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CLINICAL STUDY REPORT

Sponsor Name	Merck Sharp & Dohme LLC, Rahway, NJ, USA
Compound Name	Sitagliptin (MK-0431)
Protocol Title	A Five-year, Observational, Non-interventional Follow-up to: A Phase III, Multicenter, Double-Blind, Randomized, Placebo-Controlled Clinical Trial to Evaluate the Safety and Efficacy of Sitagliptin in Pediatric Patients with Type 2 Diabetes Mellitus with Inadequate Glycemic Control
CSR Identification	P351MK0431
Indication	Type 2 diabetes mellitus
Study Design	Multicenter, safety, observational, noninterventional, multinational, 5-year follow-up study
Phase	4
First Participant First Visit	24-DEC-2013
Study Completion Date	08-AUG-2024 last participant last visit
Report Date	27-NOV-2024
Revised Report Date	Not applicable
Previous CSR Identification	Not applicable
GCP Compliance	This study was conducted in accordance with local and/or national regulations (including all applicable data protection laws and regulations), ICH GCP, and the ethical principles that have their origin in the Declaration of Helsinki regarding IEC review, informed consent, and the protection of human participants in biomedical research.
Questions about the clinical study report should be directed to the study research staff by using the toll-free number 1-888-577-8839.	

2 SYNOPSIS

Abbreviations are defined in the list of abbreviations located at the end of the Synopsis.

SPONSOR: Merck Sharp & Dohme LLC, Rahway, NJ, USA (hereafter called the Sponsor or MSD)

COMPOUND NAME: Sitagliptin (MK-0431)

PROTOCOL TITLE: A Five-year, Observational, Non-interventional Follow-up to: A Phase III, Multicenter, Double-Blind, Randomized, Placebo -Controlled Clinical Trial to Evaluate the Safety and Efficacy of Sitagliptin in Pediatric Patients with Type 2 Diabetes Mellitus with Inadequate Glycemic Control

STUDY IDENTIFIERS:

IND: Not applicable	EudraCT: Not applicable	WHO/UTN: Not applicable	NCT: Not applicable
jRCT: Not applicable	EU CT: Not applicable	EU PAS: 4468	

STUDY PHASE: Phase 4

INDICATION: Type 2 diabetes mellitus

STUDY CENTERS: This study was conducted at 39 centers in 16 countries.

STUDY STATUS:
This study is complete; this report is based on the final analysis.

First Participant First Visit	24-DEC-2013
Last Participant Last Visit	08-AUG-2024
Database Lock Date	09-AUG-2024

METHODOLOGY:

P351 was an observational, noninterventional, multisite, follow-up study to provide an up to 5-year observational assessment of safety for participants with T2DM who were 10 to 17 years of age (inclusive) when randomized to therapy in the MK-0431-083 (hereinafter referred to as P083).

In P083, which contained Phases A and B, participants received sitagliptin ± insulin throughout the study, metformin throughout the study, placebo in Phase A followed by sitagliptin in Phase B (placebo/sitagliptin), or placebo ± insulin in Phase A followed by

metformin in Phase B (placebo ± insulin/metformin), depending on randomization and the amendment under which they were enrolled.

Participants who completed P083 were eligible to provide assent/consent for P351 at or within 6 months of the Week-54 visit of P083; participants who did not complete P083 were eligible to provide assent/consent for P351 at the time or within 6 months of when their Week-54 visit for P083 would have occurred.

Participants observed in P351 received standard of care as provided by their usual care physician. During P351, participants attended annual onsite visits and received telephone calls at 6-month intervals between visits for up to 5 years or for 2 years after reaching Tanner Stage V, whichever occurred earlier. Regardless of when the assent/consent for P351 was obtained, the last possible visit (Year +5) occurred no later than 5 years after the participant was scheduled to complete the Week-54 visit for P083.

Part of this study was conducted during the COVID-19 pandemic. The Sponsor continued to follow its SOPs for study conduct, monitoring, and oversight during the pandemic and employed a risk-based approach to assess and mitigate impact of the pandemic on study conduct.

ELIGIBILITY CRITERIA:

Randomized participants from P083 (including those who discontinued study medication and those who withdrew consent) were eligible to participate in P351 if they met enrollment criteria. Participants and/or their parent/legal guardians who were unable to or chose not to provide assent/consent when the participant completed or was scheduled for their Week-54 visit during P083 were allowed to do so within 6 months after the Week-54 visit.

OBJECTIVES AND ENDPOINTS:

Primary Objective: To assess safety for up to a 5-year period in pediatric subjects (ages 10 to 17 years at the initiation of therapy in P083) with T2DM who participated for up to one year in P083.

Endpoints: Adverse events (AEs), BMI (body mass index), BMI SDS (body mass index standard deviation score), height, body weight, Tanner Staging (pubertal progression), growth velocity, blood pressure, and heart rate

NUMBER OF PARTICIPANTS (planned and analyzed):

The number of participants enrolled in P351 was not prespecified. A total of 80 participants were enrolled in P351.

STATISTICAL AND ANALYSIS METHODS:

Safety analyses were performed in the all subjects followed-up (ASF) population, which consisted of all participants enrolled in P351. Summaries classified participants as Exposed to Sitagliptin in P083 or Not Exposed in P083, based on their randomized treatment group

from P083. Formal statistical between-group comparisons were not performed. Clinical judgment was used to assess potential differences in safety parameters between participants exposed and not exposed to sitagliptin in P083. To accommodate potentially differential follow-up durations for participants in P351, follow-up adjusted incidence rates (FAIR) are provided for AE summary measures and all specific AEs.

RESULTS:

Participant Disposition

Disposition of Participants

	Exposed to Sitagliptin in P083[a] n (%)	Not Exposed in P083[b] n (%)	Total n (%)
Enrolled in P351	36	44	80
Completed	24 (66.7)	33 (75.0)	57 (71.3)
Discontinued	12 (33.3)	11 (25.0)	23 (28.8)
Death	1 (2.8)	0 (0.0)	1 (1.3)
Lost To Follow-Up	4 (11.1)	2 (4.5)	6 (7.5)
Physician Decision	1 (2.8)	1 (2.3)	2 (2.5)
Withdrawal By Parent/Guardian	1 (2.8)	3 (6.8)	4 (5.0)
Withdrawal By Subject	5 (13.9)	5 (11.4)	10 (12.5)

Treatment groups in this follow-up study (P351) reflect the originally assigned treatment groups in P083.

[a] The Exposed to Sitagliptin in P083 includes 35 participants who were randomized to the Sitagliptin +/- insulin group, and 1 participant who was randomized to the Placebo followed by Sitagliptin group in P083. 1 participant from this group received sitagliptin as concomitant medication during P351.

[b] The Not Exposed in P083 includes 39 participants who were randomized to the Placebo +/- insulin followed by metformin group, and 5 participants who were randomized to the Metformin group in P083. 4 participants from this group received a DPP-4 inhibitor (sitagliptin or vildagliptin) as concomitant medication during P351.

Source: [P351MK0431: adam-adsl]

Demographics

Demographic and Anthropometric Characteristics
(ASF)

	Exposed to Sitagliptin in P083[a]		Not Exposed in P083[b]		Total	
	n	(%)	n	(%)	n	(%)
Participants in population	36		44		80	
Gender						
Male	16	(44.4)	13	(29.5)	29	(36.3)
Female	20	(55.6)	31	(70.5)	51	(63.8)
Age at Year 0 of P351 (Years)						
≥10 and <15	13	(36.1)	19	(43.2)	32	(40.0)
≥15 and <18	15	(41.7)	21	(47.7)	36	(45.0)
≥18	8	(22.2)	4	(9.1)	12	(15.0)
Mean	15.1		14.7		14.9	
SD	2.3		2.0		2.1	
Median	15.0		15.0		15.0	
Range	11 to 19		11 to 18		11 to 19	
Race						
American Indian Or Alaska Native	2	(5.6)	3	(6.8)	5	(6.3)
Asian	5	(13.9)	8	(18.2)	13	(16.3)
Black Or African American	1	(2.8)	1	(2.3)	2	(2.5)
Multiple	13	(36.1)	14	(31.8)	27	(33.8)
American Indian Or Alaska Native, Black Or African American	1	(2.8)	0	(0.0)	1	(1.3)
American Indian Or Alaska Native, White	8	(22.2)	9	(20.5)	17	(21.3)
Black Or African American, White	4	(11.1)	5	(11.4)	9	(11.3)
White	15	(41.7)	18	(40.9)	33	(41.3)
Ethnicity						
Hispanic Or Latino	18	(50.0)	19	(43.2)	37	(46.3)
Not Hispanic Or Latino	18	(50.0)	24	(54.5)	42	(52.5)
Not Reported	0	(0.0)	1	(2.3)	1	(1.3)
Body Mass Index at Year 0 of P351 (kg/m^2)						

Demographic and Anthropometric Characteristics
(ASF)

	Exposed to Sitagliptin in P083[a]		Not Exposed in P083[b]		Total	
	n	(%)	n	(%)	n	(%)
Mean	32.7		29.7		31.1	
SD	8.2		6.9		7.6	
Median	31.7		27.6		28.8	
Range	20.9 to 57.2		21.4 to 47.6		20.9 to 57.2	
Duration of Type 2 Diabetes Mellitus at Year 0 of P351 (years) (derived based on P083 medical history)						
Mean	1.8		2.0		2.0	
SD	1.6		1.7		1.6	
Median	1.3		1.5		1.4	
Range	1.1 to 10.1		1.1 to 9.0		1.1 to 10.1	

SD=Standard deviation.
Based on P083 enrollment:
Gender, Race, Ethnicity.
Age at baseline = (Number of days from date of birth to first day of this follow-up study + 1)/365.25.
Treatment groups in this follow-up study (P351) reflect the originally assigned treatment groups in P083.
[a] The Exposed to Sitagliptin in P083 includes 35 participants who were randomized to the Sitagliptin +/- insulin group, and 1 participant who was randomized to the Placebo followed by Sitagliptin group in P083. 1 participant from this group received sitagliptin as concomitant medication during P351.
[b] The Not Exposed in P083 includes 39 participants who were randomized to the Placebo +/- insulin followed by metformin group, and 5 participants who were randomized to the Metformin group in P083. 4 participants from this group received a DPP-4 inhibitor (sitagliptin or vildagliptin) as concomitant medication during P351.

Source: [P351MK0431: adam-adsl; adbase]

Efficacy:

No efficacy endpoints were collected.

Safety:

No meaningful safety signals were identified in P351.

- The FAIRs of AEs overall, specific AEs by SOC, and SAEs in P351 were generally similar in the Exposed to Sitagliptin in P083 and the Not Exposed in P083 groups.
- One death, in the Exposed to Sitagliptin in P083 group, was reported in P351 due to acute lymphocytic leukemia and was not considered to be related to study intervention by the investigator.
- Auxological and pubertal parameters were generally similar in participants in the Exposed to Sitagliptin in P083 and the Not Exposed in P083 groups.

Adverse Event Summary
(ASF)

	Exposed to Sitagliptin in P083[a] n (FAIR in 100-participant-years)	Not Exposed in P083[b] n (FAIR in 100-participant-years)
Participants in population	36	44
with one or more adverse events	15/72.6 (20.7)	20/99.2 (20.2)
with serious adverse events	3/103.0 (2.9)	3/140.3 (2.1)
who died	1/107.7 (0.9)	0/143.7 (0.0)
discontinued follow-up due to an adverse event	0/110.0 (0.0)	0/143.7 (0.0)

FAIR: Follow-up adjusted incidence rate = (Number of participants with ≥1 event during the follow-up study) / (Total participant-years of follow-up).

Treatment groups in this follow-up study (P351) reflect the originally assigned treatment groups in P083.

[a] The Exposed to Sitagliptin in P083 includes 35 participants who were randomized to the Sitagliptin +/- insulin group, and 1 participant who was randomized to the Placebo followed by Sitagliptin group in P083. 1 participant from this group received sitagliptin as concomitant medication during P351.

[b] The Not Exposed in P083 includes 39 participants who were randomized to the Placebo +/- insulin followed by metformin group, and 5 participants who were randomized to the Metformin group in P083. 4 participants from this group received a DPP-4 inhibitor (sitagliptin or vildagliptin) as concomitant medication during P351.

For participants who have an event, the participant-years of follow-up will be calculated as (Date of the first event - First day of the follow-up study + 1)/365.25. For participants without an event, the participant-years of follow-up will be calculated as (Last day of the follow-up window - First day of the follow-up study + 1)/365.25. The total participant-years for a treatment group will be the sum of the participant-years of follow-up of all participants in the treatment group.

Source: [P351MK0431: adam-adsl; adtte]

CONCLUSIONS:

Key safety results

In this noninterventional follow-up study (P351) of up to 5 years in pediatric participants with T2DM and inadequate glycemic control, safety was generally similar in participants exposed to sitagliptin and those not exposed to sitagliptin in P083.

LIST OF ABBREVIATIONS:

Abbreviation/Term	Definition
AE	adverse event
ASF	all subjects followed-up
BMI	body mass index
COVID-19	coronavirus disease caused by severe acute respiratory syndrome coronavirus 2
CSR	clinical study report
FAIR	follow-up adjusted incidence rate
GCP	Good Clinical Practice
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
IEC	Independent Ethics Committee
MSD	Merck Sharp & Dohme LLC, Rahway, NJ, USA
SAE	serious adverse event
SDS	standard deviation score
SOC	system organ class
SOP	standard operating procedure
T2DM	type 2 diabetes mellitus
US(A)	United States (of America)

PUBLICATION(S): As of the date of this report, there are no publications based on this study.

REPORT DATE: 27-NOV-2024

REVISED REPORT DATE: Not applicable.

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4 LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

This list serves as the first appearance in text.

The following terms may be used interchangeably in this report:

- Participant and subject
- Intervention and treatment
- Study and trial

Abbreviation/Term	Definition
AE	adverse event
ASF	all subjects followed-up
BMI	body mass index
CFR	Code of Federal Regulations
COVID-19	coronavirus disease caused by severe acute respiratory syndrome coronavirus 2
CRF	case report form
CSR	clinical study report
DPP-4	dipeptidyl peptidase 4
EMA	European Medicines Agency
ERC	Ethics Review Committee
EU	European Union
FAIR	follow-up adjusted incidence rate
FDA	Food and Drug Administration
FDC	fixed dose combination
GCP	Good Clinical Practice
GPvP	Good Pharmacovigilance Practice
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
IEC	Independent Ethics Committee
IRB	Institutional Review Board
MedDRA	Medical Dictionary for Regulatory Activities
MSD	Merck Sharp & Dohme LLC, Rahway, NJ, USA
PDCO	Pediatric Committee of the European Medicines Agency

Abbreviation/Term	Definition
PIP	Pediatric Investigation Plan
QA	quality assurance
SAE	serious adverse event
SAP	statistical analysis plan
SDV	source document verification
SDR	source data review
SDS	standard deviation score
SOC	system organ class
SOP	standard operating procedure
T2DM	type 2 diabetes mellitus
US(A)	United States (of America)

5 ETHICS

5.1 Independent Ethics Committee

The protocol, protocol amendments, informed consent form, investigator's brochure, and other relevant study documents were reviewed and approved by the IEC(s) (also referred to as an IRB, ERC, or any other ethics committee) listed in [16.1.3] before being implemented at each site, in compliance with local and/or national regulations (MSD Code of Conduct for Interventional Clinical Trials [16.1.1]). The IEC(s) consulted for this study met the definition of an "IEC" as outlined in US CFR Title 21 Part 56, or equivalent country specific regulations.

5.2 Ethical Conduct of the Study

This study was conducted in accordance with local and/or national regulations (including all applicable data protection laws and regulations), ICH GCP and with the ethical principles that have their origin in the Declaration of Helsinki regarding IEC review, informed consent, and the protection of human participants in biomedical research (MSD Code of Conduct for Interventional Clinical Trials [16.1.1]).

5.3 Participant Information and Consent

Informed consent was obtained and documented in accordance with the principles and provisions in Section 4.8 of the ICH E6 Guideline for Good Clinical Practice, US CFR Title 21 Part 50, Protection of Human Subjects, and/or local country/cultural consent practices and/or requirements where applicable. Representative written information for the participant and sample informed consent form(s) or applicable assent (if the participant was under the age of consent) are available upon request. A description of any incentives used in the study is available upon request or included, if required [16.1.3.3].

6 INVESTIGATORS AND STUDY ADMINISTRATIVE STRUCTURE

A list of investigators, including study center information, is provided in [16.1.3]. Information for the administrative structure of the study (eg, monitoring, laboratory facilities, and clinical supply) is provided in [16.1.4]. Study governance information is available in the study protocol [16.1.1].

7 INTRODUCTION

This was a follow-up study of participants from MK-0431 protocol 083 study (hereinafter referred to as P083). P083 was a 2-part (Phases A and B), multinational, placebo-controlled, double-blind, parallel-group study assessing the safety and efficacy of sitagliptin once daily in pediatric participants (ages 10 to 17 years, inclusive at initiation of therapy) with T2DM and inadequate glycemic control.

This follow-up study (P351) was designed to provide an up to 5-year noninterventional observational assessment of the safety of participants with T2DM who participated in P083. In P083, participants were randomized to receive sitagliptin ± insulin (in Phases A and B),

metformin (in Phases A and B), placebo in Phase A followed by sitagliptin in Phase B (placebo/sitagliptin), placebo ± insulin in Phase A followed by metformin in Phase B (placebo ± insulin/metformin) [16.1.1]. This follow-up study was conducted at the request of the PDCO of the EMA as a required component of the PIP (EMEA-C-000470-PIP01-08-M11), which stated: "Patients included in the study must be offered at least annual follow-up examinations, to include assessment of all infections, auxological, and pubertal parameters, for at least 5 years or for at least 2 years after reaching Tanner Stage V (whichever occurs first)."

Additional details are available in the study protocol [16.1.1]. A sample CRF is provided in [16.1.2].

Part of this study was conducted during the COVID-19 pandemic. Contingency measures implemented to manage study conduct as a result of the pandemic and the impact of those measures on study conduct, data integrity, and analyses are described in [Sec. 9.8].

8 STUDY OBJECTIVES AND ENDPOINTS

Primary Objective: To assess safety for up to a 5-year period in pediatric subjects (ages 10 to 17 years at initiation of therapy in P083) with T2DM who participated for up to one year in P083.

Endpoints: Adverse events (AEs), BMI (body mass index), BMI SDS (body mass index standard deviation score), height, body weight, Tanner Staging (pubertal progression), growth velocity, blood pressure, and heart rate.

9 INVESTIGATIONAL PLAN

9.1 Overall Study Design and Plan

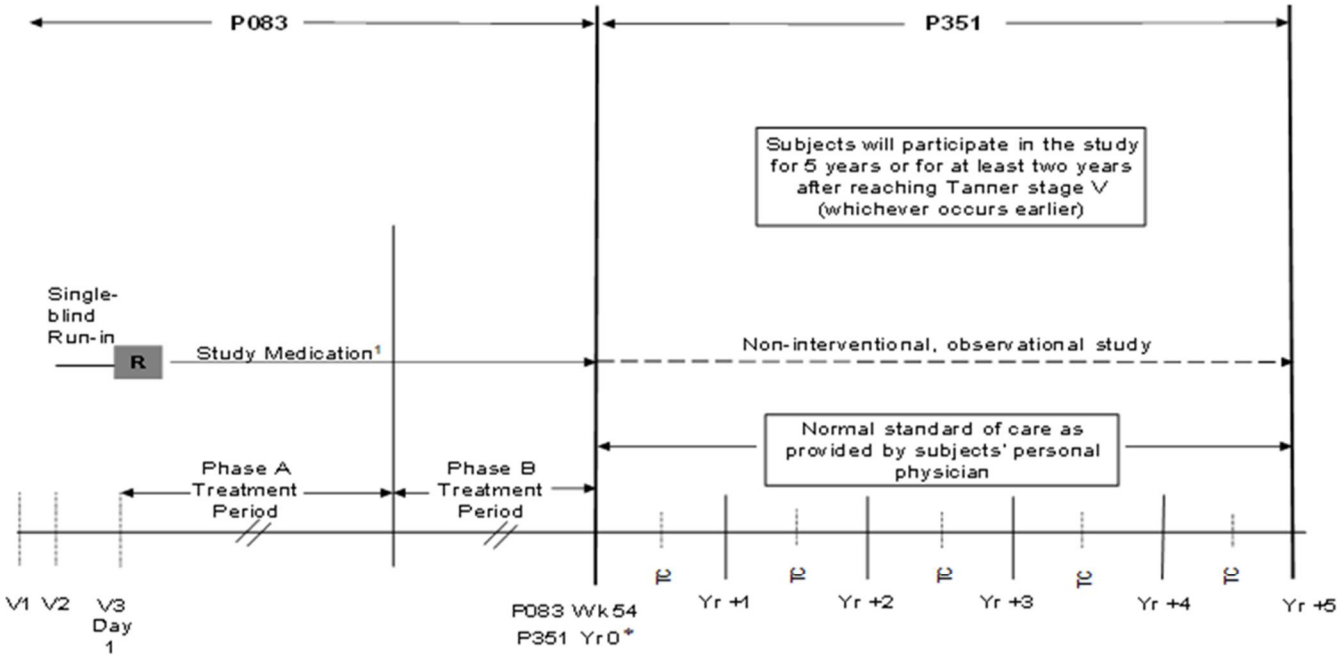
This was an observational, noninterventional, multinational study designed to provide up to a 5-year observational assessment of safety for participants with T2DM, who were 10 to 17 years of age (inclusive) at initiation of therapy in P083.

This study was conducted at 39 sites that had participated in P083. Randomized participants from P083 (including those who discontinued study medication and those who withdrew consent) from those sites were eligible to participate in P351 if they did not meet exclusion criteria [Sec. 9.3]. Participants observed in P351 received standard of care as provided by their usual care physician. The follow-up study began at Week 54 for P083, which was Year 0 for P351 [Figure 9-1]. Regardless of when the assent/consent for P351 was obtained, the last possible visit (Year +5) occurred no later than 5 years after the participant completed or was scheduled to complete the Week-54 visit for P083. Participants attended annual visits and received telephone calls at 6-month intervals between visits for up to 5 years after a participant completed or was scheduled to complete the Week-54 visit for P083 or for 2 years after reaching Tanner Stage V for genitalia/breasts, whichever occurred earlier. Participants who were at Tanner Stage V for genitalia/breasts during P083 completed P351 at Year +2.

Additional details regarding the study design of P351 are available in the study protocol [16.1.1] [16.1.9.1].

The study design is shown in [Figure 9-1] and described in the study protocol [16.1.1].

Figure 9-1
Study Design



* Subjects who have completed P083 on or off study medication and satisfy all enrollment criteria are eligible to enter P351.

[1] Participants may have received sitagliptin ± insulin, metformin, placebo in Phase A followed by sitagliptin in Phase B (placebo/sitagliptin), or placebo ± insulin in Phase A followed by metformin in Phase B (placebo ± insulin/metformin) in P083 depending on randomization and the amendment they were enrolled under.

9.2 Discussion of the Study Design

The scientific rationale for the study design is provided in the study protocol [16.1.1].

9.3 Selection of Study Population

9.3.1 Inclusion Criteria

An individual was eligible for inclusion in the study if they met all the following criteria:

- Participant and/or parent/guardian provided documented informed assent and/or consent for the study.
- Completed P083 or stopped study medication during P083.

Additional details are available in the study protocol [16.1.1].

9.3.2 Exclusion Criteria

An individual was excluded from the study if they met any of the following key exclusion criteria:

- Did not agree to refrain from participating in any double-blind interventional study while participating in P351.
- Was unlikely to adhere to the study procedures and appointment schedule.

Additional details are available in the study protocol [16.1.1].

9.3.3 Participant Withdrawal/Discontinuation Criteria

Criteria and procedures for early discontinuation from study intervention or withdrawal from the study are described in the study protocol [16.1.1].

9.4 Study Intervention

This was a noninterventional study, there was no exposure to study intervention. Additional details are available in the study protocol [16.1.1].

9.4.1 Intervention Administered

Not applicable.

9.4.2 Identity of Investigational Product

Not applicable.

9.4.3 Avoidance of Bias in the Study

9.4.3.1 Methods of Assigning Participants to Intervention Groups

This was a noninterventional study. Participants retained their randomization numbers assigned for P083 as described in the study protocol [16.1.1].

9.4.3.2 Blinding

Participants in P351 remained blinded to treatment assignment from P083 while P083 was ongoing. Investigators could inform participants about treatment assignment in P083 after P083 was completed.

9.4.4 Selection and Timing of Dose(s) for Each Participant

Not applicable. This was an observational study, eligible participants entered P351 with their originally assigned treatment group from P083 [16.1.1].

9.4.5 Intervention Compliance

Not applicable.

9.4.6 Prior and Concomitant Therapy

The medication(s)/treatment(s)/vaccination(s) allowed or disallowed before and during the study, including any exceptions to these requirements, are described in the study protocol [16.1.1].

9.5 Study Assessments and Procedures

9.5.1 Planned Measurements and Timing of Assessment(s)

The specific safety variables to be assessed, their schedule, and measurement/collection methods are displayed in the Schedule of Activities and described in the Procedures sections of the study protocol [16.1.1]. The collection and assessment of safety information during the study (evaluation, definitions, recording, and reporting of AEs, SAEs, and other reportable safety events) are detailed in the AE reporting section of the study protocol [16.1.1].

9.5.2 Appropriateness of Measurements

The safety endpoints used in this study were standard, generally reliable, and relevant to the objective set forth in the protocol [16.1.1].

9.5.3 Protocol Deviations

Protocol deviations were classified as per the ICH E3 classification of protocol deviations as important (those that may significantly impact the quality or integrity of key study data or that may significantly affect a participant's rights, safety, or well-being) or not important.

9.6 Data Quality Assurance

The CSR authors reviewed this document for accuracy of scientific content; their signatures are included in [16.1.5.2]. The coordinating investigator's signature is included in [16.1.5.1].

Quality oversight activities implemented at the study investigative site(s) or centrally by the Sponsor are intrinsic to all clinical study-related activities, in accordance with ICH GCP 5.1. For this study, such activities may have included remote and/or on-site monitoring inclusive of SDV, SDR, centralized in-house medical monitoring of clinical study data (including monitoring protocol deviations), and relevant reviews of regulatory submission documents.

Investigative study sites were monitored to assess compliance with the study protocol and with GCP. Study data were reviewed for accuracy, completeness, and consistency and verified versus source documentation according to standard operating procedures (MSD Code of Conduct for Interventional Clinical Trials [16.1.1]).

The Sponsor held investigator meeting(s) before study initiation to review all protocol procedures and investigator responsibilities under GCP. At the meeting(s), the conduct of the study was explained, and instructions were provided to ensure accuracy and consistency in data collection and performance.

Quality was also evaluated by independent GCP QA activities, which may have included QA audits of study investigative sites and third-party suppliers. The conduct of QA audits was based on a risk-based approach to assess adherence with the protocol, applicable GCP/GPvP regulations and guidance as well as applicable company policies and procedures. Audit information is provided in [16.1.8].

No serious breaches of GCP or other GCP compliance issues that were assessed as having had a significant impact on the rights, safety, or mental integrity of the study participants and/or the scientific integrity or validity of the study results occurred.

9.7 Statistical Analysis Plan

The planned analyses are described in the SAP of the protocol [16.1.1]. Prespecified changes and clarifications to the planned analyses before the database lock are described in the SAP change memo [16.1.9.1].

9.8 Changes in the Conduct of the Study or Planned Analyses

Part of this study was conducted during the COVID-19 pandemic.

9.8.1 Changes in the Conduct of the Study

Changes in the conduct of the study implemented by protocol amendment are summarized in [Table 9-1].

Table 9-1
Protocol Amendments for MK-0431-351

Document	Date Issue	Overall Rationale
Amendment 2	01-NOV-2022	Sponsor underwent an entity name change and update to the address.
Amendment 1	17-AUG-2015	To align with P083 amendments

A risk-based approach, consistent with Health Authority (FDA, EMA) guidance on conducting clinical studies during the COVID-19 pandemic, was used to assess and mitigate the impact of the pandemic on study conduct to 1) ensure the safety of study participants, study staff, and health care providers, 2) maintain compliance with GCP principles, and 3) minimize risks to study data integrity. The Sponsor continued to follow its SOPs for study conduct, monitoring, and oversight during the COVID-19 pandemic. Any contingency measures used to manage study conduct during the pandemic were implemented as per the Sponsor's SOP for exception and deviation management and as appropriate for the country, region, and individual study site. Exceptions and deviations from SOPs were documented.

Measures implemented by the Sponsor to manage key aspects of study conduct during the COVID-19 pandemic are summarized in [Table 9-2] (implementation date shown in parentheses). Not all measures were implemented at all study sites due to differences in local conditions and impact of the pandemic.

Table 9-2
Measures Implemented by the Sponsor to Manage Study Conduct During the COVID-19 Pandemic for MK-0431-351

Process	Measure (Date Implemented)
Study site monitoring	• Modifications to the frequency of on-site and remote monitoring were allowed due to national and local travel restrictions and/or study site restrictions to onsite monitoring (21-MAR-2020). • Redacted/alternate methods for source data review and verification for critical data points in absence of remote access to electronic medical records were allowed under documented circumstances (06-MAR-2020). • Critical data points for SDV were reassessed and the SMP updated without the usual approval workflow approval for resumption of on-site monitoring (01-MAY-2020).
Protocol deviations	• Study sites were queried as to the relationship of reported deviations to the COVID-19 pandemic; responses were documented (20-MAR-2020).
AE reporting	• COVID-19 infection was to be reported following data entry guidelines for AE and SAE reporting.
Data management	• Consideration was made (if required) for alternative collection of information from alternative providers of clinical care during COVID-19 if sites remain restricted for extended length of time.
Informed consent	• Oral confirmation of participant consent (eg, via telephone) was allowed when in-person discussion and signature was not possible (30-MAR-2020).

AE=adverse event; COVID-19=coronavirus disease caused by severe acute respiratory syndrome coronavirus 2; SAE=serious adverse event; SDV=source document verification; SMP=site monitoring plan

9.8.2 Changes in the Planned Analyses

Prespecified changes and clarifications to the analyses specified in the protocol P351-02 SAP before the database lock are described in [16.1.9.1] and are summarized below.

- Statistical summaries by treatment groups in P351
  - P083 included 4 treatment groups, of which 2 had limited participation. Therefore, the 4 treatment groups in P083 were collapsed into 2 treatment groups in this CSR: Exposed to Sitagliptin in P083 and Not Exposed in P083.

- Statistical Methods for Safety Analyses
  - The BMI SDS is defined only for ages <20 years. Many of the participants in P351 reached age ≥20 during this study. Hence, no summary of BMI SDS was performed.
  - The number and percentages of participants reaching Tanner Stage V by each follow-up year were summarized by sex.
  - Mean over time plots were not provided.

- Baseline measurements of P351 are described as follows:
  - Same as P083 baseline: gender, race, ethnicity, and region
  - At Year 0 of P351: age, height, body weight, and duration of T2DM (derived based on P083 medical history)

9.8.3 Changes Following Study Unblinding and Post Hoc Analyses

No changes were made to the planned analyses after the database lock, and no post hoc analyses were performed in this study.

10 STUDY PARTICIPANTS

Clinical investigator study sites were located in 16 countries: Argentina, Canada, Colombia, Dominican Republic, Guatemala, Honduras, Hungary, Israel, Italy, Malaysia, Mexico, Philippines, Poland, Romania, Russia, and the US.

Participant data listings are available upon request or, if required, provided in [16.2.1, 16.2.4, 16.2.7] with electronic data sets provided in [16.4]. Participant CRFs are available upon request or link, as applicable [16.3].

10.1 Disposition of Participants

The disposition of participants and median duration of follow-up were similar in both groups [Table 10-1] [Table 14.1-2].

A total of 80 participants enrolled in P351 across 39 study sites in 16 countries [16.1.3.1]. All participants enrolled in P351 completed P083 on or off study medication. Of the 80 participants enrolled in P351, 36 were in the Exposed to Sitagliptin in P083 group and 44 in the Not Exposed in P083 group [Table 10-1].

A total of 57/80 (71.3%) of the enrolled participants completed P351 per protocol. In the Exposed to Sitagliptin in P083 group 12/36 (33.3%) participants and in the Not Exposed in P083 group 11/44 (25.0%) participants, discontinued the study. The specific reasons for discontinuation were not notably different between the groups. The most commonly reported reason for study discontinuation in both groups was withdrawal by participant [Table 10-1] [16.2.1].

Table 10-1
Disposition of Participants

	Exposed to Sitagliptin in P083[a] n (%)	Not Exposed in P083[b] n (%)	Total n (%)
Enrolled in P351	36	44	80
Completed	24 (66.7)	33 (75.0)	57 (71.3)
Discontinued	12 (33.3)	11 (25.0)	23 (28.8)
Death	1 (2.8)	0 (0.0)	1 (1.3)
Lost To Follow-Up	4 (11.1)	2 (4.5)	6 (7.5)
Physician Decision	1 (2.8)	1 (2.3)	2 (2.5)
Withdrawal By Parent/Guardian	1 (2.8)	3 (6.8)	4 (5.0)
Withdrawal By Subject	5 (13.9)	5 (11.4)	10 (12.5)

Treatment groups in this follow-up study (P351) reflect the originally assigned treatment groups in P083.

[a] The Exposed to Sitagliptin in P083 includes 35 participants who were randomized to the Sitagliptin +/- insulin group, and 1 participant who was randomized to the Placebo followed by Sitagliptin group in P083. 1 participant from this group received sitagliptin as concomitant medication during P351.

[b] The Not Exposed in P083 includes 39 participants who were randomized to the Placebo +/- insulin followed by metformin group, and 5 participants who were randomized to the Metformin group in P083. 4 participants from this group received a DPP-4 inhibitor (sitagliptin or vildagliptin) as concomitant medication during P351.

Source: [P351MK0431: adam-adsl]

10.1.1 Confirmed Premature Unblinding Events

Not applicable. This was a noninterventional study.

10.2 Protocol Deviations

Important protocol deviations were reported for 9 (11.3%) participants [Table 10-2], with no notable trend observed.

No participant's data were excluded from the analysis due to a protocol deviation [Sec. 10.3]. No protocol deviations were classified as a serious GCP compliance issue. A listing of important protocol deviations is presented by participant and study site in [16.2.2].

Table 10-2
Summary of Important Protocol Deviations
(ASF)

	Exposed to Sitagliptin in P083[a]		Not Exposed in P083[b]		Total	
	n	(%)	n	(%)	n	(%)
Participants in population	36		44		80	
with one or more important protocol deviations	3	(8.3)	6	(13.6)	9	(11.3)
with no important protocol deviations	33	(91.7)	38	(86.4)	71	(88.8)
Safety Reporting	**1**	**(2.8)**	**3**	**(6.8)**	**4**	**(5.0)**
Participant had a reportable Safety Event and/or follow up Safety Event information that was not reported per the timelines outlined in the protocol.	1	(2.8)	3	(6.8)	4	(5.0)
Trial Procedures	**2**	**(5.6)**	**4**	**(9.1)**	**6**	**(7.5)**
Failure to conduct major / significant protocol-specified safety evaluations.	1	(2.8)	3	(6.8)	4	(5.0)
Missed weight or height measurement, or Tanner staging	1	(2.8)	1	(2.3)	2	(2.5)

Every participant is counted a single time for each applicable row and column.

Treatment groups in this follow-up study (P351) reflect the originally assigned treatment groups in P083.

[a] The Exposed to Sitagliptin in P083 includes 35 participants who were randomized to the Sitagliptin +/- insulin group, and 1 participant who was randomized to the Placebo followed by Sitagliptin group in P083. 1 participant from this group received sitagliptin as concomitant medication during P351.

[b] The Not Exposed in P083 includes 39 participants who were randomized to the Placebo +/- insulin followed by metformin group, and 5 participants who were randomized to the Metformin group in P083. 4 participants from this group received a DPP-4 inhibitor (sitagliptin or vildagliptin) as concomitant medication during P351.

Source: [P351MK0431: adam-adsl] [P351MK0431: sdtm-dv; suppdv]

10.3 Data Sets Analyzed

10.3.1 Safety Analysis Population

Safety analyses were based on the ASF population, which included all eligible participants from P083 who consented to participate in P351.

10.4 Demographics and Other Baseline Characteristics

10.4.1 Demographics and Baseline Disease Characteristics

Baseline demographics and disease characteristics were generally comparable between groups. The mean duration of T2DM at Year 0 in P351 was 2.0 years. The mean age was 14.9 years and the majority of participants (85.0%) were <18 years of age at Year 0. The proportion of female participants was lower in the Exposed to Sitagliptin in P083 group compared with the Not Exposed in P083 group, while baseline body weight and baseline BMI were higher in the Exposed to Sitagliptin in P083 group compared with the Not Exposed in P083 group [Table 10-3].

The proportion of participants from EU and EU-like countries was similar between the Exposed to Sitagliptin in P083 group and the Not Exposed in P083 group.

Table 10-3
Demographic and Anthropometric Characteristics
(ASF)

	Exposed to Sitagliptin in P083[a]		Not Exposed in P083[b]		Total	
	n	(%)	n	(%)	n	(%)
Participants in population	36		44		80	
Gender						
Male	16	(44.4)	13	(29.5)	29	(36.3)
Female	20	(55.6)	31	(70.5)	51	(63.8)
Age at Year 0 of P351 (Years)						
≥10 and <15	13	(36.1)	19	(43.2)	32	(40.0)
≥15 and <18	15	(41.7)	21	(47.7)	36	(45.0)
≥18	8	(22.2)	4	(9.1)	12	(15.0)
Mean	15.1		14.7		14.9	
SD	2.3		2.0		2.1	
Median	15.0		15.0		15.0	
Range	11 to 19		11 to 18		11 to 19	
Race						
American Indian Or Alaska Native	2	(5.6)	3	(6.8)	5	(6.3)
Asian	5	(13.9)	8	(18.2)	13	(16.3)
Black Or African American	1	(2.8)	1	(2.3)	2	(2.5)
Multiple	13	(36.1)	14	(31.8)	27	(33.8)

Demographic and Anthropometric Characteristics
(ASF)

	Exposed to Sitagliptin in P083[a]		Not Exposed in P083[b]		Total	
	n	(%)	n	(%)	n	(%)
American Indian Or Alaska Native, Black Or African American	1	(2.8)	0	(0.0)	1	(1.3)
American Indian Or Alaska Native, White	8	(22.2)	9	(20.5)	17	(21.3)
Black Or African American, White	4	(11.1)	5	(11.4)	9	(11.3)
White	15	(41.7)	18	(40.9)	33	(41.3)
Ethnicity						
Hispanic Or Latino	18	(50.0)	19	(43.2)	37	(46.3)
Not Hispanic Or Latino	18	(50.0)	24	(54.5)	42	(52.5)
Not Reported	0	(0.0)	1	(2.3)	1	(1.3)
Height at Year 0 of P351 (cm)						
Mean	162.5		160.7		161.5	
SD	10.8		10.0		10.3	
Median	162.0		161.1		162.0	
Range	143 to 184		140 to 181		140 to 184	
Body Weight at Year 0 of P351 (kg)						
Mean	85.7		77.5		81.2	
SD	19.6		22.1		21.3	
Median	86.4		72.5		77.6	
Range	53.6 to 128.8		43.8 to 128.0		43.8 to 128.8	

Demographic and Anthropometric Characteristics
(ASF)

	Exposed to Sitagliptin in P083[a]		Not Exposed in P083[b]		Total	
	n	(%)	n	(%)	n	(%)
Body Mass Index at Year 0 of P351 (kg/m^2)						
Mean	32.7		29.7		31.1	
SD	8.2		6.9		7.6	
Median	31.7		27.6		28.8	
Range	20.9 to 57.2		21.4 to 47.6		20.9 to 57.2	
Region						
EU or EU-like Countries	8	(22.2)	11	(25.0)	19	(23.8)
Other	28	(77.8)	33	(75.0)	61	(76.3)
Duration of Type 2 Diabetes Mellitus at Year 0 of P351 (years) (derived based on P083 medical history)						
Mean	1.8		2.0		2.0	
SD	1.6		1.7		1.6	
Median	1.3		1.5		1.4	

Demographic and Anthropometric Characteristics
(ASF)

	Exposed to Sitagliptin in P083[a]		Not Exposed in P083[b]		Total	
	n	(%)	n	(%)	n	(%)
Range	1.1 to 10.1		1.1 to 9.0		1.1 to 10.1	

SD=Standard deviation.

Based on P083 enrollment:

Gender, Race, Ethnicity, Region.

Bulgaria, Canada, Hungary, Italy, Latvia, Lithuania, Poland, Romania, Russian Federation, and Serbia are classified as EU or EU-like countries.

Age at baseline = (Number of days from date of birth to first day of this follow-up study + 1)/365.25.

Treatment groups in this follow-up study (P351) reflect the originally assigned treatment groups in P083.

[a] The Exposed to Sitagliptin in P083 includes 35 participants who were randomized to the Sitagliptin +/- insulin group, and 1 participant who was randomized to the Placebo followed by Sitagliptin group in P083. 1 participant from this group received sitagliptin as concomitant medication during P351.

[b] The Not Exposed in P083 includes 39 participants who were randomized to the Placebo +/- insulin followed by metformin group, and 5 participants who were randomized to the Metformin group in P083. 4 participants from this group received a DPP-4 inhibitor (sitagliptin or vildagliptin) as concomitant medication during P351.

Source: [P351MK0431: adam-adsl; adbase]

10.4.2 Medical History and Concurrent Illnesses

P351 was a follow-up study; therefore, prestudy medical conditions are those conditions present before P083 and, therefore, are not included in this report.

10.4.3 Concomitant Medications

Prior medications are those reported for P083 and, therefore, are not included in this report.

In P351, participants received standard of care as provided by their usual care physician [16.1.1]. The use of 1 or more concomitant medications was generally similar in both groups with the exception of metformin or metformin-containing FDC, which was lower in the Exposed to Sitagliptin in P083 group compared with the Not Exposed in P083 group. Besides antihyperglycemic agents, the most frequently (>4.0%) reported concomitant medications were enalapril, ibuprofen, acetaminophen, omeprazole, pantoprazole, and levothyroxine sodium [Table 14.1-5].

Antihyperglycemic agents were reported for 70 (87.5%) participants. Of these 70 participants, 5 received treatment with DPP-4 inhibitors (sitagliptin or vildagliptin) during P351 (1 in the Exposed to Sitagliptin in P083 group and 4 in the Not Exposed in P083 group) [Table 14.1-5].

10.5 Measurements of Study Intervention Compliance

Not applicable, this was a noninterventional study.

10.6 Extent of Exposure

Not applicable, this was a noninterventional study [16.1.1].

11 EFFICACY EVALUATION

No efficacy endpoints were collected for this noninterventional study.

12 SAFETY EVALUATION

Participants enrolled in P351 were a subset of the originally randomized population in P083 and, therefore, represent a population from which randomized comparisons are not available. Additionally, the number of participants in both treatment groups decreased over time. Accordingly, caution should be used when interpreting apparent imbalances between groups.

12.1 Adverse Events

A listing(s) of AEs by participant is provided in [16.2.7] [16.4].

Only AEs reported as initiating during P351 are included in this report. Follow-up adjusted incidence rates (FAIR) were used to accommodate differential follow-up for participants in P351 [16.1.1].

MedDRA version 27.0 was used for this study.

12.1.1 Brief Summary of Adverse Events

Summary measures of AEs were generally similar between groups.

The FAIRs of SAEs were generally similar for both groups. No participant discontinued this study due to an AE. One participant death was reported during this study and occurred in the Exposed to Sitagliptin in P083 group. The death was due to leukemia and was considered not related to study intervention by the investigator [Table 12-1] [Sec 12.2.1.1].

Table 12-1
Adverse Event Summary
(ASF)

	Exposed to Sitagliptin in P083[a] n (FAIR in 100-participant-years)	Not Exposed in P083[b] n (FAIR in 100-participant-years)
Participants in population	36	44
with one or more adverse events	15/72.6 (20.7)	20/99.2 (20.2)
with serious adverse events	3/103.0 (2.9)	3/140.3 (2.1)
who died	1/107.7 (0.9)	0/143.7 (0.0)
discontinued follow-up due to an adverse event	0/110.0 (0.0)	0/143.7 (0.0)

FAIR: Follow-up adjusted incidence rate = (Number of participants with ≥1 event during the follow-up study) / (Total participant-years of follow-up).

Treatment groups in this follow-up study (P351) reflect the originally assigned treatment groups in P083.

[a] The Exposed to Sitagliptin in P083 includes 35 participants who were randomized to the Sitagliptin +/- insulin group, and 1 participant who was randomized to the Placebo followed by Sitagliptin group in P083. 1 participant from this group received sitagliptin as concomitant medication during P351.

[b] The Not Exposed in P083 includes 39 participants who were randomized to the Placebo +/- insulin followed by metformin group, and 5 participants who were randomized to the Metformin group in P083. 4 participants from this group received a DPP-4 inhibitor (sitagliptin or vildagliptin) as concomitant medication during P351.

For participants who have an event, the participant-years of follow-up will be calculated as (Date of the first event - First day of the follow-up study + 1)/365.25. For participants without an event, the participant-years of follow-up will be calculated as (Last day of the follow-up window - First day of the follow-up study + 1)/365.25. The total participant-years for a treatment group will be the sum of the participant-years of follow-up of all participants in the treatment group.

Source: [P351MK0431: adam-adsl; adtte]

12.1.2 Most Frequently Reported Adverse Events

The FAIRs of AEs by SOC were generally similar between the groups in P351. AEs in the Infections and Infestations SOC were the most frequent in both groups. The FAIR for this SOC was higher in the Exposed to Sitagliptin in P083 group than in the Not Exposed in P083 group; however, there was no clinically relevant pattern or remarkable imbalance in specific AEs reported under this SOC [Table 12-2].

Seven unique participants (3 in the Exposed to Sitagliptin in P083 group and 4 in the Not Exposed in P083 group) reported AEs of upper respiratory infections (a composite of AE terms of laryngopharyngitis, nasopharyngitis, acute otitis media, pharyngitis, sinusitis, upper respiratory tract infection, and viral upper respiratory tract infection) Four AEs were in the Exposed to Sitagliptin in P083 group and 6 were in the Not Exposed in P083 group [16.2.7] [16.4].

Table 12-2
Participants with Specific Adverse Events
(Incidence >0% in One or More Treatment Groups)
(ASF)

	Exposed to Sitagliptin in P083[a] n (FAIR in 100-participant-years)	Not Exposed in P083[b] n (FAIR in 100-participant-years)
Participants in population	36	44
with one or more adverse events	15/72.6 (20.7)	20/99.2 (20.2)
Blood and lymphatic system disorders	**0/110.0 (0.0)**	**1/142.7 (0.7)**
Hypochromic anaemia	0/110.0 (0.0)	1/142.7 (0.7)
Cardiac disorders	**0/110.0 (0.0)**	**1/138.7 (0.7)**
Wandering pacemaker	0/110.0 (0.0)	1/138.7 (0.7)
Endocrine disorders	**0/110.0 (0.0)**	**1/141.9 (0.7)**
Hypothyroidism	0/110.0 (0.0)	1/141.9 (0.7)
Eye disorders	**0/110.0 (0.0)**	**2/139.3 (1.4)**
Accommodation disorder	0/110.0 (0.0)	1/140.4 (0.7)
Diabetic retinopathy	0/110.0 (0.0)	1/142.7 (0.7)
Retinal vascular disorder	0/110.0 (0.0)	1/140.4 (0.7)
Gastrointestinal disorders	**3/104.1 (2.9)**	**6/133.3 (4.5)**
Abdominal pain	1/108.3 (0.9)	1/141.9 (0.7)
Abdominal pain lower	0/110.0 (0.0)	1/142.1 (0.7)
Diarrhoea	0/110.0 (0.0)	2/140.3 (1.4)
Dyspepsia	0/110.0 (0.0)	1/143.7 (0.7)
Food poisoning	1/108.9 (0.9)	0/143.7 (0.0)
Gastritis	1/107.0 (0.9)	2/139.1 (1.4)
Lip ulceration	1/108.8 (0.9)	0/143.7 (0.0)
General disorders and administration site conditions	**1/105.2 (1.0)**	**1/143.7 (0.7)**
Non-cardiac chest pain	1/105.2 (1.0)	0/143.7 (0.0)
Pyrexia	0/110.0 (0.0)	1/143.7 (0.7)
Infections and infestations	**10/86.7 (11.5)**	**10/129.4 (7.7)**
Appendicitis	0/110.0 (0.0)	2/141.3 (1.4)
Bacteriuria	1/107.5 (0.9)	0/143.7 (0.0)
Body tinea	1/108.3 (0.9)	0/143.7 (0.0)
Bronchitis	0/110.0 (0.0)	1/142.6 (0.7)

Participants with Specific Adverse Events
(Incidence >0% in One or More Treatment Groups)
(ASF)

	Exposed to Sitagliptin in P083[a] n (FAIR in 100-participant-years)	Not Exposed in P083[b] n (FAIR in 100-participant-years)
Infections and infestations	**10/86.7 (11.5)**	**10/129.4 (7.7)**
COVID-19	1/109.9 (0.9)	0/143.7 (0.0)
Conjunctivitis	1/107.8 (0.9)	1/142.0 (0.7)
Cystitis	0/110.0 (0.0)	1/141.7 (0.7)
Enterovirus infection	0/110.0 (0.0)	2/141.0 (1.4)
Folliculitis	0/110.0 (0.0)	1/141.5 (0.7)
Fungal skin infection	1/109.7 (0.9)	0/143.7 (0.0)
Gastroenteritis	0/110.0 (0.0)	2/143.5 (1.4)
Gastrointestinal infection	1/106.1 (0.9)	0/143.7 (0.0)
Herpes simplex	1/108.0 (0.9)	0/143.7 (0.0)
Impetigo	1/109.4 (0.9)	0/143.7 (0.0)
Influenza	1/108.7 (0.9)	0/143.7 (0.0)
Laryngopharyngitis	0/110.0 (0.0)	1/141.7 (0.7)
Nasopharyngitis	2/105.9 (1.9)	1/141.2 (0.7)
Onychomycosis	1/109.8 (0.9)	0/143.7 (0.0)
Otitis media acute	0/110.0 (0.0)	1/142.2 (0.7)
Pharyngitis	0/110.0 (0.0)	1/143.1 (0.7)
Pilonidal disease	1/105.1 (1.0)	0/143.7 (0.0)
Respiratory tract infection viral	1/109.5 (0.9)	1/142.7 (0.7)
Rotavirus infection	1/108.3 (0.9)	0/143.7 (0.0)
Sinusitis	0/110.0 (0.0)	1/142.2 (0.7)
Upper respiratory tract infection	2/104.5 (1.9)	0/143.7 (0.0)
Urinary tract infection	1/108.7 (0.9)	1/142.2 (0.7)
Varicella	1/108.8 (0.9)	0/143.7 (0.0)
Viral upper respiratory tract infection	0/110.0 (0.0)	1/142.1 (0.7)
Vulvovaginal mycotic infection	0/110.0 (0.0)	1/142.2 (0.7)
Vulvovaginitis	0/110.0 (0.0)	1/143.7 (0.7)
Investigations	**2/103.9 (1.9)**	**1/140.3 (0.7)**
Blood calcium increased	1/108.9 (0.9)	0/143.7 (0.0)
High density lipoprotein decreased	1/105.0 (1.0)	0/143.7 (0.0)
Urine analysis abnormal	1/105.0 (1.0)	0/143.7 (0.0)
Weight increased	0/110.0 (0.0)	1/140.3 (0.7)
Metabolism and nutrition disorders	**4/99.8 (4.0)**	**5/134.6 (3.7)**

Participants with Specific Adverse Events
(Incidence >0% in One or More Treatment Groups)
(ASF)

	Exposed to Sitagliptin in P083[a] n (FAIR in 100-participant-years)	Not Exposed in P083[b] n (FAIR in 100-participant-years)
Metabolism and nutrition disorders	**4/99.8 (4.0)**	**5/134.6 (3.7)**
Diabetes mellitus inadequate control	1/105.4 (0.9)	2/140.1 (1.4)
Hypercholesterolaemia	0/110.0 (0.0)	1/143.7 (0.7)
Hyperglycaemia	1/107.0 (0.9)	2/138.2 (1.4)
Hypertriglyceridaemia	1/108.0 (0.9)	0/143.7 (0.0)
Hypoglycaemia	1/109.4 (0.9)	0/143.7 (0.0)
Musculoskeletal and connective tissue disorders	**1/107.2 (0.9)**	**1/141.7 (0.7)**
Arthralgia	1/107.2 (0.9)	0/143.7 (0.0)
Muscle spasms	0/110.0 (0.0)	1/141.7 (0.7)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**2/106.4 (1.9)**	**0/143.7 (0.0)**
Haemangioma of liver	1/108.7 (0.9)	0/143.7 (0.0)
Leukaemia	1/107.7 (0.9)	0/143.7 (0.0)
Nervous system disorders	**3/100.2 (3.0)**	**3/137.7 (2.2)**
Autonomic neuropathy	0/110.0 (0.0)	1/142.7 (0.7)
Burning sensation	0/110.0 (0.0)	1/142.0 (0.7)
Diabetic neuropathy	0/110.0 (0.0)	1/140.4 (0.7)
Headache	2/105.1 (1.9)	0/143.7 (0.0)
Petit mal epilepsy	1/105.2 (1.0)	0/143.7 (0.0)
Polyneuropathy	0/110.0 (0.0)	1/142.7 (0.7)
Psychiatric disorders	**1/109.7 (0.9)**	**2/140.0 (1.4)**
Anxiety	0/110.0 (0.0)	1/142.0 (0.7)
Insomnia	0/110.0 (0.0)	1/141.7 (0.7)
Intentional self-injury	1/109.7 (0.9)	0/143.7 (0.0)
Renal and urinary disorders	**3/107.8 (2.8)**	**0/143.7 (0.0)**
Microalbuminuria	1/110.0 (0.9)	0/143.7 (0.0)
Nephrolithiasis	2/107.8 (1.9)	0/143.7 (0.0)
Reproductive system and breast disorders	**0/110.0 (0.0)**	**2/137.2 (1.5)**
Menstruation irregular	0/110.0 (0.0)	1/141.5 (0.7)

Participants with Specific Adverse Events
(Incidence >0% in One or More Treatment Groups)
(ASF)

	Exposed to Sitagliptin in P083[a] n (FAIR in 100-participant-years)	Not Exposed in P083[b] n (FAIR in 100-participant-years)
Reproductive system and breast disorders	**0/110.0 (0.0)**	**2/137.2 (1.5)**
Ovarian cyst	0/110.0 (0.0)	1/139.9 (0.7)
Polycystic ovaries	0/110.0 (0.0)	1/141.0 (0.7)
Respiratory, thoracic and mediastinal disorders	**2/104.3 (1.9)**	**1/143.7 (0.7)**
Productive cough	1/108.1 (0.9)	0/143.7 (0.0)
Respiratory tract inflammation	0/110.0 (0.0)	1/143.7 (0.7)
Rhinitis allergic	1/106.2 (0.9)	0/143.7 (0.0)
Skin and subcutaneous tissue disorders	**1/106.8 (0.9)**	**2/138.7 (1.4)**
Acne	0/110.0 (0.0)	1/141.5 (0.7)
Dermatitis	1/107.7 (0.9)	0/143.7 (0.0)
Eczema	1/106.8 (0.9)	0/143.7 (0.0)
Granuloma annulare	0/110.0 (0.0)	1/140.9 (0.7)
Necrobiosis lipoidica diabeticorum	0/110.0 (0.0)	1/140.9 (0.7)

FAIR: Follow-up adjusted incidence rate = (Number of participants with ≥1 event during the follow-up study) / (Total participant-years of follow-up).

Treatment groups in this follow-up study (P351) reflect the originally assigned treatment groups in P083.

[a] The Exposed to Sitagliptin in P083 includes 35 participants who were randomized to the Sitagliptin +/- insulin group, and 1 participant who was randomized to the Placebo followed by Sitagliptin group in P083. 1 participant from this group received sitagliptin as concomitant medication during P351.

[b] The Not Exposed in P083 includes 39 participants who were randomized to the Placebo +/- insulin followed by metformin group, and 5 participants who were randomized to the Metformin group in P083. 4 participants from this group received a DPP-4 inhibitor (sitagliptin or vildagliptin) as concomitant medication during P351.

For participants who have an event, the participant-years of follow-up will be calculated as (Date of the first event - First day of the follow-up study + 1)/365.25. For participants without an event, the participant-years of follow-up will be calculated as (Last day of the follow-up window - First day of the follow-up study + 1)/365.25. The total participant-years for a treatment group will be the sum of the participant-years of follow-up of all participants in the treatment group.

Source: [P351MK0431: adam-adsl; adtte]

12.1.3 Classification of Adverse Events

Two AEs initially reported during P083 were reported as having worsened during P351 and are included in the listing [16.2.7.1.1]. Both AEs (hypertriglyceridemia [1 participant in the Exposed to Sitagliptin in P083 group] and granuloma annulare [1 participant in the Not Exposed in P083 group]) were nonserious and moderate in intensity [16.2.7.1.1].

12.2 Serious Adverse Events and Other Clinically Meaningful Adverse Events

SAEs, discontinuations due to AEs, and other clinically meaningful AEs, listed by participant, are available in [16.2.7] [16.4].

12.2.1 Serious Adverse Events

12.2.1.1 Deaths Due to Adverse Events

One death, in the Exposed to Sitagliptin in P083 group, was reported during P351. This participant had an SAE of leukemia [Table 12-3] reported on Day 71 of P351 (Day 451 of P083) and died on Day 714 of P351 (Day 1094 of P083). This death was considered not related to study intervention by the investigator. The narrative for this participant provides details for the outcome of death [16.2.7.2].

Table 12-3
Participants with Adverse Events Resulting in Death
(Incidence >0% in One or More Treatment Groups)
(ASF)

	Exposed to Sitagliptin in P083[a] n (FAIR in 100-participant-years)	Not Exposed in P083[b] n (FAIR in 100-participant-years)
Participants in population	36	44
who died	1/107.7 (0.9)	0/143.7 (0.0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**1/107.7 (0.9)**	**0/143.7 (0.0)**
Leukaemia	1/107.7 (0.9)	0/143.7 (0.0)

FAIR: Follow-up adjusted incidence rate = (Number of participants with ≥1 event during the follow-up study) / (Total participant-years of follow-up).

Treatment groups in this follow-up study (P351) reflect the originally assigned treatment groups in P083.

[a] The Exposed to Sitagliptin in P083 includes 35 participants who were randomized to the Sitagliptin +/- insulin group, and 1 participant who was randomized to the Placebo followed by Sitagliptin group in P083. 1 participant from this group received sitagliptin as concomitant medication during P351.

[b] The Not Exposed in P083 includes 39 participants who were randomized to the Placebo +/- insulin followed by metformin group, and 5 participants who were randomized to the Metformin group in P083. 4 participants from this group received a DPP-4 inhibitor (sitagliptin or vildagliptin) as concomitant medication during P351.

For participants who have an event, the participant-years of follow-up will be calculated as (Date of the first event - First day of the follow-up study + 1)/365.25. For participants without an event, the participant-years of follow-up will be calculated as (Last day of the follow-up window - First day of the follow-up study + 1)/365.25. The total participant-years for a treatment group will be the sum of the participant-years of follow-up of all participants in the treatment group.

Source: [P351MK0431: adam-adsl; adtte]

12.2.1.2 Serious Adverse Events

The FAIR of SAEs reported in P351 was low and similar in both groups. Appendicitis was the only SAE reported by more than 1 participant (2 in the Not Exposed in P083 group). No specific SAE was reported in >1 participant in the Exposed to Sitagliptin in P083 group. No participant discontinued the study due to an SAE [Table 12-4].

Table 12-4
Participants with Serious Adverse Events
(Incidence >0% in One or More Treatment Groups)
(ASF)

	Exposed to Sitagliptin in P083[a] n (FAIR in 100-participant-years)	Not Exposed in P083[b] n (FAIR in 100-participant-years)
Participants in population	36	44
with serious adverse events	3/103.0 (2.9)	3/140.3 (2.1)
Infections and infestations	**0/110.0 (0.0)**	**3/140.3 (2.1)**
Appendicitis	0/110.0 (0.0)	2/141.3 (1.4)
Urinary tract infection	0/110.0 (0.0)	1/142.7 (0.7)
Metabolism and nutrition disorders	**1/107.0 (0.9)**	**0/143.7 (0.0)**
Hyperglycaemia	1/107.0 (0.9)	0/143.7 (0.0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**1/107.7 (0.9)**	**0/143.7 (0.0)**
Leukaemia	1/107.7 (0.9)	0/143.7 (0.0)
Renal and urinary disorders	**1/108.3 (0.9)**	**0/143.7 (0.0)**
Nephrolithiasis	1/108.3 (0.9)	0/143.7 (0.0)

FAIR: Follow-up adjusted incidence rate = (Number of participants with ≥1 event during the follow-up study) / (Total participant-years of follow-up).

Treatment groups in this follow-up study (P351) reflect the originally assigned treatment groups in P083.

[a] The Exposed to Sitagliptin in P083 includes 35 participants who were randomized to the Sitagliptin +/- insulin group, and 1 participant who was randomized to the Placebo followed by Sitagliptin group in P083. 1 participant from this group received sitagliptin as concomitant medication during P351.

[b] The Not Exposed in P083 includes 39 participants who were randomized to the Placebo +/- insulin followed by metformin group, and 5 participants who were randomized to the Metformin group in P083. 4 participants from this group received a DPP-4 inhibitor (sitagliptin or vildagliptin) as concomitant medication during P351.

For participants who have an event, the participant-years of follow-up will be calculated as (Date of the first event - First day of the follow-up study + 1)/365.25. For participants without an event, the participant-years of follow-up will be calculated as (Last day of the follow-up window - First day of the follow-up study + 1)/365.25. The total participant-years for a treatment group will be the sum of the participant-years of follow-up of all participants in the treatment group.

Source: [P351MK0431: adam-adsl; adtte]

12.2.2 Discontinuations Due to Adverse Events

No participant reported an AE that led to discontinuation in P351.

12.2.3 Adverse Events of Special Interest

No AEs of special interest were identified for this study.

12.2.4 Participant Narratives

A list of participants for whom narratives were written (including events qualifying the participants for a narrative), conventions for preparing narratives, and individual participant narratives (with links to corresponding CRFs, if applicable) are presented in [16.2.7.2] [16.3].

12.3 Clinical Laboratory Evaluation

Laboratory safety tests were not collected in this study.

12.4 Vital Signs, Physical Examinations, and Other Observations Related to Safety

12.4.1 Vital Signs

There were no clinically meaningful differences in the mean changes from baseline in systolic and diastolic blood pressure and heart rate between the Exposed to Sitagliptin in P083 group and the Not Exposed in P083 group [Table 14.5-1] through [Table 14.5-3].

12.4.2 Physical Examination Findings

There were no clinically meaningful findings in physical examinations in this study.

12.4.3 Other Observations Related to Safety

12.4.3.1 Auxological and Pubertal Parameters

At entry into P351, participants in the Exposed to Sitagliptin in P083 group had higher mean body weight and BMI compared with participants in the Not Exposed in P083 group. There were no clinically meaningful differences in the mean changes from baseline in weight, BMI, and height between groups [Table 14.5-4] through [Table 14.5-7].

Tanner Stage progression (percentage of participants that reached Tanner Stage V by year) was similar between groups throughout this study [Table 12-5].

Participants who initiated the study at Tanner Stage V were followed for 2 years as described in the protocol [16.1.1]. Participants who reached Tanner Stage V at discontinuation or lost to follow-up were not considered dropouts. At study initiation, most participants (67/80 [31/36 in the Exposed to Sitagliptin in P083 group and 36/44 in the Not Exposed in P083 group]) were in late puberty (ie, Tanner Stage IV or Tanner Stage V) [Table 12-5].

Tanner Stage V was not reported for 13 participants when they completed or discontinued prematurely; of these, 8 discontinued or were lost to follow-up. A listing of participants who did not reach Tanner Stage V at the end of P351 is provided [16.2.7.1.2].

Growth velocity in females decreased progressively over the time ranges analyzed [Table 12-6]. Slightly higher growth velocities were observed in females in the Exposed to Sitagliptin in P083 group compared with the Not Exposed in P083. This may reflect the

slightly lower yearly proportion of female participants progressing to Tanner Stage V in the Exposed to Sitagliptin in P083 group compared with the Not Exposed in P083 [Table 12-5].

Growth velocity in male participants was variable over the time ranges analyzed [Table 12-7]. Pubertal progression (yearly proportion of participants progressing to Tanner V) showed minor variations between the 2 groups, but by Year 5, all male participants in both groups had progressed to Tanner V [Table 12-5].

The variability observed across groups in growth velocity and pubertal progression is not considered clinically meaningful.

Table 12-5
Participants Reaching Tanner Stage V
(ASF)

Tanner Stage at Year 0	Participants Who Reached Tanner Stage V					
	At Year 0 n/m (%)	By Year 1 n/m (%) [d]	By Year 2 n/m (%) [d]	By Year 3 n/m (%) [d]	By Year 4 n/m (%) [d]	By Year 5 n/m (%) [d]
Exposed to Sitagliptin in P083[a]						
Stage II						
Male	0/2 (0.0%)	0/2 (0.0%) [0]	0/2 (0.0%) [0]	0/2 (0.0%) [0]	1/2 (50.0%) [0]	1/1 (100.0%) [1]
Stage III						
Female	0/3 (0.0%)	0/3 (0.0%) [0]	0/3 (0.0%) [0]	2/3 (66.7%) [0]	2/3 (66.7%) [0]	2/3 (66.7%) [0]
Stage IV						
Male	0/6 (0.0%)	4/6 (66.7%) [0]	5/6 (83.3%) [0]	6/6 (100.0%) [0]	6/6 (100.0%) [0]	6/6 (100.0%) [0]
Female	0/12 (0.0%)	3/11 (27.3%) [1]	4/10 (40.0%) [2]	7/10 (70.0%) [2]	7/10 (70.0%) [2]	8/10 (80.0%) [2]
Stage V						
Male	8/8 (100.0%)	8/8 (100.0%) [0]	8/8 (100.0%) [0]	8/8 (100.0%) [0]	8/8 (100.0%) [0]	8/8 (100.0%) [0]
Female	5/5 (100.0%)	5/5 (100.0%) [0]	5/5 (100.0%) [0]	5/5 (100.0%) [0]	5/5 (100.0%) [0]	5/5 (100.0%) [0]
Overall						
Male	8/16 (50.0%)	12/16 (75.0%) [0]	13/16 (81.3%) [0]	14/16 (87.5%) [0]	15/16 (93.8%) [0]	15/15 (100.0%) [1]
Female	5/20 (25.0%)	8/19 (42.1%) [1]	9/18 (50.0%) [2]	14/18 (77.8%) [2]	14/18 (77.8%) [2]	15/18 (83.3%) [2]
Not Exposed in P083[b]						
Stage II						
Female	0/1 (0.0%)	0/1 (0.0%) [0]	0/1 (0.0%) [0]	0/1 (0.0%) [0]	1/1 (100.0%) [0]	1/1 (100.0%) [0]
Stage III						
Male	0/4 (0.0%)	0/4 (0.0%) [0]	1/4 (25.0%) [0]	2/4 (50.0%) [0]	2/4 (50.0%) [0]	4/4 (100.0%) [0]
Female	0/3 (0.0%)	0/3 (0.0%) [0]	1/3 (33.3%) [0]	1/2 (50.0%) [1]	2/2 (100.0%) [1]	2/2 (100.0%) [1]

Participants Reaching Tanner Stage V
(ASF)

Tanner Stage at Year 0	Participants Who Reached Tanner Stage V					
	At Year 0 n/m (%)	By Year 1 n/m (%) [d]	By Year 2 n/m (%) [d]	By Year 3 n/m (%) [d]	By Year 4 n/m (%) [d]	By Year 5 n/m (%) [d]
Stage IV						
Male	0/6 (0.0%)	2/6 (33.3%) [0]	3/5 (60.0%) [1]	4/5 (80.0%) [1]	5/5 (100.0%) [1]	5/5 (100.0%) [1]
Female	0/19 (0.0%)	6/17 (35.3%) [2]	10/17 (58.8%) [2]	13/16 (81.3%) [3]	14/16 (87.5%) [3]	14/16 (87.5%) [3]
Stage V						
Male	3/3 (100.0%)	3/3 (100.0%) [0]	3/3 (100.0%) [0]	3/3 (100.0%) [0]	3/3 (100.0%) [0]	3/3 (100.0%) [0]
Female	8/8 (100.0%)	8/8 (100.0%) [0]	8/8 (100.0%) [0]	8/8 (100.0%) [0]	8/8 (100.0%) [0]	8/8 (100.0%) [0]
Overall						
Male	3/13 (23.1%)	5/13 (38.5%) [0]	7/12 (58.3%) [1]	9/12 (75.0%) [1]	10/12 (83.3%) [1]	12/12 (100.0%) [1]
Female	8/31 (25.8%)	14/29 (48.3%) [2]	19/29 (65.5%) [2]	22/27 (81.5%) [4]	25/27 (92.6%) [4]	25/27 (92.6%) [4]

n = Number of participants with a Tanner Stage V at Year x or with a Tanner Stage V prior to Year x.

m = Number of participants at Year x or with a Tanner Stage V prior to Year x.

d = Cumulative number of dropouts who did not reach Tanner Stage V by Year x. Participants reaching Tanner Stage V by Year x are not considered as dropouts.

Number (%) of participants who reached Tanner Stage V (genitalia for male and breasts for female) by each follow-up year were summarized.

Treatment groups in this follow-up study (P351) reflect the originally assigned treatment groups in P083.

[a] The Exposed to Sitagliptin in P083 includes 35 participants who were randomized to the Sitagliptin +/- insulin group, and 1 participant who was randomized to the Placebo followed by Sitagliptin group in P083. 1 participant from this group received sitagliptin as concomitant medication during P351.

[b] The Not Exposed in P083 includes 39 participants who were randomized to the Placebo +/- insulin followed by metformin group, and 5 participants who were randomized to the Metformin group in P083. 4 participants from this group received a DPP-4 inhibitor (sitagliptin or vildagliptin) as concomitant medication during P351.

Source: [P351MK0431: adam-adsl; adts]

Table 12-6
Mean Change (SD) in Growth Velocity (cm/year) from Baseline over Time
(ASF, Female)

Treatment	N	Growth Velocity[a]		
		Mean (SD)	Median	Range
Year 0 to Year 1				
Exposed to Sitagliptin in P083	19	1.4 (1.6)	1.0	-0.2 to 5.3
Not Exposed in P083	27	0.8 (1.9)	0.0	-1.3 to 8.7
Year 0 to Year 2				
Exposed to Sitagliptin in P083	17	1.1 (1.4)	0.6	-0.1 to 4.7
Not Exposed in P083	26	0.8 (1.3)	0.5	-0.1 to 5.8
Year 0 to Year 3				
Exposed to Sitagliptin in P083	13	1.2 (1.0)	1.3	0.0 to 2.9
Not Exposed in P083	19	0.6 (0.8)	0.5	-1.1 to 2.5
Year 0 to Year 4				
Exposed to Sitagliptin in P083	9	0.9 (0.8)	0.5	0.0 to 2.4
Not Exposed in P083	12	0.5 (0.8)	0.3	-0.9 to 1.8
Year 0 to Year 5				
Exposed to Sitagliptin in P083	7	1.0 (0.7)	1.2	0.0 to 2.1
Not Exposed in P083	8	0.6 (0.7)	0.5	-0.3 to 1.8

[a] Growth Velocity = (Change from Baseline (Year 0) in Height)/(Change from Baseline in Chronologic Age).

N = Number of subjects with both baseline and timepoint measurements.

Treatment groups in this follow-up study (P351) reflect the originally assigned treatment groups in P083.

Exposed to Sitagliptin in P083 = The Exposed to Sitagliptin in P083 includes 35 participants who were randomized to the Sitagliptin +/- insulin group, and 1 participant who was randomized to the Placebo followed by Sitagliptin group in P083. 1 participant from this group received sitagliptin as concomitant medication during P351.

Not Exposed in P083 = The Not Exposed in P083 includes 39 participants who were randomized to the Placebo +/- insulin followed by metformin group, and 5 participants who were randomized to the Metformin group in P083. 4 participants from this group received a DPP-4 inhibitor (sitagliptin or vildagliptin) as concomitant medication during P351.

Source: [P351MK0431: adam-adsl; advs]

Table 12-7
Mean Change (SD) in Growth Velocity (cm/year) from Baseline over Time
(ASF, Male)

Treatment	N	Growth Velocity[a]		
		Mean (SD)	Median	Range
Year 0 to Year 1				
Exposed to Sitagliptin in P083	14	1.8 (3.0)	1.0	-0.7 to 10.1
Not Exposed in P083	13	1.8 (1.7)	1.3	-0.7 to 5.4
Year 0 to Year 2				
Exposed to Sitagliptin in P083	11	1.7 (2.1)	1.0	-0.3 to 6.6
Not Exposed in P083	12	1.7 (1.6)	1.5	0.0 to 5.8
Year 0 to Year 3				
Exposed to Sitagliptin in P083	6	2.2 (2.3)	1.4	0.3 to 5.9
Not Exposed in P083	9	1.8 (1.8)	1.2	0.0 to 5.8
Year 0 to Year 4				
Exposed to Sitagliptin in P083	3	3.3 (2.7)	3.9	0.3 to 5.6
Not Exposed in P083	7	1.9 (1.5)	1.2	0.7 to 4.9
Year 0 to Year 5				
Exposed to Sitagliptin in P083	2	2.5 (2.9)	2.5	0.4 to 4.5
Not Exposed in P083	5	2.0 (1.6)	1.2	0.7 to 4.4

[a] Growth Velocity = (Change from Baseline (Year 0) in Height)/(Change from Baseline in Chronologic Age).

N = Number of subjects with both baseline and timepoint measurements.

Treatment groups in this follow-up study (P351) reflect the originally assigned treatment groups in P083.

Exposed to Sitagliptin in P083 = The Exposed to Sitagliptin in P083 includes 35 participants who were randomized to the Sitagliptin +/- insulin group, and 1 participant who was randomized to the Placebo followed by Sitagliptin group in P083. 1 participant from this group received sitagliptin as concomitant medication during P351.

Not Exposed in P083 = The Not Exposed in P083 includes 39 participants who were randomized to the Placebo +/- insulin followed by metformin group, and 5 participants who were randomized to the Metformin group in P083. 4 participants from this group received a DPP-4 inhibitor (sitagliptin or vildagliptin) as concomitant medication during P351.

Source: [P351MK0431: adam-adsl; advs]

12.4.4 Pregnancy

Pregnancies were reported for 3 participants in this study (1 in the Exposed to Sitagliptin in P083 and 2 in the Not Exposed in P083 group) [16.2.7.1.3]. However, none of the participants were exposed to sitagliptin during pregnancy. The narrative for these participants provides details about the events of pregnancy and their outcomes [16.2.7.2].

12.5 Safety Results Summary

No meaningful safety signals were identified in P351.

- The FAIRs of AEs overall, specific AEs by SOC, and SAEs in P351 were generally similar in the Exposed to Sitagliptin in P083 and the Not Exposed in P083 groups.
- One death, in the Exposed to Sitagliptin in P083 group, was reported in P351 due to acute lymphocytic leukemia and was not considered to be related to study intervention by the investigator.
- Auxological and pubertal parameters were generally similar in participants in the Exposed to Sitagliptin in P083 and the Not Exposed in P083 groups.

13 CONCLUSIONS

Key Safety Results

In this noninterventional follow-up study (P351) of up to 5 years in pediatric participants with T2DM and inadequate glycemic control, safety was generally similar in participants exposed to sitagliptin and those not exposed to sitagliptin in P083.

14 SUPPLEMENTAL TABLES AND/OR FIGURES

14.1 Participant Disposition, Protocol Deviations, Demographics, Baseline Characteristics, Medical History, and Exposure

14.1.1 Disposition of Participants

Table 14.1-1
Disposition of Participants

	Exposed to Sitagliptin in P083[a] n (%)	Not Exposed in P083[b] n (%)	Total n (%)
Enrolled in P351	36	44	80
Completed	24 (66.7)	33 (75.0)	57 (71.3)
Discontinued	12 (33.3)	11 (25.0)	23 (28.8)
Death	1 (2.8)	0 (0.0)	1 (1.3)
Lost To Follow-Up	4 (11.1)	2 (4.5)	6 (7.5)
Physician Decision	1 (2.8)	1 (2.3)	2 (2.5)
Withdrawal By Parent/Guardian	1 (2.8)	3 (6.8)	4 (5.0)
Withdrawal By Subject	5 (13.9)	5 (11.4)	10 (12.5)

Treatment groups in this follow-up study (P351) reflect the originally assigned treatment groups in P083.

[a] The Exposed to Sitagliptin in P083 includes 35 participants who were randomized to the Sitagliptin +/- insulin group, and 1 participant who was randomized to the Placebo followed by Sitagliptin group in P083. 1 participant from this group received sitagliptin as concomitant medication during P351.

[b] The Not Exposed in P083 includes 39 participants who were randomized to the Placebo +/- insulin followed by metformin group, and 5 participants who were randomized to the Metformin group in P083. 4 participants from this group received a DPP-4 inhibitor (sitagliptin or vildagliptin) as concomitant medication during P351.

Source: [P351MK0431: adam-adsl]

Table 14.1-2
Summary of Follow-Up
(ASF)

	Exposed to Sitagliptin in P083[a] (n=36)	Not Exposed in P083[b] (n=44)	Total (n=80)
Length follow-up, n(%)			
1 year or less	3 (8.3)	2 (4.5)	5 (6.3)
>1 to 2 years	8 (22.2)	8 (18.2)	16 (20.0)
>2 to 3 years	7 (19.4)	10 (22.7)	17 (21.3)
>3 to 4 years	8 (22.2)	8 (18.2)	16 (20.0)
>4 years	10 (27.8)	16 (36.4)	26 (32.5)
Mean (SD) length of follow-up (years)	3.1 (1.4)	3.3 (1.4)	3.2 (1.4)
Median (Q1, Q3) length of follow-up (years)	3.0 (2.0, 4.7)	3.1 (2.0, 4.9)	3.0 (2.0, 4.9)
Total participant-years of follow-up	110.0	143.7	253.7

Follow-up time was computed for each participant as the follow-up start date to the last day of the follow-up.
SD = Standard deviation; Q1 = 25th percentile; Q3 = 75th percentile.

[a] The Exposed to Sitagliptin in P083 includes 35 participants who were randomized to the Sitagliptin +/- insulin group, and 1 participant who was randomized to the Placebo followed by Sitagliptin group in P083. 1 participant from this group received sitagliptin as concomitant medication during P351.

[b] The Not Exposed in P083 includes 39 participants who were randomized to the Placebo +/- insulin followed by metformin group, and 5 participants who were randomized to the Metformin group in P083. 4 participants from this group received a DPP-4 inhibitor (sitagliptin or vildagliptin) as concomitant medication during P351.

Source: [P351MK0431: adam-adsl]

14.1.2 Protocol Deviations

Table 14.1-3
Summary of Important Protocol Deviations
(ASF)

	Exposed to Sitagliptin in P083[a]		Not Exposed in P083[b]		Total	
	n	(%)	n	(%)	n	(%)
Participants in population	36		44		80	
with one or more important protocol deviations	3	(8.3)	6	(13.6)	9	(11.3)
with no important protocol deviations	33	(91.7)	38	(86.4)	71	(88.8)
Safety Reporting	**1**	**(2.8)**	**3**	**(6.8)**	**4**	**(5.0)**
Participant had a reportable Safety Event and/or follow up Safety Event information that was not reported per the timelines outlined in the protocol.	1	(2.8)	3	(6.8)	4	(5.0)
Trial Procedures	**2**	**(5.6)**	**4**	**(9.1)**	**6**	**(7.5)**
Failure to conduct major / significant protocol-specified safety evaluations.	1	(2.8)	3	(6.8)	4	(5.0)
Missed weight or height measurement, or Tanner staging	1	(2.8)	1	(2.3)	2	(2.5)

Every participant is counted a single time for each applicable row and column.

Treatment groups in this follow-up study (P351) reflect the originally assigned treatment groups in P083.

[a] The Exposed to Sitagliptin in P083 includes 35 participants who were randomized to the Sitagliptin +/- insulin group, and 1 participant who was randomized to the Placebo followed by Sitagliptin group in P083. 1 participant from this group received sitagliptin as concomitant medication during P351.

[b] The Not Exposed in P083 includes 39 participants who were randomized to the Placebo +/- insulin followed by metformin group, and 5 participants who were randomized to the Metformin group in P083. 4 participants from this group received a DPP-4 inhibitor (sitagliptin or vildagliptin) as concomitant medication during P351.

Source: [P351MK0431: adam-adsl] [P351MK0431: sdtm-dv; suppdv]

14.1.3 Demographics and Other Baseline Characteristics

Table 14.1-4
Demographic and Anthropometric Characteristics
(ASF)

	Exposed to Sitagliptin in P083[a]		Not Exposed in P083[b]		Total	
	n	(%)	n	(%)	n	(%)
Participants in population	36		44		80	
Gender						
Male	16	(44.4)	13	(29.5)	29	(36.3)
Female	20	(55.6)	31	(70.5)	51	(63.8)
Age at Year 0 of P351 (Years)						
≥10 and <15	13	(36.1)	19	(43.2)	32	(40.0)
≥15 and <18	15	(41.7)	21	(47.7)	36	(45.0)
≥18	8	(22.2)	4	(9.1)	12	(15.0)
Mean	15.1		14.7		14.9	
SD	2.3		2.0		2.1	
Median	15.0		15.0		15.0	
Range	11 to 19		11 to 18		11 to 19	
Race						
American Indian Or Alaska Native	2	(5.6)	3	(6.8)	5	(6.3)
Asian	5	(13.9)	8	(18.2)	13	(16.3)
Black Or African American	1	(2.8)	1	(2.3)	2	(2.5)
Multiple	13	(36.1)	14	(31.8)	27	(33.8)

Demographic and Anthropometric Characteristics
(ASF)

	Exposed to Sitagliptin in P083[a]		Not Exposed in P083[b]		Total	
	n	(%)	n	(%)	n	(%)
American Indian Or Alaska Native, Black Or African American	1	(2.8)	0	(0.0)	1	(1.3)
American Indian Or Alaska Native, White	8	(22.2)	9	(20.5)	17	(21.3)
Black Or African American, White	4	(11.1)	5	(11.4)	9	(11.3)
White	15	(41.7)	18	(40.9)	33	(41.3)
Ethnicity						
Hispanic Or Latino	18	(50.0)	19	(43.2)	37	(46.3)
Not Hispanic Or Latino	18	(50.0)	24	(54.5)	42	(52.5)
Not Reported	0	(0.0)	1	(2.3)	1	(1.3)
Height at Year 0 of P351 (cm)						
Mean	162.5		160.7		161.5	
SD	10.8		10.0		10.3	
Median	162.0		161.1		162.0	
Range	143 to 184		140 to 181		140 to 184	
Body Weight at Year 0 of P351 (kg)						
Mean	85.7		77.5		81.2	
SD	19.6		22.1		21.3	
Median	86.4		72.5		77.6	
Range	53.6 to 128.8		43.8 to 128.0		43.8 to 128.8	

Demographic and Anthropometric Characteristics
(ASF)

	Exposed to Sitagliptin in P083[a]		Not Exposed in P083[b]		Total	
	n	(%)	n	(%)	n	(%)
Body Mass Index at Year 0 of P351 (kg/m^2)						
Mean	32.7		29.7		31.1	
SD	8.2		6.9		7.6	
Median	31.7		27.6		28.8	
Range	20.9 to 57.2		21.4 to 47.6		20.9 to 57.2	
Region						
EU or EU-like Countries	8	(22.2)	11	(25.0)	19	(23.8)
Other	28	(77.8)	33	(75.0)	61	(76.3)
Duration of Type 2 Diabetes Mellitus at Year 0 of P351 (years) (derived based on P083 medical history)						
Mean	1.8		2.0		2.0	
SD	1.6		1.7		1.6	
Median	1.3		1.5		1.4	

Demographic and Anthropometric Characteristics
(ASF)

	Exposed to Sitagliptin in P083[a]		Not Exposed in P083[b]		Total	
	n	(%)	n	(%)	n	(%)
Range	1.1 to 10.1		1.1 to 9.0		1.1 to 10.1	

SD=Standard deviation.

Based on P083 enrollment:

Gender, Race, Ethnicity, Region.

Bulgaria, Canada, Hungary, Italy, Latvia, Lithuania, Poland, Romania, Russian Federation, and Serbia are classified as EU or EU-like countries.

Age at baseline = (Number of days from date of birth to first day of this follow-up study + 1)/365.25.

Treatment groups in this follow-up study (P351) reflect the originally assigned treatment groups in P083.

[a] The Exposed to Sitagliptin in P083 includes 35 participants who were randomized to the Sitagliptin +/- insulin group, and 1 participant who was randomized to the Placebo followed by Sitagliptin group in P083. 1 participant from this group received sitagliptin as concomitant medication during P351.

[b] The Not Exposed in P083 includes 39 participants who were randomized to the Placebo +/- insulin followed by metformin group, and 5 participants who were randomized to the Metformin group in P083. 4 participants from this group received a DPP-4 inhibitor (sitagliptin or vildagliptin) as concomitant medication during P351.

Source: [P351MK0431: adam-adsl; adbase]

Table 14.1-5
Participants With Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(ASF)

	Exposed to Sitagliptin in P083[a]		Not Exposed in P083[b]		Total	
	n	(%)	n	(%)	n	(%)
Participants in population	36		44		80	
with one or more concomitant medications	34	(94.4)	42	(95.5)	76	(95.0)
with no concomitant medication	2	(5.6)	2	(4.5)	4	(5.0)
Alimentary tract and metabolism						
Antidiarrheals, intestinal antiinflammatory/antiinfective agents	**2**	**(5.6)**	**3**	**(6.8)**	**5**	**(6.3)**
Bifidobacterium infantis (+) Enterococcus faecalis (+) Lactobacillus acidophilus	0	(0.0)	1	(2.3)	1	(1.3)
Nifuroxazide	1	(2.8)	2	(4.5)	3	(3.8)
Saccharomyces boulardii	1	(2.8)	1	(2.3)	2	(2.5)
Smectite	0	(0.0)	1	(2.3)	1	(1.3)
Digestives, incl. enzymes	**1**	**(2.8)**	**2**	**(4.5)**	**3**	**(3.8)**
Pancreatin	1	(2.8)	2	(4.5)	3	(3.8)
Drugs for acid related disorders	**3**	**(8.3)**	**4**	**(9.1)**	**7**	**(8.8)**
Esomeprazole	0	(0.0)	1	(2.3)	1	(1.3)
Lansoprazole	0	(0.0)	1	(2.3)	1	(1.3)
Omeprazole	1	(2.8)	3	(6.8)	4	(5.0)
Pantoprazole	2	(5.6)	2	(4.5)	4	(5.0)
Ranitidine hydrochloride	0	(0.0)	1	(2.3)	1	(1.3)
Sucralfate	0	(0.0)	2	(4.5)	2	(2.5)
Drugs for constipation	**1**	**(2.8)**	**0**	**(0.0)**	**1**	**(1.3)**
Glycerin	1	(2.8)	0	(0.0)	1	(1.3)
Drugs for functional gastrointestinal disorders	**2**	**(5.6)**	**2**	**(4.5)**	**4**	**(5.0)**
Drotaverine	1	(2.8)	0	(0.0)	1	(1.3)
Metoclopramide	1	(2.8)	0	(0.0)	1	(1.3)
Metoclopramide hydrochloride	0	(0.0)	1	(2.3)	1	(1.3)
Trimebutine	0	(0.0)	1	(2.3)	1	(1.3)
Drugs used in diabetes	**31**	**(86.1)**	**39**	**(88.6)**	**70**	**(87.5)**
Acarbose	1	(2.8)	0	(0.0)	1	(1.3)
Dapagliflozin	2	(5.6)	1	(2.3)	3	(3.8)
Dulaglutide	2	(5.6)	0	(0.0)	2	(2.5)
Empagliflozin	1	(2.8)	0	(0.0)	1	(1.3)
Gliclazide	1	(2.8)	0	(0.0)	1	(1.3)
Glyburide	0	(0.0)	2	(4.5)	2	(2.5)

Participants With Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(ASF)

	Exposed to Sitagliptin in P083[a]		Not Exposed in P083[b]		Total	
	n	(%)	n	(%)	n	(%)
Alimentary tract and metabolism						
Drugs used in diabetes	**31**	**(86.1)**	**39**	**(88.6)**	**70**	**(87.5)**
Insulin	0	(0.0)	1	(2.3)	1	(1.3)
Insulin degludec	1	(2.8)	0	(0.0)	1	(1.3)
Insulin detemir	0	(0.0)	1	(2.3)	1	(1.3)
Insulin glargine	12	(33.3)	8	(18.2)	20	(25.0)
Insulin human	1	(2.8)	3	(6.8)	4	(5.0)
Insulin human (+) insulin human, isophane	0	(0.0)	2	(4.5)	2	(2.5)
Insulin human, isophane	0	(0.0)	5	(11.4)	5	(6.3)
Insulin lispro	3	(8.3)	1	(2.3)	4	(5.0)
Insulin lispro (+) insulin lispro protamine	0	(0.0)	1	(2.3)	1	(1.3)
Insulin, isophane	1	(2.8)	0	(0.0)	1	(1.3)
Liraglutide	1	(2.8)	1	(2.3)	2	(2.5)
Metformin	22	(61.1)	35	(79.5)	57	(71.3)
Metformin hydrochloride	3	(8.3)	1	(2.3)	4	(5.0)
Metformin hydrochloride (+) sitagliptin phosphate	1	(2.8)	2	(4.5)	3	(3.8)
Metformin hydrochloride (+) vildagliptin	0	(0.0)	1	(2.3)	1	(1.3)
Semaglutide	1	(2.8)	0	(0.0)	1	(1.3)
Sitagliptin	0	(0.0)	1	(2.3)	1	(1.3)
Sitagliptin phosphate	0	(0.0)	1	(2.3)	1	(1.3)
Mineral supplements	**0**	**(0.0)**	**2**	**(4.5)**	**2**	**(2.5)**
Calcium (unspecified)	0	(0.0)	1	(2.3)	1	(1.3)
Calcium (unspecified) (+) cholecalciferol (+) magnesium (unspecified)	0	(0.0)	1	(2.3)	1	(1.3)
Stomatological preparations	**1**	**(2.8)**	**1**	**(2.3)**	**2**	**(2.5)**
Hexetidine	1	(2.8)	1	(2.3)	2	(2.5)
Vitamins	**1**	**(2.8)**	**2**	**(4.5)**	**3**	**(3.8)**
Cholecalciferol	0	(0.0)	1	(2.3)	1	(1.3)
Pyridoxine hydrochloride	0	(0.0)	1	(2.3)	1	(1.3)
Vitamin D (unspecified)	1	(2.8)	0	(0.0)	1	(1.3)
Antiinfectives for systemic use						
Antibacterials for systemic use	**6**	**(16.7)**	**11**	**(25.0)**	**17**	**(21.3)**

Participants With Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(ASF)

	Exposed to Sitagliptin in P083[a]		Not Exposed in P083[b]		Total	
	n	(%)	n	(%)	n	(%)
Antiinfectives for systemic use						
Antibacterials for systemic use	**6**	**(16.7)**	**11**	**(25.0)**	**17**	**(21.3)**
Amoxicillin	1	(2.8)	2	(4.5)	3	(3.8)
Azithromycin	0	(0.0)	1	(2.3)	1	(1.3)
Cefdinir	1	(2.8)	0	(0.0)	1	(1.3)
Cefixime	1	(2.8)	0	(0.0)	1	(1.3)
Ceftriaxone	0	(0.0)	2	(4.5)	2	(2.5)
Cefuroxime	0	(0.0)	1	(2.3)	1	(1.3)
Cefuroxime axetil	0	(0.0)	1	(2.3)	1	(1.3)
Ciprofloxacin	1	(2.8)	2	(4.5)	3	(3.8)
Fusidic acid	1	(2.8)	0	(0.0)	1	(1.3)
Levofloxacin	1	(2.8)	1	(2.3)	2	(2.5)
Lymecycline	0	(0.0)	1	(2.3)	1	(1.3)
Metronidazole	0	(0.0)	1	(2.3)	1	(1.3)
Nitrofurantoin	0	(0.0)	1	(2.3)	1	(1.3)
Norfloxacin	0	(0.0)	1	(2.3)	1	(1.3)
Antimycotics for systemic use	**0**	**(0.0)**	**1**	**(2.3)**	**1**	**(1.3)**
Fluconazole	0	(0.0)	1	(2.3)	1	(1.3)
Antivirals for systemic use	**3**	**(8.3)**	**2**	**(4.5)**	**5**	**(6.3)**
Acyclovir	2	(5.6)	0	(0.0)	2	(2.5)
Cagocel-1	1	(2.8)	0	(0.0)	1	(1.3)
Imidazolyl ethanamide pentandioic acid	1	(2.8)	1	(2.3)	2	(2.5)
Lysozyme chloride	1	(2.8)	0	(0.0)	1	(1.3)
Umifenovir	0	(0.0)	1	(2.3)	1	(1.3)
Vaccines	**2**	**(5.6)**	**1**	**(2.3)**	**3**	**(3.8)**
COVID-19 vaccine inact (Vero) CZ02	2	(5.6)	0	(0.0)	2	(2.5)
Tozinameran	0	(0.0)	1	(2.3)	1	(1.3)
Antineoplastic and immunomodulating agents						
Immunostimulants	**0**	**(0.0)**	**1**	**(2.3)**	**1**	**(1.3)**
Polyadenylate-polyuridylate potassium complex	0	(0.0)	1	(2.3)	1	(1.3)
Blood and blood forming organs						
Antianemic preparations	**0**	**(0.0)**	**1**	**(2.3)**	**1**	**(1.3)**

Participants With Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(ASF)

	Exposed to Sitagliptin in P083[a]		Not Exposed in P083[b]		Total	
	n	(%)	n	(%)	n	(%)
Blood and blood forming organs						
Antianemic preparations	**0**	**(0.0)**	**1**	**(2.3)**	**1**	**(1.3)**
Folic acid	0	(0.0)	1	(2.3)	1	(1.3)
Blood substitutes and perfusion solutions	**0**	**(0.0)**	**2**	**(4.5)**	**2**	**(2.5)**
Dextrose (+) electrolytes (unspecified)	0	(0.0)	1	(2.3)	1	(1.3)
Sodium chloride	0	(0.0)	1	(2.3)	1	(1.3)
Cardiovascular system						
Agents acting on the renin-angiotensin system	**2**	**(5.6)**	**6**	**(13.6)**	**8**	**(10.0)**
Captopril	0	(0.0)	1	(2.3)	1	(1.3)
Enalapril	2	(5.6)	2	(4.5)	4	(5.0)
Enalapril maleate	0	(0.0)	1	(2.3)	1	(1.3)
Irbesartan	0	(0.0)	1	(2.3)	1	(1.3)
Perindopril	0	(0.0)	1	(2.3)	1	(1.3)
Perindopril arginine	0	(0.0)	1	(2.3)	1	(1.3)
Beta blocking agents	**0**	**(0.0)**	**1**	**(2.3)**	**1**	**(1.3)**
Bisoprolol fumarate	0	(0.0)	1	(2.3)	1	(1.3)
Diuretics	**0**	**(0.0)**	**1**	**(2.3)**	**1**	**(1.3)**
Indapamide	0	(0.0)	1	(2.3)	1	(1.3)
Lipid modifying agents	**1**	**(2.8)**	**3**	**(6.8)**	**4**	**(5.0)**
Bezafibrate	1	(2.8)	1	(2.3)	2	(2.5)
Ciprofibrate	0	(0.0)	1	(2.3)	1	(1.3)
Omega-3 marine triglycerides	0	(0.0)	1	(2.3)	1	(1.3)
Dermatologicals						
Anti-acne preparations	**0**	**(0.0)**	**1**	**(2.3)**	**1**	**(1.3)**
Clindamycin phosphate (+) tretinoin	0	(0.0)	1	(2.3)	1	(1.3)
Erythromycin (+) zinc acetate	0	(0.0)	1	(2.3)	1	(1.3)
Antifungals for dermatological use	**3**	**(8.3)**	**1**	**(2.3)**	**4**	**(5.0)**
Econazole nitrate (+) triamcinolone acetonide	1	(2.8)	0	(0.0)	1	(1.3)
Efinaconazole	1	(2.8)	0	(0.0)	1	(1.3)
Miconazole	1	(2.8)	1	(2.3)	2	(2.5)
Antiseptics and disinfectants	**3**	**(8.3)**	**2**	**(4.5)**	**5**	**(6.3)**

Participants With Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(ASF)

	Exposed to Sitagliptin in P083[a]		Not Exposed in P083[b]		Total	
	n	(%)	n	(%)	n	(%)
Dermatologicals						
Antiseptics and disinfectants	**3**	**(8.3)**	**2**	**(4.5)**	**5**	**(6.3)**
Cetostearyl alcohol (+) phenoxyethanol (+) sodium lauryl sulfate	1	(2.8)	0	(0.0)	1	(1.3)
Chlorhexidine	1	(2.8)	0	(0.0)	1	(1.3)
Chlorhexidine gluconate (+) dichlorobenzyl alcohol (+) lactic acid (+) phenoxyethanol (+) sorbitol	0	(0.0)	1	(2.3)	1	(1.3)
Miramistin	1	(2.8)	1	(2.3)	2	(2.5)
Corticosteroids, dermatological preparations	**3**	**(8.3)**	**0**	**(0.0)**	**3**	**(3.8)**
Hydrocortisone acetate	1	(2.8)	0	(0.0)	1	(1.3)
Mometasone furoate	3	(8.3)	0	(0.0)	3	(3.8)
Genitourinary system and sex hormones						
Sex hormones and modulators of the genital system	**1**	**(2.8)**	**3**	**(6.8)**	**4**	**(5.0)**
Cyproterone acetate	0	(0.0)	1	(2.3)	1	(1.3)
Cyproterone acetate (+) ethinyl estradiol	0	(0.0)	1	(2.3)	1	(1.3)
Desogestrel (+) ethinyl estradiol	1	(2.8)	0	(0.0)	1	(1.3)
Dienogest (+) ethinyl estradiol	0	(0.0)	1	(2.3)	1	(1.3)
Estradiol	0	(0.0)	1	(2.3)	1	(1.3)
Ethinyl estradiol (+) norgestimate	0	(0.0)	1	(2.3)	1	(1.3)
Nomegestrol acetate	0	(0.0)	1	(2.3)	1	(1.3)
Urologicals	**1**	**(2.8)**	**0**	**(0.0)**	**1**	**(1.3)**
Citric acid (+) sodium bicarbonate (+) sodium citrate (+) tartaric acid	1	(2.8)	0	(0.0)	1	(1.3)
Tamsulosin hydrochloride	1	(2.8)	0	(0.0)	1	(1.3)
Musculoskeletal system						
Antiinflammatory and antirheumatic products	**6**	**(16.7)**	**5**	**(11.4)**	**11**	**(13.8)**
Benzydamine hydrochloride	2	(5.6)	0	(0.0)	2	(2.5)
Diclofenac	1	(2.8)	1	(2.3)	2	(2.5)
Diclofenac potassium	1	(2.8)	0	(0.0)	1	(1.3)

Participants With Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(ASF)

	Exposed to Sitagliptin in P083[a]		Not Exposed in P083[b]		Total	
	n	(%)	n	(%)	n	(%)
Musculoskeletal system						
Antiinflammatory and antirheumatic products	**6**	**(16.7)**	**5**	**(11.4)**	**11**	**(13.8)**
Ibuprofen	4	(11.1)	2	(4.5)	6	(7.5)
Ketorolac tromethamine	0	(0.0)	2	(4.5)	2	(2.5)
Naproxen sodium	1	(2.8)	0	(0.0)	1	(1.3)
Nervous system						
Analgesics	**5**	**(13.9)**	**1**	**(2.3)**	**6**	**(7.5)**
Acetaminophen	5	(13.9)	1	(2.3)	6	(7.5)
Morphine	1	(2.8)	0	(0.0)	1	(1.3)
Antiepileptics	**1**	**(2.8)**	**0**	**(0.0)**	**1**	**(1.3)**
Oxcarbazepine	1	(2.8)	0	(0.0)	1	(1.3)
Psychoanaleptics	**0**	**(0.0)**	**1**	**(2.3)**	**1**	**(1.3)**
Fluoxetine hydrochloride	0	(0.0)	1	(2.3)	1	(1.3)
Methylphenidate hydrochloride	0	(0.0)	1	(2.3)	1	(1.3)
Psycholeptics	**0**	**(0.0)**	**2**	**(4.5)**	**2**	**(2.5)**
Levosulpiride	0	(0.0)	1	(2.3)	1	(1.3)
Phenobarbital (+) valerian	0	(0.0)	1	(2.3)	1	(1.3)
Respiratory system						
Antihistamines for systemic use	**4**	**(11.1)**	**3**	**(6.8)**	**7**	**(8.8)**
Cetirizine hydrochloride	1	(2.8)	2	(4.5)	3	(3.8)
Diphenhydramine	1	(2.8)	0	(0.0)	1	(1.3)
Diphenhydramine hydrochloride	1	(2.8)	0	(0.0)	1	(1.3)
Loratadine	1	(2.8)	1	(2.3)	2	(2.5)
Cough and cold preparations	**2**	**(5.6)**	**1**	**(2.3)**	**3**	**(3.8)**
Ambroxol hydrochloride	1	(2.8)	1	(2.3)	2	(2.5)
Bromhexine hydrochloride	1	(2.8)	0	(0.0)	1	(1.3)
Potassium iodide	1	(2.8)	0	(0.0)	1	(1.3)
Drugs for obstructive airway diseases	**2**	**(5.6)**	**2**	**(4.5)**	**4**	**(5.0)**
Albuterol sulfate	1	(2.8)	0	(0.0)	1	(1.3)
Albuterol sulfate (+) bromhexine hydrochloride (+) guaifenesin	0	(0.0)	1	(2.3)	1	(1.3)
Beclomethasone dipropionate	0	(0.0)	1	(2.3)	1	(1.3)

Participants With Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(ASF)

	Exposed to Sitagliptin in P083[a]		Not Exposed in P083[b]		Total	
	n	(%)	n	(%)	n	(%)
Respiratory system						
Drugs for obstructive airway diseases	**2**	**(5.6)**	**2**	**(4.5)**	**4**	**(5.0)**
Fenspiride hydrochloride	1	(2.8)	0	(0.0)	1	(1.3)
Nasal preparations	**2**	**(5.6)**	**1**	**(2.3)**	**3**	**(3.8)**
Dimethindene maleate (+) phenylephrine	1	(2.8)	0	(0.0)	1	(1.3)
Naphazoline hydrochloride	1	(2.8)	0	(0.0)	1	(1.3)
Oxymetazoline hydrochloride	1	(2.8)	0	(0.0)	1	(1.3)
Xylometazoline hydrochloride	1	(2.8)	1	(2.3)	2	(2.5)
Throat preparations	**0**	**(0.0)**	**1**	**(2.3)**	**1**	**(1.3)**
Eucalyptus oil (+) peppermint oil (+) sulfanilamide (+) sulfathiazole sodium (+) thymol	0	(0.0)	1	(2.3)	1	(1.3)
Sensory organs						
Ophthalmologicals	**1**	**(2.8)**	**1**	**(2.3)**	**2**	**(2.5)**
Diphenhydramine hydrochloride (+) hypromellose (+) interferon alfa-2b (+) polyethylene oxide (+) povidone	1	(2.8)	1	(2.3)	2	(2.5)
Systemic hormonal preparations, excl. sex hormones and insulins						
Thyroid therapy	**1**	**(2.8)**	**4**	**(9.1)**	**5**	**(6.3)**
Levothyroxine sodium	1	(2.8)	4	(9.1)	5	(6.3)
Various						
All other non-therapeutic products	**0**	**(0.0)**	**1**	**(2.3)**	**1**	**(1.3)**
Cocamidopropyl betaine (+) lactic acid (+) sodium laureth sulfate (+) sorbitol	0	(0.0)	1	(2.3)	1	(1.3)
All other therapeutic products	**1**	**(2.8)**	**3**	**(6.8)**	**4**	**(5.0)**
Aconite (+) belladonna (+) calendula (+) celandine (+) cramp bark (+) precatory	0	(0.0)	1	(2.3)	1	(1.3)
Chaste tree (+) D-chiro-inositol (+) folic acid (+) hops (+) inositol (+) Salacia reticulate (+) Verbena officinalis	0	(0.0)	1	(2.3)	1	(1.3)
Cowslip (+) European elder (+) European vervain (+) gentian (+) sorrel	0	(0.0)	1	(2.3)	1	(1.3)

Participants With Concomitant Medications
(Incidence > 0% in One or More Treatment Groups)
(ASF)

	Exposed to Sitagliptin in P083[a]		Not Exposed in P083[b]		Total	
	n	(%)	n	(%)	n	(%)
Various						
All other therapeutic products	**1**	**(2.8)**	**3**	**(6.8)**	**4**	**(5.0)**
Cyanocobalamin (+) D-chiro-inositol (+) folic acid (+) manganese sulfate	0	(0.0)	1	(2.3)	1	(1.3)
English ivy	1	(2.8)	0	(0.0)	1	(1.3)

Every participant is counted a single time for each applicable specific concomitant medication. A participant with multiple concomitant medications within a medication category is counted a single time for that category.

Each specific concomitant medication is listed under all relevant medication classes based on the medication's generic name, regardless of route of administration or reason for use.

A medication that is not mapped to a second level therapeutic subgroup is classified under Other.

A medication class or specific medication appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.

Treatment groups in this follow-up study (P351) reflect the originally assigned treatment groups in P083.

[a] The Exposed to Sitagliptin in P083 includes 35 participants who were randomized to the Sitagliptin +/- insulin group, and 1 participant who was randomized to the Placebo followed by Sitagliptin group in P083. 1 participant from this group received sitagliptin as concomitant medication during P351.

[b] The Not Exposed in P083 includes 39 participants who were randomized to the Placebo +/- insulin followed by metformin group, and 5 participants who were randomized to the Metformin group in P083. 4 participants from this group received a DPP-4 inhibitor (sitagliptin or vildagliptin) as concomitant medication during P351.

Source: [P351MK0431: adam-adsl; adcm]

14.1.4 Measurements of Study Intervention Compliance

Not applicable.

14.1.5 Extent of Exposure

Not applicable.

14.2 Efficacy Data

No efficacy endpoints were collected for this noninterventional study.

14.3 Safety Data

14.3.1 Adverse Events

14.3.1.1 All Adverse Events

Table 14.3-1
Adverse Event Summary
(ASF)

	Exposed to Sitagliptin in P083[a] n (FAIR in 100-participant-years)	Not Exposed in P083[b] n (FAIR in 100-participant-years)
Participants in population	36	44
with one or more adverse events	15/72.6 (20.7)	20/99.2 (20.2)
with serious adverse events	3/103.0 (2.9)	3/140.3 (2.1)
who died	1/107.7 (0.9)	0/143.7 (0.0)
discontinued follow-up due to an adverse event	0/110.0 (0.0)	0/143.7 (0.0)

FAIR: Follow-up adjusted incidence rate = (Number of participants with ≥1 event during the follow-up study) / (Total participant-years of follow-up).

Treatment groups in this follow-up study (P351) reflect the originally assigned treatment groups in P083.

[a] The Exposed to Sitagliptin in P083 includes 35 participants who were randomized to the Sitagliptin +/- insulin group, and 1 participant who was randomized to the Placebo followed by Sitagliptin group in P083. 1 participant from this group received sitagliptin as concomitant medication during P351.

[b] The Not Exposed in P083 includes 39 participants who were randomized to the Placebo +/- insulin followed by metformin group, and 5 participants who were randomized to the Metformin group in P083. 4 participants from this group received a DPP-4 inhibitor (sitagliptin or vildagliptin) as concomitant medication during P351.

For participants who have an event, the participant-years of follow-up will be calculated as (Date of the first event - First day of the follow-up study + 1)/365.25. For participants without an event, the participant-years of follow-up will be calculated as (Last day of the follow-up window - First day of the follow-up study + 1)/365.25. The total participant-years for a treatment group will be the sum of the participant-years of follow-up of all participants in the treatment group.

Source: [P351MK0431: adam-adsl; adtte]

Table 14.3-2
Participants with Specific Adverse Events
(Incidence >0% in One or More Treatment Groups)
(ASF)

	Exposed to Sitagliptin in P083[a] n (FAIR in 100-participant-years)	Not Exposed in P083[b] n (FAIR in 100-participant-years)
Participants in population	36	44
with one or more adverse events	15/72.6 (20.7)	20/99.2 (20.2)
Blood and lymphatic system disorders	**0/110.0 (0.0)**	**1/142.7 (0.7)**
Hypochromic anaemia	0/110.0 (0.0)	1/142.7 (0.7)
Cardiac disorders	**0/110.0 (0.0)**	**1/138.7 (0.7)**
Wandering pacemaker	0/110.0 (0.0)	1/138.7 (0.7)
Endocrine disorders	**0/110.0 (0.0)**	**1/141.9 (0.7)**
Hypothyroidism	0/110.0 (0.0)	1/141.9 (0.7)
Eye disorders	**0/110.0 (0.0)**	**2/139.3 (1.4)**
Accommodation disorder	0/110.0 (0.0)	1/140.4 (0.7)
Diabetic retinopathy	0/110.0 (0.0)	1/142.7 (0.7)
Retinal vascular disorder	0/110.0 (0.0)	1/140.4 (0.7)
Gastrointestinal disorders	**3/104.1 (2.9)**	**6/133.3 (4.5)**
Abdominal pain	1/108.3 (0.9)	1/141.9 (0.7)
Abdominal pain lower	0/110.0 (0.0)	1/142.1 (0.7)
Diarrhoea	0/110.0 (0.0)	2/140.3 (1.4)
Dyspepsia	0/110.0 (0.0)	1/143.7 (0.7)
Food poisoning	1/108.9 (0.9)	0/143.7 (0.0)
Gastritis	1/107.0 (0.9)	2/139.1 (1.4)
Lip ulceration	1/108.8 (0.9)	0/143.7 (0.0)
General disorders and administration site conditions	**1/105.2 (1.0)**	**1/143.7 (0.7)**
Non-cardiac chest pain	1/105.2 (1.0)	0/143.7 (0.0)
Pyrexia	0/110.0 (0.0)	1/143.7 (0.7)
Infections and infestations	**10/86.7 (11.5)**	**10/129.4 (7.7)**
Appendicitis	0/110.0 (0.0)	2/141.3 (1.4)
Bacteriuria	1/107.5 (0.9)	0/143.7 (0.0)
Body tinea	1/108.3 (0.9)	0/143.7 (0.0)
Bronchitis	0/110.0 (0.0)	1/142.6 (0.7)

Participants with Specific Adverse Events
(Incidence >0% in One or More Treatment Groups)
(ASF)

	Exposed to Sitagliptin in P083[a] n (FAIR in 100-participant-years)	Not Exposed in P083[b] n (FAIR in 100-participant-years)
Infections and infestations	**10/86.7 (11.5)**	**10/129.4 (7.7)**
COVID-19	1/109.9 (0.9)	0/143.7 (0.0)
Conjunctivitis	1/107.8 (0.9)	1/142.0 (0.7)
Cystitis	0/110.0 (0.0)	1/141.7 (0.7)
Enterovirus infection	0/110.0 (0.0)	2/141.0 (1.4)
Folliculitis	0/110.0 (0.0)	1/141.5 (0.7)
Fungal skin infection	1/109.7 (0.9)	0/143.7 (0.0)
Gastroenteritis	0/110.0 (0.0)	2/143.5 (1.4)
Gastrointestinal infection	1/106.1 (0.9)	0/143.7 (0.0)
Herpes simplex	1/108.0 (0.9)	0/143.7 (0.0)
Impetigo	1/109.4 (0.9)	0/143.7 (0.0)
Influenza	1/108.7 (0.9)	0/143.7 (0.0)
Laryngopharyngitis	0/110.0 (0.0)	1/141.7 (0.7)
Nasopharyngitis	2/105.9 (1.9)	1/141.2 (0.7)
Onychomycosis	1/109.8 (0.9)	0/143.7 (0.0)
Otitis media acute	0/110.0 (0.0)	1/142.2 (0.7)
Pharyngitis	0/110.0 (0.0)	1/143.1 (0.7)
Pilonidal disease	1/105.1 (1.0)	0/143.7 (0.0)
Respiratory tract infection viral	1/109.5 (0.9)	1/142.7 (0.7)
Rotavirus infection	1/108.3 (0.9)	0/143.7 (0.0)
Sinusitis	0/110.0 (0.0)	1/142.2 (0.7)
Upper respiratory tract infection	2/104.5 (1.9)	0/143.7 (0.0)
Urinary tract infection	1/108.7 (0.9)	1/142.2 (0.7)
Varicella	1/108.8 (0.9)	0/143.7 (0.0)
Viral upper respiratory tract infection	0/110.0 (0.0)	1/142.1 (0.7)
Vulvovaginal mycotic infection	0/110.0 (0.0)	1/142.2 (0.7)
Vulvovaginitis	0/110.0 (0.0)	1/143.7 (0.7)
Investigations	**2/103.9 (1.9)**	**1/140.3 (0.7)**
Blood calcium increased	1/108.9 (0.9)	0/143.7 (0.0)
High density lipoprotein decreased	1/105.0 (1.0)	0/143.7 (0.0)
Urine analysis abnormal	1/105.0 (1.0)	0/143.7 (0.0)
Weight increased	0/110.0 (0.0)	1/140.3 (0.7)
Metabolism and nutrition disorders	**4/99.8 (4.0)**	**5/134.6 (3.7)**

Participants with Specific Adverse Events
(Incidence >0% in One or More Treatment Groups)
(ASF)

	Exposed to Sitagliptin in P083[a] n (FAIR in 100-participant-years)	Not Exposed in P083[b] n (FAIR in 100-participant-years)
Metabolism and nutrition disorders	**4/99.8 (4.0)**	**5/134.6 (3.7)**
Diabetes mellitus inadequate control	1/105.4 (0.9)	2/140.1 (1.4)
Hypercholesterolaemia	0/110.0 (0.0)	1/143.7 (0.7)
Hyperglycaemia	1/107.0 (0.9)	2/138.2 (1.4)
Hypertriglyceridaemia	1/108.0 (0.9)	0/143.7 (0.0)
Hypoglycaemia	1/109.4 (0.9)	0/143.7 (0.0)
Musculoskeletal and connective tissue disorders	**1/107.2 (0.9)**	**1/141.7 (0.7)**
Arthralgia	1/107.2 (0.9)	0/143.7 (0.0)
Muscle spasms	0/110.0 (0.0)	1/141.7 (0.7)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**2/106.4 (1.9)**	**0/143.7 (0.0)**
Haemangioma of liver	1/108.7 (0.9)	0/143.7 (0.0)
Leukaemia	1/107.7 (0.9)	0/143.7 (0.0)
Nervous system disorders	**3/100.2 (3.0)**	**3/137.7 (2.2)**
Autonomic neuropathy	0/110.0 (0.0)	1/142.7 (0.7)
Burning sensation	0/110.0 (0.0)	1/142.0 (0.7)
Diabetic neuropathy	0/110.0 (0.0)	1/140.4 (0.7)
Headache	2/105.1 (1.9)	0/143.7 (0.0)
Petit mal epilepsy	1/105.2 (1.0)	0/143.7 (0.0)
Polyneuropathy	0/110.0 (0.0)	1/142.7 (0.7)
Psychiatric disorders	**1/109.7 (0.9)**	**2/140.0 (1.4)**
Anxiety	0/110.0 (0.0)	1/142.0 (0.7)
Insomnia	0/110.0 (0.0)	1/141.7 (0.7)
Intentional self-injury	1/109.7 (0.9)	0/143.7 (0.0)
Renal and urinary disorders	**3/107.8 (2.8)**	**0/143.7 (0.0)**
Microalbuminuria	1/110.0 (0.9)	0/143.7 (0.0)
Nephrolithiasis	2/107.8 (1.9)	0/143.7 (0.0)
Reproductive system and breast disorders	**0/110.0 (0.0)**	**2/137.2 (1.5)**
Menstruation irregular	0/110.0 (0.0)	1/141.5 (0.7)

Participants with Specific Adverse Events (Incidence >0% in One or More Treatment Groups) (ASF)

	Exposed to Sitagliptin in P083[a] n (FAIR in 100-participant-years)	Not Exposed in P083[b] n (FAIR in 100-participant-years)
Reproductive system and breast disorders	**0/110.0 (0.0)**	**2/137.2 (1.5)**
Ovarian cyst	0/110.0 (0.0)	1/139.9 (0.7)
Polycystic ovaries	0/110.0 (0.0)	1/141.0 (0.7)
Respiratory, thoracic and mediastinal disorders	**2/104.3 (1.9)**	**1/143.7 (0.7)**
Productive cough	1/108.1 (0.9)	0/143.7 (0.0)
Respiratory tract inflammation	0/110.0 (0.0)	1/143.7 (0.7)
Rhinitis allergic	1/106.2 (0.9)	0/143.7 (0.0)
Skin and subcutaneous tissue disorders	**1/106.8 (0.9)**	**2/138.7 (1.4)**
Acne	0/110.0 (0.0)	1/141.5 (0.7)
Dermatitis	1/107.7 (0.9)	0/143.7 (0.0)
Eczema	1/106.8 (0.9)	0/143.7 (0.0)
Granuloma annulare	0/110.0 (0.0)	1/140.9 (0.7)
Necrobiosis lipoidica diabeticorum	0/110.0 (0.0)	1/140.9 (0.7)

FAIR: Follow-up adjusted incidence rate = (Number of participants with ≥1 event during the follow-up study) / (Total participant-years of follow-up).

Treatment groups in this follow-up study (P351) reflect the originally assigned treatment groups in P083.

[a] The Exposed to Sitagliptin in P083 includes 35 participants who were randomized to the Sitagliptin +/- insulin group, and 1 participant who was randomized to the Placebo followed by Sitagliptin group in P083. 1 participant from this group received sitagliptin as concomitant medication during P351.

[b] The Not Exposed in P083 includes 39 participants who were randomized to the Placebo +/- insulin followed by metformin group, and 5 participants who were randomized to the Metformin group in P083. 4 participants from this group received a DPP-4 inhibitor (sitagliptin or vildagliptin) as concomitant medication during P351.

For participants who have an event, the participant-years of follow-up will be calculated as (Date of the first event - First day of the follow-up study + 1)/365.25. For participants without an event, the participant-years of follow-up will be calculated as (Last day of the follow-up window - First day of the follow-up study + 1)/365.25. The total participant-years for a treatment group will be the sum of the participant-years of follow-up of all participants in the treatment group.

Source: [P351MK0431: adam-adsl; adtte]

14.3.1.2 Serious Adverse Events, Including Deaths

Table 14.3-3
Participants with Adverse Events Resulting in Death
(Incidence >0% in One or More Treatment Groups)
(ASF)

	Exposed to Sitagliptin in P083[a] n (FAIR in 100-participant-years)	Not Exposed in P083[b] n (FAIR in 100-participant-years)
Participants in population	36	44
who died	1/107.7 (0.9)	0/143.7 (0.0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**1/107.7 (0.9)**	**0/143.7 (0.0)**
Leukaemia	1/107.7 (0.9)	0/143.7 (0.0)

FAIR: Follow-up adjusted incidence rate = (Number of participants with ≥1 event during the follow-up study) / (Total participant-years of follow-up).

Treatment groups in this follow-up study (P351) reflect the originally assigned treatment groups in P083.

[a] The Exposed to Sitagliptin in P083 includes 35 participants who were randomized to the Sitagliptin +/- insulin group, and 1 participant who was randomized to the Placebo followed by Sitagliptin group in P083. 1 participant from this group received sitagliptin as concomitant medication during P351.

[b] The Not Exposed in P083 includes 39 participants who were randomized to the Placebo +/- insulin followed by metformin group, and 5 participants who were randomized to the Metformin group in P083. 4 participants from this group received a DPP-4 inhibitor (sitagliptin or vildagliptin) as concomitant medication during P351.

For participants who have an event, the participant-years of follow-up will be calculated as (Date of the first event - First day of the follow-up study + 1)/365.25. For participants without an event, the participant-years of follow-up will be calculated as (Last day of the follow-up window - First day of the follow-up study + 1)/365.25. The total participant-years for a treatment group will be the sum of the participant-years of follow-up of all participants in the treatment group.

Source: [P351MK0431: adam-adsl; adtte]

Table 14.3-4
Participants with Serious Adverse Events
(Incidence >0% in One or More Treatment Groups)
(ASF)

	Exposed to Sitagliptin in P083[a] n (FAIR in 100-participant-years)	Not Exposed in P083[b] n (FAIR in 100-participant-years)
Participants in population	36	44
with serious adverse events	3/103.0 (2.9)	3/140.3 (2.1)
Infections and infestations	**0/110.0 (0.0)**	**3/140.3 (2.1)**
Appendicitis	0/110.0 (0.0)	2/141.3 (1.4)
Urinary tract infection	0/110.0 (0.0)	1/142.7 (0.7)
Metabolism and nutrition disorders	**1/107.0 (0.9)**	**0/143.7 (0.0)**
Hyperglycaemia	1/107.0 (0.9)	0/143.7 (0.0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**1/107.7 (0.9)**	**0/143.7 (0.0)**
Leukaemia	1/107.7 (0.9)	0/143.7 (0.0)
Renal and urinary disorders	**1/108.3 (0.9)**	**0/143.7 (0.0)**
Nephrolithiasis	1/108.3 (0.9)	0/143.7 (0.0)

FAIR: Follow-up adjusted incidence rate = (Number of participants with ≥1 event during the follow-up study) / (Total participant-years of follow-up).

Treatment groups in this follow-up study (P351) reflect the originally assigned treatment groups in P083.

[a] The Exposed to Sitagliptin in P083 includes 35 participants who were randomized to the Sitagliptin +/- insulin group, and 1 participant who was randomized to the Placebo followed by Sitagliptin group in P083. 1 participant from this group received sitagliptin as concomitant medication during P351.

[b] The Not Exposed in P083 includes 39 participants who were randomized to the Placebo +/- insulin followed by metformin group, and 5 participants who were randomized to the Metformin group in P083. 4 participants from this group received a DPP-4 inhibitor (sitagliptin or vildagliptin) as concomitant medication during P351.

For participants who have an event, the participant-years of follow-up will be calculated as (Date of the first event - First day of the follow-up study + 1)/365.25. For participants without an event, the participant-years of follow-up will be calculated as (Last day of the follow-up window - First day of the follow-up study + 1)/365.25. The total participant-years for a treatment group will be the sum of the participant-years of follow-up of all participants in the treatment group.

Source: [P351MK0431: adam-adsl; adtte]

14.3.1.3 Other Clinically Meaningful Adverse Events

Not applicable.

14.3.1.4 Adverse Events of Special Interest

Not applicable.

14.4 Clinical Laboratory Evaluation

Not applicable.

14.5 Vital Signs and Other Observations Related to Safety

14.5.1 Vital Signs

Table 14.5-1
Summary of Change from Baseline in Systolic Blood Pressure (mmHg) over Time (ASF)

Treatment	N	Baseline Mean (SD)	Time Point Mean (SD)	Change from Baseline Mean (SD)	Median	Range
Baseline (Year 0)						
Exposed to Sitagliptin in P083	36	114.0 (9.8)				
Not Exposed in P083	44	117.0 (11.4)				
Year 1						
Exposed to Sitagliptin in P083	33	113.8 (10.1)	115.8 (11.1)	2.0 (11.4)	1.0	-18.0 to 30.0
Not Exposed in P083	40	117.0 (11.6)	117.0 (11.1)	0.0 (10.8)	0.5	-25.0 to 31.0
Year 2						
Exposed to Sitagliptin in P083	28	113.3 (10.3)	115.2 (8.5)	1.9 (13.0)	-1.5	-17.0 to 27.0
Not Exposed in P083	38	117.0 (11.9)	117.6 (10.2)	0.6 (12.8)	0.0	-40.0 to 25.0
Year 3						
Exposed to Sitagliptin in P083	19	113.9 (8.8)	118.2 (11.5)	4.2 (13.9)	1.0	-15.0 to 31.0
Not Exposed in P083	28	116.4 (12.0)	118.7 (7.8)	2.3 (10.2)	2.0	-28.0 to 23.0
Year 4						
Exposed to Sitagliptin in P083	12	112.3 (10.0)	116.2 (5.5)	3.9 (11.6)	5.0	-11.0 to 28.0
Not Exposed in P083	19	116.3 (13.8)	118.2 (9.8)	1.9 (11.2)	3.0	-23.0 to 24.0
Year 5						
Exposed to Sitagliptin in P083	9	111.8 (11.4)	115.4 (9.9)	3.7 (17.2)	-4.0	-23.0 to 29.0
Not Exposed in P083	13	114.5 (10.3)	120.8 (9.9)	6.3 (14.5)	6.0	-12.0 to 34.0

N = Number of subjects with both baseline and timepoint measurements.

Treatment groups in this follow-up study (P351) reflect the originally assigned treatment groups in P083.

Exposed to Sitagliptin in P083 = The Exposed to Sitagliptin in P083 includes 35 participants who were randomized to the Sitagliptin +/- insulin group, and 1 participant who was randomized to the Placebo followed by Sitagliptin group in P083. 1 participant from this group received sitagliptin as concomitant medication during P351.

Not Exposed in P083 = The Not Exposed in P083 includes 39 participants who were randomized to the Placebo +/- insulin followed by metformin group, and 5 participants who were randomized to the Metformin group in P083. 4 participants from this group received a DPP-4 inhibitor (sitagliptin or vildagliptin) as concomitant medication during P351.

One participant had their blood pressure measured in a semi-recumbent position that did not align with the protocol at Year 2 and Year 3 visits.

Source: [P351MK0431: adam-adsl; advs]

Table 14.5-2
Summary of Change from Baseline in Diastolic Blood Pressure (mmHg) over Time (ASF)

Treatment	N	Baseline Mean (SD)	Time Point Mean (SD)	Change from Baseline Mean (SD)	Median	Range
Baseline (Year 0)						
Exposed to Sitagliptin in P083	36	70.4 (9.0)				
Not Exposed in P083	44	73.0 (8.5)				
Year 1						
Exposed to Sitagliptin in P083	33	70.1 (9.3)	71.9 (10.2)	1.8 (8.2)	1.0	-14.0 to 23.0
Not Exposed in P083	40	73.0 (8.8)	72.6 (7.9)	-0.4 (8.8)	-0.5	-19.0 to 17.0
Year 2						
Exposed to Sitagliptin in P083	28	69.8 (8.9)	71.8 (8.8)	2.1 (9.4)	2.0	-16.0 to 20.0
Not Exposed in P083	38	73.4 (8.6)	73.5 (7.8)	0.1 (9.2)	0.0	-18.0 to 18.0
Year 3						
Exposed to Sitagliptin in P083	19	69.2 (8.8)	75.4 (7.2)	6.3 (9.5)	5.0	-6.0 to 29.0
Not Exposed in P083	28	73.1 (8.8)	75.6 (7.4)	2.5 (7.0)	3.0	-12.0 to 19.0
Year 4						
Exposed to Sitagliptin in P083	12	69.3 (8.4)	75.0 (4.7)	5.8 (11.0)	4.5	-14.0 to 31.0
Not Exposed in P083	19	72.3 (9.2)	75.1 (7.6)	2.8 (9.0)	3.0	-15.0 to 21.0
Year 5						
Exposed to Sitagliptin in P083	9	69.0 (9.6)	76.9 (7.6)	7.9 (9.1)	8.0	-3.0 to 21.0
Not Exposed in P083	13	71.4 (9.2)	74.4 (10.4)	3.0 (10.1)	1.0	-15.0 to 21.0

N = Number of subjects with both baseline and timepoint measurements.

Treatment groups in this follow-up study (P351) reflect the originally assigned treatment groups in P083.

Exposed to Sitagliptin in P083 = The Exposed to Sitagliptin in P083 includes 35 participants who were randomized to the Sitagliptin +/- insulin group, and 1 participant who was randomized to the Placebo followed by Sitagliptin group in P083. 1 participant from this group received sitagliptin as concomitant medication during P351.

Not Exposed in P083 = The Not Exposed in P083 includes 39 participants who were randomized to the Placebo +/- insulin followed by metformin group, and 5 participants who were randomized to the Metformin group in P083. 4 participants from this group received a DPP-4 inhibitor (sitagliptin or vildagliptin) as concomitant medication during P351.

One participant had their blood pressure measured in a semi-recumbent position that did not align with the protocol at Year 2 and Year 3 visits.

Source: [P351MK0431: adam-adsl; advs]

Table 14.5-3
Summary of Change from Baseline in Heart Rate (beats/min) over Time
(ASF)

Treatment	N	Baseline Mean (SD)	Time Point Mean (SD)	Change from Baseline Mean (SD)	Median	Range
Baseline (Year 0)						
Exposed to Sitagliptin in P083	36	80.5 (8.8)				
Not Exposed in P083	44	80.7 (9.7)				
Year 1						
Exposed to Sitagliptin in P083	33	80.3 (8.5)	79.3 (9.3)	-1.0 (8.9)	0.0	-22.0 to 18.0
Not Exposed in P083	40	79.9 (9.5)	80.8 (10.3)	0.8 (10.3)	1.0	-25.0 to 24.0
Year 2						
Exposed to Sitagliptin in P083	27	80.2 (8.7)	78.2 (11.0)	-2.0 (10.8)	-2.0	-25.0 to 29.0
Not Exposed in P083	38	80.6 (9.1)	82.5 (11.2)	1.9 (11.5)	1.0	-28.0 to 36.0
Year 3						
Exposed to Sitagliptin in P083	19	81.9 (8.3)	84.8 (10.4)	2.9 (12.2)	-2.0	-13.0 to 30.0
Not Exposed in P083	28	80.7 (9.9)	80.0 (10.4)	-0.7 (8.0)	-1.5	-15.0 to 18.0
Year 4						
Exposed to Sitagliptin in P083	12	82.2 (8.3)	84.7 (8.8)	2.5 (10.1)	1.5	-10.0 to 21.0
Not Exposed in P083	19	81.4 (10.6)	81.6 (9.6)	0.2 (11.2)	1.0	-25.0 to 25.0
Year 5						
Exposed to Sitagliptin in P083	9	83.0 (9.5)	81.3 (11.7)	-1.7 (8.7)	-3.0	-12.0 to 14.0
Not Exposed in P083	13	81.3 (12.5)	80.2 (12.3)	-1.1 (13.4)	0.0	-25.0 to 27.0

N = Number of subjects with both baseline and timepoint measurements.

Treatment groups in this follow-up study (P351) reflect the originally assigned treatment groups in P083.

Exposed to Sitagliptin in P083 = The Exposed to Sitagliptin in P083 includes 35 participants who were randomized to the Sitagliptin +/- insulin group, and 1 participant who was randomized to the Placebo followed by Sitagliptin group in P083. 1 participant from this group received sitagliptin as concomitant medication during P351.

Not Exposed in P083 = The Not Exposed in P083 includes 39 participants who were randomized to the Placebo +/- insulin followed by metformin group, and 5 participants who were randomized to the Metformin group in P083. 4 participants from this group received a DPP-4 inhibitor (sitagliptin or vildagliptin) as concomitant medication during P351.

Source: [P351MK0431: adam-adsl; advs]

14.5.2 Auxological and Pubertal Parameters

Table 14.5-4
Summary of Change from Baseline in Weight (kg) over Time
(ASF)

Treatment	N	Baseline Mean (SD)	Time Point Mean (SD)	Change from Baseline Mean (SD)	Median	Range
Baseline (Year 0)						
Exposed to Sitagliptin in P083	36	85.7 (19.6)				
Not Exposed in P083	44	77.5 (22.1)				
Year 1						
Exposed to Sitagliptin in P083	33	84.3 (19.1)	84.6 (19.1)	0.2 (5.4)	0.4	-20.2 to 12.1
Not Exposed in P083	40	78.0 (22.6)	79.2 (23.1)	1.2 (4.6)	1.9	-15.8 to 10.3
Year 2						
Exposed to Sitagliptin in P083	28	84.0 (20.4)	84.4 (17.9)	0.3 (9.7)	0.5	-39.5 to 14.2
Not Exposed in P083	38	77.9 (22.9)	81.1 (22.7)	3.3 (6.1)	2.8	-6.7 to 17.4
Year 3						
Exposed to Sitagliptin in P083	19	80.4 (18.5)	83.2 (17.5)	2.9 (6.6)	0.8	-6.2 to 17.7
Not Exposed in P083	28	76.1 (23.5)	81.1 (22.0)	5.0 (8.5)	4.5	-7.7 to 32.2
Year 4						
Exposed to Sitagliptin in P083	12	75.1 (19.9)	80.2 (21.0)	5.1 (8.5)	2.2	-5.9 to 19.5
Not Exposed in P083	19	77.9 (27.2)	83.4 (25.2)	5.5 (10.9)	3.5	-9.3 to 41.5
Year 5						
Exposed to Sitagliptin in P083	9	75.6 (23.0)	81.7 (23.0)	6.1 (8.5)	4.5	-4.3 to 17.9
Not Exposed in P083	13	73.1 (22.4)	83.4 (24.2)	10.3 (16.2)	7.8	-8.4 to 55.8

N = Number of subjects with both baseline and timepoint measurements.

Treatment groups in this follow-up study (P351) reflect the originally assigned treatment groups in P083.

Exposed to Sitagliptin in P083 = The Exposed to Sitagliptin in P083 includes 35 participants who were randomized to the Sitagliptin +/- insulin group, and 1 participant who was randomized to the Placebo followed by Sitagliptin group in P083. 1 participant from this group received sitagliptin as concomitant medication during P351.

Not Exposed in P083 = The Not Exposed in P083 includes 39 participants who were randomized to the Placebo +/- insulin followed by metformin group, and 5 participants who were randomized to the Metformin group in P083. 4 participants from this group received a DPP-4 inhibitor (sitagliptin or vildagliptin) as concomitant medication during P351.

Source: [P351MK0431: adam-adsl; advs]

Table 14.5-5
Summary of Change from Baseline in BMI (kg/m2) over Time
(ASF)

Treatment	N	Baseline Mean (SD)	Time Point Mean (SD)	Change from Baseline Mean (SD)	Median	Range
Baseline (Year 0)						
Exposed to Sitagliptin in P083	26	33.2 (8.5)				
Not Exposed in P083	28	30.4 (7.9)				
Year 1						
Exposed to Sitagliptin in P083	23	33.2 (8.8)	32.3 (8.3)	-0.9 (2.4)	-0.2	-9.7 to 1.9
Not Exposed in P083	26	31.0 (7.8)	31.2 (7.9)	0.2 (1.3)	0.2	-3.0 to 2.8
Year 2						
Exposed to Sitagliptin in P083	18	33.3 (9.4)	31.7 (7.9)	-1.5 (4.3)	-0.6	-16.6 to 3.9
Not Exposed in P083	26	31.0 (7.8)	31.6 (7.7)	0.6 (2.2)	0.4	-2.6 to 6.8
Year 3						
Exposed to Sitagliptin in P083	13	31.1 (7.1)	30.5 (6.6)	-0.6 (1.4)	-0.5	-3.0 to 2.5
Not Exposed in P083	18	31.0 (9.0)	31.9 (8.8)	0.9 (3.5)	0.6	-4.9 to 7.9
Year 4						
Exposed to Sitagliptin in P083	8	30.5 (7.9)	29.8 (7.0)	-0.7 (2.3)	-0.8	-2.9 to 4.0
Not Exposed in P083	13	32.4 (10.2)	32.2 (10.3)	-0.2 (4.4)	-0.6	-7.5 to 10.6
Year 5						
Exposed to Sitagliptin in P083	6	31.3 (9.2)	30.8 (7.5)	-0.4 (2.5)	-0.5	-3.9 to 3.0
Not Exposed in P083	8	30.4 (10.1)	31.4 (11.9)	1.0 (5.3)	0.9	-7.9 to 11.6

N = Number of subjects with both baseline and timepoint measurements.

Treatment groups in this follow-up study (P351) reflect the originally assigned treatment groups in P083.

Exposed to Sitagliptin in P083 = The Exposed to Sitagliptin in P083 includes 35 participants who were randomized to the Sitagliptin +/- insulin group, and 1 participant who was randomized to the Placebo followed by Sitagliptin group in P083. 1 participant from this group received sitagliptin as concomitant medication during P351.

Not Exposed in P083 = The Not Exposed in P083 includes 39 participants who were randomized to the Placebo +/- insulin followed by metformin group, and 5 participants who were randomized to the Metformin group in P083. 4 participants from this group received a DPP-4 inhibitor (sitagliptin or vildagliptin) as concomitant medication during P351.

Source: [P351MK0431: adam-adsl; advs]

Table 14.5-6
Summary of Change from Baseline in Height (cm) over Time
(ASF, Female)

Treatment	N	Baseline Mean (SD)	Time Point Mean (SD)	Change from Baseline Mean (SD)	Median	Range
Baseline (Year 0)						
Exposed to Sitagliptin in P083	20	157.1 (7.0)				
Not Exposed in P083	31	159.7 (8.4)				
Year 1						
Exposed to Sitagliptin in P083	19	157.0 (7.2)	158.4 (6.7)	1.4 (1.5)	1.0	-0.2 to 5.2
Not Exposed in P083	27	158.9 (8.6)	159.6 (8.5)	0.7 (1.3)	0.0	-1.4 to 5.0
Year 2						
Exposed to Sitagliptin in P083	17	157.0 (6.9)	159.2 (7.0)	2.2 (2.4)	1.0	-0.2 to 7.4
Not Exposed in P083	26	158.8 (8.7)	160.4 (8.5)	1.6 (2.2)	1.0	-0.2 to 9.2
Year 3						
Exposed to Sitagliptin in P083	13	157.6 (6.7)	161.1 (6.7)	3.5 (2.8)	4.0	0.0 to 7.5
Not Exposed in P083	19	156.9 (8.0)	158.9 (7.9)	2.0 (2.5)	1.5	-3.3 to 8.0
Year 4						
Exposed to Sitagliptin in P083	9	156.7 (7.4)	160.2 (6.9)	3.5 (2.9)	2.0	0.0 to 8.3
Not Exposed in P083	12	157.9 (7.2)	159.9 (8.0)	1.9 (3.1)	1.0	-3.3 to 7.2
Year 5						
Exposed to Sitagliptin in P083	7	155.0 (7.4)	159.7 (7.4)	4.7 (3.3)	6.0	0.0 to 9.3
Not Exposed in P083	8	158.5 (6.1)	161.3 (6.1)	2.9 (3.6)	2.5	-1.6 to 9.0

N = Number of subjects with both baseline and timepoint measurements.

Treatment groups in this follow-up study (P351) reflect the originally assigned treatment groups in P083.

Exposed to Sitagliptin in P083 = The Exposed to Sitagliptin in P083 includes 35 participants who were randomized to the Sitagliptin +/- insulin group, and 1 participant who was randomized to the Placebo followed by Sitagliptin group in P083. 1 participant from this group received sitagliptin as concomitant medication during P351.

Not Exposed in P083 = The Not Exposed in P083 includes 39 participants who were randomized to the Placebo +/- insulin followed by metformin group, and 5 participants who were randomized to the Metformin group in P083. 4 participants from this group received a DPP-4 inhibitor (sitagliptin or vildagliptin) as concomitant medication during P351.

Source: [P351MK0431: adam-adsl; advs]

Table 14.5-7
Summary of Change from Baseline in Height (cm) over Time
(ASF, Male)

Treatment	N	Baseline Mean (SD)	Time Point Mean (SD)	Change from Baseline Mean (SD)	Median	Range
Baseline (Year 0)						
Exposed to Sitagliptin in P083	16	169.2 (11.1)				
Not Exposed in P083	13	163.1 (13.1)				
Year 1						
Exposed to Sitagliptin in P083	14	167.3 (10.6)	169.2 (8.7)	1.9 (3.3)	0.8	-0.7 to 11.5
Not Exposed in P083	13	163.1 (13.1)	164.9 (12.3)	1.8 (1.7)	1.3	-0.5 to 5.7
Year 2						
Exposed to Sitagliptin in P083	11	167.3 (10.6)	170.6 (8.2)	3.3 (4.2)	2.0	-0.5 to 13.5
Not Exposed in P083	12	165.1 (11.6)	168.5 (9.5)	3.4 (3.5)	2.8	0.0 to 12.2
Year 3						
Exposed to Sitagliptin in P083	6	163.9 (11.5)	170.4 (7.9)	6.6 (7.1)	4.0	1.0 to 18.5
Not Exposed in P083	9	162.5 (12.1)	167.9 (9.5)	5.4 (5.5)	3.6	0.1 to 18.0
Year 4						
Exposed to Sitagliptin in P083	3	159.3 (14.0)	172.2 (3.3)	13.0 (10.8)	15.1	1.3 to 22.5
Not Exposed in P083	7	160.1 (11.5)	167.5 (8.9)	7.4 (5.9)	4.8	2.5 to 19.7
Year 5						
Exposed to Sitagliptin in P083	2	161.1 (19.2)	173.4 (4.8)	12.3 (14.4)	12.3	2.1 to 22.5
Not Exposed in P083	5	157.4 (12.8)	167.4 (11.0)	10.0 (8.0)	6.0	3.6 to 22.2

N = Number of subjects with both baseline and timepoint measurements.

Treatment groups in this follow-up study (P351) reflect the originally assigned treatment groups in P083.

Exposed to Sitagliptin in P083 = The Exposed to Sitagliptin in P083 includes 35 participants who were randomized to the Sitagliptin +/- insulin group, and 1 participant who was randomized to the Placebo followed by Sitagliptin group in P083. 1 participant from this group received sitagliptin as concomitant medication during P351.

Not Exposed in P083 = The Not Exposed in P083 includes 39 participants who were randomized to the Placebo +/- insulin followed by metformin group, and 5 participants who were randomized to the Metformin group in P083. 4 participants from this group received a DPP-4 inhibitor (sitagliptin or vildagliptin) as concomitant medication during P351.

Source: [P351MK0431: adam-adsl; advs]

Table 14.5-8
Participants Reaching Tanner Stage V
(ASF)

Tanner Stage at Year 0	Participants Who Reached Tanner Stage V					
	At Year 0 n/m (%)	By Year 1 n/m (%) [d]	By Year 2 n/m (%) [d]	By Year 3 n/m (%) [d]	By Year 4 n/m (%) [d]	By Year 5 n/m (%) [d]
Exposed to Sitagliptin in P083[a]						
Stage II						
Male	0/2 (0.0%)	0/2 (0.0%) [0]	0/2 (0.0%) [0]	0/2 (0.0%) [0]	1/2 (50.0%) [0]	1/1 (100.0%) [1]
Stage III						
Female	0/3 (0.0%)	0/3 (0.0%) [0]	0/3 (0.0%) [0]	2/3 (66.7%) [0]	2/3 (66.7%) [0]	2/3 (66.7%) [0]
Stage IV						
Male	0/6 (0.0%)	4/6 (66.7%) [0]	5/6 (83.3%) [0]	6/6 (100.0%) [0]	6/6 (100.0%) [0]	6/6 (100.0%) [0]
Female	0/12 (0.0%)	3/11 (27.3%) [1]	4/10 (40.0%) [2]	7/10 (70.0%) [2]	7/10 (70.0%) [2]	8/10 (80.0%) [2]
Stage V						
Male	8/8 (100.0%)	8/8 (100.0%) [0]	8/8 (100.0%) [0]	8/8 (100.0%) [0]	8/8 (100.0%) [0]	8/8 (100.0%) [0]
Female	5/5 (100.0%)	5/5 (100.0%) [0]	5/5 (100.0%) [0]	5/5 (100.0%) [0]	5/5 (100.0%) [0]	5/5 (100.0%) [0]
Overall						
Male	8/16 (50.0%)	12/16 (75.0%) [0]	13/16 (81.3%) [0]	14/16 (87.5%) [0]	15/16 (93.8%) [0]	15/15 (100.0%) [1]
Female	5/20 (25.0%)	8/19 (42.1%) [1]	9/18 (50.0%) [2]	14/18 (77.8%) [2]	14/18 (77.8%) [2]	15/18 (83.3%) [2]
Not Exposed in P083[b]						
Stage II						
Female	0/1 (0.0%)	0/1 (0.0%) [0]	0/1 (0.0%) [0]	0/1 (0.0%) [0]	1/1 (100.0%) [0]	1/1 (100.0%) [0]
Stage III						
Male	0/4 (0.0%)	0/4 (0.0%) [0]	1/4 (25.0%) [0]	2/4 (50.0%) [0]	2/4 (50.0%) [0]	4/4 (100.0%) [0]
Female	0/3 (0.0%)	0/3 (0.0%) [0]	1/3 (33.3%) [0]	1/2 (50.0%) [1]	2/2 (100.0%) [1]	2/2 (100.0%) [1]

Participants Reaching Tanner Stage V
(ASF)

Tanner Stage at Year 0	Participants Who Reached Tanner Stage V					
	At Year 0 n/m (%)	By Year 1 n/m (%) [d]	By Year 2 n/m (%) [d]	By Year 3 n/m (%) [d]	By Year 4 n/m (%) [d]	By Year 5 n/m (%) [d]
Stage IV						
Male	0/6 (0.0%)	2/6 (33.3%) [0]	3/5 (60.0%) [1]	4/5 (80.0%) [1]	5/5 (100.0%) [1]	5/5 (100.0%) [1]
Female	0/19 (0.0%)	6/17 (35.3%) [2]	10/17 (58.8%) [2]	13/16 (81.3%) [3]	14/16 (87.5%) [3]	14/16 (87.5%) [3]
Stage V						
Male	3/3 (100.0%)	3/3 (100.0%) [0]	3/3 (100.0%) [0]	3/3 (100.0%) [0]	3/3 (100.0%) [0]	3/3 (100.0%) [0]
Female	8/8 (100.0%)	8/8 (100.0%) [0]	8/8 (100.0%) [0]	8/8 (100.0%) [0]	8/8 (100.0%) [0]	8/8 (100.0%) [0]
Overall						
Male	3/13 (23.1%)	5/13 (38.5%) [0]	7/12 (58.3%) [1]	9/12 (75.0%) [1]	10/12 (83.3%) [1]	12/12 (100.0%) [1]
Female	8/31 (25.8%)	14/29 (48.3%) [2]	19/29 (65.5%) [2]	22/27 (81.5%) [4]	25/27 (92.6%) [4]	25/27 (92.6%) [4]

n = Number of participants with a Tanner Stage V at Year x or with a Tanner Stage V prior to Year x.

m = Number of participants at Year x or with a Tanner Stage V prior to Year x.

d = Cumulative number of dropouts who did not reach Tanner Stage V by Year x. Participants reaching Tanner Stage V by Year x are not considered as dropouts.

Number (%) of participants who reached Tanner Stage V (genitalia for male and breasts for female) by each follow-up year were summarized.

Treatment groups in this follow-up study (P351) reflect the originally assigned treatment groups in P083.

[a] The Exposed to Sitagliptin in P083 includes 35 participants who were randomized to the Sitagliptin +/- insulin group, and 1 participant who was randomized to the Placebo followed by Sitagliptin group in P083. 1 participant from this group received sitagliptin as concomitant medication during P351.

[b] The Not Exposed in P083 includes 39 participants who were randomized to the Placebo +/- insulin followed by metformin group, and 5 participants who were randomized to the Metformin group in P083. 4 participants from this group received a DPP-4 inhibitor (sitagliptin or vildagliptin) as concomitant medication during P351.

Source: [P351MK0431: adam-adsl; adts]

Table 14.5-9
Mean Change (SD) in Growth Velocity (cm/year) from Baseline over Time
(ASF, Female)

Treatment	N	Growth Velocity[a]		
		Mean (SD)	Median	Range
Year 0 to Year 1				
Exposed to Sitagliptin in P083	19	1.4 (1.6)	1.0	-0.2 to 5.3
Not Exposed in P083	27	0.8 (1.9)	0.0	-1.3 to 8.7
Year 0 to Year 2				
Exposed to Sitagliptin in P083	17	1.1 (1.4)	0.6	-0.1 to 4.7
Not Exposed in P083	26	0.8 (1.3)	0.5	-0.1 to 5.8
Year 0 to Year 3				
Exposed to Sitagliptin in P083	13	1.2 (1.0)	1.3	0.0 to 2.9
Not Exposed in P083	19	0.6 (0.8)	0.5	-1.1 to 2.5
Year 0 to Year 4				
Exposed to Sitagliptin in P083	9	0.9 (0.8)	0.5	0.0 to 2.4
Not Exposed in P083	12	0.5 (0.8)	0.3	-0.9 to 1.8
Year 0 to Year 5				
Exposed to Sitagliptin in P083	7	1.0 (0.7)	1.2	0.0 to 2.1
Not Exposed in P083	8	0.6 (0.7)	0.5	-0.3 to 1.8

[a] Growth Velocity = (Change from Baseline (Year 0) in Height)/(Change from Baseline in Chronologic Age).

N = Number of subjects with both baseline and timepoint measurements.

Treatment groups in this follow-up study (P351) reflect the originally assigned treatment groups in P083.

Exposed to Sitagliptin in P083 = The Exposed to Sitagliptin in P083 includes 35 participants who were randomized to the Sitagliptin +/- insulin group, and 1 participant who was randomized to the Placebo followed by Sitagliptin group in P083. 1 participant from this group received sitagliptin as concomitant medication during P351.

Not Exposed in P083 = The Not Exposed in P083 includes 39 participants who were randomized to the Placebo +/- insulin followed by metformin group, and 5 participants who were randomized to the Metformin group in P083. 4 participants from this group received a DPP-4 inhibitor (sitagliptin or vildagliptin) as concomitant medication during P351.

Source: [P351MK0431: adam-adsl; advs]

Table 14.5-10
Mean Change (SD) in Growth Velocity (cm/year) from Baseline over Time
(ASF, Male)

Treatment	N	Growth Velocity[a]		
		Mean (SD)	Median	Range
Year 0 to Year 1				
Exposed to Sitagliptin in P083	14	1.8 (3.0)	1.0	-0.7 to 10.1
Not Exposed in P083	13	1.8 (1.7)	1.3	-0.7 to 5.4
Year 0 to Year 2				
Exposed to Sitagliptin in P083	11	1.7 (2.1)	1.0	-0.3 to 6.6
Not Exposed in P083	12	1.7 (1.6)	1.5	0.0 to 5.8
Year 0 to Year 3				
Exposed to Sitagliptin in P083	6	2.2 (2.3)	1.4	0.3 to 5.9
Not Exposed in P083	9	1.8 (1.8)	1.2	0.0 to 5.8
Year 0 to Year 4				
Exposed to Sitagliptin in P083	3	3.3 (2.7)	3.9	0.3 to 5.6
Not Exposed in P083	7	1.9 (1.5)	1.2	0.7 to 4.9
Year 0 to Year 5				
Exposed to Sitagliptin in P083	2	2.5 (2.9)	2.5	0.4 to 4.5
Not Exposed in P083	5	2.0 (1.6)	1.2	0.7 to 4.4

[a] Growth Velocity = (Change from Baseline (Year 0) in Height)/(Change from Baseline in Chronologic Age).

N = Number of subjects with both baseline and timepoint measurements.

Treatment groups in this follow-up study (P351) reflect the originally assigned treatment groups in P083.

Exposed to Sitagliptin in P083 = The Exposed to Sitagliptin in P083 includes 35 participants who were randomized to the Sitagliptin +/- insulin group, and 1 participant who was randomized to the Placebo followed by Sitagliptin group in P083. 1 participant from this group received sitagliptin as concomitant medication during P351.

Not Exposed in P083 = The Not Exposed in P083 includes 39 participants who were randomized to the Placebo +/- insulin followed by metformin group, and 5 participants who were randomized to the Metformin group in P083. 4 participants from this group received a DPP-4 inhibitor (sitagliptin or vildagliptin) as concomitant medication during P351.

Source: [P351MK0431: adam-adsl; advs]

15 LIST OF REFERENCES

16.1.11 Publications Based on the Study

16.1.12 Important Publications Referenced in the CSR