ID: SYR-322-TZD-009 Study of Alogliptin Combined With Pioglitazone in Subjects With Type 2 Diabetes Mellitus NCT00286494

Results Preview

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## Participant Flow

Recruitment Details: Participants enrolled at 125 investigative sites in 13 countries from 24 February 2006 to 02 August 2007.

Pre-Assignment Details: Participants with a historical diagnosis of type 2 diabetes mellitus were enrolled in one of 3, once-daily (QD) treatment groups.

| Arm/Group Title | Placebo | Alogliptin 12.5 mg QD | Alogliptin 25 mg QD | Total (Not public) |
|---|---|---|---|---|
| Arm/Group Description | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | |
| Period Title: Overall Study | | | | |
| Started | 97 | 197 | 199 | 493 |
| Completed | 71 | 153 | 160 | 384 |
| Not Completed | 26 | 44 | 39 | 109 |
| Reason Not Completed | | | | |
| Hyperglycemic rescue | 12 | 19 | 18 | 49 |
| Withdrawal by Subject | 2 | 10 | 9 | 21 |
| Adverse Event | 3 | 8 | 6 | 17 |
| Physician Decision | 5 | 5 | 1 | 11 |
| Lost to Follow-up | 3 | 1 | 3 | 7 |
| Protocol Violation | 1 | 1 | 2 | 4 |
| (Not Public) | Not Completed = 26<br>Total from all reasons = 26 | Not Completed = 44<br>Total from all reasons = 44 | Not Completed = 39<br>Total from all reasons = 39 | |

## Baseline Characteristics

| Arm/Group Title | Placebo | Alogliptin 12.5 mg QD | Alogliptin 25 mg QD | Total |
|---|---|---|---|---|
| Arm/Group Description | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | |
| Overall Number of Baseline Participants | 97 | 197 | 199 | **493** |
| Baseline Analysis Population Description | [Not specified] | | | |
| **Age, Customized**<br>**Measure Type: Number**<br>**Units: participants** | | | | |
| <65 years | 83 | 165 | 160 | 408 |
| Between 65 and 74 years | 10 | 29 | 34 | 73 |
| ≥75 years | 4 | 3 | 5 | 12 |
| **Gender, Male/Female**<br>**Measure Type: Number**<br>**Units: participants** | | | | |

| | | | |
|---|---|---|---|
| Female 44 | 88 | 74 | 206 |
| Male 53 | 109 | 125 | 287 |

Outcome Measures

1. Primary Outcome

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

**Description:** The change in the value of glycosylated hemoglobin (the concentration of glucose bound to hemoglobin as a percent of the absolute maximum that can be bound) collected at week 26 or final visit and glycosylated hemoglobin collected at baseline.

**Time Frame:** Baseline and Week 26.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

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

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 95 | 196 | 195 |
| **Least Squares Mean (Standard Error) Units: percentage of Glycosylated Hemoglobin** | -0.19 (0.081) | -0.66 (0.056) | -0.80 (0.056) |

Statistical Analysis 1

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

value for the endpoint as covariates.

| | | |
|---|---|---|
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -0.47 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.67 to -0.28 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 25 mg QD |
| | **Comments** | Null Hypothesis: No difference between treatment and placebo arms in change from baseline in glycosylated hemoglobin at wk 26. Sample size calculated based on normally distributed means. For comparison of either dose vs. placebo (2-sample t-test), study sample size >=500 subjects had 95% power to detect a treatment difference as small as 0.4% in the supportive per protocol analysis set assuming SD=0.8%, 2-sided >0.05 significance level and >=80% of subjects meeting per protocol criteria. |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | <0.001 |
| | **Comments** | A step-down strategy was used for the primary analysis. First, the 25mg dose was compared to placebo at the 2-sided 0.05 significance level. The 12.5 mg dose was compared to placebo only if the comparison of the 25mg dose to placebo was significant. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, treatment regimen and geographic region as class variables; baseline pioglitazone dose and baseline value for the endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -0.61 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.80 to -0.41 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

2. Secondary Outcome

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

**Description:** The change in the value of Glycosylated Hemoglobin (the concentration of glucose bound to hemoglobin as a percent of the absolute maximum that can be bound) collected at week 4 and Glycosylated Hemoglobin collected at baseline.

**Time Frame:** Baseline and Week 4.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least one dose of study drug (Full Analysis Set), and who had measurements at baseline and at the visit. Missing data are imputed using last observation carried forward (LOCF).). Smaller "n" at earlier timepoints due to unavailable prior values to carry forward.

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 90 | 182 | 176 |
| **Least Squares Mean (Standard Error) Units: percentage of Glycosylated Hemoglobin** | -0.14 (0.042) | -0.40 (0.029) | -0.45 (0.030) |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | <0.001 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -0.26 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.36 to -0.16 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

| | | |
|---|---|---|
| **Statistical Analysis** | **Comparison Groups** | Placebo, Alogliptin 25 mg QD |

| | | |
|---|---|---|
| **Overview** | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | <0.001 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -0.31 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.41 to -0.21 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

3. Secondary Outcome

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

**Description:** The change in the value of Glycosylated Hemoglobin (the concentration of glucose bound to hemoglobin as a percent of the absolute maximum that can be bound) collected at week 8 and Glycosylated Hemoglobin collected at baseline.

**Time Frame:** Baseline and Week 8.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

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

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 95 | 196 | 195 |
| **Least Squares Mean (Standard Error) Units: percentage of Glycosylated Hemoglobin** | -0.18 (0.061) | -0.60 (0.042) | -0.73 (0.042) |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |

| | | |
|---|---|---|
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | <0.001 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -0.42 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.56 to -0.27 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 25 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | <0.001 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -0.55 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.69 to -0.40 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

4. Secondary Outcome

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

**Description:** The change in the value of Glycosylated Hemoglobin (the concentration of glucose bound to hemoglobin as a percent of the absolute maximum that can be bound) collected at week 12 and Glycosylated Hemoglobin collected at baseline.

**Time Frame:** Baseline and Week 12.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

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

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 95 | 196 | 195 |
| **Least Squares Mean (Standard Error) Units: percentage of Glycosylated Hemoglobin** | -0.23 (0.069) | -0.70 (0.048) | -0.82 (0.048) |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | <0.001 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -0.46 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.63 to -0.30 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 25 mg QD |
| | **Comments** | [Not specified] |

| | | |
|---|---|---|
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | <0.001 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -0.59 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.75 to -0.43 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

5. Secondary Outcome

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

**Description:** The change in the value of Glycosylated Hemoglobin (the concentration of glucose bound to hemoglobin as a percent of the absolute maximum that can be bound) collected at week 16 and Glycosylated Hemoglobin collected at baseline.

**Time Frame:** Baseline and Week 16.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

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

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 95 | 196 | 195 |
| **Least Squares Mean (Standard Error) Units: percentage of Glycosylated Hemoglobin** | -0.26 (0.076) | -0.70 (0.053) | -0.84 (0.053) |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |

| | | |
|---|---|---|
| **Statistical Test of Hypothesis** | **P-Value** | <0.001 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -0.45 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.63 to -0.26 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 25 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | <0.001 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -0.58 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.76 to -0.40 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

6. Secondary Outcome

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

**Description:** The change in the value of Glycosylated Hemoglobin (the concentration of glucose bound to hemoglobin as a percent of the absolute maximum that can be bound) collected at week 20 and Glycosylated Hemoglobin collected at baseline.

**Time Frame:** Baseline and Week 20.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least one dose of study drug (Full Analysis Set), and who had measurements at

baseline and at the visit. Missing data are imputed using last observation carried forward (LOCF).

| Arm/Group Title | Placebo | Alogliptin 12.5 mg QD | Alogliptin 25 mg QD |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 95 | 196 | 195 |
| **Least Squares Mean (Standard Error) Units: percentage of Glycosylated Hemoglobin** | -0.27 (0.078) | -0.68 (0.055) | -0.82 (0.055) |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | <0.001 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -0.41 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.60 to -0.22 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 25 mg QD |
| | **Comments** | [Not specified] |

| | | |
|---|---|---|
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | <0.001 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -0.55 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.74 to -0.36 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

7. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 1.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least one dose of study drug (Full Analysis Set), and who had measurements at baseline and at the visit. Missing data are imputed using last observation carried forward (LOCF).Smaller "n" at earlier timepoints due to unavailable prior values to carry forward.

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 88 | 176 | 171 |
| **Least Squares Mean (Standard Error) Units: mg/dL** | -2.7 (3.11) | -14.2 (2.20) | -18.2 (2.22) |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |

| | | |
|---|---|---|
| **Statistical Test of Hypothesis** | **P-Value** | 0.003 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -11.4 |
| | **Confidence Interval** | (2-Sided) 95%<br>-18.9 to -3.9 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 25 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | <0.001 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -15.5 |
| | **Confidence Interval** | (2-Sided) 95%<br>-23.0 to -8.0 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

8. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 2.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least one dose of study drug (Full Analysis Set), and who had measurements at baseline and at the visit. Missing data are imputed using last observation carried forward (LOCF).Smaller "n" at earlier timepoints due to unavailable prior values to carry forward.

| Arm/Group Title | Placebo | Alogliptin 12.5 mg QD | Alogliptin 25 mg QD |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 97 | 189 | 193 |
| **Least Squares Mean (Standard Error) Units: mg/dL** | -1.8 (2.97) | -21.0 (2.13) | -21.2 (2.10) |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | <0.001 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -19.2 |
| | **Confidence Interval** | (2-Sided) 95%<br>-26.4 to -11.9 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 25 mg QD |
| | **Comments** | [Not specified] |

| | | |
|---|---|---|
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | <0.001 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -19.4 |
| | **Confidence Interval** | (2-Sided) 95%<br>-26.6 to -12.3 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

9. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 4.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least one dose of study drug (Full Analysis Set), and who had measurements at baseline and at the visit. Missing data are imputed using last observation carried forward (LOCF).Smaller "n" at earlier timepoints due to unavailable prior values to carry forward

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 97 | 194 | 197 |
| **Least Squares Mean (Standard Error) Units: mg/dL** | -3.1 (2.88) | -23.7 (2.04) | -26.0 (2.02) |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |

| | | |
|---|---|---|
| **Statistical Test of Hypothesis** | **P-Value** | <0.001 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -20.6 |
| | **Confidence Interval** | (2-Sided) 95%<br>-27.5 to -13.6 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 25 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | <0.001 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -23.0 |
| | **Confidence Interval** | (2-Sided) 95%<br>-29.9 to -16.0 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

10. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 8.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

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

| Arm/Group Title | Placebo | Alogliptin 12.5 mg QD | Alogliptin 25 mg QD |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 97 | 196 | 197 |
| **Least Squares Mean (Standard Error) Units: mg/dL** | -6.1 (3.26) | -22.6 (2.30) | -27.1 (2.29) |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | <0.001 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -16.5 |
| | **Confidence Interval** | (2-Sided) 95%<br>-24.4 to -8.7 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

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

| | | |
|---|---|---|
| | **or Equivalence Analysis?** | |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | <0.001 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -21.1 |
| | **Confidence Interval** | (2-Sided) 95%<br>-28.9 to -13.3 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

11. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 12.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

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

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 97 | 196 | 197 |
| **Least Squares Mean (Standard Error) Units: mg/dL** | -9.9 (3.33) | -20.4 (2.34) | -26.2 (2.33) |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of** | **P-Value** | 0.011 |

| | | |
|---|---|---|
| **Hypothesis** | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -10.4 |
| | **Confidence Interval** | (2-Sided) 95%<br>-18.5 to -2.4 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 25 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | <0.001 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -16.3 |
| | **Confidence Interval** | (2-Sided) 95%<br>-24.3 to -8.3 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

12. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 16.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

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

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|

| | | | |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 97 | 196 | 197 |
| **Least Squares Mean (Standard Error) Units: mg/dL** | -8.3 (3.71) | -18.3 (2.61) | -22.8 (2.60) |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.029 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -10.0 |
| | **Confidence Interval** | (2-Sided) 95%<br>-18.9 to -1.0 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

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

| | | |
|---|---|---|
| | **or Equivalence Analysis?** | |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.002 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -14.4 |
| | **Confidence Interval** | (2-Sided) 95%<br>-23.3 to -5.5 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

13. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 20.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

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

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 97 | 196 | 197 |
| **Least Squares Mean (Standard Error) Units: mg/dL** | -6.4 (3.58) | -21.9 (2.52) | -21.6 (2.51) |

Statistical Analysis 1

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

| | | |
|---|---|---|
| **Hypothesis** | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -15.6 |
| | **Confidence Interval** | (2-Sided) 95%<br>-24.2 to -6.9 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 25 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | <0.001 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -15.2 |
| | **Confidence Interval** | (2-Sided) 95%<br>-23.8 to -6.7 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

14. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 26.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

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

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|

| | | | |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 97 | 196 | 197 |
| **Least Squares Mean (Standard Error) Units: mg/dL** | -5.7 (3.81) | -19.7 (2.68) | -19.9 (2.67) |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.003 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -13.9 |
| | **Confidence Interval** | (2-Sided) 95%<br>-23.1 to -4.8 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

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

| | | |
|---|---|---|
| | **or Equivalence Analysis?** | |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.003 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -14.1 |
| | **Confidence Interval** | (2-Sided) 95%<br>-23.3 to -5.0 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

15. Secondary Outcome

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

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

**Time Frame:** 26 Weeks.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least one dose of study drug (Full Analysis Set) and had at least 1 post-baseline FPG measurement.

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 97 | 196 | 198 |
| **Measure Type: Number Units: participants** | 43 | 49 | 43 |

Statistical Analysis 1

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

| | | |
|---|---|---|
| | **Method** | Regression, Logistic |
| | **Comments** | Logistic regression model includes effects for treatment, geographic region, baseline pioglitazone dose, baseline treatment regimen, & baseline HbA1c. |
| **Method of Estimation** | **Estimation Parameter** | Odds Ratio (OR) |
| | **Estimated Value** | 0.271 |
| | **Confidence Interval** | (2-Sided) 95%<br>0.147 to 0.499 |
| | **Estimation Comments** | Odd's Ratio (OR) compares alogliptin arm versus placebo.<br>OR <1.0 indicates lower incidence compared to placebo. |

Statistical Analysis 2

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 25 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | <0.001 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | Regression, Logistic |
| | **Comments** | Logistic regression model includes effects for treatment, geographic region, baseline pioglitazone dose, baseline treatment regimen, & baseline HbA1c. |
| **Method of Estimation** | **Estimation Parameter** | Odds Ratio (OR) |
| | **Estimated Value** | 0.235 |
| | **Confidence Interval** | (2-Sided) 95%<br>0.126 to 0.438 |
| | **Estimation Comments** | Odd's Ratio (OR) compares alogliptin arm versus placebo.<br>OR <1.0 indicates lower incidence compared to placebo. |

16. Secondary Outcome

**Title:** Number of Participants Requiring Rescue.

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

**Time Frame:** 26 Weeks.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least one dose of study drug (Full Analysis Set)and at least 1 post-baseline measurement.

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

| | | | |
|---|---|---|---|
| **Number of Participants Analyzed** | 97 | 196 | 199 |
| **Measure Type: Number Units: participants** | 12 | 19 | 18 |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.266 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | Regression, Logistic |
| | **Comments** | Logistic regression model includes effects for treatment, geographic region, baseline pioglitazone dose, baseline treatment regimen & baseline HbA1c. |
| **Method of Estimation** | **Estimation Parameter** | Odds Ratio (OR) |
| | **Estimated Value** | 0.628 |
| | **Confidence Interval** | (2-Sided) 95%<br>0.277 to 1.425 |
| | **Estimation Comments** | Odd's Ratio (OR) compares alogliptin arm versus placebo. OR <1.0 indicates lower incidence compared to placebo. |

Statistical Analysis 2

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

| | | |
|---|---|---|
| **Statistical Test of Hypothesis** | **P-Value** | 0.315 |
| | **Comments** | [Not specified] |
| | **Method** | Regression, Logistic |
| | **Comments** | Logistic regression model includes effects for treatment, geographic region, baseline pioglitazone dose, baseline treatment regimen & baseline HbA1c. |
| **Method of Estimation** | **Estimation Parameter** | Odds Ratio (OR) |
| | **Estimated Value** | 0.658 |
| | **Confidence Interval** | (2-Sided) 95%<br>0.292 to 1.487 |
| | **Estimation Comments** | Odd's Ratio (OR) compares alogliptin arm versus placebo.<br>OR <1.0 indicates lower incidence compared to placebo. |

17. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 4.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least one dose of study drug (Full Analysis Set), and who had measurements at baseline and at the visit. Missing data are imputed using last observation carried forward (LOCF). Smaller "n" at earlier timepoints due to unavailable prior values to carry forward.

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 87 | 172 | 169 |
| **Least Squares Mean (Standard Error) Units: pmol/L** | -0.7 (1.74) | -7.0 (1.24) | -5.6 (1.25) |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.003 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment |

| | | |
|---|---|---|
| | | regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -6.4 |
| | **Confidence Interval** | (2-Sided) 95%<br>-10.6 to -2.1 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 25 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.023 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -4.9 |
| | **Confidence Interval** | (2-Sided) 95%<br>-9.1 to -0.7 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

18. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 8.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least one dose of study drug (Full Analysis Set), and who had measurements at baseline and at the visit. Missing data are imputed using last observation carried forward (LOCF). Smaller "n" at earlier timepoints due to unavailable prior values to carry forward.

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, |

| | | | |
|---|---|---|---|
| | tablets, orally, once daily for up to 26 weeks. | tablets, orally, once daily for up to 26 weeks. | tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 92 | 186 | 188 |
| **Least Squares Mean (Standard Error) Units: pmol/L** | -2.3 (1.70) | -6.5 (1.19) | -3.7 (1.19) |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.043 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -4.2 |
| | **Confidence Interval** | (2-Sided) 95%<br>-8.3 to -0.1 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 25 mg QD |
| | **Comments** | [Not specified] |

| | | |
|---|---|---|
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.489 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -1.4 |
| | **Confidence Interval** | (2-Sided) 95%<br>-5.5 to 2.6 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

19. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 12.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

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

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 92 | 186 | 188 |
| **Least Squares Mean (Standard Error) Units: pmol/L** | 0.6 (1.88) | -3.6 (1.33) | -3.8 (1.32) |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical** | **P-Value** | 0.068 |

| | | |
|---|---|---|
| **Test of Hypothesis** | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -4.2 |
| | **Confidence Interval** | (2-Sided) 95%<br>-8.8 to 0.3 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 25 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.056 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -4.4 |
| | **Confidence Interval** | (2-Sided) 95%<br>-8.9 to 0.1 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

20. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 16.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

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

| Arm/Group Title | Placebo | Alogliptin 12.5 mg QD | Alogliptin 25 mg QD |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 92 | 186 | 188 |
| **Least Squares Mean (Standard Error) Units: pmol/L** | -3.1 (1.89) | -3.5 (1.33) | -3.1 (1.32) |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.884 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -0.3 |
| | **Confidence Interval** | (2-Sided) 95%<br>-4.9 to 4.2 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

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

| | | |
|---|---|---|
| | **or Equivalence Analysis?** | |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.993 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | 0.0 |
| | **Confidence Interval** | (2-Sided) 95%<br>-4.5 to 4.5 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

21. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 20.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

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

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 92 | 186 | 188 |
| **Least Squares Mean (Standard Error) Units: pmol/L** | -0.9 (1.67) | -6.2 (1.18) | -3.9 (1.17) |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of** | **P-Value** | 0.009 |

| | | |
|---|---|---|
| **Hypothesis** | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -5.3 |
| | **Confidence Interval** | (2-Sided) 95%<br>-9.4 to -1.3 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 25 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.143 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -3.0 |
| | **Confidence Interval** | (2-Sided) 95%<br>-7.0 to 1.0 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

22. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 26.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

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

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|

| | | | |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 92 | 186 | 188 |
| **Least Squares Mean (Standard Error) Units: pmol/L** | -1.0 (1.9) | -5.1 (1.34) | -1.7 (1.33) |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.080 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -4.1 |
| | **Confidence Interval** | (2-Sided) 95%<br>-8.6 to 0.5 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

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

| | | |
|---|---|---|
| | **or Equivalence Analysis?** | |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.782 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -0.6 |
| | **Confidence Interval** | (2-Sided) 95%<br>-5.2 to 3.9 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

23. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 4.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least one dose of study drug (Full Analysis Set), and who had measurements at baseline and at the visit. Missing data are imputed using last observation carried forward (LOCF). Smaller "n" at earlier timepoints due to unavailable prior values to carry forward.

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 86 | 166 | 165 |
| **Least Squares Mean (Standard Error) Units: mcIU/mL** | -0.09 (0.694) | -1.08 (0.501) | -0.97 (0.501) |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of** | **P-Value** | 0.249 |

| | | |
|---|---|---|
| **Hypothesis** | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -0.99 |
| | **Confidence Interval** | (2-Sided) 95%<br>-2.68 to 0.70 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 25 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.303 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -0.88 |
| | **Confidence Interval** | (2-Sided) 95%<br>-2.56 to 0.80 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

24. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 8.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

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

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|

| | | | |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 91 | 181 | 187 |
| **Least Squares Mean (Standard Error) Units: mcIU/mL** | -0.17 (0.748) | -0.82 (0.531) | 0.21 (0.522) |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.478 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -0.65 |
| | **Confidence Interval** | (2-Sided) 95%<br>-2.46 to 1.15 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

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

| | | |
|---|---|---|
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.674 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | 0.38 |
| | **Confidence Interval** | (2-Sided) 95%<br>-1.41 to 2.17 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

25. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 12.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

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

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 91 | 181 | 187 |
| **Least Squares Mean (Standard Error) Units: mcIU/mL** | 0.00 (1.085) | 0.43 (0.771) | -0.58 (0.757) |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.743 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |

| | | |
|---|---|---|
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | 0.44 |
| | **Confidence Interval** | (2-Sided) 95%<br>-2.18 to 3.06 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 25 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.662 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -0.58 |
| | **Confidence Interval** | (2-Sided) 95%<br>-3.18 to 2.02 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

26. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 16.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

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

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, |

| | | | |
|---|---|---|---|
| | tablets, orally, once daily for up to 26 weeks. | tablets, orally, once daily for up to 26 weeks. | tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 91 | 181 | 187 |
| **Least Squares Mean (Standard Error) Units: mcIU/mL** | -0.85 (0.701) | -0.10 (0.501) | -0.16 (0.492) |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.390 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | 0.75 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.96 to 2.45 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

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

| | | |
|---|---|---|
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.423 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | 0.69 |
| | **Confidence Interval** | (2-Sided) 95%<br>-1.00 to 2.38 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

27. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 20.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

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

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 91 | 181 | 187 |
| **Least Squares Mean (Standard Error) Units: mcIU/mL** | -0.19 (0.690) | -0.40 (0.490) | -0.33 (0.481) |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.807 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |

| | | |
|---|---|---|
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -0.21 |
| | **Confidence Interval** | (2-Sided) 95%<br>-1.87 to 1.46 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 25 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.867 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -0.14 |
| | **Confidence Interval** | (2-Sided) 95%<br>-1.79 to 1.51 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

28. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 26.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least one dose of study drug (Full Analysis Set), and who had measurements at baseline and at the visit. Missing data are imputed using last observation carried forward (LOCF). Smaller "n" at earlier timepoints due to unavailable prior values to carry forward.

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

| | | | |
|---|---|---|---|
| | pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 91 | 181 | 187 |
| **Least Squares Mean (Standard Error) Units: mcIU/mL** | -0.81 (0.711) | -0.19 (0.505) | 0.00 (0.495) |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.483 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | 0.61 |
| | **Confidence Interval** | (2-Sided) 95%<br>-1.10 to 2.33 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 25 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority** | |

| | | |
|---|---|---|
| | **or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.352 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | 0.81 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.89 to 2.51 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

29. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 4.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least one dose of study drug (Full Analysis Set), and who had measurements at baseline and at the visit. Missing data are imputed using last observation carried forward (LOCF). Smaller "n" at earlier timepoints due to unavailable prior values to carry forward.

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 86 | 166 | 165 |
| **Least Squares Mean (Standard Error) Units: ratio** | 0.006 (0.0144) | -0.051 (0.0104) | -0.053 (0.0104) |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |

| | | |
|---|---|---|
| **Statistical Test of Hypothesis** | **P-Value** | 0.001 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -0.057 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.092 to -0.022 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 25 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.001 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -0.059 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.093 to -0.024 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

30. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 8.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

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

| Arm/Group Title | Placebo | Alogliptin 12.5 mg QD | Alogliptin 25 mg QD |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 91 | 181 | 187 |
| **Least Squares Mean (Standard Error) Units: ratio** | -0.006 (0.0145) | -0.055 (0.0103) | -0.057 (0.0101) |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.006 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -0.049 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.084 to -0.014 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

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

| | | |
|---|---|---|
| | **or Equivalence Analysis?** | |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.004 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -0.051 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.086 to -0.016 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

31. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 12.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

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

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 91 | 181 | 187 |
| **Least Squares Mean (Standard Error) Units: ratio** | 0.017 (0.0190) | -0.029 (0.0135) | -0.040 (0.0132) |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of** | **P-Value** | 0.050 |

| | | |
|---|---|---|
| **Hypothesis** | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -0.046 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.092 to 0.000 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 25 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.014 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -0.057 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.102 to -0.012 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

32. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 16.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

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

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|

| | | | |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 91 | 181 | 187 |
| **Least Squares Mean (Standard Error) Units: ratio** | -0.015 (0.0153) | -0.042 (0.0109) | -0.045 (0.0107) |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.144 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -0.027 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.064 to 0.009 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

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

| | | |
|---|---|---|
| | **or Equivalence Analysis?** | |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.105 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -0.030 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.067 to 0.006 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

33. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 20.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

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

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 91 | 181 | 187 |
| **Least Squares Mean (Standard Error) Units: ratio** | 0.012 (0.0168) | -0.047 (0.0119) | -0.040 (0.0117) |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of** | **P-Value** | 0.004 |

| | | |
|---|---|---|
| **Hypothesis** | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -0.059 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.100 to -0.019 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 25 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.012 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -0.051 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.092 to -0.011 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

34. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 26.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

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

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|

| | | | |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 91 | 181 | 187 |
| **Least Squares Mean (Standard Error) Units: ratio** | 0.015 (0.0185) | -0.035 (0.0131) | -0.022 (0.0129) |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.028 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -0.050 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.095 to -0.005 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

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

| | | |
|---|---|---|
| | **or Equivalence Analysis?** | |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.093 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -0.038 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.082 to 0.006 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

35. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 4.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least one dose of study drug (Full Analysis Set), and who had measurements at baseline and at the visit. Missing data are imputed using last observation carried forward (LOCF). Smaller "n" at earlier timepoints due to unavailable prior values to carry forward.

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 90 | 181 | 175 |
| **Least Squares Mean (Standard Error) Units: ng/mL** | -0.144 (0.1108) | -0.156 (0.0783) | -0.088 (0.0794) |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of** | **P-Value** | 0.928 |

| | | |
|---|---|---|
| **Hypothesis** | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -0.012 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.280 to 0.255 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 25 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.683 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | 0.056 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.212 to 0.324 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

36. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 8.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

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

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|

| | | | |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 95 | 195 | 194 |
| **Least Squares Mean (Standard Error) Units: ng/mL** | -0.111 (0.1127) | -0.117 (0.0787) | 0.023 (0.0788) |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.967 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -0.006 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.277 to 0.265 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

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

| | | |
|---|---|---|
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.327 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | 0.135 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.135 to 0.405 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

37. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 12.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

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

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 95 | 195 | 194 |
| **Least Squares Mean (Standard Error) Units: ng/mL** | -0.017 (0.1226) | -0.085 (0.0856) | -0.067 (0.0856) |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.649 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |

| | | |
|---|---|---|
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -0.068 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.363 to 0.226 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 25 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.735 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -0.051 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.344 to 0.243 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

38. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 16.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

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

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, |

| | | | |
|---|---|---|---|
| | tablets, orally, once daily for up to 26 weeks. | tablets, orally, once daily for up to 26 weeks. | tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 95 | 195 | 194 |
| **Least Squares Mean (Standard Error) Units: ng/mL** | -0.290 (0.1135) | -0.071 (0.0793) | -0.052 (0.0793) |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.114 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | 0.220 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.053 to 0.492 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

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

| | | |
|---|---|---|
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.086 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | 0.238 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.033 to 0.510 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

39. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 20.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

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

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 95 | 195 | 194 |
| **Least Squares Mean (Standard Error) Units: ng/mL** | -0.255 (0.1029) | -0.228 (0.0718) | -0.123 (0.0719) |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.835 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |

| | | |
|---|---|---|
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | 0.026 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.221 to 0.273 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 25 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.296 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | 0.131 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.115 to 0.378 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

40. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 26.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

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

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, |

| | | | |
|---|---|---|---|
| | tablets, orally, once daily for up to 26 weeks. | tablets, orally, once daily for up to 26 weeks. | tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 95 | 195 | 194 |
| **Least Squares Mean (Standard Error) Units: ng/mL** | -0.356 (0.1071) | -0.233 (0.0748) | -0.133 (0.0748) |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.349 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | 0.123 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.134 to 0.380 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

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

| | | |
|---|---|---|
| | **or Equivalence Analysis?** | |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.089 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | 0.223 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.034 to 0.479 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

41. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 26.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

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

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 97 | 197 | 199 |
| **Measure Type: Number Units: participants** | 5 | 34 | 41 |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.003 |
| | **Comments** | [Not specified] |
| | **Method** | Regression, Logistic |

| | | |
|---|---|---|
| | **Comments** | Logistic regression model includes effects for treatment, geographic region, baseline pioglitazone dose, baseline treatment regimen & baseline HbA1c. |
| **Method of Estimation** | **Estimation Parameter** | Odds Ratio (OR) |
| | **Estimated Value** | 4.815 |
| | **Confidence Interval** | (2-Sided) 95%<br>1.736 to 13.358 |
| | **Estimation Comments** | Odd's Ratio (OR) compares alogliptin arm versus placebo.<br>OR <1.0 indicates lower incidence compared to placebo. |

Statistical Analysis 2

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 25 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | <0.001 |
| | **Comments** | [Not specified] |
| | **Method** | Regression, Logistic |
| | **Comments** | Logistic regression model includes effects for treatment, geographic region, baseline pioglitazone dose, baseline treatment regimen & baseline HbA1c. |
| **Method of Estimation** | **Estimation Parameter** | Odds Ratio (OR) |
| | **Estimated Value** | 5.533 |
| | **Confidence Interval** | (2-Sided) 95%<br>2.017 to 15.176 |
| | **Estimation Comments** | Odd's Ratio (OR) compares alogliptin arm versus placebo.<br>OR <1.0 indicates lower incidence compared to placebo. |

42. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 26.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

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

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 97 | 197 | 199 |

| | | | |
|---|---|---|---|
| **Measure Type: Number<br>Units: participants** | 33 | 87 | 98 |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.029 |
| | **Comments** | [Not specified] |
| | **Method** | Regression, Logistic |
| | **Comments** | Logistic regression model includes effects for treatment, geographic region, baseline pioglitazone dose, baseline treatment regimen & baseline HbA1c. |
| **Method of Estimation** | **Estimation Parameter** | Odds Ratio (OR) |
| | **Estimated Value** | 1.903 |
| | **Confidence Interval** | (2-Sided) 95%<br>1.067 to 3.393 |
| | **Estimation Comments** | Odd's Ratio (OR) compares alogliptin arm versus placebo. OR <1.0 indicates lower incidence compared to placebo. |

Statistical Analysis 2

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

| | | |
|---|---|---|
| **Statistical Test of Hypothesis** | **P-Value** | 0.005 |
| | **Comments** | [Not specified] |
| | **Method** | Regression, Logistic |
| | **Comments** | Logistic regression model includes effects for treatment, geographic region, baseline pioglitazone dose, baseline treatment regiment & baseline HbA1c. |
| **Method of Estimation** | **Estimation Parameter** | Odds Ratio (OR) |
| | **Estimated Value** | 2.301 |
| | **Confidence Interval** | (2-Sided) 95%<br>1.291 to 4.100 |
| | **Estimation Comments** | Odd's Ratio (OR) compares alogliptin arm versus placebo. OR <1.0 indicates lower incidence compared to placebo. |

43. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 26.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

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

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 97 | 197 | 199 |
| **Measure Type: Number Units: participants** | 47 | 127 | 141 |

Statistical Analysis 1

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

| | | |
|---|---|---|
| **Estimation** | **Estimated Value** | 2.783 |
| | **Confidence Interval** | (2-Sided) 95%<br>1.547 to 5.005 |
| | **Estimation Comments** | Odd's Ratio (OR) compares alogliptin arm versus placebo.<br>OR <1.0 indicates lower incidence compared to placebo. |

Statistical Analysis 2

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 25 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | <0.001 |
| | **Comments** | [Not specified] |
| | **Method** | Regression, Logistic |
| | **Comments** | Logistic regression model includes effects for treatment, geographic region, baseline pioglitazone dose, baseline treatment regimen & baseline HbA1c. |
| **Method of Estimation** | **Estimation Parameter** | Odds Ratio (OR) |
| | **Estimated Value** | 3.917 |
| | **Confidence Interval** | (2-Sided) 95%<br>2.147 to 7.146 |
| | **Estimation Comments** | Odd's Ratio (OR) compares alogliptin arm versus placebo.<br>OR <1.0 indicates lower incidence compared to placebo. |

44. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 26.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

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

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 97 | 197 | 199 |
| **Measure Type: Number Units: participants** | 26 | 118 | 128 |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | <0.001 |
| | **Comments** | [Not specified] |
| | **Method** | Regression, Logistic |
| | **Comments** | Logistic regression model includes effects for treatment, geographic region, baseline pioglitazone dose, baseline treatment regimen & baseline HbA1c. |
| **Method of Estimation** | **Estimation Parameter** | Odds Ratio (OR) |
| | **Estimated Value** | 4.134 |
| | **Confidence Interval** | (2-Sided) 95%<br>2.392 to 7.146 |
| | **Estimation Comments** | Odd's Ratio (OR) compares alogliptin arm versus placebo. OR <1.0 indicates lower incidence compared to placebo. |

Statistical Analysis 2

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 25 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | <0.001 |
| | **Comments** | [Not specified] |
| | **Method** | Regression, Logistic |
| | **Comments** | Logistic regression model includes effects for treatment, geographic region, baseline pioglitazone dose, baseline treatment regimen & baseline HbA1c. |
| **Method of Estimation** | **Estimation Parameter** | Odds Ratio (OR) |
| | **Estimated Value** | 5.247 |
| | **Confidence Interval** | (2-Sided) 95%<br>3.027 to 9.094 |
| | **Estimation Comments** | Odd's Ratio (OR) compares alogliptin arm versus placebo. OR <1.0 indicates lower incidence compared to placebo. |

45. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 26.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

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

| Arm/Group Title | Placebo | Alogliptin 12.5 mg QD | Alogliptin 25 mg QD |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 97 | 197 | 199 |
| **Measure Type: Number Units: participants** | 12 | 64 | 73 |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | <0.001 |
| | **Comments** | [Not specified] |
| | **Method** | Regression, Logistic |
| | **Comments** | Logistic regression model includes effects for treatment, geographic region, baseline pioglitazone dose, baseline treatment regimen & baseline HbA1c. |
| **Method of Estimation** | **Estimation Parameter** | Odds Ratio (OR) |
| | **Estimated Value** | 3.670 |
| | **Confidence Interval** | (2-Sided) 95%<br>1.789 to 7.532 |
| | **Estimation Comments** | Odd's Ratio (OR) compares alogliptin arm versus placebo. OR <1.0 indicates lower incidence compared to placebo. |

Statistical Analysis 2

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

| | | |
|---|---|---|
| **Statistical Test of Hypothesis** | **P-Value** | <0.001 |
| | **Comments** | [Not specified] |
| | **Method** | Regression, Logistic |
| | **Comments** | Logistic regression model includes effects for treatment, geographic region, baseline pioglitazone dose, baseline treatment regimen & baseline HbA1c. |
| **Method of Estimation** | **Estimation Parameter** | Odds Ratio (OR) |
| | **Estimated Value** | 4.693 |
| | **Confidence Interval** | (2-Sided) 95% 2.303 to 9.560 |
| | **Estimation Comments** | Odd's Ratio (OR) compares alogliptin arm versus placebo. OR <1.0 indicates lower incidence compared to placebo. |

46. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 26.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

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

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 97 | 197 | 199 |
| **Measure Type: Number Units: participants** | 5 | 32 | 37 |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.015 |
| | **Comments** | [Not specified] |
| | **Method** | Regression, Logistic |
| | **Comments** | Logistic regression model includes effects for treatment, geographic region, baseline pioglitazone dose, baseline treatment regimen & baseline HbA1c. |

| | | |
|---|---|---|
| **Method of Estimation** | **Estimation Parameter** | Odds Ratio (OR) |
| | **Estimated Value** | 3.800 |
| | **Confidence Interval** | (2-Sided) 95%<br>1.300 to 11.107 |
| | **Estimation Comments** | Odd's Ratio (OR) compares alogliptin arm versus placebo.<br>OR <1.0 indicates lower incidence compared to placebo. |

Statistical Analysis 2

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 25 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.002 |
| | **Comments** | [Not specified] |
| | **Method** | Regression, Logistic |
| | **Comments** | Logistic regression model includes effects for treatment, geographic region, baseline pioglitazone dose, baseline treatment regimen & baseline HbA1c. |
| **Method of Estimation** | **Estimation Parameter** | Odds Ratio (OR) |
| | **Estimated Value** | 5.196 |
| | **Confidence Interval** | (2-Sided) 95%<br>1.806 to 14.950 |
| | **Estimation Comments** | Odd's Ratio (OR) compares alogliptin arm versus placebo.<br>OR <1.0 indicates lower incidence compared to placebo. |

47. Secondary Outcome

**Title:** Number of Participants With Glycosylated Hemoglobin Decrease From Baseline ≥ 2.0%.

**Description:** The number of participants with a decrease from baseline in the percentage of glycosylated hemoglobin (the percentage of hemoglobin that is bound to glucose) greater than or equal to 2.0% during the 26 week study.

**Time Frame:** Baseline and Week 26.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

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

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 97 | 197 | 199 |
| **Measure Type: Number Units: participants** | 3 | 12 | 14 |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.364 |
| | **Comments** | [Not specified] |
| | **Method** | Regression, Logistic |
| | **Comments** | Logistic regression model includes effects for treatment, geographic region, baseline pioglitazone dose, baseline treatment regimen & baseline HbA1c. |
| **Method of Estimation** | **Estimation Parameter** | Odds Ratio (OR) |
| | **Estimated Value** | 1.959 |
| | **Confidence Interval** | (2-Sided) 95%<br>0.459 to 8.362 |
| | **Estimation Comments** | Odd's Ratio (OR) compares alogliptin arm versus placebo. OR <1.0 indicates lower incidence compared to placebo. |

Statistical Analysis 2

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 25 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.146 |
| | **Comments** | [Not specified] |
| | **Method** | Regression, Logistic |
| | **Comments** | Logistic regression model includes effects for treatment, geographic region, baseline pioglitazone dose, baseline treatment regimen & baseline HbA1c. |
| **Method of Estimation** | **Estimation Parameter** | Odds Ratio (OR) |
| | **Estimated Value** | 2.849 |
| | **Confidence Interval** | (2-Sided) 95%<br>0.696 to 11.672 |
| | **Estimation Comments** | Odd's Ratio (OR) compares alogliptin arm versus placebo. OR <1.0 indicates lower incidence compared to placebo. |

48. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 8.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

Randomized participants who received at least one dose of study drug (Full Analysis Set), and who had measurements at baseline and at the visit. Missing data are imputed using last observation carried forward (LOCF). Smaller "n" at earlier timepoints due to unavailable prior values to carry forward.

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 93 | 190 | 186 |
| **Least Squares Mean (Standard Error) Units: kg** | 0.36 (0.228) | 0.46 (0.160) | 0.39 (0.161) |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.718 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose,baseline value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | 0.10 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.45 to 0.65 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 25 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority** | |

| | | |
|---|---|---|
| | **or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.906 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | 0.03 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.52 to 0.58 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

49. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 12.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

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

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 94 | 193 | 189 |
| **Least Squares Mean (Standard Error) Units: kg** | 0.60 (0.267) | 0.74 (0.187) | 0.64 (0.188) |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of** | **P-Value** | 0.672 |

| | | |
|---|---|---|
| **Hypothesis** | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | 0.14 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.50 to 0.78 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 25 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.922 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | 0.03 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.61 to 0.67 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

50. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 20.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

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

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|

| | | | |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 94 | 193 | 189 |
| **Least Squares Mean (Standard Error) Units: kg** | 0.94 (0.318) | 1.14 (0.222) | 0.93 (0.224) |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.607 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | 0.20 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.56 to 0.96 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

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

| | | |
|---|---|---|
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.985 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | -0.01 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.77 to 0.76 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

51. Secondary Outcome

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

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

**Time Frame:** Baseline and Week 26.

**Safety Issue?** No

Outcome Measure Data

Analysis Population Description

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

| Arm/Group Title | **Placebo** | **Alogliptin 12.5 mg QD** | **Alogliptin 25 mg QD** |
|---|---|---|---|
| Arm/Group Description: | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |
| **Number of Participants Analyzed** | 94 | 193 | 189 |
| **Least Squares Mean (Standard Error) Units: kg** | 1.04 (0.329) | 1.46 (0.230) | 1.09 (0.232) |

Statistical Analysis 1

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 12.5 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.294 |
| | **Comments** | No multiplicity adjustments. |

| | | |
|---|---|---|
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | 0.42 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.37 to 1.22 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

Statistical Analysis 2

| | | |
|---|---|---|
| **Statistical Analysis Overview** | **Comparison Groups** | Placebo, Alogliptin 25 mg QD |
| | **Comments** | [Not specified] |
| | **Non-Inferiority or Equivalence Analysis?** | No |
| | **Comments** | [Not specified] |
| **Statistical Test of Hypothesis** | **P-Value** | 0.900 |
| | **Comments** | No multiplicity adjustments. |
| | **Method** | ANCOVA |
| | **Comments** | Treatment, geographic region and baseline treatment regimen as class variables; baseline pioglitazone dose and value for endpoint as covariates. |
| **Method of Estimation** | **Estimation Parameter** | Mean Difference (Final Values) |
| | **Estimated Value** | 0.05 |
| | **Confidence Interval** | (2-Sided) 95%<br>-0.74 to 0.84 |
| | **Estimation Comments** | Negative mean treatment difference indicates larger decrease from baseline (more negative change from baseline) in the alogliptin arm compared to the placebo arm. |

## Adverse Events

| | |
|---|---|
| Time Frame | Treatment-emergent adverse events are adverse events that started after the first dose of double-blind study drug and no more than 14 days (or 30 days for a serious event) after the last dose of double-blind drug. |
| Additional Description | At each visit the investigator had to document any occurrence of adverse events and abnormal laboratory findings. Any event spontaneously reported by the participant or observed by the investigator was recorded, irrespective of the relation to study treatment. |
| Source Vocabulary Name | MedDRA 10.0 |
| Assessment Type | Systematic Assessment |

| Arm/Group Title | Placebo | Alogliptin 12.5 mg QD | Alogliptin 25 mg QD |
|---|---|---|---|
| Arm/Group Description | Alogliptin placebo-matching tablets, orally, once daily and pioglitazone 30 mg or 45 mg, | Alogliptin 12.5 mg, tablets, orally, once daily and pioglitazone 30 mg or 45 mg, | Alogliptin 25 mg, tablets, orally, once daily and pioglitazone 30 |

| | | | |
|---|---|---|---|
| | tablets, orally, once daily for up to 26 weeks. | tablets, orally, once daily for up to 26 weeks. | mg or 45 mg, tablets, orally, once daily for up to 26 weeks. |

Serious Adverse Events

| | Placebo<br>Affected / at Risk (%) | Alogliptin 12.5 mg QD<br>Affected / at Risk (%) | Alogliptin 25 mg QD<br>Affected / at Risk (%) |
|---|---|---|---|
| Total | 4/97 (4.12%) | 5/198 (2.53%) | 13/199 (6.53%) |
| Cardiac disorders | | | |
| Angina pectoris † A | 0/97 (0%) | 1/198 (0.51%) | 1/199 (0.5%) |
| Cardiac failure congestive † A | 0/97 (0%) | 0/198 (0%) | 2/199 (1.01%) |
| Coronary artery disease † A | 0/97 (0%) | 1/198 (0.51%) | 0/199 (0%) |
| Myocardial infarction † A | 0/97 (0%) | 1/198 (0.51%) | 2/199 (1.01%) |
| Gastrointestinal disorders | | | |
| Appendicitis perforated † A | 0/97 (0%) | 1/198 (0.51%) | 0/199 (0%) |
| General disorders | | | |
| Sudden death † A | 0/97 (0%) | 1/198 (0.51%) | 0/199 (0%) |
| Immune system disorders | | | |
| Serum sickness † A | 0/97 (0%) | 0/198 (0%) | 1/199 (0.5%) |
| Infections and infestations | | | |
| Appendicitis † A | 1/97 (1.03%) | 0/198 (0%) | 1/199 (0.5%) |
| Cellulitis † A | 0/97 (0%) | 0/198 (0%) | 2/199 (1.01%) |
| Pneumonia † A | 0/97 (0%) | 0/198 (0%) | 1/199 (0.5%) |
| Viral infection † A | 0/97 (0%) | 0/198 (0%) | 1/199 (0.5%) |
| Injury, poisoning and procedural complications | | | |
| Road traffic accident † A | 0/97 (0%) | 0/198 (0%) | 1/199 (0.5%) |
| Metabolism and nutrition disorders | | | |
| Hypokalemia † A | 1/97 (1.03%) | 0/198 (0%) | 0/199 (0%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Basal cell carcinoma † A | 1/97 (1.03%) | 0/198 (0%) | 0/199 (0%) |
| Colon cancer † A | 1/97 (1.03%) | 0/198 (0%) | 0/199 (0%) |
| Nervous system disorders | | | |
| Carotid artery occlusion † A | 0/97 (0%) | 0/198 (0%) | 1/199 (0.5%) |
| Renal and urinary disorders | | | |
| Calculus ureteric † A | 1/97 (1.03%) | 0/198 (0%) | 0/199 (0%) |
| Nephrolithiasis † A | 0/97 (0%) | 1/198 (0.51%) | 0/199 (0%) |
| Reproductive system and breast disorders | | | |
| Cervical dysplasia † A | 0/97 (0%) | 0/198 (0%) | 1/199 (0.5%) |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory distress syndrome † A | 0/97 (0%) | 0/198 (0%) | 1/199 (0.5%) |

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

Other (Not Including Serious) Adverse Events

Frequency Threshold for Reporting Other Adverse Events: 3%

| | Placebo<br>Affected / at Risk (%) | Alogliptin 12.5 mg QD<br>Affected / at Risk (%) | Alogliptin 25 mg QD<br>Affected / at Risk (%) |
|---|---|---|---|
| Total | 38/97 (39.18%) | 76/198 (38.38%) | 79/199 (39.7%) |
| Gastrointestinal disorders | | | |
| Diarrhoea † A | 3/97 (3.09%) | 6/198 (3.03%) | 1/199 (0.5%) |
| Nausea † A | 2/97 (2.06%) | 9/198 (4.55%) | 6/199 (3.02%) |
| General disorders | | | |

| | | | |
|---|---|---|---|
| Fatigue † A | 3/97 (3.09%) | 4/198 (2.02%) | 4/199 (2.01%) |
| Oedema peripheral † A | 7/97 (7.22%) | 12/198 (6.06%) | 11/199 (5.53%) |
| Infections and infestations | | | |
| Bronchitis † A | 5/97 (5.15%) | 4/198 (2.02%) | 3/199 (1.51%) |
| Influenza † A | 4/97 (4.12%) | 3/198 (1.52%) | 11/199 (5.53%) |
| Nasopharyngitis † A | 6/97 (6.19%) | 8/198 (4.04%) | 14/199 (7.04%) |
| Sinusitis † A | 6/97 (6.19%) | 5/198 (2.53%) | 4/199 (2.01%) |
| Upper respiratory tract infection † A | 5/97 (5.15%) | 11/198 (5.56%) | 10/199 (5.03%) |
| Urinary tract infection † A | 1/97 (1.03%) | 9/198 (4.55%) | 4/199 (2.01%) |
| Injury, poisoning and procedural complications | | | |
| Joint injury † A | 3/97 (3.09%) | 0/198 (0%) | 1/199 (0.5%) |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia † A | 2/97 (2.06%) | 3/198 (1.52%) | 8/199 (4.02%) |
| Back Pain † A | 3/97 (3.09%) | 5/198 (2.53%) | 5/199 (2.51%) |
| Muscle spasms † A | 4/97 (4.12%) | 2/198 (1.01%) | 2/199 (1.01%) |
| Nervous system disorders | | | |
| Dizziness † A | 2/97 (2.06%) | 7/198 (3.54%) | 3/199 (1.51%) |
| Headache † A | 4/97 (4.12%) | 8/198 (4.04%) | 10/199 (5.03%) |
| Skin and subcutaneous tissue disorders | | | |
| Dry skin † A | 3/97 (3.09%) | 2/198 (1.01%) | 1/199 (0.5%) |
| Vascular disorders | | | |
| Hypertension † A | 2/97 (2.06%) | 6/198 (3.03%) | 8/199 (4.02%) |

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

## Limitations and Caveats

[Not Specified]

## More Information

### Certain Agreements

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

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

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

### Results Point of Contact


| | |
|---|---|
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