



Clinical trial results:

Effects of the PCSK9 Antibody AliroCuMab on Coronary Atherosclerosis in Patients with Acute Myocardial Infarction. A Serial, Multivessel, Intravascular Ultrasound, Near-Infrared Spectroscopy And Optical Coherence Tomography Imaging Study

Summary

EudraCT number	2017-001502-15
Trial protocol	DK AT
Global end of trial date	13 October 2021

Results information

Result version number	v1 (current)
This version publication date	11 October 2022
First version publication date	11 October 2022
Summary attachment (see zip file)	PACMAN-JAMA (PACMAN-Main_Publication-JAMA.pdf) PACMAN-JAMA-SupplMaterial (PACMAN-AMI_SupplementMaterial.pdf) PACMAN-AHJ-Design (PACMAN-Design-Publication.pdf) PACMAN-Synopsis (PACMAN_AMI_Synopsis.pdf)

Trial information

Trial identification

Sponsor protocol code	PACMAN-AMI/ 2016-01382
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03067844
WHO universal trial number (UTN)	-
Other trial identifiers	Insel-Nr.: 3277

Notes:

Sponsors

Sponsor organisation name	EU Sponsor representative AKH Vienna, Medical University of Vienna
Sponsor organisation address	Währinger Gürtel, Vienna, Austria, 1090
Public contact	Prof. Dr. Irene Lang, AKH Vienna, Medical University of Vienna, 43 14040046140, irene.lang@meduniwien.ac.at
Scientific contact	Prof. Dr. Irene Lang, AKH Vienna, Medical University of Vienna, 43 14040046140, irene.lang@meduniwien.ac.at
Sponsor organisation name	Insel Gruppe AG
Sponsor organisation address	Freiburgstrasse , Bern, Switzerland, 3010
Public contact	Prof. Dr. med. Lorenz Räber, Insel Gruppe AG, kardio.studien@insel.ch
Scientific contact	Prof. Dr. med. Lorenz Räber, Insel Gruppe AG, kardio.studien@insel.ch

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	03 April 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 October 2021
Global end of trial reached?	Yes
Global end of trial date	13 October 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effect of the PCSK9 inhibitor alirocumab on the change in percent atheroma volume (PAV) at week 52 in patients with acute myocardial infarction undergoing percutaneous coronary intervention (PCI) in the infarct-related artery and receiving guideline-recommended high-intensity statin therapy.

Protection of trial subjects:

Regular followup, Data Safety Monitoring Board (trial with approved drug / placebo but outside indication)

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 May 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 16
Country: Number of subjects enrolled	Austria: 38
Country: Number of subjects enrolled	Denmark: 34
Country: Number of subjects enrolled	Switzerland: 212
Worldwide total number of subjects	300
EEA total number of subjects	88

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)	217
From 65 to 84 years	83
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment period: 01May2017 to 01Oct2020

CH, NL, DK, AU

For further details see main manuscript: Räber L et al., JAMA. 2022 May 10;327(18):1771-1781. doi: 10.1001/jama.2022.5218. PMID: 35368058; PMCID: PMC8978048.

Pre-assignment

Screening details:

See main manuscript

Period 1

Period 1 title	overall trial (overall period)
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:

Active treatment: prefilled pen; sterile alirocumab drug product supplied at a concentration of 150 mg/mL in histidine, pH 6.0, polysorbate 20, and sucrose.

Placebo: matched for content to verum except alirocumab

Patients and treating physicians should refrain from LDL-C measurements throughout the whole study time to maintain blinding.

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment Arm

Arm description:

alirocumab arm

Arm type	Experimental
Investigational medicinal product name	Alirocumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled injector
Routes of administration	Solution for injection

Dosage and administration details:

Biweekly subcutaneous alirocumab (150 mg) for 52 weeks

Arm title	Placebo Arm
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Arm description:

Placebo Arm

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled injector
Routes of administration	Injection

Dosage and administration details:

Biweekly injection for 52 weeks

Number of subjects in period 1	Treatment Arm	Placebo Arm
Started	148	152
Completed	131	135
Not completed	17	17
Adverse event, serious fatal	2	1
Consent withdrawn by subject	13	15
Physician decision	1	1
Lost to follow-up	1	-

Baseline characteristics

Reporting groups

Reporting group title	overall trial
Reporting group description: -	

Reporting group values	overall trial	Total	
Number of subjects	300	300	
Age categorical			
Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous			
Units: years			
arithmetic mean	58.5		
standard deviation	± 9.7	-	
Gender categorical			
Units: Subjects			
Female	56	56	
Male	244	244	

Subject analysis sets

Subject analysis set title	Experimental Intervention Group
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Patients with AMI (ST-elevation or non-ST-elevation myocardial infarction) were randomly assigned to the experimental group to receive biweekly subcutaneous alirocumab (150 mg) beginning <24 hours after the acute event as add-on therapy to rosuvastatin 20 mg.

Subject analysis set title	Control Group
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Patients with AMI (ST-elevation or non-ST-elevation myocardial infarction) were randomly assigned to the placebo group to receive biweekly subcutaneous placebo beginning <24 hours after the acute event as add-on therapy to rosuvastatin 20 mg.

Reporting group values	Experimental Intervention Group	Control Group	
Number of subjects	148	152	
Age categorical			
Units: Subjects			
In utero			

Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years arithmetic mean standard deviation	58.4 ± 10	58.6 ± 9.4	
Gender categorical Units: Subjects			
Female	24	32	
Male	124	119	

End points

End points reporting groups

Reporting group title	Treatment Arm
Reporting group description: alirocumab arm	
Reporting group title	Placebo Arm
Reporting group description: Placebo Arm	
Subject analysis set title	Experimental Intervention Group
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: Patients with AMI (ST-elevation or non-ST-elevation myocardial infarction) were randomly assigned to the experimental group to receive biweekly subcutaneous alirocumab (150 mg) beginning <24 hours after the acute event as add-on therapy to rosuvastatin 20 mg.	
Subject analysis set title	Control Group
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: Patients with AMI (ST-elevation or non-ST-elevation myocardial infarction) were randomly assigned to the placebo group to receive biweekly subcutaneous placebo beginning <24 hours after the acute event as add-on therapy to rosuvastatin 20 mg.	

Primary: Change in PAV via IVUS from baseline to week 52

End point title	Change in PAV via IVUS from baseline to week 52 ^[1]
End point description:	
End point type	Primary
End point timeframe: Baseline to week 52	
Notes: [1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: Stastical Analysys for primary endpoint is specified in attached publications (main publication wit suppl. material and design publication)	

End point values	Treatment Arm	Placebo Arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	130	135		
Units: %				
arithmetic mean (full range (min-max))	-2.13 (-2.53 to -1.73)	-0.92 (-1.28 to -0.56)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Events as defined per protocol needed to be reported from ICF signature until last follow-up visit

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	23
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Frequency threshold for reporting non-serious adverse events: 0.1 %

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: See attached publications for Adverse Events (main publication with suppl. material)

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 August 2019	Increase of patient number
21 January 2020	Improved wording (re-formulation) of one exclusion criteria
27 March 2020	COVID-19 Addendum: The changes are listed in this separate protocol addendum as these changes only apply to the patient and study management affected by the SARS-CoV-2 pandemic. If possible, patient management and study conduct according the approved study protocol, should be prioritized, if in line with current local laws and regulations. <ul style="list-style-type: none">- Prolongation 52-week visit window if required by local hospital guidelines and situation- Interruption (on hold) of enrolment for the time necessary according to local hospital and national guidelines in view of the pandemic development- Changes to Visit schedule if required by local hospital guidelines and situation

Notes:

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/35368058>