Protocol Registration Receipt
08/11/2014

Grantor: CDER IND/IDE Number: 65,177 Serial Number:

Efficacy and Safety of Albiglutide in Treatment of Type 2 Diabetes

This study has been completed.

Sponsor:	GlaxoSmithKline
Collaborators:	
Information provided by (Responsible Party):	GlaxoSmithKline
ClinicalTrials.gov Identifier:	NCT00838903

Purpose

The purpose of this study is to determine if albiglutide is safe and effective in the treatment of type 2 diabetes.

Condition	Intervention	Phase
Diabetes Mellitus, Type 2	Biological/Vaccine: albiglutide Drug: sitagliptin Drug: glimepiride	Phase 3

Condition	Intervention	Phase
	Drug: metformin Biological/Vaccine: placebo albiglutide Drug: placebo sitagliptin Drug: placebo glimepiride	

Study Type: Interventional

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

Official Title: A Randomized, Double-Blind, Placebo and Active-Controlled, Parallel-Group, Multicenter Study to Determine the Efficacy and Safety of Albiglutide When Used in Combination With Metformin Compared With Metformin Plus Sitagliptin, Metformin Plus Glimepiride, and Metformin Plus Placebo in Subjects With Type 2 Diabetes Mellitus

Further study details as provided by GlaxoSmithKline:

Primary Outcome Measure:

- Change From Baseline (BL) in Glycosylated Hemoglobin (HbA1c) at Week 104 [Time Frame: Baseline and Week 104] [Designated as safety issue: No]
  HbA1c is a form of hemoglobin that is measured primarily to identify the average plasma glucose concentration over a 2- to 3-month period. The BL HbA1c value is defined as the last non-missing value before the start of treatment. Change from BL was calculated as the value at Week 104 minus the value at BL. Based on analysis of covariance (ANCOVA): change = treatment + BL HbA1c + prior myocardial infarction history + age category + region. Difference of least squares means (albiglutide - placebo, albiglutide - sitagliptin, albiglutide - glimepiride) is from the ANCOVA model. The last observation carried forward (LOCF) method was used to impute missing post-Baseline HbA1c values; the last non-missing post-BL on-treatment measurement was used to impute the missing measurement. HbA1c values obtained after hyperglycemic rescue were treated as missing and were replaced with pre-rescue values.

Secondary Outcome Measures:

- Change From Baseline in HbA1c at Week 156 [Time Frame: Baseline and Week 156] [Designated as safety issue: No]
  HbA1c is a form of hemoglobin that is measured primarily to identify the average plasma glucose concentration over a 2- to 3-month period. Baseline HbA1c value is defined as the last non-missing value before the start of treatment. Change from Baseline was calculated as the post-Baseline value minus the Baseline value. This analysis used observed HbA1c values, excluding those obtained after hyperglycemia rescue; no missing data imputation was performed .
- Change From Baseline in Fasting Plasma Glucose (FPG) at Week 104 [Time Frame: Baseline and Week 104] [Designated as safety issue: No]
  The FPG test measures blood sugar levels after the participant has not eaten (fasted) for 12 to 14 hours. The Baseline FPG value is the last non-missing value before the start of treatment. The LOCF method was used to impute missing post-Baseline FPG values. FPG values obtained after hyperglycemia rescue were treated as missing and replaced with pre-rescue values. Change from Baseline was calculated as the post-Baseline value minus the Baseline value. Based on ANCOVA: change = treatment + Baseline FPG + Baseline HbA1c category + prior myocardial infarction history + age category

+ region.

- Change From Baseline in FPG at Week 156 [Time Frame: Baseline and Week 156] [Designated as safety issue: No]

  The FPG test measures blood sugar levels after the participant has not eaten (fasted) for 12 to 14 hours. The Baseline FPG value is the last non-missing value before the start of treatment. Change from Baseline was calculated as the post-Baseline value minus the Baseline value. This analysis used observed FPG values excluding those obtained after hyperglycemia rescue; no missing data imputation was performed.

- Number of Participants Who Achieved Clinically Meaningful HbA1c Response Levels of <6.5%, <7%, and <7.5% at Week 104 [Time Frame: Week 104] [Designated as safety issue: No]

  The number of participants who achieved the HbA1c treatment goal (i.e., HbA1c response levels of <6.5%, <7%, and <7.5% at Week 52) were assessed.

- Number of Participants Who Achieved Clinically Meaningful HbA1c Response Levels of <6.5%, <7%, and <7.5% at Week 156 [Time Frame: Week 156] [Designated as safety issue: No]

  The number of participants who achieved the HbA1c treatment goal (i.e., HbA1c response levels of <6.5%, <7%, and <7.5% at Week 156) were assessed.

- Time to Hyperglycemia Rescue [Time Frame: From the start of study medication until the end of the treatment (up to Week 156)] [Designated as safety issue: No]

  Participants who experienced persistent hyperglycemia (high blood glucose) could have qualified for hyperglycemia rescue.The conditions for hyperglycemic rescue were as follows: FPG >=280 milligrams/deciliter (mg/dL) between >=Week 2 and <Week 4; FPG >=250 mg/dL between >=Week 4 and <Week 12; HbA1c >=8.5% and a <=0.5% reduction from Baseline between >=Week 12 and <Week 24; HbA1c >=8.5% between >=Week 24 and <Week 48; HbA1c >=8.0% between >= Week 48 and <Week 156. Participants could have been rescued at any time on or after Week 2. Time to hyperglycemia rescue is defined as the time between the date of the first dose of study medication and the date of hyperglycemia rescue plus 1 day, or the time between the date of the first dose of study medication and the date of the last visit during the active treatment period plus 1 day for participants not requiring rescue. This time was divided by 7 to express the result in week

- Change From Baseline in Body Weight at Week 104 [Time Frame: Baseline and Week 104] [Designated as safety issue: No]

  The Baseline value is the last non-missing value before the start of treatment. Change from Baseline was calculated as the post-Baseline weight minus the Baseline weight. The LOCF method was used to impute missing post-Baseline weight values. Weight values obtained after hyperglycemia rescue were treated as missing and replaced with prerescue values. Based on ANCOVA: change = treatment + Baseline weight + Baseline HbA1c category + prior myocardial infarction history + age category + region.

- Change From Baseline in Body Weight at Week 156 [Time Frame: Baseline and Week 156] [Designated as safety issue: No]

  The Baseline value is the last non-missing value before the start of treatment. Change from Baseline was calculated as the post-Baseline weight minus the Baseline weight. This analysis used observed body weight values excluding those obtained after hyperglycemia rescue; no missing data imputation was performed.

Enrollment: 1049
Study Start Date: February 2009
Study Completion Date: March 2013
Primary Completion Date: January 2012

Arms	Assigned Interventions
Experimental: albiglutide + metformin Albiglutide + metformin + placebo sitagliptin + placebo glimepiride	Biological/Vaccine: albiglutide albiglutide Drug: metformin Metformin Drug: placebo sitagliptin placebo to match sitagliptin Drug: placebo glimepiride placebo to match glimepiride
Active Comparator: sitagliptin + metformin Sitagliptin + metformin + placebo albiglutide + placebo glimepiride	Drug: sitagliptin sitagliptin Drug: metformin Metformin Biological/Vaccine: placebo albiglutide placebo to match albiglutide Drug: placebo glimepiride placebo to match glimepiride
Active Comparator: glimepiride + metformin Glimepiride + metformin + placebo albiglutide + placebo sitagliptin	Drug: glimepiride Glimepiride Drug: metformin Metformin Biological/Vaccine: placebo albiglutide placebo to match albiglutide Drug: placebo sitagliptin placebo to match sitagliptin
Active Comparator: metformin + placebo	Drug: metformin

Arms	Assigned Interventions
Metformin + placebo albiglutide + placebo sitagliptin + placebo glimepiride	Metformin Biological/Vaccine: placebo albiglutide placebo to match albiglutide Drug: placebo sitagliptin placebo to match sitagliptin Drug: placebo glimepiride placebo to match glimepiride

Eligibility

Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Both

Inclusion Criteria:

- type 2 diabetes
- BMI 20-45kg/m2 inclusive

Exclusion Criteria:

- females who are pregnant, lactating or <6 weeks post-partum
- current symptomatic heart failure (NYHA Class III or IV)

Contacts and Locations

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GSK Investigational Site
Houston, Texas, United States, 77055
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GSK Investigational Site
Houston, Texas, United States, 77074
GSK Investigational Site
Houston, Texas, United States, 77058
GSK Investigational Site
Houston, Texas, United States, 77036
GSK Investigational Site
Houston, Texas, United States, 77070
GSK Investigational Site
Houston, Texas, United States, 77094
GSK Investigational Site

Houston, Texas, United States, 77069

GSK Investigational Site

Houston, Texas, United States, 77074

GSK Investigational Site

Houston, Texas, United States, 77030

GSK Investigational Site

Hurst, Texas, United States, 76054

GSK Investigational Site

Katy, Texas, United States, 77450

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Katy, Texas, United States, 77450

GSK Investigational Site

Lake Jackson, Texas, United States, 77566

GSK Investigational Site

Lewisville, Texas, United States, 75067

GSK Investigational Site

Midland, Texas, United States, 79707

GSK Investigational Site

North Richland Hills, Texas, United States, 76180

GSK Investigational Site

Odessa, Texas, United States, 79761

GSK Investigational Site

San Antonio, Texas, United States, 78218

GSK Investigational Site

San Antonio, Texas, United States, 78229

GSK Investigational Site

San Antonio, Texas, United States, 78224

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San Antonio, Texas, United States, 78258

GSK Investigational Site

San Antonio, Texas, United States, 78229

GSK Investigational Site

San Antonio, Texas, United States, 78205

GSK Investigational Site

San Antonio, Texas, United States, 78215

GSK Investigational Site
San Antonio, Texas, United States, 78237
GSK Investigational Site
San Antonio, Texas, United States, 78217
GSK Investigational Site
San Antonio, Texas, United States, 78258
GSK Investigational Site
Schertz, Texas, United States, 78154
GSK Investigational Site
Sugar Land, Texas, United States, 77479
GSK Investigational Site
Sugarland, Texas, United States, 77479
GSK Investigational Site
Temple, Texas, United States, 76508

United States, Utah

GSK Investigational Site
Bountiful, Utah, United States, 84010
GSK Investigational Site
Orem, Utah, United States, 84058
GSK Investigational Site
Salt Lake City, Utah, United States, 84102
GSK Investigational Site
Salt Lake City, Utah, United States, 84107
GSK Investigational Site
Salt Lake City, Utah, United States, 84124
GSK Investigational Site
West Jordan, Utah, United States, 84088
GSK Investigational Site
West Valley City, Utah, United States, 84120
GSK Investigational Site
West Valley City, Utah, United States, 84120

United States, Vermont

GSK Investigational Site
South Burlington, Vermont, United States, 05403

United States, Virginia

GSK Investigational Site

Burke, Virginia, United States, 22015

GSK Investigational Site

Hampton, Virginia, United States, 23666

GSK Investigational Site

Manassas, Virginia, United States, 20110

GSK Investigational Site

Norfolk, Virginia, United States, 23502

GSK Investigational Site

Suffolk, Virginia, United States

GSK Investigational Site

Virgina Beach, Virginia, United States, 23455

GSK Investigational Site

Weber City, Virginia, United States, 24290

United States, Washington

GSK Investigational Site

Federal Way, Washington, United States, 98003

GSK Investigational Site

Richland, Washington, United States, 99352

GSK Investigational Site

Selah, Washington, United States, 98942

GSK Investigational Site

Spokane, Washington, United States, 99216

GSK Investigational Site

Spokane, Washington, United States, 99208

United States, West Virginia

GSK Investigational Site

Lewisburg, West Virginia, United States, 24901

United States, Wisconsin

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Milwaukee, Wisconsin, United States, 53226

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Alabaster, Albania, 35007

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Villingen-Schwenningen, Baden-Wuerttemberg, Germany, 78054

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Berlin, Berlin, Germany, 10115

GSK Investigational Site

Kelkheim, Hessen, Germany, 65779

GSK Investigational Site

Rotenburg, Hessen, Germany, 36199

GSK Investigational Site

Bad Lauterberg, Niedersachsen, Germany, 37431

GSK Investigational Site

Witten, Nordrhein-Westfalen, Germany, 58455

GSK Investigational Site

Mainz, Rheinland-Pfalz, Germany, 55116

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GSK Investigational Site

Kwun Tong, Kowloon, Hong Kong

GSK Investigational Site

Shatin, Hong Kong

GSK Investigational Site

Tai Po,, Hong Kong

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GSK Investigational Site

Distrito Federal, Mexico, 06700

GSK Investigational Site

Guadalajara, Mexico, 44600

GSK Investigational Site

Guadalajara, Mexico, 44680

GSK Investigational Site

Mexico City, Mexico, 11570

GSK Investigational Site

Mexico City, Mexico, 03300

GSK Investigational Site

Nezahualcoyotl, Mexico, 57170

GSK Investigational Site

Tijuana, Baja California Norte, Mexico, 22010

GSK Investigational Site

Torreon, Coahuila, Mexico, 27000

GSK Investigational Site

Durango, Durango, Mexico, 34080

GSK Investigational Site

Pachuca, Hidalgo, Mexico, 42086

GSK Investigational Site

Guadalajara, Jalisco, Mexico, 44670

GSK Investigational Site

Zapopan, Jalisco, Mexico, 45200

GSK Investigational Site

Morelia, Michoacán, Mexico, C.P. 58249

GSK Investigational Site

Cuernavaca, Morelos, Mexico, 62250

GSK Investigational Site

Puebla, Puebla, Mexico, 72190

GSK Investigational Site

Merida, Yucatán, Mexico, 97000

Peru

GSK Investigational Site

Ica, Ica, Peru, 11

GSK Investigational Site

Callao, Lima, Peru, Callao 2

GSK Investigational Site

Lima, Lima, Peru, 01

GSK Investigational Site

Lima, Lima, Peru, Lima 1

GSK Investigational Site

Lima, Lima, Peru, 01

GSK Investigational Site

Piura, Piura, Peru

Philippines

GSK Investigational Site

Cebu City, Philippines, 6000

GSK Investigational Site

Quezon City, Philippines, 1101

GSK Investigational Site

Quezon City, Philippines, 1102

GSK Investigational Site

San Juan, Philippines, 1500

GSK Investigational Site

Taytay Rizal, Philippines, 1920

Russian Federation

GSK Investigational Site

Arkhangelsk, Russian Federation, 163045

GSK Investigational Site

Irkutsk, Russian Federation, 664003

GSK Investigational Site

Moscow, Russian Federation, 119034

GSK Investigational Site

Nizhniy Novgorod, Russian Federation, 603126

GSK Investigational Site

Saratov, Russian Federation, 410030

GSK Investigational Site

Smolensk, Russian Federation, 214019

GSK Investigational Site

Yaroslavl, Russian Federation, 150062

South Africa

GSK Investigational Site

Cape Town, South Africa, 7530

GSK Investigational Site

Cape Town, South Africa, 7530

GSK Investigational Site

Kempton Park, South Africa, 1619

GSK Investigational Site

Parow, South Africa, 7505

GSK Investigational Site

Somerset West, South Africa, 07129

GSK Investigational Site

Soweto, South Africa, 1111

GSK Investigational Site

Port Elizabeth, Eastern Cape, South Africa, 6014

GSK Investigational Site

Boksburg North, Gauteng, South Africa, 1459

GSK Investigational Site

Johannesburg, Gauteng, South Africa, 01820

GSK Investigational Site

Lenasia, Gauteng, South Africa, 1827

GSK Investigational Site

Parktown, Gauteng, South Africa, 2193

GSK Investigational Site

Pretoria, Gauteng, South Africa, 00083

GSK Investigational Site

Durban, KwaZulu- Natal, South Africa, 4000

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Sevilla, Spain, 41003

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GSK Investigational Site

Hull, United Kingdom, HU3 2RW

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Liverpool, United Kingdom, L9 7AL

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GSK Investigational Site
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GSK Investigational Site
Port Glasgow, Renfrewshire, United Kingdom, PA14 6HW
GSK Investigational Site
Coventry, West Midlands, United Kingdom, CV2 2DX

Investigators

Study Director:	GSK Clinical Trials	GlaxoSmithKline

More Information

Responsible Party: GlaxoSmithKline
Study ID Numbers: 112753
Health Authority: United States: Food and Drug Administration

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Study Results

Participant Flow

Pre-Assignment Details

Eligible participants (par.) entered a 2-week Screening Period, a 4-week Run-in/Stabilization Period, a 156-week Treatment Period, and a 8-week post-treatment Follow-up Period. A total of 1525 par. were screened, 1049 were randomized and 1012 par. received at least 1 dose of study treatment.

Reporting Groups

	Description
Placebo Plus Metformin	Participants received metformin >=1500 milligrams (mg) daily plus

	Description
	matching albiglutide placebo as a subcutaneous injection weekly via a fully disposable pen injector system plus matching sitagliptin placebo plus matching glimepiride placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.
Sitagliptin 100 mg Plus Metformin	Participants received sitagliptin 100 mg daily plus metformin >=1500 mg daily plus matching albiglutide placebo as a subcutaneous injection weekly via a fully disposable pen injector system plus matching glimepiride placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.
Glimepiride 2 mg Plus Metformin	Participants received glimepiride 2 mg daily (with masked up-titration to 4 mg daily if required) plus metformin >=1500 mg daily plus matching albiglutide placebo as a subcutaneous injection weekly via a fully disposable pen injector system plus matching sitagliptin placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.
Albiglutide 30 mg Plus Metformin	Participants received albiglutide 30 mg weekly (with masked up-titration to 50 mg weekly if required) as a subcutaneous injection via a fully disposable pen injector system plus metformin >=1500 mg daily plus matching sitagliptin placebo plus matching glimepiride placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.

Treatment Period (156 Weeks)

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
Started	101	302	307	302
Missing Active Treatment	1	0	0	0

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
Status				
Completed	55	190	191	192
Not Completed	46	112	116	110
Adverse Event	5	13	17	25
Protocol Violation	1	6	6	5
Noncompliance	9	13	12	6
Severe or Repeated Hypoglycaemia	0	0	1	0
Lost to Follow-up	4	16	15	13
Withdrawal by Subject	20	55	56	53
Physician Decision	1	2	1	2
Termination of Study/Site by GSK	3	5	5	4
Patient and PI Decision to Discontinue	0	1	0	0
Poor Glycemic Control	0	0	0	1
Poor Therapeutic Response	1	0	0	0
Pregnancy	0	0	1	0
PI Decided for Safety Purpose	0	0	1	0
Site closed	0	0	1	0

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
Site Closed and Subject Withdrew Consent	1	0	0	0
Subject Migrated to Other Country	0	1	0	1
Missing Active Treatment Status	1	0	0	0

Follow-up Period (8 Weeks)

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
Started	101 [1]	302 [2]	307 [3]	302 [4]
Completed	75	237	243	244
Not Completed	26	65	64	58
Adverse Event	0	0	3	1
Noncompliance	2	8	5	5
Lost to Follow-up	6	28	22	24
Did Not Enter Follow-up Period	5	7	12	7
Subject Withdrawn from Follow-up	8	13	14	14
Physician Decision	1	1	1	1
Termination of Study/Site by GSK	3	4	6	4

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
ICF Withdrawn	0	1	0	0
Investigator Stopped Study at Site	0	1	0	0
Subject Moved out of Town	0	0	0	1
Missing	1	2	1	1

[1] Participants withdrawing from the Treatment Period entered the Follow-up Period.

[2] Participants withdrawing from the Treatment Period entered the Follow-up Period.

[3] Participants withdrawing from the Treatment Period entered the Follow-up Period.

[4] Participants withdrawing from the Treatment Period entered the Follow-up Period.

Baseline Characteristics

Reporting Groups

	Description
Placebo Plus Metformin	Participants received metformin >=1500 milligrams (mg) daily plus matching albiglutide placebo as a subcutaneous injection weekly via a fully disposable pen injector system plus matching sitagliptin placebo plus matching glimepiride placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.
Sitagliptin 100 mg Plus Metformin	Participants received sitagliptin 100 mg daily plus metformin >=1500 mg daily plus matching albiglutide placebo as a subcutaneous injection weekly via a fully disposable pen injector system plus matching glimepiride placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.

	Description
Glimepiride 2 mg Plus Metformin	Participants received glimepiride 2 mg daily (with masked up-titration to 4 mg daily if required) plus metformin >=1500 mg daily plus matching albiglutide placebo as a subcutaneous injection weekly via a fully disposable pen injector system plus matching sitagliptin placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.
Albiglutide 30 mg Plus Metformin	Participants received albiglutide 30 mg weekly (with masked up-titration to 50 mg weekly if required) as a subcutaneous injection via a fully disposable pen injector system plus metformin >=1500 mg daily plus matching sitagliptin placebo plus matching glimepiride placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.

Baseline Measures

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin	Total
Number of Participants	101	302	307	302	1012
Age, Continuous [units: Years] Mean (Standard Deviation)	56.1 (10.01)	54.3 (9.81)	54.4 (9.97)	54.3 (10.12)	54.5 (9.97)
Gender, Male/Female [units: Participants]					
Female	51	163	149	167	530
Male	50	139	158	135	482
Race/Ethnicity, Customized [1] [units: Participants]					
African American/African	23	35	39	53	150

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin	Total
Heritage					
American Indian or Alaskan Native	9	22	25	17	73
Asian - Central/South Asian Heritage	1	7	3	2	13
Asian - East Asian Heritage	0	2	3	5	10
Asian - Japanese Heritage	1	0	1	0	2
Asian - South East Asian Heritage	3	11	9	11	34
Native Hawaiian or Other Pacific Islander	1	0	0	1	2
White - Arabic/North African Heritage	0	1	9	3	13
White - White/Caucasian/European Heritage	64	225	220	214	723

[1] A participant may have been counted in more than one category.

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Change From Baseline (BL) in Glycosylated Hemoglobin (HbA1c) at Week 104

Measure Description	HbA1c is a form of hemoglobin that is measured primarily to identify the average plasma glucose concentration over a 2- to 3-month period. The BL HbA1c value is defined as the last non-missing value before the start of treatment. Change from BL was calculated as the value at Week 104 minus the value at BL. Based on analysis of covariance (ANCOVA): change = treatment + BL HbA1c + prior myocardial infarction history + age category + region. Difference of least squares means (albiglutide – placebo, albiglutide – sitagliptin, albiglutide - glimepiride) is from the ANCOVA model. The last observation carried forward (LOCF) method was used to impute missing post-Baseline HbA1c values; the last non-missing post-BL on-treatment measurement was used to impute the missing measurement. HbA1c values obtained after hyperglycemic rescue were treated as missing and were replaced with pre-rescue values.
Time Frame	Baseline and Week 104
Safety Issue?	No

Analysis Population Description

Intent-to-Treat (ITT) Population with LOCF: all randomized par. who received >=1 dose of study medication and who had a BL assessment and >=1 post-BL assessment of HbA1c. Only par. with a value at BL and at the specified visit were analyzed. Values were carried forward for par. who were rescued or discontinued from active treatment before Week 104.

Reporting Groups

	Description
Placebo Plus Metformin	Participants received metformin >=1500 milligrams (mg) daily plus matching albiglutide placebo as a subcutaneous injection weekly via a fully disposable pen injector system plus matching sitagliptin placebo plus matching glimepiride placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.
Sitagliptin 100 mg Plus Metformin	Participants received sitagliptin 100 mg daily plus metformin >=1500 mg daily plus matching albiglutide placebo as a subcutaneous injection

	Description
	weekly via a fully disposable pen injector system plus matching glimepiride placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.
Glimepiride 2 mg Plus Metformin	Participants received glimepiride 2 mg daily (with masked up-titration to 4 mg daily if required) plus metformin >=1500 mg daily plus matching albiglutide placebo as a subcutaneous injection weekly via a fully disposable pen injector system plus matching sitagliptin placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.
Albiglutide 30 mg Plus Metformin	Participants received albiglutide 30 mg weekly (with masked up-titration to 50 mg weekly if required) as a subcutaneous injection via a fully disposable pen injector system plus metformin >=1500 mg daily plus matching sitagliptin placebo plus matching glimepiride placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.

Measured Values

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
Number of Participants Analyzed	97	297	299	293
Change From Baseline (BL) in Glycosylated Hemoglobin (HbA1c) at Week 104 [units: Percentage of HbA1c in the blood] Least Squares Mean (Standard Error)	0.27 (0.113)	-0.28 (0.065)	-0.36 (0.064)	-0.63 (0.065)

Statistical Analysis 1 for Change From Baseline (BL) in Glycosylated Hemoglobin (HbA1c) at Week 104

Groups	Placebo Plus Metformin, Albiglutide 30 mg Plus Metformin

Method	ANCOVA
Mean Difference (Net)	-0.91
95% Confidence Interval	-1.16 to -0.65

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

[Not specified.]

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

[Not specified.]

Statistical Analysis 2 for Change From Baseline (BL) in Glycosylated Hemoglobin (HbA1c) at Week 104

Groups	Sitagliptin 100 mg Plus Metformin, Albiglutide 30 mg Plus Metformin
Method	ANCOVA
Mean Difference (Net)	-0.35
95% Confidence Interval	-0.53 to -0.17

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

[Not specified.]

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

[Not specified.]

Statistical Analysis 3 for Change From Baseline (BL) in Glycosylated Hemoglobin (HbA1c) at Week 104

Groups	Glimepiride 2 mg Plus Metformin, Albiglutide 30 mg Plus Metformin
Method	ANCOVA
Mean Difference (Net)	-0.27
95% Confidence Interval	-0.45 to -0.09

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

[Not specified.]

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

[Not specified.]

Statistical Analysis 4 for Change From Baseline (BL) in Glycosylated Hemoglobin (HbA1c) at Week 104

Groups	Placebo Plus Metformin, Albiglutide 30 mg Plus Metformin
Method	t-test, 2 sided
P-Value	<0.0001

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

[Not specified.]

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

The p-value is for superiority testing of albiglutide over placebo at 0.05 level.

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

The p-value is from a two-sided t-test to test whether the difference of least square means (albiglutide – placebo) is equal to zero

Statistical Analysis 5 for Change From Baseline (BL) in Glycosylated Hemoglobin (HbA1c) at Week 104

Groups	Sitagliptin 100 mg Plus Metformin, Albiglutide 30 mg Plus Metformin
Non-Inferiority/Equivalence Test	Yes
Method	t-test, 1 sided
P-Value	<0.0001

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

[Not specified.]

To test whether the difference of least square means (albiglutide - sitagliptin) is equal to the pre-specified non-inferiority margin of

0.3%.

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

The p-value is for non-inferiority testing of albiglutide versus sitagliptin at 0.0125 level.

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

[Not specified.]

Statistical Analysis 6 for Change From Baseline (BL) in Glycosylated Hemoglobin (HbA1c) at Week 104

Groups	Glimepiride 2 mg Plus Metformin, Albiglutide 30 mg Plus Metformin
Non-Inferiority/Equivalence Test	Yes
Method	t-test, 1 sided
P-Value	<0.0001

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

[Not specified.]

To test whether the difference of least square means (albiglutide - glimepiride) is equal to the pre-specified non-inferiority margin of 0.3%.

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

The p-value is for non-inferiority testing of albiglutide versus glimepiride at 0.0125 level.

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

[Not specified.]

Statistical Analysis 7 for Change From Baseline (BL) in Glycosylated Hemoglobin (HbA1c) at Week 104

Groups	Sitagliptin 100 mg Plus Metformin, Albiglutide 30 mg Plus Metformin
Method	t-test, 2 sided

P-Value	0.0001

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

[Not specified.]

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

The p-value is for superiority testing of albiglutide versus sitagliptin at 0.025 level.

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

The p-value is from a two-sided t-test to test whether the difference of least square means (albiglutide – sitagliptin) is equal to zero.

Statistical Analysis 8 for Change From Baseline (BL) in Glycosylated Hemoglobin (HbA1c) at Week 104

Groups	Glimepiride 2 mg Plus Metformin, Albiglutide 30 mg Plus Metformin
Method	t-test, 2 sided
P-Value	0.0033

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

[Not specified.]

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

The p-value is for superiority testing of albiglutide versus glimepiride at 0.025 level.

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

The p-value is from a two-sided t-test to test whether the difference of least square means (albiglutide - glimepiride) is equal to zero.

2. Secondary Outcome Measure:

Measure Title	Change From Baseline in HbA1c at Week 156
Measure Description	HbA1c is a form of hemoglobin that is measured primarily to identify the average plasma glucose concentration over a 2- to 3-month period. Baseline HbA1c value is defined as the last non-missing value before the start of treatment. Change from Baseline was calculated as the post-Baseline value minus the Baseline value. This analysis used observed HbA1c values, excluding those obtained after hyperglycemia rescue; no missing data imputation was performed .
Time Frame	Baseline and Week 156
Safety Issue?	No

Analysis Population Description

Intent-to-Treat (ITT) Population with observed values. Only those par. with a value at Baseline and at the specified visit were analyzed.

Reporting Groups

	Description
Placebo Plus Metformin	Participants received metformin >=1500 milligrams (mg) daily plus matching albiglutide placebo as a subcutaneous injection weekly via a fully disposable pen injector system plus matching sitagliptin placebo plus matching glimepiride placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.
Sitagliptin 100 mg Plus Metformin	Participants received sitagliptin 100 mg daily plus metformin >=1500 mg daily plus matching albiglutide placebo as a subcutaneous injection weekly via a fully disposable pen injector system plus matching glimepiride placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.
Glimepiride 2 mg Plus Metformin	Participants received glimepiride 2 mg daily (with masked up-titration to 4 mg daily if required) plus metformin >=1500 mg daily plus matching albiglutide placebo as a subcutaneous injection weekly via a fully disposable pen injector system plus matching sitagliptin placebo from

	Description
	Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.
Albiglutide 30 mg Plus Metformin	Participants received albiglutide 30 mg weekly (with masked up-titration to 50 mg weekly if required) as a subcutaneous injection via a fully disposable pen injector system plus metformin >=1500 mg daily plus matching sitagliptin placebo plus matching glimepiride placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.

Measured Values

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
Number of Participants Analyzed	16	88	102	115
Change From Baseline in HbA1c at Week 156 [units: Percentage of HbA1c in the blood] Mean (Standard Deviation)	-0.46 (0.820)	-0.56 (1.160)	-0.59 (0.999)	-0.88 (0.959)

3. Secondary Outcome Measure:

Measure Title	Change From Baseline in Fasting Plasma Glucose (FPG) at Week 104
Measure Description	The FPG test measures blood sugar levels after the participant has not eaten (fasted) for 12 to 14 hours. The Baseline FPG value is the last non-missing value before the start of treatment. The LOCF method was used to impute missing post-Baseline FPG values. FPG values obtained after hyperglycemia rescue were treated as missing and replaced with pre-rescue values. Change from Baseline was calculated

	as the post-Baseline value minus the Baseline value. Based on ANCOVA: change = treatment + Baseline FPG + Baseline HbA1c category + prior myocardial infarction history + age category + region.
Time Frame	Baseline and Week 104
Safety Issue?	No

Analysis Population Description

Intent-to-Treat (ITT) Population with LOCF. Only those participants with a value at Baseline and at the specified visit were analyzed. Values were carried forward for participants who were rescued or discontinued from active treatment before Week 104.

Reporting Groups

	Description
Placebo Plus Metformin	Participants received metformin >=1500 milligrams (mg) daily plus matching albiglutide placebo as a subcutaneous injection weekly via a fully disposable pen injector system plus matching sitagliptin placebo plus matching glimepiride placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.
Sitagliptin 100 mg Plus Metformin	Participants received sitagliptin 100 mg daily plus metformin >=1500 mg daily plus matching albiglutide placebo as a subcutaneous injection weekly via a fully disposable pen injector system plus matching glimepiride placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.
Glimepiride 2 mg Plus Metformin	Participants received glimepiride 2 mg daily (with masked up-titration to 4 mg daily if required) plus metformin >=1500 mg daily plus matching albiglutide placebo as a subcutaneous injection weekly via a fully disposable pen injector system plus matching sitagliptin placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.
Albiglutide 30 mg Plus	Participants received albiglutide 30 mg weekly (with masked

	Description
Metformin	up-titration to 50 mg weekly if required) as a subcutaneous injection via a fully disposable pen injector system plus metformin >=1500 mg daily plus matching sitagliptin placebo plus matching glimepiride placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.

Measured Values

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
Number of Participants Analyzed	100	299	302	296
Change From Baseline in Fasting Plasma Glucose (FPG) at Week 104 [units: Millimoles per liter (mmol/L)] Least Squares Mean (Standard Error)	0.55 (0.277)	-0.12 (0.160)	-0.41 (0.159)	-0.98 (0.161)

4. Secondary Outcome Measure:

Measure Title	Change From Baseline in FPG at Week 156
Measure Description	The FPG test measures blood sugar levels after the participant has not eaten (fasted) for 12 to 14 hours. The Baseline FPG value is the last non-missing value before the start of treatment. Change from Baseline was calculated as the post-Baseline value minus the Baseline value. This analysis used observed FPG values excluding those obtained after hyperglycemia rescue; no missing data imputation was performed.
Time Frame	Baseline and Week 156
Safety Issue?	No

Analysis Population Description

ITT Population with observed values. Only those participants with a value at Baseline and at the specified visit were analyzed.

Reporting Groups

	Description
Placebo Plus Metformin	Participants received metformin >=1500 milligrams (mg) daily plus matching albiglutide placebo as a subcutaneous injection weekly via a fully disposable pen injector system plus matching sitagliptin placebo plus matching glimepiride placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.
Sitagliptin 100 mg Plus Metformin	Participants received sitagliptin 100 mg daily plus metformin >=1500 mg daily plus matching albiglutide placebo as a subcutaneous injection weekly via a fully disposable pen injector system plus matching glimepiride placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.
Glimepiride 2 mg Plus Metformin	Participants received glimepiride 2 mg daily (with masked up-titration to 4 mg daily if required) plus metformin >=1500 mg daily plus matching albiglutide placebo as a subcutaneous injection weekly via a fully disposable pen injector system plus matching sitagliptin placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.
Albiglutide 30 mg Plus Metformin	Participants received albiglutide 30 mg weekly (with masked up-titration to 50 mg weekly if required) as a subcutaneous injection via a fully disposable pen injector system plus metformin >=1500 mg daily plus matching sitagliptin placebo plus matching glimepiride placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.

Measured Values

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
Number of Participants Analyzed	16	88	98	112
Change From Baseline in FPG at Week 156 [units: Millimoles per liter (mmol/L)] Mean (Standard Deviation)	-0.11 (1.498)	-0.50 (2.519)	-0.71 (2.684)	-1.30 (2.602)

5. Secondary Outcome Measure:

Measure Title	Number of Participants Who Achieved Clinically Meaningful HbA1c Response Levels of <6.5%, <7%, and <7.5% at Week 104
Measure Description	The number of participants who achieved the HbA1c treatment goal (i.e., HbA1c response levels of <6.5%, <7%, and <7.5% at Week 52) were assessed.
Time Frame	Week 104
Safety Issue?	No

Analysis Population Description

ITT Population with LOCF. Only those participants with a value at Baseline and at the specified visit were analyzed. Values were carried forward for participants who were rescued or discontinued from active treatment before Week 104.

Reporting Groups

	Description
Placebo Plus Metformin	Participants received metformin >=1500 milligrams (mg) daily plus matching albiglutide placebo as a subcutaneous injection weekly via a fully disposable pen injector system plus matching sitagliptin placebo plus matching glimepiride placebo from Week 1 to Week 156. All

	Description
	participants returned for the 8-week post-treatment Follow-up Period.
Sitagliptin 100 mg Plus Metformin	Participants received sitagliptin 100 mg daily plus metformin >=1500 mg daily plus matching albiglutide placebo as a subcutaneous injection weekly via a fully disposable pen injector system plus matching glimepiride placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.
Glimepiride 2 mg Plus Metformin	Participants received glimepiride 2 mg daily (with masked up-titration to 4 mg daily if required) plus metformin >=1500 mg daily plus matching albiglutide placebo as a subcutaneous injection weekly via a fully disposable pen injector system plus matching sitagliptin placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.
Albiglutide 30 mg Plus Metformin	Participants received albiglutide 30 mg weekly (with masked up-titration to 50 mg weekly if required) as a subcutaneous injection via a fully disposable pen injector system plus metformin >=1500 mg daily plus matching sitagliptin placebo plus matching glimepiride placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.

Measured Values

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
Number of Participants Analyzed	97	297	299	293
Number of Participants Who Achieved Clinically Meaningful HbA1c Response Levels of <6.5%, <7%, and <7.5% at Week 104				

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
[units: Participants]				
HbA1c <6.5%	7	45	40	50
HbA1c <7.0%	15	94	94	113
HbA1c <7.5%	27	132	147	172

6. Secondary Outcome Measure:

Measure Title	Number of Participants Who Achieved Clinically Meaningful HbA1c Response Levels of <6.5%, <7%, and <7.5% at Week 156
Measure Description	The number of participants who achieved the HbA1c treatment goal (i.e., HbA1c response levels of <6.5%, <7%, and <7.5% at Week 156) were assessed.
Time Frame	Week 156
Safety Issue?	No

Analysis Population Description

ITT Population with observed values. Only those participants with a value at Baseline and at the specified visit were analyzed.

Reporting Groups

	Description
Placebo Plus Metformin	Participants received metformin >=1500 milligrams (mg) daily plus matching albiglutide placebo as a subcutaneous injection weekly via a fully disposable pen injector system plus matching sitagliptin placebo plus matching glimepiride placebo from Week 1 to Week 156. All

	Description
	participants returned for the 8-week post-treatment Follow-up Period.
Sitagliptin 100 mg Plus Metformin	Participants received sitagliptin 100 mg daily plus metformin >=1500 mg daily plus matching albiglutide placebo as a subcutaneous injection weekly via a fully disposable pen injector system plus matching glimepiride placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.
Glimepiride 2 mg Plus Metformin	Participants received glimepiride 2 mg daily (with masked up-titration to 4 mg daily if required) plus metformin >=1500 mg daily plus matching albiglutide placebo as a subcutaneous injection weekly via a fully disposable pen injector system plus matching sitagliptin placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.
Albiglutide 30 mg Plus Metformin	Participants received albiglutide 30 mg weekly (with masked up-titration to 50 mg weekly if required) as a subcutaneous injection via a fully disposable pen injector system plus metformin >=1500 mg daily plus matching sitagliptin placebo plus matching glimepiride placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.

Measured Values

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
Number of Participants Analyzed	16	88	102	115
Number of Participants Who Achieved Clinically Meaningful HbA1c Response Levels of <6.5%, <7%, and <7.5% at Week 156				

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
[units: Participants]				
HbA1c <6.5%	4	23	15	31
HbA1c <7.0%	7	44	44	69
HbA1c <7.5%	13	69	69	90

7. Secondary Outcome Measure:

Measure Title	Time to Hyperglycemia Rescue
Measure Description	Participants who experienced persistent hyperglycemia (high blood glucose) could have qualified for hyperglycemia rescue.The conditions for hyperglycemic rescue were as follows: FPG >=280 milligrams/deciliter (mg/dL) between >=Week 2 and <Week 4; FPG >=250 mg/dL between >=Week 4 and <Week 12; HbA1c >=8.5% and a <=0.5% reduction from Baseline between >=Week 12 and <Week 24; HbA1c >=8.5% between >=Week 24 and <Week 48; HbA1c >=8.0% between >= Week 48 and <Week 156. Participants could have been rescued at any time on or after Week 2. Time to hyperglycemia rescue is defined as the time between the date of the first dose of study medication and the date of hyperglycemia rescue plus 1 day, or the time between the date of the first dose of study medication and the date of the last visit during the active treatment period plus 1 day for participants not requiring rescue. This time was divided by 7 to express the result in week
Time Frame	From the start of study medication until the end of the treatment (up to Week 156)
Safety Issue?	No

Analysis Population Description

ITT Population. Only those participants with a value at Baseline and at the specified visit were analyzed.

Reporting Groups

	Description
Placebo Plus Metformin	Participants received metformin >=1500 milligrams (mg) daily plus matching albiglutide placebo as a subcutaneous injection weekly via a fully disposable pen injector system plus matching sitagliptin placebo plus matching glimepiride placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.
Sitagliptin 100 mg Plus Metformin	Participants received sitagliptin 100 mg daily plus metformin >=1500 mg daily plus matching albiglutide placebo as a subcutaneous injection weekly via a fully disposable pen injector system plus matching glimepiride placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.
Glimepiride 2 mg Plus Metformin	Participants received glimepiride 2 mg daily (with masked up-titration to 4 mg daily if required) plus metformin >=1500 mg daily plus matching albiglutide placebo as a subcutaneous injection weekly via a fully disposable pen injector system plus matching sitagliptin placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.
Albiglutide 30 mg Plus Metformin	Participants received albiglutide 30 mg weekly (with masked up-titration to 50 mg weekly if required) as a subcutaneous injection via a fully disposable pen injector system plus metformin >=1500 mg daily plus matching sitagliptin placebo plus matching glimepiride placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.

Measured Values

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
Number of Participants Analyzed	100	300	302	297
Time to Hyperglycemia Rescue [units: Weeks] Median (95% Confidence Interval)	67.71 (53.14 to 122.14)	NA (NA to NA) [1]	NA (NA to NA) [2]	NA (NA to NA) [3]

[1] There were few events of hyperglycemia rescue (<50% of participants with events) to calculate the median and confidence interval.

[2] There were few events of hyperglycemia rescue (<50% of participants with events) to calculate the median and confidence interval.

[3] There were few events of hyperglycemia rescue (<50% of participants with events) to calculate the median and confidence interval.

8. Secondary Outcome Measure:

Measure Title	Change From Baseline in Body Weight at Week 104
Measure Description	The Baseline value is the last non-missing value before the start of treatment. Change from Baseline was calculated as the post-Baseline weight minus the Baseline weight. The LOCF method was used to impute missing post-Baseline weight values. Weight values obtained after hyperglycemia rescue were treated as missing and replaced with prerescue values. Based on ANCOVA: change = treatment + Baseline weight + Baseline HbA1c category + prior myocardial infarction history + age category + region.
Time Frame	Baseline and Week 104
Safety Issue?	No

Analysis Population Description

ITT Population with LOCF. Only those participants with a value at Baseline and at the specified visit were analyzed. Values were carried forward for participants who were rescued or discontinued from active treatment before Week 104.

Reporting Groups

	Description
Placebo Plus Metformin	Participants received metformin >=1500 milligrams (mg) daily plus matching albiglutide placebo as a subcutaneous injection weekly via a fully disposable pen injector system plus matching sitagliptin placebo plus matching glimepiride placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.
Sitagliptin 100 mg Plus Metformin	Participants received sitagliptin 100 mg daily plus metformin >=1500 mg daily plus matching albiglutide placebo as a subcutaneous injection weekly via a fully disposable pen injector system plus matching glimepiride placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.
Glimepiride 2 mg Plus Metformin	Participants received glimepiride 2 mg daily (with masked up-titration to 4 mg daily if required) plus metformin >=1500 mg daily plus matching albiglutide placebo as a subcutaneous injection weekly via a fully disposable pen injector system plus matching sitagliptin placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.
Albiglutide 30 mg Plus Metformin	Participants received albiglutide 30 mg weekly (with masked up-titration to 50 mg weekly if required) as a subcutaneous injection via a fully disposable pen injector system plus metformin >=1500 mg daily plus matching sitagliptin placebo plus matching glimepiride placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.

Measured Values

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
Number of Participants Analyzed	100	300	302	296
Change From Baseline in Body Weight at Week 104 [units: Kilograms] Least Squares Mean (Standard Error)	-1.00 (0.411)	-0.86 (0.237)	1.17 (0.237)	-1.21 (0.239)

9. Secondary Outcome Measure:

Measure Title	Change From Baseline in Body Weight at Week 156
Measure Description	The Baseline value is the last non-missing value before the start of treatment. Change from Baseline was calculated as the post-Baseline weight minus the Baseline weight. This analysis used observed body weight values excluding those obtained after hyperglycemia rescue; no missing data imputation was performed.
Time Frame	Baseline and Week 156
Safety Issue?	No

Analysis Population Description

ITT Population with observed values. Only those participants who were available at the indicated time points were analyzed.

Reporting Groups

	Description
Placebo Plus Metformin	Participants received metformin >=1500 milligrams (mg) daily plus matching albiglutide placebo as a subcutaneous injection weekly via a fully disposable pen injector system plus matching sitagliptin placebo plus matching glimepiride placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.

	Description
Sitagliptin 100 mg Plus Metformin	Participants received sitagliptin 100 mg daily plus metformin >=1500 mg daily plus matching albiglutide placebo as a subcutaneous injection weekly via a fully disposable pen injector system plus matching glimepiride placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.
Glimepiride 2 mg Plus Metformin	Participants received glimepiride 2 mg daily (with masked up-titration to 4 mg daily if required) plus metformin >=1500 mg daily plus matching albiglutide placebo as a subcutaneous injection weekly via a fully disposable pen injector system plus matching sitagliptin placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.
Albiglutide 30 mg Plus Metformin	Participants received albiglutide 30 mg weekly (with masked up-titration to 50 mg weekly if required) as a subcutaneous injection via a fully disposable pen injector system plus metformin >=1500 mg daily plus matching sitagliptin placebo plus matching glimepiride placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.

Measured Values

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
Number of Participants Analyzed	16	89	102	116
Change From Baseline in Body Weight at Week 156 [units: Kilograms] Mean (Standard Deviation)	-3.61 (3.460)	-2.05 (4.109)	0.98 (4.760)	-2.31 (5.093)

Reported Adverse Events

Reporting Groups

	Description
Placebo Plus Metformin	Participants received metformin >=1500 milligrams (mg) daily plus matching albiglutide placebo as a subcutaneous injection weekly via a fully disposable pen injector system plus matching sitagliptin placebo plus matching glimepiride placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.
Sitagliptin 100 mg Plus Metformin	Participants received sitagliptin 100 mg daily plus metformin >=1500 mg daily plus matching albiglutide placebo as a subcutaneous injection weekly via a fully disposable pen injector system plus matching glimepiride placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.
Glimepiride 2 mg Plus Metformin	Participants received glimepiride 2 mg daily (with masked up-titration to 4 mg daily if required) plus metformin >=1500 mg daily plus matching albiglutide placebo as a subcutaneous injection weekly via a fully disposable pen injector system plus matching sitagliptin placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.
Albiglutide 30 mg Plus Metformin	Participants received albiglutide 30 mg weekly (with masked up-titration to 50 mg weekly if required) as a subcutaneous injection via a fully disposable pen injector system plus metformin >=1500 mg daily plus matching sitagliptin placebo plus matching glimepiride placebo from Week 1 to Week 156. All participants returned for the 8-week post-treatment Follow-up Period.

Time Frame

On-treatment serious adverse events (SAEs) and non-serious AEs, defined as those events that had a start date on or after the

first day of study medication and within 56 days after the end of study medication (up to Week 156), are reported.

Additional Description

SAEs and non-serious AEs are reported for members of the Safety Population, comprised of all participants who received at least one dose of study treatment.

Serious Adverse Events

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
Total # participants affected/at risk	15/101 (14.85%)	32/302 (10.6%)	36/307 (11.73%)	44/302 (14.57%)
Cardiac disorders				
Acute myocardial infarction †[A]				
# participants affected/at risk	1/101 (0.99%)	2/302 (0.66%)	1/307 (0.33%)	2/302 (0.66%)
# events				
Angina pectoris †[A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	0/307 (0%)	2/302 (0.66%)
# events				
Angina unstable †[A]				
# participants affected/at risk	1/101 (0.99%)	0/302 (0%)	0/307 (0%)	1/302 (0.33%)
# events				
Arrhythmia †[A]				

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
# participants affected/at risk	0/101 (0%)	1/302 (0.33%)	0/307 (0%)	0/302 (0%)
# events				
Arteriospasm coronary † [A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	0/307 (0%)	1/302 (0.33%)
# events				
Cardiac failure † [A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	0/307 (0%)	1/302 (0.33%)
# events				
Cardiac failure congestive † [A]				
# participants affected/at risk	0/101 (0%)	1/302 (0.33%)	1/307 (0.33%)	2/302 (0.66%)
# events				
Cardio-respiratory arrest † [A]				
# participants affected/at risk	1/101 (0.99%)	0/302 (0%)	0/307 (0%)	1/302 (0.33%)
# events				
Coronary artery disease † [A]				
# participants affected/at risk	2/101 (1.98%)	1/302 (0.33%)	2/307 (0.65%)	1/302 (0.33%)

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
# events				
Coronary artery stenosis † [A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	1/307 (0.33%)	0/302 (0%)
# events				
Myocardial infarction † [A]				
# participants affected/at risk	1/101 (0.99%)	0/302 (0%)	1/307 (0.33%)	3/302 (0.99%)
# events				
Eye disorders				
Dacryostenosis acquired † [A]				
# participants affected/at risk	0/101 (0%)	1/302 (0.33%)	0/307 (0%)	0/302 (0%)
# events				
Retinal detachment † [A]				
# participants affected/at risk	0/101 (0%)	1/302 (0.33%)	1/307 (0.33%)	0/302 (0%)
# events				
Gastrointestinal disorders				
Abdominal pain † [A]				
# participants affected/at	0/101 (0%)	0/302 (0%)	1/307 (0.33%)	0/302 (0%)

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
risk				
# events				
Colitis ischaemic † [A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	0/307 (0%)	1/302 (0.33%)
# events				
Gastritis † [A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	0/307 (0%)	2/302 (0.66%)
# events				
Gastrointestinal haemorrhage † [A]				
# participants affected/at risk	1/101 (0.99%)	0/302 (0%)	0/307 (0%)	0/302 (0%)
# events				
Gastrooesophageal reflux disease † [A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	0/307 (0%)	1/302 (0.33%)
# events				
Intestinal obstruction † [A]				
# participants affected/at risk	0/101 (0%)	1/302 (0.33%)	1/307 (0.33%)	0/302 (0%)

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
# events				
Lower gastrointestinal haemorrhage † [A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	0/307 (0%)	1/302 (0.33%)
# events				
Oesophageal spasm † [A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	1/307 (0.33%)	0/302 (0%)
# events				
Pancreatitis acute † [A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	1/307 (0.33%)	1/302 (0.33%)
# events				
Rectal haemorrhage † [A]				
# participants affected/at risk	1/101 (0.99%)	0/302 (0%)	1/307 (0.33%)	0/302 (0%)
# events				
Small intestinal obstruction † [A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	0/307 (0%)	1/302 (0.33%)
# events				

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
General disorders				
Chest pain †[A]				
# participants affected/at risk	0/101 (0%)	1/302 (0.33%)	2/307 (0.65%)	4/302 (1.32%)
# events				
Death †[A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	0/307 (0%)	1/302 (0.33%)
# events				
Device malfunction †[A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	0/307 (0%)	1/302 (0.33%)
# events				
Non-cardiac chest pain †[A]				
# participants affected/at risk	0/101 (0%)	1/302 (0.33%)	1/307 (0.33%)	0/302 (0%)
# events				
Hepatobiliary disorders				
Bile duct stone †[A]				
# participants affected/at risk	0/101 (0%)	1/302 (0.33%)	0/307 (0%)	0/302 (0%)
# events				

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
Cholecystitis † [A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	0/307 (0%)	1/302 (0.33%)
# events				
Cholecystitis acute † [A]				
# participants affected/at risk	0/101 (0%)	1/302 (0.33%)	0/307 (0%)	1/302 (0.33%)
# events				
Cholelithiasis † [A]				
# participants affected/at risk	1/101 (0.99%)	0/302 (0%)	1/307 (0.33%)	0/302 (0%)
# events				
Immune system disorders				
Hypersensitivity † [A]				
# participants affected/at risk	0/101 (0%)	1/302 (0.33%)	0/307 (0%)	0/302 (0%)
# events				
Infections and infestations				
Abscess limb † [A]				
# participants affected/at	0/101 (0%)	0/302 (0%)	1/307 (0.33%)	0/302 (0%)

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
risk				
# events				
Appendicitis † [A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	0/307 (0%)	3/302 (0.99%)
# events				
Arthritis bacterial † [A]				
# participants affected/at risk	0/101 (0%)	1/302 (0.33%)	0/307 (0%)	0/302 (0%)
# events				
Cellulitis † [A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	2/307 (0.65%)	0/302 (0%)
# events				
Gastroenteritis † [A]				
# participants affected/at risk	0/101 (0%)	1/302 (0.33%)	2/307 (0.65%)	1/302 (0.33%)
# events				
Helicobacter infection † [A]				
# participants affected/at risk	0/101 (0%)	1/302 (0.33%)	0/307 (0%)	0/302 (0%)
# events				

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
Osteomyelitis † [A]				
# participants affected/at risk	1/101 (0.99%)	0/302 (0%)	0/307 (0%)	0/302 (0%)
# events				
Pelvic abscess † [A]				
# participants affected/at risk	0/101 (0%)	1/302 (0.33%)	0/307 (0%)	0/302 (0%)
# events				
Pneumonia † [A]				
# participants affected/at risk	1/101 (0.99%)	2/302 (0.66%)	1/307 (0.33%)	2/302 (0.66%)
# events				
Post procedural cellulitis † [A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	1/307 (0.33%)	0/302 (0%)
# events				
Pyelonephritis † [A]				
# participants affected/at risk	0/101 (0%)	1/302 (0.33%)	0/307 (0%)	1/302 (0.33%)
# events				
Pyelonephritis acute † [A]				
# participants affected/at	1/101 (0.99%)	1/302 (0.33%)	0/307 (0%)	1/302 (0.33%)

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
risk				
# events				
Subcutaneous abscess † [A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	0/307 (0%)	1/302 (0.33%)
# events				
Upper respiratory tract infection † [A]				
# participants affected/at risk	0/101 (0%)	1/302 (0.33%)	0/307 (0%)	0/302 (0%)
# events				
Urinary tract infection † [A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	0/307 (0%)	1/302 (0.33%)
# events				
Viral infection † [A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	0/307 (0%)	1/302 (0.33%)
# events				
Injury, poisoning and procedural complications				
Coronary artery restenosis †				

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
[A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	1/307 (0.33%)	0/302 (0%)
# events				
Femur fracture † [A]				
# participants affected/at risk	0/101 (0%)	1/302 (0.33%)	0/307 (0%)	0/302 (0%)
# events				
Fibula fracture † [A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	1/307 (0.33%)	0/302 (0%)
# events				
Head injury † [A]				
# participants affected/at risk	1/101 (0.99%)	0/302 (0%)	0/307 (0%)	0/302 (0%)
# events				
Intentional overdose † [A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	0/307 (0%)	1/302 (0.33%)
# events				
Joint dislocation † [A]				
# participants affected/at	0/101 (0%)	0/302 (0%)	0/307 (0%)	1/302 (0.33%)

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
risk				
# events				
Ligament sprain † [A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	1/307 (0.33%)	0/302 (0%)
# events				
Spinal fracture † [A]				
# participants affected/at risk	0/101 (0%)	1/302 (0.33%)	0/307 (0%)	0/302 (0%)
# events				
Tibia fracture † [A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	1/307 (0.33%)	0/302 (0%)
# events				
Metabolism and nutrition disorders				
Diabetes mellitus inadequate control † [A]				
# participants affected/at risk	0/101 (0%)	1/302 (0.33%)	0/307 (0%)	0/302 (0%)
# events				
Hyperglycaemia † [A]				

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
# participants affected/at risk	0/101 (0%)	0/302 (0%)	0/307 (0%)	3/302 (0.99%)
# events				
Hypoglycaemia †[A]				
# participants affected/at risk	0/101 (0%)	1/302 (0.33%)	0/307 (0%)	0/302 (0%)
# events				
Hyponatraemia †[A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	0/307 (0%)	1/302 (0.33%)
# events				
Musculoskeletal and connective tissue disorders				
Arthralgia †[A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	0/307 (0%)	1/302 (0.33%)
# events				
Arthritis †[A]				
# participants affected/at risk	0/101 (0%)	1/302 (0.33%)	0/307 (0%)	0/302 (0%)
# events				

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
Back pain †[A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	2/307 (0.65%)	0/302 (0%)
# events				
Costochondritis †[A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	0/307 (0%)	1/302 (0.33%)
# events				
Intervertebral disc protrusion †[A]				
# participants affected/at risk	1/101 (0.99%)	0/302 (0%)	0/307 (0%)	0/302 (0%)
# events				
Musculoskeletal chest pain †[A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	0/307 (0%)	1/302 (0.33%)
# events				
Myopathy †[A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	0/307 (0%)	1/302 (0.33%)
# events				
Osteoarthritis †[A]				

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
# participants affected/at risk	1/101 (0.99%)	0/302 (0%)	2/307 (0.65%)	1/302 (0.33%)
# events				
Osteoporosis † [A]				
# participants affected/at risk	0/101 (0%)	1/302 (0.33%)	0/307 (0%)	0/302 (0%)
# events				
Scoliosis † [A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	1/307 (0.33%)	0/302 (0%)
# events				
Spinal osteoarthritis † [A]				
# participants affected/at risk	1/101 (0.99%)	0/302 (0%)	0/307 (0%)	1/302 (0.33%)
# events				
Spondylolisthesis † [A]				
# participants affected/at risk	1/101 (0.99%)	0/302 (0%)	0/307 (0%)	0/302 (0%)
# events				
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
B-cell lymphoma †[A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	2/307 (0.65%)	0/302 (0%)
# events				
Bladder cancer †[A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	0/307 (0%)	1/302 (0.33%)
# events				
Breast cancer †[A]				
# participants affected/at risk	1/101 (0.99%)	1/302 (0.33%)	0/307 (0%)	0/302 (0%)
# events				
Breast cancer stage III †[A]				
# participants affected/at risk	0/101 (0%)	1/302 (0.33%)	0/307 (0%)	0/302 (0%)
# events				
Gastrointestinal cancer metastatic †[A]				
# participants affected/at risk	0/101 (0%)	1/302 (0.33%)	0/307 (0%)	0/302 (0%)
# events				
Hepatic cancer metastatic †[A]				

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
# participants affected/at risk	0/101 (0%)	0/302 (0%)	1/307 (0.33%)	0/302 (0%)
# events				
Lung cancer metastatic † [A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	2/307 (0.65%)	0/302 (0%)
# events				
Lung squamous cell carcinoma stage II † [A]				
# participants affected/at risk	0/101 (0%)	1/302 (0.33%)	0/307 (0%)	0/302 (0%)
# events				
Malignant melanoma † [A]				
# participants affected/at risk	0/101 (0%)	1/302 (0.33%)	0/307 (0%)	0/302 (0%)
# events				
Prostate cancer † [A]				
# participants affected/at risk	0/101 (0%)	1/302 (0.33%)	0/307 (0%)	0/302 (0%)
# events				
Prostate cancer metastatic † [A]				
# participants affected/at	1/101 (0.99%)	0/302 (0%)	0/307 (0%)	0/302 (0%)

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
risk				
# events				
Rectal cancer † [A]				
# participants affected/at risk	0/101 (0%)	1/302 (0.33%)	0/307 (0%)	0/302 (0%)
# events				
Renal cancer † [A]				
# participants affected/at risk	0/101 (0%)	1/302 (0.33%)	0/307 (0%)	0/302 (0%)
# events				
Squamous cell carcinoma † [A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	1/307 (0.33%)	0/302 (0%)
# events				
Thyroid cancer † [A]				
# participants affected/at risk	0/101 (0%)	2/302 (0.66%)	0/307 (0%)	1/302 (0.33%)
# events				
Uterine cancer † [A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	1/307 (0.33%)	1/302 (0.33%)

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
# events				
Uterine leiomyoma † [A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	0/307 (0%)	1/302 (0.33%)
# events				
Nervous system disorders				
Carotid artery stenosis † [A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	1/307 (0.33%)	0/302 (0%)
# events				
Cerebrovascular accident † [A]				
# participants affected/at risk	1/101 (0.99%)	0/302 (0%)	0/307 (0%)	2/302 (0.66%)
# events				
Complicated migraine † [A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	1/307 (0.33%)	0/302 (0%)
# events				
Convulsion † [A]				
# participants affected/at	0/101 (0%)	0/302 (0%)	0/307 (0%)	1/302 (0.33%)

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
risk				
# events				
Polyneuropathy † [A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	0/307 (0%)	1/302 (0.33%)
# events				
Presyncope † [A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	0/307 (0%)	1/302 (0.33%)
# events				
Subarachnoid haemorrhage † [A]				
# participants affected/at risk	1/101 (0.99%)	0/302 (0%)	0/307 (0%)	0/302 (0%)
# events				
Syncope † [A]				
# participants affected/at risk	0/101 (0%)	1/302 (0.33%)	0/307 (0%)	0/302 (0%)
# events				
Transient ischaemic attack † [A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	0/307 (0%)	1/302 (0.33%)

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
# events				
Viith nerve paralysis † [A]				
# participants affected/at risk	1/101 (0.99%)	0/302 (0%)	0/307 (0%)	0/302 (0%)
# events				
Pregnancy, puerperium and perinatal conditions				
Abortion Spontaneous † [A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	1/307 (0.33%)	0/302 (0%)
# events				
Psychiatric disorders				
Mental status changes † [A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	1/307 (0.33%)	0/302 (0%)
# events				
Suicidal ideation † [A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	0/307 (0%)	1/302 (0.33%)
# events				
Renal and urinary disorders				

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
Azotaemia † [A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	0/307 (0%)	1/302 (0.33%)
# events				
Calculus ureteric † [A]				
# participants affected/at risk	1/101 (0.99%)	0/302 (0%)	0/307 (0%)	0/302 (0%)
# events				
Nephrolithiasis † [A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	1/307 (0.33%)	1/302 (0.33%)
# events				
Reproductive system and breast disorders				
Cervical Polyp † [A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	0/307 (0%)	1/302 (0.33%)
# events				
Respiratory, thoracic and mediastinal disorders				
Atelectasis † [A]				
# participants affected/at	0/101 (0%)	0/302 (0%)	0/307 (0%)	1/302 (0.33%)

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
risk				
# events				
Chronic obstructive pulmonary disease †[A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	0/307 (0%)	1/302 (0.33%)
# events				
Epistaxis †[A]				
# participants affected/at risk	0/101 (0%)	1/302 (0.33%)	0/307 (0%)	0/302 (0%)
# events				
Pleural effusion †[A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	1/307 (0.33%)	1/302 (0.33%)
# events				
Pulmonary embolism †[A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	0/307 (0%)	2/302 (0.66%)
# events				
Skin and subcutaneous tissue disorders				
Angioedema †[A]				

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
# participants affected/at risk	1/101 (0.99%)	0/302 (0%)	2/307 (0.65%)	0/302 (0%)
# events				
Vascular disorders				
Deep vein thrombosis †[A]				
# participants affected/at risk	0/101 (0%)	0/302 (0%)	0/307 (0%)	2/302 (0.66%)
# events				
Hypertension †[A]				
# participants affected/at risk	1/101 (0.99%)	0/302 (0%)	0/307 (0%)	1/302 (0.33%)
# events				
Hypertensive crisis †[A]				
# participants affected/at risk	1/101 (0.99%)	0/302 (0%)	0/307 (0%)	0/302 (0%)
# events				
Ischaemia †[A]				
# participants affected/at risk	0/101 (0%)	1/302 (0.33%)	0/307 (0%)	0/302 (0%)
# events				
Peripheral vascular disorder †[A]				

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
# participants affected/at risk	1/101 (0.99%)	1/302 (0.33%)	1/307 (0.33%)	0/302 (0%)
# events				

† Indicates events were collected by systematic assessment.

A Term from vocabulary, MedDRA

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 2%

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
Total # participants affected/at risk	75/101 (74.26%)	229/302 (75.83%)	258/307 (84.04%)	242/302 (80.13%)
Blood and lymphatic system disorders				
Anaemia † [A]				
# participants affected/at risk	8/101 (7.92%)	14/302 (4.64%)	12/307 (3.91%)	14/302 (4.64%)
# events				
Ear and labyrinth disorders				
Vertigo † [A]				
# participants affected/at risk	3/101 (2.97%)	3/302 (0.99%)	1/307 (0.33%)	8/302 (2.65%)

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
# events				
Eye disorders				
Cataract † [A]				
# participants affected/at risk	6/101 (5.94%)	12/302 (3.97%)	20/307 (6.51%)	13/302 (4.3%)
# events				
Conjunctivitis † [A]				
# participants affected/at risk	0/101 (0%)	4/302 (1.32%)	7/307 (2.28%)	4/302 (1.32%)
# events				
Diabetic retinopathy † [A]				
# participants affected/at risk	2/101 (1.98%)	7/302 (2.32%)	14/307 (4.56%)	14/302 (4.64%)
# events				
Gastrointestinal disorders				
Abdominal discomfort † [A]				
# participants affected/at risk	0/101 (0%)	7/302 (2.32%)	2/307 (0.65%)	1/302 (0.33%)
# events				
Abdominal pain † [A]				
# participants affected/at	0/101 (0%)	12/302	8/307 (2.61%)	12/302

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
risk		(3.97%)		(3.97%)
# events				
Abdominal pain upper † [A]				
# participants affected/at risk	3/101 (2.97%)	6/302 (1.99%)	3/307 (0.98%)	4/302 (1.32%)
# events				
Constipation † [A]				
# participants affected/at risk	14/101 (13.86%)	8/302 (2.65%)	13/307 (4.23%)	19/302 (6.29%)
# events				
Dental caries † [A]				
# participants affected/at risk	3/101 (2.97%)	7/302 (2.32%)	8/307 (2.61%)	2/302 (0.66%)
# events				
Diarrhoea † [A]				
# participants affected/at risk	11/101 (10.89%)	28/302 (9.27%)	31/307 (10.1%)	46/302 (15.23%)
# events				
Dyspepsia † [A]				
# participants affected/at risk	2/101 (1.98%)	5/302 (1.66%)	8/307 (2.61%)	13/302 (4.3%)
# events				

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
Flatulence †[A]				
# participants affected/at risk	3/101 (2.97%)	1/302 (0.33%)	1/307 (0.33%)	4/302 (1.32%)
# events				
Gastritis †[A]				
# participants affected/at risk	4/101 (3.96%)	7/302 (2.32%)	7/307 (2.28%)	10/302 (3.31%)
# events				
Gastrooesophageal reflux disease †[A]				
# participants affected/at risk	4/101 (3.96%)	10/302 (3.31%)	10/307 (3.26%)	7/302 (2.32%)
# events				
Nausea †[A]				
# participants affected/at risk	13/101 (12.87%)	22/302 (7.28%)	25/307 (8.14%)	37/302 (12.25%)
# events				
Vomiting †[A]				
# participants affected/at risk	1/101 (0.99%)	14/302 (4.64%)	13/307 (4.23%)	22/302 (7.28%)
# events				
General disorders				

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
Chest pain †[A]				
# participants affected/at risk	3/101 (2.97%)	6/302 (1.99%)	5/307 (1.63%)	8/302 (2.65%)
# events				
Fatigue †[A]				
# participants affected/at risk	4/101 (3.96%)	8/302 (2.65%)	6/307 (1.95%)	8/302 (2.65%)
# events				
Injection site erythema †[A]				
# participants affected/at risk	1/101 (0.99%)	2/302 (0.66%)	3/307 (0.98%)	7/302 (2.32%)
# events				
Injection site haematoma †[A]				
# participants affected/at risk	2/101 (1.98%)	11/302 (3.64%)	11/307 (3.58%)	9/302 (2.98%)
# events				
Injection site reaction †[A]				
# participants affected/at risk	2/101 (1.98%)	5/302 (1.66%)	9/307 (2.93%)	33/302 (10.93%)
# events				
Oedema peripheral †[A]				

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
# participants affected/at risk	2/101 (1.98%)	10/302 (3.31%)	25/307 (8.14%)	13/302 (4.3%)
# events				
Immune system disorders				
Seasonal allergy † [A]				
# participants affected/at risk	1/101 (0.99%)	3/302 (0.99%)	5/307 (1.63%)	8/302 (2.65%)
# events				
Infections and infestations				
Bronchitis † [A]				
# participants affected/at risk	10/101 (9.9%)	26/302 (8.61%)	23/307 (7.49%)	24/302 (7.95%)
# events				
Cellulitis † [A]				
# participants affected/at risk	1/101 (0.99%)	7/302 (2.32%)	6/307 (1.95%)	7/302 (2.32%)
# events				
Ear infection † [A]				
# participants affected/at risk	3/101 (2.97%)	5/302 (1.66%)	6/307 (1.95%)	3/302 (0.99%)

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
# events				
Gastroenteritis †[A]				
# participants affected/at risk	4/101 (3.96%)	16/302 (5.3%)	9/307 (2.93%)	19/302 (6.29%)
# events				
Gastroenteritis viral †[A]				
# participants affected/at risk	1/101 (0.99%)	7/302 (2.32%)	5/307 (1.63%)	1/302 (0.33%)
# events				
Herpes zoster †[A]				
# participants affected/at risk	1/101 (0.99%)	2/302 (0.66%)	5/307 (1.63%)	8/302 (2.65%)
# events				
Influenza †[A]				
# participants affected/at risk	7/101 (6.93%)	17/302 (5.63%)	25/307 (8.14%)	21/302 (6.95%)
# events				
Lower respiratory tract infection †[A]				
# participants affected/at risk	4/101 (3.96%)	6/302 (1.99%)	1/307 (0.33%)	3/302 (0.99%)
# events				

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
Nasopharyngitis † [A]				
# participants affected/at risk	9/101 (8.91%)	31/302 (10.26%)	30/307 (9.77%)	24/302 (7.95%)
# events				
Otitis media † [A]				
# participants affected/at risk	1/101 (0.99%)	7/302 (2.32%)	2/307 (0.65%)	4/302 (1.32%)
# events				
Pharyngitis † [A]				
# participants affected/at risk	10/101 (9.9%)	22/302 (7.28%)	17/307 (5.54%)	17/302 (5.63%)
# events				
Pneumonia † [A]				
# participants affected/at risk	1/101 (0.99%)	2/302 (0.66%)	7/307 (2.28%)	6/302 (1.99%)
# events				
Sinusitis † [A]				
# participants affected/at risk	5/101 (4.95%)	22/302 (7.28%)	22/307 (7.17%)	17/302 (5.63%)
# events				
Tooth abscess † [A]				
# participants affected/at	6/101 (5.94%)	10/302	7/307 (2.28%)	4/302 (1.32%)

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
risk		(3.31%)		
# events				
Upper respiratory tract infection † [A]				
# participants affected/at risk	10/101 (9.9%)	33/302 (10.93%)	32/307 (10.42%)	58/302 (19.21%)
# events				
Urinary tract infection † [A]				
# participants affected/at risk	11/101 (10.89%)	37/302 (12.25%)	35/307 (11.4%)	27/302 (8.94%)
# events				
Viral infection † [A]				
# participants affected/at risk	1/101 (0.99%)	7/302 (2.32%)	4/307 (1.3%)	3/302 (0.99%)
# events				
Injury, poisoning and procedural complications				
Contusion † [A]				
# participants affected/at risk	1/101 (0.99%)	3/302 (0.99%)	7/307 (2.28%)	8/302 (2.65%)
# events				
Excoriation † [A]				

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
# participants affected/at risk	2/101 (1.98%)	2/302 (0.66%)	5/307 (1.63%)	7/302 (2.32%)
# events				
Fall †[A]				
# participants affected/at risk	1/101 (0.99%)	7/302 (2.32%)	0/307 (0%)	6/302 (1.99%)
# events				
Ligament sprain †[A]				
# participants affected/at risk	2/101 (1.98%)	8/302 (2.65%)	9/307 (2.93%)	5/302 (1.66%)
# events				
Muscle strain †[A]				
# participants affected/at risk	4/101 (3.96%)	4/302 (1.32%)	9/307 (2.93%)	6/302 (1.99%)
# events				
Investigations				
Weight Increased †[A]				
# participants affected/at risk	1/101 (0.99%)	2/302 (0.66%)	7/307 (2.28%)	5/302 (1.66%)
# events				
Metabolism and nutrition disorders				

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
Dyslipidaemia †[A]				
# participants affected/at risk	4/101 (3.96%)	11/302 (3.64%)	5/307 (1.63%)	9/302 (2.98%)
# events				
Gout †[A]				
# participants affected/at risk	2/101 (1.98%)	3/302 (0.99%)	3/307 (0.98%)	7/302 (2.32%)
# events				
Hypercholesterolaemia †[A]				
# participants affected/at risk	1/101 (0.99%)	4/302 (1.32%)	6/307 (1.95%)	7/302 (2.32%)
# events				
Hypertriglyceridaemia †[A]				
# participants affected/at risk	3/101 (2.97%)	8/302 (2.65%)	12/307 (3.91%)	8/302 (2.65%)
# events				
Hyperuricaemia †[A]				
# participants affected/at risk	2/101 (1.98%)	4/302 (1.32%)	7/307 (2.28%)	3/302 (0.99%)
# events				
Musculoskeletal and connective tissue				

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
disorders				
Arthralgia †[A]				
# participants affected/at risk	8/101 (7.92%)	31/302 (10.26%)	28/307 (9.12%)	24/302 (7.95%)
# events				
Arthritis †[A]				
# participants affected/at risk	3/101 (2.97%)	5/302 (1.66%)	3/307 (0.98%)	7/302 (2.32%)
# events				
Back pain †[A]				
# participants affected/at risk	9/101 (8.91%)	22/302 (7.28%)	19/307 (6.19%)	19/302 (6.29%)
# events				
Hypoglycaemia †[A]				
# participants affected/at risk	18/101 (17.82%)	24/302 (7.95%)	102/307 (33.22%)	35/302 (11.59%)
# events				
Muscle spasms †[A]				
# participants affected/at risk	5/101 (4.95%)	8/302 (2.65%)	9/307 (2.93%)	10/302 (3.31%)
# events				
Musculoskeletal pain †[A]				

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
# participants affected/at risk	2/101 (1.98%)	11/302 (3.64%)	6/307 (1.95%)	20/302 (6.62%)
# events				
Myalgia †[A]				
# participants affected/at risk	2/101 (1.98%)	7/302 (2.32%)	5/307 (1.63%)	6/302 (1.99%)
# events				
Osteoarthritis †[A]				
# participants affected/at risk	6/101 (5.94%)	11/302 (3.64%)	9/307 (2.93%)	10/302 (3.31%)
# events				
Pain in extremity †[A]				
# participants affected/at risk	6/101 (5.94%)	15/302 (4.97%)	21/307 (6.84%)	17/302 (5.63%)
# events				
Tendonitis †[A]				
# participants affected/at risk	2/101 (1.98%)	0/302 (0%)	7/307 (2.28%)	4/302 (1.32%)
# events				
Nervous system disorders				
Amnesia †[A]				

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
# participants affected/at risk	3/101 (2.97%)	0/302 (0%)	1/307 (0.33%)	1/302 (0.33%)
# events				
Diabetic neuropathy †[A]				
# participants affected/at risk	2/101 (1.98%)	5/302 (1.66%)	7/307 (2.28%)	5/302 (1.66%)
# events				
Dizziness †[A]				
# participants affected/at risk	5/101 (4.95%)	13/302 (4.3%)	14/307 (4.56%)	10/302 (3.31%)
# events				
Headache †[A]				
# participants affected/at risk	5/101 (4.95%)	26/302 (8.61%)	34/307 (11.07%)	22/302 (7.28%)
# events				
Neuropathy peripheral †[A]				
# participants affected/at risk	1/101 (0.99%)	5/302 (1.66%)	7/307 (2.28%)	8/302 (2.65%)
# events				
Paraesthesia †[A]				
# participants affected/at risk	3/101 (2.97%)	3/302 (0.99%)	5/307 (1.63%)	4/302 (1.32%)

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
# events				
Sciatica † [A]				
# participants affected/at risk	3/101 (2.97%)	1/302 (0.33%)	1/307 (0.33%)	2/302 (0.66%)
# events				
Psychiatric disorders				
Anxiety † [A]				
# participants affected/at risk	6/101 (5.94%)	6/302 (1.99%)	9/307 (2.93%)	8/302 (2.65%)
# events				
Depression † [A]				
# participants affected/at risk	5/101 (4.95%)	9/302 (2.98%)	10/307 (3.26%)	15/302 (4.97%)
# events				
Insomnia † [A]				
# participants affected/at risk	2/101 (1.98%)	6/302 (1.99%)	10/307 (3.26%)	12/302 (3.97%)
# events				
Reproductive system and breast disorders				
Erectile Dysfunction † [A]				
# participants affected/at	3/101 (2.97%)	4/302 (1.32%)	4/307 (1.3%)	6/302 (1.99%)

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
risk				
# events				
Respiratory, thoracic and mediastinal disorders				
Cough † [A]				
# participants affected/at risk	9/101 (8.91%)	24/302 (7.95%)	28/307 (9.12%)	26/302 (8.61%)
# events				
Nasal congestion † [A]				
# participants affected/at risk	1/101 (0.99%)	4/302 (1.32%)	10/307 (3.26%)	5/302 (1.66%)
# events				
Oropharyngeal pain † [A]				
# participants affected/at risk	1/101 (0.99%)	7/302 (2.32%)	16/307 (5.21%)	9/302 (2.98%)
# events				
Rhinitis allergic † [A]				
# participants affected/at risk	2/101 (1.98%)	5/302 (1.66%)	9/307 (2.93%)	4/302 (1.32%)
# events				
Skin and subcutaneous tissue disorders				

	Placebo Plus Metformin	Sitagliptin 100 mg Plus Metformin	Glimepiride 2 mg Plus Metformin	Albiglutide 30 mg Plus Metformin
Hyperkeratosis † [A]				
# participants affected/at risk	3/101 (2.97%)	0/302 (0%)	2/307 (0.65%)	0/302 (0%)
# events				
Rash † [A]				
# participants affected/at risk	0/101 (0%)	8/302 (2.65%)	5/307 (1.63%)	10/302 (3.31%)
# events				
Vascular disorders				
Hypertension † [A]				
# participants affected/at risk	6/101 (5.94%)	28/302 (9.27%)	32/307 (10.42%)	32/302 (10.6%)
# events				

† Indicates events were collected by systematic assessment.

A Term from vocabulary, MedDRA

More Information

Certain Agreements:

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

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

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

publication of results from all centers of a multi-center trial but requests that reports based on single-site data not precede the primary publication of the entire clinical trial.

Limitations and Caveats:

Results Point of Contact:

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