active pioglitazone (15, 30, and 45 mg).	Alogliptin 25 mg plus all active pioglitazone (15, 30, and 45 mg).
Number of Participants Analyzed	387	390	390
Least Squares Mean (Standard Error) Units: mg/dL			
Week 12 (n=337, 352, 345)	-0.6 (0.17)	-1.2 (0.16)	-1.3 (0.17)
Week 26 (n=353, 366, 355)	-0.1 (0.19)	-0.6 (0.19)	-0.6 (0.19)

125. Secondary Outcome

Title: Change From Baseline to Week 12 in Apolipoprotein C-III
Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline apolipoprotein C-III as continuous covariates.
Time Frame: Baseline and Week 12
Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	117	114	112	113	118	114	113	118	118	111	116	113
Least Squares Mean (Standard Error) **Units: mg/dL**	0.7 (0.28)	-0.4 (0.29)	-0.7 (0.29)	-0.3 (0.29)	-1.0 (0.28)	-1.4 (0.29)	-0.3 (0.29)	-1.0 (0.28)	-1.3 (0.28)	-1.1 (0.29)	-1.4 (0.29)	-1.2 (0.29)

126. Secondary Outcome

Title: Change From Baseline to Week 26 in Apolipoprotein C-III
Description: Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline apolipoprotein C-III as continuous covariates.
Time Frame: Baseline and Week 26
Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	120	118	119	117	125	116	119	121	121	117	120	118
Least Squares Mean (Standard Error) **Units: mg/dL**	0.4 (0.33)	0.5 (0.33)	-0.7 (0.33)	-0.4 (0.33)	-0.6 (0.32)	-0.7 (0.33)	0.2 (0.33)	-0.4 (0.32)	-0.6 (0.32)	0.0 (0.33)	-0.7 (0.33)	-0.5 (0.33)

127. Secondary Outcome

Title: Change From Baseline in Nuclear Magnetic Resonance Lipid Fractionation Total Triglycerides Over Time (Grouped Analysis)
Description: Nuclear Magnetic Resonance (NMR) lipid fractionation was used to assess the change from Baseline in total triglyceride levels at Weeks 12 and 26.
This analysis compared the groupings of participants who received the combination of pioglitazone with each dose of alogliptin with the grouping of participants who received pioglitazone alone. Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline NMR total triglycerides as continuous covariates.
Time Frame: Baseline and Weeks 12 and 26.
Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Pioglitazone Alone	Alogliptin 12.5 + Pioglitazone	Alogliptin 25 + Pioglitazone
Arm/Group Description:	Alogliptin placebo plus all active pioglitazone groups (15, 30, and 45 mg).	Alogliptin 12.5 mg plus all active pioglitazone (15, 30, and 45 mg).	Alogliptin 25 mg plus all active pioglitazone (15, 30, and 45 mg).
Number of Participants Analyzed	387	390	390
Least Squares Mean (Standard Error) Units: mg/dL			
Week 12 (n=332, 345, 343)	-19.6 (3.92)	-28.8 (3.85)	-31.5 (3.86)
Week 26 (n=348, 359, 357)	-11.5 (4.30)	-25.4 (4.23)	-22.9 (4.24)

128. Secondary Outcome

Title: Change From Baseline to Week 12 in NMR Lipid Fractionation Total Triglycerides
Description: NMR lipid fractionation was used to assess the change from Baseline in total triglyceride levels at Week 12.
Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline NMR total triglycerides as continuous covariates.
Time Frame: Baseline and Week 12
Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	119	113	114	113	114	117	110	113	110	109	118	116
Least Squares Mean (Standard Error) **Units: mg/dL**	20.6 (6.56)	-4.9 (6.73)	-7.8 (6.70)	-12.9 (6.72)	-21.8 (6.70)	-27.2 (6.61)	-18.3 (6.82)	-29.8 (6.73)	-31.6 (6.82)	-27.9 (6.85)	-35.1 (6.59)	-36.0 (6.64)

129. Secondary Outcome

Title: Change From Baseline to Week 26 in NMR Lipid Fractionation Total Triglycerides

Description: NMR lipid fractionation was used to assess the change from Baseline in total triglyceride levels at Week 26.
Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline NMR total triglycerides as continuous covariates.
Time Frame: Baseline and Week 26
Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	122	117	120	116	120	120	116	118	116	116	121	121
Least Squares Mean (Standard Error) Units: mg/dL	12.4 (7.26)	7.3 (7.42)	-6.8 (7.32)	-18.9 (7.44)	-20.4 (7.32)	-23.1 (7.32)	-6.9 (7.44)	-23.5 (7.38)	-19.7 (7.44)	-8.6 (7.44)	-32.1 (7.29)	-25.8 (7.29)

130. Secondary Outcome

Title: Change From Baseline in Very Low Density Lipoprotein (VLDL) / Chylomicron Particles Over Time (Grouped Analysis)
Description: The change from Baseline in levels of total VLDL/chylomicron particles and large VLDL/chylomicron particles was assessed by NMR lipid fractionation at Weeks 12 and 26.
This analysis compared the groupings of participants who received the combination of pioglitazone with each dose of alogliptin with the grouping of participants who received pioglitazone alone. Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline NMR VLDL/chylomicron particles as continuous covariates.
Time Frame: Baseline and Weeks 12 and 26
Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Pioglitazone Alone	Alogliptin 12.5 + Pioglitazone	Alogliptin 25 + Pioglitazone
Arm/Group Description:	Alogliptin placebo plus all active pioglitazone groups (15, 30, and 45 mg).	Alogliptin 12.5 mg plus all active pioglitazone (15, 30, and 45 mg).	Alogliptin 25 mg plus all active pioglitazone (15, 30, and 45 mg).
Number of Participants Analyzed	387	390	390
Least Squares Mean (Standard Error) Units: nmol/L			
Total Particles - Week 12 (n=332, 345, 343)	-1.85 (1.803)	-6.40 (1.770)	-7.26 (1.775)
Total Particles - Week 26 (n=348, 359, 357)	-1.05 (1.999)	-1.87 (1.970)	-1.31 (1.975)
Large Particles - Week 12 (n=332, 345, 343)	-1.61 (0.289)	-2.20 (0.283)	-2.17 (0.284)
Large Particles - Week 26 (n=348, 359, 357)	-1.05 (0.342)	-2.25 (0.337)	-1.98 (0.337)

131. Secondary Outcome

Title: Change From Baseline to Week 12 in VLDL / Chylomicron Particles
Description: The change from Baseline in levels of total VLDL/chylomicron particles and large VLDL/chylomicron particles was assessed by NMR lipid fractionation.
Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline NMR VLDL/chylomicron particles as continuous covariates.
Time Frame: Baseline and Week 12
Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	119	113	114	113	114	117	110	113	110	109	118	116
Least Squares Mean (Standard Error) Units: nmol/L												
Total Particles	5.82 (3.013)	-1.59 (3.092)	-5.32 (3.077)	2.52 (3.089)	-3.46 (3.077)	-5.57 (3.037)	0.45 (3.135)	-7.82 (3.092)	-6.54 (3.132)	-8.58 (3.147)	-7.99 (3.027)	-9.76 (3.051)
Large Particles	1.12 (0.482)	-0.42 (0.495)	-0.27 (0.493)	-1.20 (0.495)	-1.63 (0.493)	-1.81 (0.486)	-1.69 (0.502)	-2.19 (0.495)	-2.29 (0.501)	-1.97 (0.504)	-2.81 (0.484)	-2.45 (0.489)

132. Secondary Outcome

Title: Change From Baseline to Week 26 in VLDL / Chylomicron Particles
Description: The change from Baseline in levels of total VLDL/chylomicron particles and large VLDL/chylomicron particles was assessed by NMR lipid fractionation.
Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline NMR VLDL/chylomicron particles as continuous covariates.
Time Frame: Baseline and Week 26
Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	122	117	120	116	120	120	116	118	116	116	121	121
Least Squares Mean (Standard Error) Units: nmol/L												
Total Particles	2.80 (3.379)	0.59 (3.450)	-5.79 (3.405)	-2.99 (3.462)	-3.31 (3.405)	-5.15 (3.405)	3.68 (3.464)	-0.59 (3.436)	-0.35 (3.463)	-3.83 (3.463)	-1.70 (3.394)	1.56 (3.392)
Large Particles	1.31 (0.577)	0.94 (0.589)	-0.14 (0.582)	-1.56 (0.592)	-1.71 (0.582)	-1.80 (0.582)	-0.90 (0.592)	-2.24 (0.587)	-1.79 (0.592)	-0.67 (0.592)	-2.80 (0.580)	-2.36 (0.580)

133. Secondary Outcome

Title: Change From Baseline in VLDL / Chylomicron Triglycerides Over Time (Grouped Analysis)
Description: The change from Baseline in levels of VLDL/chylomicron triglycerides was assessed by NMR lipid fractionation at Weeks 12 and 26.
This analysis compared the groupings of participants who received the combination of pioglitazone with each dose of alogliptin with the grouping of participants who received pioglitazone alone. Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline NMR VLDL/chylomicron triglycerides as continuous covariates.
Time Frame: Baseline and Weeks 12 and 26
Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Pioglitazone Alone	Alogliptin 12.5 + Pioglitazone	Alogliptin 25 + Pioglitazone
Arm/Group Description:	Alogliptin placebo plus all active pioglitazone groups (15, 30, and 45 mg).	Alogliptin 12.5 mg plus all active pioglitazone (15, 30, and 45 mg).	Alogliptin 25 mg plus all active pioglitazone (15, 30, and 45 mg).
Number of Participants Analyzed	387	390	390
Least Squares Mean (Standard Error)			

Units: mg/dL			
Week 12 (n=332, 345, 343)	-20.4 (3.90)	-28.5 (3.83)	-30.3 (3.84)
Week 26 (n=348, 359, 357)	-13.0 (4.28)	-25.4 (4.22)	-23.0 (4.23)

134. Secondary Outcome

Title: Change From Baseline to Week 12 in VLDL / Chylomicron Triglycerides

Description: The change from Baseline in VLDL/chylomicron triglyceride levels was assessed by NMR lipid fractionation. Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline NMR VLDL/chylomicron triglycerides as continuous covariates.

Time Frame: Baseline and Week 12

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Placebo**	**Alogliptin 12.5 + Placebo**	**Alogliptin 25 + Placebo**	**Placebo + Pioglitazone 15**	**Alogliptin 12.5 + Pioglitazone 15**	**Alogliptin 25 + Pioglitazone 15**	**Placebo + Pioglitazone 30**	**Alogliptin 12.5 + Pioglitazone 30**	**Alogliptin 25 + Pioglitazone 30**	**Placebo + Pioglitazone 45**	**Alogliptin 12.5 + Pioglitazone 45**	**Alogliptin 25 + Pioglitazone 45**
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	119	113	114	113	114	117	110	113	110	109	118	116
Least Squares Mean (Standard Error) Units: mg/dL	19.9 (6.51)	-3.5 (6.69)	-6.4 (6.65)	-14.2 (6.68)	-21.1 (6.65)	-26.5 (6.56)	-19.1 (6.78)	-29.5 (6.69)	-30.1 (6.77)	-28.4 (6.80)	-35.5 (6.55)	-34.8 (6.60)

135. Secondary Outcome

Title: Change From Baseline to Week 26 in VLDL / Chylomicron Triglycerides

Description: The change from Baseline in VLDL/chylomicron triglyceride levels was assessed by NMR lipid fractionation. Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline NMR VLDL/chylomicron triglycerides as continuous covariates.

Time Frame: Baseline and Week 26

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Placebo**	**Alogliptin 12.5 + Placebo**	**Alogliptin 25 + Placebo**	**Placebo + Pioglitazone 15**	**Alogliptin 12.5 + Pioglitazone 15**	**Alogliptin 25 + Pioglitazone 15**	**Placebo + Pioglitazone 30**	**Alogliptin 12.5 + Pioglitazone 30**	**Alogliptin 25 + Pioglitazone 30**	**Placebo + Pioglitazone 45**	**Alogliptin 12.5 + Pioglitazone 45**	**Alogliptin 25 + Pioglitazone 45**
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	122	117	120	116	120	120	116	118	116	116	121	121
Least Squares Mean (Standard Error) Units: mg/dL	11.9 (7.23)	8.3 (7.39)	-7.0 (7.29)	-20.4 (7.41)	-20.4 (7.29)	-23.8 (7.29)	-8.2 (7.41)	-23.5 (7.35)	-18.9 (7.41)	-10.4 (7.41)	-32.3 (7.26)	-26.2 (7.26)

136. Secondary Outcome

Title: Change From Baseline in VLDL Particles Over Time (Grouped Analysis)

Description: The change from Baseline in levels of medium VLDL particles and small VLDL particles was assessed by NMR fractionation at Weeks 12 and 26. This analysis compared the groupings of participants who received the combination of pioglitazone with each dose of alogliptin with the grouping of participants who received pioglitazone alone. Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline NMR VLDL particles as continuous covariates.

Time Frame: Baseline and Weeks 12 and 26

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Pioglitazone Alone**	**Alogliptin 12.5 + Pioglitazone**	**Alogliptin 25 + Pioglitazone**
Arm/Group Description:	Alogliptin placebo plus all active pioglitazone groups (15, 30, and 45 mg).	Alogliptin 12.5 mg plus all active pioglitazone (15, 30, and 45 mg).	Alogliptin 25 mg plus all active pioglitazone (15, 30, and 45 mg).
Number of Participants Analyzed	387	390	390
Least Squares Mean (Standard Error) Units: nmol/L			
Medium Particles - Week 12 (n=332, 345, 343)	-4.44 (1.174)	-5.36 (1.152)	-7.30 (1.155)
Medium Particles - Week 26 (n=348, 359, 357)	-2.28 (1.346)	-3.02 (1.326)	-4.88 (1.329)
Small Particles - Week 12 (n=332, 345, 343)	4.16 (1.053)	1.33 (1.033)	1.91 (1.035)
Small Particles - Week 26 (n=348, 359, 357)	2.30 (1.084)	3.55 (1.067)	5.22 (1.070)

137. Secondary Outcome

Title: Change From Baseline to Week 12 in VLDL Particles

Description: The change from Baseline in levels of medium VLDL particles and small VLDL particles was assessed by NMR lipid fractionation. Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline NMR VLDL particles as continuous covariates.

Time Frame: Baseline and Week 12

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Placebo**	**Alogliptin 12.5 + Placebo**	**Alogliptin 25 + Placebo**	**Placebo + Pioglitazone 15**	**Alogliptin 12.5 + Pioglitazone 15**	**Alogliptin 25 + Pioglitazone 15**	**Placebo + Pioglitazone 30**	**Alogliptin 12.5 + Pioglitazone 30**	**Alogliptin 25 + Pioglitazone 30**	**Placebo + Pioglitazone 45**	**Alogliptin 12.5 + Pioglitazone 45**	**Alogliptin 25 + Pioglitazone 45**
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	119	113	114	113	114	117	110	113	110	109	118	116
Least Squares Mean (Standard Error) Units: nmol/L												
Medium Particles	2.13 (1.962)	-1.13 (2.014)	-2.88 (2.003)	-2.25 (2.011)	-3.16 (2.004)	-6.51 (1.977)	-2.59 (2.041)	-6.70 (2.013)	-7.05 (2.039)	-8.64 (2.048)	-6.38 (1.971)	-8.50 (1.987)
Small Particles	2.76 (1.758)	0.39 (1.804)	-2.30 (1.797)	5.99 (1.803)	1.16 (1.796)	2.60 (1.772)	4.39 (1.829)	1.15 (1.806)	2.51 (1.828)	2.22 (1.839)	1.80 (1.765)	0.73 (1.780)

138. Secondary Outcome

Title: Change From Baseline to Week 26 in VLDL Particles

Description: The change from Baseline in levels of medium VLDL particles and small VLDL particles was assessed by NMR lipid fractionation.
Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline NMR VLDL particles as continuous covariates

Time Frame: Baseline and Week 26

Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	122	117	120	116	120	120	116	118	116	116	121	121
Least Squares Mean (Standard Error)												
Units: nmol/L												
Medium Particles	1.54 (2.275)	0.85 (2.324)	-2.94 (2.292)	-4.43 (2.331)	-1.78 (2.293)	-5.42 (2.292)	0.28 (2.332)	-2.17 (2.313)	-4.38 (2.331)	-2.70 (2.331)	-5.09 (2.285)	-4.83 (2.284)
Small Particles	0.26 (1.831)	-0.87 (1.868)	-2.91 (1.846)	2.83 (1.876)	-0.19 (1.845)	1.90 (1.845)	4.16 (1.877)	4.07 (1.863)	5.45 (1.876)	-0.08 (1.878)	6.77 (1.837)	8.33 (1.837)

139. Secondary Outcome

Title: Change From Baseline in Mean VLDL Particle Size Over Time (Grouped Analysis)

Description: The change from Baseline in mean VLDL particle size was assessed by NMR lipid fractionation at Weeks 12 and 26.
This analysis compared the groupings of participants who received the combination of pioglitazone with each dose of alogliptin with the grouping of participants who received pioglitazone alone. Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline mean VLDL particle size as continuous covariates.

Time Frame: Baseline and Weeks 12 and 26

Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Pioglitazone Alone	Alogliptin 12.5 + Pioglitazone	Alogliptin 25 + Pioglitazone
Arm/Group Description:	Alogliptin placebo plus all active pioglitazone groups (15, 30, and 45 mg).	Alogliptin 12.5 mg plus all active pioglitazone (15, 30, and 45 mg).	Alogliptin 25 mg plus all active pioglitazone (15, 30, and 45 mg).
Number of Participants Analyzed	387	390	390
Least Squares Mean (Standard Error)			
Units: nm			
Week 12 (n=332, 344, 343)	-2.77 (0.398)	-2.98 (0.390)	-3.02 (0.391)
Week 26 (n=348, 358, 357)	-2.49 (0.406)	-3.67 (0.400)	-3.26 (0.400)

140. Secondary Outcome

Title: Change From Baseline to Week 12 in Mean VLDL Particle Size

Description: The change from Baseline in mean VLDL particle size was assessed by NMR lipid fractionation.
Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline mean VLDL particle size as continuous covariates.

Time Frame: Baseline and Week 12

Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	119	113	114	113	113	117	110	113	110	109	118	116
Least Squares Mean (Standard Error)	0.65 (0.664)	0.12 (0.681)	-0.18 (0.678)	-2.81 (0.681)	-2.10 (0.681)	-2.56 (0.669)	-3.16 (0.690)	-2.88 (0.681)	-2.49 (0.690)	-2.37 (0.694)	-4.00 (0.666)	-4.03 (0.672)
Units: nm												

141. Secondary Outcome

Title: Change From Baseline to Week 26 in Mean VLDL Particle Size

Description: The change from Baseline in mean VLDL particle size was assessed by NMR lipid fractionation.
Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline mean VLDL particle size as continuous covariates.

Time Frame: Baseline and Week 26

Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.

Number of Participants Analyzed	122	117	120	116	119	120	116	118	116	116	121	121
Least Squares Mean (Standard Error)	0.26 (0.685)	0.52 (0.700)	0.35 (0.691)	-2.99 (0.703)	-2.66 (0.694)	-2.36 (0.691)	-2.88 (0.703)	-3.69 (0.697)	-3.30 (0.702)	-1.60 (0.703)	-4.65 (0.688)	-4.12 (0.688)
Units: nm												

142. Secondary Outcome

Title: Change From Baseline in Intermediate Density Lipoprotein (IDL) Particles Over Time (Grouped Analysis)

Description: The change from Baseline in levels of IDL particles was assessed by NMR lipid fractionation at Weeks 12 and 26.
This analysis compared the groupings of participants who received the combination of pioglitazone with each dose of alogliptin with the grouping of participants who received pioglitazone alone. Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline NMR IDL particles as continuous covariates.

Time Frame: Baseline and Weeks 12 and 26

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Pioglitazone Alone**	**Alogliptin 12.5 + Pioglitazone**	**Alogliptin 25 + Pioglitazone**
Arm/Group Description:	Alogliptin placebo plus all active pioglitazone groups (15, 30, and 45 mg).	Alogliptin 12.5 mg plus all active pioglitazone (15, 30, and 45 mg).	Alogliptin 25 mg plus all active pioglitazone (15, 30, and 45 mg).
Number of Participants Analyzed	387	390	390
Least Squares Mean (Standard Error) Units: nmol/L			
Week 12 (n=332, 345, 343)	0.4 (2.16)	-3.9 (2.12)	-5.7 (2.12)
Week 26 (n=348, 359, 357)	2.8 (2.16)	-4.2 (2.13)	-1.5 (2.13)

143. Secondary Outcome

Title: Change From Baseline to Week 12 in IDL Particles

Description: The change from Baseline in levels of IDL particles was assessed by NMR lipid fractionation.
Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline NMR IDL particles as continuous covariates.

Time Frame: Baseline and Week 12

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Placebo**	**Alogliptin 12.5 + Placebo**	**Alogliptin 25 + Placebo**	**Placebo + Pioglitazone 15**	**Alogliptin 12.5 + Pioglitazone 15**	**Alogliptin 25 + Pioglitazone 15**	**Placebo + Pioglitazone 30**	**Alogliptin 12.5 + Pioglitazone 30**	**Alogliptin 25 + Pioglitazone 30**	**Placebo + Pioglitazone 45**	**Alogliptin 12.5 + Pioglitazone 45**	**Alogliptin 25 + Pioglitazone 45**
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	119	113	114	113	114	117	110	113	110	109	118	116
Least Squares Mean (Standard Error)	1.6 (3.60)	-11.1 (3.70)	-6.0 (3.68)	5.1 (3.70)	-6.0 (3.68)	-2.3 (3.64)	-2.2 (3.75)	-6.3 (3.70)	-8.1 (3.75)	-1.5 (3.76)	0.7 (3.62)	-6.5 (3.65)
Units: nmol/L												

144. Secondary Outcome

Title: Change From Baseline to Week 26 in IDL Particles

Description: The change from Baseline in levels of IDL particles was assessed by NMR lipid fractionation.
Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline NMR IDL particles as continuous covariates.

Time Frame: Baseline and Week 26

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Placebo**	**Alogliptin 12.5 + Placebo**	**Alogliptin 25 + Placebo**	**Placebo + Pioglitazone 15**	**Alogliptin 12.5 + Pioglitazone 15**	**Alogliptin 25 + Pioglitazone 15**	**Placebo + Pioglitazone 30**	**Alogliptin 12.5 + Pioglitazone 30**	**Alogliptin 25 + Pioglitazone 30**	**Placebo + Pioglitazone 45**	**Alogliptin 12.5 + Pioglitazone 45**	**Alogliptin 25 + Pioglitazone 45**
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	122	117	120	116	120	120	116	118	116	116	121	121
Least Squares Mean (Standard Error)	5.1 (3.65)	-7.3 (3.73)	-3.2 (3.68)	5.2 (3.74)	-2.4 (3.67)	0.0 (3.68)	3.0 (3.74)	-5.0 (3.71)	-5.5 (3.74)	0.1 (3.74)	-5.0 (3.66)	1.0 (3.66)
Units: nmol/L												

145. Secondary Outcome

Title: Change From Baseline in Low Density Lipoprotein (LDL) Particles Over Time (Grouped Analysis)

Description: The change from Baseline in levels of total, large, medium-small, total small and very small LDL particles was assessed by NMR fractionation at Weeks 12 and 26.
This analysis compared the groupings of participants who received the combination of pioglitazone with each dose of alogliptin with the grouping of participants who received pioglitazone alone. Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline NMR LDL particles as continuous covariates.

Time Frame: Baseline and Weeks 12 and 26

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Pioglitazone Alone**	**Alogliptin 12.5 + Pioglitazone**	**Alogliptin 25 + Pioglitazone**
Arm/Group Description:	Alogliptin placebo plus all active pioglitazone groups (15, 30, and 45 mg).	Alogliptin 12.5 mg plus all active pioglitazone (15, 30, and 45 mg).	Alogliptin 25 mg plus all active pioglitazone (15, 30, and 45 mg).
Number of Participants Analyzed	387	390	390
Least Squares Mean (Standard Error) Units: nmol/L			
Total Particles - Week 12 (n=332, 345, 343)	-104.1 (17.46)	-180.5 (17.13)	-236.8 (17.18)
Total Particles - Week 26 (n=348, 359, 357)	-78.2 (17.83)	-146.2 (17.55)	-182.9 (17.60)
Large Particles - Week 12 (n=332, 345, 343)	85.5 (10.02)	111.6 (9.83)	102.3 (9.85)
Large Particles - Week 26 (n=348, 359, 357)	95.8 (11.11)	93.9 (10.93)	106.1 (10.96)
Medium-Small Particles - Week 12 (n=332, 345, 343)	-36.6 (4.11)	-55.3 (4.03)	-60.1 (4.04)
Medium-Small Particles - Week 26 (n=348, 359, 357)	-34.3 (4.22)	-44.9 (4.16)	-49.6 (4.17)

Total Small Particles - Week 12 (n=332, 345, 343)	-191.4 (20.32)	-287.5 (19.94)	-331.4 (20.00)
Total Small Particles - Week 26 (n=348, 359, 357)	-178.1 (21.13)	-235.0 (20.81)	-285.9 (20.87)
Very Small Particles - Week 12 (n=332, 345, 343)	-154.6 (16.53)	-232.3 (16.23)	-271.3 (16.27)
Very Small Particles - Week 26 (n=348, 359, 357)	-143.6 (17.23)	-190.3 (16.97)	-236.2 (17.02)

146. Secondary Outcome

Title: Change From Baseline to Week 12 in LDL Particles

Description: The change from Baseline in levels of total, large, medium-small, total small and very small LDL particles was assessed by NMR lipid fractionation.
Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline NMR LDL particles as continuous covariates.

Time Frame: Baseline and Week 12

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	119	113	114	113	114	117	110	113	110	109	118	116
Least Squares Mean (Standard Error) Units: nmol/L												
Total Particles	52.0 (29.17)	-39.1 (29.92)	-69.9 (29.80)	-48.8 (29.91)	-143.5 (29.79)	-175.6 (29.43)	-96.2 (30.37)	-195.8 (29.93)	-248.8 (30.31)	-167.0 (30.46)	-202.2 (29.27)	-285.8 (29.52)
Large Particles	4.7 (16.74)	21.1 (17.16)	-8.0 (17.09)	56.2 (17.15)	73.8 (17.08)	85.7 (16.86)	83.9 (17.43)	126.2 (17.18)	105.7 (17.39)	116.9 (17.48)	135.2 (16.79)	116.1 (16.95)
Medium-Small Particles	9.4 (6.87)	-7.7 (7.04)	-5.1 (7.02)	-20.3 (7.04)	-41.1 (7.01)	-48.0 (6.93)	-34.4 (7.14)	-58.2 (7.05)	-64.1 (7.14)	-55.4 (7.17)	-66.8 (6.89)	-68.2 (6.96)
Total Small Particles	45.1 (33.98)	-52.0 (34.83)	-56.5 (34.70)	-109.9 (34.83)	-211.0 (34.69)	-256.3 (34.26)	-184.1 (35.32)	-313.7 (34.85)	-345.4 (35.29)	-280.4 (35.46)	-337.9 (34.08)	-392.7 (34.38)
Very Small Particles	36.4 (27.65)	-44.1 (28.34)	-51.9 (28.23)	-89.2 (28.33)	-170.3 (28.22)	-207.6 (27.87)	-149.8 (28.74)	-255.7 (28.36)	-281.5 (28.72)	-225.0 (28.85)	-271.0 (27.73)	-325.0 (27.97)

147. Secondary Outcome

Title: Change From Baseline to Week 26 in LDL Particles

Description: The change from Baseline in levels of total, large, medium-small, total small and very small LDL particles was assessed by NMR lipid fractionation.
Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline NMR LDL particles as continuous covariates.

Time Frame: Baseline and Week 26

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	122	117	120	116	120	120	116	118	116	116	121	121
Least Squares Mean (Standard Error) Units: nmol/L												
Total Particles	15.0 (30.11)	-14.5 (30.73)	-30.8 (30.36)	-46.3 (30.86)	-115.1 (30.35)	-119.4 (30.37)	-68.6 (30.90)	-158.9 (30.62)	-209.4 (30.85)	-119.7 (30.87)	-164.6 (30.22)	-219.9 (30.21)
Large Particles	-23.8 (18.77)	-12.3 (19.14)	15.3 (18.91)	70.5 (19.22)	63.2 (18.90)	93.1 (18.90)	79.3 (19.27)	96.6 (19.09)	102.7 (19.22)	137.7 (19.23)	121.9 (18.83)	122.7 (18.83)
Medium-Small Particles	9.1 (7.14)	0.0 (7.28)	-6.9 (7.20)	-25.8 (7.31)	-29.9 (7.19)	-36.2 (7.20)	-30.0 (7.32)	-47.4 (7.26)	-55.0 (7.31)	-47.1 (7.31)	-57.6 (7.16)	-57.8 (7.17)
Total Small Particles	32.4 (35.72)	2.2 (36.44)	-42.9 (36.00)	-122.5 (36.59)	-175.1 (35.99)	-211.5 (36.01)	-154.9 (36.60)	-248.7 (36.31)	-304.9 (36.58)	-256.9 (36.58)	-281.1 (35.82)	-341.3 (35.82)
Very Small Particles	24.0 (29.13)	2.5 (29.71)	-36.6 (29.36)	-96.3 (29.84)	-145.7 (29.35)	-174.5 (29.37)	-124.9 (29.85)	-201.6 (29.61)	-250.0 (29.83)	-209.6 (29.83)	-223.6 (29.22)	-283.9 (29.21)

148. Secondary Outcome

Title: Change From Baseline in Mean LDL Particle Size Over Time (Grouped Analysis)

Description: The change from Baseline in mean LDL particle size was assessed by NMR lipid fractionation at Weeks 12 and 26.
This analysis compared the groupings of participants who received the combination of pioglitazone with each dose of alogliptin with the grouping of participants who received pioglitazone alone.
Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline mean LDL particle size as continuous covariates.

Time Frame: Baseline and Weeks 12 and 26

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Pioglitazone Alone	Alogliptin 12.5 + Pioglitazone	Alogliptin 25 + Pioglitazone
Arm/Group Description:	Alogliptin placebo plus all active pioglitazone groups (15, 30, and 45 mg).	Alogliptin 12.5 mg plus all active pioglitazone (15, 30, and 45 mg).	Alogliptin 25 mg plus all active pioglitazone (15, 30, and 45 mg).
Number of Participants Analyzed	387	390	390
Least Squares Mean (Standard Error) Units: nm			
Week 12 (n=332, 345, 343)	0.43 (0.034)	0.58 (0.034)	0.61 (0.034)
Week 26 (n=348, 359, 357)	0.41 (0.036)	0.47 (0.035)	0.54 (0.036)

149. Secondary Outcome

Title: Change From Baseline to Week 12 in Mean LDL Particle Size

Description: The change from Baseline in mean LDL particle size was assessed by NMR lipid fractionation.
Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline mean LDL particle size as continuous covariates.

Time Frame: Baseline and Week 12

Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	119	113	114	113	114	117	110	113	110	109	118	116
Least Squares Mean (Standard Error) **Units: nm**	-0.05 (0.057)	0.13 (0.059)	0.06 (0.059)	0.25 (0.059)	0.43 (0.059)	0.49 (0.058)	0.44 (0.060)	0.61 (0.059)	0.61 (0.060)	0.58 (0.060)	0.68 (0.058)	0.73 (0.058)

150. Secondary Outcome

Title: Change From Baseline to Week 26 in Mean LDL Particle Size
Description: The change from Baseline in mean LDL particle size was assessed by NMR lipid fractionation.
Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline mean LDL particle size as continuous covariates.
Time Frame: Baseline and Week 26
Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	122	117	120	116	120	120	116	118	116	116	121	121
Least Squares Mean (Standard Error) **Units: nm**	-0.06 (0.061)	-0.01 (0.062)	0.07 (0.061)	0.26 (0.062)	0.38 (0.061)	0.41 (0.061)	0.38 (0.062)	0.48 (0.062)	0.57 (0.062)	0.59 (0.062)	0.55 (0.061)	0.63 (0.061)

151. Secondary Outcome

Title: Change From Baseline in High Density Lipoprotein (HDL) Particles Over Time (Grouped Analysis)
Description: The change from Baseline in levels of total, large, medium and small HDL particles was assessed by NMR fractionation at Weeks 12 and 26.
This analysis compared the groupings of participants who received the combination of pioglitazone with each dose of alogliptin with the grouping of participants who received pioglitazone alone. Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline NMR HDL particles as continuous covariates.
Time Frame: Baseline and Weeks 12 and 26.
Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Pioglitazone Alone	Alogliptin 12.5 + Pioglitazone	Alogliptin 25 + Pioglitazone
Arm/Group Description:	Alogliptin placebo plus all active pioglitazone groups (15, 30, and 45 mg).	Alogliptin 12.5 mg plus all active pioglitazone (15, 30, and 45 mg).	Alogliptin 25 mg plus all active pioglitazone (15, 30, and 45 mg).
Number of Participants Analyzed	387	390	390
Least Squares Mean (Standard Error) Units: µMOL/L			
Total Particles - Week 12 (n=332, 345, 343)	0.86 (0.220)	0.58 (0.216)	0.43 (0.216)
Total Particles - Week 26 (n=348, 359, 357)	0.62 (0.235)	1.18 (0.231)	0.78 (0.232)
Large Particles - Week 12 (n=332, 345, 343)	0.89 (0.111)	0.78 (0.109)	0.89 (0.109)
Large Particles - Week 26 (n=348, 359, 357)	0.81 (0.123)	0.90 (0.121)	1.01 (0.122)
Medium Particles - Week 12 (n=332, 345, 343)	1.38 (0.195)	1.16 (0.191)	1.63 (0.191)
Medium Particles - Week 26 (n=348, 359, 357)	1.34 (0.195)	1.10 (0.192)	1.46 (0.192)
Small Particles - Week 12 (n=332, 345, 343)	-1.35 (0.261)	-1.39 (0.256)	-2.12 (0.256)
Small Particles - Week 26 (n=348, 359, 357)	-1.45 (0.261)	-0.85 (0.257)	-1.73 (0.258)

152. Secondary Outcome

Title: Change From Baseline to Week 12 in HDL Particles
Description: The change from Baseline in levels of total, large, medium and small HDL particles was assessed by NMR lipid fractionation.
Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline NMR HDL particles as continuous covariates.
Time Frame: Baseline and Week 12
Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	119	113	114	113	114	117	110	113	110	109	118	116
Least Squares Mean (Standard Error) Units: µmol/L												
Total Particles	-0.08 (0.368)	-0.06 (0.377)	0.16 (0.375)	0.90 (0.377)	0.37 (0.375)	0.55 (0.370)	1.29 (0.382)	0.75 (0.377)	0.15 (0.382)	0.40 (0.384)	0.63 (0.369)	0.60 (0.372)
Large Particles	-0.21 (0.185)	-0.29 (0.190)	-0.10 (0.189)	0.53 (0.190)	0.24 (0.189)	0.50 (0.186)	1.09 (0.192)	0.95 (0.190)	1.12 (0.192)	1.06 (0.193)	1.17 (0.186)	1.06 (0.187)
Medium Particles	0.17 (0.325)	-0.24 (0.333)	-0.01 (0.332)	0.81 (0.334)	1.15 (0.332)	0.65 (0.328)	1.21 (0.338)	0.97 (0.334)	1.89 (0.338)	2.06 (0.339)	1.30 (0.326)	2.31 (0.329)
Small Particles	-0.07 (0.435)	0.43 (0.447)	0.27 (0.445)	-0.25 (0.446)	-1.09 (0.445)	-0.63 (0.439)	-0.92 (0.453)	-1.18 (0.447)	-2.82 (0.452)	-2.82 (0.455)	-1.84 (0.437)	-2.84 (0.441)

153. Secondary Outcome

Title: Change From Baseline to Week 26 in HDL Particles
Description: The change from Baseline in levels of total, large, medium and small HDL particles was assessed by NMR lipid fractionation.
Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline NMR HDL particles as continuous covariates.
Time Frame: Baseline and Week 26
Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone	Alogliptin 12.5 +	Alogliptin 25 +	Placebo + Pioglitazone	Alogliptin 12.5 +	Alogliptin 25 +	Placebo + Pioglitazone	Alogliptin 12.5 +	Alogliptin 25 +

Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	122	117	120	116	120	120	116	118	116	116	121	121
Least Squares Mean (Standard Error) Units: µmol/L												
Total Particles	0.18 (0.397)	0.43 (0.405)	1.03 (0.400)	0.37 (0.407)	0.77 (0.400)	1.31 (0.400)	0.67 (0.407)	1.15 (0.403)	0.26 (0.406)	0.83 (0.407)	1.61 (0.398)	0.77 (0.398)
Large Particles	0.02 (0.208)	-0.16 (0.212)	0.39 (0.210)	0.53 (0.213)	0.55 (0.210)	0.75 (0.210)	0.64 (0.213)	1.13 (0.212)	1.34 (0.213)	1.26 (0.213)	1.02 (0.209)	0.95 (0.209)
Medium Particles	0.13 (0.330)	0.16 (0.336)	0.54 (0.332)	0.81 (0.338)	0.86 (0.332)	0.67 (0.332)	1.48 (0.338)	1.47 (0.335)	1.69 (0.337)	1.71 (0.337)	0.96 (0.331)	2.01 (0.330)
Small Particles	0.00 (0.441)	0.41 (0.450)	0.10 (0.444)	-0.78 (0.452)	-0.68 (0.444)	-0.17 (0.444)	-1.35 (0.452)	-1.47 (0.448)	-2.77 (0.452)	-2.21 (0.452)	-0.40 (0.443)	-2.24 (0.442)

154. Secondary Outcome

Title: Change From Baseline in Mean HDL Particle Size Over Time (Grouped Analysis)

Description: The change from Baseline in mean HDL particle size was assessed by NMR lipid fractionation at Weeks 12 and 26.
This analysis compared the groupings of participants who received the combination of pioglitazone with each dose of alogliptin with the grouping of participants who received pioglitazone alone. Least squares means are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline mean HDL particle size as continuous covariates.

Time Frame: Baseline and Weeks 12 and 26

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Pioglitazone Alone**	**Alogliptin 12.5 + Pioglitazone**	**Alogliptin 25 + Pioglitazone**
Arm/Group Description:	Alogliptin placebo plus all active pioglitazone groups (15, 30, and 45 mg).	Alogliptin 12.5 mg plus all active pioglitazone (15, 30, and 45 mg).	Alogliptin 25 mg plus all active pioglitazone (15, 30, and 45 mg).
Number of Participants Analyzed	387	390	390
Least Squares Mean (Standard Error) Units: nm			
Week 12 (n=332, 345, 343)	0.11 (0.013)	0.13 (0.013)	0.16 (0.013)
Week 26 (n=348, 359, 357)	0.11 (0.015)	0.12 (0.014)	0.17 (0.014)

155. Secondary Outcome

Title: Change From Baseline to Week 12 in Mean HDL Particle Size

Description: The change from Baseline in mean HDL particle size was assessed by NMR lipid fractionation. Least squares means are from are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline mean HDL particle size as continuous covariates.

Time Frame: Baseline and Week 12

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Placebo**	**Alogliptin 12.5 + Placebo**	**Alogliptin 25 + Placebo**	**Placebo + Pioglitazone 15**	**Alogliptin 12.5 + Pioglitazone 15**	**Alogliptin 25 + Pioglitazone 15**	**Placebo + Pioglitazone 30**	**Alogliptin 12.5 + Pioglitazone 30**	**Alogliptin 25 + Pioglitazone 30**	**Placebo + Pioglitazone 45**	**Alogliptin 12.5 + Pioglitazone 45**	**Alogliptin 25 + Pioglitazone 45**
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	119	113	114	113	114	117	110	113	110	109	118	116
Least Squares Mean (Standard Error) **Units: nm**	0.00 (0.023)	0.00 (0.023)	0.00 (0.023)	0.06 (0.023)	0.07 (0.023)	0.09 (0.023)	0.10 (0.023)	0.15 (0.023)	0.17 (0.023)	0.18 (0.024)	0.17 (0.023)	0.21 (0.023)

156. Secondary Outcome

Title: Change From Baseline to Week 26 in Mean HDL Particle Size

Description: The change from Baseline in mean HDL particle size was assessed by NMR lipid fractionation. Least squares means are from are from an ANCOVA model with treatment and geographic region as class variables, and baseline metformin dose and baseline mean HDL particle size as continuous covariates.

Time Frame: Baseline and Week 26

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set where Baseline and at least 1 postbaseline assessment were available. Last observation carried forward imputation was utilized.

Arm/Group Title	**Placebo**	**Alogliptin 12.5 + Placebo**	**Alogliptin 25 + Placebo**	**Placebo + Pioglitazone 15**	**Alogliptin 12.5 + Pioglitazone 15**	**Alogliptin 25 + Pioglitazone 15**	**Placebo + Pioglitazone 30**	**Alogliptin 12.5 + Pioglitazone 30**	**Alogliptin 25 + Pioglitazone 30**	**Placebo + Pioglitazone 45**	**Alogliptin 12.5 + Pioglitazone 45**	**Alogliptin 25 + Pioglitazone 45**
Arm/Group Description:	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.
Number of Participants Analyzed	122	117	120	116	120	120	116	118	116	116	121	121
Least Squares Mean (Standard Error) **Units: nm**	0.03 (0.025)	0.00 (0.025)	0.07 (0.025)	0.06 (0.025)	0.06 (0.025)	0.11 (0.025)	0.10 (0.025)	0.15 (0.025)	0.20 (0.025)	0.19 (0.025)	0.16 (0.025)	0.19 (0.025)

Adverse Events

Time Frame	Adverse events were collected from the time of informed consent until the end of the study, and from spontaneous reporting for 30 days after the end of treatment.
Additional Description	At each study visit, the investigator assessed whether any events had occurred. Patients could report events at any other time during the study. All events, whether reported by the patient or observed by the investigator, were documented, whether or not the investigator concluded the event to be related to the drug treatment.
Source Vocabulary Name	MedDRA (10.0)
Assessment Type	Systematic Assessment

Arm/Group Title	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
Arm/Group Description	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone placebo-matching tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 15 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.	Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 45 mg, tablets, orally, once daily for up to 26 weeks.

Serious Adverse Events

	Placebo	**Alogliptin 12.5 + Placebo**	**Alogliptin 25 + Placebo**	**Placebo + Pioglitazone 15**	**Alogliptin 12.5 + Pioglitazone 15**	**Alogliptin 25 + Pioglitazone 15**	**Placebo + Pioglitazone 30**	**Alogliptin 12.5 + Pioglitazone 30**	**Alogliptin 25 + Pioglitazone 30**	**Placebo + Pioglitazone 45**	**Alogliptin 12.5 + Pioglitazone 45**	**Alogliptin 25 + Pioglitazone 45**
	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)
Total	2/129 (1.55%)	5/128 (3.91%)	6/129 (4.65%)	1/129 (0.78%)	2/130 (1.54%)	1/130 (0.77%)	2/129 (1.55%)	3/130 (2.31%)	6/130 (4.62%)	10/129 (7.75%)	2/130 (1.54%)	5/130 (3.85%)

Cardiac disorders												
Angina unstable †A	0/129 (0%)	0/128 (0%)	0/129 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	1/130 (0.77%)	0/130 (0%)
Coronary artery disease †A	0/129 (0%)	0/128 (0%)	0/129 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	1/129 (0.78%)	0/130 (0%)	0/130 (0%)
Coronary artery stenosis †A	0/129 (0%)	0/128 (0%)	0/129 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	1/130 (0.77%)
Myocardial infarction †A	0/129 (0%)	0/128 (0%)	0/129 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	1/129 (0.78%)	0/130 (0%)	0/130 (0%)
Myocardial ischaemia †A	0/129 (0%)	0/128 (0%)	0/129 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	1/130 (0.77%)
Gastrointestinal disorders												
Gastritis †A	0/129 (0%)	0/128 (0%)	0/129 (0%)	0/129 (0%)	0/130 (0%)	1/130 (0.77%)	0/129 (0%)	1/130 (0.77%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)
Pancreatitis †A	0/129 (0%)	1/128 (0.78%)	0/129 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)
Periodontitis †A	0/129 (0%)	1/128 (0.78%)	0/129 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)
Reflux oesophagitis †A	0/129 (0%)	0/128 (0%)	0/129 (0%)	0/129 (0%)	0/130 (0%)	1/130 (0.77%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)
Umbilical hernia †A	0/129 (0%)	0/128 (0%)	0/129 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	1/129 (0.78%)	0/130 (0%)	0/130 (0%)
General disorders												
Non-cardiac chest pain †A	0/129 (0%)	0/128 (0%)	1/129 (0.78%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	1/129 (0.78%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)
Pyrexia †A	1/129 (0.78%)	0/128 (0%)	0/129 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	1/130 (0.77%)	0/129 (0%)	0/130 (0%)	0/130 (0%)
Sudden cardiac death †A	0/129 (0%)	0/128 (0%)	0/129 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	1/129 (0.78%)	0/130 (0%)	0/130 (0%)
Hepatobiliary disorders												
Cholangitis †A	0/129 (0%)	0/128 (0%)	1/129 (0.78%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)
Cholecystitis †A	0/129 (0%)	0/128 (0%)	1/129 (0.78%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)
Cholecystitis acute †A	0/129 (0%)	0/128 (0%)	0/129 (0%)	0/129 (0%)	1/130 (0.77%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)
Cholelithiasis †A	0/129 (0%)	1/128 (0.78%)	0/129 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)
Hepatitis †A	0/129 (0%)	0/128 (0%)	0/129 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	1/129 (0.78%)	0/130 (0%)	0/130 (0%)
Infections and infestations												
Appendicitis †A	0/129 (0%)	0/128 (0%)	1/129 (0.78%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	1/130 (0.77%)
Arthritis bacterial †A	0/129 (0%)	0/128 (0%)	1/129 (0.78%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)
Bronchopneumonia †A	0/129 (0%)	0/128 (0%)	0/129 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	1/129 (0.78%)	0/130 (0%)	0/130 (0%)
Gastroenteritis viral †A	0/129 (0%)	0/128 (0%)	0/129 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	1/129 (0.78%)	0/130 (0%)	0/130 (0%)
Lower respiratory tract infection †A	0/129 (0%)	0/128 (0%)	0/129 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	1/129 (0.78%)	0/130 (0%)	0/130 (0%)
Osteomyelitis †A	0/129 (0%)	0/128 (0%)	0/129 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	1/130 (0.77%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)
Perirectal abscess †A	0/129 (0%)	0/128 (0%)	0/129 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	1/130 (0.77%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)
Pneumonia †A	0/129 (0%)	0/128 (0%)	0/129 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	1/130 (0.77%)	1/129 (0.78%)	0/130 (0%)	0/130 (0%)
Pyelonephritis †A	0/129 (0%)	0/128 (0%)	0/129 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	1/129 (0.78%)	0/130 (0%)	0/130 (0%)
Pyelonephritis acute †A	0/129 (0%)	0/128 (0%)	0/129 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	1/129 (0.78%)	0/130 (0%)	0/130 (0%)
Urinary tract infection †A	0/129 (0%)	1/128 (0.78%)	0/129 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)
Injury, poisoning and procedural complications												
Ankle fracture †A	0/129 (0%)	0/128 (0%)	0/129 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	1/129 (0.78%)	0/130 (0%)	0/130 (0%)
Foreign body in eye †A	0/129 (0%)	0/128 (0%)	0/129 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	1/130 (0.77%)	0/129 (0%)	0/130 (0%)	0/130 (0%)
Nervous system disorders												
Carotid artery occlusion †A	0/129 (0%)	0/128 (0%)	1/129 (0.78%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)
Cerebrovascular accident †A	1/129 (0.78%)	0/128 (0%)	0/129 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)
Convulsion †A	0/129 (0%)	0/128 (0%)	1/129 (0.78%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)
Disturbance in attention †A	0/129 (0%)	0/128 (0%)	0/129 (0%)	1/129 (0.78%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)
Ischaemic stroke †A	0/129 (0%)	0/128 (0%)	0/129 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	1/130 (0.77%)	0/129 (0%)	0/130 (0%)	0/130 (0%)
Lacunar infarction †A	0/129 (0%)	0/128 (0%)	0/129 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	1/130 (0.77%)
Migraine with aura †A	0/129 (0%)	0/128 (0%)	0/129 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	1/130 (0.77%)	0/129 (0%)	0/130 (0%)	0/130 (0%)
Nerve compression †A	0/129 (0%)	1/128 (0.78%)	0/129 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)
Syncope †A	0/129 (0%)	0/128 (0%)	1/129 (0.78%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)
Pregnancy, puerperium and perinatal conditions												
Abortion spontaneous †A	0/129 (0%)	1/128 (0.78%)	0/129 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)
Psychiatric disorders												
Anxiety †A	0/129 (0%)	0/128 (0%)	0/129 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	1/129 (0.78%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)
Renal and urinary disorders												
Calculus ureteric †A	0/129 (0%)	0/128 (0%)	0/129 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	1/130 (0.77%)
Nephrolithiasis †A	0/129 (0%)	0/128 (0%)	0/129 (0%)	0/129 (0%)	1/130 (0.77%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)
Respiratory, thoracic and mediastinal disorders												
Lung cyst benign †A	0/129 (0%)	0/128 (0%)	0/129 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	1/130 (0.77%)	0/129 (0%)	0/130 (0%)	0/130 (0%)
Pulmonary congestion †A	0/129 (0%)	0/128 (0%)	0/129 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	1/130 (0.77%)	0/130 (0%)
Pulmonary embolism †A	0/129 (0%)	0/128 (0%)	1/129 (0.78%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)
Vascular disorders												
Peripheral vascular disorder †A	0/129 (0%)	0/128 (0%)	0/129 (0%)	0/129 (0%)	0/130 (0%)	0/130 (0%)	0/129 (0%)	1/130 (0.77%)	0/130 (0%)	0/129 (0%)	0/130 (0%)	0/130 (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: 5%

	Placebo	Alogliptin 12.5 + Placebo	Alogliptin 25 + Placebo	Placebo + Pioglitazone 15	Alogliptin 12.5 + Pioglitazone 15	Alogliptin 25 + Pioglitazone 15	Placebo + Pioglitazone 30	Alogliptin 12.5 + Pioglitazone 30	Alogliptin 25 + Pioglitazone 30	Placebo + Pioglitazone 45	Alogliptin 12.5 + Pioglitazone 45	Alogliptin 25 + Pioglitazone 45
	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)
Total	41/129 (31.78%)	40/128 (31.25%)	46/129 (35.66%)	51/129 (39.53%)	45/130 (34.62%)	44/130 (33.85%)	40/129 (31.01%)	35/130 (26.92%)	51/130 (39.23%)	40/129 (31.01%)	47/130 (36.15%)	41/130 (31.54%)
Blood and lymphatic system disorders												
Anaemia †A	2/129 (1.55%)	0/128 (0%)	0/129 (0%)	2/129 (1.55%)	2/130 (1.54%)	2/130 (1.54%)	3/129 (2.33%)	3/130 (2.31%)	7/130 (5.38%)	0/129 (0%)	3/130 (2.31%)	5/130 (3.85%)
Gastrointestinal disorders												
Abdominal pain upper †A	2/129 (1.55%)	0/128 (0%)	7/129 (5.43%)	0/129 (0%)	1/130 (0.77%)	2/130 (1.54%)	1/129 (0.78%)	1/130 (0.77%)	3/130 (2.31%)	1/129 (0.78%)	5/130 (3.85%)	0/130 (0%)
Diarrhoea †A	11/129 (8.53%)	2/128 (1.56%)	4/129 (3.1%)	5/129 (3.88%)	3/130 (2.31%)	6/130 (4.62%)	4/129 (3.1%)	2/130 (1.54%)	7/130 (5.38%)	5/129 (3.88%)	4/130 (3.08%)	7/130 (5.38%)
General disorders												
Oedema peripheral †A	2/129 (1.55%)	2/128 (1.56%)	2/129 (1.55%)	2/129 (1.55%)	2/130 (1.54%)	7/130 (5.38%)	6/129 (4.65%)	4/130 (3.08%)	1/130 (0.77%)	2/129 (1.55%)	4/130 (3.08%)	6/130 (4.62%)
Infections and infestations												
Influenza †A	3/129 (2.33%)	4/128 (3.12%)	4/129 (3.1%)	9/129 (6.98%)	4/130 (3.08%)	8/130 (6.15%)	7/129 (5.43%)	2/130 (1.54%)	8/130 (6.15%)	5/129 (3.88%)	3/130 (2.31%)	2/130 (1.54%)
Nasopharyngitis †A	5/129 (3.88%)	5/128 (3.91%)	4/129 (3.1%)	3/129 (2.33%)	8/130 (6.15%)	8/130 (6.15%)	4/129 (3.1%)	5/130 (3.85%)	9/130 (6.92%)	4/129 (3.1%)	6/130 (4.62%)	4/130 (3.08%)
Upper respiratory tract infection †A	5/129 (3.88%)	3/128 (2.34%)	8/129 (6.2%)	3/129 (2.33%)	2/130 (1.54%)	4/130 (3.08%)	1/129 (0.78%)	5/130 (3.85%)	4/130 (3.08%)	2/129 (1.55%)	4/130 (3.08%)	4/130 (3.08%)
Urinary tract infection †A	6/129 (4.65%)	6/128 (4.69%)	5/129 (3.88%)	7/129 (5.43%)	5/130 (3.85%)	6/130 (4.62%)	8/129 (6.2%)	4/130 (3.08%)	4/130 (3.08%)	8/129 (6.2%)	5/130 (3.85%)	5/130 (3.85%)
Metabolism and nutrition disorders												
Dyslipidaemia †A	0/129 (0%)	1/128 (0.78%)	1/129 (0.78%)	3/129 (2.33%)	3/130 (2.31%)	1/130 (0.77%)	2/129 (1.55%)	1/130 (0.77%)	4/130 (3.08%)	7/129 (5.43%)	1/130 (0.77%)	2/130 (1.54%)
Hypertriglyceridaemia †A	3/129 (2.33%)	7/128 (5.47%)	6/129 (4.65%)	5/129 (3.88%)	2/130 (1.54%)	3/130 (2.31%)	5/129 (3.88%)	2/130 (1.54%)	4/130 (3.08%)	3/129 (2.33%)	3/130 (2.31%)	1/130 (0.77%)
Musculoskeletal and connective tissue disorders												
Back pain †A	5/129 (3.88%)	1/128 (0.78%)	7/129 (5.43%)	5/129 (3.88%)	6/130 (4.62%)	5/130 (3.85%)	3/129 (2.33%)	2/130 (1.54%)	8/130 (6.15%)	4/129 (3.1%)	12/130 (9.23%)	3/130 (2.31%)
Nervous system disorders												
Dizziness †A	4/129 (3.1%)	3/128 (2.34%)	2/129 (1.55%)	5/129 (3.88%)	7/130 (5.38%)	2/130 (1.54%)	4/129 (3.1%)	5/130 (3.85%)	5/130 (3.85%)	6/129 (4.65%)	6/130 (4.62%)	1/130 (0.77%)
Headache †A	6/129 (4.65%)	5/128 (3.91%)	9/129 (6.98%)	16/129 (12.4%)	5/130 (3.85%)	3/130 (2.31%)	2/129 (1.55%)	2/130 (1.54%)	5/130 (3.85%)	5/129 (3.88%)	6/130 (4.62%)	6/130 (4.62%)
Vascular disorders												
Hypertension †A	4/129 (3.1%)	6/128 (4.69%)	4/129 (3.1%)	6/129 (4.65%)	9/130 (6.92%)	3/130 (2.31%)	2/129 (1.55%)	3/130 (2.31%)	3/130 (2.31%)	2/129 (1.55%)	5/130 (3.85%)	1/130 (0.77%)

† 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.

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