ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: May 8, 2015

ClinicalTrials.gov ID: NCT00757588

Study Identification

Unique Protocol ID:	CV181-057
Brief Title:	Safety and Efficacy of Saxagliptin Plus Insulin With or Without Metformin
Official Title:	A Multicenter, Randomized, Double-Blind, Phase 3 Trial to Evaluate the Efficacy and Safety of Saxagliptin Added to Insulin Monotherapy or to Insulin in Combination With Metformin in Subjects With Type 2 Diabetes Who Have Inadequate Glycemic Control on Insulin Alone or on Insulin in Combination With Metformin
Secondary IDs:	Eudract-2008-001089-10

Study Status

Record Verification:	May 2015
Overall Status:	Completed
Study Start:	November 2008
Primary Completion:	April 2010 [Actual]
Study Completion:	April 2010 [Actual]

Sponsor/Collaborators

Sponsor:	AstraZeneca
Responsible Party:	Sponsor
Collaborators:	AstraZeneca

Oversight

FDA Regulated?:	Yes

Applicable Trial?:	Section 801 Clinical Trial? Yes Delayed Posting? No
IND/IDE Protocol?:	Yes
IND/IDE Information:	Grantor: CDER IND/IDE Number: 63,634 Serial Number: 0281 Has Expanded Access? No
Review Board:	Approval Status: Board Name: Board Affiliation: Phone: Email:
Data Monitoring?:	Yes
Plan to Share IPD?:	
Oversight Authorities:	United States: Food and Drug Administration Russia: Ethics Committee India: Central Drugs Standard Control Organization Poland: Office for Registration of Medicinal Products, Medical Devices and Biocidal Products United Kingdom: Medicines and Healthcare Products Regulatory Agency France: Afssaps - Agence française de sécurité sanitaire des produits de santé (Saint-Denis) Brazil: National Health Surveillance Agency South Africa: Medicines Control Council Canada: Canadian Institutes of Health Research

Study Description

Brief Summary:	The purpose of this study is to compare the effects of saxagliptin with those of placebo as add-on therapy to insulin and insulin with metformin in improving glycemic control at 24 and 52 weeks.
Detailed Description:	

Conditions

Conditions:	Type 2 Diabetes
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 3
Intervention Model:	Parallel Assignment
Number of Arms:	2
Masking:	Double Blind (Subject, Investigator)
Allocation:	Randomized
Endpoint Classification:	Safety/Efficacy Study
Enrollment:	455 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Saxagliptin, 5 mg + insulin Saxagliptin, 5 mg, plus insulin, administered to participants with Type 2 diabetes inadequately controlled with insulin alone or with insulin plus metformin	Drug: Saxagliptin, 5 mg + insulin Saxagliptin, 5-mg tablets (plus stable insulin dose), given orally once daily (24 weeks short-term, 28 weeks long-term); participants stratified by use of stable metformin dose; flexible insulin dose (as needed for rescue) Other Names: • BMS-477118
Placebo Comparator: Placebo + insulin Placebo administered to participants with Type 2 diabetes inadequately controlled with insulin alone or with insulin plus metformin	Drug: Placebo + insulin Placebo tablets given orally once daily for 24 weeks (short-term period)+ insulin with metformin

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age:	18 Years
Maximum Age:	78 Years
Gender:	Both
Accepts Healthy Volunteers?:	No

Criteria: Inclusion Criteria:

- Type 2 diabetes mellitus
- Must have been taking a stable dose of basal or premixed insulin for 8 weeks or longer prior to screening
- If taking metformin, must have been taking the same daily dose for 8 weeks or longer prior to screening
- Insulin type should be intermediate- or long-acting (basal) or premixed (premixed formulation may include short- or rapid-acting insulin as 1 component).
- Inadequate glycemic control (A1C of 7.5% to 11.0%, inclusive)
- Body mass index of 45 kg/m² or lower
- Fasting C-peptide level of 0.8 ng/mL or higher

Exclusion Criteria:

- Symptoms of poorly controlled diabetes, including but not limited to marked polyuria and polydipsia with greater than 10% weight loss during the last 3 months prior to screening or other signs and symptoms
- History of diabetic ketoacidosis or hyperosmolar nonketotic coma
- Women of childbearing potential unable or unwilling to use acceptable birth control
- Women who are pregnant or breastfeeding
- Active liver disease
- Anemia
- Chronic or repeated intermittent corticosteroid treatment (participants receiving stable doses of replacement corticosteroid (except dexamethasone) therapy may be enrolled)
- Use of short- or rapid-acting insulin
- Significant cardiovascular history defined as: myocardial infarction, coronary angioplasty or bypass graft, valvular disease or repair, unstable angina pectoris, transient ischemic attack, or cerebrovascular accident
- Congestive heart failure
- Unstable or rapidly progressing renal disease
- History of alcohol or drug abuse within the previous year
- History of hemoglobinopathies
- Unstable major psychiatric disorders
- Immunocompromised status

Contacts/Locations

Study Officials: Bristol-Myers Squibb
Study Director
Bristol-Myers Squibb

Locations: France
Local Institution
Montpellier Cedex 5, France, 34295

Local Institution
Valenciennes, France, 59300

United States, Mississippi
Danny W. Jackson P.A.
Rolling Fork, Mississippi, United States, 39159

United States, Florida
Panhandle Family Care Assoc. & Coastal Palms Res. Grp Inc.
Marianna, Florida, United States, 32446

United States, California
Ritchken & First M.D.'S
San Diego, California, United States, 92117

United States, Wisconsin
Aurora Advanced Healthcare
Milwaukee, Wisconsin, United States, 53209

Poland
Local Institution
Wroclaw, Poland, 50-088

Local Institution
Elblag, Poland, 82-300

South Africa
Local Institution
Tygerberg, Western Cape, South Africa, 7505

Local Institution
Parktown, Gauteng, South Africa, 2193

Local Institution
Durban, Kwa Zulu Natal, South Africa, 4001

Local Institution
Umhlanga Rocks, Kwa Zulu Natal, South Africa, 4319

Local Institution
Goodwood, Western Cape, South Africa, 7460

United Kingdom
Local Institution
Middlesborough, Cleveland, United Kingdom, TS4 3BW

Local Institution
Sheffield, Yorkshire, United Kingdom, S5 7AU

Local Institution
Salford, Greater Manchester, United Kingdom, M6 8HD

Local Institution
Newcastle Upon Tyne, Tyne And Wear, United Kingdom, NE4 6BE

Local Institution
Birmingham, West Midlands, United Kingdom, B9 5SS

France
Local Institution
Nantes, France, 44093

Local Institution
Besancon Cedex, France, 25030

Canada, Quebec
Local Institution
Laval, Quebec, Canada, H7T 2P5

Local Institution
Gatineau, Quebec, Canada, J8V 2P5

Local Institution
Sherbrooke, Quebec, Canada, J1G 5K2

Canada, Ontario
Local Institution
London, Ontario, Canada, N6A 4V2

Canada, New Brunswick
Local Institution
Bathurst, New Brunswick, Canada, E2A 4X7

Canada, British Columbia
Local Institution
Vancouver, British Columbia, Canada, V6E 1M7

Canada, Saskatchewan
Local Institution
Regina, Saskatchewan, Canada, S4P 0W5

Canada, Prince Edward Island
Local Institution
Charlottetown, Prince Edward Island, Canada, C1A 5Y9

United States, Florida
Family Care Associates Of Nw Florida
Chipley, Florida, United States, 32428

United States, California
Diabetes Medical Center Of California
Northridge, California, United States, 91325

United States, South Carolina
Southeastern Research Associates, Inc.
Taylors, South Carolina, United States, 29687

United States, Florida
Central Florida Clinical Trials, Inc.
Altamonte Springs, Florida, United States, 32701

United States, New York
Southgate Medical Group
West Seneca, New York, United States, 14224

United States, California
Encompass Clinical Research
Spring Valley, California, United States, 91978

United States, Texas
Texas Center For Drug Development
Houston, Texas, United States, 77081

United States, California
Valley Research
Fresno, California, United States, 93720

Torrance-Lomita Medical Center
Lomita, California, United States, 90717

United States, Georgia
Endocrine Research Solutions, Inc.
Roswell, Georgia, United States, 30076

United States, Arizona
Clinical Research Advantage, Inc
Tempe, Arizona, United States, 85282

Mexico
Local Institution
Monterrey, Nuevo Leon, Mexico, 64240

Local Institution
Ciudad De Mexico, Distrito Federal, Mexico, 14000

Local Institution
Monterrey, Nuevo Leon, Mexico, 64710

Local Institution
Aguascalientes, Aguascalientes, Mexico, 20127

Local Institution
Mexico City, Mexico, Mexico, 06700

Local Institution
Veracruz, Veracruz, Mexico, 91700

Local Institution
Zapopan, Jal., Jalisco, Mexico, 45150

Local Institution
Monterrey, Nuevo Leon, Mexico, 64060

Hungary
Local Institution
Zalaegerszeg-Pozva, Hungary, 8900

Local Institution
Budapest, Hungary, 1041

Local Institution
Szentes, Hungary, 6600

Local Institution
Budapest, Hungary, 1212

Local Institution
Balatonfured, Hungary, 8230

Mexico
Local Institution
Monterrrey, Nuevo Leon, Mexico, 64700

Canada, Alberta
Local Institution
Calgary, Alberta, Canada, T3B 0M3

United States, Texas

Dgd Research, Inc.
San Antonio, Texas, United States, 78229

Hungary
Local Institution
Budapest, Hungary, 1083

Russian Federation
Local Institution
St. Petersburg, Russian Federation, 195257

Local Institution
Smolensk, Russian Federation, 214018

Local Institution
St. Petersburg, Russian Federation, 194156

Local Institution
St Petersburg, Russian Federation, 198013

Local Institution
Saint-Petersburg, Russian Federation, 191015

Local Institution
St.Petersburg, Russian Federation, 197022

Local Institution
Yaroslaval, Russian Federation, 150062

Local Institution
Kursk, Russian Federation, 305035

Poland
Local Institution
Gdansk, Poland, 80-286

Local Institution
Sopot, Poland, 81-756

Local Institution
Lublin, Poland, 20-950

Local Institution
Krakow, Poland, 30-510

Local Institution

Lodz, Poland, 90-153

Local Institution
Szczecin, Poland, 71-455

Local Institution
Zabrze, Poland, 41-800

Russian Federation
Local Institution
Saratov, Russian Federation, 410031

Mexico
Local Institution
Aguascalientes, Aguascalientes, Mexico, 20230

India
Local Institution
Hariyana, India, 132001

Local Institution
Mumbai, India, 400007

Local Institution
Vellore, India, 632004

Local Institution
Indore, Madhya Pradesh, India, 452001

Local Institution
Pune, India, 411037

Local Institution
Pune, India, 411 030

Local Institution
Pune, India, 411011

References

Citations:

Links: URL: http://ctr.bms.com/ctd/start.do
Description BMS Clinical Trials Disclosure

URL: http://www.bms.com/clinical_trials/Pages/Investigator_Inquiry_form.aspx
Description Investigator Inquiry form

URL: http://www.fda.gov/MEDWATCH/safety.htm
Description For FDA Safety Alerts and Recalls refer to the following link: http://www.fda.gov/MEDWATCH/safety.htm

URL: http://www.clinicalstudyresults.org/drugdetails/?company_id=4&drug_name_id=1235&sort=c.c...
Description Pharma web posting

Study Data/Documents:

Study Results

Participant Flow

Pre-Assignment Details	Of 455 participants randomized, 402 received treatment and completed the 24-week phase. Two participants were mistakenly identified as not completing the short-term (ST) treatment period, although they did. The discrepancy was identified after the ST phase database lock. In reality, 404 completed the ST phase.

Reporting Groups

	Description
Saxagliptin, 5 mg + Insulin	Saxagliptin, 5 mg, added to ongoing insulin with or without metformin therapy for up to 24 weeks in patients with type 2 diabetes
Placebo + Insulin	Placebo added to ongoing insulin with metformin therapy for up to 24 weeks in patients with type 2 diabetes

Period 1: Short-term (24-week) Phase

	Saxagliptin, 5 mg + Insulin	Placebo + Insulin
Started	304	151
Completed	268 [1]	134
Not Completed	36	17
Lack of Efficacy	3	2
Adverse Event	6	3
Withdrawal by Subject	13	5

	Saxagliptin, 5 mg + Insulin	Placebo + Insulin
Death	1	0
Lost to Follow-up	3	5
Poor compliance or noncompliance	5	1
No longer meets study criteria	5	0
Not specified	0	1

[1] Does not include 2 who completed Period 1 but were erroneously reported in the CSR as noncompleters.

Period 2: Long-term (52-week) Phase

	Saxagliptin, 5 mg + Insulin	Placebo + Insulin
Started	268 [1]	134
Completed	246	125
Not Completed	22	9
Lack of Efficacy	1	0
Adverse Event	4	0
Withdrawal by Subject	4	2
Lost to Follow-up	1	1
Poor or noncompliance	5	2
Pregnancy	1	0
No longer meets study criteria	5	4

	Saxagliptin, 5 mg + Insulin	Placebo + Insulin
Not specified	1	0

[1] 270 participants completed short-term phase; 2 of these did not enter long-term phase.

Baseline Characteristics

Reporting Groups

	Description
Saxagliptin, 5 mg + Insulin	Saxagliptin, 5 mg, added to ongoing insulin with or without metformin therapy for up to 24 weeks in patients with type 2 diabetes
Placebo + Insulin	Placebo added to ongoing insulin with metformin therapy for up to 24 weeks in patients with type 2 diabetes

Baseline Measures

		Saxagliptin, 5 mg + Insulin	Placebo + Insulin	Total
Overall Number of Participants		304	151	455
Age, Customized Median (Full Range) Unit of measure: years	Number Analyzed	304 participants	151 participants	455 participants
[Not specified]		58 (18 to 77)	58 (30 to 77)	58 (18 to 77)
Age, Customized Measure Type: Number Unit of measure: participants	Number Analyzed	304 participants	151 participants	455 participants
Younger than 65 years		233	118	351
65 years to younger than 75 years		65	30	95
75 years and older		6	3	9

		Saxagliptin, 5 mg + Insulin	Placebo + Insulin	Total
Age, Customized Mean (Standard Deviation) Unit of measure: Years	Number Analyzed	304 participants	151 participants	455 participants
[Not specified]		57.2 (9.43)	57.3 (9.27)	57.2 (9.37)
Gender, Male/ Female Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	304 participants	151 participants	455 participants
	Female	184 60.53%	83 54.97%	267 58.68%
	Male	120 39.47%	68 45.03%	188 41.32%
Race (NIH/OMB) Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	304 participants	151 participants	455 participants
	American Indian or Alaska Native	0 0%	0 0%	0 0%
	Asian	40 13.16%	19 12.58%	59 12.97%
	Native Hawaiian or Other Pacific Islander	0 0%	0 0%	0 0%
	Black or African American	13 4.28%	9 5.96%	22 4.84%
	White	237 77.96%	118 78.15%	355 78.02%
	More than one race	0 0%	0 0%	0 0%
	Unknown or Not Reported	14 4.61%	5 3.31%	19 4.18%

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Adjusted Mean Change From Baseline in A1C Levels (Last Observation Carried Forward [LOCF])
Measure Description	Change from baseline: post-pre. Adjusted for baseline (value and metformin use). ANCOVA model: difference between week t and baseline values=baseline values + treatment + metformin use
Time Frame	Baseline to Week 24
Safety Issue?	No

Analysis Population Description

Randomized participants who received at least 1 dose of double-blind study medication. Participants must also have had both a baseline and at least 1 postrandomization measurement in the 24- and 52-week periods.

Reporting Groups

	Description
Saxagliptin, 5 mg + Insulin	Saxagliptin, 5 mg, added to ongoing insulin with or without metformin therapy for up to 24 weeks in patients with type 2 diabetes
Placebo + Insulin	Placebo added to ongoing insulin with metformin therapy for up to 24 weeks in patients with type 2 diabetes

Measured Values

	Saxagliptin, 5 mg + Insulin	Placebo + Insulin
Number of Participants Analyzed	300	149
Adjusted Mean Change From Baseline in A1C Levels (Last Observation Carried Forward [LOCF]) Mean (Standard Error) Unit of measure: Percentage of change	-0.73 (0.054)	-0.32 (0.074)

Statistical Analysis 1 for Adjusted Mean Change From Baseline in A1C Levels (Last Observation Carried Forward [LOCF])

Statistical Analysis Overview	Comparison Groups	Saxagliptin, 5 mg + Insulin
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	Significance testing based on hierarchical testing. Primary and secondary endpoints are presented in order of testing.
	Method	ANCOVA
	Comments	Adjusted mean difference for saxagliptin groups vs placebo in Week 24 (LOCF). Adjusted for baseline.

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.41
	Confidence Interval	(2-Sided) 95% -0.59 to -0.24
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.089
	Estimation Comments	ANCOVA model: difference between week t and baseline values = baseline values + treatment + metformin use

2. Secondary Outcome Measure:

Measure Title	Change From Baseline in Postprandial Glucose (PPG) Area Under the Curve (AUC) Response to an Meal Tolerance Test (MTT)
Measure Description	An MTT is a 2-part test that measures glucose and insulin levels after an overnight fast and before ingesting a meal consisting of a nutritional drink and power bar and again at prespecified times (30, 60, 120, and 180 minutes) after the start of ingestion of the meal
Time Frame	Baseline to Week 24
Safety Issue?	No

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
Saxagliptin, 5 mg + Insulin	Saxagliptin, 5 mg, added to ongoing insulin with or without metformin therapy for up to 24 weeks in patients with type 2 diabetes
Placebo + Insulin	Placebo added to ongoing insulin with metformin therapy for up to 24 weeks in patients with type 2 diabetes

Measured Values

	Saxagliptin, 5 mg + Insulin	Placebo + Insulin
Number of Participants Analyzed	258	122
Change From Baseline in Postprandial Glucose (PPG) Area Under the Curve (AUC) Response to an Meal Tolerance Test (MTT) Mean (Standard Error) Unit of measure: mg*min/dL	-4548.5 (687.65)	-718.8 (981.63)

Statistical Analysis 1 for Change From Baseline in Postprandial Glucose (PPG) Area Under the Curve (AUC) Response to an Meal Tolerance Test (MTT)

Statistical Analysis Overview	Comparison Groups	Saxagliptin, 5 mg + Insulin, Placebo + Insulin
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0011
	Comments	Significance testing based on hierarchical testing. Primary and secondary endpoints are presented in order of testing.
	Method	ANCOVA
	Comments	Adjusted mean difference for saxagliptin groups vs placebo in Week 24 (LOCF). Adjusted for baseline.

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-3829.8
	Confidence Interval	(2-Sided) 95% -6122.4 to -1537.1
	Parameter Dispersion	Type: Standard Error of the mean Value: 1165.99
	Estimation Comments	ANCOVA model: difference between week t and baseline values = baseline values + treatment + metformin use

3. Secondary Outcome Measure:

Measure Title	Change From Baseline in 120-minute PPG Values During an MTT

Measure Description	An MTT is a 2-part test that measures glucose and insulin levels after an overnight fast and before ingesting a meal consisting of a nutritional drink and power bar and again at prespecified times (30, 60, 120, and 180 minutes) after the start of ingestion of the meal.
Time Frame	Baseline to Week 24
Safety Issue?	No

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Saxagliptin, 5 mg + Insulin	Saxagliptin, 5 mg, added to ongoing insulin with or without metformin therapy for up to 24 weeks in patients with type 2 diabetes
Placebo + Insulin	Placebo added to ongoing insulin with metformin therapy for up to 24 weeks in patients with type 2 diabetes

Measured Values

	Saxagliptin, 5 mg + Insulin	Placebo + Insulin
Number of Participants Analyzed	262	129
Change From Baseline in 120-minute PPG Values During an MTT Mean (Standard Error) Unit of measure: mg/dL	-27.2 (4.35)	-4.2 (6.08)

Statistical Analysis 1 for Change From Baseline in 120-minute PPG Values During an MTT

Statistical Analysis Overview	Comparison Groups	Saxagliptin, 5 mg + Insulin, Placebo + Insulin
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0016
	Comments	Significance testing based on hierarchical testing. Primary and secondary endpoints are presented in order of testing.
	Method	ANCOVA

	Comments	Adjusted mean difference for saxagliptin groups vs placebo in Week 24 (LOCF). Adjusted for baseline.

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-23.0
	Confidence Interval	(2-Sided) 95% -37.2 to -8.7
	Parameter Dispersion	Type: Standard Error of the mean Value: 7.24
	Estimation Comments	ANCOVA model: difference between week t and baseline values = baseline values + treatment + metformin use

4. Secondary Outcome Measure:

Measure Title	Change From Baseline in Fasting Plasma Glucose Values
Measure Description	
Time Frame	Baseline to Week 24
Safety Issue?	No

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
Saxagliptin, 5 mg + Insulin	Saxagliptin, 5 mg, added to ongoing insulin with or without metformin therapy for up to 24 weeks in patients with type 2 diabetes
Placebo + Insulin	Placebo added to ongoing insulin with metformin therapy for up to 24 weeks in patients with type 2 diabetes

Measured Values

	Saxagliptin, 5 mg + Insulin	Placebo + Insulin
Number of Participants Analyzed	300	149
Change From Baseline in Fasting Plasma Glucose Values Mean (Standard Error) Unit of measure: mg/dL	-10.1 (2.87)	-6.1 (3.98)

Statistical Analysis 1 for Change From Baseline in Fasting Plasma Glucose Values

Statistical Analysis Overview	Comparison Groups	Saxagliptin, 5 mg + Insulin, Placebo + Insulin
	Comments	.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.3958
	Comments	Significance testing based on hierarchical testing. Primary and secondary endpoints are presented in order of testing.
	Method	ANCOVA
	Comments	Adjusted mean difference for saxagliptin groups vs placebo in Week 24 (LOCF). Adjusted for baseline.

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-4.02
	Confidence Interval	(2-Sided) 95% -13.32 to 5.28
	Parameter Dispersion	Type: Standard Error of the mean Value: 4.732
	Estimation Comments	ANCOVA model: difference between week t and baseline values = baseline values + treatment + metformin use

5. Secondary Outcome Measure:

Measure Title	Percentage of Participants Achieving a Therapeutic Glycemic Response
Measure Description	Therapeutic glycemic response is defined as an A1C<7%. Significance was not interpreted with a p value.
Time Frame	Baseline to Week 24
Safety Issue?	No

Analysis Population Description

Randomized participants who received at least 1 dose of double-blind study medication. Participants must also have had both a baseline and at least 1 postrandomization measurement in the 24-week period.

Reporting Groups

	Description
Saxagliptin, 5 mg + Insulin	Saxagliptin, 5 mg, added to ongoing insulin with or without metformin therapy for up to 24 weeks in patients with type 2 diabetes
Placebo + Insulin	Placebo added to ongoing insulin with metformin therapy for up to 24 weeks in patients with type 2 diabetes

Measured Values

	Saxagliptin, 5 mg + Insulin	Placebo + Insulin
Number of Participants Analyzed	300	149
Percentage of Participants Achieving a Therapeutic Glycemic Response Measure Type: Number Unit of measure: Percentage of participants	17.3	6.7

6. Secondary Outcome Measure:

Measure Title	Change From Baseline in Mean Total Daily Dose of Insulin (MTDDI) (LOCF)
Measure Description	Based on information recorded in the participant's daily diary. The MTDDI was calculated at every visit using the values patients recorded since the last regularly scheduled visit (minimum of 80% of days with a value). At every visit, the MTDDI was compared with the participant's baseline MTDDI (measured during a 4-week lead-in period) to identify any changes in insulin use at that visit compared with insulin use at baseline.
Time Frame	Baseline to Week 24
Safety Issue?	No

Analysis Population Description

Randomized participants who received at least 1 dose of double-blind study medication. Participants must also have had both a baseline and at least 1 postrandomization measurement in the 24-week period.

Reporting Groups

	Description
Saxagliptin, 5 mg + Insulin	Saxagliptin, 5 mg, added to ongoing insulin with or without metformin therapy for up to 24 weeks in patients with type 2 diabetes
Placebo + Insulin	Placebo added to ongoing insulin with metformin therapy for up to 24 weeks in patients with type 2 diabetes

Measured Values

	Saxagliptin, 5 mg + Insulin	Placebo + Insulin
Number of Participants Analyzed	299	151
Change From Baseline in Mean Total Daily Dose of Insulin (MTDDI) (LOCF) Mean (Standard Error) Unit of measure: Units	1.71 (0.704)	5.01 (0.970)

Statistical Analysis 1 for Change From Baseline in Mean Total Daily Dose of Insulin (MTDDI) (LOCF)

Statistical Analysis Overview	Comparison Groups	Saxagliptin, 5 mg + Insulin
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	
	Comments	Significance testing based on hierarchical testing. Primary and secondary endpoints are presented in order of testing.
	Method	ANCOVA
	Comments	Adjusted mean difference for saxagliptin groups vs placebo in Week 24 (LOCF). Adjusted for baseline.

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-3.3
	Confidence Interval	(2-Sided) 95% -5.6 to -1.1
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.16
	Estimation Comments	ANCOVA model: difference between week t and baseline values = baseline values + treatment + metformin use

7. Other Pre-specified Outcome Measure:

Measure Title	Number of Participants With Abnormal Changes From Baseline in Electrocardiogram (ECG) Results

Measure Description	ECG abnormalities included those in nonspecific "other" categories (Other nonspecific ST/T, Other intraventricular conduction defect, Other, and Other rhythm abnormalities)and nonspecific findings, such as sinus bradycardia, sinus arrythmia, sinus tachycardia, poor R-wave progression, and ventricular premature contractions.
Time Frame	Baseline to Week 52
Safety Issue?	Yes

Analysis Population Description

Participants who had normal ECG findings at baseline and who received at least 1 dose of study medication.

Reporting Groups

	Description
Saxagliptin, 5 mg + Insulin	Saxagliptin, 5 mg, added to ongoing insulin with or without metformin therapy for up to 24 weeks in patients with type 2 diabetes
Placebo + Insulin	Placebo added to ongoing insulin with metformin therapy for up to 24 weeks in patients with type 2 diabetes

Measured Values

	Saxagliptin, 5 mg + Insulin	Placebo + Insulin
Number of Participants Analyzed	153	75
Number of Participants With Abnormal Changes From Baseline in Electrocardiogram (ECG) Results Measure Type: Number Unit of measure: Participants	15	11

8. Other Pre-specified Outcome Measure:

Measure Title	Shift in Absolute Lymphocyte Counts From Baseline to Selected Visits (LOCF)
Measure Description	Absolute lymphocyte count=value*10^3 c/uL
Time Frame	Baseline and Weeks 24 and 52
Safety Issue?	Yes

Analysis Population Description

All participants who received at least 1 dose of double-blind study medication.

Reporting Groups

	Description
Saxagliptin, 5 mg + Insulin	Saxagliptin, 5 mg, added to ongoing insulin with or without metformin therapy for up to 24 weeks in patients with type 2 diabetes
Placebo + Insulin	Placebo added to ongoing insulin with metformin therapy for up to 24 weeks in patients with type 2 diabetes

Measured Values

	Saxagliptin, 5 mg + Insulin	Placebo + Insulin
Number of Participants Analyzed	304	151
Shift in Absolute Lymphocyte Counts From Baseline to Selected Visits (LOCF) Measure Type: Number Unit of measure: Participants		
Baseline <= 0.75; Week 24 <= 0.75	0	0
Baseline <= 0.75; Week 24 >0.75- <= 5.00	0	2
Baseline <= 0.75; Week 24 >5.00	0	0
Baseline >0.75- <= 5.00; Week 24 <= 0.75	1	0
Baseline >0.75- <= 5.00; Week 24 >0.75- <= 5.00	293	148
Baseline >0.75- <= 5.00; Week 24 >5.00	1	0
Baseline >5.00; Week 24 <= 0.75	0	0
Baseline >5.00; Week 24 >0.75- <= 5.00	0	0
Baseline >5.00; Week 24 >5.00	1	0
Baseline <= 0.75; Week 52 <= 0.75	0	0
Baseline <= 0.75; Week 52 >0.75- <= 5.00	0	2
Baseline <= 0.75; Week 52 >5.00	0	0
Baseline >0.75- <= 5.00; Week 52 <= 0.75	0	0
Baseline >0.75- <= 5.00; Week 52 >0.75- <= 5.00	295	147
Baseline >0.75- <= 5.00; Week 52 >5.00	0	1
Baseline >5.00; Week 52 <= 0.75	0	0
Baseline >5.00; Week 52 >0.75- <= 5.00	0	0
Baseline >5.00; Week 52 >5.00	1	0

9. Other Pre-specified Outcome Measure:

Measure Title	Number of Participants With at Least 1 Adverse Event (AE), at Least 1 Treatment-related AE, Death as Outcome, at Least 1 Serious Adverse Event (SAE), at Least 1 Treatment-related SAE, Discontinuations Due to SAEs, and Discontinuations Due to AEs
Measure Description	An AE is any new untoward medical occurrence or worsening of a preexisting medical condition that does not necessarily have a causal relationship with this treatment. An SAE is any untoward medical event that at any dose: results in death, persistent or significant disability/incapacity, or drug dependency or abuse; is life-threatening, an important medical event, or a congenital anomaly/birth defect; requires inpatient hospitalization; or prolongs existing hospitalization. Treatment-related=possibly, probably, or certainly related to and of unknown relationship to study treatment.
Time Frame	Baseline to Week 52, continuously
Safety Issue?	Yes

Analysis Population Description

All participants who received at least 1 dose of double-blind study medication.

Reporting Groups

	Description
Saxagliptin, 5 mg + Insulin	Saxagliptin, 5 mg, added to ongoing insulin with or without metformin therapy for up to 24 weeks in patients with type 2 diabetes
Placebo + Insulin	Placebo added to ongoing insulin with metformin therapy for up to 24 weeks in patients with type 2 diabetes

Measured Values

	Saxagliptin, 5 mg + Insulin	Placebo + Insulin
Number of Participants Analyzed	304	151
Number of Participants With at Least 1 Adverse Event (AE), at Least 1 Treatment-related AE, Death as Outcome, at Least 1 Serious Adverse Event (SAE), at Least 1 Treatment-related SAE, Discontinuations Due to SAEs, and Discontinuations Due to AEs Measure Type: Number Unit of measure: Participants		
At least 1 AE	202	108
At least 1 treatment-related AE	56	34
Deaths	2	0

	Saxagliptin, 5 mg + Insulin	Placebo + Insulin
At least 1 SAE	25	13
At least 1 treatment-related SAE	3	0
Discontinuations due to SAEs	4	0
Discontinuations due to AEs	9	3

10. Other Pre-specified Outcome Measure:

Measure Title	Mean Changes From Baseline in Systolic and Diastolic Blood Pressure Readings
Measure Description	
Time Frame	Baseline to Weeks 2, 4, 6, 8, 12, 16, 20, 24, 28, 36, 44, and 52
Safety Issue?	Yes

Analysis Population Description

All participants who received at least 1 dose of double-blind study medication.

Reporting Groups

	Description
Saxagliptin, 5 mg + Insulin	Saxagliptin, 5 mg, added to ongoing insulin with or without metformin therapy for up to 24 weeks in patients with type 2 diabetes
Placebo + Insulin	Placebo added to ongoing insulin with metformin therapy for up to 24 weeks in patients with type 2 diabetes

Measured Values

	Saxagliptin, 5 mg + Insulin	Placebo + Insulin
Number of Participants Analyzed	304	151
Mean Changes From Baseline in Systolic and Diastolic Blood Pressure Readings Number (95% Confidence Interval) Unit of measure: mm Hg		
Systolic blood pressure (Week 2) (n=294, 147)	-1.0 (-2.3 to 0.4)	2.3 (-0.0 to 4.6)
Systolic blood pressure (Week 4) (n=293, 144)	-1.2 (-2.6 to 0.2)	0.0 (-2.3 to 2.4)
Systolic blood pressure (Week 6) (n=280, 141)	-0.8 (-2.4 to 0.7)	1.0 (-1.2 to 3.2)

	Saxagliptin, 5 mg + Insulin	Placebo + Insulin
Systolic blood pressure (Week 8) (n=290, 142)	-0.8 (-2.4 to 0.8)	2.4 (-0.2 to 4.9)
Systolic blood pressure (Week 12) (n=286, 144)	-1.7 (-3.2 to -0.2)	2.2 (0.0 to 4.3)
Systolic blood pressure (Week 16) (n=278, 139)	-1.2 (-2.9 to 0.5)	1.1 (-1.1 to 3.3)
Systolic blood pressure (Week 20) (n=276, 137)	-0.6 (-2.0 to 0.9)	1.3 (-1.0 to 3.7)
Systolic blood pressure (Week 24) (n=273, 134)	-1.5 (-3.2 to 0.1)	-0.1 (-2.2 to 2.0)
Systolic blood pressure (Week 28) (n=264, 132)	-1.4 (-3.0 to 0.1)	1.8 (-0.6 to 4.2)
Systolic blood pressure (Week 36) (n=261, 129)	-0.7 (-2.4 to 1.1)	3.6 (1.2 to 6.0)
Systolic blood pressure (Week 44) (n=250, 125)	-0.6 (-2.2 to 1.0)	2.6 (0.4 to 4.8)
Systolic blood pressure (Week 52) (n=246, 125)	0.0 (-1.7 to 1.7)	1.0 (-1.3 to 3.3)
Diastolic blood pressure (Week 2) (n=294, 147)	0.1 (-0.9 to 1.0)	1.4 (-0.0 to 2.8)
Diastolic blood pressure (Week 4) (n=293, 144)	0.0 (-1.0 to 1.1)	1.8 (0.4 to 3.2)
Diastolic blood pressure (Week 6) (n=280, 141)	0.0 (-1.0 to 1.1)	0.3 (-1.1 to 1.8)
Diastolic blood pressure (Week 8) (n=290, 142)	-0.5 (-1.5 to 0.4)	2.1 (0.6 to 3.6)
Diastolic blood pressure (Week 12) (n=286, 144)	-0.8 (-1.8 to 0.2)	1.0 (-0.3 to 2.4)
Diastolic blood pressure (Week 16) (n=278, 139)	-1.1 (-2.1 to -0.1)	1.3 (-0.0 to 2.6)
Diastolic blood pressure (Week 20) (n=276, 137)	-0.7 (-1.8 to 0.4)	1.1 (-0.3 to 2.5)
Diastolic blood pressure (Week 24) (n=273, 134)	-1.7 (-2.8 to -0.6)	0.5 (-0.9 to 1.9)
Diastolic blood pressure (Week 28) (n=264, 132)	-1.6 (-2.7 to -0.5)	0.2 (-1.3 to 1.7)
Diastolic blood pressure (Week 36) (n=261, 129)	-1.2 (-2.4 to 0.1)	0.2 (-1.1 to 1.6)
Diastolic blood pressure (Week 44) (n=250, 125)	-0.3 (-1.5 to 1.0)	0.4 (-1.0 to 1.8)
Diastolic blood pressure (Week 52) (n=246, 125)	-0.5 (-1.7 to 0.7)	0.1 (-1.4 to 1.6)

11. Other Pre-specified Outcome Measure:

Measure Title	Mean Changes From Baseline in Heart Rate
Measure Description	
Time Frame	Baseline to Weeks 2, 4, 6, 8, 12, 16, 20, 24, 28, 36, 44, and 52
Safety Issue?	Yes

Analysis Population Description

All participants who received at least 1 dose of double-blind study medication.

Reporting Groups

	Description
Saxagliptin, 5 mg + Insulin	Saxagliptin, 5 mg, added to ongoing insulin with or without metformin therapy for up to 24 weeks in patients with type 2 diabetes
Placebo + Insulin	Placebo added to ongoing insulin with metformin therapy for up to 24 weeks in patients with type 2 diabetes

Measured Values

	Saxagliptin, 5 mg + Insulin	Placebo + Insulin
Number of Participants Analyzed	304	151
Mean Changes From Baseline in Heart Rate Number (95% Confidence Interval) Unit of measure: Beats per minute		
Week 2 (n=294, 147)	-0.5 (-1.4 to 0.4)	-0.7 (-1.8 to 0.4)
Week 4 (n=293, 144)	-0.5 (-1.5 to 0.5)	-1.0 (-2.1 to 0.2)
Week 6 (n=280, 141)	-0.5 (-1.5 to 0.4)	-0.9 (-2.3 to 0.4)
Week 8 (n=290, 142)	-0.0 (-1.0 to 1.0)	-0.7 (-2.0 to 0.6)
Week 12 (n=286, 144)	0.3 (-0.7 to 1.3)	0.2 (-1.0 to 1.4)
Week 16 (n=278, 139)	-1.0 (-2.1 to 0.1)	-0.6 (-2.1 to 1.0)
Week 20 (n=276, 137)	-0.5 (-1.6 to 0.6)	0.4 (-0.9 to 1.8)
Week 24 (n=273, 134)	0.0 (-1.2 to 1.3)	-1.0 (-2.5 to 0.4)
Week 28 (n=264, 132)	-1.0 (-2.1 to 0.2)	-0.6 (-2.1 to 0.9)
Week 36 (n=261, 129)	0.0 (-1.1 to 1.2)	-0.0 (-1.4 to 1.4)
Week 44 (n=250, 125)	0.2 (-0.9 to 1.4)	-0.7 (-2.3 to 1.0)
Week 52 (n=246, 125)	-0.3 (-1.5 to 0.8)	0.2 (-1.7 to 2.1)

12. Other Pre-specified Outcome Measure:

Measure Title	Shift in Platelet Counts From Baseline to Selected Visits (LOCF)

Measure Description	Platelet count=value*10^9 c/L
Time Frame	Baseline and Weeks 24 and 52
Safety Issue?	Yes

Analysis Population Description

All participants who received at least 1 dose of double-blind study medication.

Reporting Groups

	Description
Saxagliptin, 5 mg + Insulin	Saxagliptin, 5 mg, added to ongoing insulin with or without metformin therapy for up to 24 weeks in patients with type 2 diabetes
Placebo + Insulin	Placebo added to ongoing insulin with metformin therapy for up to 24 weeks in patients with type 2 diabetes

Measured Values

	Saxagliptin, 5 mg + Insulin	Placebo + Insulin
Number of Participants Analyzed	304	151
Shift in Platelet Counts From Baseline to Selected Visits (LOCF) Measure Type: Number Unit of measure: Participants		
Baseline <= 100; Week 24 <= 100	0	0
Baseline <= 100; Week 24 >100 - <= 600	0	0
Baseline <= 100; Week 24 >600	0	0
Baseline >100 - <= 600; Week 24 <= 100	1	1
Baseline >100 - <= 600; Week 24 >100 - <= 600	296	143
Baseline >100 - <= 600; Week 24 >600	0	0
Baseline >600; Week 24 <= 100	0	0
Baseline >600; Week 24 >100 - <= 600	0	0
Baseline >600; Week 24 >600	0	0
Baseline <= 100; Week 52 <= 100	0	0
Baseline <= 100; Week 52 >100 - <= 600	0	1
Baseline <= 100; Week 52 >600	0	0

	Saxagliptin, 5 mg + Insulin	Placebo + Insulin
Baseline >100 - <= 600; Week 52 <= 100	2	0
Baseline >100 - <= 600; Week 52 >100 - <= 600	295	144
Baseline >100 - <= 600; Week 52 >600	0	0
Baseline >600; Week 52 <= 100	0	0
Baseline >600; Week 52 >100 - <= 600	0	0
Baseline >600; Week 52 >600	0	0

13. Other Pre-specified Outcome Measure:

Measure Title	Number of Participants With Marked Laboratory Abnormalities During the 24-Week ST + 52-Week LT Treatment Period
Measure Description	Marked abnormality=a laboratory value lying outside the predefined criteria and more extreme (farther from the limit)on-treatment than at baseline. ULN=upper limit of normal; LLN=lower limit of normal; prx=pre-RX=pretreatment. Criteria 1: if prx=0 use >=2, if prx=0.5 or 1 use >=3, if prx=2 use 4.
Time Frame	Baseline and during and up to 14 days after last dose of study drug (in Week 52)
Safety Issue?	Yes

Analysis Population Description

All participants who received at least 1 dose of double-blind study medication.

Reporting Groups

	Description
Saxagliptin, 5 mg + Insulin	Saxagliptin, 5 mg, added to ongoing insulin with or without metformin therapy for up to 24 weeks in patients with type 2 diabetes
Placebo + Insulin	Placebo added to ongoing insulin with metformin therapy for up to 24 weeks in patients with type 2 diabetes

Measured Values

	Saxagliptin, 5 mg + Insulin	Placebo + Insulin
Number of Participants Analyzed	304	151

	Saxagliptin, 5 mg + Insulin	Placebo + Insulin
Number of Participants With Marked Laboratory Abnormalities During the 24-Week ST + 52-Week LT Treatment Period Measure Type: Number Unit of measure: Participants		
Hemoglobin <8 g/dL (n=300; 150)	2	0
Hematocrit <0.75*prx (n=300; 150)	2	2
Platelets <50*10^9 c/L (n=297; 145)	0	0
Platelets >1.5*ULN (n=297; 145)	0	0
Leukocytes <2*1000 c/uL (n=300; 150)	0	1
Neutrophils <1*1000 c/uL (n=296; 150)	1	0
Eosinophils >0.9*1000 c/uL (n=296; 150)	9	7
Lymphocytes <=0.75*1000 c/uL (n=296; 150)	3	2
Alkaline phosphatase >3*prx & >ULN (n=302; 150)	2	1
Alkaline phosphatase >1.5 ULN (n=302; 150)	10	5
Aspartate aminotransferase >3* ULN (n=298; 148)	2	0
Aspartate aminotransferase>5* ULN (n=298; 148)	1	0
Aspartate aminotransferase >10*ULN (n=298; 148)	0	0
Aspartate aminotransferase >20*ULN (n=298; 148)	0	0
Alanine transaminase >3*ULN (n=300; 148)	5	3
Alanine transaminase >5*ULN (n=300; 148)	1	0
Alanine transaminase >10*ULN (n=300; 148)	0	0
Alanine transaminase >20*ULN (n=300; 148)	0	0
Bilirubin, total >2 mg/dL (n=301; 150)	0	0
Bilirubin, total >1.5*ULN (n=301; 150)	0	1
Bilirubin, total >2*ULN (n=301; 150)	0	0
Blood urea nitrogen >2*prx & >ULN (n=302; 150)	5	7
Creatinine >2.5 mg/dL (n=303; 150)	0	0
Glucose, serum fasting <50 mg/dL (n=0; 0)	0	0

	Saxagliptin, 5 mg + Insulin	Placebo + Insulin
Glucose, serum fasting >500 mg/dL (n=0; 0)	0	0
Glucose, serum unspecified <50 mg/dL (n=0; 0)	0	0
Glucose, serum unspecified >500 mg/dL (n=0; 0)	0	0
Glucose, plasma fasting <50 mg/dL (n=301;150)	5	0
Glucose, plasma fasting >500 mg/dL (n=301;150)	0	1
Glucose, plasma unspecified <50 mg/dL (n=272; 133)	5	1
Glucose, plasma unspecified >500 mg/d (n=272; 133)	1	1
Sodium, serum <0.9*prx & <=130 mEq/L (n=302; 150)	1	0
Sodium, serum >1.1*prx & >=150 mEq/L (n=302; 150)	0	0
Potassium, serum <0.8 prx &<=3.2 mEq/L(n=300; 148)	3	1
Potassium, serum >1.2*prx&>= 6.0 mEq/L(n=300; 148)	8	8
Chloride, serum <90 mEq/L (n=302; 150)	1	0
Chloride, serum >120 mEq/L (n=302; 150)	0	0
Albumin <0.9*LLN; if prx<LLN, 0.75*prx (n=302,150)	1	0
Creatine kinase >5*ULN (n=301, 148)	6	2
Uric acid >1.5*ULN; if prx >ULN, >2 (n=0,0)	0	0
Protein urine (see criteria 1) (n=297,146)	8	3
Blood urine (see criteria 1) (n=297; 146)	14	2
Red blood cells urine (see criteria 1) (n=53; 31)	8	3
White blood cells urine (see criteria 1)(n=115;53)	35	10

14. Other Pre-specified Outcome Measure:

Measure Title	Percentage of Participants With Reported and Confirmed Hypoglycemia
Measure Description	Confirmed hypoglycemia=fingerstick glucose measurement of ≤50 mg/dL with associated symptoms/
Time Frame	Baseline to Week 52
Safety Issue?	Yes

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Saxagliptin, 5 mg + Insulin	Saxagliptin, 5 mg, added to ongoing insulin with or without metformin therapy for up to 24 weeks in patients with type 2 diabetes
Placebo + Insulin	Placebo added to ongoing insulin with metformin therapy for up to 24 weeks in patients with type 2 diabetes

Measured Values

	Saxagliptin, 5 mg + Insulin	Placebo + Insulin
Number of Participants Analyzed	300	149
Percentage of Participants With Reported and Confirmed Hypoglycemia Measure Type: Number Unit of measure: Percentage of Participants		
Reported	19.4	24.5
Confirmed	7.6	6.6

Reported Adverse Events

Time Frame	Baseline to Week 52
Additional Description	[Not specified]

Reporting Groups

	Description
Placebo + Insulin	Placebo added to ongoing insulin with metformin therapy for up to 24 weeks in patients with type 2 diabetes
Saxagliptin, 5 mg + Insulin	Saxagliptin, 5 mg, added to ongoing insulin with or without metformin therapy for up to 24 weeks in patients with type 2 diabetes

Serious Adverse Events

	Placebo + Insulin	Saxagliptin, 5 mg + Insulin
	Affected/At Risk (%)	Affected/At Risk (%)
Total	13/151 (8.61%)	25/304 (8.22%)
Blood and lymphatic system disorders		
ANAEMIA VITAMIN B12 DEFICIENCY [A] †	1/151 (0.66%)	0/304 (0%)
IRON DEFICIENCY ANAEMIA [A] †	1/151 (0.66%)	0/304 (0%)
Cardiac disorders		
ACUTE CORONARY SYNDROME [A] †	0/151 (0%)	1/304 (0.33%)
ACUTE MYOCARDIAL INFARCTION [A] †	0/151 (0%)	1/304 (0.33%)
ANGINA PECTORIS [A] †	0/151 (0%)	1/304 (0.33%)
CARDIAC FAILURE [A] †	0/151 (0%)	2/304 (0.66%)
CORONARY ARTERY OCCLUSION [A] †	0/151 (0%)	1/304 (0.33%)
MYOCARDIAL INFARCTION [A] †	0/151 (0%)	1/304 (0.33%)
MYOCARDIAL ISCHAEMIA [A] †	0/151 (0%)	1/304 (0.33%)
Eye disorders		
DIABETIC RETINOPATHY [A] †	0/151 (0%)	1/304 (0.33%)
Gastrointestinal disorders		
CONSTIPATION [A] †	0/151 (0%)	1/304 (0.33%)
CROHN'S DISEASE [A] †	0/151 (0%)	1/304 (0.33%)
PANCREATITIS CHRONIC [A] †	1/151 (0.66%)	0/304 (0%)
General disorders		
CHEST PAIN [A] †	0/151 (0%)	1/304 (0.33%)
INFLUENZA LIKE ILLNESS [A] †	1/151 (0.66%)	0/304 (0%)
Hepatobiliary disorders		
CHOLANGITIS [A] †	1/151 (0.66%)	0/304 (0%)

	Placebo + Insulin	Saxagliptin, 5 mg + Insulin
	Affected/At Risk (%)	Affected/At Risk (%)
CHOLANGITIS ACUTE [A] †	1/151 (0.66%)	0/304 (0%)
JAUNDICE [A] †	1/151 (0.66%)	0/304 (0%)
Infections and infestations		
ABSCESS LIMB [A] †	2/151 (1.32%)	0/304 (0%)
ARTHRITIS INFECTIVE [A] †	1/151 (0.66%)	0/304 (0%)
BRONCHITIS [A] †	1/151 (0.66%)	0/304 (0%)
CELLULITIS [A] †	1/151 (0.66%)	0/304 (0%)
DENGUE FEVER [A] †	0/151 (0%)	1/304 (0.33%)
DIVERTICULITIS [A] †	0/151 (0%)	1/304 (0.33%)
INTESTINAL GANGRENE [A] †	0/151 (0%)	1/304 (0.33%)
OSTEOMYELITIS [A] †	1/151 (0.66%)	0/304 (0%)
PNEUMONIA [A] †	0/151 (0%)	1/304 (0.33%)
URINARY TRACT INFECTION [A] †	0/151 (0%)	1/304 (0.33%)
Injury, poisoning and procedural complications		
ANKLE FRACTURE [A] †	0/151 (0%)	1/304 (0.33%)
CONTUSION [A] †	0/151 (0%)	1/304 (0.33%)
Investigations		
LIVER FUNCTION TEST ABNORMAL [A] †	0/151 (0%)	1/304 (0.33%)
Metabolism and nutrition disorders		
HYPOGLYCAEMIA [A] †	0/151 (0%)	1/304 (0.33%)
Musculoskeletal and connective tissue disorders		
ARTHRALGIA [A] †	0/151 (0%)	1/304 (0.33%)

	Placebo + Insulin	Saxagliptin, 5 mg + Insulin
	Affected/At Risk (%)	Affected/At Risk (%)
INTERVERTEBRAL DISC PROTRUSION [A] †	1/151 (0.66%)	0/304 (0%)
NECK PAIN [A] †	0/151 (0%)	1/304 (0.33%)
OSTEOARTHRITIS [A] †	0/151 (0%)	2/304 (0.66%)
OSTEOPOROSIS [A] †	1/151 (0.66%)	0/304 (0%)
PAIN IN EXTREMITY [A] †	1/151 (0.66%)	0/304 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
BREAST CANCER [A] †	0/151 (0%)	1/304 (0.33%)
PANCREATIC CARCINOMA [A] †	0/151 (0%)	1/304 (0.33%)
PITUITARY TUMOUR [A] †	1/151 (0.66%)	0/304 (0%)
PROSTATE CANCER METASTATIC [A] †	1/151 (0.66%)	0/304 (0%)
UTERINE LEIOMYOMA [A] †	0/151 (0%)	1/304 (0.33%)
Nervous system disorders		
SCIATICA [A] †	1/151 (0.66%)	0/304 (0%)
THALAMIC INFARCTION [A] †	1/151 (0.66%)	0/304 (0%)
TRANSIENT ISCHAEMIC ATTACK [A] †	1/151 (0.66%)	0/304 (0%)
Renal and urinary disorders		
RENAL FAILURE ACUTE [A] †	1/151 (0.66%)	0/304 (0%)
RENAL IMPAIRMENT [A] †	0/151 (0%)	1/304 (0.33%)
Vascular disorders		
HYPERTENSION [A] †	0/151 (0%)	1/304 (0.33%)
PERIPHERAL ISCHAEMIA [A] †	1/151 (0.66%)	0/304 (0%)
PERIPHERAL VASCULAR DISORDER [A] †	1/151 (0.66%)	0/304 (0%)

	Placebo + Insulin	Saxagliptin, 5 mg + Insulin
	Affected/At Risk (%)	Affected/At Risk (%)
THROMBOPHLEBITIS SUPERFICIAL [A] †	0/151 (0%)	1/304 (0.33%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 13.1

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	Placebo + Insulin	Saxagliptin, 5 mg + Insulin
	Affected/At Risk (%)	Affected/At Risk (%)
Total	64/151 (42.38%)	96/304 (31.58%)
Infections and infestations		
BRONCHITIS [A] †	4/151 (2.65%)	16/304 (5.26%)
INFLUENZA [A] †	14/151 (9.27%)	10/304 (3.29%)
NASOPHARYNGITIS [A] †	10/151 (6.62%)	19/304 (6.25%)
PHARYNGITIS [A] †	8/151 (5.3%)	11/304 (3.62%)
UPPER RESPIRATORY TRACT INFECTION [A] †	11/151 (7.28%)	19/304 (6.25%)
URINARY TRACT INFECTION [A] †	12/151 (7.95%)	23/304 (7.57%)
Musculoskeletal and connective tissue disorders		
PAIN IN EXTREMITY [A] †	10/151 (6.62%)	7/304 (2.3%)
Nervous system disorders		
HEADACHE [A] †	6/151 (3.97%)	18/304 (5.92%)
Vascular disorders		
HYPERTENSION [A] †	8/151 (5.3%)	8/304 (2.63%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 13.1

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.

Bristol-Myers Squibb Co. agreements with investigators vary; constant is our right to embargo communications regarding trial results prior to public release for a period ≤60 days from submittal for review. We will not prohibit investigators from publishing, but will prohibit the disclosure of previously undisclosed confidential information other than study results, and request postponement of single-center publications until after disclosure of the clinical trial's primary publication

Results Point of Contact:

Name/Official Title: Boaz Hirschberg
Organization: AstraZeneca Pharmaceuticals
Phone:
Email: ClinicalTrialTransparency@astrazeneca.com