Clinical trial results:
A Pooled Analysis of the Safety and Efficacy of MK-0431A and MK-0431A XR in Pediatric Patients with Type 2 Diabetes Mellitus With Inadequate Glycemic Control on Metformin Therapy (Alone or in Combination with Insulin).

Summary

EudraCT number	2014-003583-20
Trial protocol	DE GB
Global end of trial date	17 September 2019

Results information

Result version number	v1
This version publication date	25 March 2020
First version publication date	25 March 2020

Trial information

Trial identification

Sponsor protocol code	0431A-170 and 0431A-289

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01472367
WHO universal trial number (UTN)	-
Other trial identifiers	EudraCT Number: 2012-004035-23, NCT Number: NCT01760447, EudraCT Number: 2011-002529-23

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	17 September 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 September 2019
Global end of trial reached?	Yes
Global end of trial date	17 September 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to assess the effect of the addition of sitagliptin (administered as MK-0431A or MK-0431A XR) relative to the addition of placebo on glycated hemoglobin (A1C), and the safety and tolerability of the addition of sitagliptin, in pediatric participants (ages 10-17 years) with type 2 diabetes mellitus with inadequate glycemic control on metformin therapy (alone or in combination with insulin).

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research. The following additional measure defined for this individual study was in place for the protection of trial subjects: Insulin as glycemic rescue therapy. In protocol MK-0431A-170, the type of insulin used as glycemic rescue therapy was at the investigator's discretion during Weeks 0-20, but only insulin glargine was used as glycemic rescue therapy during Weeks 20-54. In protocol MK-0431A-289, only insulin glargine was used as glycemic rescue therapy throughout Weeks 0-54.

Background therapy:

Participants who were on insulin at screening continued receiving insulin during the study.

Evidence for comparator: -

Actual start date of recruitment	07 December 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 1
Country: Number of subjects enrolled	Australia: 1
Country: Number of subjects enrolled	Brazil: 1
Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	Chile: 4
Country: Number of subjects enrolled	Colombia: 2
Country: Number of subjects enrolled	Costa Rica: 4
Country: Number of subjects enrolled	Dominican Republic: 10
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Greece: 1
Country: Number of subjects enrolled	Guatemala: 8
Country: Number of subjects enrolled	Hungary: 2
Country: Number of subjects enrolled	Israel: 15
Country: Number of subjects enrolled	Italy: 4

Country: Number of subjects enrolled	Malaysia: 22
Country: Number of subjects enrolled	Mauritius: 6
Country: Number of subjects enrolled	Mexico: 30
Country: Number of subjects enrolled	Philippines: 4
Country: Number of subjects enrolled	Russian Federation: 20
Country: Number of subjects enrolled	Saudi Arabia: 6
Country: Number of subjects enrolled	South Africa: 1
Country: Number of subjects enrolled	Sri Lanka: 23
Country: Number of subjects enrolled	Taiwan: 1
Country: Number of subjects enrolled	Thailand: 4
Country: Number of subjects enrolled	Ukraine: 8
Country: Number of subjects enrolled	United Arab Emirates: 4
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	United States: 31
Worldwide total number of subjects	223
EEA total number of subjects	16

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	21
Adolescents (12-17 years)	202
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study recruited participants in clinics/clinical offices in 28 countries.

Pre-assignment

Screening details:

The Pre-Assignment Period included a one-week single-blind placebo run-in prior to randomization during which participants received metformin with sitagliptin/metformin placebo or metformin XR with sitagliptin/metformin XR placebo each day.

Period 1

Period 1 title	Randomization
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Sitagliptin/Metformin

Arm description:

Participants received one tablet of sitagliptin/metformin and one tablet of metformin-placebo, administered twice daily prior to the morning and evening meals, during Weeks 0-20. Participants in this arm were enrolled in protocol MK-0431A-170.

Arm type	Experimental
Investigational medicinal product name	Sitagliptin plus metformin
Investigational medicinal product code	
Other name	MK-0431A
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 2 tablets daily, one taken with a morning meal and one taken with an evening meal, to provide a total daily dose of 100 mg of sitagliptin and 1000mg, 1700mg or 2000 mg of metformin. Dosage of metformin was based on each participant's daily metformin dose prior to enrollment.

Investigational medicinal product name	Placebo to metformin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 2 tablets daily, one taken with a morning meal and one taken with an evening meal. Each tablet contained placebo to metformin.

Investigational medicinal product name	Insulin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants who met protocol-specific glycemic rescue criteria received insulin as glycemic rescue therapy; participants on background insulin had their insulin dose increased for glycemic rescue.

Arm title	Metformin

Arm description:

Participants received one tablet of metformin and one tablet of placebo to sitagliptin/metformin, administered twice daily prior to the morning and evening meals, during Weeks 0-20. Participants in this arm were enrolled in protocol MK-0431A-170.

Arm type	Placebo
Investigational medicinal product name	Metformin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 2 tablets daily, one taken with a morning meal and one taken with an evening meal, to provide a total daily dose of 1000 mg, 1700 mg or 2000 mg of metformin. Dosage was based on each participant's daily metformin dose prior to enrollment.

Investigational medicinal product name	Placebo to sitagliptin plus metformin
Investigational medicinal product code	
Other name	Placebo to MK-0431A
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 2 tablets daily, one taken with a morning meal and one taken with an evening meal. Each tablet contained placebo to sitagliptin plus metformin.

Investigational medicinal product name	Insulin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants who met protocol-specific glycemic rescue criteria received insulin as glycemic rescue therapy; participants on background insulin had their insulin dose increased for glycemic rescue.

Arm title	Sitagliptin/Metformin XR

Arm description:

Participants received two tablets of sitagliptin/metformin XR and two tablets of metformin XR placebo, administered once daily with a meal, during Weeks 0-20. Participants in this arm were enrolled in protocol MK-0431A-289.

Arm type	Experimental
Investigational medicinal product name	Sitagliptin plus metformin XR
Investigational medicinal product code	
Other name	MK-0431A XR
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 2 tablets daily, both taken together with a meal, to provide a total daily dose of 100 mg of sitagliptin and 1000mg, 1500mg or 2000 mg of metformin. Dosage of metformin XR was based on each participant's daily metformin dose prior to enrollment.

Investigational medicinal product name	Placebo to metformin XR
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 2 tablets daily, both taken together with a meal. Each tablet contained placebo to metformin XR.

Investigational medicinal product name	Insulin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants who met protocol-specific glycemic rescue criteria received insulin glargine as glycemic rescue therapy; participants on background insulin had their insulin dose increased for glycemic rescue.

Arm title	Metformin XR

Arm description:

Participants received two tablets of metformin XR and two tablets of placebo to sitagliptin/metformin XR, administered once daily with a meal, during Weeks 0-20. Participants in this arm were enrolled in protocol MK-0431A-289.

Arm type	Placebo
Investigational medicinal product name	Placebo to sitagliptin plus metformin XR
Investigational medicinal product code	
Other name	Placebo to MK-0431A XR
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 2 tablets daily, both taken together with a meal. Each tablet contained placebo to sitagliptin plus metformin XR.

Investigational medicinal product name	Insulin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants who met protocol-specific glycemic rescue criteria received insulin glargine as glycemic rescue therapy; participants on background insulin had their insulin dose increased for glycemic rescue.

Investigational medicinal product name	Metformin XR
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 2 tablets daily, both taken together with a meal, to provide a total daily dose of 1000 mg, 1500 mg or 2000 mg of metformin XR. Dosage was based on each participant's daily metformin dose prior to enrollment.

Number of subjects in period 1	Sitagliptin/Metformin	Metformin	Sitagliptin/Metformin XR
Started	63	62	47
Completed	62	62	45
Not completed	1	0	2
Randomized but not treated	1	-	2

Number of subjects in period 1	Metformin XR
Started	51

Completed	51
Not completed	0
Randomized but not treated	-

Period 2

Period 2 title	Weeks 0-20
Is this the baseline period?	Yes[1]
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Sitagliptin/Metformin

Arm description:

Participants received one tablet of sitagliptin/metformin and one tablet of metformin-placebo, administered twice daily prior to the morning and evening meals, during Weeks 0-20. Participants in this arm were enrolled in protocol MK-0431A-170.

Arm type	Experimental
Investigational medicinal product name	Sitagliptin plus metformin
Investigational medicinal product code	
Other name	MK-0431A
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 2 tablets daily, one taken with a morning meal and one taken with an evening meal, to provide a total daily dose of 100 mg of sitagliptin and 1000mg, 1700mg or 2000 mg of metformin. Dosage of metformin was based on each participant's daily metformin dose prior to enrollment.

Investigational medicinal product name	Placebo to metformin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 2 tablets daily, one taken with a morning meal and one taken with an evening meal. Each tablet contained placebo to metformin.

Investigational medicinal product name	Insulin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants who met protocol-specific glycemic rescue criteria received insulin as glycemic rescue therapy; participants on background insulin had their insulin dose increased for glycemic rescue.

Arm title	Metformin

Arm description:

Participants received one tablet of metformin and one tablet of placebo to sitagliptin/metformin, administered twice daily prior to the morning and evening meals, during Weeks 0-20. Participants in this arm were enrolled in protocol MK-0431A-170.

Arm type	Placebo
Investigational medicinal product name	Metformin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 2 tablets daily, one taken with a morning meal and one taken with an evening meal, to provide a total daily dose of 1000 mg, 1700 mg or 2000 mg of metformin. Dosage was based on each participant's daily metformin dose prior to enrollment.

Investigational medicinal product name	Placebo to sitagliptin plus metformin
Investigational medicinal product code	
Other name	Placebo to MK-0431A
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 2 tablets daily, one taken with a morning meal and one taken with an evening meal. Each tablet contained placebo to sitagliptin plus metformin.

Investigational medicinal product name	Insulin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants who met protocol-specific glycemic rescue criteria received insulin as glycemic rescue therapy; participants on background insulin had their insulin dose increased for glycemic rescue.

Arm title	Sitagliptin/Metformin XR

Arm description:

Participants received two tablets of sitagliptin/metformin XR and two tablets of metformin XR placebo, administered once daily with a meal, during Weeks 0-20. Participants in this arm were enrolled in protocol MK-0431A-289.

Arm type	Experimental
Investigational medicinal product name	Sitagliptin plus metformin XR
Investigational medicinal product code	
Other name	MK-0431A XR
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 2 tablets daily, both taken together with a meal, to provide a total daily dose of 100 mg of sitagliptin and 1000mg, 1500mg or 2000 mg of metformin. Dosage of metformin XR was based on each participant's daily metformin dose prior to enrollment.

Investigational medicinal product name	Insulin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants who met protocol-specific glycemic rescue criteria received insulin glargine as glycemic rescue therapy; participants on background insulin had their insulin dose increased for glycemic rescue.

Investigational medicinal product name	Placebo to metformin XR
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 2 tablets daily, both taken together with a meal. Each tablet contained placebo to metformin XR.

Arm title	Metformin XR

Arm description:

Participants received two tablets of metformin XR and two tablets of placebo to sitagliptin/metformin XR, administered once daily with a meal, during Weeks 0-20. Participants in this arm were enrolled in protocol MK-0431A-289.

Arm type	Placebo
Investigational medicinal product name	Placebo to sitagliptin plus metformin XR
Investigational medicinal product code	
Other name	Placebo to MK-0431A XR
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 2 tablets daily, both taken together with a meal. Each tablet contained placebo to sitagliptin plus metformin XR.

Investigational medicinal product name	Metformin XR
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 2 tablets daily, both taken together with a meal, to provide a total daily dose of 1000 mg, 1500 mg or 2000 mg of metformin XR. Dosage was based on each participant's daily metformin dose prior to enrollment.

Investigational medicinal product name	Insulin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants who met protocol-specific glycemic rescue criteria received insulin glargine as glycemic rescue therapy; participants on background insulin had their insulin dose increased for glycemic rescue.

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: Period 1 includes all participants randomized. Period 2 includes all participants who were both randomized and treated with study medication, which is the population used for baseline characteristics.

Number of subjects in period 2[2]	Sitagliptin/Metformin	Metformin	Sitagliptin/Metformin XR
Started	62	62	45
Treated	62	62	45
Completed	59	62	42
Not completed	3	0	3
Consent withdrawn by subject	2	-	1
Lost to follow-up	1	-	1

Consent withdrawn by Parent/Guardian	-	-	1

Number of subjects in period 2[2]	Metformin XR
Started	51
Treated	51
Completed	47
Not completed	4
Consent withdrawn by subject	-
Lost to follow-up	1
Consent withdrawn by Parent/Guardian	3

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The baseline period used all participants both randomized and treated with study medication rather than all participants randomized, which was used as the worldwide total.

Period 3

Period 3 title	Weeks 20-54
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Sitagliptin/Metformin

Arm description:

Participants received one tablet of sitagliptin/metformin and one tablet of metformin-placebo, administered twice daily prior to the morning and evening meals, during Weeks 20-54. Participants in this arm were enrolled in protocol MK-0431A-170.

Arm type	Experimental
Investigational medicinal product name	Sitagliptin plus metformin
Investigational medicinal product code	
Other name	MK-0431A
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 2 tablets daily, one taken with a morning meal and one taken with an evening meal, to provide a total daily dose of 100 mg of sitagliptin and 1000mg, 1700mg or 2000 mg of metformin. Dosage of metformin was based on each participant's daily metformin dose prior to enrollment.

Investigational medicinal product name	Placebo to metformin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 2 tablets daily, one taken with a morning meal and one taken with an evening meal. Each tablet contained placebo to metformin.

Investigational medicinal product name	Insulin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants who met protocol-specific glycemic rescue criteria received insulin glargine as glycemic rescue therapy; participants on background insulin had their insulin dose increased for glycemic rescue.

Arm title	Metformin

Arm description:

Participants received one tablet of metformin and one tablet of placebo to sitagliptin/metformin, administered twice daily prior to the morning and evening meals, during Weeks 20-54. Participants in this arm were enrolled in protocol MK-0431A-170.

Arm type	Placebo
Investigational medicinal product name	Metformin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 2 tablets daily, one taken with a morning meal and one taken with an evening meal, to provide a total daily dose of 1000 mg, 1700 mg or 2000 mg of metformin. Dosage was based on each participant's daily metformin dose prior to enrollment.

Investigational medicinal product name	Insulin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants who met protocol-specific glycemic rescue criteria received insulin glargine as glycemic rescue therapy; participants on background insulin had their insulin dose increased for glycemic rescue.

Investigational medicinal product name	Placebo to sitagliptin plus metformin
Investigational medicinal product code	
Other name	Placebo to MK-0431A
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 2 tablets daily, one taken with a morning meal and one taken with an evening meal. Each tablet contained placebo to sitagliptin plus metformin.

Arm title	Sitagliptin/Metformin XR

Arm description:

Participants received two tablets of sitagliptin/metformin XR and two tablets of metformin XR placebo, administered once daily with a meal, during Weeks 20-54. Participants in this arm were enrolled in protocol MK-0431A-289.

Arm type	Experimental
Investigational medicinal product name	Sitagliptin plus metformin XR
Investigational medicinal product code	
Other name	MK-0431A XR
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 2 tablets daily, both taken together with a meal, to provide a total daily dose of 100 mg of sitagliptin and 1000mg, 1500mg or 2000 mg of metformin. Dosage of metformin XR was based on each participant's daily metformin dose prior to enrollment.

Investigational medicinal product name	Insulin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants who met protocol-specific glycemic rescue criteria received insulin glargine as glycemic rescue therapy; participants on background insulin had their insulin dose increased for glycemic rescue.

Investigational medicinal product name	Placebo to metformin XR
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 2 tablets daily, both taken together with a meal. Each tablet contained placebo to metformin XR.

Arm title	Metformin XR

Arm description:

Participants received two tablets of metformin XR and two tablets of placebo to sitagliptin/metformin XR, administered once daily with a meal, during Weeks 20-54. Participants in this arm were enrolled in protocol MK-0431A-289.

Arm type	Placebo
Investigational medicinal product name	Placebo to sitagliptin plus metformin XR
Investigational medicinal product code	
Other name	Placebo to MK-0431A XR
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 2 tablets daily, both taken together with a meal. Each tablet contained placebo to sitagliptin plus metformin XR.

Investigational medicinal product name	Metformin XR
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 2 tablets daily, both taken together with a meal, to provide a total daily dose of 1000 mg, 1500 mg or 2000 mg of metformin XR. Dosage was based on each participant's daily metformin dose prior to enrollment.

Investigational medicinal product name	Insulin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants who met protocol-specific glycemic rescue criteria received insulin glargine as glycemic rescue therapy; participants on background insulin had their insulin dose increased for glycemic rescue.

Number of subjects in period 3[3]	Sitagliptin/Metformin	Metformin	Sitagliptin/Metformin XR
Started	28	30	42
Completed	25	28	39
Not completed	3	2	3
Consent withdrawn by subject	2	1	1
Lost to follow-up	-	-	1
Consent withdrawn by Parent/Guardian	1	1	1

Number of subjects in period 3[3]	Metformin XR
Started	47
Completed	43
Not completed	4
Consent withdrawn by subject	2
Lost to follow-up	2
Consent withdrawn by Parent/Guardian	-

Notes:

[3] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Not all participants who completed the Weeks 0-20 Period continued in the Weeks 20-54 Period. In protocol MK-0431A-170, participants were required to re-consent to enter the Weeks 20-54 period, and many did not do so.

Baseline characteristics

Reporting groups	
Reporting group title	Sitagliptin/Metformin
Reporting group description:	
Participants received one tablet of sitagliptin/metformin and one tablet of metformin-placebo, administered twice daily prior to the morning and evening meals, during Weeks 0-20. Participants in this arm were enrolled in protocol MK-0431A-170.	
Reporting group title	Metformin
Reporting group description:	
Participants received one tablet of metformin and one tablet of placebo to sitagliptin/metformin, administered twice daily prior to the morning and evening meals, during Weeks 0-20. Participants in this arm were enrolled in protocol MK-0431A-170.	
Reporting group title	Sitagliptin/Metformin XR
Reporting group description:	
Participants received two tablets of sitagliptin/metformin XR and two tablets of metformin XR placebo, administered once daily with a meal, during Weeks 0-20. Participants in this arm were enrolled in protocol MK-0431A-289.	
Reporting group title	Metformin XR
Reporting group description:	
Participants received two tablets of metformin XR and two tablets of placebo to sitagliptin/metformin XR, administered once daily with a meal, during Weeks 0-20. Participants in this arm were enrolled in protocol MK-0431A-289.	

Reporting group values	Sitagliptin/Metformin	Metformin	Sitagliptin/Metformin XR
Number of subjects	62	62	45
Age Categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	10	7	3
Adolescents (12-17 years)	52	55	42
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	14.4	13.9	14.8
standard deviation	± 2.2	± 1.8	± 1.9
Gender Categorical Units: Subjects			
Female	41	40	32
Male	21	22	13
Race Units: Subjects			
American Indian Or Alaska Native	0	1	3
Asian	21	22	15

Native Hawaiian or Other Pacific Islander	1	1	0
Black or African American	2	2	2
White	24	23	22
More than one race	14	13	3
Ethnicity			
Units: Subjects			
Hispanic or Latino	23	23	11
Not Hispanic or Latino	35	36	29
Unknown or Not Reported	4	3	5
Glycated Hemoglobin (A1C)			
A1C is a blood marker used to report average blood glucose levels over prolonged periods of time. A1C is the ratio of glycated hemoglobin to total hemoglobin x 100. The analysis population includes all randomized participants who received ≥1 dose of study medication and had a baseline measurement of A1C.			
Units: Percentage			
arithmetic mean	8.02	8.13	7.87
standard deviation	± 1.22	± 1.08	± 0.94

Reporting group values	Metformin XR	Total	
Number of subjects	51	220	
Age Categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	1	21	
Adolescents (12-17 years)	50	199	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous			
Units: years			
arithmetic mean	14.9		
standard deviation	± 1.6	-	
Gender Categorical			
Units: Subjects			
Female	32	145	
Male	19	75	
Race			
Units: Subjects			
American Indian Or Alaska Native	9	13	
Asian	6	64	
Native Hawaiian or Other Pacific Islander	0	2	
Black or African American	4	10	
White	27	96	
More than one race	5	35	
Ethnicity			
Units: Subjects			

Hispanic or Latino	20	77	
Not Hispanic or Latino	28	128	
Unknown or Not Reported	3	15	

Glycated Hemoglobin (A1C)			
A1C is a blood marker used to report average blood glucose levels over prolonged periods of time. A1C is the ratio of glycated hemoglobin to total hemoglobin x 100. The analysis population includes all randomized participants who received ≥1 dose of study medication and had a baseline measurement of A1C.			
Units: Percentage			
arithmetic mean	7.97		
standard deviation	± 1.05	-	

Subject analysis sets

Subject analysis set title	Sitagliptin/Metformin and Sitagliptin/Metformin XR Pooled
Subject analysis set type	Full analysis

Subject analysis set description:

This analysis set contains the pooled population of treated participants from the experimental-drug groups "Sitagliptin/Metformin" (from protocol MK-0431A-170) and "Sitagliptin/Metformin XR" (from protocol MK-0431A-289).

Subject analysis set title	Metformin and Metformin XR Pooled
Subject analysis set type	Full analysis

Subject analysis set description:

This analysis set contains the pooled population of treated participants from the placebo groups "Metformin" (from protocol MK-0431A-170) and "Metformin XR" (from protocol MK-0431A-289).

Reporting group values	Sitagliptin/Metformin and Sitagliptin/Metformin XR Pooled	Metformin and Metformin XR Pooled	
Number of subjects	107	113	
Age Categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	13	8	
Adolescents (12-17 years)	94	105	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous Units: years			
arithmetic mean	14.5	14.4	
standard deviation	± 2.1	± 1.8	
Gender Categorical Units: Subjects			
Female	73	72	
Male	34	41	
Race Units: Subjects			
American Indian Or Alaska Native	3	10	

Asian	36	28	
Native Hawaiian or Other Pacific Islander	1	1	
Black or African American	4	6	
White	46	50	
More than one race	17	18	
Ethnicity Units: Subjects			
Hispanic or Latino	34	43	
Not Hispanic or Latino	64	64	
Unknown or Not Reported	9	6	
Glycated Hemoglobin (A1C)			
A1C is a blood marker used to report average blood glucose levels over prolonged periods of time. A1C is the ratio of glycated hemoglobin to total hemoglobin x 100. The analysis population includes all randomized participants who received ≥1 dose of study medication and had a baseline measurement of A1C.			
Units: Percentage			
arithmetic mean	7.96	8.06	
standard deviation	± 1.11	± 1.07	

End points

End points reporting groups

Reporting group title	Sitagliptin/Metformin
Reporting group description:	
Participants received one tablet of sitagliptin/metformin and one tablet of metformin-placebo, administered twice daily prior to the morning and evening meals, during Weeks 0-20. Participants in this arm were enrolled in protocol MK-0431A-170.	
Reporting group title	Metformin
Reporting group description:	
Participants received one tablet of metformin and one tablet of placebo to sitagliptin/metformin, administered twice daily prior to the morning and evening meals, during Weeks 0-20. Participants in this arm were enrolled in protocol MK-0431A-170.	
Reporting group title	Sitagliptin/Metformin XR
Reporting group description:	
Participants received two tablets of sitagliptin/metformin XR and two tablets of metformin XR placebo, administered once daily with a meal, during Weeks 0-20. Participants in this arm were enrolled in protocol MK-0431A-289.	
Reporting group title	Metformin XR
Reporting group description:	
Participants received two tablets of metformin XR and two tablets of placebo to sitagliptin/metformin XR, administered once daily with a meal, during Weeks 0-20. Participants in this arm were enrolled in protocol MK-0431A-289.	
Reporting group title	Sitagliptin/Metformin
Reporting group description:	
Participants received one tablet of sitagliptin/metformin and one tablet of metformin-placebo, administered twice daily prior to the morning and evening meals, during Weeks 0-20. Participants in this arm were enrolled in protocol MK-0431A-170.	
Reporting group title	Metformin
Reporting group description:	
Participants received one tablet of metformin and one tablet of placebo to sitagliptin/metformin, administered twice daily prior to the morning and evening meals, during Weeks 0-20. Participants in this arm were enrolled in protocol MK-0431A-170.	
Reporting group title	Sitagliptin/Metformin XR
Reporting group description:	
Participants received two tablets of sitagliptin/metformin XR and two tablets of metformin XR placebo, administered once daily with a meal, during Weeks 0-20. Participants in this arm were enrolled in protocol MK-0431A-289.	
Reporting group title	Metformin XR
Reporting group description:	
Participants received two tablets of metformin XR and two tablets of placebo to sitagliptin/metformin XR, administered once daily with a meal, during Weeks 0-20. Participants in this arm were enrolled in protocol MK-0431A-289.	
Reporting group title	Sitagliptin/Metformin
Reporting group description:	
Participants received one tablet of sitagliptin/metformin and one tablet of metformin-placebo, administered twice daily prior to the morning and evening meals, during Weeks 20-54. Participants in this arm were enrolled in protocol MK-0431A-170.	
Reporting group title	Metformin
Reporting group description:	
Participants received one tablet of metformin and one tablet of placebo to sitagliptin/metformin, administered twice daily prior to the morning and evening meals, during Weeks 20-54. Participants in this arm were enrolled in protocol MK-0431A-170.	
Reporting group title	Sitagliptin/Metformin XR
Reporting group description:	
Participants received two tablets of sitagliptin/metformin XR and two tablets of metformin XR placebo, administered once daily with a meal, during Weeks 20-54. Participants in this arm were enrolled in	

protocol MK-0431A-289.

Reporting group title	Metformin XR

Reporting group description:

Participants received two tablets of metformin XR and two tablets of placebo to sitagliptin/metformin XR, administered once daily with a meal, during Weeks 20-54. Participants in this arm were enrolled in protocol MK-0431A-289.

Subject analysis set title	Sitagliptin/Metformin and Sitagliptin/Metformin XR Pooled
Subject analysis set type	Full analysis

Subject analysis set description:

This analysis set contains the pooled population of treated participants from the experimental-drug groups "Sitagliptin/Metformin" (from protocol MK-0431A-170) and "Sitagliptin/Metformin XR" (from protocol MK-0431A-289).

Subject analysis set title	Metformin and Metformin XR Pooled
Subject analysis set type	Full analysis

Subject analysis set description:

This analysis set contains the pooled population of treated participants from the placebo groups "Metformin" (from protocol MK-0431A-170) and "Metformin XR" (from protocol MK-0431A-289).

Primary: Change from Baseline in A1C at Week 20

End point title	Change from Baseline in A1C at Week 20

End point description:

Glycated hemoglobin (A1C) is a blood marker used to report average blood glucose levels over prolonged periods of time. Percentage A1C is the ratio of glycated hemoglobin to total hemoglobin x 100. Mean change from baseline at Week 20 was estimated from a longitudinal data analysis model. The analysis population includes all randomized participants who received ≥1 dose of study medication and who had at least 1 measurement of A1C. Per protocol, only the pooled analysis groups were analyzed for this primary endpoint.

End point type	Primary

End point timeframe:

Baseline and Week 20

End point values	Sitagliptin/Metformin and Sitagliptin/Metformin XR Pooled	Metformin and Metformin XR Pooled		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	107	113		
Units: Percentage				
least squares mean (confidence interval 95%)				
Change from Baseline at Week 20	-0.58 (-0.94 to -0.22)	-0.09 (-0.43 to 0.26)		

Statistical analyses

Statistical analysis title	Difference in Change from Baseline

Statistical analysis description:

The Least Squares (LS) Mean for the arm "Sitagliptin/Metformin and Sitagliptin/Metformin XR Pooled" is compared against that of "Metformin and Metformin XR Pooled."

Comparison groups	Sitagliptin/Metformin and Sitagliptin/Metformin XR Pooled v Metformin and Metformin XR Pooled

Number of subjects included in analysis	220
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.018
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-0.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	-0.09

Primary: Number of participants who experienced ≥1 Adverse Event During Weeks 0-20

End point title	Number of participants who experienced ≥1 Adverse Event During Weeks 0-20

End point description:

The number of participants experiencing ≥1 adverse event during Weeks 0-20 was reported. An adverse event is defined as any untoward medical occurrence in a person administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. The analysis population includes all randomized participants who received ≥1 dose of study medication.

End point type	Primary

End point timeframe:

Up to Week 20

End point values	Sitagliptin/Metformin	Metformin	Sitagliptin/Metformin XR	Metformin XR
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	62	62	45	51
Units: Participants	42	46	29	30

End point values	Sitagliptin/Metformin and Sitagliptin/Metformin XR Pooled	Metformin and Metformin XR Pooled		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	107	113		
Units: Participants	71	76		

Statistical analyses

Statistical analysis title	Difference in Percentage
Comparison groups	Sitagliptin/Metformin and Sitagliptin/Metformin XR Pooled v Metformin and Metformin XR Pooled
Number of subjects included in analysis	220
Analysis specification	Pre-specified
Analysis type	other[1]
Parameter estimate	Difference in Percentage
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.9
upper limit	11.3

Notes:

[1] - The percentage of participants who experienced ≥1 adverse event for the arm "Sitagliptin/Metformin and Sitagliptin/Metformin XR Pooled" is compared against that of "Metformin and Metformin XR Pooled."

Primary: Number of Participants Who Discontinued Study Drug Due to Experiencing an Adverse Event During Weeks 0-20

End point title	Number of Participants Who Discontinued Study Drug Due to Experiencing an Adverse Event During Weeks 0-20

End point description:

The number of participants who discontinued from study drug due to an adverse event during Weeks 0-20 was reported. An adverse event is defined as any untoward medical occurrence in a person administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. The analysis population includes all randomized participants who received ≥1 dose of study medication.

End point type	Primary

End point timeframe:

Up to Week 20

End point values	Sitagliptin/Metformin	Metformin	Sitagliptin/Metformin XR	Metformin XR
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	62	62	45	51
Units: Participants	1	2	2	2

End point values	Sitagliptin/Metformin and Sitagliptin/Metformin XR Pooled	Metformin and Metformin XR Pooled		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	107	113		
Units: Participants	3	4		

Statistical analyses

Statistical analysis title	Difference in Percentage

Statistical analysis description:

The percentage of participants who discontinued study drug due to experiencing an adverse event for the arm "Sitagliptin/Metformin and Sitagliptin/Metformin XR Pooled" is compared against that of "Metformin and Metformin XR Pooled."

Comparison groups	Sitagliptin/Metformin and Sitagliptin/Metformin XR Pooled v Metformin and Metformin XR Pooled
Number of subjects included in analysis	220
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Percentage
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.2
upper limit	5

Primary: Number of Participants Who Experienced ≥1 Adverse Event During Weeks 0-56

End point title	Number of Participants Who Experienced ≥1 Adverse Event During Weeks 0-56

End point description:

The number of participants experiencing ≥1 adverse event during Weeks 0-56 were reported. An adverse event is defined as any untoward medical occurrence in a person administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. The analysis population includes all randomized participants who received ≥1 dose of study medication and continued in the study beyond Week 20.

End point type	Primary

End point timeframe:

Up to approximately Week 56

End point values	Sitagliptin/Metformin	Metformin	Sitagliptin/Metformin XR	Metformin XR
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	30	42	47
Units: Participants	26	27	36	39

End point values	Sitagliptin/Metformin and Sitagliptin/Metformin XR Pooled	Metformin and Metformin XR Pooled		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	70	77		
Units: Participants	62	66		

Statistical analyses

Statistical analysis title	Difference in Percentage
Statistical analysis description:	
The percentage of participants who experienced ≥1 adverse event for the arm "Sitagliptin/Metformin and Sitagliptin/Metformin XR Pooled" is compared against that of "Metformin and Metformin XR Pooled."	
Comparison groups	Sitagliptin/Metformin and Sitagliptin/Metformin XR Pooled v Metformin and Metformin XR Pooled
Number of subjects included in analysis	147
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Percentage
Point estimate	2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.9
upper limit	14.4

Primary: Number of Participants Who Discontinued Study Drug Due to Experiencing an Adverse Event During Weeks 0-54

End point title	Number of Participants Who Discontinued Study Drug Due to Experiencing an Adverse Event During Weeks 0-54
End point description:	
The number of participants who discontinued from study drug due to an adverse event during Weeks 0-54 was reported. An adverse event is defined as any untoward medical occurrence in a person administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. The analysis population includes all randomized participants who received ≥1 dose of study medication and continued in the study beyond Week 20.	
End point type	Primary
End point timeframe:	
Up to Week 54	

End point values	Sitagliptin/Metformin	Metformin	Sitagliptin/Metformin XR	Metformin XR
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	30	42	47
Units: Participants	1	1	1	3

End point values	Sitagliptin/Metformin and Sitagliptin/Metformin XR Pooled	Metformin and Metformin XR Pooled		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	70	77		
Units: Participants	2	4		

Statistical analyses

Statistical analysis title	Difference in Percentage

Statistical analysis description:

The percentage of participants who discontinued study drug due to experiencing an adverse event for the arm "Sitagliptin/Metformin and Sitagliptin/Metformin XR Pooled" is compared against that of "Metformin and Metformin XR Pooled."

Comparison groups	Sitagliptin/Metformin and Sitagliptin/Metformin XR Pooled v Metformin and Metformin XR Pooled
Number of subjects included in analysis	147
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Percentage
Point estimate	-2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.1
upper limit	5.8

Secondary: Change from baseline in A1C at Week 54

End point title	Change from baseline in A1C at Week 54

End point description:

A1C is a blood marker used to report average blood glucose levels over prolonged periods of time. Percentage A1C is the ratio of glycated hemoglobin to total hemoglobin x 100. Mean change from baseline at Week 54 was estimated from a longitudinal data analysis model. The analysis population includes all randomized participants who received ≥1 dose of study medication, had at least 1 measurement of A1C, and continued in the study beyond Week 20. Per protocol, only the pooled analysis groups were analyzed for this secondary endpoint.

End point type	Secondary

End point timeframe:

Baseline and Week 54

End point values	Sitagliptin/Metformin and Sitagliptin/Metformin XR Pooled	Metformin and Metformin XR Pooled		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	70	77		
Units: Percentage				
least squares mean (confidence interval 95%)	0.35 (-0.48 to 1.19)	0.73 (-0.08 to 1.54)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Fasting Plasma Glucose (FPG) at Week 20

End point title	Change from Baseline in Fasting Plasma Glucose (FPG) at Week 20

End point description:

Blood glucose was measured on a fasting basis. Mean change from baseline at Week 20 was estimated from a longitudinal data analysis model. The analysis population includes all randomized participants who received ≥1 dose of study medication, and who had at least 1 measurement of FPG. Per protocol, only the pooled analysis groups were analyzed for this secondary endpoint.

End point type	Secondary

End point timeframe:

Baseline and Week 20

End point values	Sitagliptin/Metformin and Sitagliptin/Metformin XR Pooled	Metformin and Metformin XR Pooled		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	107	113		
Units: mg/dL				
least squares mean (confidence interval 95%)	-2.5 (-16.7 to 11.7)	8.3 (-5.0 to 21.6)		

Statistical analyses

Statistical analysis title	Difference in Change from Baseline

Statistical analysis description:

The Least Squares (LS) Mean for the arm "Sitagliptin/Metformin and Sitagliptin/Metformin XR Pooled" is compared against that of "Metformin and Metformin XR Pooled."

Comparison groups	Sitagliptin/Metformin and Sitagliptin/Metformin XR Pooled v Metformin and Metformin XR Pooled

Number of subjects included in analysis	220
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.159
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-10.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-25.9
upper limit	4.3

Secondary: Change from Baseline in FPG at Week 54

End point title	Change from Baseline in FPG at Week 54

End point description:

Blood glucose was measured on a fasting basis. Mean change from baseline at Week 54 was estimated from a longitudinal data analysis model. The analysis population includes all randomized participants who received ≥1 dose of study medication, had at least 1 measurement of FPG, and continued in the study beyond Week 20. Per protocol, only the pooled analysis groups were analyzed for this secondary endpoint.

End point type	Secondary

End point timeframe:

Baseline and Week 54

End point values	Sitagliptin/Metformin and Sitagliptin/Metformin XR Pooled	Metformin and Metformin XR Pooled		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	70	77		
Units: mg/dL				
least squares mean (confidence interval 95%)	16.8 (-8.4 to 42.0)	16.9 (-7.0 to 40.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with A1C at Goal (<7.0%) at Week 20

End point title	Percentage of Participants with A1C at Goal (<7.0%) at Week 20

End point description:

Percentage of participants with A1C at goal (<7.0%) at Week 20 was presented. The analysis population includes all randomized participants who received ≥1 dose of study medication. Per protocol, only the pooled analysis groups were analyzed for this secondary endpoint.

End point type	Secondary

End point timeframe:

Week 20

End point values	Sitagliptin/Metformin and Sitagliptin/Metformin XR Pooled	Metformin and Metformin XR Pooled		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	107	113		
Units: Percentage				
number (not applicable)	43.0	31.0		

Statistical analyses

Statistical analysis title	Difference in Percentage

Statistical analysis description:

The percentage of participants with A1C at the A1C goal (<7.0%) in the arm "Sitagliptin/Metformin and Sitagliptin/Metformin XR Pooled" is compared against that of "Metformin and Metformin XR Pooled." For estimating the treatment difference, when the A1C result for a participant at Week 20 was not available, a multiple imputation method was used to impute whether the participant had met the goal.

Comparison groups	Sitagliptin/Metformin and Sitagliptin/Metformin XR Pooled v Metformin and Metformin XR Pooled
Number of subjects included in analysis	220
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.017
Method	Miettinen and Nurminen
Parameter estimate	Difference in Percentage
Point estimate	16
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.9
upper limit	28.9

Secondary: Percentage of Participants with A1C at Goal (<6.5%) at Week 20

End point title	Percentage of Participants with A1C at Goal (<6.5%) at Week 20

End point description:

Percentage of participants with A1C at goal (<6.5%) at Week 20 was presented. The analysis population includes all randomized participants who received ≥1 dose of study medication. Per protocol, only the pooled analysis groups were analyzed for this secondary endpoint.

End point type	Secondary

End point timeframe:

Week 20

End point values	Sitagliptin/Metformin and Sitagliptin/Metformin XR Pooled	Metformin and Metformin XR Pooled		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	107	113		
Units: Percentage				
number (not applicable)	29.0	20.4		

Statistical analyses

Statistical analysis title	Difference in Percentage

Statistical analysis description:

The percentage of participants with A1C at the A1C goal (<6.5%) in the arm "Sitagliptin/Metformin and Sitagliptin/Metformin XR Pooled" is compared against that of "Metformin and Metformin XR Pooled." For estimating the treatment difference, when the A1C result for a participant at Week 20 was not available, a multiple imputation method was used to impute whether the participant had met the goal.

Comparison groups	Sitagliptin/Metformin and Sitagliptin/Metformin XR Pooled v Metformin and Metformin XR Pooled
Number of subjects included in analysis	220
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.049
Method	Miettinen and Nurminen
Parameter estimate	Difference in Percentage
Point estimate	12.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	24.8

Secondary: Percentage of Participants with A1C at Goal (<7.0%) at Week 54

End point title	Percentage of Participants with A1C at Goal (<7.0%) at Week 54

End point description:

Percentage of participants with A1C at goal (<7.0%) at Week 54 was presented. The analysis population includes all randomized participants who received ≥1 dose of study medication and continued in the study beyond Week 20. Per protocol, only the pooled analysis groups were analyzed for this secondary endpoint.

End point type	Secondary

End point timeframe:

Week 54

End point values	Sitagliptin/Metformin and Sitagliptin/Metformin XR Pooled	Metformin and Metformin XR Pooled		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	70	77		
Units: Percentage				
number (not applicable)	31.4	27.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with A1C at Goal (<6.5%) at Week 54

End point title	Percentage of Participants with A1C at Goal (<6.5%) at Week 54

End point description:

Percentage of participants with A1C at goal (<6.5%) at Week 54 was presented. The analysis population includes all randomized participants who received ≥1 dose of study medication and continued in the study beyond Week 20. Per protocol, only the pooled analysis groups were analyzed for this secondary endpoint.

End point type	Secondary

End point timeframe:

Week 54

End point values	Sitagliptin/Metformin and Sitagliptin/Metformin XR Pooled	Metformin and Metformin XR Pooled		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	70	77		
Units: Percentage				
number (not applicable)	18.6	19.5		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Initiating Glycemic Rescue Therapy by Week 20

End point title	Percentage of Participants Initiating Glycemic Rescue Therapy by Week 20

End point description:

Percentage of participants who initiated glycemic rescue therapy prior to Week 20 was reported. The analysis population includes all randomized participants who received ≥1 dose of study medication.

End point type	Secondary

End point timeframe:

Up to Week 20

End point values	Sitagliptin/Metformin	Metformin	Sitagliptin/Metformin XR	Metformin XR
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	62	62	45	51
Units: Percentage				
number (not applicable)	3.2	19.4	4.4	13.7

End point values	Sitagliptin/Metformin and Sitagliptin/Metformin XR Pooled	Metformin and Metformin XR Pooled		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	107	113		
Units: Percentage				
number (not applicable)	3.7	16.8		

Statistical analyses

Statistical analysis title	Difference in Percentage

Statistical analysis description:

The percentage of participants initiating glycemic rescue therapy in the arm "Sitagliptin/Metformin and Sitagliptin/Metformin XR Pooled" is compared against that of "Metformin and Metformin XR Pooled."

Comparison groups	Sitagliptin/Metformin and Sitagliptin/Metformin XR Pooled v Metformin and Metformin XR Pooled
Number of subjects included in analysis	220
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Log-Rank Test
Parameter estimate	Kaplan-Meier Difference in Percentage
Point estimate	-13.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.1
upper limit	-5.3

Secondary: Percentage of Participants Initiating Insulin Glargine During Weeks 20-54

End point title	Percentage of Participants Initiating Insulin Glargine During Weeks 20-54

End point description:

Percentage of participants who initiated insulin glargine therapy from Weeks 20 through 54 was reported. The analysis population includes all randomized participants who received ≥1 dose of study medication and continued in the study beyond Week 20 without initiating glycemic rescue therapy before Week 20. Per protocol, only the pooled analysis groups were analyzed for this secondary endpoint.

End point type	Secondary

End point timeframe:

Week 20 up to Week 54

End point values	Sitagliptin/Metformin and Sitagliptin/Metformin XR Pooled	Metformin and Metformin XR Pooled		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	66	64		
Units: Percentage				
number (not applicable)	22.7	26.6		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 56 weeks for non serious adverse events. Up to approximately 8 years for serious adverse events and deaths.

Adverse event reporting additional description:

"Pooled Sita/Met FDC" = "Sita/Met IR FDC" plus "Sita/Met XR FDC." "Pooled Metformin" = "Metformin IR" plus "Metformin XR."

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	Sita/Met IR FDC
Reporting group description: -	
Reporting group title	Metformin IR
Reporting group description: -	
Reporting group title	Sita/Met XR FDC
Reporting group description: -	
Reporting group title	Metformin XR
Reporting group description: -	
Reporting group title	Pooled Sita/Met FDC
Reporting group description: -	
Reporting group title	Pooled Metformin

Reporting group description: -

Serious adverse events	Sita/Met IR FDC	Metformin IR	Sita/Met XR FDC
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 62 (6.45%)	3 / 62 (4.84%)	3 / 45 (6.67%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Blood glucose increased			
subjects affected / exposed	0 / 62 (0.00%)	1 / 62 (1.61%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Epilepsy			
subjects affected / exposed	0 / 62 (0.00%)	1 / 62 (1.61%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 62 (1.61%)	0 / 62 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Immune system disorders			
Type I hypersensitivity			
subjects affected / exposed	1 / 62 (1.61%)	0 / 62 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 62 (0.00%)	0 / 62 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 62 (0.00%)	0 / 62 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 62 (0.00%)	0 / 62 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 62 (1.61%)	0 / 62 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	0 / 62 (0.00%)	0 / 62 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			

Synovial cyst			
subjects affected / exposed	1 / 62 (1.61%)	0 / 62 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 62 (0.00%)	0 / 62 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
H1N1 influenza			
subjects affected / exposed	0 / 62 (0.00%)	0 / 62 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	1 / 62 (1.61%)	0 / 62 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 62 (0.00%)	0 / 62 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 62 (0.00%)	1 / 62 (1.61%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Metformin XR	Pooled Sita/Met FDC	Pooled Metformin
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 51 (5.88%)	7 / 107 (6.54%)	6 / 113 (5.31%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Blood glucose increased			

subjects affected / exposed	0 / 51 (0.00%)	0 / 107 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Epilepsy			
subjects affected / exposed	0 / 51 (0.00%)	0 / 107 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 51 (0.00%)	1 / 107 (0.93%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Immune system disorders			
Type I hypersensitivity			
subjects affected / exposed	0 / 51 (0.00%)	1 / 107 (0.93%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 51 (1.96%)	0 / 107 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 51 (0.00%)	1 / 107 (0.93%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 51 (1.96%)	0 / 107 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			

subjects affected / exposed	0 / 51 (0.00%)	1 / 107 (0.93%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	1 / 51 (1.96%)	0 / 107 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Synovial cyst			
subjects affected / exposed	0 / 51 (0.00%)	1 / 107 (0.93%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 51 (0.00%)	1 / 107 (0.93%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
H1N1 influenza			
subjects affected / exposed	1 / 51 (1.96%)	0 / 107 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 51 (0.00%)	1 / 107 (0.93%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 51 (0.00%)	1 / 107 (0.93%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyperglycaemia			

subjects affected / exposed	1 / 51 (1.96%)	0 / 107 (0.00%)	2 / 113 (1.77%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Sita/Met IR FDC	Metformin IR	Sita/Met XR FDC
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 62 (54.84%)	40 / 62 (64.52%)	30 / 45 (66.67%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 62 (3.23%)	3 / 62 (4.84%)	3 / 45 (6.67%)
occurrences (all)	3	3	3
Blood creatine phosphokinase increased			
subjects affected / exposed	3 / 62 (4.84%)	1 / 62 (1.61%)	3 / 45 (6.67%)
occurrences (all)	3	1	3
Blood glucose increased			
subjects affected / exposed	3 / 62 (4.84%)	0 / 62 (0.00%)	2 / 45 (4.44%)
occurrences (all)	4	0	2
Creatinine renal clearance increased			
subjects affected / exposed	4 / 62 (6.45%)	0 / 62 (0.00%)	0 / 45 (0.00%)
occurrences (all)	4	0	0
Urine albumin/creatinine ratio increased			
subjects affected / exposed	4 / 62 (6.45%)	2 / 62 (3.23%)	0 / 45 (0.00%)
occurrences (all)	5	2	0
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 62 (4.84%)	8 / 62 (12.90%)	2 / 45 (4.44%)
occurrences (all)	4	10	4
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 62 (3.23%)	4 / 62 (6.45%)	4 / 45 (8.89%)
occurrences (all)	2	4	4
Abdominal pain upper			

subjects affected / exposed	1 / 62 (1.61%)	2 / 62 (3.23%)	0 / 45 (0.00%)
occurrences (all)	2	2	0
Diarrhoea			
subjects affected / exposed	7 / 62 (11.29%)	4 / 62 (6.45%)	1 / 45 (2.22%)
occurrences (all)	8	4	1
Nausea			
subjects affected / exposed	2 / 62 (3.23%)	5 / 62 (8.06%)	4 / 45 (8.89%)
occurrences (all)	5	5	6
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 62 (3.23%)	3 / 62 (4.84%)	3 / 45 (6.67%)
occurrences (all)	2	4	3
Oropharyngeal pain			
subjects affected / exposed	2 / 62 (3.23%)	1 / 62 (1.61%)	3 / 45 (6.67%)
occurrences (all)	2	1	3
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	5 / 62 (8.06%)	3 / 62 (4.84%)	3 / 45 (6.67%)
occurrences (all)	6	3	3
Influenza			
subjects affected / exposed	1 / 62 (1.61%)	4 / 62 (6.45%)	2 / 45 (4.44%)
occurrences (all)	1	5	3
Nasopharyngitis			
subjects affected / exposed	7 / 62 (11.29%)	7 / 62 (11.29%)	1 / 45 (2.22%)
occurrences (all)	11	7	2
Pharyngitis			
subjects affected / exposed	1 / 62 (1.61%)	3 / 62 (4.84%)	1 / 45 (2.22%)
occurrences (all)	1	3	1
Upper respiratory tract infection			
subjects affected / exposed	9 / 62 (14.52%)	6 / 62 (9.68%)	5 / 45 (11.11%)
occurrences (all)	11	8	9
Urinary tract infection			
subjects affected / exposed	0 / 62 (0.00%)	5 / 62 (8.06%)	3 / 45 (6.67%)
occurrences (all)	0	6	3
Metabolism and nutrition disorders			

Hyperglycaemia			
subjects affected / exposed	3 / 62 (4.84%)	5 / 62 (8.06%)	3 / 45 (6.67%)
occurrences (all)	3	6	3
Hypoglycaemia			
subjects affected / exposed	10 / 62 (16.13%)	6 / 62 (9.68%)	9 / 45 (20.00%)
occurrences (all)	106	15	70

Non-serious adverse events	Metformin XR	Pooled Sita/Met FDC	Pooled Metformin
Total subjects affected by non-serious adverse events			
subjects affected / exposed	36 / 51 (70.59%)	64 / 107 (59.81%)	76 / 113 (67.26%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 51 (5.88%)	5 / 107 (4.67%)	6 / 113 (5.31%)
occurrences (all)	3	6	6
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 51 (1.96%)	6 / 107 (5.61%)	2 / 113 (1.77%)
occurrences (all)	1	6	2
Blood glucose increased			
subjects affected / exposed	3 / 51 (5.88%)	5 / 107 (4.67%)	3 / 113 (2.65%)
occurrences (all)	5	6	5
Creatinine renal clearance increased			
subjects affected / exposed	0 / 51 (0.00%)	4 / 107 (3.74%)	0 / 113 (0.00%)
occurrences (all)	0	4	0
Urine albumin/creatinine ratio increased			
subjects affected / exposed	0 / 51 (0.00%)	4 / 107 (3.74%)	2 / 113 (1.77%)
occurrences (all)	0	5	2
Nervous system disorders			
Headache			
subjects affected / exposed	10 / 51 (19.61%)	5 / 107 (4.67%)	18 / 113 (15.93%)
occurrences (all)	15	8	25
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 51 (7.84%)	6 / 107 (5.61%)	8 / 113 (7.08%)
occurrences (all)	4	6	8
Abdominal pain upper			

subjects affected / exposed	3 / 51 (5.88%)	1 / 107 (0.93%)	5 / 113 (4.42%)
occurrences (all)	4	2	6
Diarrhoea			
subjects affected / exposed	3 / 51 (5.88%)	8 / 107 (7.48%)	7 / 113 (6.19%)
occurrences (all)	10	9	14
Nausea			
subjects affected / exposed	2 / 51 (3.92%)	6 / 107 (5.61%)	7 / 113 (6.19%)
occurrences (all)	3	11	8
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 51 (3.92%)	5 / 107 (4.67%)	5 / 113 (4.42%)
occurrences (all)	2	5	6
Oropharyngeal pain			
subjects affected / exposed	1 / 51 (1.96%)	5 / 107 (4.67%)	2 / 113 (1.77%)
occurrences (all)	6	5	7
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	2 / 51 (3.92%)	8 / 107 (7.48%)	5 / 113 (4.42%)
occurrences (all)	2	9	5
Influenza			
subjects affected / exposed	3 / 51 (5.88%)	3 / 107 (2.80%)	7 / 113 (6.19%)
occurrences (all)	5	4	10
Nasopharyngitis			
subjects affected / exposed	2 / 51 (3.92%)	8 / 107 (7.48%)	9 / 113 (7.96%)
occurrences (all)	3	13	10
Pharyngitis			
subjects affected / exposed	5 / 51 (9.80%)	2 / 107 (1.87%)	8 / 113 (7.08%)
occurrences (all)	6	2	9
Upper respiratory tract infection			
subjects affected / exposed	3 / 51 (5.88%)	14 / 107 (13.08%)	9 / 113 (7.96%)
occurrences (all)	5	20	13
Urinary tract infection			
subjects affected / exposed	1 / 51 (1.96%)	3 / 107 (2.80%)	6 / 113 (5.31%)
occurrences (all)	1	3	7
Metabolism and nutrition disorders			

Hyperglycaemia			
subjects affected / exposed	4 / 51 (7.84%)	6 / 107 (5.61%)	9 / 113 (7.96%)
occurrences (all)	4	6	10
Hypoglycaemia			
subjects affected / exposed	10 / 51 (19.61%)	19 / 107 (17.76%)	16 / 113 (14.16%)
occurrences (all)	45	176	60

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 September 2012	MK-0431A-170 AM01 (Base study): Incorporated procedural and administrative changes.
17 April 2014	MK-0431A-170 AM02 (Base study): Updated analyses to reflect the pooled analysis. Reduced the sample size from 240 to 90 participants and analysis was combined with study MK-0431A-289 with adequate power for the primary analysis at Week 20. The timeframe required for participants to be off insulin therapy before Visit 1 was reduced from 6 months to 12 weeks. A1C lower limit for inclusion changed from ≥7.0% to ≥6.5%.
17 April 2014	MK-0431A-170 AM03 (Extension study): Created the 34-week extension study.
17 April 2014	MK-0431A-289 AM04: Modified the timeframe for prior treatment with insulin from 6 months to 12 weeks. A1C lower limit for inclusion changed from ≥7% to ≥6.5%. Sample size was reduced from 240 to 90 participants and analysis was combined with study MK-0431A-170 with adequate power for the primary analysis at Week 20.
09 January 2015	MK-0431A-170 AM04 (Base study): Included participants on background insulin.
09 January 2015	MK-0431A-170 AM05 (Extension study): Included participants on background insulin.
20 January 2015	MK-0431A-289 AM05: Included participants on background insulin.
10 April 2015	MK-0431A-170 AM07 (Base study): Changed "adverse experience" to "adverse event."
10 April 2015	MK-0431A-170 AM08 (Extension study): Changed "adverse experience" to "adverse event."
09 September 2015	MK-0431A-289 AM07: Changed "adverse experience" to "adverse event." Complied with recommendations from the FDA to minimize missing data.
04 November 2015	MK-0431A-170 AM11 (Base study): Complied with recommendations from the FDA to minimize missing data. Updated sample size from approximately 90 participants to approximately 130 participants.
04 November 2015	MK-0431A-170 AM12 (Extension study): Complied with recommendations from the FDA to minimize missing data. Updated sample size from approximately 90 participants to approximately 130 participants.
12 April 2018	MK-0431A-289 AM10: Complied with the recommendations from a health authority. Increased sample size. Clarified statistical methods for analyses using the Treatment Effect estimand. Added analyses using the Treatment Policy estimand.
12 April 2018	MK-0431A-170 AM15 (Base study): Modified sample size. Beginning and end of study were defined. Clarified statistical methods for analyses using the Treatment Effect estimand. Added analyses using the Treatment Policy estimand.
12 April 2018	MK-0431A-170 AM16 (Extension study): Modified sample size. Beginning and end of study were defined.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported