EU Clinical Trials Register

Clinical trial results:
Effects of PCSK9 inhibition by Evolocumab on postprandial lipid metabolism in type 2 diabetes

Summary

EudraCT number	2016-001176-30
Trial protocol	FI
Global end of trial date	23 May 2018

Results information

Result version number	v1 (current)
This version publication date	27 March 2021
First version publication date	27 March 2021

Trial information

Trial identification

Sponsor protocol code	20167169

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02948777
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Clinical Research Institute, HUCH Ltd.
Sponsor organisation address	Haartmaninkatu 8, Helsinki, Finland,
Public contact	Research Program Unit, University of Helsinki, Research Program Unit, University of Helsinki, +358 947171990, marja-riitta.taskinen@helsinki.fi
Scientific contact	Research Program Unit, University of Helsinki, Research Program Unit, University of Helsinki, +358 947171990, marja-riitta.taskinen@helsinki.fi

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	Interim
Date of interim/final analysis	24 December 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 May 2018
Global end of trial reached?	Yes
Global end of trial date	23 May 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The overall aim is to clarify the postprandial dynamics of PCSK9 on the pathophysiology of postprandial hypertriglyceridemia in people with type 2 diabetes. The effect of 12 weeks treatment with Evolocumab 140 mg s.c. Q2W on postprandial lipid and lipoprotein metabolism will be assessed in patients with type 2 diabetes (n=12) in an one-arm unblinded clinical trial.

Protection of trial subjects:

Evolocumab is a prescription medicine and the subjects having analyses have minimal pain and no distress, so no protection was needed.

Background therapy:

Statin

Evidence for comparator: -

Actual start date of recruitment	01 September 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	Finland: 14
Worldwide total number of subjects	14
EEA total number of subjects	14

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)	7
From 65 to 84 years	7

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited from previous studies and by using two advertisement in the biggest daily newspaper in Finland, Helsingin Sanomat on 2nd October 2016 and 26th March 2019.

Pre-assignment

Screening details:

Screening period: Telefone screening (195 subjects) and Screening visit 1 (77 subjects).
Run-in period: Screening visit 2 including physician visit and atorvastatin + metformin start (37 subjects) and Screening visit 3 including lipid values check (22 subjects).
Inclusion and exclusion criteria are listed in protocol.

Period 1

Period 1 title	Baseline run-in period 2-4 weeks
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Analyses

Arm description:

Lipoprotein kinetic analyses using stable isotopes in the postprandial state. A measurements of liver fat content in the fasting state by MRI was performed within 7 days before the start of the kinetic procedure.

Arm type	Experimental
Investigational medicinal product name	atorvastatin is initiated if other statin is used
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The subjects will use metformin at a stable dose (500-3000 mg per day) throughout the study. If the patient uses another statin than atorvastatin (20 mg) at screening visit the used statin is stopped and atorvastatin 20 mg is initiated. If the patient is not using any statin, atorvastatin 20 mg will be initiated and the lipid values will be checked after 4 weeks. If eligible (LDL>1.8 mmol/L), the patient can be recruited. The subjects will continue using atorvastatin 20 mg throughout the study. However, patients using atorvastatin 40 mg / day will continue on atorvastatin 40 mg / day (it is not ethical to reduce the dose if LDL-C is >1.8 mmol/L). The subjects will use the metformin as a prescription medication. Atorvastatin will be administered by the study centre to the subjects.

Number of subjects in period 1	Analyses
Started	14
Completed	14

Period 2

Period 2 title	Treatment period evolocumab
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	Kinetic visit 1

Arm description:

Injections of stable isotopes and blood sampling for kinetic procedure and standard oral fat tolerance test, MRI and heparin tests on separate dates.

Arm type	Experimental
Investigational medicinal product name	Evolocumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Evolocumab (AMG 145) is supplied as a sterile, single-use, preservative free solution for subcutaneous injection in a disposable, spring-based prefilled autoinjector (AI)/pen. The AI/pen contains a 1.0 mL deliverable volume of 140 mg/mL Evolocumab in 220 mM proline, 20 mM acetate, 0.01% (w/v) polysorbate 80, pH 5.0. Evolocumab will be administered 140 mg s.c. Q2W without any dose adjustments or escalation.

Arm title	Week 2

Arm description:

Study visit with safety monitoring.

Arm type	Experimental
Investigational medicinal product name	Evolocumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Evolocumab (AMG 145) is supplied as a sterile, single-use, preservative free solution for subcutaneous injection in a disposable, spring-based prefilled autoinjector (AI)/pen. The AI/pen contains a 1.0 mL deliverable volume of 140 mg/mL Evolocumab in 220 mM proline, 20 mM acetate, 0.01% (w/v) polysorbate 80, pH 5.0. Evolocumab will be administered 140 mg s.c. Q2W without any dose adjustments or escalation.

Arm title	Week 4

Arm description:

Study visit with safety monitoring.

Arm type	Experimental
Investigational medicinal product name	Evolocumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Evolocumab (AMG 145) is supplied as a sterile, single-use, preservative free solution for subcutaneous

injection in a disposable, spring-based prefilled autoinjector (AI)/pen. The AI/pen contains a 1.0 mL deliverable volume of 140 mg/mL Evolocumab in 220 mM proline, 20 mM acetate, 0.01% (w/v) polysorbate 80, pH 5.0. Evolocumab will be administered 140 mg s.c. Q2W without any dose adjustments or escalation.

Arm title	Week 8

Arm description:

Study visit with safety monitoring.

Arm type	Experimental
Investigational medicinal product name	Evolocumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Evolocumab (AMG 145) is supplied as a sterile, single-use, preservative free solution for subcutaneous injection in a disposable, spring-based prefilled autoinjector (AI)/pen. The AI/pen contains a 1.0 mL deliverable volume of 140 mg/mL Evolocumab in 220 mM proline, 20 mM acetate, 0.01% (w/v) polysorbate 80, pH 5.0. Evolocumab will be administered 140 mg s.c. Q2W without any dose adjustments or escalation.

Arm title	Kinetic visit 2

Arm description:

Injections of stable isotopes and blood sampling for kinetic procedure and a standard oral fat tolerance test repeated.

Arm type	Experimental
Investigational medicinal product name	Evolocumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Evolocumab (AMG 145) is supplied as a sterile, single-use, preservative free solution for subcutaneous injection in a disposable, spring-based prefilled autoinjector (AI)/pen. The AI/pen contains a 1.0 mL deliverable volume of 140 mg/mL Evolocumab in 220 mM proline, 20 mM acetate, 0.01% (w/v) polysorbate 80, pH 5.0. Evolocumab will be administered 140 mg s.c. Q2W without any dose adjustments or escalation.

Number of subjects in period 2	Kinetic visit 1	Week 2	Week 4
Started	14	14	14
Completed	14	14	14

Number of subjects in period 2	Week 8	Kinetic visit 2
Started	14	14
Completed	14	14

Baseline characteristics

Reporting groups

Reporting group title	Baseline run-in period 2-4 weeks

Reporting group description: -

Reporting group values	Baseline run-in period 2-4 weeks	Total	
Number of subjects	14	14	
Age categorical			
Units: Subjects			
Adults (18-64 years)	7	7	
From 65-84 years	7	7	
Gender categorical			
Units: Subjects			
Female	8	8	
Male	6	6	
BMI			
Units: BMI			
arithmetic mean	30		
full range (min-max)	25 to 40	-	
Triglycerides			
Units: mmol/l			
arithmetic mean	1.6		
full range (min-max)	1.0 to 4.5	-	

End points

End points reporting groups

Reporting group title	Analyses
Reporting group description:	
Lipoprotein kinetic analyses using stable isotopes in the postprandial state. A measurements of liver fat content in the fasting state by MRI was performed within 7 days before the start of the kinetic procedure.	
Reporting group title	Kinetic visit 1
Reporting group description:	
Injections of stable isotopes and blood sampling for kinetic procedure and standard oral fat tolerance test, MRI and heparin tests on separate dates.	
Reporting group title	Week 2
Reporting group description:	
Study visit with safety monitoring.	
Reporting group title	Week 4
Reporting group description:	
Study visit with safety monitoring.	
Reporting group title	Week 8
Reporting group description:	
Study visit with safety monitoring.	
Reporting group title	Kinetic visit 2
Reporting group description:	
Injections of stable isotopes and blood sampling for kinetic procedure and a standard oral fat tolerance test repeated.	

Primary: TRL-C kinetic study

End point title	TRL-C kinetic study
End point description:	
More end point parameters found in published paper by Taskinen MR, Björnson E, Kahri J, Söderlund S, Matikainen N, Porthan K, Ainola M, Hakkarainen A, Lundbom N, Fermanelli V, Fuchs J, Thorsell A, Kronenberg F, Andersson L, Adiels M, Packard CJ, Borén J. Effects of Evolocumab on the Postprandial Kinetics of Apo (Apolipoprotein) B100- and B48-Containing Lipoproteins in Subjects With Type 2 Diabetes. Arterioscler Thromb Vasc Biol. 2020 Dec 24:ATVBAHA120315446.	
End point type	Primary
End point timeframe:	
Difference in the parameter between kinetic visit 1 and kinetic visit 2.	

End point values	Kinetic visit 1	Kinetic visit 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	14		
Units: mg/dL				
arithmetic mean (standard deviation)	33.4 (± 10.9)	17.8 (± 6.5)		

Attachments (see zip file)	Table 1. Taskinen MR et al. ATVB. 2020, ATVBAHA120315446..

Statistical analyses

Statistical analysis title	TRL-C
Comparison groups	Kinetic visit 1 v Kinetic visit 2
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Notes:

[1] - The trial was a single-phase, nonrandomized study of 12-week treatment with evolocumab 140 mg subcutaneously every 2 weeks in 14 patients with type II diabetes on background statin therapy. Cardiometabolic responses to a high-fat mixed meal were assessed before and at the end of the intervention period.

Primary: VLDL2 pool

End point title	VLDL2 pool

End point description:

More end point parameters found in published paper by Taskinen MR, Björnson E, Kahri J, Söderlund S, Matikainen N, Porthan K, Ainola M, Hakkarainen A, Lundbom N, Fermanelli V, Fuchs J, Thorsell A, Kronenberg F, Andersson L, Adiels M, Packard CJ, Borén J. Effects of Evolocumab on the Postprandial Kinetics of Apo (Apolipoprotein) B100- and B48-Containing Lipoproteins in Subjects With Type 2 Diabetes. Arterioscler Thromb Vasc Biol. 2020 Dec 24:ATVBAHA120315446.

End point type	Primary

End point timeframe:

Difference in the parameter between kinetic visit 1 and kinetic visit 2.

End point values	Kinetic visit 1	Kinetic visit 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	14		
Units: mg				
arithmetic mean (standard deviation)	130 (± 47)	93 (± 58)		

Attachments (see zip file)	Table 2. Taskinen MR et al. ATVB. 2020, ATVBAHA120315446..

Statistical analyses

Statistical analysis title	VLDL2 pool
Comparison groups	Kinetic visit 1 v Kinetic visit 2
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other[2]
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Notes:

[2] - The trial was a single-phase, nonrandomized study of 12-week treatment with evolocumab 140 mg subcutaneously every 2 weeks in 14 patients with type II diabetes on background statin therapy. Cardiometabolic responses to a high-fat mixed meal were assessed before and at the end of the intervention period.

Primary: ApoC-III

End point title	ApoC-III

End point description:

More end point parameters found in published paper by Taskinen MR, Björnson E, Kahri J, Söderlund S, Matikainen N, Porthan K, Ainola M, Hakkarainen A, Lundbom N, Fermanelli V, Fuchs J, Thorsell A, Kronenberg F, Andersson L, Adiels M, Packard CJ, Borén J. Effects of Evolocumab on the Postprandial Kinetics of Apo (Apolipoprotein) B100- and B48-Containing Lipoproteins in Subjects With Type 2 Diabetes. Arterioscler Thromb Vasc Biol. 2020 Dec 24:ATVBAHA120315446.

End point type	Primary

End point timeframe:

Difference in the parameter between kinetic visit 1 and kinetic visit 2.

End point values	Kinetic visit 1	Kinetic visit 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	14		
Units: mg/dL				
arithmetic mean (standard deviation)	12.2 (± 4.3)	10.4 (± 5.2)		

Attachments (see zip file)	Table 1. Taskinen MR et al. ATVB. 2020, ATVBAHA120315446..

Statistical analyses

Statistical analysis title	ApoC-III
Comparison groups	Kinetic visit 2 v Kinetic visit 1
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Notes:

[3] - The trial was a single-phase, nonrandomized study of 12-week treatment with evolocumab 140 mg subcutaneously every 2 weeks in 14 patients with type II diabetes on background statin therapy. Cardiometabolic responses to a high-fat mixed meal were assessed before and at the end of the intervention period.

Primary: VLDL2 FCR

End point title	VLDL2 FCR

End point description:

More end point parameters found in published paper by Taskinen MR, Björnson E, Kahri J, Söderlund S, Matikainen N, Porthan K, Ainola M, Hakkarainen A, Lundbom N, Fermanelli V, Fuchs J, Thorsell A, Kronenberg F, Andersson L, Adiels M, Packard CJ, Borén J. Effects of Evolocumab on the Postprandial Kinetics of Apo (Apolipoprotein) B100- and B48-Containing Lipoproteins in Subjects With Type 2 Diabetes. Arterioscler Thromb Vasc Biol. 2020 Dec 24:ATVBAHA120315446.

End point type	Primary

End point timeframe:

Difference in the parameter between kinetic visit 1 and kinetic visit 2.

End point values	Kinetic visit 1	Kinetic visit 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	14		
Units: pools/d				
arithmetic mean (standard deviation)	6.6 (± 3.3)	9.5 (± 4.2)		

Attachments (see zip file)	Table 2. Taskinen MR et al. ATVB. 2020, ATVBAHA120315446..

Statistical analyses

Statistical analysis title	VLDL2 FCR
Comparison groups	Kinetic visit 1 v Kinetic visit 2
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other[4]
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Notes:

[4] - The trial was a single-phase, nonrandomized study of 12-week treatment with evolocumab 140 mg subcutaneously every 2 weeks in 14 patients with type II diabetes on background statin therapy. Cardiometabolic responses to a high-fat mixed meal were assessed before and at the end of the intervention period.

Primary: IDL pool

End point title	IDL pool

End point description:

More end point parameters found in published paper by Taskinen MR, Björnson E, Kahri J, Söderlund S, Matikainen N, Porthan K, Ainola M, Hakkarainen A, Lundbom N, Fermanelli V, Fuchs J, Thorsell A, Kronenberg F, Andersson L, Adiels M, Packard CJ, Borén J. Effects of Evolocumab on the Postprandial Kinetics of Apo (Apolipoprotein) B100- and B48-Containing Lipoproteins in Subjects With Type 2 Diabetes. Arterioscler Thromb Vasc Biol. 2020 Dec 24:ATVBAHA120315446.

End point type	Primary

End point timeframe:

Difference in the parameter between kinetic visit 1 and kinetic visit 2.

End point values	Kinetic visit 1	Kinetic visit 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	14		
Units: mg				
arithmetic mean (standard deviation)	190 (± 50)	130 (± 49)		

Attachments (see zip file)	Table 2. Taskinen MR et al. ATVB. 2020, ATVBAHA120315446..

Statistical analyses

Statistical analysis title	IDL pool
Comparison groups	Kinetic visit 1 v Kinetic visit 2
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other[5]
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Notes:

[5] - The trial was a single-phase, nonrandomized study of 12-week treatment with evolocumab 140 mg subcutaneously every 2 weeks in 14 patients with type II diabetes on background statin therapy. Cardiometabolic responses to a high-fat mixed meal were assessed before and at the end of the intervention period.

Primary: IDL to LDL transfer

End point title	IDL to LDL transfer

End point description:

More end point parameters found in published paper by Taskinen MR, Björnson E, Kahri J, Söderlund S, Matikainen N, Porthan K, Ainola M, Hakkarainen A, Lundbom N, Fermanelli V, Fuchs J, Thorsell A, Kronenberg F, Andersson L, Adiels M, Packard CJ, Borén J. Effects of Evolocumab on the Postprandial Kinetics of Apo (Apolipoprotein) B100- and B48-Containing Lipoproteins in Subjects With Type 2 Diabetes. Arterioscler Thromb Vasc Biol. 2020 Dec 24:ATVBAHA120315446.

End point type	Primary

End point timeframe:

Difference in the parameter between kinetic visit 1 and kinetic visit 2.

End point values	Kinetic visit 1	Kinetic visit 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	14		
Units: mg/d				
arithmetic mean (standard deviation)	450 (± 190)	310 (± 140)		

Attachments (see zip file)	Table 2. Taskinen MR et al. ATVB. 2020, ATVBAHA120315446..

Statistical analyses

Statistical analysis title	IDL to LDL transfer
Comparison groups	Kinetic visit 1 v Kinetic visit 2

Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other[6]
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Notes:

[6] - The trial was a single-phase, nonrandomized study of 12-week treatment with evolocumab 140 mg subcutaneously every 2 weeks in 14 patients with type II diabetes on background statin therapy. Cardiometabolic responses to a high-fat mixed meal were assessed before and at the end of the intervention period.

Primary: VLDL2 pool

End point title	VLDL2 pool

End point description:

More end point parameters found in published paper by Taskinen MR, Björnson E, Kahri J, Söderlund S, Matikainen N, Porthan K, Ainola M, Hakkarainen A, Lundbom N, Fermanelli V, Fuchs J, Thorsell A, Kronenberg F, Andersson L, Adiels M, Packard CJ, Borén J. Effects of Evolocumab on the Postprandial Kinetics of Apo (Apolipoprotein) B100- and B48-Containing Lipoproteins in Subjects With Type 2 Diabetes. Arterioscler Thromb Vasc Biol. 2020 Dec 24:ATVBAHA120315446.

End point type	Primary

End point timeframe:

Difference in the parameter between kinetic visit 1 and kinetic visit 2.

End point values	Kinetic visit 1	Kinetic visit 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	14		
Units: g				
arithmetic mean (standard deviation)	1.1 (± 0.43)	0.75 (± 0.43)		

Attachments (see zip file)	Table 2. Taskinen MR et al. ATVB. 2020, ATVBAHA120315446..

Statistical analyses

Statistical analysis title	VLDL2 pool
Comparison groups	Kinetic visit 1 v Kinetic visit 2
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other[7]
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Notes:

[7] - The trial was a single-phase, nonrandomized study of 12-week treatment with evolocumab 140 mg subcutaneously every 2 weeks in 14 patients with type II diabetes on background statin therapy. Cardiometabolic responses to a high-fat mixed meal were assessed before and at the end of the intervention period.

Primary: VLDL2 FCR

End point title	VLDL2 FCR

End point description:

More end point parameters found in published paper by Taskinen MR, Björnson E, Kahri J, Söderlund S, Matikainen N, Porthan K, Ainola M, Hakkarainen A, Lundbom N, Fermanelli V, Fuchs J, Thorsell A, Kronenberg F, Andersson L, Adiels M, Packard CJ, Borén J. Effects of Evolocumab on the Postprandial Kinetics of Apo (Apolipoprotein) B100- and B48-Containing Lipoproteins in Subjects With Type 2 Diabetes. Arterioscler Thromb Vasc Biol. 2020 Dec 24:ATVBAHA120315446.

End point type	Primary

End point timeframe:

Difference in the parameter between kinetic visit 1 and kinetic visit 2.

End point values	Kinetic visit 1	Kinetic visit 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	14		
Units: pools/d				
arithmetic mean (standard deviation)	10 (± 6.3)	15 (± 8.7)		

Attachments (see zip file)	Table 2. Taskinen MR et al. ATVB. 2020, ATVBAHA120315446..

Statistical analyses

Statistical analysis title	VLDL2 FCR
Comparison groups	Kinetic visit 1 v Kinetic visit 2
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other[8]
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Notes:

[8] - The trial was a single-phase, nonrandomized study of 12-week treatment with evolocumab 140 mg subcutaneously every 2 weeks in 14 patients with type II diabetes on background statin therapy. Cardiometabolic responses to a high-fat mixed meal were assessed before and at the end of the intervention period.

Primary: CM-apoB48 FCR

End point title	CM-apoB48 FCR

End point description:

More end point parameters found in published paper by Taskinen MR, Björnson E, Kahri J, Söderlund S, Matikainen N, Porthan K, Ainola M, Hakkarainen A, Lundbom N, Fermanelli V, Fuchs J, Thorsell A, Kronenberg F, Andersson L, Adiels M, Packard CJ, Borén J. Effects of Evolocumab on the Postprandial Kinetics of Apo (Apolipoprotein) B100- and B48-Containing Lipoproteins in Subjects With Type 2 Diabetes. Arterioscler Thromb Vasc Biol. 2020 Dec 24:ATVBAHA120315446.

End point type	Primary

End point timeframe:

Difference in the parameter between kinetic visit 1 and kinetic visit 2.

End point values	Kinetic visit 1	Kinetic visit 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	14		
Units: pools/d				
arithmetic mean (standard deviation)	37 (± 24)	46 (± 32)		

Attachments (see zip file)	Table 2. Taskinen MR et al. ATVB. 2020, ATVBAHA120315446..

Statistical analyses

Statistical analysis title	CM-apoB48 FCR
Comparison groups	Kinetic visit 1 v Kinetic visit 2
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other[9]
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Notes:

[9] - The trial was a single-phase, nonrandomized study of 12-week treatment with evolocumab 140 mg subcutaneously every 2 weeks in 14 patients with type II diabetes on background statin therapy. Cardiometabolic responses to a high-fat mixed meal were assessed before and at the end of the intervention period.

Primary: CM-TG FCR

End point title	CM-TG FCR

End point description:

More end point parameters found in published paper by Taskinen MR, Björnson E, Kahri J, Söderlund S, Matikainen N, Porthan K, Ainola M, Hakkarainen A, Lundbom N, Fermanelli V, Fuchs J, Thorsell A, Kronenberg F, Andersson L, Adiels M, Packard CJ, Borén J. Effects of Evolocumab on the Postprandial Kinetics of Apo (Apolipoprotein) B100- and B48-Containing Lipoproteins in Subjects With Type 2 Diabetes. Arterioscler Thromb Vasc Biol. 2020 Dec 24:ATVBAHA120315446.

End point type	Primary

End point timeframe:

Difference in the parameter between kinetic visit 1 and kinetic visit 2.

End point values	Kinetic visit 1	Kinetic visit 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	14		
Units: pools/d				
arithmetic mean (standard deviation)	41 (± 27)	54 (± 31)		

Attachments (see zip file)	Table 2. Taskinen MR et al. ATVB. 2020, ATVBAHA120315446..

Statistical analyses

Statistical analysis title	CM-TG FCR
Comparison groups	Kinetic visit 1 v Kinetic visit 2
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other[10]
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Notes:

[10] - The trial was a single-phase, nonrandomized study of 12-week treatment with evolocumab 140 mg subcutaneously every 2 weeks in 14 patients with type II diabetes on background statin therapy. Cardiometabolic responses to a high-fat mixed meal were assessed before and at the end of the intervention period.

Primary: TRL-C cardiometabolic study

End point title	TRL-C cardiometabolic study

End point description:

More end point parameters found in published paper by Taskinen MR, Björnson E, Andersson L, Kahri J, Porthan K, Matikainen N, Söderlund S, Pietiläinen K, Hakkarainen A, Lundbom N, Nilsson R, Ståhlman M, Adiels M, Parini P, Packard C, Borén J. Impact of proprotein convertase subtilisin/kexin type 9 inhibition with evolocumab on the postprandial responses of triglyceride-rich lipoproteins in type II diabetic subjects. J Clin Lipidol. 2020 Jan-Feb;14(1):77-87.

End point type	Primary

End point timeframe:

Difference in the parameter between kinetic visit 1 and kinetic visit 2.

End point values	Kinetic visit 1	Kinetic visit 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	14		
Units: mg/dL				
arithmetic mean (standard deviation)	33.4 (± 11)	17.8 (± 6.5)		

Attachments (see zip file)	Figure 1. Taskinen MR et al. J Clin Lipidol. 2020,14, 77-87..pdf
	Table 1. Taskinen MR et al. J Clin Lipidol. 2020,14, 77-87..pdf

Statistical analyses

Statistical analysis title	TRL-C
Comparison groups	Kinetic visit 1 v Kinetic visit 2
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other[11]
P-value	< 0.05
Method	t-test, 1-sided

Notes:

[11] - The trial was a single-phase, nonrandomized study of 12-week treatment with evolocumab 140 mg subcutaneously every 2 weeks in 14 patients with type II diabetes on background statin therapy. Cardiometabolic responses to a high-fat mixed meal were assessed before and at the end of the intervention period.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

21 November 2016-23 April 2018

Assessment type	Systematic

Dictionary used

Dictionary name	Duodecim
Dictionary version	2020

Reporting groups

Reporting group title	Treatment period evolocumab

Reporting group description: -

Serious adverse events	Treatment period evolocumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 14 (14.29%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Blood and lymphatic system disorders			
Increase in blood glucose			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Iron deficiency anemia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Non-cardiac chest pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Treatment period evolocumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 14 (100.00%)		
Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Hypertension			
subjects affected / exposed	3 / 14 (21.43%)		
occurrences (all)	3		
Tachycardia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Nervous system disorders			
Postural vertigo			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Tiredness			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	2		
Dizziness			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Tinnitus			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	2		
Eosinophilia			

subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Thrombocytosis			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Macrocytosis			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Microcytosis			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Gastrointestinal disorders			
Heartburn			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Gastroenteritis			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			
Respiratory infection / flu			
subjects affected / exposed	10 / 14 (71.43%)		
occurrences (all)	10		
Exacerbation of asthma			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Bronchitis			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Skin eruption			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	2		
Edema			

subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Renal and urinary disorders			
Pyuria			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Urinary tract infection			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	2		
Hematuria			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Infections and infestations			
Fungal nail disease			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Maxillary sinusitis			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Herpes simplex labialis			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Worsening of diabetes			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Hypokalemia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

 None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/33356392

http://www.ncbi.nlm.nih.gov/pubmed/31917184