Protocol Registration Receipt
02/07/2013

Grantor: CDER IND/IDE Number: 43,468 Serial Number: 0483

Rosiglitazone Versus a Sulfonylurea On Progression Of Atherosclerosis In Patients With Heart Disease And Type 2 Diabetes

This study has been completed.

Sponsor:	GlaxoSmithKline
Collaborators:	
Information provided by (Responsible Party):	GlaxoSmithKline
ClinicalTrials.gov Identifier:	NCT00116831

Purpose

The purpose of this study is to test the safety and effectiveness of rosiglitazone against a sulfonylurea in reducing or slowing the development of atherosclerosis in the blood vessels of the heart.

Condition	Intervention	Phase
Non-Insulin-Dependent Diabetes Mellitus	Drug: Glipizide	Phase 3

Condition	Intervention	Phase
Atherosclerosis Cardiovascular Disease	Drug: rosiglitazone maleate	

Study Type: Interventional

Study Design: Treatment, Parallel Assignment, Double Blind (Subject, Caregiver, Investigator), Randomized, Safety/Efficacy Study

Official Title: A Phase III, 18 Month, Multicenter, Randomized, Double-Blind, Active-Controlled Clinical Trial to Compare Rosiglitazone Versus Glipizide on the Progression of Atherosclerosis in Subjects With Type 2 Diabetes Mellitus and Cardiovascular Disease (APPROACH)

Further study details as provided by GlaxoSmithKline:

Primary Outcome Measure:

- Change From Baseline in Percent Atheroma Volume (PAV) to Month 18 [Time Frame: Baseline to Month 18] [Designated as safety issue: No]
  The primary efficacy endpoint was change in PAV (defined as total atheroma volume divided by total vessel volume x 100) within a 40 mm segment in non-intervened coronary arteries from Baseline to Month 18, based upon Intravascular Ultrasound (IVUS) assessment.
- Model Adjusted Change From Baseline in Percent Atheroma Volume (PAV) to Month 18 [Time Frame: Baseline to Month 18] [Designated as safety issue: No]
  Model Adjusted Change (MAC) = Baseline + Region + Sex + Treatment + Cardiac Procedure + Prior Oral Anti-Hyperglycemic Diabetic Medications(s) (OAD).

Secondary Outcome Measures:

- Change From Baseline in Atheroma, Vessel, and Lumen Volume to Month 18 [Time Frame: Baseline to Month 18] [Designated as safety issue: No]
  IVUS-derived endpoints measured within the same segment (in non-intervened coronary arteries) from Baseline to Month 18
- Model Adjusted Change From Baseline in Atheroma Volume to Month 18 [Time Frame: Baseline to Month 18] [Designated as safety issue: No]
  IVUS-derived endpoints measured within the same segment (in non-intervened coronary arteries) from Baseline to Month 18. Model Adjusted Change (MAC) = Baseline + Region + Sex + Treatment + Cardiac Procedure + Prior OAD Medication.
- Model Adjusted Change From Baseline in Lumen Volume to Month 18 [Time Frame: Baseline to Month 18] [Designated as safety issue: No]
  IVUS-derived endpoints measured within the same segment (in non-intervened coronary arteries) from Baseline to Month 18. Model Adjusted Change (MAC) = Baseline + Region + Sex + Treatment + Cardiac Procedure + Prior OAD Medication.
- Model Adjusted Change From Baseline in Vessel Volume to Month 18 [Time Frame: Baseline to Month 18] [Designated as safety issue: No]
  IVUS-derived endpoints measured within the same segment (in non-intervened coronary arteries) from Baseline to Month 18. Model Adjusted Change (MAC) = Baseline + Region + Sex + Treatment + Cardiac Procedure + Prior OAD Medication.
- Change From Baseline in Atheroma, Vessel, and Lumen Area to Month 18 [Time Frame: Baseline to Month 18] [Designated as safety issue: No]
  IVUS-derived endpoints measured within the same segment (in non-intervened coronary arteries) from Baseline to Month 18
- Model Adjusted Change From Baseline in Atheroma Area to Month 18 [Time Frame: Baseline to Month 18] [Designated as safety issue: No]

IVUS-derived endpoints measured within the same segment (in non-intervened coronary arteries) from Baseline to Month 18. Model Adjusted Change (MAC) = Baseline + Region + Sex + Treatment + Cardiac Procedure + Prior OAD Medication.

- Model Adjusted Change From Baseline in Lumen Area to Month 18 [Time Frame: Baseline to Month 18] [Designated as safety issue: No]
  IVUS-derived endpoints measured within the same segment (in non-intervened coronary arteries) from Baseline to Month 18. Model Adjusted Change (MAC) = Baseline + Region + Sex + Treatment + Cardiac Procedure + Prior OAD Medication.
- Model Adjusted Change From Baseline in Vessel Area to Month 18 [Time Frame: Baseline to Month 18] [Designated as safety issue: No]
  IVUS-derived endpoints measured within the same segment (in non-intervened coronary arteries) from Baseline to Month 18. Model Adjusted Change (MAC) = Baseline + Region + Sex + Treatment + Cardiac Procedure + Prior OAD Medication.
- Change From Baseline in Normalized Atheroma Volume [Time Frame: Baseline to Month 18] [Designated as safety issue: No]
  IVUS-derived endpoints measured within the same segment (in non-intervened coronary arteries) from Baseline to Month 18. Normalized atheroma volume is defined as mean atheroma area x median segment length in cohort.
- Model Adjusted Change From Baseline in Normalized Atheroma Volume [Time Frame: Baseline to Month 18] [Designated as safety issue: No]
  IVUS-derived endpoints measured within the same segment (in non-intervened coronary arteries) from Baseline to Month 18. Normalized atheroma volume is defined as mean atheroma area x median segment length in cohort. Model Adjusted Change = Baseline + Region + Sex + Treatment + Cardiac Procedure + Prior OAD Medication.
- Change in Atheroma Volume Within the 10 mm of the Non-intervened Vessel Segment With the Greatest Atheroma Volume at Baseline [Time Frame: Baseline to Month 18] [Designated as safety issue: No]
  IVUS-derived endpoints measured within the same 10 mm segment of non-intervened coronary arteries with the greatest degree of atheroma volume at Baseline, from Baseline to Month 18, including the nominal change in atheroma volume and atheroma area
- Model Adjusted Change in Atheroma Volume Within the 10 mm of the Non-intervened Vessel Segment With the Greatest Atheroma Volume at Baseline [Time Frame: Baseline to Month 18] [Designated as safety issue: No]
  IVUS-derived endpoints measured within the same 10 mm segment of non-intervened coronary arteries with the greatest degree of atheroma volume at Baseline, from Baseline to Month 18, including the nominal change in atheroma volume and atheroma area. Model Adjusted Change = Baseline + Region + Sex + Treatment + Cardiac Procedure + Prior OAD Medication.
- Change in Atheroma Area Within the 10 mm of the Non-intervened Vessel Segment With the Greatest Atheroma Volume at Baseline [Time Frame: Baseline to Month 18] [Designated as safety issue: No]
  IVUS-derived endpoints measured within the same 10 mm segment of non-intervened coronary arteries with the greatest degree of atheroma volume at Baseline, from Baseline to Month 18, including the nominal change in atheroma volume and atheroma area
- Model Adjusted Change in Atheroma Area Within the 10 mm of the Non-intervened Vessel Segment With the Greatest Atheroma Volume at Baseline [Time Frame: Baseline to Month 18] [Designated as safety issue: No]
  IVUS-derived endpoints measured within the same 10 mm segment of non-intervened coronary arteries with the greatest degree of atheroma volume at Baseline, from Baseline to Month 18, including the nominal change in atheroma volume and atheroma area. Model Adjusted Change = Baseline + Region + Sex + Treatment + Cardiac Procedure + Prior OAD Medication.
- Model Adjusted Change in Glycated Hemoglobin (HbA1c) From Baseline to Month 18 [Time Frame: Baseline to Month 18] [Designated as safety issue: No]
  From repeated measures analysis model: Change = Baseline + visit + sex + region + treatment + prior Oral Anti-Hyperglycemic Diabetic Medications(s)

(OAD) + cardiac procedure + treatment x visit.

- Model Adjusted Change in Fasting Plasma Glucose (FPG) From Baseline to Month 18 [Time Frame: Baseline to Month 18] [Designated as safety issue: No]

  From repeated measures analysis model: Change = Baseline + visit + sex + region + treatment + prior OAD + cardiac procedure + treatment x visit.
- Repeated Measures Analysis of Percent Change in hsCRP From Baseline to Month 18 [Time Frame: Baseline to Month 18] [Designated as safety issue: No]

  Changes in cardiovascular biomarkers from Baseline to Month 18, such as high sensitivity C-reactive protein (hsCRP) . Repeated measures analysis model: Log(value) - log(baseline) = log(baseline) + visit + sex + region + treatment + prior OAD + cardiac procedure + treatment x visit.
- Repeated Measures Analysis of Percent Change in MMP 9 From Baseline to Month 18 [Time Frame: Baseline to Month 18] [Designated as safety issue: No]

  Changes in cardiovascular biomarkers from Baseline to Month 18, such as matrix metalloproteinase-9 (MMP-9). Repeated measures analysis model: Log(value) - log(baseline) = log(baseline) + visit + sex + region + treatment + prior OAD + cardiac procedure + treatment x visit.
- Percent Change in Brain Natriuretic Peptide (BNP) From Baseline to Month 18 [Time Frame: Baseline to Month 18] [Designated as safety issue: No]

  It was measured as ratio to baseline as percentage change based on log-transformed data : 100 x (exp(Mean change on log scale) - 1)It was measured as ratio to baseline as percentage change based on log-transformed data : 100 x (exp(Mean change on log scale) - 1). Ratio to baseline as %change mean (%) was used as the estimation parameter for both groups.
- Model Adjusted Percent Change in Brain Natriuretic Peptide (BNP) From Baseline to Month 18 [Time Frame: Baseline to Month 18] [Designated as safety issue: No]

  It was measured as ratio to baseline as percentage change based on log-transformed data : 100 x (exp(Mean change on log scale) - 1). Model Adjusted change based on ANCOVA: Log(value) - log(Baseline) = log(Baseline) + sex + region + treatment + prior OAD + cardiac procedure.
- Percent Change From Baseline to Month 18 in Total Cholesterol (TC) [Time Frame: Baseline to Month 18] [Designated as safety issue: No]

  Repeated measures analysis model: Log(value) - log (Baseline) = log(Baseline) + visit + sex + region + treatment + prior OAD + cardiac procedure + treatment x visit.
- Percent Change From Baseline to Month 18 in High Density Lipoprotein Cholesterol (HDL-c) [Time Frame: Baseline to Month 18] [Designated as safety issue: No]

  Repeated measures analysis model: Log(value) - log (Baseline) = log(Baseline) + visit + sex + region + treatment + prior OAD + cardiac procedure + treatment x visit.
- Percent Change From Baseline to Month 18 in HDL-2 [Time Frame: Baseline to Month 18] [Designated as safety issue: No]

  Repeated measures analysis model: Log(value) - log (Baseline) = log(Baseline) + visit + sex + region + treatment + prior OAD + cardiac procedure + treatment x visit.
- Percent Change From Baseline to Month 18 in HDL-3 [Time Frame: Baseline to Month 18] [Designated as safety issue: No]

  Repeated measures analysis model: Log(value) - log (Baseline) = log(Baseline) + visit + sex + region + treatment + prior OAD + cardiac procedure + treatment x visit.
- Percent Change From Baseline to Month 18 in Low Density Lipoprotein Cholesterol (LDL-c) [Time Frame: Baseline to Month 18] [Designated as safety issue: No]

Repeated measures analysis model: Log(value) - log (Baseline) = log(Baseline) + visit + sex + region + treatment + prior OAD + cardiac procedure + treatment x visit.

- Percent Change From Baseline to Month 18 in Triglycerides (TG) [Time Frame: Baseline to Month 18] [Designated as safety issue: No]
  Repeated measures analysis model: Log(value) - log (Baseline) = log(Baseline) + visit + sex + region + treatment + prior OAD + cardiac procedure + treatment x visit.
- Percent Change From Baseline to Month 18 in Free Fatty Acids (FFA) [Time Frame: Baseline to Month 18] [Designated as safety issue: No]
  Repeated measures analysis model: Log(value) - log (Baseline) = log(Baseline) + visit + sex + region + treatment + prior OAD + cardiac procedure + treatment x visit.
- Percent Change From Baseline to Month 18 in Apoprotein B (apoB) [Time Frame: Baseline to Month 18] [Designated as safety issue: No]
  Repeated measures analysis model: Log(value) - log (Baseline) = log(Baseline) + visit + sex + region + treatment + prior OAD + cardiac procedure + treatment x visit.
- Change From Baseline to Month 18 in LDL-c Peak Particle Density Measured by LDL Relative Flotation [Time Frame: Baseline to Month 18] [Designated as safety issue: No]
  From repeated measures analysis model: Change = baseline + visit + sex + region + treatment + prior OAD + cardiac procedure + treatment x visit.
- Change From Baseline to Month 18 in Total Cholesterol/HDL-c Ratio [Time Frame: Baseline to Month 18] [Designated as safety issue: No]
  From repeated measures analysis model: Change = baseline + visit + sex + region + treatment + prior OAD + cardiac procedure + treatment x visit.
- Change From Baseline to Month 18 in LDL-c/HDL-c Ratio [Time Frame: Baseline to Month 18] [Designated as safety issue: No]
  From repeated measures analysis model: Change = baseline + visit + sex + region + treatment + prior OAD + cardiac procedure + treatment x visit.
- Number of Participants With the Indicated Treatment Emergent Major Cardiovascular Events (MACE) for All-cause Death, Non-fatal MI, Non-fatal Stroke, Coronary Revascularization, or Hospitalization for Recurrent Myocardial Ischemia (MACE Composite 1) [Time Frame: Baseline to Month 21] [Designated as safety issue: No]
  This was 1 of 2 MACE composite endpoints and was a secondary efficacy endpoint.
- Number of Participants With the Indicated Treatment Emergent Major Cardiovascular Events (MACE) for Cardiovascular Death, Nonfatal MI, or Nonfatal Stroke (MACE Composite 2) [Time Frame: Baseline to Month 21] [Designated as safety issue: No]
  This was 1 of 2 MACE composite endpoints and was a secondary efficacy endpoint.
- Number of Other Cardiovascular Events [Time Frame: Baseline to Month 21] [Designated as safety issue: No]
  This was one of the secondary endpoints of the study.

Enrollment: 672
Study Start Date: January 2005
Study Completion Date: August 2008
Primary Completion Date: August 2008

Arms	Assigned Interventions
Active Comparator: Glipizide oral anti-diabetic medication	Drug: Glipizide oral anti-diabetic medication
Experimental: rosiglitazone maleate oral anti-diabetic medication	Drug: rosiglitazone maleate oral antidiabetic medication

Eligibility

Ages Eligible for Study: 30 Years to 80 Years
Genders Eligible for Study: Both

Inclusion criteria:

- Male or female between 30 to 80 years of age, inclusive.
- Established diagnosis of T2DM (based on diagnostic criteria of the American Diabetes Association (ADA), WHO guidelines or local national guidelines).
- Subjects who are undergoing coronary angiography for evaluation of suspected or previously diagnosed coronary artery disease or who are undergoing PCI.
- Subjects' prior anti-hyperglycemic diabetic therapy:

Diet and exercise only (drug naïve), with HbA1c >7.0 and £ 10.0%. HbA1c > 6.5 and <= 8.5%.

- Left ventricular ejection fraction (EF) ³ 40% as assessed by contrast ventriculography (or previously documented in medical notes within one month prior to index procedure by other methods e.g. echocardiography or nuclear study)
- Female subjects must be postmenopausal (i.e., >6 months without menstrual period), surgically sterile, or using effective contraceptive measures (oral contraceptives, Norplant, Depo-Provera, an intra-uterine device (IUD), a diaphragm with spermicide or a condom with spermicide). Women of childbearing potential must use effective contraceptive measures for at least 1 month prior to visit 1a, and should continue to use the same contraceptive method during the study and for 30 days after discontinuing study medication.
- Willingness and ability to give informed consent prior to entering the study and available to complete the study.

Exclusion Criteria:

- Type 1 diabetes and/or history of diabetic ketoacidosis.
- Exposure to a TZD or other PPAR-g agonist within the 6 months prior to screening visit.
- Subjects treated with triple OAD therapy or high dose dual combination OAD therapy [1].

- Subjects who have required chronic insulin use in the last 6 months (except during pregnancy or acute episodes such as hospitalization, trauma or infection).
- ST segment elevation myocardial infarction in the last 30 days.
- Subjects who have a history or are scheduled to receive coronary artery bypass graft surgery (CABG), valve repair or replacement, aneurysmectomy or planned major non-cardiac surgery during the study period.
- Subjects who have severe cardiac valvular disease
- Stroke or resuscitated in the past 6 months
- History of congestive heart failure (NYHA class I – IV)
- History of significant hypersensitivity or reaction (e.g., difficulty swallowing, difficulty breathing, tachycardia or skin reaction) to any TZD, SU, biguanide or insulin
- Prior history of severe edema or edema requiring medical treatment.
- Chronic disease requiring chronic or intermittent treatment with oral, intravenous, or injected corticosteroids (use of topical, inhaled, or nasal corticosteroids is permissible).
- Recent history or suspicion of current drug abuse or alcohol abuse within the last 6 months.
- Untreated hypo- or hyperthyroidism
- A diagnosis of cancer (other than superficial squamous, basal cell skin cancer, or adequately treated cervical carcinoma in situ) in the past 3 years or current treatment for the active cancer.
- Any clinically significant abnormality identified at the screening visit, physical examination, laboratory tests, or electrocardiogram which, in the judgement of the Investigator, would preclude safe completion of the study.
- Blood pressure: SBP >170 or DBP > 100 mmHg
- Significant anemia (Hemoglobin < 11 g/dL for males and < 10 g/dL for females).
- Significant renal disease manifested by serum creatinine (> 1.5mg/dL for males or > 1.4mg/dL for females), or where the use of metformin is contra-indicated.
- Hepatic disease or biliary tract obstruction, or significant hepatic enzyme elevation (ALT or AST > 2.5 times upper limit of normal (ULN) or bilirubin >2x ULN).
- History of myopathy or history of elevated creatine kinase (CK) > 3 times upper normal limit.
- Use of an investigational drug within 30 days or 5 half-lives (whichever is the longer).
- Women who are lactating, pregnant or planning to become pregnant during the course of the study.
- Unwillingness or inability to comply with the procedures described in this protocol.

Contacts and Locations

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Study Director:	GSK Clinical Trials	GlaxoSmithKline

More Information

Publications:

García-García H, Garg S, Brugaletta S, Morocutti G, Ratner R, Kolatkar N, Kravitz B, Miller D, Huang C,. Nesto R, Serruys P, and the APPROACH study group. Evaluation of In-stent Restenosis in the APPROACH trial (Assessment on the Prevention of Progression by Rosiglitazone On Atherosclerosis in Diabetes Patients with Cardiovascular History) Running title: In-stent restenosis in the APPROACH trial . [Int J Cardiovasc Imaging]. 2011;Feb 27(.):Epub ahead of print .

Gerstein HC, Ratner RE, Cannon CP, Serruys PW, García-García HM, van Es G-A, Kolatkar NS, Kravitz BG, Miller DM, Huang C, Fitzgerald PJ, Nesto RW;

APPROACH study group. Effect of Rosiglitazone on Progression of Coronary Atherosclerosis in Patients with Type 2 Diabetes and Coronary Artery Disease: The APPROACH trial. (Submitted for publication).

Ratner RE, Cannon CP, Gerstein HC, Nesto RW, Serruys PW, Van Es GA, Kolatkar NS, Kravitz BG, Zalewski A, Fitzgerald PJ; APPROACH Study Group. Assessment on the Prevention of Progression by Rosiglitazone on Atherosclerosis in diabetes patients with Cardiovascular History (APPROACH): study design and baseline characteristics. Am Heart J. 2008 Dec;156(6):1074-1079.

Nesto RW. Effect of rosiglitazone versus glipizide on progression of coronary atherosclerosis in patients with type 2 diabetes and coronary artery disease. American Heart Association Scientific Sessions. November 12, 2008, New Orleans, LA. (http://directnews.americanheart.org/extras/pdfs/approach_slides.pdf)

Responsible Party: GlaxoSmithKline
Study ID Numbers: AVD100521
Health Authority: Germany: Federal Institute for Drugs and Medical Devices
Canada: Health Canada
United States: Food and Drug Administration

Study Results

Participant Flow

Reporting Groups

	Description
Glipizide (GLP) 5 mg	Glipizide (GLP) 5 mg once daily for 18 months
Rosiglitazone (RSG) 4 mg	Rosiglitazone (RSG) 4 mg once daily for 18 months

Overall Study

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Started	337	331

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Completed	264	259
Not Completed	73	72
Adverse Event	14	16
Baseline IVUS determined unevaluable	12	11
Lost to Follow-up	8	6
Protocol Violation	3	6
Hypoglycaemic events	1	0
Low haemoglobin on screening	1	0
Withdrawn investigational product	1	0
Withdrawal by Subject	32	32
Insufficient therapeutic effect	0	1
Missing data for participant	1	0

Baseline Characteristics

Reporting Groups

	Description
Glipizide (GLP) 5 mg	Glipizide (GLP) 5 mg once daily for 18 months
Rosiglitazone (RSG) 4 mg	Rosiglitazone (RSG) 4 mg once daily for 18 months

Baseline Measures

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg	Total
Number of Participants	337	331	668
Age, Continuous [units: years] Mean (Standard Deviation)	60.2 (9.05)	61.8 (8.38)	61.0 (8.76)
Gender, Male/Female [units: participants]			
Female	116	98	214
Male	221	233	454
Race/Ethnicity, Customized [units: Participants]			
White	255	240	495
Oriental	70	82	152
Black	7	4	11
Mixed race	4	2	6
Missing	0	1	1
American Indian/Alaska native	1	2	3
Study-Specific Measure [1] [units: Participants]			
Diet and exercise regimen only	64	56	120
Oral anti-diabetic monotherapy	183	182	365
Oral anti-diabetic dual	90	93	183

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg	Total
therapy			
Study-Specific Measure [2] [units: Participants]			
Never smoked	152	151	303
Current smoker	57	55	112
Former smoker	128	124	252
Missing	0	1	1
Study-Specific Measure [3] [units: kilograms per square meter (kg/m2)] Median (Full Range)	29 (19 to 52)	28 (17 to 58)	29 (17 to 58)
Study-Specific Measure [4] [units: Years] Mean (Full Range)	0.79 (0.01 to 28.58)	0.59 (0.00 to 25.19)	0.73 (0.00 to 28)
Study-Specific Measure [5] [units: Years] Median (Full Range)	4.62 (0 to 35.82)	4.96 (0.02 to 31.66)	4.74 (0 to 35.82)

[1] Pre-study treatment in the Safety Population

[2] Smoking history in the Safety Population

[3] Median BMI in the Safety Population

[4] Duration of cardiovascular disease in the Safety Population

[5] Duration of diabetes in the Safety Population

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Change From Baseline in Percent Atheroma Volume (PAV) to Month 18
Measure Description	The primary efficacy endpoint was change in PAV (defined as total atheroma volume divided by total vessel volume x 100) within a 40 mm segment in non-intervened coronary arteries from Baseline to Month 18, based upon Intravascular Ultrasound (IVUS) assessment.
Time Frame	Baseline to Month 18
Safety Issue?	No

Analysis Population Description

IVUS Evaluable Population (Defined as all randomized participants who received at least one dose of study medication, with an evaluable Baseline and exit [≥ 9 months] IVUS imaging assessment.)

Reporting Groups

	Description
Glipizide (GLP) 5 mg	Glipizide (GLP) 5 mg once daily for 18 months
Rosiglitazone (RSG) 4 mg	Rosiglitazone (RSG) 4 mg once daily for 18 months

Measured Values

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Number of Participants Analyzed	229	233
Change From Baseline in Percent Atheroma Volume (PAV) to Month 18 [units: percent (absolute change)] Mean (Standard Deviation)		
Baseline	40.593 (10.9717)	40.422 (11.7506)

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Month 18	41.013 (11.1572)	40.182 (11.4257)
Change from Baseline	0.420 (4.8085)	-0.240 (4.2421)

2. Primary Outcome Measure:

Measure Title	Model Adjusted Change From Baseline in Percent Atheroma Volume (PAV) to Month 18
Measure Description	Model Adjusted Change (MAC) = Baseline + Region + Sex + Treatment + Cardiac Procedure + Prior Oral Anti-Hyperglycemic Diabetic Medications(s) (OAD).
Time Frame	Baseline to Month 18
Safety Issue?	No

Analysis Population Description

IVUS Evaluable Population (Defined as all randomized participants who received at least one dose of study medication, with an evaluable Baseline and exit [≥ 9 months] IVUS imaging assessment.)

Reporting Groups

	Description
Glipizide (GLP) 5 mg	Glipizide (GLP) 5 mg once daily for 18 months
Rosiglitazone (RSG) 4 mg	Rosiglitazone (RSG) 4 mg once daily for 18 months

Measured Values

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Number of Participants Analyzed	229	233
Model Adjusted Change From Baseline in Percent Atheroma Volume (PAV) to Month 18 [units: percent (absolute change)] Mean (Standard Error)	0.43 (0.331)	-0.21 (0.331)

Statistical Analysis 1 for Model Adjusted Change From Baseline in Percent Atheroma Volume (PAV) to Month 18

Groups	Glipizide (GLP) 5 mg, Rosiglitazone (RSG) 4 mg
Method	ANCOVA
P-Value	0.1221
Other Estimated Parameter [Model adjusted mean diff. (RSG-GLP)]	-0.64
95% Confidence Interval	-1.457 to 0.173

Additional details about the analysis, such as null hypothesis and power calculation:

[Not specified.]

Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:

[Not specified.]

Other relevant information, such as adjustments or degrees of freedom:

[Not specified.]

3. Secondary Outcome Measure:

Measure Title	Change From Baseline in Atheroma, Vessel, and Lumen Volume to Month 18

Measure Description	IVUS-derived endpoints measured within the same segment (in non-intervened coronary arteries) from Baseline to Month 18
Time Frame	Baseline to Month 18
Safety Issue?	No

Analysis Population Description

IVUS Evaluable Population

Reporting Groups

	Description
Glipizide (GLP) 5 mg	Glipizide (GLP) 5 mg once daily for 18 months
Rosiglitazone (RSG) 4 mg	Rosiglitazone (RSG) 4 mg once daily for 18 months

Measured Values

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Number of Participants Analyzed	229	233
Change From Baseline in Atheroma, Vessel, and Lumen Volume to Month 18 [units: millimeters cubed (mm3)] Mean (Standard Deviation)		
Atheroma Volume, Baseline	249.747 (150.4095)	222.431 (137.4193)
Atheroma Volume, Month 18	249.625 (149.7098)	218.576 (134.3462)
Change from Baseline in Atheroma Volume	-0.123 (28.1627)	-3.854 (25.8846)

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Vessel Volume, Baseline	609.378 (311.7587)	555.062 (297.9848)
Vessel Volume, Month 18	603.088 (304.3434)	547.186 (298.2100)
Change from Baseline in Vessel Volume	-6.290 (52.7032)	-7.876 (40.4948)
Lumen Volume, Baseline	359.726 (195.6810)	332.688 (192.3850)
Lumen Volume, Month 18	353.513 (192.2419)	328.676 (191.9313)
Change from Baseline in Lumen Volume	-6.213 (56.0042)	-4.012 (38.5260)

4. Secondary Outcome Measure:

Measure Title	Model Adjusted Change From Baseline in Atheroma Volume to Month 18
Measure Description	IVUS-derived endpoints measured within the same segment (in non-intervened coronary arteries) from Baseline to Month 18. Model Adjusted Change (MAC) = Baseline + Region + Sex + Treatment + Cardiac Procedure + Prior OAD Medication.
Time Frame	Baseline to Month 18
Safety Issue?	No

Analysis Population Description

IVUS Evaluable Population

Reporting Groups

	Description
Glipizide (GLP) 5 mg	Glipizide (GLP) 5 mg once daily for 18 months
Rosiglitazone (RSG) 4 mg	Rosiglitazone (RSG) 4 mg once daily for 18 months

Measured Values

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Number of Participants Analyzed	229	233
Model Adjusted Change From Baseline in Atheroma Volume to Month 18 [units: millimeters cubed (mm3)] Mean (Standard Error)	0.98 (2.001)	-3.60 (2.002)

Statistical Analysis 1 for Model Adjusted Change From Baseline in Atheroma Volume to Month 18

Groups	Glipizide (GLP) 5 mg, Rosiglitazone (RSG) 4 mg
Method	
Other Estimated Parameter [Mean diff (RSG-GLP) for atheroma volume]	-4.58

Additional details about the analysis, such as null hypothesis and power calculation:

[Not specified.]

5. Secondary Outcome Measure:

Measure Title	Model Adjusted Change From Baseline in Lumen Volume to Month 18

Measure Description	IVUS-derived endpoints measured within the same segment (in non-intervened coronary arteries) from Baseline to Month 18. Model Adjusted Change (MAC) = Baseline + Region + Sex + Treatment + Cardiac Procedure + Prior OAD Medication.
Time Frame	Baseline to Month 18
Safety Issue?	No

Analysis Population Description

IVUS Evaluable Population

Reporting Groups

	Description
Glipizide (GLP) 5 mg	Glipizide (GLP) 5 mg once daily for 18 months
Rosiglitazone (RSG) 4 mg	Rosiglitazone (RSG) 4 mg once daily for 18 months

Measured Values

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Number of Participants Analyzed	229	233
Model Adjusted Change From Baseline in Lumen Volume to Month 18 [units: millimeters cubed (mm3)] Mean (Standard Error)	-4.91 (3.545)	-4.59 (3.526)

Statistical Analysis 1 for Model Adjusted Change From Baseline in Lumen Volume to Month 18

Groups	Glipizide (GLP) 5 mg, Rosiglitazone (RSG) 4 mg
Method	
Other Estimated Parameter [Mean diff	0.32

(RSG-GLP) for lumen volume]	

Additional details about the analysis, such as null hypothesis and power calculation:

[Not specified.]

6. Secondary Outcome Measure:

Measure Title	Model Adjusted Change From Baseline in Vessel Volume to Month 18
Measure Description	IVUS-derived endpoints measured within the same segment (in non-intervened coronary arteries) from Baseline to Month 18. Model Adjusted Change (MAC) = Baseline + Region + Sex + Treatment + Cardiac Procedure + Prior OAD Medication.
Time Frame	Baseline to Month 18
Safety Issue?	No

Analysis Population Description

IVUS Evaluable Population

Reporting Groups

	Description
Glipizide (GLP) 5 mg	Glipizide (GLP) 5 mg once daily for 18 months
Rosiglitazone (RSG) 4 mg	Rosiglitazone (RSG) 4 mg once daily for 18 months

Measured Values

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Number of Participants Analyzed	229	233

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Model Adjusted Change From Baseline in Vessel Volume to Month 18 [units: millimeters cubed (mm3)] Mean (Standard Error)	-4.56 (3.479)	-8.13 (3.466)

Statistical Analysis 1 for Model Adjusted Change From Baseline in Vessel Volume to Month 18

Groups	Glipizide (GLP) 5 mg, Rosiglitazone (RSG) 4 mg
Method	
Other Estimated Parameter [Mean diff (RSG-GLP) for vessel volume]	-3.56

Additional details about the analysis, such as null hypothesis and power calculation:

[Not specified.]

7. Secondary Outcome Measure:

Measure Title	Change From Baseline in Atheroma, Vessel, and Lumen Area to Month 18
Measure Description	IVUS-derived endpoints measured within the same segment (in non-intervened coronary arteries) from Baseline to Month 18
Time Frame	Baseline to Month 18
Safety Issue?	No

Analysis Population Description

IVUS Evaluable Population

Reporting Groups

	Description
Glipizide (GLP) 5 mg	Glipizide (GLP) 5 mg once daily for 18 months
Rosiglitazone (RSG) 4 mg	Rosiglitazone (RSG) 4 mg once daily for 18 months

Measured Values

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Number of Participants Analyzed	229	233
Change From Baseline in Atheroma, Vessel, and Lumen Area to Month 18 [units: millimeters squared (mm2)] Mean (Standard Deviation)		
Atheroma Area, Baseline	5.918 (2.9281)	5.748 (2.5585)
Atheroma Area, Month 18	5.928 (2.9615)	5.634 (2.5594)
Change from Baseline in Atheroma Area	0.010 (0.6448)	-0.114 (0.6990)
Vessel Area, Baseline	14.364 (5.1946)	14.166 (4.8231)
Vessel Area, Month 18	14.261 (5.1699)	13.977 (4.8595)
Change from Baseline in Vessel Area	-0.102 (1.1954)	-0.189 (0.9918)
Lumen Area, Baseline	8.447 (3.2037)	8.419 (3.2847)
Lumen Area, Month 18	8.335	8.344

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
	(3.2056)	(3.3077)
Change from Baseline in Lumen Area	-0.113 (1.2166)	-0.075 (0.9207)

8. Secondary Outcome Measure:

Measure Title	Model Adjusted Change From Baseline in Atheroma Area to Month 18
Measure Description	IVUS-derived endpoints measured within the same segment (in non-intervened coronary arteries) from Baseline to Month 18. Model Adjusted Change (MAC) = Baseline + Region + Sex + Treatment + Cardiac Procedure + Prior OAD Medication.
Time Frame	Baseline to Month 18
Safety Issue?	No

Analysis Population Description

IVUS Evaluable Population

Reporting Groups

	Description
Glipizide (GLP) 5 mg	Glipizide (GLP) 5 mg once daily for 18 months
Rosiglitazone (RSG) 4 mg	Rosiglitazone (RSG) 4 mg once daily for 18 months

Measured Values

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Number of Participants Analyzed	229	233
Model Adjusted Change From Baseline in Atheroma Area to Month 18 [units: millimeters square (mm2)] Mean (Standard Error)	0.03 (0.050)	-0.10 (0.050)

Statistical Analysis 1 for Model Adjusted Change From Baseline in Atheroma Area to Month 18

Groups	Glipizide (GLP) 5 mg, Rosiglitazone (RSG) 4 mg
Method	
Other Estimated Parameter [Mean diff (RSG-GLP) for atheroma area]	-0.13

Additional details about the analysis, such as null hypothesis and power calculation:

[Not specified.]

9. Secondary Outcome Measure:

Measure Title	Model Adjusted Change From Baseline in Lumen Area to Month 18
Measure Description	IVUS-derived endpoints measured within the same segment (in non-intervened coronary arteries) from Baseline to Month 18. Model Adjusted Change (MAC) = Baseline + Region + Sex + Treatment + Cardiac Procedure + Prior OAD Medication.
Time Frame	Baseline to Month 18
Safety Issue?	No

Analysis Population Description

IVUS Evaluable Population

Reporting Groups

	Description
Glipizide (GLP) 5 mg	Glipizide (GLP) 5 mg once daily for 18 months
Rosiglitazone (RSG) 4 mg	Rosiglitazone (RSG) 4 mg once daily for 18 months

Measured Values

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Number of Participants Analyzed	229	233
Model Adjusted Change From Baseline in Lumen Area to Month 18 [units: millimeters square (mm2)] Mean (Standard Error)	-0.14 (0.079)	-0.11 (0.079)

Statistical Analysis 1 for Model Adjusted Change From Baseline in Lumen Area to Month 18

Groups	Glipizide (GLP) 5 mg, Rosiglitazone (RSG) 4 mg
Method	
Other Estimated Parameter [Mean diff (RSG-GLP) for lumen area]	0.02

Additional details about the analysis, such as null hypothesis and power calculation:

[Not specified.]

10. Secondary Outcome Measure:

Measure Title	Model Adjusted Change From Baseline in Vessel Area to Month 18

Measure Description	IVUS-derived endpoints measured within the same segment (in non-intervened coronary arteries) from Baseline to Month 18. Model Adjusted Change (MAC) = Baseline + Region + Sex + Treatment + Cardiac Procedure + Prior OAD Medication.
Time Frame	Baseline to Month 18
Safety Issue?	No

Analysis Population Description

IVUS Evaluable Population

Reporting Groups

	Description
Glipizide (GLP) 5 mg	Glipizide (GLP) 5 mg once daily for 18 months
Rosiglitazone (RSG) 4 mg	Rosiglitazone (RSG) 4 mg once daily for 18 months

Measured Values

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Number of Participants Analyzed	229	233
Model Adjusted Change From Baseline in Vessel Area to Month 18 [units: millimeters square (mm2)] Mean (Standard Error)	-0.10 (0.082)	-0.21 (0.082)

Statistical Analysis 1 for Model Adjusted Change From Baseline in Vessel Area to Month 18

Groups	Glipizide (GLP) 5 mg, Rosiglitazone (RSG) 4 mg
Method	
Other Estimated Parameter [Mean diff	-0.11

(RSG-GLP) for vessel area]	

Additional details about the analysis, such as null hypothesis and power calculation:

[Not specified.]

11. Secondary Outcome Measure:

Measure Title	Change From Baseline in Normalized Atheroma Volume
Measure Description	IVUS-derived endpoints measured within the same segment (in non-intervened coronary arteries) from Baseline to Month 18. Normalized atheroma volume is defined as mean atheroma area x median segment length in cohort.
Time Frame	Baseline to Month 18
Safety Issue?	No

Analysis Population Description

IVUS Evaluable Population

Reporting Groups

	Description
Glipizide (GLP) 5 mg	Glipizide (GLP) 5 mg once daily for 18 months
Rosiglitazone (RSG) 4 mg	Rosiglitazone (RSG) 4 mg once daily for 18 months

Measured Values

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Number of Participants Analyzed	229	233
Change From Baseline in Normalized		

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Atheroma Volume [units: millimeters cubed (mm3)] Mean (Standard Deviation)		
Baseline	232.772 (115.1630)	226.075 (100.6261)
Month 18	233.153 (116.4765)	221.599 (100.6606)
Change from Baseline	0.381 (25.3600)	-4.476 (27.4901)

12. Secondary Outcome Measure:

Measure Title	Model Adjusted Change From Baseline in Normalized Atheroma Volume
Measure Description	IVUS-derived endpoints measured within the same segment (in non-intervened coronary arteries) from Baseline to Month 18. Normalized atheroma volume is defined as mean atheroma area x median segment length in cohort. Model Adjusted Change = Baseline + Region + Sex + Treatment + Cardiac Procedure + Prior OAD Medication.
Time Frame	Baseline to Month 18
Safety Issue?	No

Analysis Population Description

IVUS Evaluable Population

Reporting Groups

	Description
Glipizide (GLP) 5 mg	Glipizide (GLP) 5 mg once daily for 18 months
Rosiglitazone (RSG) 4 mg	Rosiglitazone (RSG) 4 mg once daily for 18 months

Measured Values

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Number of Participants Analyzed	229	233
Model Adjusted Change From Baseline in Normalized Atheroma Volume [units: millimeters cubed (mm3)] Mean (Standard Error)	1.20 (1.974)	-3.92 (1.983)

Statistical Analysis 1 for Model Adjusted Change From Baseline in Normalized Atheroma Volume

Groups	Glipizide (GLP) 5 mg, Rosiglitazone (RSG) 4 mg
Method	
Other Estimated Parameter [Model adjusted mean diff. (RSG-GLP)]	-5.12

Additional details about the analysis, such as null hypothesis and power calculation:

[Not specified.]

13. Secondary Outcome Measure:

Measure Title	Change in Atheroma Volume Within the 10 mm of the Non-intervened Vessel Segment With the Greatest Atheroma Volume at Baseline
Measure Description	IVUS-derived endpoints measured within the same 10 mm segment of

	non-intervened coronary arteries with the greatest degree of atheroma volume at Baseline, from Baseline to Month 18, including the nominal change in atheroma volume and atheroma area
Time Frame	Baseline to Month 18
Safety Issue?	No

Analysis Population Description

IVUS Evaluable Population with last observation carried forward (LOCF)

Reporting Groups

	Description
Glipizide (GLP) 5 mg	Glipizide (GLP) 5 mg once daily for 18 months
Rosiglitazone (RSG) 4 mg	Rosiglitazone (RSG) 4 mg once daily for 18 months

Measured Values

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Number of Participants Analyzed	229	233
Change in Atheroma Volume Within the 10 mm of the Non-intervened Vessel Segment With the Greatest Atheroma Volume at Baseline [units: millimeters cubed (mm3)] Mean (Standard Deviation)		
Baseline	75.649 (32.6125)	70.961 (29.9610)
Month 18	72.225 (33.2887)	66.020 (30.7228)

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Change from Baseline	-3.424 (11.9263)	-4.941 (12.2005)

14. Secondary Outcome Measure:

Measure Title	Model Adjusted Change in Atheroma Volume Within the 10 mm of the Non-intervened Vessel Segment With the Greatest Atheroma Volume at Baseline
Measure Description	IVUS-derived endpoints measured within the same 10 mm segment of non-intervened coronary arteries with the greatest degree of atheroma volume at Baseline, from Baseline to Month 18, including the nominal change in atheroma volume and atheroma area. Model Adjusted Change = Baseline + Region + Sex + Treatment + Cardiac Procedure + Prior OAD Medication.
Time Frame	Baseline to Month 18
Safety Issue?	No

Analysis Population Description

IVUS Evaluable Population with last observation carried forward (LOCF)

Reporting Groups

	Description
Glipizide (GLP) 5 mg	Glipizide (GLP) 5 mg once daily for 18 months
Rosiglitazone (RSG) 4 mg	Rosiglitazone (RSG) 4 mg once daily for 18 months

Measured Values

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Number of Participants Analyzed	229	233
Model Adjusted Change in Atheroma Volume Within the 10 mm of the Non-intervened Vessel Segment With the Greatest Atheroma Volume at Baseline [units: millimeters cubed (mm3)] Mean (Standard Error)	-3.56 (0.892)	-5.28 (0.898)

Statistical Analysis 1 for Model Adjusted Change in Atheroma Volume Within the 10 mm of the Non-intervened Vessel Segment With the Greatest Atheroma Volume at Baseline

Groups	Glipizide (GLP) 5 mg, Rosiglitazone (RSG) 4 mg
Method	
Other Estimated Parameter [Model adjusted mean diff. (RSG-GLP)]	-1.72

Additional details about the analysis, such as null hypothesis and power calculation:

[Not specified.]

15. Secondary Outcome Measure:

Measure Title	Change in Atheroma Area Within the 10 mm of the Non-intervened Vessel Segment With the Greatest Atheroma Volume at Baseline
Measure Description	IVUS-derived endpoints measured within the same 10 mm segment of non-intervened coronary arteries with the greatest degree of atheroma volume at Baseline, from Baseline to Month 18, including the nominal change in atheroma volume and atheroma area
Time Frame	Baseline to Month 18

Safety Issue?	No

Analysis Population Description

IVUS Evaluable Population with last observation carried forward (LOCF)

Reporting Groups

	Description
Glipizide (GLP) 5 mg	Glipizide (GLP) 5 mg once daily for 18 months
Rosiglitazone (RSG) 4 mg	Rosiglitazone (RSG) 4 mg once daily for 18 months

Measured Values

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Number of Participants Analyzed	229	233
Change in Atheroma Area Within the 10 mm of the Non-intervened Vessel Segment With the Greatest Atheroma Volume at Baseline [units: millimeters squared (mm2)] Mean (Standard Deviation)		
Baseline	7.569 (3.2718)	7.093 (3.0042)
Month 18	7.185 (3.2957)	6.625 (3.0741)
Change from Baseline	-0.384 (1.0608)	-0.468 (1.1370)

16. Secondary Outcome Measure:

Measure Title	Model Adjusted Change in Atheroma Area Within the 10 mm of the Non-intervened Vessel Segment With the Greatest Atheroma Volume at Baseline
Measure Description	IVUS-derived endpoints measured within the same 10 mm segment of non-intervened coronary arteries with the greatest degree of atheroma volume at Baseline, from Baseline to Month 18, including the nominal change in atheroma volume and atheroma area. Model Adjusted Change = Baseline + Region + Sex + Treatment + Cardiac Procedure + Prior OAD Medication.
Time Frame	Baseline to Month 18
Safety Issue?	No

Analysis Population Description

IVUS Evaluable Population with last observation carried forward (LOCF)

Reporting Groups

	Description
Glipizide (GLP) 5 mg	Glipizide (GLP) 5 mg once daily for 18 months
Rosiglitazone (RSG) 4 mg	Rosiglitazone (RSG) 4 mg once daily for 18 months

Measured Values

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Number of Participants Analyzed	229	233
Model Adjusted Change in Atheroma Area Within the 10 mm of the Non-intervened Vessel Segment With the Greatest Atheroma Volume at Baseline	-0.39 (0.081)	-0.50 (0.082)

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
[units: millimeters squared (mm2)] Mean (Standard Error)		

Statistical Analysis 1 for Model Adjusted Change in Atheroma Area Within the 10 mm of the Non-intervened Vessel Segment With the Greatest Atheroma Volume at Baseline

Groups	Glipizide (GLP) 5 mg, Rosiglitazone (RSG) 4 mg
Method	
Other Estimated Parameter [Model adjusted mean diff. (RSG-GLP)]	-0.11

Additional details about the analysis, such as null hypothesis and power calculation:

[Not specified.]

17. Secondary Outcome Measure:

Measure Title	Model Adjusted Change in Glycated Hemoglobin (HbA1c) From Baseline to Month 18
Measure Description	From repeated measures analysis model: Change = Baseline + visit + sex + region + treatment + prior Oral Anti-Hyperglycemic Diabetic Medications(s) (OAD) + cardiac procedure + treatment x visit.
Time Frame	Baseline to Month 18
Safety Issue?	No

Analysis Population Description

Intent-to-Treat (ITT) Population without Last Observation Carried Forward (LOCF). ITT population was defined as all participants in the study who were randomized and have at least one on-therapy value for an efficacy assessment.

Reporting Groups

	Description
Glipizide (GLP) 5 mg	Glipizide (GLP) 5 mg once daily for 18 months
Rosiglitazone (RSG) 4 mg	Rosiglitazone (RSG) 4 mg once daily for 18 months

Measured Values

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Number of Participants Analyzed	321	311
Model Adjusted Change in Glycated Hemoglobin (HbA1c) From Baseline to Month 18 [units: Percentage] Mean (Standard Error)	-0.20 (0.051)	-0.30 (0.053)

Statistical Analysis 1 for Model Adjusted Change in Glycated Hemoglobin (HbA1c) From Baseline to Month 18

Groups	Glipizide (GLP) 5 mg, Rosiglitazone (RSG) 4 mg
Method	
Other Estimated Parameter [Treatment difference (RSG-GLP)]	-0.10

Additional details about the analysis, such as null hypothesis and power calculation:

[Not specified.]

18. Secondary Outcome Measure:

Measure Title	Model Adjusted Change in Fasting Plasma Glucose (FPG) From Baseline to Month 18
Measure Description	From repeated measures analysis model: Change = Baseline + visit + sex + region + treatment + prior OAD + cardiac procedure + treatment

	x visit.
Time Frame	Baseline to Month 18
Safety Issue?	No

Analysis Population Description

ITT Population without LOCF

Reporting Groups

	Description
Glipizide (GLP) 5 mg	Glipizide (GLP) 5 mg once daily for 18 months
Rosiglitazone (RSG) 4 mg	Rosiglitazone (RSG) 4 mg once daily for 18 months

Measured Values

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Number of Participants Analyzed	273	255
Model Adjusted Change in Fasting Plasma Glucose (FPG) From Baseline to Month 18 [units: millimole/Liter (mmol/L)] Mean (Standard Error)	-0.46 (0.138)	-1.34 (0.145)

Statistical Analysis 1 for Model Adjusted Change in Fasting Plasma Glucose (FPG) From Baseline to Month 18

Groups	Glipizide (GLP) 5 mg, Rosiglitazone (RSG) 4 mg
Method	
Other Estimated Parameter [Treatment difference (RSG-GLP)]	-0.88

Additional details about the analysis, such as null hypothesis and power calculation:

[Not specified.]

19. Secondary Outcome Measure:

Measure Title	Repeated Measures Analysis of Percent Change in hsCRP From Baseline to Month 18
Measure Description	Changes in cardiovascular biomarkers from Baseline to Month 18, such as high sensitivity C-reactive protein (hsCRP) . Repeated measures analysis model: Log(value) - log(baseline) = log(baseline) + visit + sex + region + treatment + prior OAD + cardiac procedure + treatment x visit.
Time Frame	Baseline to Month 18
Safety Issue?	No

Analysis Population Description

ITT Population without LOCF

Reporting Groups

	Description
Glipizide (GLP) 5 mg	Glipizide (GLP) 5 mg once daily for 18 months
Rosiglitazone (RSG) 4 mg	Rosiglitazone (RSG) 4 mg once daily for 18 months

Measured Values

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Number of Participants Analyzed	316	302
Repeated Measures Analysis of Percent		

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Change in hsCRP From Baseline to Month 18 [units: percent change]		
Adjusted Geometric Mean + Standard Error	-62.82	-80.33
Adjusted Geometric Mean	-65.18	-81.63
Adjusted Geometric Mean - Standard Error	-67.40	-82.84

Statistical Analysis 1 for Repeated Measures Analysis of Percent Change in hsCRP From Baseline to Month 18

Groups	Glipizide (GLP) 5 mg, Rosiglitazone (RSG) 4 mg
Method	
Other Estimated Parameter [Treatment difference (RSG-GLP)]	-47.23

Additional details about the analysis, such as null hypothesis and power calculation:

[Not specified.]

20. Secondary Outcome Measure:

Measure Title	Repeated Measures Analysis of Percent Change in MMP 9 From Baseline to Month 18
Measure Description	Changes in cardiovascular biomarkers from Baseline to Month 18, such as matrix metalloproteinase-9 (MMP-9). Repeated measures analysis model: Log(value) - log(baseline) = log(baseline) + visit + sex + region + treatment + prior OAD + cardiac procedure + treatment x visit.

Time Frame	Baseline to Month 18
Safety Issue?	No

Analysis Population Description

ITT Population without LOCF

Reporting Groups

	Description
Glipizide (GLP) 5 mg	Glipizide (GLP) 5 mg once daily for 18 months
Rosiglitazone (RSG) 4 mg	Rosiglitazone (RSG) 4 mg once daily for 18 months

Measured Values

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Number of Participants Analyzed	298	291
Repeated Measures Analysis of Percent Change in MMP 9 From Baseline to Month 18 [units: percent change]		
Adjusted Geometric Mean + Standard Error	-26.5	-38.8
Adjusted Geometric Mean	-30.5	-42.2
Adjusted Geometric Mean - Standard Error	-34.3	-45.5

Statistical Analysis 1 for Repeated Measures Analysis of Percent Change in MMP 9 From Baseline to Month 18

Groups	Glipizide (GLP) 5 mg, Rosiglitazone (RSG) 4 mg
Method	

Other Estimated Parameter [Treatment difference (RSG-GLP)]	-16.9

Additional details about the analysis, such as null hypothesis and power calculation:

[Not specified.]

21. Secondary Outcome Measure:

Measure Title	Percent Change in Brain Natriuretic Peptide (BNP) From Baseline to Month 18
Measure Description	It was measured as ratio to baseline as percentage change based on log-transformed data : 100 x (exp(Mean change on log scale) - 1)It was measured as ratio to baseline as percentage change based on log-transformed data : 100 x (exp(Mean change on log scale) - 1). Ratio to baseline as %change mean (%) was used as the estimation parameter for both groups.
Time Frame	Baseline to Month 18
Safety Issue?	No

Analysis Population Description

ITT Population with LOCF

Reporting Groups

	Description
Glipizide (GLP) 5 mg	Glipizide (GLP) 5 mg once daily for 18 months
Rosiglitazone (RSG) 4 mg	Rosiglitazone (RSG) 4 mg once daily for 18 months

Measured Values

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Number of Participants Analyzed	212	199
Percent Change in Brain Natriuretic Peptide (BNP) From Baseline to Month 18 [units: percent change]		
Mean + Standard Error	1.141	30.189
Mean	-6.608	20.582
Mean - Standard Error	-13.764	11.683

22. Secondary Outcome Measure:

Measure Title	Model Adjusted Percent Change in Brain Natriuretic Peptide (BNP) From Baseline to Month 18
Measure Description	It was measured as ratio to baseline as percentage change based on log-transformed data : 100 x (exp(Mean change on log scale) - 1). Model Adjusted change based on ANCOVA: Log(value) - log(Baseline) = log(Baseline) + sex + region + treatment + prior OAD + cardiac procedure.
Time Frame	Baseline to Month 18
Safety Issue?	No

Analysis Population Description

ITT Population with LOCF

Reporting Groups

	Description
Glipizide (GLP) 5 mg	Glipizide (GLP) 5 mg once daily for 18 months

	Description
Rosiglitazone (RSG) 4 mg	Rosiglitazone (RSG) 4 mg once daily for 18 months

Measured Values

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Number of Participants Analyzed	212	199
Model Adjusted Percent Change in Brain Natriuretic Peptide (BNP) From Baseline to Month 18 [units: percent change]		
Adjusted Geometric Mean + Standard Error	-4.865	24.576
Adjusted Geometric Mean	-11.388	15.720
Adjusted Geometric Mean - Standard Error	-17.465	7.499

Statistical Analysis 1 for Model Adjusted Percent Change in Brain Natriuretic Peptide (BNP) From Baseline to Month 18

Groups	Glipizide (GLP) 5 mg, Rosiglitazone (RSG) 4 mg
Method	
Other Estimated Parameter [Ratio to GLP as % difference from GLP]	30.591

Additional details about the analysis, such as null hypothesis and power calculation:

[Not specified.]

23. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline to Month 18 in Total Cholesterol (TC)
Measure Description	Repeated measures analysis model: Log(value) - log (Baseline) = log(Baseline) + visit + sex + region + treatment + prior OAD + cardiac procedure + treatment x visit.
Time Frame	Baseline to Month 18
Safety Issue?	No

Analysis Population Description

ITT Population without LOCF

Reporting Groups

	Description
Glipizide (GLP) 5 mg	Glipizide (GLP) 5 mg once daily for 18 months
Rosiglitazone (RSG) 4 mg	Rosiglitazone (RSG) 4 mg once daily for 18 months

Measured Values

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Number of Participants Analyzed	272	263
Percent Change From Baseline to Month 18 in Total Cholesterol (TC) [units: percent change]		
Adjusted Geometric Mean + Standard Error	-4.205	3.151
Adjusted Geometric Mean	-5.644	1.567
Adjusted Geometric Mean - Standard	-7.062	0.007

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Error		

Statistical Analysis 1 for Percent Change From Baseline to Month 18 in Total Cholesterol (TC)

Groups	Glipizide (GLP) 5 mg, Rosiglitazone (RSG) 4 mg
Method	
Other Estimated Parameter [Treatment difference (RSG-GLP)]	7.642

Additional details about the analysis, such as null hypothesis and power calculation:

[Not specified.]

24. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline to Month 18 in High Density Lipoprotein Cholesterol (HDL-c)
Measure Description	Repeated measures analysis model: Log(value) - log (Baseline) = log(Baseline) + visit + sex + region + treatment + prior OAD + cardiac procedure + treatment x visit.
Time Frame	Baseline to Month 18
Safety Issue?	No

Analysis Population Description

ITT Population without LOCF

Reporting Groups

	Description
Glipizide (GLP) 5 mg	Glipizide (GLP) 5 mg once daily for 18 months

	Description
Rosiglitazone (RSG) 4 mg	Rosiglitazone (RSG) 4 mg once daily for 18 months

Measured Values

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Number of Participants Analyzed	269	261
Percent Change From Baseline to Month 18 in High Density Lipoprotein Cholesterol (HDL-c) [units: percent change]		
Adjusted Geometric Mean + Standard Error	7.208	15.104
Adjusted Geometric Mean	5.710	13.440
Adjusted Geometric Mean - Standard Error	4.233	11.808

Statistical Analysis 1 for Percent Change From Baseline to Month 18 in High Density Lipoprotein Cholesterol (HDL-c)

Groups	Glipizide (GLP) 5 mg, Rosiglitazone (RSG) 4 mg
Method	
Other Estimated Parameter [Treatment difference (RSG-GLP)]	7.316

Additional details about the analysis, such as null hypothesis and power calculation:

[Not specified.]

25. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline to Month 18 in HDL-2
Measure Description	Repeated measures analysis model: Log(value) - log (Baseline) = log(Baseline) + visit + sex + region + treatment + prior OAD + cardiac procedure + treatment x visit.
Time Frame	Baseline to Month 18
Safety Issue?	No

Analysis Population Description

ITT Population without LOCF

Reporting Groups

	Description
Glipizide (GLP) 5 mg	Glipizide (GLP) 5 mg once daily for 18 months
Rosiglitazone (RSG) 4 mg	Rosiglitazone (RSG) 4 mg once daily for 18 months

Measured Values

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Number of Participants Analyzed	269	260
Percent Change From Baseline to Month 18 in HDL-2 [units: percent change]		
Adjusted Geometric Mean + Standard Error	2.065	18.241
Adjusted Geometric Mean	-0.783	14.821
Adjusted Geometric Mean - Standard Error	-3.550	11.507

Statistical Analysis 1 for Percent Change From Baseline to Month 18 in HDL-2

Groups	Glipizide (GLP) 5 mg, Rosiglitazone (RSG) 4 mg
Method	
Other Estimated Parameter [Treatment difference (RSG-GLP)]	15.731

Additional details about the analysis, such as null hypothesis and power calculation:

[Not specified.]

26. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline to Month 18 in HDL-3
Measure Description	Repeated measures analysis model: Log(value) - log (Baseline) = log(Baseline) + visit + sex + region + treatment + prior OAD + cardiac procedure + treatment x visit.
Time Frame	Baseline to Month 18
Safety Issue?	No

Analysis Population Description

ITT Population without LOCF

Reporting Groups

	Description
Glipizide (GLP) 5 mg	Glipizide (GLP) 5 mg once daily for 18 months
Rosiglitazone (RSG) 4 mg	Rosiglitazone (RSG) 4 mg once daily for 18 months

Measured Values

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Number of Participants Analyzed	269	260
Percent Change From Baseline to Month 18 in HDL-3 [units: percent change]		
Adjusted Geometric Mean + Standard Error	10.683	15.165
Adjusted Geometric Mean	9.074	13.440
Adjusted Geometric Mean - Standard Error	7.490	11.732

Statistical Analysis 1 for Percent Change From Baseline to Month 18 in HDL-3

Groups	Glipizide (GLP) 5 mg, Rosiglitazone (RSG) 4 mg
Method	
Other Estimated Parameter [Treatment difference (RSG-GLP)]	3.998

Additional details about the analysis, such as null hypothesis and power calculation:

[Not specified.]

27. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline to Month 18 in Low Density Lipoprotein Cholesterol (LDL-c)
Measure Description	Repeated measures analysis model: Log(value) - log (Baseline) = log(Baseline) + visit + sex + region + treatment + prior OAD + cardiac procedure + treatment x visit.

Time Frame	Baseline to Month 18
Safety Issue?	No

Analysis Population Description

ITT Population without LOCF

Reporting Groups

	Description
Glipizide (GLP) 5 mg	Glipizide (GLP) 5 mg once daily for 18 months
Rosiglitazone (RSG) 4 mg	Rosiglitazone (RSG) 4 mg once daily for 18 months

Measured Values

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Number of Participants Analyzed	261	252
Percent Change From Baseline to Month 18 in Low Density Lipoprotein Cholesterol (LDL-c) [units: percent change]		
Adjusted Geometric Mean + Standard Error	-8.955	1.795
Adjusted Geometric Mean	-11.600	-1.237
Adjusted Geometric Mean - Standard Error	-14.172	-4.180

Statistical Analysis 1 for Percent Change From Baseline to Month 18 in Low Density Lipoprotein Cholesterol (LDL-c)

Groups	Glipizide (GLP) 5 mg, Rosiglitazone (RSG) 4 mg
Method	

Other Estimated Parameter [Treatment difference (RSG-GLP)]	11.728

Additional details about the analysis, such as null hypothesis and power calculation:

[Not specified.]

28. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline to Month 18 in Triglycerides (TG)
Measure Description	Repeated measures analysis model: Log(value) - log (Baseline) = log(Baseline) + visit + sex + region + treatment + prior OAD + cardiac procedure + treatment x visit.
Time Frame	Baseline to Month 18
Safety Issue?	No

Analysis Population Description

ITT Population without LOCF

Reporting Groups

	Description
Glipizide (GLP) 5 mg	Glipizide (GLP) 5 mg once daily for 18 months
Rosiglitazone (RSG) 4 mg	Rosiglitazone (RSG) 4 mg once daily for 18 months

Measured Values

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Number of Participants Analyzed	241	229

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Percent Change From Baseline to Month 18 in Triglycerides (TG) [units: percent change]		
Adjusted Geometric Mean + Standard Error	-7.415	-13.601
Adjusted Geometric Mean	-10.309	-16.381
Adjusted Geometric Mean - Standard Error	-13.110	-19.067

Statistical Analysis 1 for Percent Change From Baseline to Month 18 in Triglycerides (TG)

Groups	Glipizide (GLP) 5 mg, Rosiglitazone (RSG) 4 mg
Method	
Other Estimated Parameter [Treatment difference (RSG-GLP)]	-6.768

Additional details about the analysis, such as null hypothesis and power calculation:

[Not specified.]

29. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline to Month 18 in Free Fatty Acids (FFA)
Measure Description	Repeated measures analysis model: Log(value) - log (Baseline) = log(Baseline) + visit + sex + region + treatment + prior OAD + cardiac procedure + treatment x visit.
Time Frame	Baseline to Month 18

Safety Issue?	No

Analysis Population Description

ITT Population without LOCF

Reporting Groups

	Description
Glipizide (GLP) 5 mg	Glipizide (GLP) 5 mg once daily for 18 months
Rosiglitazone (RSG) 4 mg	Rosiglitazone (RSG) 4 mg once daily for 18 months

Measured Values

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Number of Participants Analyzed	236	229
Percent Change From Baseline to Month 18 in Free Fatty Acids (FFA) [units: percent change]		
Adjusted Geometric Mean + Standard Error	32.909	13.835
Adjusted Geometric Mean	27.303	8.880
Adjusted Geometric Mean - Standard Error	21.943	4.142

Statistical Analysis 1 for Percent Change From Baseline to Month 18 in Free Fatty Acids (FFA)

Groups	Glipizide (GLP) 5 mg, Rosiglitazone (RSG) 4 mg
Method	
Other Estimated Parameter [Treatment difference (RSG-GLP)]	-14.478

Additional details about the analysis, such as null hypothesis and power calculation:

[Not specified.]

30. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline to Month 18 in Apoprotein B (apoB)
Measure Description	Repeated measures analysis model: Log(value) - log (Baseline) = log(Baseline) + visit + sex + region + treatment + prior OAD + cardiac procedure + treatment x visit.
Time Frame	Baseline to Month 18
Safety Issue?	No

Analysis Population Description

ITT Population without LOCF

Reporting Groups

	Description
Glipizide (GLP) 5 mg	Glipizide (GLP) 5 mg once daily for 18 months
Rosiglitazone (RSG) 4 mg	Rosiglitazone (RSG) 4 mg once daily for 18 months

Measured Values

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Number of Participants Analyzed	280	273
Percent Change From Baseline to Month 18 in Apoprotein B (apoB) [units: percent change]		

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Adjusted Geometric Mean + Standard Error	-6.588	-6.967
Adjusted Geometric Mean	-8.320	-8.744
Adjusted Geometric Mean - Standard Error	-10.021	-10.488

Statistical Analysis 1 for Percent Change From Baseline to Month 18 in Apoprotein B (apoB)

Groups	Glipizide (GLP) 5 mg, Rosiglitazone (RSG) 4 mg
Method	
Other Estimated Parameter [Treatment difference (RSG-GLP)]	-0.462

Additional details about the analysis, such as null hypothesis and power calculation:

[Not specified.]

31. Secondary Outcome Measure:

Measure Title	Change From Baseline to Month 18 in LDL-c Peak Particle Density Measured by LDL Relative Flotation
Measure Description	From repeated measures analysis model: Change = baseline + visit + sex + region + treatment + prior OAD + cardiac procedure + treatment x visit.
Time Frame	Baseline to Month 18
Safety Issue?	No

Analysis Population Description

ITT Population without LOCF

Reporting Groups

	Description
Glipizide (GLP) 5 mg	Glipizide (GLP) 5 mg once daily for 18 months
Rosiglitazone (RSG) 4 mg	Rosiglitazone (RSG) 4 mg once daily for 18 months

Measured Values

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Number of Participants Analyzed	267	262
Change From Baseline to Month 18 in LDL-c Peak Particle Density Measured by LDL Relative Flotation [units: Ratio] Mean (Standard Error)	0.0040 (0.00158)	0.0204 (0.001630)

Statistical Analysis 1 for Change From Baseline to Month 18 in LDL-c Peak Particle Density Measured by LDL Relative Flotation

Groups	Glipizide (GLP) 5 mg, Rosiglitazone (RSG) 4 mg
Method	
Other Estimated Parameter [Treatment difference (RSG-GLP)]	0.0164

Additional details about the analysis, such as null hypothesis and power calculation:

[Not specified.]

32. Secondary Outcome Measure:

Measure Title	Change From Baseline to Month 18 in Total Cholesterol/HDL-c Ratio

Measure Description	From repeated measures analysis model: Change = baseline + visit + sex + region + treatment + prior OAD + cardiac procedure + treatment x visit.
Time Frame	Baseline to Month 18
Safety Issue?	No

Analysis Population Description

ITT Population without LOCF

Reporting Groups

	Description
Glipizide (GLP) 5 mg	Glipizide (GLP) 5 mg once daily for 18 months
Rosiglitazone (RSG) 4 mg	Rosiglitazone (RSG) 4 mg once daily for 18 months

Measured Values

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Number of Participants Analyzed	263	253
Change From Baseline to Month 18 in Total Cholesterol/HDL-c Ratio [units: ratio] Mean (Standard Error)	-0.495 (0.08380)	-0.377 (0.08620)

Statistical Analysis 1 for Change From Baseline to Month 18 in Total Cholesterol/HDL-c Ratio

Groups	Glipizide (GLP) 5 mg, Rosiglitazone (RSG) 4 mg
Method	
Other Estimated Parameter [Treatment difference (RSG-GLP)]	0.118

Additional details about the analysis, such as null hypothesis and power calculation:

[Not specified.]

33. Secondary Outcome Measure:

Measure Title	Change From Baseline to Month 18 in LDL-c/HDL-c Ratio
Measure Description	From repeated measures analysis model: Change = baseline + visit + sex + region + treatment + prior OAD + cardiac procedure + treatment x visit.
Time Frame	Baseline to Month 18
Safety Issue?	No

Analysis Population Description

ITT Population without LOCF

Reporting Groups

	Description
Glipizide (GLP) 5 mg	Glipizide (GLP) 5 mg once daily for 18 months
Rosiglitazone (RSG) 4 mg	Rosiglitazone (RSG) 4 mg once daily for 18 months

Measured Values

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Number of Participants Analyzed	252	242
Change From Baseline to Month 18 in LDL-c/HDL-c Ratio [units: ratio] Mean (Standard Error)	-0.365 (0.0610)	-0.226 (0.0629)

Statistical Analysis 1 for Change From Baseline to Month 18 in LDL-c/HDL-c Ratio

Groups	Glipizide (GLP) 5 mg, Rosiglitazone (RSG) 4 mg
Method	
Other Estimated Parameter [Treatment difference (RSG-GLP)]	0.140

Additional details about the analysis, such as null hypothesis and power calculation:

[Not specified.]

34. Secondary Outcome Measure:

Measure Title	Number of Participants With the Indicated Treatment Emergent Major Cardiovascular Events (MACE) for All-cause Death, Non-fatal MI, Non-fatal Stroke, Coronary Revascularization, or Hospitalization for Recurrent Myocardial Ischemia (MACE Composite 1)
Measure Description	This was 1 of 2 MACE composite endpoints and was a secondary efficacy endpoint.
Time Frame	Baseline to Month 21
Safety Issue?	No

Analysis Population Description

Safety Population

Reporting Groups

	Description
Glipizide (GLP) 5 mg	Glipizide (GLP) 5 mg once daily for 18 months
Rosiglitazone (RSG) 4 mg	Rosiglitazone (RSG) 4 mg once daily for 18 months

Measured Values

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Number of Participants Analyzed	337	331
Number of Participants With the Indicated Treatment Emergent Major Cardiovascular Events (MACE) for All-cause Death, Non-fatal MI, Non-fatal Stroke, Coronary Revascularization, or Hospitalization for Recurrent Myocardial Ischemia (MACE Composite 1) [units: Participants]	38	39

35. Secondary Outcome Measure:

Measure Title	Number of Participants With the Indicated Treatment Emergent Major Cardiovascular Events (MACE) for Cardiovascular Death, Nonfatal MI, or Nonfatal Stroke (MACE Composite 2)
Measure Description	This was 1 of 2 MACE composite endpoints and was a secondary efficacy endpoint.
Time Frame	Baseline to Month 21
Safety Issue?	No

Analysis Population Description

Safety Population

Reporting Groups

	Description
Glipizide (GLP) 5 mg	Glipizide (GLP) 5 mg once daily for 18 months
Rosiglitazone (RSG) 4 mg	Rosiglitazone (RSG) 4 mg once daily for 18 months

Measured Values

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Number of Participants Analyzed	337	331
Number of Participants With the Indicated Treatment Emergent Major Cardiovascular Events (MACE) for Cardiovascular Death, Nonfatal MI, or Nonfatal Stroke (MACE Composite 2) [units: Participants]	10	14

36. Secondary Outcome Measure:

Measure Title	Number of Other Cardiovascular Events
Measure Description	This was one of the secondary endpoints of the study.
Time Frame	Baseline to Month 21
Safety Issue?	No

Analysis Population Description

Safety Population

Reporting Groups

	Description
Glipizide (GLP) 5 mg	Glipizide (GLP) 5 mg once daily for 18 months
Rosiglitazone (RSG) 4 mg	Rosiglitazone (RSG) 4 mg once daily for 18 months

Measured Values

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Number of Participants Analyzed	337	331
Number of Other Cardiovascular Events [units: Number of events]		
All-cause death	7	8
Cardiovascular death	3	4
Non-fatal myocardial infarction	6	7
Non-fatal stroke	1	5
Coronary revascularization	27	26
Hospitalization for recurrent myocardial ischemia	7	11
Non-MACE congestive heart failure	3	8

Reported Adverse Events

Reporting Groups

	Description
Glipizide (GLP) 5 mg	Glipizide (GLP) 5 mg once daily for 18 months

	Description
Rosiglitazone (RSG) 4 mg	Rosiglitazone (RSG) 4 mg once daily for 18 months

Serious Adverse Events

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Total # participants affected/at risk	71/337 (21.07%)	71/331 (21.45%)
Blood and lymphatic system disorders		
Anaemia † [A]		
# participants affected/at risk	1/337 (0.3%)	3/331 (0.91%)
# events		
Lymphadenitis † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Cardiac disorders		
Acute coronary syndrome † [A]		
# participants affected/at risk	2/337 (0.59%)	0/331 (0%)
# events		
Acute myocardial infarction		

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
† [A]		
# participants affected/at risk	2/337 (0.59%)	0/331 (0%)
# events		
Angina pectoris † [A]		
# participants affected/at risk	10/337 (2.97%)	12/331 (3.63%)
# events		
Angina unstable † [A]		
# participants affected/at risk	8/337 (2.37%)	4/331 (1.21%)
# events		
Arrhythmia † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Atrial flutter † [A]		
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)
# events		
Atrioventricular block second degree † [A]		
# participants affected/at	0/337 (0%)	1/331 (0.3%)

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
risk		
# events		
Bradycardia † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Cardiac arrest † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Cardiac failure † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Cardiac failure congestive † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Cardiogenic shock † [A]		
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)
# events		

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Cardiovascular disorder † [A]		
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)
# events		
Congestive cardiomyopathy † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Coronary artery disease † [A]		
# participants affected/at risk	2/337 (0.59%)	1/331 (0.3%)
# events		
Coronary artery stenosis † [A]		
# participants affected/at risk	3/337 (0.89%)	2/331 (0.6%)
# events		
Myocardial infarction † [A]		
# participants affected/at risk	1/337 (0.3%)	1/331 (0.3%)
# events		
Palpitations † [A]		
# participants affected/at	0/337 (0%)	1/331 (0.3%)

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
risk		
# events		
Prinzmetal angina † [A]		
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)
# events		
Ear and labyrinth disorders		
Vertigo † [A]		
# participants affected/at risk	1/337 (0.3%)	1/331 (0.3%)
# events		
Eye disorders		
Macular hole † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Gastrointestinal disorders		
Abdominal pain † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
# events		
Abdominal pain upper † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Colitis † [A]		
# participants affected/at risk	1/337 (0.3%)	1/331 (0.3%)
# events		
Gastric ulcer † [A]		
# participants affected/at risk	0/337 (0%)	2/331 (0.6%)
# events		
Gastric ulcer haemorrhage † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Gastritis † [A]		
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)
# events		
Pancreatitis † [A]		

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)
# events		
Peritonitis † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
General disorders		
Chest pain † [A]		
# participants affected/at risk	8/337 (2.37%)	6/331 (1.81%)
# events		
Constipation † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Death † [A]		
# participants affected/at risk	1/337 (0.3%)	1/331 (0.3%)
# events		
Dyspepsia † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
# events		
Enteritis † [A]		
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)
# events		
Fatigue † [A]		
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)
# events		
Gastrointestinal haemorrhage † [A]		
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)
# events		
Ill-defined disorder † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Non-cardiac chest pain † [A]		
# participants affected/at risk	4/337 (1.19%)	1/331 (0.3%)
# events		
Oedema peripheral † [A]		

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Pyrexia †[A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Sudden cardiac death †[A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Umbilical hernia †[A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Vessel puncture site haemorrhage †[A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Hepatobiliary disorders		
Biliary tract disorder †[A]		
# participants affected/at	0/337 (0%)	1/331 (0.3%)

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
risk		
# events		
Cholecystitis acute † [A]		
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)
# events		
Cholelithiasis † [A]		
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)
# events		
Hepatitis toxic † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Infections and infestations		
Bronchitis † [A]		
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)
# events		
Dengue fever † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
# events		
Erysipelas † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Febrile infection † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Gastroenteritis † [A]		
# participants affected/at risk	1/337 (0.3%)	1/331 (0.3%)
# events		
Influenza † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Pneumonia † [A]		
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)
# events		
Respiratory tract infection † [A]		

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)
# events		
Septic shock † [A]		
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)
# events		
Urinary tract infection † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Injury, poisoning and procedural complications		
Cervical vertebral fracture † [A]		
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)
# events		
Chest injury † [A]		
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)
# events		
Fall † [A]		

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
In-stent arterial restenosis † [A]		
# participants affected/at risk	0/337 (0%)	3/331 (0.91%)
# events		
In-stent coronary artery restenosis † [A]		
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)
# events		
Joint injury † [A]		
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)
# events		
Meniscus lesion † [A]		
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)
# events		
Muscle injury † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
# events		
Post procedural haematoma † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Post procedural myocardial infarction † [A]		
# participants affected/at risk	0/337 (0%)	2/331 (0.6%)
# events		
Post procedural swelling † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Postoperative thrombosis † [A]		
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)
# events		
Spinal fracture † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Subdural haematoma †[A]		
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)
# events		
Therapeutic agent toxicity †[A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Investigations		
Cardiac enzymes increased †[A]		
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)
# events		
Metabolism and nutrition disorders		
Dehydration †[A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Diabetes mellitus inadequate control †[A]		

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)
# events		
Fluid retention † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Gout † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Musculoskeletal and connective tissue disorders		
Gouty arthritis † [A]		
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)
# events		
Osteoarthritis † [A]		
# participants affected/at risk	2/337 (0.59%)	0/331 (0%)
# events		
Spinal osteoarthritis † [A]		

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)
# events		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Benign neoplasm of thyroid gland † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Breast cancer in situ † [A]		
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)
# events		
Lung neoplasm malignant † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Lymphoma † [A]		
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
# events		
Malignant melanoma † [A]		
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)
# events		
Renal neoplasm † [A]		
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)
# events		
Nervous system disorders		
Brain stem infarction † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Carotid artery stenosis † [A]		
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)
# events		
Cerebral artery embolism † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
# events		
Cerebrovascular accident † [A]		
# participants affected/at risk	1/337 (0.3%)	2/331 (0.6%)
# events		
Dizziness † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Loss of consciousness † [A]		
# participants affected/at risk	1/337 (0.3%)	1/331 (0.3%)
# events		
Presyncope † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Syncope vasovagal † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Vertebrobasilar insufficiency		

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
† [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Pregnancy, puerperium and perinatal conditions		
Abortion spontaneous † [A]		
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)
# events		
Psychiatric disorders		
Adjustment disorder with mixed disturbance of emotion and cond † [A]		
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)
# events		
Anxiety † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Depression † [A]		
# participants affected/at	1/337 (0.3%)	0/331 (0%)

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
risk		
# events		
Renal and urinary disorders		
Calculus ureteric †[A]		
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)
# events		
Diabetic nephropathy †[A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Nephroangiosclerosis †[A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Proteinuria †[A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Renal colic †[A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
# events		
Renal failure † [A]		
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)
# events		
Renal failure acute † [A]		
# participants affected/at risk	1/337 (0.3%)	1/331 (0.3%)
# events		
Urinary incontinence † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Reproductive system and breast disorders		
Benign prostatic hyperplasia † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Prostatitis † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
# events		
Respiratory, thoracic and mediastinal disorders		
Acute respiratory failure † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Dyspnoea † [A]		
# participants affected/at risk	2/337 (0.59%)	2/331 (0.6%)
# events		
Epistaxis † [A]		
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)
# events		
Hiccups † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Hydrothorax † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Pleural effusion † [A]		
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)
# events		
Pleurisy † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Pulmonary embolism † [A]		
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)
# events		
Pulmonary oedema † [A]		
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)
# events		
Vascular disorders		
Haematoma † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Haemorrhage † [A]		

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)
# events		
Hypertension † [A]		
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)
# events		
Hypertensive crisis † [A]		
# participants affected/at risk	1/337 (0.3%)	0/331 (0%)
# events		
Hypotension † [A]		
# participants affected/at risk	0/337 (0%)	2/331 (0.6%)
# events		
Intermittent claudication † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		
Thrombophlebitis † [A]		
# participants affected/at risk	0/337 (0%)	1/331 (0.3%)
# events		

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Vascular pseudoaneurysm † [A]		
# participants affected/at risk	2/337 (0.59%)	0/331 (0%)
# events		

† Indicates events were collected by systematic assessment.

A Term from vocabulary, MedDRA

Other Adverse Events

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

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Total # participants affected/at risk	117/337 (34.72%)	98/331 (29.61%)
Cardiac disorders		
Angina pectoris † [A]		
# participants affected/at risk	33/337 (9.79%)	31/331 (9.37%)
# events		
General disorders		
Chest pain † [A]		
# participants affected/at risk	17/337 (5.04%)	11/331 (3.32%)
# events		
Edema peripheral † [A]		

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
# participants affected/at risk	24/337 (7.12%)	29/331 (8.76%)
# events		
Fatigue †[A]		
# participants affected/at risk	13/337 (3.86%)	18/331 (5.44%)
# events		
Nervous system disorders		
Dizziness †[A]		
# participants affected/at risk	17/337 (5.04%)	16/331 (4.83%)
# events		
Headache †[A]		
# participants affected/at risk	20/337 (5.93%)	11/331 (3.32%)
# events		
Respiratory, thoracic and mediastinal disorders		
Cough †[A]		
# participants affected/at risk	20/337 (5.93%)	13/331 (3.93%)
# events		

	Glipizide (GLP) 5 mg	Rosiglitazone (RSG) 4 mg
Vascular disorders		
Hypertension † [A]		
# participants affected/at risk	21/337 (6.23%)	13/331 (3.93%)
# events		

† Indicates events were collected by systematic assessment.

A Term from vocabulary, MedDRA

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.

GSK agreements may vary with individual investigators, but will not prohibit any investigator from publishing. GSK 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.

Limitations and Caveats:

Results Point of Contact:

Name/Official Title: GSK Response Center

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