Protocol Registration Receipt
04/05/2013

Grantor: CDER IND/IDE Number: 43,468 Serial Number: 637

# Study In Postmenopausal Women With Type 2 Diabetes Looking At Approved Diabetes Drugs And How They Affect Bone Health

This study has been completed.

| | |
|---|---|
| Sponsor: | GlaxoSmithKline |
| Collaborators: | |
| Information provided by (Responsible Party): | GlaxoSmithKline |
| ClinicalTrials.gov Identifier: | NCT00679939 |

## Purpose

The purpose of this study is to determine the effects of rosiglitazone on the bone in postmenopausal women with type 2 diabetes mellitus

| Condition | Intervention | Phase |
|---|---|---|
| Diabetes Mellitus, Type 2 | Drug: Rosiglitazone<br>Drug: Metformin | Phase 4 |

Study Type: Interventional

Study Design: Treatment, Parallel Assignment, Double Blind (Subject, Investigator), Randomized, Pharmacodynamics Study

Official Title: A 52 Week Randomized, Double-Blind, Multicenter, Mechanistic Study With a 24 Week Open-Label Follow-Up to Evaluate the Effect of AVANDIA TM on Bone in Postmenopausal Women With Type 2 Diabetes Mellitus

## Further study details as provided by GlaxoSmithKline:

Primary Outcome Measure:

- Adjusted Percent Change From Baseline in Femoral Neck (FN) Bone Mineral Density (BMD) Via Dual-energy X-ray Absorptiometry (DXA) at Week 52 [Time Frame: Baseline and Week 52] [Designated as safety issue: Yes]

  FN BMD (measured in grams per centimeters squared [g/cm^2]) was measured by DXA. Bone mineral density is calculated as the mineral content of a bone divided by the area of the bone. DXA is the principal technique used for measuring BMD. Percent change from Baseline at Week 52 was calculated as (BMD at Week 52 minus BMD at Baseline)/BMD at Baseline x 100% and was assessed by analysis of covariance (ANCOVA) with terms for treatment, baseline value, prior therapy, and region. Change in FN BMD at Week 52 was only analyzed within the Rosiglitazone arm.
- Adjusted Percent Change From Baseline in Femoral Neck (FN) Bone Mineral Density (BMD) Via Dual-energy X-ray Absorptiometry (DXA) at Week 76+10 Days [Time Frame: Baseline and Week 76+10 days] [Designated as safety issue: No]

  FN BMD (measured in grams per centimeters squared [g/cm^2]) was measured by DXA. Bone mineral density is calculated as the mineral content of a bone divided by the area of the bone. DXA is the principal technique used for measuring BMD. Percent change from Baseline at Week 76+10 days was calculated as (BMD at Week 76+10 days minus BMD at Baseline)/BMD at Baseline x 100% and was assessed by analysis of covariance (ANCOVA) with terms for treatment, baseline value, prior therapy, and region.
- Adjusted Percent Change in Femoral Neck (FN) Bone Mineral Density (BMD) Via Dual-energy X-ray Absorptiometry (DXA) From Week 52 +10 Days to Week 76+10 Days [Time Frame: Week 52+10 days and Week 76+10 days] [Designated as safety issue: No]

  FN BMD (measured in grams per centimeters squared [g/cm^2]) was measured by DXA. Bone mineral density is calculated as the mineral content of a bone divided by the area of the bone. DXA is the principal technique used for measuring BMD. Percent change from Week 52+10 days to Week 76+10 days was calculated as (BMD at Week 76+10 days minus BMD at Week 52+10 days)/BMD at Week 52+10 days x 100% and was assessed by analysis of covariance (ANCOVA) with terms for treatment, baseline value, prior therapy, and region.

Secondary Outcome Measures:

- Adjusted Percent Change From Baseline in Femoral Neck, Total Hip, Trochanter, and Lumbar Spine BMD Via DXA at Week 52 [Time Frame: Baseline and Week 52] [Designated as safety issue: Yes]

  BMD (measured in grams per centimeters squared [g/cm^2]) was measured by DXA. Percent change from Baseline at Week 52 was calculated as (BMD at Week 52 minus BMD at Baseline)/BMD at Baseline x 100% and was assessed by analysis of covariance (ANCOVA) with terms for treatment, baseline value, prior therapy, and region.
- Adjusted Percent Change in Femoral Neck, Total Hip, Trochanter, and Lumbar Spine BMD Via DXA From Week 52+10 Days to Week 76 + 10 Days [Time Frame: Week 52 + 10 days and Week 76 + 10 days] [Designated as safety issue: No]

  BMD (measured in grams per centimeters squared [g/cm^2]) was measured by DXA. Percent change from Week 52 + 10 days toat Week 76 + 10 days

was calculated as (BMD at Week 76 + 10 days minus BMD at Week 52 + 10 days)/BMD at Week 52 + 10 days x 100% and was assessed by analysis of covariance (ANCOVA) with terms for treatment, baseline value, prior therapy, and region.

- Adjusted Percent Change in Femoral Neck, Total Hip, Trochanter, and Lumbar Spine BMD Via DXA From Week 52+30 Days to Week 76 + 30 Days [Time Frame: Week 52 + 30 days and Week 76 + 30 days] [Designated as safety issue: Yes]

  BMD (measured in grams per centimeters squared [g/cm^2]) was measured by DXA. Percent change from Week 52 + 30 days to Week 76 + 30 days was calculated as (BMD at Week 76 + 30 days minus BMD at Week 52 + 30 days)/BMD at Week 52 + 30 days x 100% and was assessed by analysis of covariance (ANCOVA) with terms for treatment, baseline value, prior therapy, and region.

- Adjusted Percent Change From Baseline in Bone Specific Alkaline Phosphatase (BSAP) and Procollagen Type 1 N-propeptide (P1NP) at Week 52 and Week 76 [Time Frame: Baseline, Week 52, and Week 76] [Designated as safety issue: Yes]

  BSAP and P1NP levels were measured in micrograms per liter (mcg/L) from blood samples. BSAP and P1NP are indicators of bone buildup or formation. GM, geometric mean; SE, standard error. Percent change was based on log-transformed data and was assessed by an ANCOVA with terms for treatment, baseline value, prior therapy, and region.

- Adjusted Percent Change in Bone Specific Alkaline Phosphatase (BSAP) and Procollagen Type 1 N-propeptide (P1NP) From Week 52 to Week 76 [Time Frame: Week 52 and Week 76] [Designated as safety issue: Yes]

  BSAP and P1NP levels were measured in micrograms per liter (mcg/L) from blood samples. BSAP and P1NP are indicators of bone buildup or formation. GM, geometric mean; SE, standard error. Percent change was based on log-transformed data and was assessed by an ANCOVA with terms for treatment, baseline value, prior therapy, and region.

- Adjusted Percent Change From Baseline in Carboxyterminal Cross-linked Telopeptide of Type 1 Collagen (CTX) at Week 52 and Week 76 [Time Frame: Baseline, Week 52, and Week 76] [Designated as safety issue: Yes]

  CTX levels were measured in picograms per milliliter (pg/ml) from blood samples. CTX is an indicator of bone break down or resorption. Percent change was based on log-transformed data and was assessed by an ANCOVA with terms for treatment, baseline value, prior therapy, and region.

- Adjusted Percent Change in Carboxyterminal Cross-linked Telopeptide of Type 1 Collagen (CTX) From Week 52 to Week 76 [Time Frame: Week 52 and Week 76] [Designated as safety issue: Yes]

  CTX levels were measured in picograms per milliliter (pg/ml) from blood samples. CTX is an indicator of bone break down or resorption. Percent change was based on log-transformed data and was assessed by an ANCOVA with terms for treatment, baseline value, prior therapy, and region.

- Adjusted Percent Change From Baseline in 25-Hydroxyvitamin D (Vitamin D) at Week 52 and Week 76 [Time Frame: Baseline, Week 52, and Week 76] [Designated as safety issue: Yes]

  Vitamin D levels were measured in nanomoles per Liter (nmol/L) from blood samples. Vitamin D is required for good bone health. Percent change was based on log-transformed data and was assessed by an ANCOVA with terms for treatment, baseline value, prior therapy, and region.

- Adjusted Percent Change in 25-Hydroxyvitamin D (Vitamin D) From Week 52 to Week 76 [Time Frame: Week 52 and Week 76] [Designated as safety issue: Yes]

  Vitamin D levels were measured in nanomoles per Liter (nmol/L) from blood samples. Vitamin D is required for good bone health. Percent change was based on log-transformed data and was assessed by an ANCOVA with terms for treatment, baseline value, prior therapy, and region.

- Adjusted Percent Change From Baseline in Intact Parathyroid Hormone (PTH) at Week 52 and Week 76 [Time Frame: Baseline, Week 52, and Week 76] [Designated as safety issue: Yes]

Intact PTH levels were measured in nanograms per Liter (ng/L) from blood samples. Intact PTH is the amount of PTH circulating in the blood and influences bone health. Percent change was based on log-transformed data and was assessed by an ANCOVA with terms for treatment, baseline value, prior therapy, and region.

- Adjusted Percent Change in Intact Parathyroid Hormone (PTH) From Week 52 to Week 76 [Time Frame: Week 52 and Week 76] [Designated as safety issue: Yes]

  Intact PTH levels were measured in nanograms per Liter (ng/L) from blood samples. Intact PTH is the amount of PTH circulating in the blood and influences bone health. Percent change was based on log-transformed data and was assessed by an ANCOVA with terms for treatment, baseline value, prior therapy, and region.
- Percent Change From Baseline in Serum Estradiol at Week 52 and Week 76 [Time Frame: Baseline, Week 52, and Week 76] [Designated as safety issue: Yes]

  Serum estradiol levels were measured in picomoles per Liter (pmol/L) from blood samples. Estradiol is one form of the female sex hormone estrogen and influences bone health. Percent change from baseline was based on log-transformed data.
- Percent Change in Serum Estradiol From Week 52 to Week 76 [Time Frame: Week 52 and Week 76] [Designated as safety issue: Yes]

  Serum estradiol levels were measured in picomoles per Liter (pmol/L) from blood samples. Estradiol is one form of the female sex hormone estrogen and influences bone health. Percent change from baseline was based on log-transformed data.
- Percent Change From Baseline in Total Testosterone at Week 52 and Week 76 [Time Frame: Baseline, Week 52, and Week 76] [Designated as safety issue: Yes]

  Total testosterone levels were measured in nanomoles per Liter (nmol/L) from blood samples. Testosterone is a male sex hormone and influences bone health; total testosterone is the entire amount circulating in blood. Percent change from baseline was based on log-transformed data.
- Percent Change in Total Testosterone From Week 52 to Week 76 [Time Frame: Week 52 and Week 76] [Designated as safety issue: Yes]

  Total testosterone levels were measured in nanomoles per Liter (nmol/L) from blood samples. Testosterone is a male sex hormone and influences bone health; total testosterone is the entire amount circulating in blood. Percent change from baseline was based on log-transformed data.
- Percent Change From Baseline in Free Testosterone at Week 52 and Week 76 [Time Frame: Baseline, Week 52, and Week 76] [Designated as safety issue: Yes]

  Free testosterone levels were measured as a percentage of total testosterone from blood samples. Free testosterone is the amount of testosterone available to the body for use. Percent change from baseline was based on log-transformed data.
- Percent Change in Free Testosterone From Week 52 to Week 76 [Time Frame: Week 52 and Week 76] [Designated as safety issue: Yes]

  Free testosterone levels were measured as a percentage of total testosterone from blood samples. Free testosterone is the amount of testosterone available to the body for use. Percent change from baseline was based on log-transformed data.
- Percent Change From Baseline in Sex Hormone Binding Globulin (SHBG) at Week 52 and Week 76 [Time Frame: Baseline, Week 52, and Week 76] [Designated as safety issue: Yes]

  SHBG levels were measured in nanomoles per liter (nmol/L) from blood samples. SHBG binds to estradiol and testosterone and influences the amount of estradiol or testosterone available to the body for use. Percent change from baseline was based on log-transformed data.
- Percent Change in Sex Hormone Binding Globulin (SHBG) From Week 52 to Week 76 [Time Frame: Week 52 and Week 76] [Designated as safety issue: Yes]

SHBG levels were measured in nanomoles per liter (nmol/L) from blood samples. SHBG binds to estradiol and testosterone and influences the amount of estradiol or testosterone available to the body for use. Percent change from baseline was based on log-transformed data.

Other Pre-specified Outcome Measures:

- Percent Change in Percentage of Free Estradiol From Week 52 to Week 76 [Time Frame: Week 52 and Week 76] [Designated as safety issue: Yes]
  Free estradiol levels were measured as a percentage of serum estrogen from blood samples. Free estradiol is the amount of estrogen available to the body for use. Percent change was based on log-transformed data.
- Percent Change in Free Estradiol From Week 52 to Week 76 [Time Frame: Week 52 and Week 76] [Designated as safety issue: Yes]
  Free estradiol levels were measured in picomoles per Liter (pmol/L) from blood samples. Free estrodial is the amount of estrogen available to the body for use. Change was based on log-transformed data.

Enrollment: 226
Study Start Date: April 2008
Study Completion Date: September 2010
Primary Completion Date: March 2010

| Arms | Assigned Interventions |
|---|---|
| Active Comparator: Arm 1 Treatment A<br>rosiglitazone up to 8mg/day | Drug: Rosiglitazone<br>up to 8mg/day<br><br>Other Names:<br>Rosiglitazone |
| Active Comparator: Arm 2 Treatment B<br>metformin up to 2000mg/day | Drug: Metformin<br>up to 2000mg/day |

## Eligibility

Ages Eligible for Study: 55 Years to 80 Years
Genders Eligible for Study: Female

Inclusion Criteria:

- Female, >55 to <80 years
- >5 years menopausal

- Type 2 Diabetes Mellitus (T2DM) diagnosis according to American Diabetes Association (ADA), American Association of Clinical Endocrinologists (AACE), Canadian Diabetes Association (CDA), World Health Organization/International Diabetes Federation (WHO/IDF)
- Drug-naïve (HbA1c < or = 9.0%); OR Prior monotherapy, submaximal doses of metformin (< or = 1000mg Metformin), sulfonylureas (< or = 5mg Glyburide, < or = 10mg Glipizide or < or = 8mg glimepiride) or full dose Januvia (100mg) (HbA1c < or = 8.5%); OR Prior monotherapy, > submaximal doses of metformin (>1000mg) or sulfonylureas (>5mg Glyburide, >10mg Glipizide or >8mg glimepiride) (HbA1c < or = 7.0%)
- Weighs <300 lbs (136.4 kg)
- Two or more vertebra (L1-L4) suitable for BMD measurement by dual x-ray absorptiometry (DXA)
- Absolute BMD value consistent with T-score >-2.5 at femoral neck, lumbar spine and total hip

Exclusion Criteria:

- Type 1 Diabetes Mellitus (T1DM) or history of diabetic ketoacidosis (DKA)
- Renal or hepatic disease (clinically significant)
- Hepatocellular reaction, severe edema, or medically serious fluid event associated with thiazolidinedione (TZD)
- Recent (<6mos) history or clinical intervention for angina or myocardial infarction or is taking nitrates
- Any stage of heart failure, i.e. New York Heart Association (NYHA) class I-IV
- Systolic BP >160mmHg or diastolic BP >90mmHg while on antihypertensive
- Hypersensitivity to TZDs, biguanides
- Prior treatment with two or more oral anti-diabetic (OAD) agents
- Bilateral hip replacements
- Concurrent diseases affecting bone metabolism
- Active malabsorption syndrome
- Serum calcium outside the central lab reference range
- Thyroid replacement therapy, serum thyroid stimulating hormone (TSH) must be within range
- Vitamin D deficiency
- Previous treatment with: strontium, intravenous (IV) bisphosphonate, fluoride, hormones, calcineurin inhibitors or methotrexate
- Chronic systemic corticosteroid [e.g. glucocorticoid, mineralocorticoid] treatment of no more than two intra-articular injections within the past year or use of oral parenteral, or long-term, high-dose inhaled corticosteroids

## Contacts and Locations

### Investigators

| | | |
|---|---|---|
| Study Director: | GSK Clinical Trials | GlaxoSmithKline |

## More Information

Publications:

Fitzpatrick L, BilezikianJ, Wooddell M, Paul G, Kolatkar N, Nino A, Miller C, Bogado C, Arnaud C, Cobitz A. AVD111179 Mechanism of Action Study to Evaluate the Effect of Rosiglitazone on Bone in Postmenopausal Women with Type 2 Diabetes Mellitus: Study Design and Baseline Characteristics. J Drug Asses. 2011;1(.):11-19.

Responsible Party: GlaxoSmithKline
Study ID Numbers: AVD111179
Health Authority: Canada: Health Canada
United States: Food and Drug Administration

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# Study Results

## Participant Flow

### Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be |

| | Description |
|---|---|
| | down-titrated to alleviate any MET-related tolerability issues. |

52-Week Double-Blind (DB) Period

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Started | 114 | 112 |
| Completed | 77 | 85 |
| Not Completed | 37 | 27 |
| Withdrew Consent | 17 | 13 |
| Adverse Event | 14 | 12 |
| Investigator Discretion | 5 | 0 |
| Protocol Violation | 1 | 0 |
| Lost to Follow-up | 0 | 2 |

24-Week Open-Label (OL) Period

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Started | 76 [1] | 84 [2] |
| Completed | 69 | 80 |
| Not Completed | 7 | 4 |
| Adverse Event | 0 | 1 |

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Protocol Violation | 1 | 1 |
| Met Stopping Criteria | 3 | 1 |
| Physician Decision | 1 | 0 |
| Withdrawal by Subject | 2 | 1 |

[1] One participant who completed the DB Period did not receive the OL dose of MET.

[2] One participant who completed the DB Period did not receive the OL dose of MET.

## Baseline Characteristics

### Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

Baseline Measures

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period | Total |
|---|---|---|---|
| Number of Participants | 114 | 111 | 225 |
| Age, Continuous [1]<br>Years [units: Years]<br>Mean (Standard Deviation) | 63.6 (6.61) | 64.0 (6.46) | 63.8 (6.52) |
| Gender, Male/Female [2]<br>[units: Participants] | | | |
| Female | 114 | 111 | 225 |
| Male | 0 | 0 | 0 |
| Race/Ethnicity, Customized [3]<br>[units: participants] | | | |
| White - White/Caucasian/European | 82 | 78 | 160 |
| African American/African | 2 | 8 | 10 |
| American Indian or Alaskan Native | 6 | 5 | 11 |
| Asian - Central/South Asian | 13 | 10 | 23 |
| South East Asian | 4 | 6 | 10 |
| Mixed Race | 3 | 2 | 5 |
| East Asia | 4 | 2 | 6 |

[1] Baseline Characteristics were summarized for all participants in the Safety Population, comprised of all randomized participants who received at least one dose of study medication. One participant in the Metformin arm did not receive study medication and was not included in

the Safety Population.

[2] Baseline Characteristics were summarized for all participants in the Safety Population, comprised of all randomized participants who received at least one dose of study medication. One participant in the Metformin arm did not receive study medication and was not included in the Safety Population.

[3] Baseline Characteristics were summarized for all participants in the Safety Population, comprised of all randomized participants who received at least one dose of study medication. One participant in the Metformin arm did not receive study medication and was not included in the Safety Population.

## Outcome Measures

### 1. Primary Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Percent Change From Baseline in Femoral Neck (FN) Bone Mineral Density (BMD) Via Dual-energy X-ray Absorptiometry (DXA) at Week 52 |
| Measure Description | FN BMD (measured in grams per centimeters squared [g/cm^2]) was measured by DXA. Bone mineral density is calculated as the mineral content of a bone divided by the area of the bone. DXA is the principal technique used for measuring BMD. Percent change from Baseline at Week 52 was calculated as (BMD at Week 52 minus BMD at Baseline)/BMD at Baseline x 100% and was assessed by analysis of covariance (ANCOVA) with terms for treatment, baseline value, prior therapy, and region. Change in FN BMD at Week 52 was only analyzed within the Rosiglitazone arm. |
| Time Frame | Baseline and Week 52 |
| Safety Issue? | Yes |

Analysis Population Description

Safety Population. Only evaluable participants with a value at baseline and at Week 52 for the parameter of interest were analyzed. Only participants with Baseline DXA and Week 52 DXA measurements performed on or prior to initiating open-label MET are included in this primary analysis.

Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period |
|---|---|
| Number of Participants Analyzed | 52 |
| Adjusted Percent Change From Baseline in Femoral Neck (FN) Bone Mineral Density (BMD) Via Dual-energy X-ray Absorptiometry (DXA) at Week 52<br>[units: percent change]<br>Mean (Standard Error) | -1.24 (0.619) |

## 2. Primary Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Percent Change From Baseline in Femoral Neck (FN) Bone Mineral Density (BMD) Via Dual-energy X-ray Absorptiometry (DXA) at Week 76+10 Days |

| | |
|---|---|
| Measure Description | FN BMD (measured in grams per centimeters squared [g/cm^2]) was measured by DXA. Bone mineral density is calculated as the mineral content of a bone divided by the area of the bone. DXA is the principal technique used for measuring BMD. Percent change from Baseline at Week 76+10 days was calculated as (BMD at Week 76+10 days minus BMD at Baseline)/BMD at Baseline x 100% and was assessed by analysis of covariance (ANCOVA) with terms for treatment, baseline value, prior therapy, and region. |
| Time Frame | Baseline and Week 76+10 days |
| Safety Issue? | No |

## Analysis Population Description

Safety Population. Only evaluable participants with a value at baseline and at Week 76 performed up to 10 days after stopping OL MET for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 65 | 70 |
| Adjusted Percent Change From Baseline in Femoral Neck (FN) Bone Mineral Density (BMD) Via Dual-energy X-ray Absorptiometry (DXA) at Week 76+10 Days<br>[units: percent change]<br>Mean (Standard Error) | -1.91 (0.624) | 0.31 (0.636) |

3. Primary Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Percent Change in Femoral Neck (FN) Bone Mineral Density (BMD) Via Dual-energy X-ray Absorptiometry (DXA) From Week 52 +10 Days to Week 76+10 Days |
| Measure Description | FN BMD (measured in grams per centimeters squared [g/cm^2]) was measured by DXA. Bone mineral density is calculated as the mineral content of a bone divided by the area of the bone. DXA is the principal technique used for measuring BMD. Percent change from Week 52+10 days to Week 76+10 days was calculated as (BMD at Week 76+10 days minus BMD at Week 52+10 days)/BMD at Week 52+10 days x 100% and was assessed by analysis of covariance (ANCOVA) with terms for treatment, baseline value, prior therapy, and region. |
| Time Frame | Week 52+10 days and Week 76+10 days |
| Safety Issue? | No |

## Analysis Population Description

Safety Population. Only evaluable participants with a value at Week 52 performed up to 10 days after initiating OL MET and at Week 76 performed up to 10 days after stopping OL MET for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

## Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 56 | 62 |
| Adjusted Percent Change in Femoral Neck (FN) Bone Mineral Density (BMD) Via Dual-energy X-ray Absorptiometry (DXA) From Week 52 +10 Days to Week | -0.07 (0.589) | -0.02 (0.585) |

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| 76+10 Days<br>[units: percent change]<br>Mean (Standard Error) | | |

4. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Percent Change From Baseline in Femoral Neck, Total Hip, Trochanter, and Lumbar Spine BMD Via DXA at Week 52 |
| Measure Description | BMD (measured in grams per centimeters squared [g/cm^2]) was measured by DXA. Percent change from Baseline at Week 52 was calculated as (BMD at Week 52 minus BMD at Baseline)/BMD at Baseline x 100% and was assessed by analysis of covariance (ANCOVA) with terms for treatment, baseline value, prior therapy, and region. |
| Time Frame | Baseline and Week 52 |
| Safety Issue? | Yes |

### Analysis Population Description

Safety Population. Only evaluable participants with a value at baseline and at Week 52 for the parameter of interest were analyzed. Only participants with Baseline DXA and Week 52 DXA measurements performed on or prior to initiating open-label MET were analyzed. Not all participants had correct positioning for the DXA lumbar spine measurement.

### Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) |

| | Description |
|---|---|
| Metformin in OL Period | in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

## Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 52 | 54 |
| Adjusted Percent Change From Baseline in Femoral Neck, Total Hip, Trochanter, and Lumbar Spine BMD Via DXA at Week 52<br>[units: percent change]<br>Mean (Standard Error) | | |
| Femoral neck, n=52, 54 | -1.24 (0.619) | 0.72 (0.659) |
| Total hip, n=52, 54 | -0.77 (0.417) | -0.38 (0.440) |
| Trochanter, n=52, 54 | -0.21 (0.725) | -0.78 (0.768) |

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Lumbar spine, n=51, 53 | -1.21 (0.473) | 0.12 (0.505) |

5. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Percent Change in Femoral Neck, Total Hip, Trochanter, and Lumbar Spine BMD Via DXA From Week 52+10 Days to Week 76 + 10 Days |
| Measure Description | BMD (measured in grams per centimeters squared [g/cm^2]) was measured by DXA. Percent change from Week 52 + 10 days toat Week 76 + 10 days was calculated as (BMD at Week 76 + 10 days minus BMD at Week 52 + 10 days)/BMD at Week 52 + 10 days x 100% and was assessed by analysis of covariance (ANCOVA) with terms for treatment, baseline value, prior therapy, and region. |
| Time Frame | Week 52 + 10 days and Week 76 + 10 days |
| Safety Issue? | No |

## Analysis Population Description

Safety Population. Only evaluable participants with a value at Week 52 performed up to 10 days after initiating OL MET and at Week 76 performed up to 10 days after stopping OL MET for the parameter of interest were analyzed. Not all participants had correct positioning for the DXA lumbar spine measurement.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to |

| | Description |
|---|---|
| | open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

## Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 56 | 62 |
| Adjusted Percent Change in Femoral Neck, Total Hip, Trochanter, and Lumbar Spine BMD Via DXA From Week 52+10 Days to Week 76 + 10 Days<br>[units: percent change]<br>Mean (Standard Error) | | |
| Femoral neck, n=56, 62 | -0.07 (0.589) | -0.02 (0.585) |
| Total hip, n=56, 62 | 0.40 (0.304) | -0.13 (0.301) |
| Trochanter, n=56, 62 | -0.02 (0.475) | -0.68 (0.469) |
| Lumbar spine, n=55, 62 | 0.26 (0.440) | 1.03 (0.442) |

6. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Percent Change in Femoral Neck, Total Hip, Trochanter, and Lumbar Spine BMD Via DXA From Week 52+30 Days to Week 76 + 30 Days |
| Measure Description | BMD (measured in grams per centimeters squared [g/cm^2]) was measured by DXA. Percent change from Week 52 + 30 days to Week 76 + 30 days was calculated as (BMD at Week 76 + 30 days minus BMD at Week 52 + 30 days)/BMD at Week 52 + 30 days x 100% and was assessed by analysis of covariance (ANCOVA) with terms for treatment, baseline value, prior therapy, and region. |
| Time Frame | Week 52 + 30 days and Week 76 + 30 days |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population. Only evaluable participants with a value at Week 52 performed up to 30 days after initiating OL MET and Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed. Not all participants had correct positioning for all of the DXA measurements.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were |

| | Description |
|---|---|
| | switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 65 | 73 |
| Adjusted Percent Change in Femoral Neck, Total Hip, Trochanter, and Lumbar Spine BMD Via DXA From Week 52+30 Days to Week 76 + 30 Days<br>[units: percent change]<br>Mean (Standard Error) | | |
| Femoral neck, n=64, 73 | -0.27 (0.559) | -0.25 (0.535) |
| Total hip, n=64, 73 | 0.00 (0.298) | -0.27 (0.283) |
| Trochanter, n=64, 73 | -0.17 (0.495) | -0.47 (0.470) |
| Lumbar spine, n=65, 70 | 0.54 (0.445) | 0.90 (0.442) |

7. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Percent Change From Baseline in Bone Specific Alkaline Phosphatase (BSAP) and Procollagen Type 1 N-propeptide (P1NP) at Week 52 and Week 76 |

| | |
|---|---|
| Measure Description | BSAP and P1NP levels were measured in micrograms per liter (mcg/L) from blood samples. BSAP and P1NP are indicators of bone buildup or formation. GM, geometric mean; SE, standard error. Percent change was based on log-transformed data and was assessed by an ANCOVA with terms for treatment, baseline value, prior therapy, and region. |
| Time Frame | Baseline, Week 52, and Week 76 |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population. Only evaluable participants with a value at Baseline and at Week 52 or Week 76 for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg). RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin | Metformin (MET) initiated at a total daily dose of 1000 mg. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

## Measured Values

| | Rosiglitazone | Metformin |
|---|---|---|
| Number of Participants Analyzed | 78 | 84 |
| Adjusted Percent Change From Baseline in Bone Specific Alkaline Phosphatase (BSAP) and Procollagen Type 1 N-propeptide (P1NP) at Week 52 and Week 76<br>[units: percent change] | | |
| Week 52, GM - SE, BSAP, n=78, 84 | -15.2 | -29.7 |
| Week 52, GM, BSAP, n=78, 84 | -12.3 | -27.3 |
| Week 52, GM + SE, BSAP, n=78, 84 | -9.3 | -24.8 |
| Week 76, GM - SE, BSAP, n=64, 77 | -18.7 | -26.7 |
| Week 76, GM, BSAP, n=64, 77 | -15.9 | -24.3 |
| Week 76, GM + SE, BSAP, n=64, 77 | -12.9 | -21.8 |
| Week 52, GM - SE, P1NP, n=76, 83 | 5.0 | -16.5 |
| Week 52, GM, P1NP, n=76, 83 | 9.0 | -13.3 |
| Week 52, GM + SE, P1NP, n=76, 83 | 13.3 | -9.9 |
| Week 76 GM - SE, P1NP, n=63, 75 | -11.2 | -14.5 |
| Week 76, GM, P1NP, n=63, 75 | -6.9 | -10.5 |
| Week 76, GM + SE, P1NP, n=63, 75 | -2.4 | -6.4 |

8. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Percent Change in Bone Specific Alkaline Phosphatase (BSAP) and Procollagen Type 1 N-propeptide (P1NP) From Week 52 to Week 76 |

| | |
|---|---|
| Measure Description | BSAP and P1NP levels were measured in micrograms per liter (mcg/L) from blood samples. BSAP and P1NP are indicators of bone buildup or formation. GM, geometric mean; SE, standard error. Percent change was based on log-transformed data and was assessed by an ANCOVA with terms for treatment, baseline value, prior therapy, and region. |
| Time Frame | Week 52 and Week 76 |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population. Only evaluable participants with a value at Week 52 and at Week 76 for the parameter of interest were analyzed. One participant did not have P1NP measured.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

## Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 64 | 76 |
| Adjusted Percent Change in Bone Specific Alkaline Phosphatase (BSAP) and Procollagen Type 1 N-propeptide (P1NP) From Week 52 to Week 76 [units: percent change] | | |
| GM - SE, BSAP, n=64, 76 | -5.6 | 4.3 |
| GM, BSAP, n=64, 76 | -2.0 | 8.0 |
| GM + SE, BSAP, n=64, 76 | 1.8 | 11.8 |
| GM - SE, P1NP, n=63, 76 | -15.8 | 3.2 |
| GM, P1NP, n=63, 76 | -12.4 | 7.0 |
| GM + SE, P1NP, n=63, 76 | -9.0 | 11.0 |

9. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Percent Change From Baseline in Carboxyterminal Cross-linked Telopeptide of Type 1 Collagen (CTX) at Week 52 and Week 76 |
| Measure Description | CTX levels were measured in picograms per milliliter (pg/ml) from blood samples. CTX is an indicator of bone break down or resorption. Percent change was based on log-transformed data and was assessed by an ANCOVA with terms for treatment, baseline value, prior therapy, and region. |

| | |
|---|---|
| Time Frame | Baseline, Week 52, and Week 76 |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population. Only evaluable participants with a value at Baseline and at Week 52 or Week 76 for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

## Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 77 | 84 |
| Adjusted Percent Change From Baseline | | |

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| in Carboxyterminal Cross-linked Telopeptide of Type 1 Collagen (CTX) at Week 52 and Week 76<br>[units: percent change] | | |
| Week 52, GM - SE, n=77, 84 | 11.3 | -7.8 |
| Week 52, GM, n=77, 84 | 18.1 | -2.3 |
| Week 52, GM + SE, n=77, 84 | 25.4 | 3.7 |
| Week 76, GM - SE, n=63, 77 | -19.5 | -4.5 |
| Week 76, GM, n=63, 77 | -13.1 | 2.6 |
| Week 76, GM + SE, n=63, 77 | -6.1 | 10.3 |

10. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Percent Change in Carboxyterminal Cross-linked Telopeptide of Type 1 Collagen (CTX) From Week 52 to Week 76 |
| Measure Description | CTX levels were measured in picograms per milliliter (pg/ml) from blood samples. CTX is an indicator of bone break down or resorption. Percent change was based on log-transformed data and was assessed by an ANCOVA with terms for treatment, baseline value, prior therapy, and region. |
| Time Frame | Week 52 and Week 76 |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population. Only evaluable participants with a value at Week 52 and at Week 76 for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

## Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 64 | 76 |
| Adjusted Percent Change in Carboxyterminal Cross-linked Telopeptide of Type 1 Collagen (CTX) From Week 52 to Week 76<br>[units: percent change] | | |

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| GM - SE | -31.2 | 2.2 |
| GM | -26.7 | 8.4 |
| GM + SE | -21.9 | 14.9 |

11. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Percent Change From Baseline in 25-Hydroxyvitamin D (Vitamin D) at Week 52 and Week 76 |
| Measure Description | Vitamin D levels were measured in nanomoles per Liter (nmol/L) from blood samples. Vitamin D is required for good bone health. Percent change was based on log-transformed data and was assessed by an ANCOVA with terms for treatment, baseline value, prior therapy, and region. |
| Time Frame | Baseline, Week 52, and Week 76 |
| Safety Issue? | Yes |

Analysis Population Description

Safety Population. Only evaluable participants with a value at Baseline and at Week 52 or Week 76 for the parameter of interest were analyzed.

Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the |

| | Description |
|---|---|
| | follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

## Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 61 | 65 |
| Adjusted Percent Change From Baseline in 25-Hydroxyvitamin D (Vitamin D) at Week 52 and Week 76<br>[units: percent change] | | |
| Week 52, GM - SE, n=61, 65 | -27.9 | -15.9 |
| Week 52, GM, n=61, 65 | -24.7 | -12.2 |
| Week 52, GM + SE, n=61, 65 | -21.4 | -8.4 |
| Week 76, GM - SE, n=55, 58 | -21.3 | -12.5 |
| Week 76, GM, n=55, 58 | -18.1 | -8.9 |
| Week 76, GM + SE, n=55, 58 | -14.6 | -5.2 |

12. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Percent Change in 25-Hydroxyvitamin D (Vitamin D) From Week 52 to Week 76 |
| Measure Description | Vitamin D levels were measured in nanomoles per Liter (nmol/L) from blood samples. Vitamin D is required for good bone health. Percent change was based on log-transformed data and was assessed by an ANCOVA with terms for treatment, baseline value, prior therapy, and region. |
| Time Frame | Week 52 and Week 76 |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population. Only evaluable participants with a value at Week 52 and at Week 76 for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be |

| | Description |
|---|---|
| | down-titrated to alleviate any MET-related tolerability issues. |

Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 63 | 76 |
| Adjusted Percent Change in 25-Hydroxyvitamin D (Vitamin D) From Week 52 to Week 76 [units: percent change] | | |
| GM - SE | -4.7 | -7.7 |
| GM | 0.1 | -3.2 |
| GM + SE | 5.1 | 1.5 |

13. Secondary Outcome Measure:

| Measure Title | Adjusted Percent Change From Baseline in Intact Parathyroid Hormone (PTH) at Week 52 and Week 76 |
|---|---|
| Measure Description | Intact PTH levels were measured in nanograms per Liter (ng/L) from blood samples. Intact PTH is the amount of PTH circulating in the blood and influences bone health. Percent change was based on log-transformed data and was assessed by an ANCOVA with terms for treatment, baseline value, prior therapy, and region. |
| Time Frame | Baseline, Week 52, and Week 76 |

| | |
|---|---|
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population. Only evaluable participants with a value at Baseline and at Week 52 or Week 76 for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

## Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 64 | 71 |
| Adjusted Percent Change From Baseline in Intact Parathyroid Hormone (PTH) at Week 52 and Week 76 | | |

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| [units: percent change] | | |
| Week 52, GM - SE, n=64, 71 | -16.5 | -25.9 |
| Week 52, GM, n=64, 71 | -12.0 | -22.0 |
| Week 52, GM + SE, n=64, 71 | -7.2 | -17.8 |
| Week 76, GM - SE, n=56, 64 | -28.8 | -26.2 |
| Week 76, GM, n=56, 64 | -23.1 | -20.8 |
| Week 76, GM + SE, n=56, 64 | -17.0 | -15.0 |

14. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Percent Change in Intact Parathyroid Hormone (PTH) From Week 52 to Week 76 |
| Measure Description | Intact PTH levels were measured in nanograms per Liter (ng/L) from blood samples. Intact PTH is the amount of PTH circulating in the blood and influences bone health. Percent change was based on log-transformed data and was assessed by an ANCOVA with terms for treatment, baseline value, prior therapy, and region. |
| Time Frame | Week 52 and Week 76 |
| Safety Issue? | Yes |

### Analysis Population Description

Safety Population. Only evaluable participants with a value at Week 52 and at Week 76 for the parameter of interest were analyzed.

### Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

## Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 64 | 75 |
| Adjusted Percent Change in Intact Parathyroid Hormone (PTH) From Week 52 to Week 76<br>[units: percent change] | | |
| GM - SE | -13.2 | -1.7 |
| GM | -7.4 | 4.3 |
| GM + SE | -1.3 | 10.7 |

15. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Percent Change From Baseline in Serum Estradiol at Week 52 and Week 76 |
| Measure Description | Serum estradiol levels were measured in picomoles per Liter (pmol/L) from blood samples. Estradiol is one form of the female sex hormone estrogen and influences bone health. Percent change from baseline was based on log-transformed data. |
| Time Frame | Baseline, Week 52, and Week 76 |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population. Only evaluable participants with a value at Baseline and at Week 52 or Week 76 for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 74 | 82 |
| Percent Change From Baseline in Serum Estradiol at Week 52 and Week 76 [units: percent change] | | |
| Week 52, GM - SE, n=74, 82 | -17.0838 | -31.4166 |
| Week 52, GM, n=74, 82 | -3.453 | -17.280 |
| Weel 52, GM + SE, n=74, 82 | 12.4189 | -0.2292 |
| Week 76, GM - SE, n=64, 76 | -16.0971 | 0.4372 |
| Week 76, GM, n=64, 76 | 0.215 | 21.389 |
| Week 76, GM - SE, n=64, 76 | 19.6987 | 46.7122 |

16. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Percent Change in Serum Estradiol From Week 52 to Week 76 |
| Measure Description | Serum estradiol levels were measured in picomoles per Liter (pmol/L) from blood samples. Estradiol is one form of the female sex hormone estrogen and influences bone health. Percent change from baseline was based on log-transformed data. |
| Time Frame | Week 52 and Week 76 |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population. Only evaluable participants with a value at Week 52 and at Week 76 for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

## Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 64 | 77 |
| Percent Change in Serum Estradiol From Week 52 to Week 76<br>[units: percent change] | | |
| GM - SE | -15.2056 | 29.3058 |

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| GM | 0.513 | 50.823 |
| GM + SE | 19.1447 | 75.9217 |

17. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Percent Change From Baseline in Total Testosterone at Week 52 and Week 76 |
| Measure Description | Total testosterone levels were measured in nanomoles per Liter (nmol/L) from blood samples. Testosterone is a male sex hormone and influences bone health; total testosterone is the entire amount circulating in blood. Percent change from baseline was based on log-transformed data. |
| Time Frame | Baseline, Week 52, and Week 76 |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population. Only evaluable participants with a value at Baseline and at Week 52 or Week 76 for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day |

| | Description |
|---|---|
| | to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

## Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 74 | 82 |
| Percent Change From Baseline in Total Testosterone at Week 52 and Week 76 [units: percent change] | | |
| Week 52, GM - SE, n=74, 82 | 14.1569 | -5.8206 |
| Week 52, GM, n=74, 82 | 19.689 | 1.044 |
| Week 52, GM + SE, n=74, 82 | 25.4897 | 8.4082 |
| Week 76, GM - SE, n=64, 75 | -12.5441 | -8.2870 |
| Week 76, GM, n=64, 75 | -8.156 | -2.932 |
| Week 76, GM + SE, n=64, 75 | -3.5470 | 2.7363 |

18. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Percent Change in Total Testosterone From Week 52 to Week 76 |
| Measure Description | Total testosterone levels were measured in nanomoles per Liter (nmol/L) from blood samples. Testosterone is a male sex hormone and influences bone health; total testosterone is the entire amount circulating in blood. Percent change from baseline was based on log-transformed data. |
| Time Frame | Week 52 and Week 76 |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population. Only evaluable participants with a value at Week 52 and at Week 76 for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be |

| | Description |
|---|---|
| | down-titrated to alleviate any MET-related tolerability issues. |

Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 64 | 76 |
| Percent Change in Total Testosterone From Week 52 to Week 76 [units: percent change] | | |
| GM - SE | -29.0307 | -13.9923 |
| GM | -24.373 | -7.102 |
| GM + SE | -19.4104 | 0.3411 |

19. Secondary Outcome Measure:

| Measure Title | Percent Change From Baseline in Free Testosterone at Week 52 and Week 76 |
|---|---|
| Measure Description | Free testosterone levels were measured as a percentage of total testosterone from blood samples. Free testosterone is the amount of testosterone available to the body for use. Percent change from baseline was based on log-transformed data. |
| Time Frame | Baseline, Week 52, and Week 76 |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population. Only evaluable participants with a value at Baseline and at Week 52 or Week 76 for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

## Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 74 | 82 |
| Percent Change From Baseline in Free Testosterone at Week 52 and Week 76 [units: percent change] | | |
| Week 52, GM - SE, n=74, 82 | -9.9964 | 2.5725 |

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Week 52, GM, n=74, 82 | -5.940 | 6.266 |
| Week 52, GM + SE, n=74, 82 | 1.7006 | 10.0934 |
| Week 76, GM - SE, n=64, 75 | -0.3232 | -1.9532 |
| Week 76, GM, n=64, 75 | 3.687 | 2.478 |
| Week 76, GM + SE, n=64, 75 | 7.8593 | 7.1093 |

20. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Percent Change in Free Testosterone From Week 52 to Week 76 |
| Measure Description | Free testosterone levels were measured as a percentage of total testosterone from blood samples. Free testosterone is the amount of testosterone available to the body for use. Percent change from baseline was based on log-transformed data. |
| Time Frame | Week 52 and Week 76 |
| Safety Issue? | Yes |

### Analysis Population Description

Safety Population. Only evaluable participants with a value at Week 52 and at Week 76 for the parameter of interest were analyzed.

### Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose |

| | Description |
|---|---|
| | of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 64 | 76 |
| Percent Change in Free Testosterone From Week 52 to Week 76 [units: percent change] | | |
| GM - SE | 3.1109 | -6.9549 |
| GM | 8.993 | -3.537 |
| GM + SE | 15.2100 | 0.0073 |

21. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Percent Change From Baseline in Sex Hormone Binding Globulin (SHBG) at Week 52 and Week 76 |
| Measure Description | SHBG levels were measured in nanomoles per liter (nmol/L) from blood samples. SHBG binds to estradiol and testosterone and influences the amount of estradiol or testosterone available to the body for use. Percent change from baseline was based on log-transformed data. |
| Time Frame | Baseline, Week 52, and Week 76 |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population. Only evaluable participants with a value at Baseline and at Week 52 or Week 76 for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 74 | 83 |
| Percent Change From Baseline in Sex Hormone Binding Globulin (SHBG) at Week 52 and Week 76 [units: percent change] | | |
| Week 52, GM - SE, n=74, 83 | 33.2608 | 4.3929 |
| Week 52, GM, n=74, 83 | 37.563 | 8.146 |
| Week 52, GM + SE, n=74, 83 | 42.0049 | 12.0349 |
| Week 76, GM - SE, n=61, 67 | -0.2973 | 4.0983 |
| Week 76, GM, n=61, 67 | 3.137 | 9.846 |
| Week 76, GM + SE, n=61, 67 | 6.6896 | 15.9116 |

22. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Percent Change in Sex Hormone Binding Globulin (SHBG) From Week 52 to Week 76 |
| Measure Description | SHBG levels were measured in nanomoles per liter (nmol/L) from blood samples. SHBG binds to estradiol and testosterone and influences the amount of estradiol or testosterone available to the body for use. Percent change from baseline was based on log-transformed data. |
| Time Frame | Week 52 and Week 76 |

| | |
|---|---|
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population. Only evaluable participants with a value at Week 52 and at Week 76 for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

## Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 62 | 66 |
| Percent Change in Sex Hormone Binding Globulin (SHBG) From Week 52 to Week 76 | | |

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| [units: percent change] | | |
| GM - SE | -27.0129 | -3.9036 |
| GM | -24.624 | -0.825 |
| GM + SE | -22.1566 | 2.3517 |

23. Other Pre-specified Outcome Measure:

| | |
|---|---|
| Measure Title | Percent Change in Percentage of Free Estradiol From Week 52 to Week 76 |
| Measure Description | Free estradiol levels were measured as a percentage of serum estrogen from blood samples. Free estradiol is the amount of estrogen available to the body for use. Percent change was based on log-transformed data. |
| Time Frame | Week 52 and Week 76 |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population. Only evaluable participants with a value at Week 52 and Week 76 for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to |

| | Description |
|---|---|
| | open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 33 | 38 |
| Percent Change in Percentage of Free Estradiol From Week 52 to Week 76 [units: percent change] | | |
| GM - SE | -7.6337 | -5.4666 |
| GM | -2.683 | -0.975 |
| GM + SE | 2.5337 | 3.7301 |

24. Other Pre-specified Outcome Measure:

| | |
|---|---|
| Measure Title | Percent Change in Free Estradiol From Week 52 to Week 76 |
| Measure Description | Free estradiol levels were measured in picomoles per Liter (pmol/L) from blood samples. Free estrodial is the amount of estrogen available to the body for use. Change was based on log-transformed data. |
| Time Frame | Week 52 and Week 76 |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population. Only evaluable participants with a value at Week 52 and Week 76 for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

## Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 27 | 33 |
| Percent Change in Free Estradiol From Week 52 to Week 76<br>[units: percent change] | | |
| GM - SE | -29.5250 | 96.1843 |
| GM | -3.239 | 173.932 |
| GM + SE | 32.8525 | 282.4903 |

25. Post-Hoc Outcome Measure:

| Measure Title | Adjusted Percent Change From Baseline in Femoral Neck, Total Hip, Trochanter, and Lumbar Spine BMD Via DXA at Week 52 + 10 Days and Week 76 + 10 Days |
|---|---|
| Measure Description | BMD (measured in grams per centimeters squared [g/cm^2]) was measured by DXA. Percent change from Baseline at Week 52 + 10 days or Week 76 + 10 days was calculated as (BMD at Week 52 + 10 days (or Week 76 + 10 days ) minus BMD at Baseline)/BMD at Baseline x 100% and was assessed by analysis of covariance (ANCOVA) with terms for treatment, baseline value, prior therapy, and region. |
| Time Frame | Baseline, Week 52 + 10 days, and Week 76 + 10 days |
| Safety Issue? | Yes |

Analysis Population Description

Safety Population. Only evaluable participants with a value at Baseline and at Week 52 performed up to 10 days after initiating OL MET or at Week 76 performed up to 10 days after stopping OL MET for the parameter of interest were analyzed. Not all participants had the correct positioning for the DXA lumbar spine measurement.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

## Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 70 | 78 |
| Adjusted Percent Change From Baseline in Femoral Neck, Total Hip, Trochanter, and Lumbar Spine BMD Via DXA at Week 52 + 10 Days and Week 76 + 10 Days [units: percent change] | | |

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Mean (Standard Error) | | |
| Week 52 + 10 days; Femoral neck (FN), n=70, 78 | -1.47 (0.521) | 0.22 (0.512) |
| Week 52 + 10 days; Total hip (TH), n=70, 78 | -1.62 (0.386) | -0.72 (0.379) |
| Week 52 + 10 days; Trochanter (Tro.), n=70, 78 | -1.45 (0.602) | -1.04 (0.589) |
| Week 52 + 10 days; Lumbar spine (LS), n=70, 76 | -1.41 (0.416) | 0.04 (0.419) |
| Week 76 + 10 days; FN, n=65, 70 | -1.91 (0.624) | 0.31 (0.636) |
| Week 76 + 10 days; TH, n=65, 70 | -1.70 (0.415) | -0.83 (0.420) |
| Week 76 + 10 days; Tro., n=65, 70 | -2.14 (0.644) | -1.35 (0.650) |
| Week 76 + 10 days; LS, n=65, 71 | -1.24 (0.452) | 0.85 (0.457) |

26. Post-Hoc Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Percent Change From Baseline in Femoral Neck, Total Hip, Trochanter, and Lumbar Spine BMD Via DXA at Week 52 + 30 Days and Week 76 + 30 Days |
| Measure Description | BMD (measured in grams per centimeters squared [g/cm^2]) was measured by DXA. Percent change from Baseline at Week 52 + 30 days or Week 76 + 30 days was calculated as (BMD at Week 52 + 30 days (or Week 76 + 30 days) minus BMD at Baseline)/BMD at Baseline x 100% and was assessed by analysis of covariance |

| | |
|---|---|
| | (ANCOVA) with terms for treatment, baseline value, prior therapy, and region. |
| Time Frame | Baseline, Week 52 + 30 days, and Week 76 + 30 days |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population. Only evaluable participants with a value at Baseline and at Week 52 performed up to 30 days after initiating OL MET or at Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed. Not all participants had the correct positioning for all of the DXA measurements.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

## Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 79 | 83 |
| Adjusted Percent Change From Baseline in Femoral Neck, Total Hip, Trochanter, and Lumbar Spine BMD Via DXA at Week 52 + 30 Days and Week 76 + 30 Days<br>[units: percent change]<br>Mean (Standard Error) | | |
| Week 52 + 30 days; Femoral neck (FN), n=77, 83 | -1.59 (0.503) | 0.24 (0.498) |
| Week 52 + 30 days; Total hip (TH), n=77, 83 | -1.79 (0.370) | -0.72 (0.364) |
| Week 52 + 30 days; Trochanter (Tro.), n=77, 83 | -1.83 (0.583) | -1.01 (0.574) |
| Week 52 + 30 days; Lumbar spine (LS), n=79, 81 | -1.60 (0.417) | 0.11 (0.421) |
| Week 76 + 30 days; FN, n=66, 74 | -2.05 (0.620) | 0.29 (0.619) |
| Week 76 + 30 days; TH, n=66, 74 | -1.79 (0.408) | -0.68 (0.404) |
| Week 76 + 30 days; Tro., n=66, 74 | -2.53 (0.508) | -0.96 (0.575) |
| Week 76 + 30 days; LS, n=66, 72 | -1.15 (0.464) | 1.13 (0.467) |

27. Post-Hoc Outcome Measure:

| Measure Title | Adjusted Percent Change From Baseline in Femoral Neck, Total Hip, Trochanter, and Intertrochanter Areal BMD Via |
|---|---|

| | Quantitative Computed Tomography (QCT) at Week 52 + 30 Days and Week 76 + 30 Days |
|---|---|
| Measure Description | BMD (measured in grams per centimeters squared [g/cm^2]) was measured by QCT. BMD by QCT is the 2-dimensional volume that mimics the DXA measurement for the same region. Percent change from Baseline at Week 52 + 30 days orWeek 76 + 30 days was calculated as (BMD at Week 52 + 30 days (orWeek 76 + 30 days) minus BMD at baseline)/BMD at Baseline x 100% and was assessed by an analysis of covariance (ANCOVA) with terms for treatment, baseline value, prior therapy, and region. |
| Time Frame | Baseline, Week 52 + 30 days, and Week 76 + 30 days |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Baseline and at Week 52 performed up to 30 days after initiating OL MET or at Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up |

| | Description |
|---|---|
| | phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

## Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 32 | 35 |
| Adjusted Percent Change From Baseline in Femoral Neck, Total Hip, Trochanter, and Intertrochanter Areal BMD Via Quantitative Computed Tomography (QCT) at Week 52 + 30 Days and Week 76 + 30 Days<br>[units: percent change]<br>Mean (Standard Error) | | |
| Week 52 + 30 days; Femoral neck (FN), n=32, 35 | -2.39 (0.895) | 0.09 (0.986) |
| Week 52 + 30 days; Total hip (TH), n=32, 35 | -3.39 (0.475) | 0.09 (0.521) |
| Week 52 + 30 days; Trochanter (Tro.), n=32, 35 | -4.53 (0.612) | -0.23 (0.669) |
| Week 52+30 days; Intertrochanter (Inter.),n=32, 35 | -3.36 (0.515) | 0.77 (0.565) |
| Week 76+30 days; Femoral neck (FN), n=31, 30 | -1.98 (0.587) | -1.52 (0.705) |

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Week 76 + 30 days; TH, n=31, 30 | -2.11 (0.495) | -0.32 (0.591) |
| Week 76 + 30 days; Tro., n=31, 30 | -2.86 (0.752) | -1.28 (0.892) |
| Week 76 + 30 days; Inter., n=31, 30 | -1.66 (0.525) | 0.30 (0.627) |

28. Post-Hoc Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Percent Change in Femoral Neck, Total Hip, Trochanter, and Intertrochanter Areal BMD Via Quantitative Computed Tomography (QCT) From Week 52+30 Days to Week 76 + 30 Days |
| Measure Description | BMD (measured in grams per centimeters squared [g/cm^2]) was measured by QCT. BMD by QCT is the 2-dimensional volume that mimics the DXA measurement for the same region. Percent change from Week 52 + 30 days to Week 76 + 30 days was calculated as (BMD at Week 76 + 30 days minus BMD at Week 52 + 30 days)/BMD at Week 52 + 30 days x 100% and was assessed by an analysis of covariance (ANCOVA) with terms for treatment, baseline value, prior therapy, and region. |
| Time Frame | Week 52 + 30 days and Week 76 + 30 days |
| Safety Issue? | Yes |

Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Week 52 performed up to 30 days after initiating OL MET or at Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

## Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 30 | 30 |
| Adjusted Percent Change in Femoral Neck, Total Hip, Trochanter, and Intertrochanter Areal BMD Via Quantitative Computed Tomography (QCT) From Week 52+30 Days to Week 76 + 30 Days<br>[units: percent change]<br>Mean (Standard Error) | | |

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| percent change | 0.95 (0.728) | -1.39 (0.866) |
| Total hip | 1.61 (0.346) | -0.18 (0.411) |
| Trochanter | 1.81 (0.534) | -0.91 (0.632) |
| Intertrochanter | 2.05 (0.428) | -0.25 (0.507) |

29. Post-Hoc Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Percent Change From Baseline in Total Hip (TH) Integral, TH Trabecular, and TH Cortical vBMD Via QCT at Week 52 + 30 Days and at Week 76 + 30 Days |
| Measure Description | Volumetric (v)BMD (measured in milligrams per centimeters cubed [mg/cm^3]) was measured by QCT. vBMD is the 3-dimensional density of a region of bone. Cortical bone is dense bone. Trabecular bone is spongy bone. Integral bone is the sum of cortical and trabecular bone measurements. Cortical thickness is the width of the cortical shell. Percent change from Baseline was calculated as (vBMD at Week 52+30 days (or Week 76+30 days) minus vBMD at baseline)/vBMD at Baseline x 100% and was assessed by ANCOVA with terms for treatment, baseline value, prior therapy, and region. |
| Time Frame | Baseline, Week 52 + 30 days, and Week 76 + 30 days |
| Safety Issue? | Yes |

Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Baseline and at Week 52 performed up to 30 days after initiating OL MET or at Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 32 | 35 |
| Adjusted Percent Change From Baseline in Total Hip (TH) Integral, TH Trabecular, and TH Cortical vBMD Via QCT at Week 52 + 30 Days and at Week 76 + 30 Days<br>[units: percent change]<br>Mean (Standard Error) | | |
| Week 52 + 30 days; Integral, n=32, 35 | -3.60 (0.587) | 0.99 (0.645) |

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Week 52 + 30 days; Trabecular, n=32, 35 | -3.63 (1.243) | 0.21 (1.376) |
| Week 52 + 30 days; Cortical, n=32, 35 | -0.54 (0.537) | 0.52 (0.603) |
| Week 76 + 30 days; Integral, n=31, 30 | -1.70 (0.657) | 0.85 (0.786) |
| Week 76 + 30 days; Trabecular, n=31, 30 | -2.66 (1.211) | 0.70 (1.445) |
| Week 76 + 30 days; Cortical, n=31, 30 | 0.23 (0.421) | 0.50 (0.518) |

30. Post-Hoc Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Percent Change in Total Hip (TH) Integral, TH Trabecular, and TH Cortical vBMD Via QCT From Week 52+30 Days to Week 76 + 30 Days |
| Measure Description | Volumetric (v)BMD (measured in milligrams per centimeters cubed [mg/cm^3]) was measured by QCT. vBMD is the 3-dimensional density of a region of bone. Cortical bone is dense bone. Trabecular bone is spongy bone. Integral bone is the sum of cortical and trabecular bone measurements. Cortical thickness is the width of the cortical shell. Percent change from Week 52 + 30 days was calculated as (vBMD at Week 76 + 30 days minus vBMD at Week 52 + 30 days)/ vBMD at Week 52 + 30 days x 100% and was assessed by an ANCOVA with terms for treatment, baseline value, prior therapy, and region. |
| Time Frame | Week 52 + 30 days and Week 76 + 30 days |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Week 52 performed up to 30 days after initiating OL MET or at Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

## Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 30 | 30 |
| Adjusted Percent Change in Total Hip (TH) Integral, TH Trabecular, and TH Cortical vBMD Via QCT From Week 52+30 Days to Week 76 + 30 Days | | |

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| [units: percent change]<br>Mean (Standard Error) | | |
| Integral | 2.24 (0.483) | -0.20 (0.5746) |
| Trabecular | 0.90 (1.252) | 1.15 (1.491) |
| Cortical | 0.94 (0.449) | -0.06 (0.548) |

31. Post-Hoc Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Percent Change From Baseline in Femoral Neck (FN) Integral, FN Trabecular, and FN Cortical vBMD Via QCT at Week 52 + 30 Days and Week 76 + 30 Days |
| Measure Description | vBMD (measured in milligrams per centimeters cubed [mg/cm^3]) was measured by QCT. Percent change from Baseline at Week 52 + 30 days or Week 76 + 30 days was calculated as (vBMD at Week 52 + 30 days (orWeek 76 + 30 days) minus vBMD at baseline)/vBMD at Baseline x 100% and was assessed by an analysis of covariance (ANCOVA) with terms for treatment, baseline value, prior therapy, and region. |
| Time Frame | Baseline, Week 52 + 30 days, and Week 76 + 30 days |
| Safety Issue? | Yes |

Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Baseline and at Week 52 performed up to 30 days after initiating OL MET or at Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 32 | 35 |
| Adjusted Percent Change From Baseline in Femoral Neck (FN) Integral, FN Trabecular, and FN Cortical vBMD Via QCT at Week 52 + 30 Days and Week 76 + 30 Days<br>[units: percent change]<br>Mean (Standard Error) | | |
| Week 52 + 30 days, Integral, n=32, 35 | -3.72 (1.097) | 0.58 (1.208) |

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Week 52 + 30 days, Trabecular, n=32, 35 | -1.83 (1.695) | 0.91 (1.867) |
| Week 52 + 30 days, Cortical, n=32, 35 | -1.00 (0.735) | -0.20 (0.819) |
| Week 76 + 30 days, Integral, n=31, 30 | -2.13 (0.946) | -0.61 (1.141) |
| Week 76 + 30 days, Trabecular, n=31, 30 | -1.05 (1.798) | 2.27 (2.141) |
| Week 76 + 30 days, Cortical, n=31, 30 | -0.46 (0.599) | -1.60 (0.723) |

32. Post-Hoc Outcome Measure:

| Measure Title | Adjusted Percent Change in Femoral Neck (FN) Integral, FN Trabecular, and FN Cortical vBMD Via QCT From Week 52+30 Days to Week 76 + 30 Days |
|---|---|
| Measure Description | vBMD (measured in milligrams per centimeters cubed [mg/cm^3]) was measured by QCT. Percent change from Week 52 + 30 days to Week 76 + 30 days was calculated as (vBMD at Week 76 + 30 days minus vBMD at Week 52 + 30 days)/vBMD at Week 52 + 30 days x 100% and was assessed by an analysis of covariance (ANCOVA) with terms for treatment, baseline value, prior therapy, and region. |
| Time Frame | Week 52 + 30 days and Week 76 + 30 days |
| Safety Issue? | No |

Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Week 52 performed up to 30 days after initiating OL MET or at Week 76

performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

## Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 30 | 30 |
| Adjusted Percent Change in Femoral Neck (FN) Integral, FN Trabecular, and FN Cortical vBMD Via QCT From Week 52+30 Days to Week 76 + 30 Days<br>[units: percent change]<br>Mean (Standard Error) | | |

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Integral | 2.21 (0.871) | -1.37 (1.040) |
| Trabecular | 0.27 (1.721) | 2.21 (2.044) |
| Cortical | 1.03 (0.774) | -1.30 (0.929) |

33. Post-Hoc Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Percent Change From Baseline in Trochanter Integral, Trochanter Trabecular, and Trochanter Cortical vBMD Via QCT at Week 52 + 30 Days and Week 76 + 30 Days |
| Measure Description | vBMD (measured in milligrams per centimeters cubed [mg/cm^3]) was measured by QCT. Percent change from Baseline at Week 52 + 30 days or Week 76 + 30 days was calculated as (vBMD at Week 52 + 30 days (or Week 76 + 30 days) minus vBMD at baseline)/vBMD at Baseline x 100% and was assessed by an analysis of covariance (ANCOVA) with terms for treatment, baseline value, prior therapy, and region. |
| Time Frame | Baseline, Week 52 + 30 days, and Week 76 + 30 days |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Baseline and at Week 52 performed up to 30 days after initiating OL MET or at Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

## Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 32 | 35 |
| Adjusted Percent Change From Baseline in Trochanter Integral, Trochanter Trabecular, and Trochanter Cortical vBMD Via QCT at Week 52 + 30 Days and Week 76 + 30 Days<br>[units: percent change]<br>Mean (Standard Error) | | |
| Week 52 + 30 days, Integral, n=32, 35 | -4.80 (0.666) | 0.01 (0.730) |

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Week 52 + 30 days, Trabecular, n=32, 35 | -3.43 (1.157) | 0.67 (1.275) |
| Week 52 + 30 days, Cortical, n=32, 35 | -1.26 (0.490) | -0.18 (0.540) |
| Week 76 + 30 days, Integral, n=31, 30 | -2.88 (0.748) | -0.93 (0.889) |
| Week 76 + 30 days, Trabecular, n=31, 30 | -2.42 (1.085) | 0.92 (1.293) |
| Week 76 + 30 days, Cortical, n=31, 30 | -0.49 (0.384) | -0.64 (0.462) |

34. Post-Hoc Outcome Measure:

| Measure Title | Adjusted Percent Change in Trochanter Integral, Trochanter Trabecular, and Trochanter Cortical vBMD Via QCT From Week 52+30 Days to Week 76 + 30 Days |
|---|---|
| Measure Description | vBMD (measured in milligrams per centimeters cubed [mg/cm^3]) was measured by QCT. Percent change from Week 52 + 30 days to Week 76 + 30 days was calculated as (vBMD at Week 76 + 30 days minus vBMD at Week 52 + 30 days)/vBMD at Week 52 + 30 days x 100% and was assessed by an analysis of covariance (ANCOVA) with terms for treatment, baseline value, prior therapy, and region. |
| Time Frame | Week 52 + 30 days and Week 76 + 30 days |
| Safety Issue? | Yes |

Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Week 52 performed up to 30 days after initiating OL MET or at Week 76

performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

## Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 30 | 30 |
| Adjusted Percent Change in Trochanter Integral, Trochanter Trabecular, and Trochanter Cortical vBMD Via QCT From Week 52+30 Days to Week 76 + 30 Days<br>[units: percent change]<br>Mean (Standard Error) | | |

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| percent change | 2.22 (0.506) | -0.90 (0.600) |
| Trabecular | 1.07 (1.138) | 0.95 (1.353) |
| Cortical | 0.78 (0.396) | -0.65 (0.474) |

35. Post-Hoc Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Percent Change From Baseline in Intertrochanter Integral, Intertrochanter Trabecular, and Intertrochanter Cortical vBMD Via QCT at Week 52 + 30 Days and Week 76 + 30 Days |
| Measure Description | vBMD (measured in milligrams per centimeters cubed [mg/cm^3]) was measured by QCT. Percent change from Baseline at Week 52 + 30 days or Week 76 + 30 days was calculated as (vBMD at Week 52 + 30 days (or Week 76 + 30 days) minus vBMD at baseline)/vBMD at Baseline x 100% and was assessed by an analysis of covariance (ANCOVA) with terms for treatment, baseline value, prior therapy, and region. |
| Time Frame | Baseline, Week 52 + 30 days, and Week 76 + 30 days |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Baseline and at Week 52 performed up to 30 days after initiating OL MET or at Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

## Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 32 | 35 |
| Adjusted Percent Change From Baseline in Intertrochanter Integral, Intertrochanter Trabecular, and Intertrochanter Cortical vBMD Via QCT at Week 52 + 30 Days and Week 76 + 30 Days<br>[units: percent change]<br>Mean (Standard Error) | | |
| Week 52 + 30 days, Integral, n=32, 35 | -3.47 (0.621) | 2.18 (0.683) |

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Week 52 + 30 days, Trabecular, n=32, 35 | -4.26 (1.341) | -0.22 (1.485) |
| Week 52 + 30 days, Cortical, n=32, 35 | -0.76 (0.568) | 0.99 (0.631) |
| Week 76 + 30 days, Integral, n=31, 30 | -0.92 (0.746) | 1.88 (0.895) |
| Week 76 + 30 days, Trabecular, n=31, 30 | -3.09 (1.278) | 0.27 (1.525) |
| Week 76 + 30 days, Cortical, n=31, 30 | 0.41 (0.472) | 0.79 (0.573) |

36. Post-Hoc Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Percent Change in Intertrochanter Integral, Intertrochanter Trabecular, and Intertrochanter Cortical vBMD Via QCT From Week 52+30 Days to Week 76 + 30 Days |
| Measure Description | vBMD (measured in milligrams per centimeters cubed [mg/cm^3]) was measured by QCT. Percent change from Week 52 + 30 days to Week 76 + 30 days was calculated as (vBMD at Week 76 + 30 days minus vBMD at Week 52 + 30 days)/vBMD at Week 52 + 30 days x 100% and was assessed by an analysis of covariance (ANCOVA) with terms for treatment, baseline value, prior therapy, and region. |
| Time Frame | Week 52 + 30 days and Week 76 + 30 days |
| Safety Issue? | Yes |

Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Week 52 performed up to 30 days after initiating OL MET or at Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

## Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 30 | 30 |
| Adjusted Percent Change in Intertrochanter Integral, Intertrochanter Trabecular, and Intertrochanter Cortical vBMD Via QCT From Week 52+30 Days to Week 76 + 30 Days<br>[units: percent change] | | |

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Mean (Standard Error) | | |
| percent change | 2.83 (0.563) | -0.46 (0.671) |
| Trabecular | 1.16 (1.298) | 1.21 (1.545) |
| Cortical | 1.29 (0.479) | -0.27 (0.577) |

37. Post-Hoc Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Percent Change From Baseline in Vertebral Trabecular vBMD Via QCT at Week 52 + 30 Days and Week 76 + 30 Days |
| Measure Description | BMD (measured in milligrams per centimeters cubed [mg/cm^3]) was measured by QCT. Percent change from Baseline at Week 52 + 30 days or Week 76 + 30 days was calculated as (vBMD at Week 52 + 30 days (orWeek 76 + 30 days) minus vBMD at baseline)/vBMD at Baseline x 100% and was assessed by an analysis of covariance (ANCOVA) with terms for treatment, baseline value, prior therapy, and region. |
| Time Frame | Baseline, Week 52 + 30 days, and Week 76 + 30 days |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Baseline and at Week 52 performed up to 30 days after initiating OL MET or at Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

## Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 32 | 35 |
| Adjusted Percent Change From Baseline in Vertebral Trabecular vBMD Via QCT at Week 52 + 30 Days and Week 76 + 30 Days<br>[units: percent change]<br>Mean (Standard Error) | | |
| Week 52 + 30 days, n=32, 35 | -6.71 (1.454) | -1.72 (1.601) |
| Week 76 + 30 days, n=31, 30 | -5.15 (1.121) | -3.91 (1.337) |

38. Post-Hoc Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Percent Change in Vertebral Trabecular vBMD Via QCT From Week 52+30 Days to Week 76 + 30 Days |
| Measure Description | BMD (measured in milligrams per centimeters cubed [mg/cm^3]) was measured by QCT. Percent change from Week 52 + 30 days to Week 76 + 30 days was calculated as (vBMD at Week 76 + 30 days minus vBMD at Week 52 + 30 days)/vBMD at Week 52 + 30 days x 100% and was assessed by an analysis of covariance (ANCOVA) with terms for treatment, baseline value, prior therapy, and region. |
| Time Frame | Week 52 + 30 days and Week 76 + 30 days |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Week 52 performed up to 30 days after initiating OL MET or at Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up |

| | Description |
|---|---|
| | phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 30 | 30 |
| Adjusted Percent Change in Vertebral Trabecular vBMD Via QCT From Week 52+30 Days to Week 76 + 30 Days<br>[units: percent change]<br>Mean (Standard Error) | 3.53 (1.454) | -2.11 (1.727) |

39. Post-Hoc Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Percent Change From Baseline in Femoral Neck (FN) Supero-posterior Integral, Trabecular, and Cortical vBMD Via QCT at Week 52 + 30 Days and Week 76 + 30 Days |
| Measure Description | vBMD (measured in milligrams per centimeters cubed [mg/cm^3]) was measured by QCT. Percent change from Baseline at Week 52 + 30 days orWeek 76 + 30 days was calculated as (vBMD at Week 52 + 30 days (or Week 76 + 30 days) minus vBMD at baseline)/vBMD at Baseline x 100% and was assessed by an analysis of covariance (ANCOVA) with terms for treatment, baseline value, prior therpay, and region. Supero-posterior is the upper and back section of the FN. |

| | |
|---|---|
| Time Frame | Baseline, Week 52 + 30 days, and Week 76 + 30 days |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Baseline and at Week 52 performed up to 30 days after initiating OL MET or Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

## Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 32 | 35 |

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Adjusted Percent Change From Baseline in Femoral Neck (FN) Supero-posterior Integral, Trabecular, and Cortical vBMD Via QCT at Week 52 + 30 Days and Week 76 + 30 Days<br>[units: percent change]<br>Mean (Standard Error) | | |
| Week 52 + 30 days, Integral, n=32, 35 | -10.26 (2.194) | -0.03 (2.417) |
| Week 52 + 30 days, Trabecular, n=32, 35 | 2.77 (5.848) | 5.57 (6.420) |
| Week 52 + 30 days, Cortical, n=32, 35 | -3.76 (0.836) | -0.66 (0.922) |
| Week 76 + 30 days, Integral, n=31, 30 | -4.21 (2.094) | 1.07 (2.508) |
| Week 76 + 30 days, Trabecular, n=31, 30 | 2.37 (7.040) | 10.24 (8.362) |
| Week 76 + 30 days, Cortical, n=31, 30 | -1.65 (0.730) | -1.30 (0.877) |

40. Post-Hoc Outcome Measure:

| Measure Title | Adjusted Change From Baseline in Femoral Neck (FN) Supero-posterior and Cortical vBMD Via QCT at Week 76 + 30 Days |
|---|---|
| Measure Description | vBMD was measured by QCT. Change from Baseline at Week 76 + 30 days was calculated as vBMD at Week 76 + 30 days minus vBMD at baseline and was assessed by an analysis of covariance (ANCOVA) with terms for treatment, baseline value, prior therapy, and region. |

| | |
|---|---|
| | Supero-posterior is the upper and back section of the FN. |
| Time Frame | Baseline and Week 76 + 30 days |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Baseline and at Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

## Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 31 | 30 |
| Adjusted Change From Baseline in Femoral Neck (FN) Supero-posterior and Cortical vBMD Via QCT at Week 76 + 30 Days<br>[units: mg/cm^3]<br>Mean (Standard Error) | -8.007<br>(3.4199) | -7.006<br>(4.1114) |

41. Post-Hoc Outcome Measure:

| Measure Title | Adjusted Percent Change in Femoral Neck (FN) Supero-posterior Integral, Trabecular, and Cortical vBMD Via QCT From Week 52+30 Days to Week 76 + 30 Days |
|---|---|
| Measure Description | vBMD (measured in milligrams per centimeters cubed [mg/cm^3]) was measured by QCT. Percent change from Week 52 + 30 days to Week 76 + 30 days was calculated as (vBMD at Week 76 + 30 days minus vBMD at Week 52 + 30 days)/vBMD at Week 52 + 30 days x 100% and was assessed by an analysis of covariance (ANCOVA) with terms for treatment, baseline value, prior therpay, and region.<br>Supero-posterior is the upper and back section of the FN. |
| Time Frame | Week 52 + 30 days and Week 76 + 30 days |
| Safety Issue? | Yes |

Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Week 52 performed up to 30 days after initiating OL MET or at Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 30 | 30 |
| Adjusted Percent Change in Femoral Neck (FN) Supero-posterior Integral, Trabecular, and Cortical vBMD Via QCT From Week 52+30 Days to Week 76 + 30 Days<br>[units: percent change]<br>Mean (Standard Error) | | |
| Integral | 8.29 (3.262) | 0.52 (3.884) |

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Trabecular | 36.05 (31.815) | -11.69 (37.721) |
| Cortical | 2.17 (0.944) | -0.94 (1.129) |

## 42. Post-Hoc Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Change in Femoral Neck (FN) Supero-posterior Cortical vBMD Via QCT From Week 52 + 30 Days to Week 76 + 30 Days |
| Measure Description | vBMD was measured by QCT. Change from Week 52 + 30 days to Week 76 + 30 days was calculated as vBMD at Week 76 + 30 days minus vBMD at Week 52 + 30 days and was assessed by an analysis of covariance (ANCOVA) with terms for treatment, baseline value, prior therpay, and region. Supero-posterior is the upper and back section of the FN. |
| Time Frame | Week 52 + 30 days and Week 76 + 30 days |
| Safety Issue? | Yes |

### Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Week 52 performed up to 30 days after initiating OL MET or at Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

### Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) |

| | Description |
|---|---|
| Metformin in OL Period | in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 30 | 30 |
| Adjusted Change in Femoral Neck (FN) Supero-posterior Cortical vBMD Via QCT From Week 52 + 30 Days to Week 76 + 30 Days<br>[units: mg/cm^3]<br>Mean (Standard Error) | 9.30 (4.287) | -4.92 (5.130) |

43. Post-Hoc Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Percent Change From Baseline in Femoral Neck (FN) Supero-posterior Cortical Thickness Via QCT at Week 52 + 30 Days and Week 76 + 30 Days |
| Measure Description | Cortical thickness (measured in millimeters) was measured by QCT. Percent change was calculated as (thickness at Week 52 + 30 days (or Week 76 + 30 days) minus thickness at Baseline)/thickness at Baseline x 100% |
| Time Frame | Baseline, Week 52 + 30 days, and Week 76 + 30 days |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Baseline and at Week 52 performed up to 30 days after initiating OL MET or at Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 32 | 35 |
| Adjusted Percent Change From Baseline in Femoral Neck (FN) Supero-posterior Cortical Thickness Via QCT at Week 52 + 30 Days and Week 76 + 30 Days<br>[units: percent change]<br>Mean (Standard Error) | | |
| Week 52 + 30 days, n=32, 35 | -20.48 (3.614) | 1.00 (3.986) |
| Week 76 + 30 days, n=31,30 | -3.52 (3.674) | -1.50 (4.423) |

## 44. Post-Hoc Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Change From Baseline in Femoral Neck (FN) Supero-posterior Cortical Thickness Via QCT at Week 76 + 30 Days |
| Measure Description | Cortical thickness was measured by QCT. Change from baseline was calculated as thickness at Week 76 + 30 days minus thickness at Baseline. |
| Time Frame | Baseline and Week 76 + 30 days |
| Safety Issue? | Yes |

### Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Baseline and at Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 31 | 30 |
| Adjusted Change From Baseline in Femoral Neck (FN) Supero-posterior Cortical Thickness Via QCT at Week 76 + 30 Days<br>[units: millimeters]<br>Mean (Standard Error) | -0.95 (0.0537) | -0.067 (0.0647) |

45. Post-Hoc Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Percent Change in Femoral Neck (FN) Supero-posterior Cortical Thickness Via QCT From Week 52+30 Days to Week 76 + 30 Days |
| Measure Description | Cortical thickness (measured in millimeters) was measured by QCT. Percent change was calculated as (thickness at Week 76 + 30 days minus thickness at Week 52 + 30 days)/thickness at Week 52 + 30 days x 100%. |
| Time Frame | Week 52 + 30 days and Week 76 + 30 days |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Week 52 performed up to 30 days after initiating OL MET or at Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 |

| | Description |
|---|---|
| | mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 30 | 30 |
| Adjusted Percent Change in Femoral Neck (FN) Supero-posterior Cortical Thickness Via QCT From Week 52+30 Days to Week 76 + 30 Days<br>[units: percent change]<br>Mean (Standard Error) | 32.42 (10.358) | -7.80 (2.383) |

46. Post-Hoc Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Change in Femoral Neck (FN) Supero-posterior Cortical Thickness Via QCT From Week 52 + 30 Days to Week 76 + 30 Days |
| Measure Description | Cortical thickness was measured by QCT. Change was calculated as thickness at Week 76 + 30 days minus thickness at Week 52 + 30 days. |
| Time Frame | Week 52 + 30 days and Week 76 + 30 days |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Week 52 performed up to 30 days after initiating OL MET or at Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

## Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 30 | 30 |
| Adjusted Change in Femoral Neck (FN) Supero-posterior Cortical Thickness Via QCT From Week 52 + 30 Days to Week 76 + 30 Days | 0.18 (0.049) | -0.05 (0.059) |

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| [units: millimeters]<br>Mean (Standard Error) | | |

47. Post-Hoc Outcome Measure:

| Measure Title | Adjusted Percent Change From Baseline in Femoral Neck (FN) Supero-anterior Integral, Trabecular, and Cortical vBMD Via QCT at Week 52 + 30 Days and Week 76 + 30 Days |
|---|---|
| Measure Description | vBMD (measured in milligrams per centimeters cubed [mg/cm^3]) was measured by QCT. Percent change from Baseline at Week 52 + 30 daysor Week 76 + 30 days was calculated as (vBMD at Week 52 + 30 days(or Week 76 + 30 days) minus vBMD at baseline)/vBMD at Baseline x 100% and was assessed by an analysis of covariance (ANCOVA) with terms for treatment, baseline value, prior therapy, and region. Supero-anterior is the upper and front section of the FN. |
| Time Frame | Baseline, Week 52 plus 30 days, and Week 76 + 30 days |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Baseline and at Week 52 performed up to 30 days after initiating OL MET or at Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) |

| | Description |
|---|---|
| Metformin in OL Period | in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

## Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 32 | 35 |
| Adjusted Percent Change From Baseline in Femoral Neck (FN) Supero-anterior Integral, Trabecular, and Cortical vBMD Via QCT at Week 52 + 30 Days and Week 76 + 30 Days<br>[units: percent change]<br>Mean (Standard Error) | | |
| Week 52 + 30 days, Integral, n=32, 35 | -6.56 (2.106) | -0.58 (2.311) |
| Week 52 + 30 days, Trabecular, n=32, | 3.59 (4.719) | 2.82 (5.180) |

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| 35 | | |
| Week 52 + 30 days, Cortical, n=32, 35 | -1.91 (0.901) | -0.25 (0.977) |
| Week 76 + 30 days, Integral, n=31, 30 | -4.97 (2.384) | -2.45 (2.838) |
| Week 76 + 30 days, Trabecular, n=31, 30 | -0.85 (6.050) | 3.98 (7.171) |
| Week 76 + 30 days, Cortical, n=31, 30 | -0.93 (0.745) | -1.49 (0.876) |

48. Post-Hoc Outcome Measure:

| Measure Title | Adjusted Change From Baseline in Femoral Neck (FN) Supero-anterior Cortical vBMD Via QCT at Week 76 + 30 Days |
|---|---|
| Measure Description | vBMD was measured by QCT. Change from Baseline at Week 76 + 30 days was calculated as vBMD at Week 76 + 30 days minus vBMD at baseline and was assessed by an analysis of covariance (ANCOVA) with terms for treatment, baseline value, prior therapy, and region. Supero-anterior is the upper and front section of the FN. |
| Time Frame | Baseline and Week 76 + 30 days |
| Safety Issue? | Yes |

Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Baseline and at Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 31 | 30 |
| Adjusted Change From Baseline in Femoral Neck (FN) Supero-anterior Cortical vBMD Via QCT at Week 76 + 30 Days<br>[units: mg/cm^3]<br>Mean (Standard Error) | -4.555<br>(3.5006) | -7.553<br>(4.1177) |

49. Post-Hoc Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Percent Change in Femoral Neck (FN) Supero-anterior Integral, Trabecular, and Cortical vBMD Via QCT From Week 52+30 Days to Week 76 + 30 Days |
| Measure Description | vBMD (measured in milligrams per centimeters cubed [mg/cm^3]) was measured by QCT. Percent change from Week 52 + 30 days to Week 76 + 30 days was calculated as (vBMD at Week 76 + 30 days minus vBMD at Week 52 + 30 days)/vBMD at Week 52 + 30 days x 100% and was assessed by an analysis of covariance (ANCOVA) with terms for treatment, baseline value, prior therapy, and region. Supero-anterior is the upper and front section of the FN. |
| Time Frame | Week 52 + 30 days and Week 76 + 30 days |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Week 52 performed up to 30 days after initiating OL MET or at Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week |

| | Description |
|---|---|
| | 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 30 | 30 |
| Adjusted Percent Change in Femoral Neck (FN) Supero-anterior Integral, Trabecular, and Cortical vBMD Via QCT From Week 52+30 Days to Week 76 + 30 Days<br>[units: percent change]<br>Mean (Standard Error) | | |
| Integral | 2.96 (2.202) | -1.81 (2.609) |
| Trabecular | -2.78 (4.677) | 6.63 (5.531) |
| Cortical | 1.19 (0.778) | -1.28 (0.912) |

50. Post-Hoc Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Change in Femoral Neck (FN) Supero-anterior Cortical vBMD Via QCT From Week 52+30 Days to Week 76 + 30 Days |

| | |
|---|---|
| Measure Description | vBMD was measured by QCT. Change from Week 52 + 30 days to Week 76 + 30 days was calculated as vBMD at Week 76 + 30 days minus vBMD at Week 52 + 30 days and was assessed by an analysis of covariance (ANCOVA) with terms for treatment, baseline value, prior therapy, and region. Supero-anterior is the upper and front section of the FN. |
| Time Frame | Week 52 + 30 days and Week 76 + 30 days |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Week 52 performed up to 30 days after initiating OL MET or at Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

## Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 30 | 30 |
| Adjusted Change in Femoral Neck (FN) Supero-anterior Cortical vBMD Via QCT From Week 52+30 Days to Week 76 + 30 Days<br>[units: mg/cm^3]<br>Mean (Standard Error) | 5.19 (3.686) | -6.24 (4.319) |

51. Post-Hoc Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Percent Change From Baseline in Femoral Neck (FN) Supero-anterior Cortical Thickness Via QCT at Week 52 + 30 Days and Week 76 + 30 Days |
| Measure Description | Cortical thickness (measured in millimeters) was measured by QCT. Percent change was calculated as (thickness at Week 52 + 30 days(or Week 76 + 30 days) minus thickness at Baseline)/thickness at Baseline x 100%. |
| Time Frame | Baseline, Week 52 + 30 days, and Week 76 + 30 days |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Baseline and at Week 52 performed up to 30 days after initiating OL MET or at Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

## Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 32 | 35 |
| Adjusted Percent Change From Baseline in Femoral Neck (FN) Supero-anterior Cortical Thickness Via QCT at Week 52 + 30 Days and Week 76 + 30 Days<br>[units: percent change]<br>Mean (Standard Error) | | |
| Week 52 + 30 days, n=32, 35 | -13.45 (5.002) | 5.05 (5.453) |
| Week 76 + 30 days, n=31, 30 | -4.23 (4.491) | -4.78 (5.327) |

52. Post-Hoc Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Change From Baseline in Femoral Neck (FN) Supero-anterior Cortical Thickness Via QCT at Week 76 + 30 Days |
| Measure Description | Cortical thickness was measured by QCT. Change from baseline was calculated as thickness at Week 76 + 30 days minus thickness at Baseline. |
| Time Frame | Baseline and Week 76 + 30 days |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Baseline and at Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be |

| | Description |
|---|---|
| | down-titrated to alleviate any MET-related tolerability issues. |

Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 31 | 30 |
| Adjusted Change From Baseline in Femoral Neck (FN) Supero-anterior Cortical Thickness Via QCT at Week 76 + 30 Days<br>[units: millimeters]<br>Mean (Standard Error) | -0.117<br>(0.0484) | -0.087<br>(0.0575) |

53. Post-Hoc Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Percent Change in Femoral Neck (FN) Supero-anterior Cortical Thickness Via QCT From Week 52 + 30 Days to Week 76 + 30 Days |
| Measure Description | Cortical thickness (measured in millimeters) was measured by QCT. Percent change was calculated as (thickness at Week 76 + 30 days minus thickness at Week 52 + 30 days)/thickness at Week 52 + 30 days x 100%. |
| Time Frame | Week 52 + 30 days and Week 76 + 30 days |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Week 52 performed up to 30 days after initiating OL MET or at Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

## Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 30 | 30 |
| Adjusted Percent Change in Femoral Neck (FN) Supero-anterior Cortical Thickness Via QCT From Week 52 + 30 Days to Week 76 + 30 Days | 14.02 (6.779) | -13.65 (7.995) |

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| [units: percent change]<br>Mean (Standard Error) | | |

54. Post-Hoc Outcome Measure:

| Measure Title | Adjusted Change in Femoral Neck (FN) Supero-anterior Cortical Thickness Via QCT From Week 52+30 Days to Week 76 + 30 Days |
|---|---|
| Measure Description | Cortical thickness was measured by QCT. Change was calculated as thickness at Week 76 + 30 days minus thickness at Week 52 + 30 days. |
| Time Frame | Week 52 + 30 days and Week 76 + 30 days |
| Safety Issue? | Yes |

### Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Week 52 performed up to 30 days after initiating OL MET or at Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

### Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be |

| | Description |
|---|---|
| | down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 30 | 30 |
| Adjusted Change in Femoral Neck (FN) Supero-anterior Cortical Thickness Via QCT From Week 52+30 Days to Week 76 + 30 Days<br>[units: millimeters]<br>Mean (Standard Error) | 0.11 (0.052) | -0.13 (0.061) |

55. Post-Hoc Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Percent Change From Baseline in Femoral Neck (FN) Infero-posterior Integral, Trabecular, and Cortical vBMD Via QCT at Week 52 + 30 Days and Week 76 + 30 Days |

| | |
|---|---|
| Measure Description | vBMD (measured in milligrams per centimeters cubed [mg/cm^3]) was measured by QCT. Percent change from Baseline at Week 52 + 30 days or Week 76 + 30 days was calculated as (vBMD at Week 52 + 30 days (or Week 76 + 30 days) minus vBMD at baseline)/vBMD at Baseline x 100% and was assessed by an analysis of covariance (ANCOVA) with terms for treatment, baseline value, prior therapy, and region. Infero-posterior is the lower and back section of the FN. |
| Time Frame | Baseline, Week 52 + 30 days, and Week 76 + 30 days |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Baseline and at Week 52 performed up to 30 days after initiating OL MET or at Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 32 | 35 |
| Adjusted Percent Change From Baseline in Femoral Neck (FN) Infero-posterior Integral, Trabecular, and Cortical vBMD Via QCT at Week 52 + 30 Days and Week 76 + 30 Days<br>[units: percent change]<br>Mean (Standard Error) | | |
| Week 52 + 30 days, Integral, n=32, 35 | -4.11 (1.074) | 1.74 (1.200) |
| Week 52 + 30 days, Trabecular, n=32, 35 | -84.08 (270.700) | 282.16 (297.445) |
| Week 52 + 30 days, Cortical, n=32, 35 | -3.42 (1.531) | 1.14 (1.694) |
| Week 76 + 30 days, Integral, n=31, 30 | -3.11 (0.933) | 0.01 (1.147) |
| Week 76 + 30 days, Trabecular, n=31, 30 | 24.46 (17.473) | 13.54 (20.790) |
| Week 76 + 30 days, Cortical, n=31, 30 | -1.32 (1.234) | -1.17 (1.492) |

56. Post-Hoc Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Change From Baseline in Femoral Neck (FN) Infero-posterior Cortical vBMD Via QCT at Week 76 + 30 Days |
| Measure Description | vBMD was measured by QCT. Change from Baseline at Week 76 + 30 days was calculated as vBMD at Week 76 + 30 days minus vBMD at |

| | |
|---|---|
| | baseline and was assessed by an analysis of covariance (ANCOVA) with terms for treatment, baseline value, prior therapy, and region. Infero-posterior is the lower and back section of the FN. |
| Time Frame | Baseline and Week 76 + 30 days |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Baseline and at Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

## Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 31 | 30 |
| Adjusted Change From Baseline in Femoral Neck (FN) Infero-posterior Cortical vBMD Via QCT at Week 76 + 30 Days<br>[units: mg/cm^3]<br>Mean (Standard Error) | -12.424 (8.9945) | -10.244 (10.8703) |

57. Post-Hoc Outcome Measure:

| Measure Title | Adjusted Percent Change in Femoral Neck (FN) Infero-posterior Integral, Trabecular, and Cortical vBMD Via QCT From Week 52+30 Days to Week 76 + 30 Days |
|---|---|
| Measure Description | vBMD (measured in milligrams per centimeters cubed [mg/cm^3]) was measured by QCT. Percent change from Week 52 + 30 days to Week 76 + 30 days was calculated as (vBMD at Week 76 + 30 days minus vBMD at Week 52 + 30 days)/vBMD at Week 52 + 30 days x 100% and was assessed by an analysis of covariance (ANCOVA) with terms for treatment, baseline value, prior therapy, and region. Infero-posterior is the lower and back section of the FN. |
| Time Frame | Week 52 + 30 days and Week 76 + 30 days |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Week 52 performed up to 30 days after initiating OL MET or at Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 30 | 30 |
| Adjusted Percent Change in Femoral Neck (FN) Infero-posterior Integral, Trabecular, and Cortical vBMD Via QCT From Week 52+30 Days to Week 76 + 30 Days<br>[units: percent change]<br>Mean (Standard Error) | | |
| Integral | 1.47 (1.183) | -1.87 (1.435) |

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Trabecular | -39.81 (130.071) | 161.81 (154.179) |
| Cortical | 2.67 (1.728) | -2.50 (2.076) |

58. Post-Hoc Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Change in Femoral Neck (FN) Infero-posterior Cortical vBMD Via QCT From Week 52 + 30 Days to Week 76 + 30 Days |
| Measure Description | vBMD was measured by QCT. Change from Week 52 + 30 days to Week 76 + 30 days was calculated as vBMD at Week 76 + 30 days minus vBMD at Week 52 + 30 days and was assessed by an analysis of covariance (ANCOVA) with terms for treatment, baseline value, prior therapy, and region. Infero-posterior is the lower and back section of the FN. |
| Time Frame | Week 52 + 30 days and Week 76 + 30 days |
| Safety Issue? | Yes |

### Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Week 52 performed up to 30 days after initiating OL MET or at Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

### Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) |

| | Description |
|---|---|
| Metformin in OL Period | in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 30 | 30 |
| Adjusted Change in Femoral Neck (FN) Infero-posterior Cortical vBMD Via QCT From Week 52 + 30 Days to Week 76 + 30 Days<br>[units: mg/cm^3]<br>Mean (Standard Error) | 15.48<br>(11.544) | -17.59<br>(13.865) |

59. Post-Hoc Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Percent Change From Baseline in Femoral Neck (FN) Infero-posterior Cortical Thickness Via QCT at Week 52 + 30 Days and Week 76 + 30 Days |
| Measure Description | Cortical thickness (measured in millimeters) was measured by QCT. Percent change was calculated as (thickness at Week 52 + 30 days (or Week 76 + 30 days) minus thickness at Baseline)/thickness at Baseline x 100%. |
| Time Frame | Baseline, Week 52 + 30 days, and Week 76 + 30 days |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Baseline and at Week 52 performed up to 30 days after initiating OL MET or Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 32 | 35 |
| Adjusted Percent Change From Baseline in Femoral Neck (FN) Infero-posterior Cortical Thickness Via QCT at Week 52 + 30 Days and Week 76 + 30 Days<br>[units: percent change]<br>Mean (Standard Error) | | |
| Week 52 + 30 days, n=32, 35 | 0.47 (1.977) | -1.27 (2.180) |
| Week 76 + 30 days, n=31, 30 | -1.46 (1.593) | -0.11 (1.910) |

60. Post-Hoc Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Change From Baseline in Femoral Neck (FN) Infero-posterior Cortical Thickness Via QCT at Week 76 + 30 Days |
| Measure Description | Cortical thickness was measured by QCT. Change from Baseline was calculated as thickness at Week 76 + 30 days minus thickness at Baseline. |
| Time Frame | Baseline and Week 76 + 30 days |
| Safety Issue? | Yes |

Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Baseline and at Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

## Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 31 | 30 |
| Adjusted Change From Baseline in Femoral Neck (FN) Infero-posterior Cortical Thickness Via QCT at Week 76 + 30 Days<br>[units: millimeters]<br>Mean (Standard Error) | -0.082<br>(0.0816) | -0.048<br>(0.0978) |

61. Post-Hoc Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Percent Change in Femoral Neck (FN) Infero-posterior Cortical Thickness Via QCT From Week 52 + 30 Days to Week 76 + 30 Days |
| Measure Description | Cortical thickness (measured in millimeters) was measured by QCT. Percent change was calculated as (thickness at Week 76 + 30 days minus thickness at Week 52 + 30 days)/thickness at Week 52 + 30 days x 100%. |
| Time Frame | Week 52 + 30 days and Week 76 + 30 days |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Week 52 performed up to 30 days after initiating OL MET or at Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 |

| | Description |
|---|---|
| | mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 30 | 30 |
| Adjusted Percent Change in Femoral Neck (FN) Infero-posterior Cortical Thickness Via QCT From Week 52 + 30 Days to Week 76 + 30 Days<br>[units: percent change]<br>Mean (Standard Error) | -1.48 (1.552) | 2.04 (1.846) |

62. Post-Hoc Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Change in Femoral Neck (FN) Infero-posterior Cortical Thickness Via QCT From Week 52 + 30 Days to Week 76 + 30 Days |
| Measure Description | Cortical thickness was measured by QCT. Change was calculated as thickness at Week 76 + 30 days minus thickness at Week 52 + 30 days. |
| Time Frame | Week 52 + 30 days and Week 76 + 30 days |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Week 52 performed up to 30 days after initiating OL MET or at Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

## Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 30 | 30 |
| Adjusted Change in Femoral Neck (FN) Infero-posterior Cortical Thickness Via QCT From Week 52 + 30 Days to Week 76 + 30 Days | -0.08 (0.078) | 0.07 (0.093) |

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| [units: millimeters]<br>Mean (Standard Error) | | |

63. Post-Hoc Outcome Measure:

| Measure Title | Adjusted Percent Change From Baseline in Femoral Neck (FN) Infero-anterior Integral, Trabecular, and Cortical vBMD Via QCT at Week 52 + 30 Days and Week 76 + 30 Days |
|---|---|
| Measure Description | vBMD (measured in milligrams per centimeters cubed [mg/cm^3]) was measured by QCT. Percent change from Baseline at Week 52 + 30 days or Week 76 + 30 days was calculated as (vBMD at Week 52 + 30 days (orWeek 76 + 30 days) minus vBMD at baseline)/vBMD at Baseline x 100% and was assessed by an analysis of covariance (ANCOVA) with terms for treatment, baseline value, prior therapy, and region. Infero-anterior is the lower and front section of the FN. |
| Time Frame | Baseline, Week 52 + 30 days, and Week 76 + 30 days |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Baseline and at Week 52 performed up to 30 days after initiating OL MET or at Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) |

| | Description |
|---|---|
| Metformin in OL Period | in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

## Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 32 | 35 |
| Adjusted Percent Change From Baseline in Femoral Neck (FN) Infero-anterior Integral, Trabecular, and Cortical vBMD Via QCT at Week 52 + 30 Days and Week 76 + 30 Days<br>[units: percent change]<br>Mean (Standard Error) | | |
| Week 52 + 30 days, Integral, n=32, 35 | -4.35 (1.950) | 1.26 (2.163) |
| Week 52, Trabecular, n=32, 35 | -161.59 | 930.71 |

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| | (774.589) | (851.727) |
| Week 52, Cortical, n=32, 35 | -1.85 (1.309) | 0.85 (1.563) |
| Week 76 + 30 days, Integral, n=31, 30 | -0.29 (2.301) | 0.54 (2.810) |
| Week 76 + 30 days, Trabecular, n=31, 30 | 81.29 (35.959) | 37.81 (42.791) |
| Week 76 + 30 days, Cortical, n=31, 30 | 1.45 (1.149) | -0.63 (1.409) |

64. Post-Hoc Outcome Measure:

| Measure Title | Adjusted Change From Baseline in Femoral Neck (FN) Infero-anterior Cortical vBMD Via QCT at Week 76 + 30 Days |
|---|---|
| Measure Description | vBMD was measured by QCT. Change from Baseline at Week 76 + 30 days was calculated as vBMD at Week 76 + 30 days minus vBMD at baseline and was assessed by an analysis of covariance (ANCOVA) with terms for treatment, baseline value, prior therapy, and region. Infero-anterior is the lower and front section of the FN. |
| Time Frame | Baseline and Week 76 + 30 days |
| Safety Issue? | Yes |

Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Baseline and at Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 31 | 30 |
| Adjusted Change From Baseline in Femoral Neck (FN) Infero-anterior Cortical vBMD Via QCT at Week 76 + 30 Days<br>[units: mg/cm^3]<br>Mean (Standard Error) | 7.901<br>(6.9912) | -5.025<br>(8.5722) |

65. Post-Hoc Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Percent Change in Femoral Neck (FN) Infero-anterior Integral, Trabecular, and Cortical vBMD Via QCT From Week 52+30 Days to Week 76 + 30 Days |
| Measure Description | vBMD (measured in milligrams per centimeters cubed [mg/cm^3]) was measured by QCT. Percent change from Week 52 + 30 days to Week 76 + 30 days was calculated as (vBMD at Week 76 + 30 days minus vBMD at Week 52 + 30 days)/vBMD at Week 52 + 30 days x 100% and was assessed by an analysis of covariance (ANCOVA) with terms for treatment, baseline value, prior therapy, and region. Infero-anterior is the lower and front section of the FN. |
| Time Frame | Week 52 + 30 days and Week 76 + 30 days |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Week 52 performed up to 30 days after initiating OL MET or at Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up |

| | Description |
|---|---|
| | phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 30 | 30 |
| Adjusted Percent Change in Femoral Neck (FN) Infero-anterior Integral, Trabecular, and Cortical vBMD Via QCT From Week 52+30 Days to Week 76 + 30 Days<br>[units: percent change]<br>Mean (Standard Error) | | |
| Integral | 5.05 (1.878) | 0.38 (2.268) |
| Trabecular | -90.60 (167.792) | 260.13 (199.323) |
| Cortical | 3.68 (1.649) | -1.64 (2.016) |

66. Post-Hoc Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Change in Femoral Neck (FN) Infero-anterior Cortical vBMD Via QCT From Week 52 + 30 Days to Week 76 + 30 Days |
| Measure Description | vBMD was measured by QCT. Change from Week 52 + 30 days to |

| | |
|---|---|
| | Week 76 + 30 days was calculated as vBMD at Week 76 + 30 days minus vBMD at Week 52 + 30 days and was assessed by an analysis of covariance (ANCOVA) with terms for treatment, baseline value, prior therapy, and region. Infero-anterior is the lower and front section of the FN. |
| Time Frame | Week 52 + 30 days and Week 76 + 30 days |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Week 52 performed up to 30 days after initiating OL MET or at Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

## Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 30 | 30 |
| Adjusted Change in Femoral Neck (FN) Infero-anterior Cortical vBMD Via QCT From Week 52 + 30 Days to Week 76 + 30 Days<br>[units: mg/cm^3]<br>Mean (Standard Error) | 20.15 (9.677) | -10.73 (11.830) |

67. Post-Hoc Outcome Measure:

| Measure Title | Adjusted Percent Change From Baseline in Femoral Neck (FN) Infero-anterior Cortical Thickness Via QCT at Week 52 + 30 Days and Week 76 + 30 Days |
|---|---|
| Measure Description | Cortical thickness (measured in millimeters) was measured by QCT. Percent change was calculated as (thickness at Week 52 + 30 days (orWeek 76 + 30 days) minus thickness at Baseline)/thickness at Baseline x 100%. |
| Time Frame | Baseline, Week 52 + 30 days, and Week 76 + 30 days |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Baseline and at Week 52 performed up to 30 days after initiating OL MET or at Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

## Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 32 | 35 |
| Adjusted Percent Change From Baseline in Femoral Neck (FN) Infero-anterior Cortical Thickness Via QCT at Week 52 + 30 Days and Week 76 + 30 Days<br>[units: percent change]<br>Mean (Standard Error) | | |
| Week 52 + 30 days, n=32, 35 | -6.05 (2.393) | 0.64 (2.656) |
| Week 76 + 30 days, n=31, 30 | -3.59 (2.804) | 0.39 (3.421) |

68. Post-Hoc Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Change From Baseline in Femoral Neck (FN) Infero-anterior Cortical Thickness Via QCT at Week 76 + 30 Days |
| Measure Description | Cortical thickness was measured by QCT. Change was calculated as thickness at Week 76 + 30 days minus thickness at Baseline. |
| Time Frame | Baseline and Week 76 + 30 days |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Baseline and at Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 31 | 30 |
| Adjusted Change From Baseline in Femoral Neck (FN) Infero-anterior Cortical Thickness Via QCT at Week 76 + 30 Days<br>[units: millimeters]<br>Mean (Standard Error) | -0.120<br>(0.0931) | -0.040<br>(0.1135) |

69. Post-Hoc Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Percent Change in Femoral Neck (FN) Infero-anterior Cortical Thickness Via QCT From Week 52 + 30 Days to Week 76 + 30 Days |
| Measure Description | Cortical thickness (measured in millimeters) was measured by QCT. Percent change was calculated as (thickness at Week 76 + 30 days minus thickness at Week 52 + 30 days)/thickness at Week 52 + 30 days x 100%. |
| Time Frame | Week 52 + 30 days and Week 76 + 30 days |
| Safety Issue? | Yes |

Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Week 52 performed up to 30 days after initiating OL MET or at Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 30 | 30 |
| Adjusted Percent Change in Femoral Neck (FN) Infero-anterior Cortical Thickness Via QCT From Week 52 + 30 Days to Week 76 + 30 Days<br>[units: percent change]<br>Mean (Standard Error) | 3.12 (2.127) | 1.56 (2.257) |

70. Post-Hoc Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Change in Femoral Neck (FN) Infero-anterior Cortical Thickness Via QCT From Week 52 + 30 Days to Week 76 + 30 Days |
| Measure Description | Cortical thickness was measured by QCT. Change was calculated as thickness at Week 76 + 30 days minus thickness at Week 52 + 30 days. |
| Time Frame | Week 52 + 30 days and Week 76 + 30 days |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population, QCT subset. Only evaluable participants with a value at Week 52 performed up to 30 days after initiating OL MET or at Week 76 performed up to 30 days after stopping OL MET for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 30 | 30 |
| Adjusted Change in Femoral Neck (FN) Infero-anterior Cortical Thickness Via QCT From Week 52 + 30 Days to Week 76 + 30 Days<br>[units: millimeters]<br>Mean (Standard Error) | 0.09 (0.065) | 0.01 (0.078) |

71. Post-Hoc Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Change From Baseline in Albumin-adjusted Serum Calcium (AASC) at Week 52 and Week 76 |
| Measure Description | AASC levels were measured from blood samples. AASC is the amount of free calcium circulating in the blood and calcium is required for good bone health. Change from baseline was calculated as the Week 52or Week 76 value minus the baseline value and was assessed by an ANCOVA with terms for treatment, baseline value, prior therapy, and region. |
| Time Frame | Baseline, Week 52, and Week 76 |
| Safety Issue? | Yes |

Analysis Population Description

Safety Population. Only evaluable participants with a value at Baseline and at Week 52 or Week 76 for the parameter of interest were analyzed.

Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

## Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 73 | 83 |
| Adjusted Change From Baseline in Albumin-adjusted Serum Calcium (AASC) at Week 52 and Week 76<br>[units: millimoles per Liter (mmol/L)]<br>Mean (Standard Error) | | |
| Week 52, n=73, 83 | 0.01 (0.009) | 0.03 (0.009) |
| Week 76, n=64, 75 | 0.03 (0.010) | 0.04 (0.010) |

72. Post-Hoc Outcome Measure:

| | |
|---|---|
| Measure Title | Adjusted Change in Albumin-adjusted Serum Calcium (AASC) From Week 52 to Week 76 |
| Measure Description | AASC levels were measured from blood samples. AASC is the amount of free calcium circulating in the blood and calcium is required for good bone health. Change from Week 52 was calculated as the Week 76 value minus the Week 52 value and was assessed by an ANCOVA with terms for treatment, baseline value, prior therapy, and region. |
| Time Frame | Week 52 and Week 76 |
| Safety Issue? | Yes |

## Analysis Population Description

Safety Population. Only evaluable participants with a value at Week 52 and at Week 76 for the parameter of interest were analyzed.

## Reporting Groups

| | Description |
|---|---|
| Rosiglitazone in DB Period; Metformin in OL Period | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg) in the 52-week DB Period. RSG could be uptitrated to a total daily dose of 8 mg at Week 4. At Week 52, all participants were switched to open-label (OL) Metformin (MET) therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin in DB Period; Metformin in OL Period | Metformin (MET) initiated at a total daily dose of 1000 mg in the 52-week DB Period. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4. At Week 52, all participants were switched to open-label MET therapy for 24 weeks during the follow-up phase; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be |

| | Description |
|---|---|
| | down-titrated to alleviate any MET-related tolerability issues. |

Measured Values

| | Rosiglitazone in DB Period; Metformin in OL Period | Metformin in DB Period; Metformin in OL Period |
|---|---|---|
| Number of Participants Analyzed | 64 | 74 |
| Adjusted Change in Albumin-adjusted Serum Calcium (AASC) From Week 52 to Week 76<br>[units: millimoles per Liter (mmol/L)]<br>Mean (Standard Error) | 0.01 (0.011) | 0.00 (0.010) |

## Reported Adverse Events

Reporting Groups

| | Description |
|---|---|
| Rosiglitazone: DB | Rosiglitazone (RSG) initiated at a total daily dose of 4 milligrams (mg). RSG could be uptitrated to a total daily dose of 8 mg at Week 4 in the 52-week Double-Blind (DB) Period. |
| Metformin: DB | Metformin (MET) initiated at a total daily dose of 1000 mg. MET could be uptitrated to 1500 mg/day at Week 2 and to 2000 mg/day at Week 4 in the 52-week DB Period. |
| Rosiglitazone: MET OL | At Week 52, all participants receiving RSG in the DB Period were switched to open-label Metformin (MET) therapy for 24 weeks during the Open-label (OL) Period; all participants were force-titrated from |

| | Description |
|---|---|
| | 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |
| Metformin: MET OL | At Week 52, all participants receiving MET in the DB Period were switched to open-label MET therapy for 24 weeks during the OL Period; all participants were force-titrated from 1000 mg/day to 2000 mg/day over a 4-week period. However, participants could be down-titrated to alleviate any MET-related tolerability issues. |

Time Frame

76 weeks

Additional Description

Serious adverse events (SAEs) and AEs were collected in the Safety Population, comprised of all randomized participants who received at least one dose of study medication.

Serious Adverse Events

| | Rosiglitazone: DB | Metformin: DB | Rosiglitazone: MET OL | Metformin: MET OL |
|---|---|---|---|---|
| Total # participants affected/at risk | 7/114 (6.14%) | 5/111 (4.5%) | 0/76 (0%) | 0/84 (0%) |
| Cardiac disorders | | | | |
| Coronary artery disease †[A] | | | | |
| # participants affected/at risk | 0/114 (0%) | 1/111 (0.9%) | 0/76 (0%) | 0/84 (0%) |
| # events | | | | |
| Gastrointestinal | | | | |

| | Rosiglitazone: DB | Metformin: DB | Rosiglitazone: MET OL | Metformin: MET OL |
|---|---|---|---|---|
| disorders | | | | |
| Umbilical hernia, obstructive † [A] | | | | |
| # participants affected/at risk | 1/114 (0.88%) | 0/111 (0%) | 0/76 (0%) | 0/84 (0%) |
| # events | | | | |
| General disorders | | | | |
| Device dislocation † [A] | | | | |
| # participants affected/at risk | 1/114 (0.88%) | 0/111 (0%) | 0/76 (0%) | 0/84 (0%) |
| # events | | | | |
| Generalised oedema † [A] | | | | |
| # participants affected/at risk | 1/114 (0.88%) | 0/111 (0%) | 0/76 (0%) | 0/84 (0%) |
| # events | | | | |
| Sudden cardiac death † [A] | | | | |
| # participants affected/at risk | 1/114 (0.88%) | 0/111 (0%) | 0/76 (0%) | 0/84 (0%) |
| # events | | | | |
| Infections and infestations | | | | |
| Enteritis infectious † [A] | | | | |

| | Rosiglitazone: DB | Metformin: DB | Rosiglitazone: MET OL | Metformin: MET OL |
|---|---|---|---|---|
| # participants affected/at risk | 0/114 (0%) | 1/111 (0.9%) | 0/76 (0%) | 0/84 (0%) |
| # events | | | | |
| Escherichia infection † [A] | | | | |
| # participants affected/at risk | 1/114 (0.88%) | 0/111 (0%) | 0/76 (0%) | 0/84 (0%) |
| # events | | | | |
| Pyelonephritis † [A] | | | | |
| # participants affected/at risk | 1/114 (0.88%) | 0/111 (0%) | 0/76 (0%) | 0/84 (0%) |
| # events | | | | |
| Urinary tract infection † [A] | | | | |
| # participants affected/at risk | 1/114 (0.88%) | 1/111 (0.9%) | 0/76 (0%) | 0/84 (0%) |
| # events | | | | |
| Injury, poisoning and procedural complications | | | | |
| Wrist fracture † [A] | | | | |
| # participants affected/at risk | 0/114 (0%) | 1/111 (0.9%) | 0/76 (0%) | 0/84 (0%) |
| # events | | | | |
| Investigations | | | | |
| Alanine aminotransferase | | | | |

| | Rosiglitazone: DB | Metformin: DB | Rosiglitazone: MET OL | Metformin: MET OL |
|---|---|---|---|---|
| increased † [A] | | | | |
| # participants affected/at risk | 0/114 (0%) | 1/111 (0.9%) | 0/76 (0%) | 0/84 (0%) |
| # events | | | | |
| Nervous system disorders | | | | |
| Cerebral infarction † [A] | | | | |
| # participants affected/at risk | 0/114 (0%) | 1/111 (0.9%) | 0/76 (0%) | 0/84 (0%) |
| # events | | | | |
| Presyncope † [A] | | | | |
| # participants affected/at risk | 1/114 (0.88%) | 0/111 (0%) | 0/76 (0%) | 0/84 (0%) |
| # events | | | | |
| Respiratory, thoracic and mediastinal disorders | | | | |
| Asthma † [A] | | | | |
| # participants affected/at risk | 0/114 (0%) | 1/111 (0.9%) | 0/76 (0%) | 0/84 (0%) |
| # events | | | | |
| Pleural effusion † [A] | | | | |
| # participants affected/at risk | 1/114 (0.88%) | 0/111 (0%) | 0/76 (0%) | 0/84 (0%) |

| | Rosiglitazone: DB | Metformin: DB | Rosiglitazone: MET OL | Metformin: MET OL |
|---|---|---|---|---|
| # events | | | | |
| Vascular disorders | | | | |
| Hypertension † [A] | | | | |
| # participants affected/at risk | 1/114 (0.88%) | 0/111 (0%) | 0/76 (0%) | 0/84 (0%) |
| # events | | | | |

† Indicates events were collected by systematic assessment.

A Term from vocabulary, MedDRA, v13

## Other Adverse Events

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

| | Rosiglitazone: DB | Metformin: DB | Rosiglitazone: MET OL | Metformin: MET OL |
|---|---|---|---|---|
| Total # participants affected/at risk | 47/115 (40.87%) | 45/111 (40.54%) | 12/76 (15.79%) | 8/84 (9.52%) |
| Gastrointestinal disorders | | | | |
| Diarrhoea † [A] | | | | |
| # participants affected/at risk | 3/115 (2.61%) | 15/111 (13.51%) | 6/76 (7.89%) | 1/84 (1.19%) |
| # events | | | | |
| Dyspepsia † [A] | | | | |
| # participants affected/at risk | 2/115 (1.74%) | 6/111 (5.41%) | 0/76 (0%) | 0/84 (0%) |

| | Rosiglitazone: DB | Metformin: DB | Rosiglitazone: MET OL | Metformin: MET OL |
|---|---|---|---|---|
| # events | | | | |
| Nausea † [A] | | | | |
| # participants affected/at risk | 3/115 (2.61%) | 3/111 (2.7%) | 3/76 (3.95%) | 5/84 (5.95%) |
| # events | | | | |
| General disorders | | | | |
| Fatigue † [A] | | | | |
| # participants affected/at risk | 6/115 (5.22%) | 4/111 (3.6%) | 0/76 (0%) | 0/84 (0%) |
| # events | | | | |
| Oedemal peripheral † [A] | | | | |
| # participants affected/at risk | 17/115 (14.78%) | 0/111 (0%) | 0/76 (0%) | 0/84 (0%) |
| # events | | | | |
| Infections and infestations | | | | |
| Influenza † [A] | | | | |
| # participants affected/at risk | 3/115 (2.61%) | 6/111 (5.41%) | 0/76 (0%) | 1/84 (1.19%) |
| # events | | | | |
| Nasopharyngitis † [A] | | | | |
| # participants affected/at risk | 7/115 (6.09%) | 7/111 (6.31%) | 1/76 (1.32%) | 0/84 (0%) |

| | Rosiglitazone: DB | Metformin: DB | Rosiglitazone: MET OL | Metformin: MET OL |
|---|---|---|---|---|
| # events | | | | |
| Investigations | | | | |
| Weight increased † [A] | | | | |
| # participants affected/at risk | 9/115 (7.83%) | 1/111 (0.9%) | 0/76 (0%) | 0/84 (0%) |
| # events | | | | |
| Musculoskeletal and connective tissue disorders | | | | |
| Arthralgia † [A] | | | | |
| # participants affected/at risk | 5/115 (4.35%) | 6/111 (5.41%) | 1/76 (1.32%) | 0/84 (0%) |
| # events | | | | |
| Back pain † [A] | | | | |
| # participants affected/at risk | 6/115 (5.22%) | 5/111 (4.5%) | 1/76 (1.32%) | 0/84 (0%) |
| # events | | | | |
| Nervous system disorders | | | | |
| Headache † [A] | | | | |
| # participants affected/at risk | 9/115 (7.83%) | 5/111 (4.5%) | 1/76 (1.32%) | 1/84 (1.19%) |
| # events | | | | |

| | Rosiglitazone: DB | Metformin: DB | Rosiglitazone: MET OL | Metformin: MET OL |
|---|---|---|---|---|
| Respiratory, thoracic and mediastinal disorders | | | | |
| Cough † [A] | | | | |
| # participants affected/at risk | 6/115 (5.22%) | 1/111 (0.9%) | 1/76 (1.32%) | 1/84 (1.19%) |
| # events | | | | |

† Indicates events were collected by systematic assessment.

A Term from vocabulary, MedDRA, v13

## 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
Organization: GlaxoSmithKline
Phone: 866-435-7343

Email: