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

ClinicalTrials.gov ID: NCT00885378

Study Identification

Unique Protocol ID:	CV181-080
Brief Title:	Efficacy and Safety Study of Saxagliptin + Metformin Immediate Release (IR) Versus Metformin IR Alone in Type 2 Diabetes Mellitus
Official Title:	A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Phase 3 Trial to Evaluate the Efficacy and Safety of 2.5 mg Saxagliptin, Twice Daily, in Combination With Metformin IR in Subjects With Type 2 Diabetes Mellitus Who Have Inadequate Glycemic Control on Metformin IR Alone
Secondary IDs:	EUDRACT #: 2009-010224-25

Study Status

Record Verification:	May 2015
Overall Status:	Completed
Study Start:	May 2009
Primary Completion:	February 2010 [Actual]
Study Completion:	February 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: 302 Has Expanded Access? No
Review Board:	Approval Status: Board Name: Board Affiliation: Phone: Email:
Data Monitoring?:	No
Plan to Share IPD?:	
Oversight Authorities:	Germany: Federal Institute for Drugs and Medical Devices Germany: Ethics Commission Hungary: National Institute of Pharmacy Hungary: Medical Research Council Ethic Committee for Clinical Pharmacology (MRC-ECCP) Mexico: Federal Commission for Sanitary Risks Protection Mexico: Ethics Committee United States: Food and Drug Administration

Study Description

Brief Summary:	The purpose of this study is to compare the reduction in hemoglobin A1C (A1C) for participants taking saxagliptin in combination with metformin immediate release (IR) versus metformin IR alone.
Detailed Description:	

Conditions

Conditions:	Type 2 Diabetes Mellitus
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, Caregiver, Investigator, Outcomes Assessor)
Allocation:	Randomized
Endpoint Classification:	Safety/Efficacy Study
Enrollment:	166 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Active Comparator: Saxagliptin plus metformin IR	Drug: Saxagliptin plus metformin IR Tablets, Oral, 2.5 mg, Twice daily, 12 weeks Other Names: • BMS-477118 • Onglyza
Placebo Comparator: Placebo plus metformin IR	Drug: Placebo plus metformin IR Tablets, Oral, Placebo, Twice daily, 12 weeks

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
- 18-78 years of age
- Taking stable twice daily (BID) dosing of metformin IR (at least 1500 mg) for at least 8 weeks
- A1C: 7-10%
- C-peptide: ≥ 0.8 ng/mL
- Body mass index (BMI): ≤45 kg/m^2

Exclusion Criteria:

- Women of childbearing potential unable or unwilling to use acceptable birth control
- Women who are pregnant or breastfeeding
- Fasting plasma glucose (FPG) >270 mg/dL
- Significant cardiovascular history
- Symptoms of poorly controlled diabetes
- History of diabetic ketoacidosis or hyperosmolar nonketotic coma
- Insulin therapy within one year of screening
- Cardiovascular even within the prior 6 months
- New York Heart Association Stage III/IV congestive heart failure and/or known left ventricular ejection fraction <=40%
- Significant history of renal or hepatic disease
- History of a psychiatric disorder, alcohol or drug abuse within the previous year
- Treatment with potent CYP3A4 inhibitors or inducers
- Immunocompromised participants
- Active liver disease or clinically significant abnormal hepatic, renal , endocrine, metabolic, or hematological screening tests

Contacts/Locations

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

Locations: United States, Florida
Clinical Therapeutics Corporation
Coral Gables, Florida, United States, 33134

United States, Ohio
Wells Institute For Health Awareness
Kettering, Ohio, United States, 45429

United States, Virginia
Tidewater Integrated Medical Research
Virginia Beach, Virginia, United States, 23454

United States, California
Southland Clinical Research Center, Inc.
Fountain Valley, California, United States, 92708

United States, Georgia
Middle Georgia Drug Study Center, Llc
Perry, Georgia, United States, 31069

United States, Ohio
Newark Physician Associates
Newark, Ohio, United States, 43055

United States, Texas
Village Family Practice
Houston, Texas, United States, 77024

United States, Tennessee
Holston Medical Group
Kingsport, Tennessee, United States, 37660

United States, Pennsylvania
Integrated Medical Group Pc/Fleetwood Clinical Research
Fleetwood, Pennsylvania, United States, 19522

Puerto Rico
Local Institution
San Juan, Puerto Rico, 00920

Local Institution
San Juan, Puerto Rico, 00926

Local Institution
Ponce, Puerto Rico, 00716

Local Institution
San Juan, Puerto Rico, 00909

United States, Oklahoma
Integris Family Care Yukon
Yukon, Oklahoma, United States, 73099

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

United States, Texas
Southwest Clinical Research Centers, Llc
Pearland, Texas, United States, 77584

United States, Ohio

Community Health Care Of Manchester
Akron, Ohio, United States, 44319

United States, California
John Muir Physician Network Clinical Research Center
Concord, California, United States, 94520

Germany
Local Institution
Wuestensachsen, Germany, 36115

Local Institution
Ludwigshafen, Germany, 67067

Local Institution
Pirna, Germany, 01796

Local Institution
Saarbrucken, Germany, 66119

Local Institution
Magdeberg, Germany, 39112

Hungary
Local Institution
Eger, Hungary, 3300

Germany
Local Institution
Tann, Germany, 36142

Hungary
Local Institution
Balatonfured, Hungary, Hungary, 8230

Local Institution
Budapest, Hungary, 1036

Germany
Local Institution
Saarlouis, Germany, 66740

Hungary
Local Institution
Szigetvar, Hungary, 7900

Local Institution
Zalaegerszeg, Hungary, 8900

United States, Ohio
Midwest Regional Research, Inc.
Bellbrook, Ohio, United States, 45305

United States, Oregon
Williamette Valley Clinical Studies
Eugene, Oregon, United States, 97404

United States, Florida
Nextphase Clinical Trials, Inc.
Miami, Florida, United States, 33145

United States, Oklahoma
Integris Family Care South
Oklahoma, Oklahoma, United States, 73170

United States, Texas
Jolene K. Berg, Md., Dgd Research, Inc.
San Antonio, Texas, United States, 78229

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

United States, Mississippi
Jackson Clinic
Rolling Fork, Mississippi, United States, 39159

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

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

United States, Louisiana
Louisiana Heart Center Research
Slidell, Louisiana, United States, 70458

United States, California
Torrance Clinical Research

Lomita, California, United States, 90717

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 Clinical Study Results.org

Study Data/Documents:

Study Results

Participant Flow

Recruitment Details	Participants at 43 sites in 4 countries (25 sites in the United States [US], 9 in Germany, 5 in Hungary, and 4 in Puerto Rico) received study medication and participated in this study.
Pre-Assignment Details	Of the 166 subjects who entered the lead-in period, 6 discontinued: 3 withdrawal of consent, 1 poor/ noncompliance, 1 adverse event (AE; abdominal pain secondary to partial small bowel obstruction), and 1 elevated liver enzymes that did not meet study exclusion criteria but was discontinued by the investigator.

Reporting Groups

	Description
Saxagliptin 2.5 mg + Metformin Immediate Release (IR)	Saxagliptin 2.5 mg tablets orally (PO) plus a flexible metformin IR dose twice daily (BID).
Placebo + Metformin IR	2.5 mg placebo tablets PO BID plus flexible metformin IR dose.

Overall Study

	Saxagliptin 2.5 mg + Metformin Immediate Release (IR)	Placebo + Metformin IR
Started	74 [1]	86 [1]
Completed	66	78
Not Completed	8	8
Lack of Efficacy	2	2
Withdrawal by Subject	1	2
Lost to Follow-up	1	2
Poor/ Noncompliance	2	2
Protocol Violation	2	0

[1] Number randomized.

Baseline Characteristics

Reporting Groups

	Description
Saxagliptin 2.5 mg + Metformin Immediate Release (IR)	Saxagliptin 2.5 mg tablets orally (PO) plus a flexible metformin IR dose twice daily (BID).
Placebo + Metformin IR	2.5 mg placebo tablets PO BID plus flexible metformin IR dose.

Baseline Measures

		Saxagliptin 2.5 mg + Metformin Immediate Release (IR)	Placebo + Metformin IR	Total
Overall Number of Participants		74	86	160
Age, Continuous Mean (Standard Deviation) Unit of measure: years	Number Analyzed	74 participants	86 participants	160 participants
		53.90 (10.35)	56.60 (9.97)	55.4 (10.20)

		Saxagliptin 2.5 mg + Metformin Immediate Release (IR)	Placebo + Metformin IR	Total
Gender, Male/ Female Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	74 participants	86 participants	160 participants
	Female	34 45.95%	41 47.67%	75 46.88%
	Male	40 54.05%	45 52.33%	85 53.12%
Race (NIH/OMB) Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	74 participants	86 participants	160 participants
	American Indian or Alaska Native	0 0%	1 1.16%	1 0.63%
	Asian	2 2.7%	2 2.33%	4 2.5%
	Native Hawaiian or Other Pacific Islander	0 0%	0 0%	0 0%
	Black or African American	8 10.81%	3 3.49%	11 6.88%
	White	64 86.49%	80 93.02%	144 90%
	More than one race	0 0%	0 0%	0 0%
	Unknown or Not Reported	0 0%	0 0%	0 0%
Region of Enrollment Measure Type: Number Unit of measure: participants	Number Analyzed	74 participants	86 participants	160 participants
United States		49	56	105

		Saxagliptin 2.5 mg + Metformin Immediate Release (IR)	Placebo + Metformin IR	Total
Hungary		8	8	16
Puerto Rico		8	10	18
Germany		9	12	21
Mean Height Mean (Standard Deviation) Unit of measure: cm	Number Analyzed	74 participants	86 participants	160 participants
		168.38 (9.56)	167.77 (8.99)	168.05 (9.23)
Mean Weight Mean (Standard Deviation) Unit of measure: kg	Number Analyzed	74 participants	86 participants	160 participants
		95.85 (21.40)	91.74 (19.87)	93.64 (20.63)
Mean Body Mass Index (BMI) Mean (Standard Deviation) Unit of measure: kg / m^2	Number Analyzed	74 participants	86 participants	160 participants
		33.68 (5.94)	32.51 (6.18)	33.05 (6.08)
Participant Body Mass Index Measure Type: Number Unit of measure: Participants	Number Analyzed	74 participants	86 participants	160 participants
< 30 kg / m^2		19	35	54
>= 30 kg / m^2		55	51	106
Mean Duration of Type 2 Diabetes Mellitus [1] Mean (Standard Deviation) Unit of measure: Years	Number Analyzed	74 participants	86 participants	160 participants
		5.81 (6.37)	6.17 (4.21)	6.00 (5.30)
		[1] Measure Description: Mean time since the time of diagnosis of Type 2 Diabetes Mellitus.		

		Saxagliptin 2.5 mg + Metformin Immediate Release (IR)	Placebo + Metformin IR	Total
Mean Metformin Dose at Baseline	Number Analyzed	74 participants	86 participants	160 participants
Mean (Standard Deviation) Unit of measure: mg		1911.5 (376.59)	1855.8 (330.19)	1881.6 (352.38)

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Mean Hemoglobin A1C (A1c) and Change From Baseline to Week 12
Measure Description	Mean change was adjusted for baseline.
Time Frame	Baseline, Week 12
Safety Issue?	No

Analysis Population Description

Randomized participants with both a baseline value and post-baseline value (up to Week 12).

Reporting Groups

	Description
Saxagliptin 2.5 mg + Metformin Immediate Release (IR)	Saxagliptin 2.5 mg tablets orally (PO) plus a flexible metformin IR dose twice daily (BID).
Placebo + Metformin IR	2.5 mg placebo tablets PO BID plus flexible metformin IR dose.

Measured Values

	Saxagliptin 2.5 mg + Metformin Immediate Release (IR)	Placebo + Metformin IR
Number of Participants Analyzed	74	84
Mean Hemoglobin A1C (A1c) and Change From Baseline to Week 12 Mean (Standard Error) Unit of measure: Percentage of glycosylated hemoglobins		
Baseline	7.92 (0.11)	7.97 (0.09)
Adjusted Mean Change From Baseline	-0.56 (0.09)	-0.22 (0.08)

Statistical Analysis 1 for Mean Hemoglobin A1C (A1c) and Change From Baseline to Week 12

Statistical Analysis Overview	Comparison Groups	Saxagliptin 2.5 mg + Metformin Immediate Release (IR), Placebo + Metformin IR
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0063
	Comments	Between-group comparisons significant at alpha = 0.05, significance testing based on hierarchical testing.
	Method	ANCOVA
	Comments	Adjusted mean difference for saxagliptin groups vs placebo at Week 12(LOCF) was adjusted for baseline.

Method of Estimation	Estimation Parameter	Other [Standard Error of the Mean]
	Estimated Value	-0.34
	Confidence Interval	(2-Sided) 95% -0.58 to -0.10
	Estimation Comments	difference between week t value - baseline value = baseline value + treatment.

2. Secondary Outcome Measure:

Measure Title	Mean Baseline and Change From Baseline in Fasting Plasma Glucose (FPG)
Measure Description	Mean change was adjusted for baseline.
Time Frame	Baseline, Week 12
Safety Issue?	No

Analysis Population Description

Randomized participants with a measurement at the specified timepoint with Last Observation Carried Forward (LOCF).

Reporting Groups

	Description
Saxagliptin 2.5 mg + Metformin Immediate Release (IR)	Saxagliptin 2.5 mg tablets orally (PO) plus a flexible metformin IR dose twice daily (BID).

	Description
Placebo + Metformin IR	2.5 mg placebo tablets PO BID plus flexible metformin IR dose.

Measured Values

	Saxagliptin 2.5 mg + Metformin Immediate Release (IR)	Placebo + Metformin IR
Number of Participants Analyzed	73	84
Mean Baseline and Change From Baseline in Fasting Plasma Glucose (FPG) Mean (Standard Error) Unit of measure: mg / dL		
Mean Baseline	164.22 (5.512)	161.25 (4.624)
Adjusted Mean Change from Baseline	-13.73 (4.51)	-4.22 (4.20)

Statistical Analysis 1 for Mean Baseline and Change From Baseline in Fasting Plasma Glucose (FPG)

Statistical Analysis Overview	Comparison Groups	Saxagliptin 2.5 mg + Metformin Immediate Release (IR), Placebo + Metformin IR
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.1248
	Comments	[Not specified]
	Method	ANCOVA
	Comments	ANCOVA model: post - pre = pretreatment.

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-9.51
	Confidence Interval	(2-Sided) 95% -21.68 to 2.66
	Parameter Dispersion	Type: Standard Error of the mean Value: 6.162
	Estimation Comments	Estimate = adjusted mean change for Saxagliptin - adjusted mean change for Placebo.

3. Secondary Outcome Measure:

Measure Title	Percentage of Participants Achieving a Therapeutic Glycemic Response (A1C < 7.0%) at Week 12
Measure Description	Adjusted for baseline. Calculated using the method by Zhang et al. (Zhang M, Tsiatis A, Davidian M. Improving efficiency of inference in randomized clinical trials using auxiliary covariates. Biometrics. Published online on January 11, 2008; Digital Object Identifier: 10.1111/j.1541-0420.2007.00976.x.)
Time Frame	Week 12
Safety Issue?	No

Analysis Population Description

Randomized participants with measurement at timepoint with LOCF.

Reporting Groups

	Description
Saxagliptin 2.5 mg + Metformin Immediate Release (IR)	Saxagliptin 2.5 mg tablets orally (PO) plus a flexible metformin IR dose twice daily (BID).
Placebo + Metformin IR	2.5 mg placebo tablets PO BID plus flexible metformin IR dose.

Measured Values

	Saxagliptin 2.5 mg + Metformin Immediate Release (IR)	Placebo + Metformin IR
Number of Participants Analyzed	73	84
Percentage of Participants Achieving a Therapeutic Glycemic Response (A1C < 7.0%) at Week 12 Number (95% Confidence Interval) Unit of measure: Percentage of Participants	37.5 (27.4 to 47.6)	24.2 (15.8 to 32.7)

Statistical Analysis 1 for Percentage of Participants Achieving a Therapeutic Glycemic Response (A1C < 7.0%) at Week 12

Statistical Analysis Overview	Comparison Groups	Saxagliptin 2.5 mg + Metformin Immediate Release (IR), Placebo + Metformin IR
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	13.2
	Confidence Interval	(2-Sided) 95% 1.1 to 25.4
	Estimation Comments	Adjusted for baseline.

4. Secondary Outcome Measure:

Measure Title	Percentage of Participants Achieving a Therapeutic Glycemic Response (A1C <= 6.5%) at Week 12
Measure Description	Adjusted for baseline. Calculated using the method by Zhang et al. (Zhang M, Tsiatis A, Davidian M. Improving efficiency of inference in randomized clinical trials using auxiliary covariates. Biometrics. Published online on January 11, 2008; Digital Object Identifier: 10.1111/j.1541-0420.2007.00976.x.)
Time Frame	Week 12
Safety Issue?	No

Analysis Population Description

Randomized participants with measurement at timepoint with LOCF.

Reporting Groups

	Description
Saxagliptin 2.5 mg + Metformin Immediate Release (IR)	Saxagliptin 2.5 mg tablets orally (PO) plus a flexible metformin IR dose twice daily (BID).
Placebo + Metformin IR	2.5 mg placebo tablets PO BID plus flexible metformin IR dose.

Measured Values

	Saxagliptin 2.5 mg + Metformin Immediate Release (IR)	Placebo + Metformin IR
Number of Participants Analyzed	74	84
Percentage of Participants Achieving a Therapeutic Glycemic Response (A1C <= 6.5%) at Week 12 Number (95% Confidence Interval) Unit of measure: Percentage of Participants	24.6 (15.1 to 34.1)	10.7 (4.6 to 16.9)

Statistical Analysis 1 for Percentage of Participants Achieving a Therapeutic Glycemic Response (A1C <= 6.5%) at Week 12

Statistical Analysis Overview	Comparison Groups	Saxagliptin 2.5 mg + Metformin Immediate Release (IR), Placebo + Metformin IR
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	13.8
	Confidence Interval	(2-Sided) 95% 3.0 to 24.7
	Estimation Comments	Adjusted for baseline.

5. Other Pre-specified Outcome Measure:

Measure Title	Participant Adverse Event (AE), Related AE, Serious Adverse Event (SAE), Related SAE, and Discontinued Due to AEs Summary
Measure Description	AE = any new untoward medical occurrence/worsening of a pre-existing medical condition which does not necessarily have a causal relationship with this treatment.SAE = any untoward medical occurrence that at any dose: results in death, is life-threatening, requires inpatient hospitalization or causes prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect, results in development of drug dependency or drug abuse, is an important medical event. Treatment-related=Possible, Probable, or Certain relationship to drug.
Time Frame	Week 1 to Week 12; AEs are included up to the last treatment day + 1 day or the last visit in the double-blind (DB) period. SAEs are included up to the last of 1) the last treatment day + 30 days or 2) the last visit day + 30 days in the DB period.
Safety Issue?	Yes

Analysis Population Description

All treated participants.

Reporting Groups

	Description
Saxagliptin 2.5 mg + Metformin Immediate Release (IR)	Saxagliptin 2.5 mg tablets orally (PO) plus a flexible metformin IR dose twice daily (BID).
Placebo + Metformin IR	2.5 mg placebo tablets PO BID plus flexible metformin IR dose.

Measured Values

	Saxagliptin 2.5 mg + Metformin Immediate Release (IR)	Placebo + Metformin IR
Number of Participants Analyzed	74	86
Participant Adverse Event (AE), Related AE, Serious Adverse Event (SAE), Related SAE, and Discontinued Due to AEs Summary Measure Type: Number Unit of measure: Participants		
At Least 1 AE	19	34
At Least 1 Related AE	1	3
Deaths	0	0
At Least 1 SAE	1	1
At Least 1 Related SAE	0	0
Discontinued Due to SAEs	0	0
Discontinued Due to AEs	0	0

6. Other Pre-specified Outcome Measure:

Measure Title	Participants With Reported Hypoglycemia AEs During Double-Blind Treatment Period
Measure Description	Hypoglycemic Events are based upon the Saxagliptin Predefined List of Events, which included hypoglycemia, blood glucose decreased, and hypoglycemic unconsciousness.
Time Frame	Week 1 to Week 12; AEs are included up to the last treatment day + 1 day or the last visit in the DB period. SAEs are included up to the last of 1) the last treatment day + 30 days or 2) the last visit day + 30 days in the DB period.
Safety Issue?	Yes

Analysis Population Description

All treated participants.

Reporting Groups

	Description
Saxagliptin 2.5 mg + Metformin Immediate Release (IR)	Saxagliptin 2.5 mg tablets orally (PO) plus a flexible metformin IR dose twice daily (BID).
Placebo + Metformin IR	2.5 mg placebo tablets PO BID plus flexible metformin IR dose.

Measured Values

	Saxagliptin 2.5 mg + Metformin Immediate Release (IR)	Placebo + Metformin IR
Number of Participants Analyzed	74	86
Participants With Reported Hypoglycemia AEs During Double-Blind Treatment Period Measure Type: Number Unit of measure: Participants	4	1

7. Other Pre-specified Outcome Measure:

Measure Title	Participants With Confirmed Hypoglycemia
Measure Description	Confirmed hypoglycemia was defined by a fingerstick glucose value <= 50 mg/dL with associated hypoglycemia symptoms.
Time Frame	Week 1 to Week 12; AEs are included up to the last treatment day + 1 day or the last visit in the DB period. SAEs are included up to the last of 1) the last treatment day + 30 days or 2) the last visit day + 30 days in the DB period.
Safety Issue?	Yes

Analysis Population Description
All treated participants.

Reporting Groups

	Description
Saxagliptin 2.5 mg + Metformin Immediate Release (IR)	Saxagliptin 2.5 mg tablets orally (PO) plus a flexible metformin IR dose twice daily (BID).
Placebo + Metformin IR	2.5 mg placebo tablets PO BID plus flexible metformin IR dose.

Measured Values

	Saxagliptin 2.5 mg + Metformin Immediate Release (IR)	Placebo + Metformin IR
Number of Participants Analyzed	74	86
Participants With Confirmed Hypoglycemia Measure Type: Number Unit of measure: Participants	0	1

8. Other Pre-specified Outcome Measure:

Measure Title	Participant Electrocardiogram (ECG) Status at Baseline and Week 12
Measure Description	Abnormal ECGs were defined as those not within the normal limits for the participant, according to the investigator. 'Shifted Normal to Abnormal' and 'Shifted Abnormal to Normal' references a change from measurements at Baseline to those at Week 12.
Time Frame	Baseline, Week 12
Safety Issue?	Yes

Analysis Population Description

All treated participants, excluding those with missing values.

Reporting Groups

	Description
Saxagliptin 2.5 mg + Metformin Immediate Release (IR)	Saxagliptin 2.5 mg tablets orally (PO) plus a flexible metformin IR dose twice daily (BID).
Placebo + Metformin IR	2.5 mg placebo tablets PO BID plus flexible metformin IR dose.

Measured Values

	Saxagliptin 2.5 mg + Metformin Immediate Release (IR)	Placebo + Metformin IR
Number of Participants Analyzed	71	78
Participant Electrocardiogram (ECG) Status at Baseline and Week 12 Measure Type: Number Unit of measure: Participants		
Baseline Normal	36	42
Baseline Abnormal	35	36
Week 12 Normal	39	50
Week 12 Abnormal	32	28
Shifted Normal to Abnormal	5	4
Shifted Abnormal to Normal	8	12

9. Other Pre-specified Outcome Measure:

Measure Title	Baseline and Mean Change From Baseline in Participant Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP)
Measure Description	Baseline values reference the measurement for the cohort of participants evaluated at the given time point.
Time Frame	Baseline, Week 4, Week 8, Week 12
Safety Issue?	Yes

Analysis Population Description

All treated participants. n= number of participants with measurement at time point.

Reporting Groups

	Description
Saxagliptin 2.5 mg + Metformin Immediate Release (IR)	Saxagliptin 2.5 mg tablets orally (PO) plus a flexible metformin IR dose twice daily (BID).
Placebo + Metformin IR	2.5 mg placebo tablets PO BID plus flexible metformin IR dose.

Measured Values

	Saxagliptin 2.5 mg + Metformin Immediate Release (IR)	Placebo + Metformin IR
Number of Participants Analyzed	74	86
Baseline and Mean Change From Baseline in Participant Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) Mean (Standard Error) Unit of measure: mm Hg		
Baseline SBP for Week 4 cohort (n=74, 84)	128.89 (1.67)	127.57 (1.53)
Baseline DBP for Week 4 cohort (n=74, 84)	78.99 (1.07)	77.07 (1.05)
SBP Change From Baseline at Week 4 (n=74, 84)	-0.47 (1.43)	0.17 (1.16)
DBP Change From Baseline at Week 4 (n=74, 84)	-0.81 (0.84)	0.95 (0.86)
Baseline SBP for Week 8 cohort (n=70, 81)	128.33 (1.67)	127.60 (1.57)
Baseline DBP for Week 8 cohort (n=70, 81)	78.87 (1.08)	77.32 (1.03)
SBP Change From Baseline at Week 8 (n=70, 81)	0.60 (1.66)	-0.43 (1.48)
DBP Change From Baseline at Week 8 (n=70, 81)	0.37 (0.94)	0.86 (0.93)

	Saxagliptin 2.5 mg + Metformin Immediate Release (IR)	Placebo + Metformin IR
Baseline SBP for Week 12 cohort (n=66, 77)	128.18 (1.76)	127.38 (1.56)
Baseline DBP for Week 12 cohort (n=66, 77)	78.85 (1.13)	77.23 (1.06)
SBP Change From Baseline at Week 12 (n=66, 77)	1.59 (1.51)	0.83 (1.26)
DBP Change From Baseline at Week 12 (n=66, 77)	1.03 (0.75)	1.29 (0.85)

10. Other Pre-specified Outcome Measure:

Measure Title	Baseline and Mean Change From Baseline in Participant Heart Rate (HR)
Measure Description	Baseline values reference the measurement for the cohort of participants evaluated at the given time point.
Time Frame	Baseline, Week 4, Week 8, Week 12
Safety Issue?	Yes

Analysis Population Description

All treated participants. n= number of participants with measurement at time point.

Reporting Groups

	Description
Saxagliptin 2.5 mg + Metformin Immediate Release (IR)	Saxagliptin 2.5 mg tablets orally (PO) plus a flexible metformin IR dose twice daily (BID).
Placebo + Metformin IR	2.5 mg placebo tablets PO BID plus flexible metformin IR dose.

Measured Values

	Saxagliptin 2.5 mg + Metformin Immediate Release (IR)	Placebo + Metformin IR
Number of Participants Analyzed	74	86
Baseline and Mean Change From Baseline in Participant Heart Rate (HR) Mean (Standard Error) Unit of measure: mm Hg		
Baseline HR for Week 4 cohort (n=74, 84)	73.45 (1.072)	73.77 (0.968)
HR Change From Baseline at Week 4 (n=74, 84)	0.97 (0.881)	1.18 (0.778)

	Saxagliptin 2.5 mg + Metformin Immediate Release (IR)	Placebo + Metformin IR
Baseline HR for Week 8 cohort (n=70, 81)	73.51 (1.091)	73.56 (0.990)
HR Change From Baseline at Week 8 (n=70, 81)	2.70 (0.914)	0.28 (0.727)
Baseline HR for Week 12 cohort (n=66, 77)	73.71 (1.142)	73.55 (1.035)
HR Change From Baseline at Week 12 (n=66, 77)	0.61 (1.061)	0.60 (0.866)

11. Other Pre-specified Outcome Measure:

Measure Title	Participants Experiencing Changes From Baseline in Laboratory Parameters That Met the Marked Abnormality Criteria
Measure Description	A laboratory value was considered a marked abnormality if it is outside the pre-defined criteria for marked abnormality and the on-treatment value was more extreme (farther from the limit) than the baseline value. ULN=upper limit of normal; LLN=lower limit of normal.
Time Frame	Baseline, Week 12
Safety Issue?	Yes

Analysis Population Description

All treated participants.

Reporting Groups

	Description
Saxagliptin 2.5 mg + Metformin Immediate Release (IR)	Saxagliptin 2.5 mg tablets orally (PO) plus a flexible metformin IR dose twice daily (BID).
Placebo + Metformin IR	2.5 mg placebo tablets PO BID plus flexible metformin IR dose.

Measured Values

	Saxagliptin 2.5 mg + Metformin Immediate Release (IR)	Placebo + Metformin IR
Number of Participants Analyzed	74	86
Participants Experiencing Changes From Baseline in Laboratory Parameters That Met the Marked Abnormality Criteria Measure Type: Number Unit of measure: Participants		

	Saxagliptin 2.5 mg + Metformin Immediate Release (IR)	Placebo + Metformin IR
Hemoglobin < 8 g/dL	0	0
Hematocrit < 0.75 prior to dosing	0	0
Platelets < 50 x 10^9 c/L	0	0
Platelets > 1.5 x ULN	0	0
Leukocytes < 2 x 10^3 c/uL	0	0
Neutrophils < 1 x 10^3 c/uL	1	0
Eosinophils > 0.9 x 10^3 c/uL	0	2
Lymphocytes <= 0.75 x 10^3 c/uL	1	0
Alkaline Phosphatase >3x prior to dosing and > ULN	0	0
Aspartate Aminotransferase > 3x ULN	1	0
Aspartate Aminotransferase > 5x ULN	0	0
Alanine Aminotransferase > 3x ULN	1	0
Alanine Aminotransferase > 5x ULN	0	0
Total Bilirubin > 2 mg/dL	0	0
Total Bilirubin > 1.5x ULN	0	1
Blood Urea Nitrogen > 2x prior to dosing and > ULN	0	0
Creatinine > 2.5 mg/dL	0	0
Serum Sodium <0.9x pre-Rx and <= 130 mEq/	0	0
Serum Sodium >1.1x pre-Rx and >= 150 mEq/L	0	0
Serum Potassium <=0.8x pre-Rx and <= 3.2 mEq/L	0	0
Serum Potassium >=1.2x pre-Rx and >= 6.0 mEq/L	1	0
Serum Chloride <90 mEq/L	0	0
Serum Chloride > 120 mEq/L	0	0
Albumin <0.9x LLN, or if pre-Rx<LLN use <0.75x	0	0
Creatinine Kinase > 5x ULN	0	1
Fasting Plasma Glucose < 50 mg/dL	1	0
Fasting Plasma Glucose > 500 mg/dL	0	0

	Saxagliptin 2.5 mg + Metformin Immediate Release (IR)	Placebo + Metformin IR
Plasma Glucose Unspecified < 50 mg/dL	0	0
Plasma Glucose Unspecified > 500 mg/dL	0	0

12. Other Pre-specified Outcome Measure:

Measure Title	Participants Experiencing Changes From Baseline in Urinalysis Parameters That Met the Marked Abnormality Criteria
Measure Description	Marked abnormality criteria were urine protein: if pre-Rx=o use >=2, if pre-Rx =0.5 or 1 use >=3, if pre-Rx =2, use >=4; urine blood: if pre-Rx=0, use >=2, if pre-Rx=0.5 or 1, use >=3, if pre-Rx=2, use >=4; Urine red blood cell count (RBC): if pre-Rx=o use >=2, if pre-Rx =0.5 or 1 use >=3, if pre-Rx =2, use >=4; urine white blood cell count (WBC): if pre-Rx=o use >=2, if pre-Rx =0.5 or 1 use >=3, if pre-Rx =2, use >=4.
Time Frame	Baseline, Week 12
Safety Issue?	Yes

Analysis Population Description

All treated participants. N = number of participants analyzed and n = the number of participants with values available for each specific measurement.

Reporting Groups

	Description
Saxagliptin 2.5 mg + Metformin Immediate Release (IR)	Saxagliptin 2.5 mg tablets orally (PO) plus a flexible metformin IR dose twice daily (BID).
Placebo + Metformin IR	2.5 mg placebo tablets PO BID plus flexible metformin IR dose.

Measured Values

	Saxagliptin 2.5 mg + Metformin Immediate Release (IR)	Placebo + Metformin IR
Number of Participants Analyzed	74	86
Participants Experiencing Changes From Baseline in Urinalysis Parameters That Met the Marked Abnormality Criteria Measure Type: Number Unit of measure: Participants		
Urine Protein (n=74, 84)	0	0
Urine Blood (n=74, 84)	1	1

	Saxagliptin 2.5 mg + Metformin Immediate Release (IR)	Placebo + Metformin IR
Urine Red Blood Cells (n=7, 10)	0	0
Urine White Blood Cells (n=16, 18)	2	2

Reported Adverse Events

Time Frame	[Not specified]
Additional Description	[Not specified]

Reporting Groups

	Description
Placebo + Metformin IR	2.5 mg placebo tablets PO BID plus flexible metformin IR dose.
Saxagliptin 2.5 mg + Metformin Immediate Release (IR)	Saxagliptin 2.5 mg tablets orally (PO) plus a flexible metformin IR dose twice daily (BID).

Serious Adverse Events

	Placebo + Metformin IR	Saxagliptin 2.5 mg + Metformin Immediate Release (IR)
	Affected/At Risk (%)	Affected/At Risk (%)
Total	1/86 (1.16%)	1/74 (1.35%)
Cardiac disorders		
MYOCARDIAL INFARCTION [A] †	0/86 (0%)	1/74 (1.35%)
Musculoskeletal and connective tissue disorders		
BACK PAIN [A] †	1/86 (1.16%)	0/74 (0%)
Respiratory, thoracic and mediastinal disorders		
PULMONARY OEDEMA [A] †	0/86 (0%)	1/74 (1.35%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 12.1

Other Adverse Events

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

	Placebo + Metformin IR	Saxagliptin 2.5 mg + Metformin Immediate Release (IR)
	Affected/At Risk (%)	Affected/At Risk (%)
Total	0/86 (0%)	0/74 (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.

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