



Clinical trial results:

A Phase 3, Multi-Center, Placebo-Controlled, Randomized, Double-Blind, 12-Week Study With a 40-Week, Active-Controlled, Double-Blind Extension to Evaluate the Efficacy and Safety of K-877 in Adult Patients With Fasting Triglyceride Levels ≥ 500 mg/dL and < 2000 mg/dL and Normal Renal Function.

Summary

EudraCT number	2015-003511-37
Trial protocol	HU CZ BG PL
Global end of trial date	24 June 2019

Results information

Result version number	v1 (current)
This version publication date	05 July 2020
First version publication date	05 July 2020

Trial information

Trial identification

Sponsor protocol code	K-877-301
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03001817
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Kowa Research Institute, Inc.
Sponsor organisation address	430 Davis Drive, Suite 200, Morrisville, United States, 27560
Public contact	Regulatory Affairs, Kowa Research Institute, Inc., 1 919-433-1600,
Scientific contact	Regulatory Affairs, Kowa Research Institute, Inc., 1 919-433-1600,

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	17 March 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 October 2018
Global end of trial reached?	Yes
Global end of trial date	24 June 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to demonstrate the efficacy of K-877 0.2 mg twice daily compared to placebo from baseline to Week 12 in lowering fasting triglyceride (TG) levels in patients with fasting TG levels ≥ 500 mg/dL (5.65 mmol/L) and < 2000 mg/dL (22.60 mmol/L).

Protection of trial subjects:

The study was conducted in accordance with the World Medical Association Declaration of Helsinki; ICH GCP; General Data Protection Regulation or Directive 2001/20/EC (in the EU); the FDA GCP, as described in 21 CFR Parts 11, 50, 54, 56, and 312 and Health Insurance Portability and Accountability Act (in the US); and the laws and regulations of the country where the study was conducted. Prior to the initiation of any study procedures, each patient signed and dated an approved informed consent form. Each patient was assured of his/her right to withdraw from the study at any time.

Background therapy: -

Evidence for comparator:

Fenofibrate (145 mg once daily) was chosen as the active comparator for the 40-week Extension Period of this study based on current guidelines for the management of severe hypertriglyceridemia.

Actual start date of recruitment	28 November 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Bulgaria: 41
Country: Number of subjects enrolled	Czech Republic: 33
Country: Number of subjects enrolled	Hungary: 44
Country: Number of subjects enrolled	Poland: 25
Country: Number of subjects enrolled	Belarus: 58
Country: Number of subjects enrolled	Georgia: 37
Country: Number of subjects enrolled	Russian Federation: 114
Country: Number of subjects enrolled	Ukraine: 58
Country: Number of subjects enrolled	United States: 141
Worldwide total number of subjects	551
EEA total number of subjects	143

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	527
From 65 to 84 years	24
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Eligible patients entered a 4- to 6-week lifestyle stabilization period. The stabilization period was followed by a 2-week TG qualifying period and patient eligibility was assessed based on the visits in this period.

Period 1

Period 1 title	12-week Efficacy
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

Key results from lipid parameters were blinded prior to Week 16. Investigators received an alert for TG levels >2000 mg/dL (22.60 mmol/L) at any time during the study as well as a sham alert for TG elevation during the 12-week Efficacy Period to ensure study blinding was maintained.

Arms

Are arms mutually exclusive?	Yes
Arm title	K-877

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Pemafibrate
Investigational medicinal product code	K-877
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

0.2 mg BID

Arm title	Placebo
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Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo matching K-877
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo BID

Number of subjects in period 1	K-877	Placebo
Started	368	183
Completed	350	176
Not completed	18	7
Consent withdrawn by subject	9	3
Adverse event, non-fatal	6	2
Persistent significant abnormal laboratory values	-	1
Lost to follow-up	3	-
Protocol deviation	-	1

Period 2

Period 2 title	40-week Extension
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

Starting at Visit 7 (Week 12), patients received an oral dose of K-877 0.2 mg BID and placebo matching fenofibrate once daily, or fenofibrate 145 mg once daily and placebo matching K-877 BID with double dummy techniques.

Arms

Are arms mutually exclusive?	Yes
Arm title	K-877

Arm description:

Patients randomized to receive K-877 0.2 mg BID in the 12-week Efficacy Period continued to receive K-877 0.2 mg BID, as well as placebo matching fenofibrate 145 mg once daily, in the 40-week Extension Period.

Arm type	Experimental and Placebo Comparator
Investigational medicinal product name	Pemafibrate
Investigational medicinal product code	K-877
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

0.2 mg BID

Investigational medicinal product name	Placebo matching fenofibrate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Placebo once daily over-encapsulated for double dummy techniques

Arm title	Placebo/Fenofibrate
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Arm description:

Patients randomized to receive placebo matching K-877 0.2 mg BID in the 12-week Efficacy Period received fenofibrate 145 mg once daily and placebo matching K-877 0.2 mg BID in the 40-week Extension Period.

Arm type	Active Comparator and Placebo
Investigational medicinal product name	Fenofibrate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

145 mg once daily over-encapsulated for double dummy techniques

Investigational medicinal product name	Placebo matching K-877
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo BID

Number of subjects in period 2	K-877	Placebo/Fenofibrate
Started	350	176
Completed	335	163
Not completed	15	14
Adverse event, serious fatal	3	-
Consent withdrawn by subject	5	8
Adverse event, non-fatal	-	2
Persistent significant abnormal laboratory values	1	1
Use of prohibited medication	-	1
Lost to follow-up	6	2
Joined	0	1
Protocol Deviation	-	1

Baseline characteristics

Reporting groups

Reporting group title	K-877
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	K-877	Placebo	Total
Number of subjects	368	183	551
Age categorical Units: Subjects			
18-64 years	351	176	527
65-84 years	17	7	24
≥85 years	0	0	0
Gender categorical Units: Subjects			
Female	97	39	136
Male	271	144	415

Subject analysis sets

Subject analysis set title	Full Analysis Set (FAS)
Subject analysis set type	Full analysis
Subject analysis set description: The FAS consisted of all randomized patients who took at least 1 dose of double-blind study drug and had a baseline TG measurement.	
Subject analysis set title	Safety Analysis Set
Subject analysis set type	Safety analysis
Subject analysis set description: The Safety Analysis Set included all randomized patients who received at least 1 dose of study drug.	

Reporting group values	Full Analysis Set (FAS)	Safety Analysis Set	
Number of subjects	551	551	
Age categorical Units: Subjects			
18-64 years	527		
65-84 years	24		
≥85 years	0		
Gender categorical Units: Subjects			
Female	136		
Male	415		

End points

End points reporting groups

Reporting group title	K-877
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	K-877
Reporting group description:	
Patients randomized to receive K-877 0.2 mg BID in the 12-week Efficacy Period continued to receive K-877 0.2 mg BID, as well as placebo matching fenofibrate 145 mg once daily, in the 40-week Extension Period.	
Reporting group title	Placebo/Fenofibrate
Reporting group description:	
Patients randomized to receive placebo matching K-877 0.2 mg BID in the 12-week Efficacy Period received fenofibrate 145 mg once daily and placebo matching K-877 0.2 mg BID in the 40-week Extension Period.	
Subject analysis set title	Full Analysis Set (FAS)
Subject analysis set type	Full analysis
Subject analysis set description:	
The FAS consisted of all randomized patients who took at least 1 dose of double-blind study drug and had a baseline TG measurement.	
Subject analysis set title	Safety Analysis Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
The Safety Analysis Set included all randomized patients who received at least 1 dose of study drug.	

Primary: Percent Change of Fasting Triglyceride (TG) Levels From Baseline to Week 12

End point title	Percent Change of Fasting Triglyceride (TG) Levels From Baseline to Week 12
End point description:	
End point type	Primary
End point timeframe:	
Baseline to Week 12	

End point values	K-877	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	368	183		
Units: Percent				
median (inter-quartile range (Q1-Q3))	-56.00 (-72.08 to -32.40)	-7.97 (-44.78 to 49.87)		

Statistical analyses

Statistical analysis title	Hodges-Lehmann estimator with multiple imputation
Statistical analysis description: A pattern mixture model was used as the primary imputation method as part of the primary analysis for the Week 12 percent change from baseline in fasting TG.	
Comparison groups	K-877 v Placebo
Number of subjects included in analysis	551
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Hodges-Lehmann, multiple imputation

Secondary: Percent Change From Baseline to Week 52 in Fasting TG

End point title	Percent Change From Baseline to Week 52 in Fasting TG
End point description:	
End point type	Secondary
End point timeframe: Baseline to Week 52	

End point values	K-877	Placebo/Fenofibrate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	335	163		
Units: percent				
median (inter-quartile range (Q1-Q3))	-57.93 (-73.76 to -31.97)	-55.45 (-68.95 to -28.74)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

52 Weeks

Adverse event reporting additional description:

Non-serious adverse events are reported in the table when frequency exceeded the threshold 5% within either reporting group. In overall period, total subjects affected by any non-serious adverse events regardless of the threshold were 167/368 (45.4%) in the K-877 group and 89/183 (48.6%) in the Placebo/Fenofibrate group.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.0
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Reporting groups

Reporting group title	K-877
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Reporting group description:

Patients randomized to receive K-877 0.2 mg BID in the 12-week Efficacy Period continued to receive K-877 0.2 mg BID, as well as placebo matching fenofibrate 145 mg once daily, in the 40-week Extension Period.

Reporting group title	Placebo/Fenofibrate
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Reporting group description:

Patients randomized to receive placebo matching K-877 0.2 mg BID in the 12-week Efficacy Period received fenofibrate 145 mg once daily and placebo matching K-877 0.2 mg BID in the 40-week Extension Period.

Serious adverse events	K-877	Placebo/Fenofibrate	
Total subjects affected by serious adverse events			
subjects affected / exposed	39 / 368 (10.60%)	8 / 183 (4.37%)	
number of deaths (all causes)	3	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Endometrial cancer			
subjects affected / exposed	1 / 368 (0.27%)	0 / 183 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 368 (0.27%)	0 / 183 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			

subjects affected / exposed	1 / 368 (0.27%)	0 / 183 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery aneurysm			
subjects affected / exposed	1 / 368 (0.27%)	0 / 183 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral ischaemia			
subjects affected / exposed	0 / 368 (0.00%)	1 / 183 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	1 / 368 (0.27%)	0 / 183 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			
subjects affected / exposed	1 / 368 (0.27%)	0 / 183 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Immune system disorders			
Allergic granulomatous angiitis			
subjects affected / exposed	1 / 368 (0.27%)	0 / 183 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 368 (0.27%)	0 / 183 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			

subjects affected / exposed	1 / 368 (0.27%)	0 / 183 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	1 / 368 (0.27%)	0 / 183 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 368 (0.00%)	1 / 183 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Limb traumatic amputation			
subjects affected / exposed	1 / 368 (0.27%)	0 / 183 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist fracture			
subjects affected / exposed	1 / 368 (0.27%)	0 / 183 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 368 (0.27%)	0 / 183 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Coronary artery disease			
subjects affected / exposed	2 / 368 (0.54%)	1 / 183 (0.55%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 368 (0.27%)	0 / 183 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Myocardial ischaemia			
subjects affected / exposed	1 / 368 (0.27%)	0 / 183 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	3 / 368 (0.82%)	1 / 183 (0.55%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Altered state of consciousness			
subjects affected / exposed	1 / 368 (0.27%)	0 / 183 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paralysis			
subjects affected / exposed	1 / 368 (0.27%)	0 / 183 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	1 / 368 (0.27%)	0 / 183 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 368 (0.27%)	0 / 183 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Visual impairment			
subjects affected / exposed	0 / 368 (0.00%)	1 / 183 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Dental cyst			

subjects affected / exposed	1 / 368 (0.27%)	0 / 183 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal inflammation			
subjects affected / exposed	0 / 368 (0.00%)	1 / 183 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 368 (0.27%)	0 / 183 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedematous pancreatitis			
subjects affected / exposed	1 / 368 (0.27%)	0 / 183 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	1 / 368 (0.27%)	0 / 183 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 368 (0.27%)	0 / 183 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	1 / 368 (0.27%)	0 / 183 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatotoxicity			
subjects affected / exposed	1 / 368 (0.27%)	0 / 183 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			

Toxic skin eruption			
subjects affected / exposed	0 / 368 (0.00%)	1 / 183 (0.55%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Calculus urinary			
subjects affected / exposed	1 / 368 (0.27%)	0 / 183 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glomerulonephritis chronic			
subjects affected / exposed	0 / 368 (0.00%)	1 / 183 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Spinal pain			
subjects affected / exposed	1 / 368 (0.27%)	0 / 183 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 368 (0.27%)	0 / 183 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 368 (0.27%)	0 / 183 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 368 (0.27%)	0 / 183 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Diabetes mellitus inadequate control			

subjects affected / exposed	2 / 368 (0.54%)	0 / 183 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	1 / 368 (0.27%)	0 / 183 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	K-877	Placebo/Fenofibrate	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 368 (8.70%)	14 / 183 (7.65%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	23 / 368 (6.25%)	5 / 183 (2.73%)	
occurrences (all)	23	6	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	11 / 368 (2.99%)	11 / 183 (6.01%)	
occurrences (all)	12	11	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 August 2017	<ul style="list-style-type: none">• Defined inclusion criteria that patients on a low-intensity statin or not on a statin needed to meet. They were consistent with, and further clarify, the American College of Cardiology/American Heart Association Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults (2013).• Clarified eGFR criteria and procedures for screen failures and potential transfer to the other parallel study, Study K-877-303. For patients who were transferred from Study K-877-303, their Visit 1 procedures were to be skipped and a written consent was required prior to any other procedures at Visit 2.• Permitted the inclusion of patients with Type 2 Diabetes Mellitus on fixed-dose regimens insulin or insulin analogues to make this study available to a wider population.• Permitted the inclusion of patients with positive HCV antibody, but no detectable HCV RNA or evidence of active HCV infection, to exclude only patients who have evidence of active HCV infection.• Simplified thyroid exclusions for patients on replacement therapy to make them consistent for both patients on therapy or untreated.• Specified an exception for prohibited medications based on the result of the drug-drug interaction study with clarithromycin known as an inhibitor of OATP1B1, OATP1B3, and CYP3A4.• Updated precautions for coadministering medications based on the result of the drug-drug interaction study with clopidogrel (CYP2C8 inhibitor).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported