ID: SYR-322_305 Efficacy and Safety of Alogliptin Plus Metformin Compared to Glipizide Plus Metformin in Patients With Type 2 Diabetes Mellitus NCT00856284

Uploaded Record
Results Preview

Close

Hide All

Participant Flow

Recruitment Details: Participants took part in the study at 310 study sites worldwide from 05 March 2009 to 17 October 2012.

Pre-Assignment Details: Participants with type 2 diabetes mellitus experiencing inadequate glycemic control while on metformin therapy were enrolled equally in 1 of 3 treatment groups: alogliptin 12.5 mg once daily (QD), alogliptin 25 mg QD, and glipizide 5 mg QD.

Arm/Group Title	**Metformin + Alogliptin 12.5 mg**	**Metformin + Alogliptin 25 mg**	**Metformin + Glipizide**	Total (Not public)
Arm/Group Description	Alogliptin 12.5 mg, tablets, orally, once daily and the maximum tolerated dose of metformin (1500 mg to 3300 mg daily) for up to 104 weeks.	Alogliptin 25 mg, tablets, orally, once daily and the maximum tolerated dose of metformin (1500 mg to 3300 mg daily) for up to 104 weeks.	Glipizide 5 mg, tablets, orally, once daily and the maximum tolerated dose of metformin (1500 mg to 3300 mg daily) for up to 104 weeks. After at least 2 weeks of treatment but prior to Week 20, participants with persistent hyperglycemia (fasting plasma glucose ≥250 mg/dL) underwent a dose titration of glipizide up to 20 mg in 5-mg increments in 4-week intervals.	
Period Title: Overall Study				
Started	880	885	874	2639
Received Study Drug	873	878	869	2620
Completed	472	493	427	1392
Not Completed	408	392	447	1247
Reason Not Completed				
Hyperglycemic rescue	231	201	235	667
Adverse Event	60	74	82	216
Major protocol deviation	24	16	15	55
Lost to Follow-up	20	22	28	70
Voluntary withdrawal	48	52	62	162
Pregnancy	1	2	0	3
Investigator discretion	9	8	10	27
Other	15	17	14	46
NOTE : "Other" is not sufficiently descriptive for "Other" Reason Not Completed. Please provide a more descriptive label.				
Randomized in error	0	0	1	1
(Not Public)	Not Completed = 408 Total from all reasons = 408	Not Completed = 392 Total from all reasons = 392	Not Completed = 447 Total from all reasons = 447	

Baseline Characteristics

Arm/Group Title	**Metformin + Alogliptin 12.5 mg**	**Metformin + Alogliptin 25 mg**	**Metformin + Glipizide**	**Total**
Arm/Group Description	Alogliptin 12.5 mg, tablets, orally, once daily and the	Alogliptin 25 mg, tablets, orally, once daily and the	Glipizide 5 mg, tablets, orally, once daily and the maximum	

	maximum tolerated dose of metformin (1500 mg to 3300 mg daily) for up to 104 weeks.	maximum tolerated dose of metformin (1500 mg to 3300 mg daily) for up to 104 weeks.	tolerated dose of metformin (1500 mg to 3300 mg daily) for up to 104 weeks. After at least 2 weeks of treatment but prior to Week 20, participants with persistent hyperglycemia (fasting plasma glucose ≥250 mg/dL) underwent a dose titration of glipizide up to 20 mg in 5-mg increments in 4-week intervals.	
Overall Number of Baseline Participants	880	885	874	**2639**
Baseline Analysis Population Description	The Randomized Set included all enrolled subjects who were subsequently randomized.			
Age, Continuous Mean (Standard Deviation) Units: years	55.2 (9.60)	55.5 (9.81)	55.4 (9.60)	55.4 (9.67)
Age, Customized [1] Measure Type: Number Units: participants				
<65 years	734	710	723	2167
	NOTE : The sum of participants in all Categories for the Measure does not equal the Overall Number of Baseline Participants in the Arm/Group.	NOTE : The sum of participants in all Categories for the Measure does not equal the Overall Number of Baseline Participants in the Arm/Group.	NOTE : The sum of participants in all Categories for the Measure does not equal the Overall Number of Baseline Participants in the Arm/Group.	
≥65 years	146	175	151	472
≥75 years	13	17	15	45
	[1] Categories ≥65 years and ≥75 years are not mutually exclusive. Participants ≥75 years are counted in both categories.			
Gender, Male/Female Measure Type: Number Units: participants				
Female	461	433	433	1327
Male	419	452	441	1312
Race/Ethnicity, Customized Measure Type: Number Units: participants				
American Indian or Alaska Native	40	42	36	118
Asian	191	207	203	601
Black or African American	74	66	81	221
Native Hawaiian or Other Pacific Islander	7	1	4	12
White	557	555	533	1645
Multiracial	11	14	17	42
Race/Ethnicity, Customized Measure Type: Number Units: participants				
Hispanic or Latino	192	204	192	588
Not Hispanic or Latino	688	681	682	2051
Body Mass Index (BMI) [1] Mean (Standard Deviation) Units: kg/m^2	31.27 (5.417)	31.27 (5.341)	31.11 (5.320)	31.22 (5.358)
	[1] BMI data available for 879, 885 and 872 participants in each treatment arm, respectively.			
Glycosylated hemoglobin (HbA1c) [1] Mean (Standard Deviation) Units: percentage	7.59 (0.599)	7.61 (0.606)	7.60 (0.617)	7.60 (0.607)
	[1] Mean HbA1c data includes 877, 883 and 870 participants in each treatment arm, respectively.			
Baseline HbA1c Category Measure Type: Number Units: participants				
<8.0%	615	620	613	1848

≥8.0%	265	265	261	791
Diabetes duration [1] Mean (Standard Deviation) Units: years	5.65 (5.324)	5.42 (4.730)	5.48 (4.884)	5.52 (4.985)

[1] Diabetes duration data available for 880, 884 and 874 participants in each treatment arm, respectively.

Metformin dose Mean (Standard Deviation) Units: mg	1825.2 (405.59)	1837.2 (373.06)	1823.4 (390.63)	1828.6 (389.85)
Glomerular filtration rate [1] Mean (Standard Deviation) Units: mL/min/1.73m^2				
MDRD	83.04 (16.586)	82.35 (16.199)	82.28 (16.994)	82.56 (16.591)
Cockcroft-Gault	109.3 (33.40)	109.3 (32.85)	108.0 (32.64)	108.9 (32.96)

[1] Glomerular filtration rate (GFR) was calculated using the modification of diet in renal disease (MDRD) formula and the Cockcroft-Gault formula. Data include 877, 883 and 870 participants in each treatment arm, respectively.

Smoking history Measure Type: Number Units: participants				
Never smoked	543	586	578	1707
Current smoker	135	122	111	368
Ex-smoker	202	177	185	564

Outcome Measures

1. Primary Outcome

Title: Change From Baseline in Glycosylated Hemoglobin (HbA1c) at Week 52

Description: The change from Baseline to Week 52 in HbA1c (the concentration of glucose bound to hemoglobin as a percent of the absolute maximum that can be bound). The least squares (LS) means are from an analysis of covariance (ANCOVA) model with treatment, study schedule, and geographic region as class variables, and Baseline metformin dose and Baseline HbA1c as covariates.

Time Frame: Baseline and Week 52

Safety Issue? No

Outcome Measure Data

Analysis Population Description

The Per-protocol set included all randomized patients who took at least 1 dose of double-blind study drug, with a Baseline assessment and at least 1 post-baseline assessment for that variable and who had no major protocol violations. Last observation carried forward (LOCF) was used.

Arm/Group Title	**Metformin + Alogliptin 12.5 mg**	**Metformin + Alogliptin 25 mg**	**Metformin + Glipizide**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and the maximum tolerated dose of metformin (1500 mg to 3300 mg daily) for up to 104 weeks.	Alogliptin 25 mg, tablets, orally, once daily and the maximum tolerated dose of metformin (1500 mg to 3300 mg daily) for up to 104 weeks.	Glipizide 5 mg, tablets, orally, once daily and the maximum tolerated dose of metformin (1500 mg to 3300 mg daily) for up to 104 weeks. After at least 2 weeks of treatment but prior to Week 20, participants with persistent hyperglycemia (fasting plasma glucose ≥250 mg/dL) underwent a dose titration of glipizide up to 20 mg in 5-mg increments in 4-week intervals.
Number of Participants Analyzed	371	382	336
Least Squares Mean (Standard Error) Units: percentage glycosylated hemoglobin	-0.81 (0.027)	-0.76 (0.027)	-0.73 (0.029)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Metformin + Alogliptin 25 mg, Metformin + Glipizide
	Comments	The null hypotheses were tested in a fixed order at the 1-sided 0.0125 significance level at Weeks 52 and 104, independently: H01: Alogliptin 25 mg was inferior in HbA1c change from Baseline vs glipizide. H02: Alogliptin 12.5 mg was inferior vs glipizide. H03: Alogliptin 25 mg was not superior vs glipizide. H04: Alogliptin 12.5 mg was not superior vs glipizide. Each subsequent null hypothesis was tested only if all previously tested null hypotheses were rejected with respect to Weeks 52 and 104.
	Non-Inferiority or Equivalence Analysis?	Yes
	Comments	Non-inferiority was met if the upper limit of the 1-sided 98.75% CI for the difference between alogliptin 25 mg and glipizide in HbA1c change from Baseline was less than 0.3%. If the null hypothesis H01 was rejected, then H02 was tested to show noninferiority of alogliptin 12.5 mg versus glipizide with a margin of 0.3%. Non-inferiority was met if the upper limit of the 1-sided 98.75% CI for the difference between alogliptin 12.5 mg and glipizide in HbA1c change from Baseline was less than 0.3%.
Method of Estimation	**Estimation Parameter**	Other[LS Mean Difference]
	Estimated Value	-0.03

	Confidence Interval	(1-Sided) 98.75% 0.059
	Estimation Comments	[Not specified]

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Metformin + Alogliptin 12.5 mg, Metformin + Glipizide
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	Yes
	Comments	Non-inferiority was met if the upper limit of the 1-sided 98.75% CI for the difference between alogliptin 25 mg and glipizide in HbA1c change from Baseline was less than 0.3%. If the null hypothesis H01 was rejected, then H02 was tested to show noninferiority of alogliptin 12.5 mg versus glipizide with a margin of 0.3%. Non-inferiority was met if the upper limit of the 1-sided 98.75% CI for the difference between alogliptin 12.5 mg and glipizide in HbA1c change from Baseline was less than 0.3%.
Method of Estimation	**Estimation Parameter**	Other[LS Mean Difference]
	Estimated Value	-0.09
	Confidence Interval	(1-Sided) 98.75% 0.003
	Estimation Comments	[Not specified]

2. Primary Outcome

Title:	Change From Baseline in Glycosylated Hemoglobin (HbA1c) at Week 104
Description:	The change from Baseline to Week 104 in HbA1c (the concentration of glucose bound to hemoglobin as a percent of the absolute maximum that can be bound). The least squares (LS) means are from an analysis of covariance (ANCOVA) model with treatment, study schedule, and geographic region as class variables, and Baseline metformin dose and Baseline HbA1c as covariates.
Time Frame:	Baseline and Week 104
Safety Issue?	No

Outcome Measure Data

Analysis Population Description

The Per-protocol set included all randomized patients who took at least 1 dose of double-blind study drug, with a Baseline assessment and at least 1 post-baseline assessment for that variable and who had no major protocol violations. Last observation carried forward was used (LOCF).

Arm/Group Title	**Metformin + Alogliptin 12.5 mg**	**Metformin + Alogliptin 25 mg**	**Metformin + Glipizide**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and the maximum tolerated dose of metformin (1500 mg to 3300 mg daily) for up to 104 weeks.	Alogliptin 25 mg, tablets, orally, once daily and the maximum tolerated dose of metformin (1500 mg to 3300 mg daily) for up to 104 weeks.	Glipizide 5 mg, tablets, orally, once daily and the maximum tolerated dose of metformin (1500 mg to 3300 mg daily) for up to 104 weeks. After at least 2 weeks of treatment but prior to Week 20, participants with persistent hyperglycemia (fasting plasma glucose ≥250 mg/dL) underwent a dose titration of glipizide up to 20 mg in 5-mg increments in 4-week intervals.
Number of Participants Analyzed	371	382	336
Least Squares Mean (Standard Error) Units: percentage glycosylated hemoglobin	-0.68 (0.037)	-0.72 (0.037)	-0.59 (0.039)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Metformin + Alogliptin 25 mg, Metformin + Glipizide
	Comments	The null hypotheses were tested in a fixed order at the 1-sided 0.0125 significance level at Weeks 52 and 104, independently: H01: Alogliptin 25 mg was inferior in HbA1c change from Baseline vs glipizide. H02: Alogliptin 12.5 mg was inferior vs glipizide. H03: Alogliptin 25 mg was not superior vs glipizide. H04: Alogliptin 12.5 mg was not superior vs glipizide. Each subsequent null hypothesis was tested only if all previously tested null hypotheses were rejected with respect to Weeks 52 and 104.
	Non-Inferiority or Equivalence Analysis?	Yes
	Comments	Non-inferiority was met if the upper limit of the 1-sided 98.75% CI for the difference between alogliptin 25 mg and glipizide in HbA1c change from Baseline was less than 0.3%. If the null hypothesis H01 was rejected, then H02 was tested to show noninferiority of alogliptin 12.5 mg versus glipizide with a margin of 0.3%. Non-inferiority was met if the upper limit of the 1-sided 98.75% CI for the difference between alogliptin 12.5 mg and glipizide in HbA1c change from Baseline was less than 0.3%.
Method of Estimation	**Estimation Parameter**	Other[LS Mean Difference]
	Estimated Value	-0.13

	Confidence Interval	(1-Sided) 98.75% -0.006
	Estimation Comments	[Not specified]

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Metformin + Alogliptin 12.5 mg, Metformin + Glipizide
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	Yes
	Comments	Non-inferiority was met if the upper limit of the 1-sided 98.75% CI for the difference between alogliptin 25 mg and glipizide in HbA1c change from Baseline was less than 0.3%. If the null hypothesis H01 was rejected, then H02 was tested to show noninferiority of alogliptin 12.5 mg versus glipizide with a margin of 0.3%. Non-inferiority was met if the upper limit of the 1-sided 98.75% CI for the difference between alogliptin 12.5 mg and glipizide in HbA1c change from Baseline was less than 0.3%.
Method of Estimation	**Estimation Parameter**	Other[LS Mean Difference]
	Estimated Value	-0.09
	Confidence Interval	(1-Sided) 98.75% 0.035
	Estimation Comments	[Not specified]

3. Secondary Outcome

Title:	Change From Baseline in Glycosylated Hemoglobin at Other Time Points
Description:	The change from Baseline over time in HbA1c (the concentration of glucose bound to hemoglobin as a percent of the absolute maximum that can be bound). LS means are from an ANCOVA model with treatment, study schedule, and geographic region as class variables, and Baseline metformin dose and Baseline HbA1c as covariates.
Time Frame:	Baseline and Weeks 4, 8, 12, 16, 20, 26, 39, 65, 78, and 91.
Safety Issue?	No

Outcome Measure Data

Analysis Population Description
Per-protocol set; LOCF was used.

Arm/Group Title	**Metformin + Alogliptin 12.5 mg**	**Metformin + Alogliptin 25 mg**	**Metformin + Glipizide**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and the maximum tolerated dose of metformin (1500 mg to 3300 mg daily) for up to 104 weeks.	Alogliptin 25 mg, tablets, orally, once daily and the maximum tolerated dose of metformin (1500 mg to 3300 mg daily) for up to 104 weeks.	Glipizide 5 mg, tablets, orally, once daily and the maximum tolerated dose of metformin (1500 mg to 3300 mg daily) for up to 104 weeks. After at least 2 weeks of treatment but prior to Week 20, participants with persistent hyperglycemia (fasting plasma glucose ≥250 mg/dL) underwent a dose titration of glipizide up to 20 mg in 5-mg increments in 4-week intervals.
Number of Participants Analyzed	371	382	336
Least Squares Mean (Standard Error) Units: percentage of glycosylated hemoglobin			
Week 4 (n=341, 354, 318)	-0.37 (0.020)	-0.40 (0.020)	-0.41 (0.021)

Week 8 (n=370, 382, 336)	-0.56 (0.024)	-0.60 (0.024)	-0.66 (0.025)
Week 12 (n=371, 382, 336)	-0.69 (0.025)	-0.71 (0.025)	-0.78 (0.026)
Week 16 (n=371, 382, 336)	-0.74 (0.026)	-0.76 (0.025)	-0.78 (0.027)
Week 20 (n=371, 382, 336)	-0.76 (0.026)	-0.78 (0.025)	-0.79 (0.027)
Week 26 (n=371, 382, 336)	-0.80 (0.027)	-0.79 (0.026)	-0.80 (0.028)
Week 39 (n=371, 382, 336)	-0.81 (0.026)	-0.81 (0.025)	-0.74 (0.027)
Week 65 (n=371, 382, 336)	-0.81 (0.029)	-0.83 (0.028)	-0.76 (0.030)
Week 78 (n=371, 382, 336)	-0.82 (0.030)	-0.80 (0.030)	-0.73 (0.032)
Week 91 (n=371, 382, 336)	-0.76 (0.033)	-0.77 (0.033)	-0.68 (0.035)

4. Secondary Outcome

Title: Change From Baseline in Fasting Plasma Glucose Over Time

Description: The change from Baseline in fasting plasma glucose (FPG) was assessed at Weeks 2, 4, 8, 12, 16, 20, 26, 39, 52, 65, 78, 91, and 104. LS means are from an ANCOVA model with treatment, study schedule, and geographic region as class variables, and Baseline FPG and Baseline metformin dose as covariates.

Time Frame: Baseline and Weeks 2, 4, 8, 12, 16, 20, 26, 39, 52, 65, 78, 91, and 104.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set, which included all randomized patients who received at least 1 dose of double-blind study drug who had a Baseline assessment and at least 1 post-baseline assessment for FPG. LOCF was used.

Arm/Group Title	**Metformin + Alogliptin 12.5 mg**	**Metformin + Alogliptin 25 mg**	**Metformin + Glipizide**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and the maximum tolerated dose of metformin (1500 mg to 3300 mg daily) for up to 104 weeks.	Alogliptin 25 mg, tablets, orally, once daily and the maximum tolerated dose of metformin (1500 mg to 3300 mg daily) for up to 104 weeks.	Glipizide 5 mg, tablets, orally, once daily and the maximum tolerated dose of metformin (1500 mg to 3300 mg daily) for up to 104 weeks. After at least 2 weeks of treatment but prior to Week 20, participants with persistent hyperglycemia (fasting plasma glucose ≥250 mg/dL) underwent a dose titration of glipizide up to 20 mg in 5-mg increments in 4-week intervals.
Number of Participants Analyzed	867	867	859
Least Squares Mean (Standard Error) Units: mg/dL			
Week 2 (n=781, 803, 777)	-10.2 (0.89)	-11.4 (0.87)	-7.7 (0.89)
Week 4 (n=863, 865, 855)	-10.6 (0.85)	-11.6 (0.85)	-10.2 (0.85)
Week 8 (n=867, 867, 859)	-9.2 (0.91)	-11.6 (0.91)	-9.3 (0.92)
Week 12 (n=867, 867, 859)	-10.7 (0.94)	-11.2 (0.94)	-9.4 (0.95)
Week 16 (n=867, 867, 859)	-8.6 (0.98)	-9.9 (0.98)	-7.1 (0.98)
Week 20 (n=867, 867, 859)	-7.6 (1.02)	-10.1 (1.02)	-5.5 (1.02)
Week 26 (n=867, 867, 859)	-7.5 (1.06)	-10.1 (1.06)	-4.3 (1.06)
Week 39 (n=867, 867, 859)	-6.9 (1.14)	-8.4 (1.14)	-0.6 (1.15)
Week 52 (n=867, 867, 859)	-5.0 (1.22)	-7.0 (1.22)	0.9 (1.23)
Week 65 (n=867, 867, 859)	-3.4 (1.21)	-5.9 (1.21)	1.4 (1.21)
Week 78 (n=867, 867, 859)	-2.8 (1.47)	-5.1 (1.47)	5.1 (1.48)
Week 91 (n=867, 867, 859)	-0.9 (1.27)	-3.4 (1.27)	4.9 (1.28)
Week 104 (n=867, 867, 859)	-0.9 (1.28)	-3.2 (1.28)	5.4 (1.29)

5. Secondary Outcome

Title: Percentage of Participants With Glycosylated Hemoglobin Less Than or Equal to 6.5%

Description: The percentage of participants with HbA1c less than or equal to 6.5% at Weeks 26, 52, 78, and 104. Participants who did not complete the scheduled Week 104 visit were assessed based on their response at the

time of discontinuation.

Time Frame: Weeks 26, 52, 78, and 104.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set. Participants who did not complete the scheduled Week 26, Week 52, Week 78 or Week 104 visit were assessed based on their response at the time of discontinuation.

Arm/Group Title	**Metformin + Alogliptin 12.5 mg**	**Metformin + Alogliptin 25 mg**	**Metformin + Glipizide**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and the maximum tolerated dose of metformin (1500 mg to 3300 mg daily) for up to 104 weeks.	Alogliptin 25 mg, tablets, orally, once daily and the maximum tolerated dose of metformin (1500 mg to 3300 mg daily) for up to 104 weeks.	Glipizide 5 mg, tablets, orally, once daily and the maximum tolerated dose of metformin (1500 mg to 3300 mg daily) for up to 104 weeks. After at least 2 weeks of treatment but prior to Week 20, participants with persistent hyperglycemia (fasting plasma glucose ≥250 mg/dL) underwent a dose titration of glipizide up to 20 mg in 5-mg increments in 4-week intervals.
Number of Participants Analyzed	873	878	869
Measure Type: Number Units: percentage of participants			
Week 26	25.6	26.2	24.8
Week 52	24.5	24.8	20.8
Week 78	24.2	26.4	21.8
Week 104	23.5	24.1	19.0

6. Secondary Outcome

Title: Percentage of Participants With Glycosylated Hemoglobin Less Than or Equal to 7.0%

Description: Percentage of participants with HbA1c ≤ 7.0% at Weeks 26, 52, 78, and 104. Participants who did not complete the scheduled Week 104 visit were assessed based on their response at the time of discontinuation.

Time Frame: Weeks 26, 52, 78, and 104.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set. Participants who did not complete the scheduled Week 26, Week 52, Week 78 or Week 104 visit were assessed based on their response at the time of discontinuation.

Arm/Group Title	**Metformin + Alogliptin 12.5 mg**	**Metformin + Alogliptin 25 mg**	**Metformin + Glipizide**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and the maximum tolerated dose of metformin (1500 mg to 3300 mg daily) for up to 104 weeks.	Alogliptin 25 mg, tablets, orally, once daily and the maximum tolerated dose of metformin (1500 mg to 3300 mg daily) for up to 104 weeks.	Glipizide 5 mg, tablets, orally, once daily and the maximum tolerated dose of metformin (1500 mg to 3300 mg daily) for up to 104 weeks. After at least 2 weeks of treatment but prior to Week 20, participants with persistent hyperglycemia (fasting plasma glucose ≥250 mg/dL) underwent a dose titration of

			glipizide up to 20 mg in 5-mg increments in 4-week intervals.
Number of Participants Analyzed	873	878	869
Measure Type: Number Units: percentage of participants			
Week 26	56.4	59.2	56.1
Week 52	51.7	55.5	47.4
Week 78	48.8	52.4	46.6
Week 104	45.6	48.5	42.8

7. Secondary Outcome

Title: Change From Baseline in Body Weight Over Time

Description: LS Means are from an ANCOVA model with treatment, study schedule and geographic region as class variables, and Baseline weight and Baseline metformin dose as covariates.

Time Frame: Baseline and Weeks 12, 26, 39, 52, 65, 78, 91, and 104.

Safety Issue? No

Outcome Measure Data

Analysis Population Description
Full analysis set, LOCF was used.

Arm/Group Title	**Metformin + Alogliptin 12.5 mg**	**Metformin + Alogliptin 25 mg**	**Metformin + Glipizide**
Arm/Group Description:	Alogliptin 12.5 mg, tablets, orally, once daily and the maximum tolerated dose of metformin (1500 mg to 3300 mg daily) for up to 104 weeks.	Alogliptin 25 mg, tablets, orally, once daily and the maximum tolerated dose of metformin (1500 mg to 3300 mg daily) for up to 104 weeks.	Glipizide 5 mg, tablets, orally, once daily and the maximum tolerated dose of metformin (1500 mg to 3300 mg daily) for up to 104 weeks. After at least 2 weeks of treatment but prior to Week 20, participants with persistent hyperglycemia (fasting plasma glucose ≥250 mg/dL) underwent a dose titration of glipizide up to 20 mg in 5-mg increments in 4-week intervals.

Number of Participants Analyzed	867	868	861
Least Squares Mean (Standard Error) Units: kg			
Week 12	-0.51 (0.076)	-0.53 (0.076)	0.71 (0.077)
Week 26	-0.65 (0.101)	-0.71 (0.101)	0.86 (0.101)
Week 39	-0.60 (0.109)	-0.86 (0.109)	0.97 (0.110)
Week 52	-0.63 (0.117)	-0.90 (0.117)	0.89 (0.117)
Week 65	-0.70 (0.122)	-0.92 (0.122)	0.87 (0.123)
Week 78	-0.78 (0.124)	-0.94 (0.124)	0.88 (0.125)
Week 91	-0.67 (0.127)	-0.88 (0.127)	0.89 (0.127)
Week 104	-0.68 (0.127)	-0.89 (0.127)	0.95 (0.127)

Adverse Events

Time Frame	Collection of adverse events commenced from the time the participant was first administered double-blind study medication until the end of the study and from spontaneous reporting for 30 days after the end of treatment (up to 108 weeks).
Additional Description	At each visit the investigator had to document any occurrence of adverse events and abnormal laboratory findings. Any event spontaneously reported by the participant or observed by the investigator was recorded, irrespective of the relation to study treatment.
Source Vocabulary Name	MedDRA 15.0
Assessment Type	Systematic Assessment

Arm/Group Title	Metformin + Alogliptin 12.5 mg	Metformin + Alogliptin 25 mg	Metformin + Glipizide
Arm/Group Description	Alogliptin 12.5 mg, tablets, orally, once daily and the maximum tolerated dose of metformin (1500 mg to 3300 mg daily) for up to 104 weeks.	Alogliptin 25 mg, tablets, orally, once daily and the maximum tolerated dose of metformin (1500 mg to 3300 mg daily) for up to 104 weeks.	Glipizide 5 mg, tablets, orally, once daily and the maximum tolerated dose of metformin (1500 mg to 3300 mg daily) for up to 104 weeks. After at least 2 weeks of treatment but prior to Week 20, participants with persistent hyperglycemia (fasting plasma glucose ≥250 mg/dL)

underwent a dose titration of glipizide up to 20 mg in 5-mg increments in 4-week intervals.

Serious Adverse Events

	Metformin + Alogliptin 12.5 mg	Metformin + Alogliptin 25 mg	Metformin + Glipizide
	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)
Total	86/873 (9.85%)	97/878 (11.05%)	81/869 (9.32%)
Blood and lymphatic system disorders			
Anaemia † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Iron deficiency anaemia † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Cardiac disorders			
Acute coronary syndrome † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Acute myocardial infarction † A	0/873 (0%)	1/878 (0.11%)	5/869 (0.58%)
Angina pectoris † A	0/873 (0%)	2/878 (0.23%)	1/869 (0.12%)
Angina unstable † A	1/873 (0.11%)	4/878 (0.46%)	4/869 (0.46%)
Arteriosclerosis coronary artery † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Atrial fibrillation † A	1/873 (0.11%)	3/878 (0.34%)	2/869 (0.23%)
Atrial flutter † A	2/873 (0.23%)	2/878 (0.23%)	1/869 (0.12%)
Atrioventricular block † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Atrioventricular block complete † A	1/873 (0.11%)	0/878 (0%)	1/869 (0.12%)
Atrioventricular block second degree † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Bradycardia † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Cardiac failure † A	0/873 (0%)	3/878 (0.34%)	1/869 (0.12%)
Cardiac failure congestive † A	2/873 (0.23%)	1/878 (0.11%)	1/869 (0.12%)
Cardiomyopathy † A	0/873 (0%)	1/878 (0.11%)	1/869 (0.12%)
Congestive cardiomyopathy † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Coronary artery disease † A	5/873 (0.57%)	3/878 (0.34%)	2/869 (0.23%)
Coronary artery occlusion † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Left ventricular failure † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Myocardial infarction † A	0/873 (0%)	1/878 (0.11%)	3/869 (0.35%)
Myocardial ischaemia † A	1/873 (0.11%)	0/878 (0%)	2/869 (0.23%)
Pericardial effusion † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Right ventricular failure † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Silent myocardial infarction † A	0/873 (0%)	2/878 (0.23%)	0/869 (0%)
Tachyarrhythmia † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Ear and labyrinth disorders			
Acute vestibular syndrome † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Vertigo † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Vertigo positional † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Endocrine disorders			
Primary hyperaldosteronism † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Eye disorders			
Cataract † A	1/873 (0.11%)	1/878 (0.11%)	1/869 (0.12%)
Cataract nuclear † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Cataract subcapsular † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Iridocyclitis † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Retinal detachment † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Vision blurred † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Gastrointestinal disorders			
Abdominal pain † A	1/873 (0.11%)	0/878 (0%)	2/869 (0.23%)
Anal fistula † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Colitis † A	2/873 (0.23%)	2/878 (0.23%)	0/869 (0%)
Colitis ischaemic † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Diarrhoea † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Diverticulum † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Dyspepsia † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)

Enterocolitis	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Gastritis † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Gastrointestinal haemorrhage † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Haematemesis † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Haemorrhoids † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Inguinal hernia † A	1/873 (0.11%)	1/878 (0.11%)	1/869 (0.12%)
Intestinal ischaemia † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Mallory-Weiss syndrome † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Nausea † A	0/873 (0%)	1/878 (0.11%)	1/869 (0.12%)
Pancreatitis † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Pancreatitis acute † A	0/873 (0%)	1/878 (0.11%)	1/869 (0.12%)
Umbilical hernia † A	0/873 (0%)	1/878 (0.11%)	1/869 (0.12%)
Umbilical hernia, obstructive † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Upper gastrointestinal haemorrhage † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Vomiting † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
General disorders			
Chest pain † A	0/873 (0%)	2/878 (0.23%)	0/869 (0%)
Hernia † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Non-cardiac chest pain † A	3/873 (0.34%)	4/878 (0.46%)	3/869 (0.35%)
Sudden death † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Hepatobiliary disorders			
Bile duct stone † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Cholecystitis † A	1/873 (0.11%)	1/878 (0.11%)	1/869 (0.12%)
Cholecystitis acute † A	0/873 (0%)	3/878 (0.34%)	0/869 (0%)
Cholelithiasis † A	0/873 (0%)	1/878 (0.11%)	1/869 (0.12%)
Drug-induced liver injury † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Immune system disorders			
Anaphylactic reaction † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Infections and infestations			
Abdominal abscess † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Abscess limb † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Acute sinusitis † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Amoebiasis † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Appendicitis † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Bronchitis † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Cellulitis † A	3/873 (0.34%)	1/878 (0.11%)	3/869 (0.35%)
Cystitis † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Dengue fever † A	1/873 (0.11%)	0/878 (0%)	2/869 (0.23%)
Diverticulitis † A	1/873 (0.11%)	1/878 (0.11%)	1/869 (0.12%)
Gangrene † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Gastroenteritis † A	2/873 (0.23%)	2/878 (0.23%)	0/869 (0%)
Gastroenteritis salmonella † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Hepatitis viral † A	1/873 (0.11%)	0/878 (0%)	2/869 (0.23%)
Lobar pneumonia † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Malaria † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Osteomyelitis † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Pneumocystis jiroveci pneumonia † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Pneumonia † A	1/873 (0.11%)	2/878 (0.23%)	2/869 (0.23%)
Scrotal abscess † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Sepsis † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Septic shock † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Staphylococcal infection † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Urinary tract infection † A	1/873 (0.11%)	1/878 (0.11%)	1/869 (0.12%)
Urosepsis † A	0/873 (0%)	1/878 (0.11%)	1/869 (0.12%)
Injury, poisoning and procedural complications			
Ankle fracture † A	1/873 (0.11%)	2/878 (0.23%)	1/869 (0.12%)
Comminuted fracture † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Craniocerebral injury † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Facial bones fracture † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)

Fall	2/873 (0.23%)	0/878 (0%)	0/869 (0%)
Femur fracture † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Incisional hernia † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Joint dislocation † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Joint injury † A	0/873 (0%)	0/878 (0%)	2/869 (0.23%)
Ligament rupture † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Lower limb fracture † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Patella fracture † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Peripheral nerve injury † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Road traffic accident † A	1/873 (0.11%)	0/878 (0%)	1/869 (0.12%)
Tendon rupture † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Tibia fracture † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Metabolism and nutrition disorders			
Dehydration † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Diabetic ketoacidosis † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Hypoglycaemia † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Musculoskeletal and connective tissue disorders			
Arthralgia † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Back pain † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Bursitis † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Haemarthrosis † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Intervertebral disc protrusion † A	1/873 (0.11%)	1/878 (0.11%)	0/869 (0%)
Muscle haemorrhage † A	2/873 (0.23%)	0/878 (0%)	0/869 (0%)
Musculoskeletal chest pain † A	1/873 (0.11%)	2/878 (0.23%)	1/869 (0.12%)
Myalgia intercostal † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Osteoarthritis † A	2/873 (0.23%)	3/878 (0.34%)	4/869 (0.46%)
Polymyositis † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Spinal column stenosis † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Spinal osteoarthritis † A	1/873 (0.11%)	1/878 (0.11%)	0/869 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Basal cell carcinoma † A	1/873 (0.11%)	1/878 (0.11%)	0/869 (0%)
Bladder transitional cell carcinoma † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Breast cancer † A	2/873 (0.23%)	0/878 (0%)	1/869 (0.12%)
Colon adenoma † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Colon cancer † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Colon cancer stage 0 † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Endometrial cancer † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Gastrointestinal tract adenoma † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Lipoma † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Lung adenocarcinoma † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Non-Hodgkin's lymphoma † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Non-small cell lung cancer stage IIIB † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Ovarian adenoma † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Ovarian cancer † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Rectal cancer metastatic † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Renal oncocytoma † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Small cell lung cancer stage unspecified † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Squamous cell carcinoma of skin † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Uterine leiomyoma † A	2/873 (0.23%)	0/878 (0%)	0/869 (0%)
Nervous system disorders			
Carotid artery stenosis † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Cerebral infarction † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Cerebrovascular accident † A	1/873 (0.11%)	1/878 (0.11%)	3/869 (0.35%)
Dizziness † A	1/873 (0.11%)	0/878 (0%)	1/869 (0.12%)

Epilepsy † A	1/873 (0.11%)	0/878 (0%)	1/869 (0.12%)
Haemorrhagic stroke † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Headache † A	1/873 (0.11%)	1/878 (0.11%)	0/869 (0%)
Intercostal neuralgia † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Ischaemic stroke † A	1/873 (0.11%)	1/878 (0.11%)	0/869 (0%)
Neuralgia † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Parkinsonism † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Presyncope † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Radiculopathy † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Syncope † A	2/873 (0.23%)	0/878 (0%)	1/869 (0.12%)
Tension headache † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Transient ischaemic attack † A	0/873 (0%)	2/878 (0.23%)	0/869 (0%)
VIIth nerve paralysis † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
VIth nerve paralysis † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Vertebrobasilar insufficiency † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Pregnancy, puerperium and perinatal conditions			
Abortion † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Psychiatric disorders			
Alcohol withdrawal syndrome † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Bipolar disorder † A	1/873 (0.11%)	0/878 (0%)	1/869 (0.12%)
Depressed mood † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Depression † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Schizophrenia † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Renal and urinary disorders			
Calculus urinary † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Diabetic nephropathy † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Nephrolithiasis † A	2/873 (0.23%)	2/878 (0.23%)	0/869 (0%)
Renal colic † A	1/873 (0.11%)	1/878 (0.11%)	1/869 (0.12%)
Renal failure acute † A	1/873 (0.11%)	2/878 (0.23%)	3/869 (0.35%)
Urinary retention † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Reproductive system and breast disorders			
Adenomyosis † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Benign prostatic hyperplasia † A	1/873 (0.11%)	1/878 (0.11%)	0/869 (0%)
Cervical dysplasia † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Cervix disorder † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Cystocele † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Dysmenorrhoea † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Epididymitis † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Metrorrhagia † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Ovarian cyst † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Rectocele † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Uterine prolapse † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Uterovaginal prolapse † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Asthma † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Chronic obstructive pulmonary disease † A	2/873 (0.23%)	0/878 (0%)	1/869 (0.12%)
Dyspnoea † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Emphysema † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Granulomatous pneumonitis † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Interstitial lung disease † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Pleuritic pain † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Pulmonary embolism † A	1/873 (0.11%)	0/878 (0%)	1/869 (0.12%)
Pulmonary oedema † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Respiratory failure † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Skin and subcutaneous tissue disorders			
Rash maculo-papular † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)

Vascular disorders			
Aortic aneurysm † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Arterial thrombosis limb † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Deep vein thrombosis † A	1/873 (0.11%)	1/878 (0.11%)	0/869 (0%)
Embolism † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Femoral artery occlusion † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Hypertension † A	1/873 (0.11%)	3/878 (0.34%)	0/869 (0%)
Hypertensive crisis † A	0/873 (0%)	2/878 (0.23%)	1/869 (0.12%)
Iliac artery occlusion † A	0/873 (0%)	1/878 (0.11%)	0/869 (0%)
Orthostatic hypotension † A	0/873 (0%)	0/878 (0%)	1/869 (0.12%)
Peripheral arterial occlusive disease † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)
Thrombophlebitis † A	1/873 (0.11%)	0/878 (0%)	0/869 (0%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 15.0

Other (Not Including Serious) Adverse Events

Frequency Threshold for Reporting Other Adverse Events	3%

	Metformin + Alogliptin 12.5 mg	Metformin + Alogliptin 25 mg	Metformin + Glipizide
	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)
Total	688/873 (78.81%)	687/878 (78.25%)	668/869 (76.87%)
Blood and lymphatic system disorders			
Anaemia † A	16/873 (1.83%)	37/878 (4.21%)	32/869 (3.68%)
Gastrointestinal disorders			
Diarrhoea † A	60/873 (6.87%)	60/878 (6.83%)	63/869 (7.25%)
Nausea † A	28/873 (3.21%)	32/878 (3.64%)	20/869 (2.3%)
General disorders			
Asthenia † A	14/873 (1.6%)	15/878 (1.71%)	27/869 (3.11%)
Fatigue † A	20/873 (2.29%)	19/878 (2.16%)	28/869 (3.22%)
Infections and infestations			
Bronchitis † A	39/873 (4.47%)	36/878 (4.1%)	36/869 (4.14%)
Influenza † A	36/873 (4.12%)	36/878 (4.1%)	42/869 (4.83%)
Nasopharyngitis † A	78/873 (8.93%)	67/878 (7.63%)	61/869 (7.02%)
Sinusitis † A	26/873 (2.98%)	29/878 (3.3%)	23/869 (2.65%)
Upper respiratory tract infection † A	84/873 (9.62%)	90/878 (10.25%)	76/869 (8.75%)
Urinary tract infection † A	41/873 (4.7%)	33/878 (3.76%)	38/869 (4.37%)
Investigations			
Creatinine renal clearance decreased † A	23/873 (2.63%)	34/878 (3.87%)	32/869 (3.68%)
Metabolism and nutrition disorders			
Dyslipidaemia † A	22/873 (2.52%)	20/878 (2.28%)	34/869 (3.91%)
Hypoglycaemia † A	18/873 (2.06%)	6/878 (0.68%)	91/869 (10.47%)
Musculoskeletal and connective tissue disorders			
Arthralgia † A	38/873 (4.35%)	42/878 (4.78%)	40/869 (4.6%)
Back pain † A	54/873 (6.19%)	45/878 (5.13%)	49/869 (5.64%)
Pain in extremity † A	28/873 (3.21%)	28/878 (3.19%)	33/869 (3.8%)
Nervous system disorders			
Dizziness † A	24/873 (2.75%)	24/878 (2.73%)	29/869 (3.34%)
Headache † A	45/873 (5.15%)	60/878 (6.83%)	46/869 (5.29%)
Tremor † A	5/873 (0.57%)	3/878 (0.34%)	29/869 (3.34%)
Respiratory, thoracic and mediastinal disorders			
Cough † A	35/873 (4.01%)	26/878 (2.96%)	33/869 (3.8%)
Vascular disorders			
Hypertension † A	45/873 (5.15%)	67/878 (7.63%)	65/869 (7.48%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 15.0

Limitations and Caveats

The Week 52 results summarized in herein differ from the Week 52 results summarized in an interim analysis, because the per protocol set (PPS) defined for the final analysis included fewer subjects than the PPS defined for the interim analysis.

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.

The first study related publication will be a multi-center publication submitted within 24 months after conclusion or termination of a study at all sites. After such multi site publication, all proposed site publications and presentations will be submitted to sponsor for review 60 days in advance of publication. Site will remove Sponsor confidential information unrelated to study results. Sponsor can delay a proposed publication for another 60 days to preserve intellectual property.

Results Point of Contact

Name/Official Title:	Medical Director, Clinical Science
Organization:	Takeda
Phone:	800-778-2860
Email:	clinicaltrialregistry@tpna.com

Close