This report may include approved and non-approved uses, formulations, or treatment regimens. The results reported may not reflect the overall profile of a product. Before prescribing any product mentioned in this report, healthcare professionals should consult local prescribing information for the product approved in their country.

END OF TRIAL STUDY SUMMARY REPORT

MK-3577

Generic Name: MK-3577	Protocol 009
EudraCT Number:	
Dosage Form: tablet	Phase: IIa
Indication: Type 2 Diabetes Mellitus (T2DM)	Study Design: randomized, crossover, incomplete block design
Sponsor Name:	Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc. (hereafter referred to as Merck)
Clinical Monitor:	[redacted]
Study Initiation Date (FPI):	29-May-2009
Study Early Termination Date (if applicable):	12-Jul-2010
Study Completion Date (LPO):	Not applicable
Investigator Name/Affiliation:	Multicenter (57)

MERCK SHARP & DOHME CORP., A SUBSIDIARY OF MERCK & CO., INC. MK-3577, tablet Type 2 Diabetes Mellitus (T2DM)	**END OF TRIAL STUDY SUMMARY REPORT**

PROTOCOL TITLE/NO.: A Phase IIa, Multicenter, Randomized, Placebo- and Active-Comparator Controlled, Cross-Over Clinical Trial to Study the Safety and Efficacy of MK-3577 in Patients with Type 2 Diabetes Mellitus Who Have Inadequate Glycemic Control #009

INVESTIGATOR(S)/STUDY CENTER(S): Fifty-seven sites received IRB/ERC approval and were shipped clinical supplies: 13 sites in the USA, 6 sites in 3 countries in Europe, 10 sites in 3 countries in the Asia/Pacific region, 13 sites in 4 countries in Latin America, 8 sites in 2 countries in Central Europe, and 7 sites in South Africa.

PRIMARY THERAPY PERIOD: 29-May-2009 to 16-Jun-2010 **CLINICAL PHASE:** IIa

DURATION OF TREATMENT: 16 weeks

OBJECTIVE(S): In patients with type 2 diabetes with inadequate control on diet and exercise,

Primary:

(1) **Objective:** To assess the 24-hour weighted mean glucose (WMG)-lowering efficacy of MK-3577 compared to placebo after 4 weeks of treatment.

Hypothesis: After 4 weeks of treatment, either the morning administration or the evening administration of MK-3577 provides superior WMG reduction compared to placebo.

(2) **Objective:** To assess the safety and tolerability of MK-3577 compared to placebo.

Hypothesis: MK-3577 is well tolerated.

Secondary:

(1) **Objective:** To assess the effect of evening administration of MK-3577 on fasting plasma glucose (FPG) levels.

Hypothesis: After 4 weeks of treatment, MK-3577 administered in the evening provides superior reduction in FPG levels compared to placebo.

(2) **Objective:** To assess the effect of morning administration of MK-3577 on 2-hour post-meal plasma glucose (PMG) levels after the morning meal.

Hypothesis: After 4 weeks of treatment, MK-3577 administered in the morning provides superior reduction in 2-hour PMG levels after the morning meal compared to placebo.

(3) **Objective:** To assess the effect of morning or evening administration of MK-3577 on LDL-Cholesterol (LDL-C).

Hypothesis: After 4 weeks of treatment, either the morning administration or the evening administration of MK-3577 does not increase LDL-C compared to placebo.

(4) **Objective:** To assess the effect of evening administration of MK-3577 on 2-hour PMG levels after the morning meal.

(5) **Objective:** To assess the effect of morning administration of MK-3577 on FPG levels.

Exploratory:

(1) **Objective:** To estimate the difference in reduction in 24-hour WMG between morning, evening and twice-daily administration of MK-3577.

(2) **Objective:** To assess the effect of MK-3577 compared to placebo on change from baseline in 24-hour systolic and diastolic ambulatory blood pressure.

(3) **Objective:** To estimate the effect of MK-3577 administered twice daily compared to placebo on change from baseline in LDL-C.

(4) **Objective:** To assess the effect of metformin on 24-hour WMG and to compare the effect on 24-hour WMG between metformin and MK-3577.

(5) **Objective:** To explore the relationship between plasma MK-3577 concentration and pharmacodynamic parameters.

STUDY STATUS: Terminated

STUDY DESIGN: This was a phase IIa, multicenter, randomized, double-blind, placebo- and active-controlled, 4-period/5-treatment incomplete cross-over study in patients with T2DM. Treatments consisted of MK-3577 10-mg in the morning, MK-3577 6-mg in the evening, MK-3577 25-mg twice daily, metformin 1000-mg twice daily, or placebo. This study consisted of a 1-week screening period, an up-to-4-week AHA wash-off period, a 2-week run-in period, four consecutive 4-week double-blind treatment periods, and a 2-week post-treatment follow-up period (referred to as the "post-study period"). Approximately 276 patients were to be randomized among one of 14 treatment sequences. At sites which were selected as Domiciled Visit Sites, a subset of approximately 60 patients was to be domiciled at randomization and at the end of the first two treatment periods, and undergo 24-hour blood sampling. At sites which were not Domiciled Visit Sites, the remaining subset of approximately 216 patients was to have 24-hour ambulatory blood pressure monitoring and a 3-Point Meal Tolerance Test (MTT) performed at randomization and at the end of the first treatment period.

An pre-specified interim analysis (IA) was performed after the first 118 patients completed the first 2 periods of the study to assess the glucose-lowering efficacy and safety profile of the MK-3577 treatment regimens, and guide potential dose adaptation. The standing internal Data Monitoring Committee met and reviewed the efficacy and safety data for the initial cohort of patients participating in this study. Based upon their review of the data, the committee recommended discontinuing the protocol as sufficient data had been accrued to assess the study hypotheses. No new safety issues were identified. On June 3, 2010, all participating sites received a communication regarding study termination and instructions to have patients discontinue study medication and to complete protocol-specified discontinuation procedures.

DISPOSITION:

	n	(%)
SCREENING FAILURES:	342	
RANDOMIZED:	118	
Male (age range)	63 (32 to 70)	(53.4)
Female (age range)	55 (31 to 69)	(46.6)
COMPLETED:	81	(68.6)
DISCONTINUED:	37	(31.4)
Adverse experience	11	(9.3)
ALT/AST	1	(0.8)
Excluded Medication	3	(2.5)
Lost to Follow-Up	4	(3.4)
Protocol Violation	2	(1.7)
Study Terminated by Sponsor	10	(8.5)
Triglycerides	1	(0.8)
Withdrawal by Subject	5	(4.2)

DOSAGE/FORMULATION NOS.: MK-3577 was supplied as 2-mg, 5-mg, 10-mg or matching placebo capsules. Metformin was supplied as 500-mg or matching placebo tablets. All medications were supplied in a double-blinded manner.

The formulation numbers used for this study were:

Compound	Dose	Bulk Lot / Formulation Number
MK-3577	2mg	[redacted]
MK-3577	5mg	
MK-3577	10mg	
Placebo to match MK-3577	2mg 5mg 10mg	
Placebo to match MK-3577	10mg	
Metformin HCl	500mg	
Metformin HCl	500mg	
Metformin HCl	500mg	
Placebo to match Metformin HCl	500mg	
Placebo to match Metformin HCl	500mg	
Placebo to match Metformin HCl	500mg	

DIAGNOSIS/INCLUSION CRITERIA: Male and female patients were ≥18 and ≤70 years of age with T2DM. At screening, eligible patients were required to meet one of the following criteria:

- Not on antihyperglycemic medications for at least 10 weeks, with an A1C of ≥ 6.5% and ≤ 9.5%, or
- On a single oral antihyperglycemic medication (but not on a PPAR-γ agonist), with an A1C of ≥ 6.0% and ≤ 9.0%, or
- On a low-dose combination oral antihyperglycemic medication (but not on a PPAR-γ agonist) at a dose less than or equal to 50% of the maximum recommended dose (per label of individual country) of each component, with an A1C of ≥ 6.0% and ≤ 9.0%.

Patients eligible for randomization were required to have an FPG of ≥140 and ≤240 mg/dL (≥7.8 and ≤13.3 mmol/L) at Visit 3/Week -2 and a site fasting fingerstick glucose of ≤240 mg/dL (13.3 mmol/L) at Visit 4/Day 1.

EVALUATION CRITERIA:

Efficacy Measurements included laboratory assessment of FPG, WMG (in domiciled group only), PMG, insulin, and glucagon.

Safety Measurements included monitoring of adverse experiences, clinical evaluation of body weight, vital signs, physical examination, laboratory assessments including blood chemistry (including sodium, potassium, chloride, carbon dioxide, albumin, uric acid, ALT, AST, alkaline phosphatase, creatinine, total and direct bilirubin), CPK, hematology (including CBC, differential, absolute neutrophil count), lipid panel (including ApoB-100 and ApoA1), and urinalysis, ECG assessments, and 24-hour Ambulatory Blood Pressure Monitoring (in the non-domiciled group only).

RESULTS: **Table 1** presents the disposition of patients by treatment group.

EFFICACY: **Tables 2, 3, and 4** below show the efficacy results for change from baseline for 24-hour WMG, FPG, and 2-hour PMG, respectively, in the Full Analysis Set (FAS) population. The results for the 24-hour WMG at Week 4 show a significant decrease compared to placebo in both MK-3577 QD treatment groups. The results for FPG at Week 4 show a significant decrease compared to placebo in all three MK-3577 treatment groups. The results for 2-hour PMG at Week 4 show a significant decrease compared to placebo in the MK-3577 25mg BID treatment group.

SAFETY: Safety data is presented in Tables 5 through 14 below for the All Patients as Treated (APaT)/Data as Observed (DAO) population. A summary of adverse events is presented in **Table 5**; no meaningful differences in the summary measures of adverse events were observed among the treatment groups. **Table 6** displays specific adverse events (incidence ≥5% in one or more treatment groups). No meaningful differences among treatment groups were observed. **Table 7** provides a listing of patients who had a serious adverse event. **Table 8** displays the incidence of patients who were discontinued due to an adverse event. No meaningful differences were observed among treatment groups.

Tables 9 through 12 present the summary of percent change from baseline of lipid parameters. At Week 4, all three MK-3577 treatment groups showed increases in total cholesterol, LDL-C, HDL-C, and TG. **Tables 13 and 14** present the summary of percent change from baseline of hepatic transaminases. At Week 4, all three MK-3577 treatment groups showed an increase in ALT and AST, with the MK-3577 25 mg BID group showing the largest increase.

AUTHORS: [redacted]

Table 1

Disposition of Patients by Treatment
(APaT)

	Placebo		MK-3577 10 mg QAM		MK-3577 6 mg QPM		MK-3577 25 mg BID		Metformin 1000 mg BID ‡		Post Study †		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Patients in Treatment Group	108		106		105		89		18		85			
Study Disposition														
COMPLETED	102	(94.4)	95	(89.6)	99	(94.3)	81	(91.0)	16	(88.9)	81	(95.3)		
DISCONTINUED	6	(5.6)	11	(10.4)	6	(5.7)	8	(9.0)	2	(11.1)	4	(4.7)	37	(31.4)
ADVERSE EVENT	2	(1.9)	1	(0.9)	3	(2.9)	4	(4.5)	1	(5.6)	0	(0.0)	11	(9.3)
ALT/AST	0	(0.0)	1	(0.9)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
EXCLUDED MEDICATION	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	3	(3.5)	3	(2.5)
LOST TO FOLLOW-UP	1	(0.9)	2	(1.9)	1	(1.0)	0	(0.0)	0	(0.0)	0	(0.0)	4	(3.4)
PROTOCOL VIOLATION	1	(0.9)	1	(0.9)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	2	(1.7)
STUDY TERMINATED BY SPONSOR	0	(0.0)	5	(4.7)	1	(1.0)	4	(4.5)	0	(0.0)	0	(0.0)	10	(8.5)
TRIGLYCERIDES	1	(0.9)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
WITHDRAWAL BY SUBJECT	1	(0.9)	1	(0.9)	1	(1.0)	0	(0.0)	1	(5.6)	1	(1.2)	5	(4.2)

Each patient is counted once per treatment for Study Disposition based on the latest corresponding disposition record.

† Post-study contains patients who have complete all 4 study periods without discontinuation in any period.

‡ Allocation to treatment groups was unbalanced.

Table 2

Constrained Longitudinal Data Analysis of Change From Baseline in 24-Hour Weighted Mean Glucose (mg/dL) at Week 4
(FAS/DAO)

Treatment Group	N †	Baseline Mean (SD)	On Treatment Mean (SD)	Change From Baseline Mean (SE)	Change From Baseline LS Mean (SE) ‡	Change From Baseline 90% CI for LS Mean
Placebo	38	164.7 (38.9)	163.2 (43.2)	-1.5 (4.6)	-1.6 (4.1)	(-8.5, 5.3)
MK-3577 10 mg QAM	10	157.7 (44.0)	143.0 (37.6)	-14.7 (10.4)	-18.8 (6.8)	(-30.2, -7.4)
MK-3577 6 mg QPM	11	148.2 (26.9)	131.0 (19.2)	-17.3 (5.0)	-25.0 (6.7)	(-36.3, -13.7)
Metformin 1000 mg BID	15	181.1 (40.1)	139.5 (34.0)	-41.7 (5.7)	-36.5 (6.1)	(-46.7, -26.3)

Between Treatment Group Comparison	Difference in LS Means (90% CI)	p-Value
MK-3577 10 mg QAM vs. Placebo	-17.2 (-28.3, -6.1)	0.013
MK-3577 6 mg QPM vs. Placebo	-23.4 (-34.5, -12.4)	<0.001
Metformin 1000 mg BID vs. Placebo	-34.9 (-44.8, -25.0)	<0.001
MK-3577 10 mg QAM vs. Metformin 1000 mg BID	17.7 (3.6, 31.7)	0.040
MK-3577 6 mg QPM vs. Metformin 1000 mg BID	11.4 (-2.5, 25.4)	0.176

† N = Number of individuals included in the LDA model.

‡ Based on an LDA model including terms for treatment, period, the interaction of treatment by period, prior antihyperglycemic therapy status (yes/no), randomization stratum (participation in domiciled visits/no participation in domiciled visits), and subject effect, with a restriction of same baseline mean across patients in all treatment sequences (due to randomization).

Patients on MK-3577 25 mg BID did not undergo 24-hour glucose sampling."

Table 3

Constrained Longitudinal Data Analysis of Change From Baseline in FPG (mg/dL) at Week 4
(FAS/DAO)

Treatment Group	N †	Baseline Mean (SD)	On Treatment Mean (SD)	Change From Baseline Mean (SE)	Change From Baseline LS Mean (SE) ‡	Change From Baseline 90% CI for LS Mean
Placebo	104	150.4 (34.0)	155.6 (39.0)	5.2 (3.5)	4.3 (3.8)	(-2.1, 10.6)
MK-3577 10 mg QAM	100	150.7 (32.5)	143.5 (33.6)	-7.2 (3.5)	-7.2 (3.5)	(-13.0, -1.4)
MK-3577 6 mg QPM	98	150.2 (32.6)	133.8 (30.6)	-16.4 (3.3)	-17.5 (3.5)	(-23.3, -11.7)
MK-3577 25 mg BID	86	146.4 (31.9)	117.5 (24.7)	-29.0 (3.7)	-31.7 (3.5)	(-37.5, -26.0)
Metformin 1000 mg BID	18	167.5 (32.2)	142.9 (32.4)	-24.6 (5.7)	-14.4 (6.2)	(-24.7, -4.2)

Between Treatment Group Comparison	Difference in LS Means (90% CI)	p-Value
MK-3577 10 mg QAM vs. Placebo	-11.5 (-17.5, -5.4)	0.002
MK-3577 6 mg QPM vs. Placebo	-21.8 (-27.8, -15.8)	<0.001
MK-3577 25 mg BID vs. Placebo	-36.0 (-42.0, -30.0)	<0.001
Metformin 1000 mg BID vs. Placebo	-20.0 (-30.0, -10.1)	0.001

† N = Number of individuals included in the LDA model.

‡ Based on an LDA model including terms for treatment, period, the interaction of treatment by period, prior antihyperglycemic therapy status (yes/no), randomization stratum (participation in domiciled visits/no participation in domiciled visits), and subject effect, with a restriction of same baseline mean across patients in all treatment sequences (due to randomization).

Table 4

Constrained Longitudinal Data Analysis of Change From Baseline in 2-Hour Post-Meal Glucose (mg/dL) at Week 4
(FAS/DAO)

Treatment Group	N [†]	Baseline Mean (SD)	On Treatment Mean (SD)	Change From Baseline Mean (SE)	Change From Baseline LS Mean (SE) [‡]	Change From Baseline 90% CI for LS Mean
Placebo	59	231.9 (58.3)	227.3 (68.3)	-3.6 (6.3)	-5.2 (5.9)	(-15.0, 4.6)
MK-3577 10 mg QAM	17	212.8 (65.0)	182.7 (60.4)	-23.9 (13.0)	-20.1 (10.3)	(-37.2, -3.0)
MK-3577 6 mg QPM	19	217.9 (53.8)	190.4 (43.3)	-28.2 (7.5)	-25.6 (10.2)	(-42.6, -8.6)
MK-3577 25 mg BID	21	199.9 (57.7)	135.7 (24.9)	-62.8 (11.0)	-73.0 (9.3)	(-88.5, -57.5)
Metformin 1000 mg BID	15	247.4 (62.2)	183.2 (49.2)	-64.2 (10.5)	-54.6 (10.3)	(-71.7, -37.4)

Between Treatment Group Comparison	Difference in LS Means (90% CI)	p-Value
MK-3577 10 mg QAM vs. Placebo	-14.9 (-33.0, 3.2)	0.174
MK-3577 6 mg QPM vs. Placebo	-20.4 (-38.4, -2.4)	0.063
MK-3577 25 mg BID vs. Placebo	-78.1 (-96.4, -59.8)	<0.001
Metformin 1000 mg BID vs. Placebo	-49.4 (-66.9, -31.8)	<0.001

[†] N = Number of individuals included in the LDA model.

[‡] Based on an LDA model including terms for treatment, period, the interaction of treatment by period, prior antihyperglycemic therapy status (yes/no), randomization stratum (participation in domiciled visits/no participation in domiciled visits), and subject effect, with a restriction of same baseline mean across patients in all treatment sequences (due to randomization).

Table 5

Adverse Event Summary
in Treatment and Post-Treatment Periods
(APaT)

	Placebo		MK-3577 10 mg QAM		MK-3577 6 mg QPM		MK-3577 25 mg BID		Metformin 1000 mg BID	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Patients in treatment group	108		106		105		89		18	
with one or more adverse events	28	(25.9)	30	(28.3)	22	(21.0)	28	(31.5)	6	(33.3)
with no adverse event	80	(74.1)	76	(71.7)	83	(79.0)	61	(68.5)	12	(66.7)
with drug-related[†] adverse events	8	(7.4)	8	(7.5)	5	(4.8)	9	(10.1)	2	(11.1)
with serious adverse events	1	(0.9)	2	(1.9)	2	(1.9)	0	(0.0)	0	(0.0)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	1	(1.0)	0	(0.0)	0	(0.0)
who died	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued[‡] due to an adverse event	2	(1.9)	2	(1.9)	2	(1.9)	3	(3.4)	1	(5.6)
discontinued due to a drug-related adverse event	1	(0.9)	1	(0.9)	1	(1.0)	2	(2.2)	1	(5.6)
discontinued due to a serious adverse event	1	(0.9)	1	(0.9)	2	(1.9)	0	(0.0)	0	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	1	(1.0)	0	(0.0)	0	(0.0)

[†] Determined by the investigator to be related to the drug.

[‡] Study medication withdrawn.

AEs in the Post-Treatment Period are included with the AEs of the immediately preceding treatment.

Table 6

Patients With Adverse Events (Incidence ≥ 5% in One or More Treatment Groups) in Treatment and Post-Treatment Periods (APaT)

	Placebo		MK-3577 10 mg QAM		MK-3577 6 mg QPM		MK-3577 25 mg BID		Metformin 1000 mg BID	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Patients in treatment group	108		106		105		89		18	
with one or more adverse events	28	(25.9)	30	(28.3)	22	(21.0)	28	(31.5)	6	(33.3)
with no adverse events	80	(74.1)	76	(71.7)	83	(79.0)	61	(68.5)	12	(66.7)
Gastrointestinal disorders	**3**	**(2.8)**	**4**	**(3.8)**	**3**	**(2.9)**	**11**	**(12.4)**	**1**	**(5.6)**
Diarrhoea	1	(0.9)	1	(0.9)	1	(1.0)	3	(3.4)	1	(5.6)
General disorders and administration site conditions	**3**	**(2.8)**	**2**	**(1.9)**	**2**	**(1.9)**	**3**	**(3.4)**	**1**	**(5.6)**
Pyrexia	0	(0.0)	2	(1.9)	1	(1.0)	1	(1.1)	1	(5.6)
Infections and infestations	**6**	**(5.6)**	**11**	**(10.4)**	**8**	**(7.6)**	**8**	**(9.0)**	**0**	**(0.0)**
Injury, poisoning and procedural complications	**3**	**(2.8)**	**3**	**(2.8)**	**0**	**(0.0)**	**2**	**(2.2)**	**1**	**(5.6)**
Injury, poisoning and procedural complications	**3**	**(2.8)**	**3**	**(2.8)**	**0**	**(0.0)**	**2**	**(2.2)**	**1**	**(5.6)**
Excoriation	1	(0.9)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.6)
Investigations	**2**	**(1.9)**	**6**	**(5.7)**	**2**	**(1.9)**	**6**	**(6.7)**	**1**	**(5.6)**
Heart rate increased	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.6)

Patients With Adverse Events (Incidence ≥ 5% in One or More Treatment Groups) in Treatment and Post-Treatment Periods (APaT) (Cont.)

	Placebo		MK-3577 10 mg QAM		MK-3577 6 mg QPM		MK-3577 25 mg BID		Metformin 1000 mg BID	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Musculoskeletal and connective tissue disorders	**2**	**(1.9)**	**3**	**(2.8)**	**5**	**(4.8)**	**3**	**(3.4)**	**1**	**(5.6)**
Musculoskeletal chest pain	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.6)
Pain in extremity	0	(0.0)	1	(0.9)	0	(0.0)	1	(1.1)	1	(5.6)
Nervous system disorders	**4**	**(3.7)**	**6**	**(5.7)**	**1**	**(1.0)**	**4**	**(4.5)**	**1**	**(5.6)**
Headache	1	(0.9)	1	(0.9)	0	(0.0)	0	(0.0)	1	(5.6)
Sinus headache	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.6)
Respiratory, thoracic and mediastinal disorders	**3**	**(2.8)**	**3**	**(2.8)**	**0**	**(0.0)**	**2**	**(2.2)**	**1**	**(5.6)**
Epistaxis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.6)
Vascular disorders	**2**	**(1.9)**	**0**	**(0.0)**	**1**	**(1.0)**	**1**	**(1.1)**	**1**	**(5.6)**
Hypertension	0	(0.0)	0	(0.0)	1	(1.0)	1	(1.1)	1	(5.6)

AEs in the Post-Treatment Period are included with the AEs of the immediately preceding treatment.

Every patient is counted a single time for each applicable specific adverse event. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class.

A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns is greater than or equal to the percent incidence specified in the report title, after rounding.

Table 7

Listing of Patients With Serious Adverse Events
(APaT)

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Table 8

Patients With Adverse Events Resulting in Discontinuation of Study Medication
(Incidence > 0% in One or More Treatment Groups)
(APaT)

	Placebo		MK-3577 10 mg QAM		MK-3577 6 mg QPM		MK-3577 25 mg BID		Metformin 1000 mg BID	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Patients in treatment group	108		106		105		89		18	
with one or more adverse events resulting in discontinuation of study medication	2	(1.9)	2	(1.9)	2	(1.9)	3	(3.4)	1	(5.6)
with no adverse events resulting in discontinuation of study medication	106	(98.1)	104	(98.1)	103	(98.1)	86	(96.6)	17	(94.4)
Cardiac disorders	**0**	**(0.0)**	**0**	**(0.0)**	**2**	**(1.9)**	**0**	**(0.0)**	**0**	**(0.0)**
Coronary artery disease	0	(0.0)	0	(0.0)	1	(1.0)	0	(0.0)	0	(0.0)
Myocardial infarction	0	(0.0)	0	(0.0)	1	(1.0)	0	(0.0)	0	(0.0)
Gastrointestinal disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(5.6)**
Diarrhoea	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.6)

Patients With Adverse Events Resulting in Discontinuation of Study Medication
(Incidence > 0% in One or More Treatment Groups)
(APaT) (Cont.)

	Placebo		MK-3577 10 mg QAM		MK-3577 6 mg QPM		MK-3577 25 mg BID		Metformin 1000 mg BID	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Infections and infestations	**1**	**(0.9)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**
Cellulitis	1	(0.9)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Investigations	**0**	**(0.0)**	**1**	**(0.9)**	**0**	**(0.0)**	**2**	**(2.2)**	**0**	**(0.0)**
Alanine aminotransferase increased	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)	0	(0.0)
Transaminases increased	0	(0.0)	1	(0.9)	0	(0.0)	1	(1.1)	0	(0.0)
Metabolism and nutrition disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(1.1)**	**0**	**(0.0)**
Hypoglycaemia	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)	0	(0.0)
Respiratory, thoracic and mediastinal disorders	**0**	**(0.0)**	**1**	**(0.9)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**
Chronic obstructive pulmonary disease	0	(0.0)	1	(0.9)	0	(0.0)	0	(0.0)	0	(0.0)

Patients With Adverse Events Resulting in Discontinuation of Study Medication
(Incidence > 0% in One or More Treatment Groups)
(APaT) (Cont.)

	Placebo		MK-3577 10 mg QAM		MK-3577 6 mg QPM		MK-3577 25 mg BID		Metformin 1000 mg BID	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Skin and subcutaneous tissue disorders	**1**	**(0.9)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**
Hyperhidrosis	1	(0.9)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

AEs in the Post-Treatment Period are included with the AEs of the immediately preceding treatment.

Every patient is counted a single time for each applicable specific adverse event. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class.

A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns is greater than or equal to the percent incidence specified in the report title, after rounding.

Table 9

Summary of Percent Change From Baseline in Total Cholesterol (mg/dL) by Week (APaT/DAO)

		Baseline	Timepoint	Percent Change from Baseline			
Treatment	N[†]	Mean (SD)	Mean (SD)	Mean (SD)	Median	(Q1, Q3)	Range
Week 4							
Placebo	102	174.9 (31.9)	177.1 (35.3)	1.7 (13.5)	0.0	(-5.8 , 6.6)	-18.7 to 72.4
MK-3577 10 mg QAM	100	174.5 (31.8)	183.0 (35.7)	5.6 (16.1)	2.6	(-3.2 , 9.1)	-24.5 to 91.5
MK-3577 6 mg QPM	99	174.1 (31.7)	185.6 (35.6)	7.4 (16.5)	4.9	(-2.3 , 11.6)	-21.7 to 83.4
MK-3577 25 mg BID	86	177.2 (31.9)	196.6 (40.6)	11.5 (17.2)	10.3	(3.2 , 16.5)	-20.2 to 125.6
Metformin 1000 mg BID	18	171.1 (45.4)	175.8 (44.3)	3.4 (13.1)	3.5	(-3.8 , 10.4)	-19.1 to 35.7
Post-Study							
Placebo	9	185.7 (38.5)	182.1 (27.6)	-0.2 (13.4)	0.9	(-6.8 , 3.8)	-19.3 to 25.3
MK-3577 10 mg QAM	37	182.0 (30.2)	182.1 (32.6)	1.0 (16.1)	-0.3	(-8.5 , 5.8)	-22.1 to 59.0
MK-3577 6 mg QPM	36	169.6 (31.3)	164.6 (31.4)	-2.0 (13.6)	-2.7	(-7.0 , 4.0)	-37.7 to 33.6
MK-3577 25 mg BID	18	172.7 (27.2)	183.5 (28.5)	7.3 (16.4)	4.8	(-0.8 , 9.6)	-15.9 to 50.9
Metformin 1000 mg BID	2	177.3 (10.3)	149.0 (18.4)	-15.5 (15.3)	-15.5	(-26.3 , -4.7)	-26.3 to -4.7

[†]N = Number of individuals who have valid reading at timepoint.

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Table 10

Summary of Percent Change From Baseline in LDL-C (mg/dL) by Week
(APaT/DAO)

		Baseline	Timepoint	Percent Change from Baseline			
Treatment	N[†]	Mean (SD)	Mean (SD)	Mean (SD)	Median	(Q1, Q3)	Range
Week 4							
Placebo	102	101.3 (26.7)	104.1 (28.2)	4.8 (25.0)	1.4	(-7.1 , 7.6)	-34.9 to 140.3
MK-3577 10 mg QAM	100	101.8 (27.5)	104.7 (29.4)	5.4 (27.9)	0.9	(-6.8 , 9.3)	-62.9 to 140.3
MK-3577 6 mg QPM	99	101.4 (27.3)	109.0 (29.1)	10.6 (27.9)	3.5	(-4.3 , 15.7)	-38.3 to 133.1
MK-3577 25 mg BID	86	104.7 (27.7)	112.4 (29.9)	9.1 (21.8)	6.3	(-1.7 , 15.4)	-32.2 to 138.6
Metformin 1000 mg BID	18	96.7 (35.6)	101.8 (32.4)	7.6 (23.4)	5.7	(-7.0 , 7.5)	-26.1 to 72.3
Post-Study							
Placebo	9	107.7 (27.8)	100.9 (25.2)	-4.1 (19.8)	-8.6	(-11.2 , 0.4)	-25.5 to 38.7
MK-3577 10 mg QAM	37	107.7 (24.3)	108.4 (26.0)	2.8 (23.9)	3.9	(-10.2 , 11.4)	-32.3 to 87.1
MK-3577 6 mg QPM	36	99.2 (31.2)	94.5 (29.2)	-0.6 (24.4)	-2.3	(-14.0 , 8.2)	-50.5 to 66.7
MK-3577 25 mg BID	17	103.1 (24.0)	106.0 (26.3)	3.6 (15.5)	0.5	(-3.5 , 9.2)	-18.4 to 46.9
Metformin 1000 mg BID	2	109.3 (3.2)	80.0 (19.8)	-26.5 (20.3)	-26.5	(-40.8 , -12.1)	-40.8 to -12.1

[†]N = Number of individuals who have valid reading at timepoint.

Table 11

Summary of Percent Change From Baseline in HDL-C (mg/dL) by Week
(APaT/DAO)

		Baseline	Timepoint	Percent Change from Baseline			
Treatment	N[†]	Mean (SD)	Mean (SD)	Mean (SD)	Median	(Q1, Q3)	Range
Week 4							
Placebo	102	42.6 (10.5)	43.7 (10.0)	3.8 (14.5)	2.1	(-6.3 , 12.3)	-23.1 to 47.8
MK-3577 10 mg QAM	100	43.1 (10.5)	46.5 (11.2)	9.1 (17.1)	7.8	(-2.4 , 17.6)	-35.2 to 58.5
MK-3577 6 mg QPM	99	42.7 (10.6)	46.6 (11.9)	10.3 (17.8)	7.8	(-1.6 , 16.9)	-23.3 to 73.3
MK-3577 25 mg BID	86	42.9 (11.3)	48.2 (14.7)	12.6 (17.6)	10.5	(0.9 , 21.7)	-16.7 to 77.8
Metformin 1000 mg BID	18	43.2 (12.9)	45.3 (13.2)	5.7 (9.2)	6.9	(-1.0 , 10.2)	-9.6 to 27.3
Post-Study							
Placebo	9	48.9 (19.4)	52.4 (20.7)	10.3 (31.2)	11.5	(-4.2 , 16.7)	-28.8 to 75.6
MK-3577 10 mg QAM	37	42.8 (9.6)	46.8 (9.9)	11.0 (17.2)	13.0	(3.9 , 19.5)	-40.8 to 56.0
MK-3577 6 mg QPM	36	42.0 (9.0)	43.4 (10.8)	3.7 (15.0)	6.6	(-2.3 , 12.4)	-40.0 to 41.7
MK-3577 25 mg BID	18	42.0 (11.0)	44.5 (10.9)	6.9 (12.5)	4.4	(1.7 , 12.9)	-12.5 to 41.4
Metformin 1000 mg BID	2	36.5 (15.6)	42.5 (14.8)	18.5 (9.8)	18.5	(11.6 , 25.5)	11.6 to 25.5

[†]N = Number of individuals who have valid reading at timepoint.

Table 12

Summary of Percent Change From Baseline in TG (mg/dL) by Week
(APaT/DAO)

		Baseline	Timepoint	Percent Change from Baseline			
Treatment	N[†]	Mean (SD)	Mean (SD)	Mean (SD)	Median	(Q1, Q3)	Range
Week 4							
Placebo	102	156.9 (99.8)	147.5 (81.0)	-0.3 (29.8)	-1.5	(-22.9 , 16.2)	-61.5 to 95.4
MK-3577 10 mg QAM	100	149.0 (78.5)	162.7 (115.5)	11.5 (37.2)	9.3	(-5.8 , 26.9)	-67.6 to 154.8
MK-3577 6 mg QPM	99	151.4 (79.5)	151.2 (89.9)	4.3 (33.7)	-2.8	(-17.5 , 23.2)	-71.0 to 101.0
MK-3577 25 mg BID	86	149.0 (76.4)	183.6 (191.7)	18.9 (42.9)	11.4	(-8.8 , 35.5)	-55.3 to 221.2
Metformin 1000 mg BID	18	158.1 (88.5)	143.4 (69.8)	-2.5 (30.2)	-3.1	(-13.5 , 4.0)	-56.3 to 79.3
Post-Study							
Placebo	9	145.1 (56.3)	143.7 (44.4)	7.8 (45.4)	-1.0	(-26.3 , 40.7)	-44.4 to 98.1
MK-3577 10 mg QAM	37	157.3 (69.1)	134.4 (69.0)	-12.8 (23.7)	-11.0	(-26.4 , -0.3)	-66.7 to 48.3
MK-3577 6 mg QPM	36	145.4 (100.5)	133.4 (85.6)	1.5 (43.0)	-10.6	(-19.4 , 9.6)	-62.3 to 174.2
MK-3577 25 mg BID	18	150.3 (58.8)	181.4 (133.3)	19.0 (71.9)	-5.3	(-15.7 , 35.3)	-40.1 to 275.1
Metformin 1000 mg BID	2	158.5 (43.8)	133.0 (67.9)	-18.9 (20.4)	-18.9	(-33.3 , -4.5)	-33.3 to -4.5

[†]N = Number of individuals who have valid reading at timepoint.

Table 13

Summary of Percent Change From Baseline in ALT (IU/L) by Week
(APaT/DAO)

		Baseline	Timepoint	Percent Change from Baseline			
Treatment	N[†]	Mean (SD)	Mean (SD)	Mean (SD)	Median	(Q1, Q3)	Range
Week 2							
Placebo	101	26.3 (14.0)	26.7 (20.7)	5.5 (48.7)	-4.3	(-20.0 , 14.7)	-80.0 to 320.0
MK-3577 10 mg QAM	101	27.1 (14.4)	31.3 (21.5)	20.0 (50.6)	9.1	(-8.6 , 38.5)	-58.3 to 300.0
MK-3577 6 mg QPM	98	26.6 (14.0)	32.9 (25.9)	32.0 (79.5)	15.5	(-10.5 , 54.2)	-75.0 to 547.1
MK-3577 25 mg BID	84	25.9 (13.1)	39.9 (26.3)	66.4 (95.4)	48.1	(2.9 , 101.1)	-73.3 to 515.0
Metformin 1000 mg BID	18	30.0 (17.3)	26.1 (13.7)	-10.0 (15.5)	-12.0	(-19.4 , 3.1)	-35.5 to 19.4
Week 4							
Placebo	99	26.2 (13.8)	26.0 (17.2)	4.7 (47.9)	0.0	(-20.0 , 18.2)	-75.0 to 373.3
MK-3577 10 mg QAM	96	27.2 (14.3)	35.0 (29.1)	47.2 (202.6)	12.0	(-9.4 , 47.8)	-78.3 to 1877.8
MK-3577 6 mg QPM	98	27.1 (14.2)	29.3 (16.2)	17.7 (67.0)	6.5	(-12.9 , 32.1)	-80.0 to 555.6
MK-3577 25 mg BID	82	25.6 (13.1)	38.5 (24.8)	65.4 (115.9)	31.7	(0.0 , 91.7)	-75.0 to 575.0
Metformin 1000 mg BID	16	30.3 (18.3)	23.3 (14.9)	-21.7 (13.9)	-18.4	(-32.8 , -12.7)	-47.8 to 0.0
Post-Study							
Placebo	10	31.0 (15.3)	24.6 (12.5)	-7.5 (41.0)	-12.1	(-30.0 , 31.8)	-83.3 to 46.4
MK-3577 10 mg QAM	37	26.8 (18.3)	30.1 (21.0)	24.0 (75.7)	0.0	(-18.1 , 26.9)	-67.4 to 346.7
MK-3577 6 mg QPM	36	25.0 (10.9)	25.5 (12.0)	9.2 (45.1)	0.0	(-23.1 , 34.1)	-63.9 to 147.1
MK-3577 25 mg BID	18	26.4 (7.2)	31.3 (11.9)	22.0 (42.8)	12.2	(-3.0 , 32.4)	-29.7 to 137.0
Metformin 1000 mg BID	2	28.0 (5.7)	24.0 (2.8)	-13.5 (7.4)	-13.5	(-18.8 , -8.3)	-18.8 to -8.3

[†]N = Number of individuals who have valid reading at timepoint.

Table 14

Summary of Percent Change From Baseline in AST (IU/L) by Week
(APaT/DAO)

		Baseline	Timepoint	Percent Change from Baseline			
Treatment	N[†]	Mean (SD)	Mean (SD)	Mean (SD)	Median	(Q1, Q3)	Range
Week 2							
Placebo	101	22.5 (10.0)	23.2 (15.6)	4.8 (38.7)	0.0	(-17.6 , 13.8)	-50.0 to 235.3
MK-3577 10 mg QAM	101	22.8 (10.1)	26.0 (12.6)	19.0 (41.5)	11.8	(-6.7 , 40.0)	-45.0 to 211.8
MK-3577 6 mg QPM	98	22.6 (10.0)	26.1 (13.1)	19.2 (39.1)	13.0	(0.0 , 30.8)	-46.2 to 213.8
MK-3577 25 mg BID	84	21.7 (9.5)	33.2 (20.0)	60.2 (72.2)	43.7	(11.3 , 86.0)	-42.9 to 329.4
Metformin 1000 mg BID	18	26.1 (11.0)	23.2 (9.6)	-9.7 (15.9)	-7.7	(-20.6 , 0.0)	-41.3 to 22.7
Week 4							
Placebo	99	22.4 (9.8)	23.5 (12.6)	9.2 (45.3)	0.0	(-11.8 , 20.7)	-38.5 to 331.3
MK-3577 10 mg QAM	96	23.0 (10.1)	28.5 (17.2)	27.5 (58.0)	15.0	(-5.6 , 42.3)	-42.4 to 329.4
MK-3577 6 mg QPM	98	23.0 (10.2)	25.2 (11.2)	13.3 (29.5)	8.2	(-8.7 , 29.6)	-45.5 to 117.6
MK-3577 25 mg BID	82	21.5 (9.2)	31.6 (16.4)	57.7 (95.3)	26.0	(9.1 , 81.8)	-29.4 to 550.0
Metformin 1000 mg BID	16	26.6 (11.5)	21.6 (10.5)	-16.0 (18.8)	-16.7	(-30.6 , -1.9)	-50.0 to 20.0
Post-Study							
Placebo	10	20.3 (6.6)	19.9 (8.1)	-0.0 (25.3)	-7.9	(-13.8 , 0.0)	-31.3 to 50.0
MK-3577 10 mg QAM	37	22.5 (12.0)	24.6 (13.1)	15.5 (57.8)	3.7	(-10.5 , 21.4)	-48.5 to 300.0
MK-3577 6 mg QPM	36	22.4 (8.4)	22.2 (9.5)	3.5 (37.7)	-5.7	(-21.4 , 26.5)	-46.2 to 150.0
MK-3577 25 mg BID	18	23.1 (9.9)	25.3 (9.7)	16.0 (33.0)	10.6	(-4.8 , 23.5)	-44.1 to 81.8
Metformin 1000 mg BID	2	22.0 (5.7)	17.0 (2.8)	-21.8 (7.3)	-21.8	(-26.9 , -16.7)	-26.9 to -16.7

[†]N = Number of individuals who have valid reading at timepoint.