Sitagliptin Added-on to Insulin Study (0431-051)

This study has been completed.

Sponsor:
Merck Sharp & Dohme Corp.

Information provided by (Responsible Party):
Merck Sharp & Dohme Corp.

ClinicalTrials.gov Identifier:
NCT00395343

First received: November 1, 2006
Last updated: April 24, 2015
Last verified: April 2015
History of Changes

Purpose

A clinical study to determine the safety and efficacy of sitagliptin in patients with Type 2 Diabetes Mellitus who have inadequate glycemic control on insulin or insulin/metformin combination therapy.

Condition	Intervention	Phase
Type 2 Diabetes Mellitus	Drug: sitagliptin phosphate Drug: Comparator : placebo (unspecified)	Phase 3

Study Type: Interventional
Study Design: Allocation: Randomized
Endpoint Classification: Safety/Efficacy Study
Intervention Model: Parallel Assignment
Masking: Double Blind (Subject, Investigator)
Primary Purpose: Treatment

Official Title: A Phase III, Multicenter, Randomized, Double-Blind Clinical Trial to Study the Safety and Efficacy of the Addition of Sitagliptin (MK0431) to Patients With Type 2 Diabetes Mellitus Who Have Inadequate Glycemic Control on Insulin Therapy (Alone or In Combination With Metformin)

Resource links provided by NLM:

MedlinePlus related topics: Diabetes Type 2

Drug Information available for: Sitagliptin Sitagliptin phosphate

U.S. FDA Resources

Further study details as provided by Merck Sharp & Dohme Corp.:

Primary Outcome Measures:

- Change From Baseline in A1C at Week 24 [Time Frame: Baseline and Week 24] [Designated as safety issue: No]

  A1C is measured as a percent. Thus, this change from baseline reflects the Week 24 A1C percent minus the Week 0 A1C percent.

Secondary Outcome Measures:

- Change From Baseline in Fasting Plasma Glucose (FPG) at Week 24 [Time Frame: Baseline and Week 24] [Designated as safety issue: No]

  Change from baseline at Week 24 is defined as Week 24 minus Week 0.

- Change From Baseline in 2-hour Post-meal Glucose (PMG) at Week 24 [Time Frame: Baseline and Week 24] [Designated as safety issue: No]

  Change from baseline at Week 24 is defined as Week 24 minus Week 0.

- Percent Change From Baseline in Index of Static Beta-Cell Sensitivity to Glucose at Week 24 [Time Frame: Baseline and Week 24] [Designated as safety issue: No]

  Static sensitivity is a measure of the effect of glucose on beta-cell secretion and is the ratio between the insulin secretion rate and glucose concentration above the threshold level at steady state. (See Breda and Cobelli, Annals of Biomedical Engineering 29, 692-700 (2001) for more details.)

- Percent of Patients With A1C < 7.0% at Week 24 [Time Frame: 24 Weeks] [Designated as safety issue: No]
- Percent of Patients With A1C < 6.5% at Week 24 [Time Frame: Week 24] [Designated as safety issue: Yes]

Other Outcome Measures:

- Change From Baseline in A1C at Week 24 [Time Frame: Baseline and Week 24] [Designated as safety issue: No]

  A1C in subset of patients on long-acting or intermediate-acting insulin. A1C is measured as a percent. Thus, this change from baseline reflects the Week 24 A1C percent minus the Week 0 A1C percent.

Enrollment:	641
Study Start Date:	December 2006
Study Completion Date:	October 2008
Primary Completion Date:	October 2008 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: 1 sitagliptin	Drug: sitagliptin phosphate sitagliptin 100 mg tablet qd for a 24-wk treatment period. Other Names: • MK0431 • Januvia™
Placebo Comparator: 2 Placebo	Drug: Comparator : placebo (unspecified) sitagliptin 100 mg Pbo tablet qd for a 24-wk treatment period.

Eligibility

Ages Eligible for Study:	21 Years and older
Genders Eligible for Study:	Both
Accepts Healthy Volunteers:	No

Criteria

Inclusion Criteria:

- Patient has type 2 diabetes mellitus
- Patient is poorly controlled while on insulin or insulin and metformin

Exclusion Criteria:

- Patient has a history of type 1 diabetes mellitus or history of ketoacidosis
- Patient is taking oral antidiabetic agents other than metformin during the past 3 months
- Patient is currently on treatment with daily use of pre-prandial short-acting or rapid-acting insulin

Contacts and Locations

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the Contacts provided below. For general information, see Learn About Clinical Studies.

Please refer to this study by its ClinicalTrials.gov identifier: NCT00395343

Sponsors and Collaborators

Merck Sharp & Dohme Corp.

Investigators

Study Director: Medical Monitor Merck Sharp & Dohme Corp.

More Information

Additional Information:

(MedWatch - FDA maintained medical product safety Information) EXIT

(Merck: Patient & Caregiver U.S. Product Web Site) EXIT

Publications:

Vilsbøll T, Rosenstock J, Yki-Järvinen H, Cefalu WT, Chen Y, Luo E, Musser B, Andryuk PJ, Ling Y, Kaufman KD, Amatruda JM, Engel SS, Katz L. Efficacy and safety of sitagliptin when added to insulin therapy in patients with type 2 diabetes. Diabetes Obes Metab. 2010 Feb;12(2):167-77. doi: 10.1111/j.1463-1326.2009.01173.x.

Responsible Party:	Merck Sharp & Dohme Corp.
ClinicalTrials.gov Identifier:	NCT00395343 History of Changes
Other Study ID Numbers:	0431-051 MK0431-051 2006_532
Study First Received:	November 1, 2006
Results First Received:	September 18, 2009
Last Updated:	April 24, 2015
Health Authority:	United States: Food and Drug Administration

Additional relevant MeSH terms:

Diabetes Mellitus	Hormones
Diabetes Mellitus, Type 2	Hormones, Hormone Substitutes, and Hormone Antagonists
Endocrine System Diseases	Hypoglycemic Agents
Glucose Metabolism Disorders	Incretins
Metabolic Diseases	Molecular Mechanisms of Pharmacological Action
Sitagliptin	Pharmacologic Actions
Dipeptidyl-Peptidase IV Inhibitors	Physiological Effects of Drugs
Enzyme Inhibitors	Protease Inhibitors

ClinicalTrials.gov processed this record on April 13, 2016

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For Patients and Families | For Researchers | For Study Record Managers

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ClinicalTrials.gov Identifier:
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First received: November 1, 2006
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Last verified: April 2015
History of Changes

Results First Received: September 18, 2009

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Safety/Efficacy Study; Intervention Model: Parallel Assignment; Masking: Double Blind (Subject, Investigator); Primary Purpose: Treatment
Condition:	Type 2 Diabetes Mellitus
Interventions:	Drug: sitagliptin phosphate Drug: Comparator : placebo (unspecified)

Participant Flow

Hide Participant Flow

Recruitment Details

Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations

Phase III

First Patient In: 29-Jan-2007 Last Patient Last Visit: 13-Oct-2008; 100 study centers worldwide

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment

Patients at least 21 years of age with type 2 diabetes mellitus with inadequate glycemic control (A1C ≥7.5 and ≤11.0%) on stable-dose insulin (alone or in combination with stable-dose metformin) were eligible to enter the 24 week study. 1-week screening, followed by a 2-week single-blind placebo run-in.

Reporting Groups

	Description
Sitagliptin 100 mg q.d.	The Sitagliptin 100 mg q.d. (q.d. = once daily) group includes data from patients randomized to receive treatment with 100 mg oral tablets of sitagliptin once daily (blinded) in addition to ongoing treatment with insulin (pre-mixed, intermediate-acting, or long-acting) alone or in combination with open-label metformin 500 mg oral tablets (≥1500 mg/day).
Placebo	The Placebo group includes data from patients randomized to receive treatment with a placebo of the sitagliptin 100 mg oral tablet once daily (blinded) in addition to ongoing treatment with insulin (pre-mixed, intermediate-acting, or long-acting) alone or in combination with open-label metformin 500 mg oral tablets (≥1500 mg/day).

Participant Flow: Overall Study

	Sitagliptin 100 mg q.d.	Placebo
STARTED	322	319
COMPLETED	281	283
NOT COMPLETED	41	36
Adverse Event	13	5
Lack of Efficacy	0	1
Lost to Follow-up	4	4
Physician Decision	2	4
Protocol Violation	6	8
Withdrawal by Subject	11	12
Unspecified	5	2

Baseline Characteristics

Hide Baseline Characteristics

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No text entered.

Reporting Groups

	Description
Sitagliptin 100 mg q.d.	The Sitagliptin 100 mg q.d. (q.d. = once daily) group includes data from patients randomized to receive treatment with 100 mg oral tablets of sitagliptin once daily (blinded) in addition to ongoing treatment with insulin (pre-mixed, intermediate-acting, or long-acting) alone or in combination with open-label metformin 500 mg oral tablets (≥1500 mg/day).
Placebo	The Placebo group includes data from patients randomized to receive treatment with a placebo of the sitagliptin 100 mg oral tablet once daily (blinded) in addition to ongoing treatment with insulin (pre-mixed, intermediate-acting, or long-acting) alone or in combination with open-label metformin 500 mg oral tablets (≥1500 mg/day).
Total	Total of all reporting groups

Baseline Measures

	Sitagliptin 100 mg q.d.	Placebo	Total
Number of Participants [units: participants]	322	319	641
Age [units: years] Mean (Standard Deviation)	58.3 (9.1)	57.2 (9.3)	57.8 (9.2)
Gender [units: participants]			
Female	165	150	315
Male	157	169	326
Race/Ethnicity, Customized [units: participants]			
White	228	219	447
Black	21	23	44
Asian	55	61	116
Other	18	16	34
A1C (Hemoglobin A1c) [units: Percent] Mean (Standard Deviation)	8.7 (0.9)	8.6 (0.9)	8.7 (0.9)

Outcome Measures

Hide All Outcome Measures

1. Primary: Change From Baseline in A1C at Week 24 [Time Frame: Baseline and Week 24]

Measure Type	Primary
Measure Title	Change From Baseline in A1C at Week 24
Measure Description	A1C is measured as a percent. Thus, this change from baseline reflects the Week 24 A1C percent minus the Week 0 A1C percent.
Time Frame	Baseline and Week 24
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The Full Analysis Set (FAS) included all patients with a baseline value and ≥1 post-baseline value for this outcome. Data following glycemic rescue were treated as missing. For FAS patients with no data at Week 24, the last non-baseline observed measurement was carried forward to Week 24.

Reporting Groups

	Description
Sitagliptin 100 mg q.d.	The Sitagliptin 100 mg q.d. (q.d. = once daily) group includes data from patients randomized to receive treatment with 100 mg oral tablets of sitagliptin once daily (blinded) in addition to ongoing treatment with insulin (pre-mixed,

	intermediate-acting, or long-acting) alone or in combination with open-label metformin 500 mg oral tablets (≥1500 mg/day).
Placebo	The Placebo group includes data from patients randomized to receive treatment with a placebo of the sitagliptin 100 mg oral tablet once daily (blinded) in addition to ongoing treatment with insulin (pre-mixed, intermediate-acting, or long-acting) alone or in combination with open-label metformin 500 mg oral tablets (≥1500 mg/day).

Measured Values

	Sitagliptin 100 mg q.d.	Placebo
Number of Participants Analyzed [units: participants]	**305**	**312**
Change From Baseline in A1C at Week 24 [units: Percent] Least Squares Mean (95% Confidence Interval)	**-0.59 (-0.70 to -0.48)**	**-0.03 (-0.14 to 0.08)**

Statistical Analysis 1 for Change From Baseline in A1C at Week 24

Groups [1]	All groups
Method [2]	ANCOVA
P Value [3]	<0.001
Mean Difference (Net) [4]	-0.56
95% Confidence Interval	-0.70 to -0.42

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Model terms: treatment; baseline; metformin stratum (on vs. not on metformin); insulin stratum (pre-mixed vs. intermediate or long-acting)
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

2. Secondary: Change From Baseline in Fasting Plasma Glucose (FPG) at Week 24 [Time Frame: Baseline and Week 24]

Measure Type	Secondary
Measure Title	Change From Baseline in Fasting Plasma Glucose (FPG) at Week 24
Measure Description	Change from baseline at Week 24 is defined as Week 24 minus Week 0.
Time Frame	Baseline and Week 24
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The Full Analysis Set (FAS) included all patients with a baseline value and ≥1 post-baseline value for this outcome. Data following glycemic rescue were treated as missing. For FAS patients with no data at Week 24, the last non-baseline observed measurement was carried forward to Week 24.

Reporting Groups

	Description
Sitagliptin 100 mg q.d.	The Sitagliptin 100 mg q.d. (q.d. = once daily) group includes data from patients randomized to receive treatment with 100 mg oral tablets of sitagliptin once daily (blinded) in addition to ongoing treatment with insulin (pre-mixed, intermediate-acting, or long-acting) alone or in combination with open-label metformin 500 mg oral tablets (≥1500 mg/day).
Placebo	The Placebo group includes data from patients randomized to receive treatment with a placebo of the sitagliptin 100 mg oral tablet once daily (blinded) in addition to ongoing treatment with insulin (pre-mixed, intermediate-acting, or long-acting) alone or in combination with open-label metformin 500 mg oral tablets (≥1500 mg/day).

Measured Values

	Sitagliptin 100 mg q.d.	**Placebo**
Number of Participants Analyzed [units: participants]	**310**	**313**
Change From Baseline in Fasting Plasma Glucose (FPG) at Week 24 [units: mg/dL] Least Squares Mean (95% Confidence Interval)	**-18.5 (-25.1 to -11.9)**	**-3.5 (-10.2 to 3.1)**

Statistical Analysis 1 for Change From Baseline in Fasting Plasma Glucose (FPG) at Week 24

Groups [1]	All groups
Method [2]	ANCOVA
P Value [3]	<0.001
Mean Difference (Net) [4]	-15.0
95% Confidence Interval	-23.4 to -6.5

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Model terms: treatment; baseline; metformin stratum; insulin stratum
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

3. Secondary: Change From Baseline in 2-hour Post-meal Glucose (PMG) at Week 24 [Time Frame: Baseline and Week 24]

Measure Type	Secondary
Measure Title	Change From Baseline in 2-hour Post-meal Glucose (PMG) at Week 24
Measure Description	Change from baseline at Week 24 is defined as Week 24 minus Week 0.
Time Frame	Baseline and Week 24
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The Full Analysis Set (FAS) included all patients with a baseline value and ≥1 post-baseline value for this outcome. Data following glycemic rescue were treated as missing. For FAS patients with no data at Week 24, the last non-baseline observed measurement was carried forward to Week 24.

Reporting Groups

	Description
Sitagliptin 100 mg q.d.	The Sitagliptin 100 mg q.d. (q.d. = once daily) group includes data from patients randomized to receive treatment with 100 mg oral tablets of sitagliptin once daily (blinded) in addition to ongoing treatment with insulin (pre-mixed, intermediate-acting, or long-acting) alone or in combination with open-label metformin 500 mg oral tablets (≥1500 mg/day).
Placebo	The Placebo group includes data from patients randomized to receive treatment with a placebo of the sitagliptin 100 mg oral tablet once daily (blinded) in addition to ongoing treatment with insulin (pre-mixed, intermediate-acting, or long-acting) alone or in combination with open-label metformin 500 mg oral tablets (≥1500 mg/day).

Measured Values

	Sitagliptin 100 mg q.d.	**Placebo**
Number of Participants Analyzed [units: participants]	**240**	**257**
Change From Baseline in 2-hour Post-meal Glucose (PMG) at Week 24 **[units: mg/dL]** **Least Squares Mean (95% Confidence Interval)**	**-30.9 (-40.0 to -21.8)**	**5.2 (-3.6 to 13.9)**

Statistical Analysis 1 for Change From Baseline in 2-hour Post-meal Glucose (PMG) at Week 24

Groups [1]	All groups
Method [2]	ANCOVA
P Value [3]	<0.001
Mean Difference (Net) [4]	-36.1
95% Confidence Interval	-47.1 to -25.1

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.

[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Model terms: treatment; baseline; metformin stratum; insulin stratum
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

4. Secondary: Percent Change From Baseline in Index of Static Beta-Cell Sensitivity to Glucose at Week 24 [Time Frame: Baseline and Week 24]

Measure Type	Secondary
Measure Title	Percent Change From Baseline in Index of Static Beta-Cell Sensitivity to Glucose at Week 24
Measure Description	Static sensitivity is a measure of the effect of glucose on beta-cell secretion and is the ratio between the insulin secretion rate and glucose concentration above the threshold level at steady state. (See Breda and Cobelli, Annals of Biomedical Engineering 29, 692-700 (2001) for more details.)
Time Frame	Baseline and Week 24
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The Full Analysis Set (FAS) included all patients who participated in the 10-point meal tolerance test and had a baseline value and ≥1 post-baseline value for this outcome. Data following glycemic rescue were treated as missing. For FAS patients with no data at Week 24, the last non-baseline observed measurement was carried forward to Week 24.

Reporting Groups

	Description
Sitagliptin 100 mg q.d.	The Sitagliptin 100 mg q.d. (q.d. = once daily) group includes data from patients randomized to receive treatment with 100 mg oral tablets of sitagliptin once daily (blinded) in addition to ongoing treatment with insulin (pre-mixed, intermediate-acting, or long-acting) alone or in combination with open-label metformin 500 mg oral tablets (≥1500 mg/day).
Placebo	The Placebo group includes data from patients randomized to receive treatment with a placebo of the sitagliptin 100 mg oral tablet once daily (blinded) in addition to ongoing treatment with insulin (pre-mixed, intermediate-acting, or long-acting) alone or in combination with open-label metformin 500 mg oral tablets (≥1500 mg/day).

Measured Values

	Sitagliptin 100 mg q.d.	**Placebo**
Number of Participants Analyzed [units: participants]	**35**	**45**
Percent Change From Baseline in Index of Static Beta-Cell Sensitivity to Glucose at Week 24 [units: Percent] Least Squares Mean (95% Confidence Interval)	**28.4 (5.4 to 56.6)**	**-8.1 (-22.6 to 9.2)**

Statistical Analysis 1 for Percent Change From Baseline in Index of Static Beta-Cell Sensitivity to Glucose at Week 24

Groups [1]	All groups
Method [2]	ANCOVA
P Value [3]	0.01
Geometric Mean Difference [4]	36.5
95% Confidence Interval	8.9 to 64.7

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Model terms: treatment; log-scaled baseline value; metformin stratum; insulin stratum
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

5. Secondary: Percent of Patients With A1C < 7.0% at Week 24 [Time Frame: 24 Weeks]

Measure Type	Secondary
Measure Title	Percent of Patients With A1C < 7.0% at Week 24
Measure Description	No text entered.
Time Frame	24 Weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The Full Analysis Set (FAS) included all patients with a baseline value and ≥1 post-baseline value for this outcome. Data following glycemic rescue were treated as missing. For FAS patients with no data at Week 24, the last non-baseline observed measurement was carried forward to Week 24.

Reporting Groups

	Description
Sitagliptin 100 mg q.d.	The Sitagliptin 100 mg q.d. (q.d. = once daily) group includes data from patients randomized to receive treatment with 100 mg oral tablets of sitagliptin once daily (blinded) in addition to ongoing treatment with insulin (pre-mixed, intermediate-acting, or long-acting) alone or in combination with open-label metformin 500 mg oral tablets (≥1500 mg/day).
Placebo	The Placebo group includes data from patients randomized to receive treatment with a placebo of the sitagliptin 100 mg oral tablet once daily (blinded) in addition to ongoing treatment with insulin (pre-mixed, intermediate-acting, or long-acting) alone or in combination with open-label metformin 500 mg oral tablets (≥1500 mg/day).

Measured Values

	Sitagliptin 100 mg q.d.	Placebo
Number of Participants Analyzed [units: participants]	305	312
Percent of Patients With A1C < 7.0% at Week 24 [units: Percent]	12.8	5.1

Statistical Analysis 1 for Percent of Patients With A1C < 7.0% at Week 24

Groups [1]	All groups
Method [2]	Logistic Regression
P Value [3]	<0.001
Odds Ratio (OR) [4]	3.60
95% Confidence Interval	1.89 to 6.85

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Model terms: treatment; baseline; Metformin stratum; and insulin stratum
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	Based on a test of the odds ratio = 1, comparing the odds of having A1C <7.0% at Week 24 in the Sitagliptin 100 mg q.d. group vs. the Placebo group.
[4]	Other relevant estimation information:
	No text entered.

6. Secondary: Percent of Patients With A1C < 6.5% at Week 24 [Time Frame: Week 24]

Measure Type	Secondary
Measure Title	Percent of Patients With A1C < 6.5% at Week 24
Measure Description	No text entered.
Time Frame	Week 24
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The Full Analysis Set (FAS) included all patients with a baseline value and ≥1 post-baseline value for this outcome. Data following glycemic rescue were treated as missing. For FAS patients with no data at Week 24, the last non-baseline observed measurement was carried forward to Week 24.

Reporting Groups

	Description
Sitagliptin 100 mg q.d.	The Sitagliptin 100 mg q.d. (q.d. = once daily) group includes data from patients randomized to receive treatment with 100 mg oral tablets of sitagliptin once daily (blinded) in addition to ongoing treatment with insulin (pre-mixed, intermediate-acting, or long-acting) alone or in combination with open-label metformin 500 mg oral tablets (≥1500 mg/day).
Placebo	The Placebo group includes data from patients randomized to receive treatment with a placebo of the sitagliptin 100 mg oral tablet once daily (blinded) in addition to ongoing treatment with insulin (pre-mixed, intermediate-acting, or long-acting) alone or in combination with open-label metformin 500 mg oral tablets (≥1500 mg/day).

Measured Values

	Sitagliptin 100 mg q.d.	Placebo
Number of Participants Analyzed [units: participants]	**305**	**312**
Percent of Patients With A1C < 6.5% at Week 24 [units: Percent]	**2.3**	**1.9**

Statistical Analysis 1 for Percent of Patients With A1C < 6.5% at Week 24

Groups [1]	All groups
Method [2]	Logistic Regression
P Value [3]	0.584
Odds Ratio (OR) [4]	1.37
95% Confidence Interval	0.45 to 4.18

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Model terms: treatment; baseline; Metformin stratum; and insulin stratum
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	Based on a test of the odds ratio = 1, comparing the odds of having A1C <7.0% at Week 24 in the Sitagliptin 100 mg q.d. group vs. the Placebo group.
[4]	Other relevant estimation information:
	This parameter estimate and 95% confidence interval correspond to the odds of having A1C <6.5% at Week 24 in the Sitagliptin 100 mg q.d. group vs. the Placebo group.

7. Other Pre-specified: Change From Baseline in A1C at Week 24 [Time Frame: Baseline and Week 24]

Measure Type	Other Pre-specified
Measure Title	Change From Baseline in A1C at Week 24

Measure Description	A1C in subset of patients on long-acting or intermediate-acting insulin. A1C is measured as a percent. Thus, this change from baseline reflects the Week 24 A1C percent minus the Week 0 A1C percent.
Time Frame	Baseline and Week 24
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The Full Analysis Set (FAS) included the subset of patients on long-acting or intermediate-acting insulin with a baseline value and ≥1 post-baseline value for this outcome. Data following glycemic rescue were treated as missing. For FAS patients with no data at Week 24, the last non-baseline observed measurement was carried forward to Week 24.

Reporting Groups

	Description
Sitagliptin 100 mg q.d.	The Sitagliptin 100 mg q.d. (q.d. = once daily) group includes data from patients randomized to receive treatment with 100 mg oral tablets of sitagliptin once daily (blinded) in addition to ongoing treatment with insulin (pre-mixed, intermediate-acting, or long-acting) alone or in combination with open-label metformin 500 mg oral tablets (≥1500 mg/day).
Placebo	The Placebo group includes data from patients randomized to receive treatment with a placebo of the sitagliptin 100 mg oral tablet once daily (blinded) in addition to ongoing treatment with insulin (pre-mixed, intermediate-acting, or long-acting) alone or in combination with open-label metformin 500 mg oral tablets (≥1500 mg/day).

Measured Values

	Sitagliptin 100 mg q.d.	**Placebo**
Number of Participants Analyzed [units: participants]	**225**	**232**
Change From Baseline in A1C at Week 24 [units: Percent] Least Squares Mean (95% Confidence Interval)	**-0.61 (-0.73 to -0.48)**	**-0.04 (-0.16 to 0.08)**

Statistical Analysis 1 for Change From Baseline in A1C at Week 24

Groups [1]	All groups
Method [2]	ANCOVA
P Value [3]	<0.001
Mean Difference (Net) [4]	-0.56
95% Confidence Interval	-0.72 to -0.40

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Model terms: treatment; baseline; metformin stratum; insulin stratum, treatment by insulin stratum interaction
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:

	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	No text entered.
Additional Description	No text entered.

Reporting Groups

	Description
Sitagliptin 100 mg q.d.	The Sitagliptin 100 mg q.d. (q.d. = once daily) group includes data from patients randomized to receive treatment with 100 mg oral tablets of sitagliptin once daily (blinded) in addition to ongoing treatment with insulin (pre-mixed, intermediate-acting, or long-acting) alone or in combination with open-label metformin 500 mg oral tablets (≥1500 mg/day).
Placebo	The Placebo group includes data from patients randomized to receive treatment with a placebo of the sitagliptin 100 mg oral tablet once daily (blinded) in addition to ongoing treatment with insulin (pre-mixed, intermediate-acting, or long-acting) alone or in combination with open-label metformin 500 mg oral tablets (≥1500 mg/day).

Serious Adverse Events

	Sitagliptin 100 mg q.d.	Placebo
Total, serious adverse events		
# participants affected / at risk	**20/322 (6.21%)**	**11/319 (3.45%)**
Cardiac disorders		
Any Cardiac disorders [*1]		
# participants affected / at risk	**4/322 (1.24%)**	**5/319 (1.57%)**
Acute myocardial infarction [*1]		
# participants affected / at risk	**1/322 (0.31%)**	**1/319 (0.31%)**
Angina pectoris [*1]		
# participants affected / at risk	**2/322 (0.62%)**	**0/319 (0.00%)**
Angina unstable [*1]		
# participants affected / at risk	**0/322 (0.00%)**	**1/319 (0.31%)**
Cardiac failure congestive [*1]		
# participants affected / at risk	**0/322 (0.00%)**	**2/319 (0.63%)**
Coronary artery disease [*1]		
# participants affected / at risk	**0/322 (0.00%)**	**1/319 (0.31%)**
Myocardial infarction [*1]		

# participants affected / at risk	0/322 (0.00%)	1/319 (0.31%)
Trifascicular block [*1]		
# participants affected / at risk	1/322 (0.31%)	0/319 (0.00%)
Gastrointestinal disorders		
Any Gastrointestinal Disorders [*1]		
# participants affected / at risk	2/322 (0.62%)	1/319 (0.31%)
Abdominal pain [*1]		
# participants affected / at risk	1/322 (0.31%)	0/319 (0.00%)
Inguinal hernia [*1]		
# participants affected / at risk	0/322 (0.00%)	1/319 (0.31%)
Oesophageal spasm [*1]		
# participants affected / at risk	1/322 (0.31%)	0/319 (0.00%)
Hepatobiliary disorders		
Any Hepatobiliary disorders [*1]		
# participants affected / at risk	1/322 (0.31%)	1/319 (0.31%)
Cholecystitis acute [*1]		
# participants affected / at risk	0/322 (0.00%)	1/319 (0.31%)
Cholelithiasis obstructive [*1]		
# participants affected / at risk	1/322 (0.31%)	0/319 (0.00%)
Infections and infestations		
Any Infections and Infestations [*1]		
# participants affected / at risk	3/322 (0.93%)	1/319 (0.31%)
Bronchitis [*1]		
# participants affected / at risk	1/322 (0.31%)	0/319 (0.00%)
Genital abscess [*1]		
# participants affected / at risk	1/322 (0.31%)	0/319 (0.00%)
Perianal abscess [*1]		
# participants affected / at risk	0/322 (0.00%)	1/319 (0.31%)
Pyelonephritis chronic [*1]		
# participants affected / at risk	1/322 (0.31%)	0/319 (0.00%)
Injury, poisoning and procedural complications		
Any Injury, Poisoning and Procedural Complications [*1]		
# participants affected / at risk	2/322 (0.62%)	1/319 (0.31%)
Incisional hernia [*1]		
# participants affected / at risk	0/322 (0.00%)	1/319 (0.31%)
Pelvic fracture [*1]		
# participants affected / at risk	1/322 (0.31%)	0/319 (0.00%)
Traumatic ulcer [*1]		
# participants affected / at risk	1/322 (0.31%)	0/319 (0.00%)
Investigations		
Any Investigations [*1]		

# participants affected / at risk	1/322 (0.31%)	0/319 (0.00%)
Blood glucose increased [*1]		
# participants affected / at risk	1/322 (0.31%)	0/319 (0.00%)
Metabolism and nutrition disorders		
Any Metabolism and nutrition disorders [*1]		
# participants affected / at risk	2/322 (0.62%)	0/319 (0.00%)
Hypoglycaemia [*1]		
# participants affected / at risk	2/322 (0.62%)	0/319 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Any Neoplasms Benign, Malignant and Unspecified (Incl Cysts and Polyps) [*1]		
# participants affected / at risk	2/322 (0.62%)	0/319 (0.00%)
Breast cancer [*1]		
# participants affected / at risk	1/322 (0.31%)	0/319 (0.00%)
Rectal cancer [*1]		
# participants affected / at risk	1/322 (0.31%)	0/319 (0.00%)
Nervous system disorders		
Any Nervous System Disorders [*1]		
# participants affected / at risk	0/322 (0.00%)	2/319 (0.63%)
Headache [*1]		
# participants affected / at risk	0/322 (0.00%)	1/319 (0.31%)
Syncope [*1]		
# participants affected / at risk	0/322 (0.00%)	1/319 (0.31%)
Psychiatric disorders		
Any Psychiatric Disorders [*1]		
# participants affected / at risk	1/322 (0.31%)	1/319 (0.31%)
Depression [*1]		
# participants affected / at risk	0/322 (0.00%)	1/319 (0.31%)
Major depression [*1]		
# participants affected / at risk	1/322 (0.31%)	0/319 (0.00%)
Reproductive system and breast disorders		
Any Reproductive System and Breast Disorders [*1]		
# participants affected / at risk	1/322 (0.31%)	0/319 (0.00%)
Balanoposthitis [*1]		
# participants affected / at risk	1/322 (0.31%)	0/319 (0.00%)
Respiratory, thoracic and mediastinal disorders		
Any Respiratory, Thoracic and Mediastinal Disorders [*1]		
# participants affected / at risk	0/322 (0.00%)	1/319 (0.31%)
Asthma [*1]		
# participants affected / at risk	0/322 (0.00%)	1/319 (0.31%)
Skin and subcutaneous tissue disorders		

Any Skin and Subcutaneous Tissue Disorders * 1		
# participants affected / at risk	**2/322 (0.62%)**	**0/319 (0.00%)**
Leukocytoclastic vasculitis * 1		
# participants affected / at risk	**1/322 (0.31%)**	**0/319 (0.00%)**
Skin ulcer * 1		
# participants affected / at risk	**1/322 (0.31%)**	**0/319 (0.00%)**
Vascular disorders		
Any Vascular Disorders * 1		
# participants affected / at risk	**1/322 (0.31%)**	**0/319 (0.00%)**
Extremity necrosis * 1		
# participants affected / at risk	**1/322 (0.31%)**	**0/319 (0.00%)**

* Events were collected by non-systematic assessment
1 Term from vocabulary, MedDRA 11.0

Other Adverse Events

Hide Other Adverse Events

Time Frame	No text entered.
Additional Description	No text entered.

Frequency Threshold

Threshold above which other adverse events are reported	5%

Reporting Groups

	Description
Sitagliptin 100 mg q.d.	The Sitagliptin 100 mg q.d. (q.d. = once daily) group includes data from patients randomized to receive treatment with 100 mg oral tablets of sitagliptin once daily (blinded) in addition to ongoing treatment with insulin (pre-mixed, intermediate-acting, or long-acting) alone or in combination with open-label metformin 500 mg oral tablets (≥1500 mg/day).
Placebo	The Placebo group includes data from patients randomized to receive treatment with a placebo of the sitagliptin 100 mg oral tablet once daily (blinded) in addition to ongoing treatment with insulin (pre-mixed, intermediate-acting, or long-acting) alone or in combination with open-label metformin 500 mg oral tablets (≥1500 mg/day).

Other Adverse Events

	Sitagliptin 100 mg q.d.	**Placebo**
Total, other (not including serious) adverse events		
# participants affected / at risk	**49/322 (15.22%)**	**25/319 (7.84%)**
Metabolism and nutrition disorders		
Any Metabolism and nutrition disorders * 1		

# participants affected / at risk	49/322 (15.22%)	25/319 (7.84%)
Hypoglycaemia * 1		
# participants affected / at risk	49/322 (15.22%)	25/319 (7.84%)

* Events were collected by non-systematic assessment
1 Term from vocabulary, MedDRA 11.0

Limitations and Caveats

Hide Limitations and Caveats

Limitations of the study, such as early termination leading to small numbers of participants analyzed and technical problems with measurement leading to unreliable or uninterpretable data
No text entered.

More Information

Hide More Information

Certain Agreements:

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

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

The agreement is:

☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **less than or equal to 60 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **more than 60 days but less than or equal to 180 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

☑ Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed.

Restriction Description: Merck agreements may vary with individual investigators, but will not prohibit any investigator from publishing. Merck supports the publication of results from all centers of a multi-center trial but requests that reports based on single-site data not precede the primary publication of the entire clinical trial.

Results Point of Contact:

Name/Title: Senior Vice President, Global Clinical Development
Organization: Merck Sharp & Dohme Corp.
phone: 1-800-672-6372
e-mail: ClinicalTrialsDisclosure@merck.com

Publications of Results:

Vilsbøll T, Rosenstock J, Yki-Järvinen H, Cefalu WT, Chen Y, Luo E, Musser B, Andryuk PJ, Ling Y, Kaufman KD, Amatruda JM, Engel SS, Katz L. Efficacy and safety of sitagliptin when added to insulin therapy in patients with type 2 diabetes. Diabetes Obes Metab. 2010 Feb;12(2):167-77. doi: 10.1111/j.1463-1326.2009.01173.x.

Responsible Party: Merck Sharp & Dohme Corp.
ClinicalTrials.gov Identifier: NCT00395343 History of Changes
Other Study ID Numbers: 0431-051

	MK0431-051
	2006_532
Study First Received:	November 1, 2006
Results First Received:	September 18, 2009
Last Updated:	April 24, 2015
Health Authority:	United States: Food and Drug Administration

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For Patients and Families | For Researchers | For Study Record Managers

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