Clinical trial results:
A phase IIa, placebo-controlled, double blind, randomised multicentre pilot study to investigate the efficacy, safety and tolerability of the monoclonal antibody ATH3G10 in patients with ST-elevation myocardial infarction

Summary

EudraCT number	2018-003676-12
Trial protocol	SE DK NL
Global end of trial date	12 March 2021

Results information

Result version number	v1 (current)
This version publication date	03 November 2021
First version publication date	03 November 2021

Trial information

Trial identification

Sponsor protocol code	ATH3G10-006

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03991143
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Athera Biotechnologies AB
Sponsor organisation address	Olof Palmes gata 29, Stockholm, Sweden, 11122
Public contact	James Hall, CEO, Athera Biotechnologies AB, +46 8501 37000, j.hall@athera.se
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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	21 April 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 March 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main goal of this study was to evaluate the efficacy of a single administration of ATH3G10 in patients presenting with an acute ST-segment elevation myocardial infarction (STEMI) undergoing percutaneous coronary intervention (PCI).

Protection of trial subjects:

The study was performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki that are consistent with International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH)/Good Clinical Practice (GCP) and applicable regulatory requirements. Informed consent was obtained from all subjects prior to initiation of the study.

To avoid antibody aggregates in the solution, the investigational medicinal product (IMP) was passed through a 0.2 µm filter just before the connection to the intravenous catheter. If a patient experienced an adverse event assessed as related to the IMP during the slow injection, the dosing was to be immediately stopped. If the dosing was stopped due to technical reason (e.g. change of needle), a re-start of dosing was allowed within 30 minutes.

Patients previously exposed to ATH3G10 were excluded.

Any apparent side effect experienced by a patient was assessed from the time of the IMP dose and throughout the the study (until the 12-month follow-up visit, Visit 5) and were reported as adverse events (AEs).

Background therapy:

No background therapy was used in this study.

Evidence for comparator:

No comparator was used in this study.

Actual start date of recruitment	01 February 2019
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	1 Years
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	Sweden: 60
Country: Number of subjects enrolled	Denmark: 6
Worldwide total number of subjects	82
EEA total number of subjects	82

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)	38
From 65 to 84 years	44
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The first patient's first visit in the study (first patient screened) was on 2019-04-25 and the last patient's last visit was on 2021-03-12.

Pre-assignment

Screening details:

A total of 82 patients were screened. All 82 patients (43 patients in the ATH3G10 group and 39 patients in the placebo group) were randomised and treated, as planned.

Period 1

Period 1 title	Visit 1- prior to treatment
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Carer, Assessor, Subject

Blinding implementation details:

This was a double-blinded study, the treatment was blinded to the patient, the Investigators and the personnel administrating the IMP. The Investigator could only break the treatment code if the appropriate future management of the patient necessitated knowledge of current treatment.

Arms

Are arms mutually exclusive?	Yes
Arm title	ATH3G10

Arm description:

Patients were allocated to the ATH3G10 group.

Arm type	Experimental
Investigational medicinal product name	ATH3G10
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

The test product, ATH3G10, was a clear to slightly opalescent, colourless to faintly yellowish concentrated solution in 10 mL clear type 1 glass vials filled with 5 mL. The vials were sealed with bromobutyl rubber stoppers, covered with aluminium caps and stored at 2-8 °C.
Each patient received a single intravenous dose of the IMP within 120 minutes of the PCI procedure start, defined as the time when the guide wire was passed through the stenosis. To avoid antibody aggregates in the solution, the IMP was passed through a 0.2 µm filter just before the connection to the intravenous catheter. If a patient experienced an AE assessed as related to the IMP during the slow injection, the dosing was to be immediately stopped. If the dosing was stopped due to technical reason (e.g. change of needle), a re-start of dosing was allowed within 30 minutes.

Arm title	Placebo

Arm description:

Patients were allocated to the placebo group.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

The placebo was a sterile sodium chloride 0.9% solution for infusion in 10 mL clear type 1 glass vials

filled with 5 mL. The reference product was stored at 2-8 °C.
If a patient experienced an AE assessed as related to the IMP during the slow injection, the dosing was to be immediately stopped. If the dosing was stopped due to technical reason (e.g. change of needle), a re-start of dosing was allowed within 30 minutes.

Number of subjects in period 1	ATH3G10	Placebo
Started	43	39
Completed	43	39

Period 2

Period 2 title	Visit 1- treatment
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Assessor

Blinding implementation details:

This was a double-blinded study, the treatment was blinded to the patient, the Investigators and the personnel administrating the IMP. The Investigator could only break the treatment code if the appropriate future management of the patient necessitated knowledge of current treatment.

Arms

Are arms mutually exclusive?	Yes
Arm title	ATH3G10

Arm description:

Patients were allocated to receive a single dose of 250 mg of ATH3G10 at Visit 1.

Arm type	Experimental
Investigational medicinal product name	ATH3G10
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

The test product, ATH3G10, was a clear to slightly opalescent, colourless to faintly yellowish concentrated solution in 10 mL clear type 1 glass vials filled with 5 mL. The vials were sealed with bromobutyl rubber stoppers, covered with aluminium caps and stored at 2-8 °C.
Each patient received a single intravenous dose of the IMP within 120 minutes of the PCI procedure start, defined as the time when the guide wire was passed through the stenosis. To avoid antibody aggregates in the solution, the IMP was passed through a 0.2 µm filter just before the connection to the intravenous catheter. If a patient experienced an AE assessed as related to the IMP during the slow injection, the dosing was to be immediately stopped. If the dosing was stopped due to technical reason (e.g. change of needle), a re-start of dosing was allowed within 30 minutes.

Arm title	Placebo

Arm description:

Patients were allocated to receive a single dose of placebo at Visit 1.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

The placebo was a sterile sodium chloride 0.9% solution for infusion in 10 mL clear type 1 glass vials filled with 5 mL. The reference product was stored at 2-8 °C.
If a patient experienced an AE assessed as related to the IMP during the slow injection, the dosing was to be immediately stopped. If the dosing was stopped due to technical reason (e.g. change of needle), a re-start of dosing was allowed within 30 minutes.

Number of subjects in period 2	ATH3G10	Placebo
Started	43	39
Completed	41	37
Not completed	2	2
Consent withdrawn by subject	2	2

Period 3

Period 3 title	Visit 2- MRI examination
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Assessor

Blinding implementation details:

This was a double-blinded study, the treatment was blinded to the patient, the Investigators and the personnel administrating the IMP. The Investigator could only break the treatment code if the appropriate future management of the patient necessitated knowledge of current treatment.

Arms

Are arms mutually exclusive?	Yes
Arm title	ATH3G10

Arm description:

Patients were allocated to receive a single dose of 250 mg of ATH3G10 at Visit 1.

Arm type	Experimental
Investigational medicinal product name	ATH3G10
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

The test product, ATH3G10, was a clear to slightly opalescent, colourless to faintly yellowish

concentrated solution in 10 mL clear type 1 glass vials filled with 5 mL. The vials were sealed with bromobutyl rubber stoppers, covered with aluminium caps and stored at 2-8 °C.
Each patient received a single intravenous dose of the IMP within 120 minutes of the PCI procedure start, defined as the time when the guide wire was passed through the stenosis. To avoid antibody aggregates in the solution, the IMP was passed through a 0.2 µm filter just before the connection to the intravenous catheter. If a patient experienced an AE assessed as related to the IMP during the slow injection, the dosing was to be immediately stopped. If the dosing was stopped due to technical reason (e.g. change of needle), a re-start of dosing was allowed within 30 minutes.

Arm title	Placebo
Arm description: -	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

The placebo was a sterile sodium chloride 0.9% solution for infusion in 10 mL clear type 1 glass vials filled with 5 mL. The reference product was stored at 2-8 °C.
If a patient experienced an AE assessed as related to the IMP during the slow injection, the dosing was to be immediately stopped. If the dosing was stopped due to technical reason (e.g. change of needle), a re-start of dosing was allowed within 30 minutes.

Number of subjects in period 3	ATH3G10	Placebo
Started	41	37
Completed	41	37

Period 4

Period 4 title	Visit 3- 3-month follow-up and 2nd MRI
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Assessor

Blinding implementation details:

This was a double-blinded study, the treatment was blinded to the patient, the Investigators and the personnel administrating the IMP. The Investigator could only break the treatment code if the appropriate future management of the patient necessitated knowledge of current treatment.

Arms

Are arms mutually exclusive?	Yes

Arm title	ATH3G10

Arm description:

Patients were allocated to receive a single dose of 250 mg of ATH3G10 at Visit 1.

Arm type	Experimental
Investigational medicinal product name	ATH3G10
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

The test product, ATH3G10, was a clear to slightly opalescent, colourless to faintly yellowish concentrated solution in 10 mL clear type 1 glass vials filled with 5 mL. The vials were sealed with bromobutyl rubber stoppers, covered with aluminium caps and stored at 2-8 °C.
Each patient received a single intravenous dose of the IMP within 120 minutes of the PCI procedure start, defined as the time when the guide wire was passed through the stenosis. To avoid antibody aggregates in the solution, the IMP was passed through a 0.2 µm filter just before the connection to the intravenous catheter. If a patient experienced an AE assessed as related to the IMP during the slow injection, the dosing was to be immediately stopped. If the dosing was stopped due to technical reason (e.g. change of needle), a re-start of dosing was allowed within 30 minutes.

Arm title	Placebo

Arm description:

Patients were allocated to receive a single dose of placebo at Visit 1.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

The placebo was a sterile sodium chloride 0.9% solution for infusion in 10 mL clear type 1 glass vials filled with 5 mL. The reference product was stored at 2-8 °C.
If a patient experienced an AE assessed as related to the IMP during the slow injection, the dosing was to be immediately stopped. If the dosing was stopped due to technical reason (e.g. change of needle), a re-start of dosing was allowed within 30 minutes.

Number of subjects in period 4	ATH3G10	Placebo
Started	41	37
Completed	41	37

Period 5

Period 5 title	Visit 4- 6-month follow-up
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind

Roles blinded	Subject, Investigator, Monitor, Carer, Assessor

Blinding implementation details:

This was a double-blinded study, the treatment was blinded to the patient, the Investigators and the personnel administrating the IMP. The Investigator could only break the treatment code if the appropriate future management of the patient necessitated knowledge of current treatment.

Arms

Are arms mutually exclusive?	Yes
Arm title	ATH3G10

Arm description:

Patients were allocated to receive a single dose of 250 mg of ATH3G10 at Visit 1.

Arm type	Experimental
Investigational medicinal product name	ATH3G10
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

The test product, ATH3G10, was a clear to slightly opalescent, colourless to faintly yellowish concentrated solution in 10 mL clear type 1 glass vials filled with 5 mL. The vials were sealed with bromobutyl rubber stoppers, covered with aluminium caps and stored at 2-8 °C.
Each patient received a single intravenous dose of the IMP within 120 minutes of the PCI procedure start, defined as the time when the guide wire was passed through the stenosis. To avoid antibody aggregates in the solution, the IMP was passed through a 0.2 µm filter just before the connection to the intravenous catheter. If a patient experienced an AE assessed as related to the IMP during the slow injection, the dosing was to be immediately stopped. If the dosing was stopped due to technical reason (e.g. change of needle), a re-start of dosing was allowed within 30 minutes.

Arm title	Placebo

Arm description:

Patients were allocated to receive a single dose of placebo at Visit 1.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

The placebo was a sterile sodium chloride 0.9% solution for infusion in 10 mL clear type 1 glass vials filled with 5 mL. The reference product was stored at 2-8 °C.
If a patient experienced an AE assessed as related to the IMP during the slow injection, the dosing was to be immediately stopped. If the dosing was stopped due to technical reason (e.g. change of needle), a re-start of dosing was allowed within 30 minutes.

Number of subjects in period 5	ATH3G10	Placebo
Started	41	37
Completed	41	36
Not completed	0	1
not willing to continue the study	-	1

Period 6

Period 6 title	Visit 5- 12-month follow-up
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Assessor

Blinding implementation details:

This was a double-blinded study, the treatment was blinded to the patient, the Investigators and the personnel administrating the IMP. The Investigator could only break the treatment code if the appropriate future management of the patient necessitated knowledge of current treatment.

Arms

Are arms mutually exclusive?	Yes
Arm title	ATH3G10

Arm description:

Patients were allocated to receive a single dose of 250 mg of ATH3G10 at Visit 1.

Arm type	Experimental
Investigational medicinal product name	ATH3G10
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

The test product, ATH3G10, was a clear to slightly opalescent, colourless to faintly yellowish concentrated solution in 10 mL clear type 1 glass vials filled with 5 mL. The vials were sealed with bromobutyl rubber stoppers, covered with aluminium caps and stored at 2-8 °C.
Each patient received a single intravenous dose of the IMP within 120 minutes of the PCI procedure start, defined as the time when the guide wire was passed through the stenosis. To avoid antibody aggregates in the solution, the IMP was passed through a 0.2 µm filter just before the connection to the intravenous catheter. If a patient experienced an AE assessed as related to the IMP during the slow injection, the dosing was to be immediately stopped. If the dosing was stopped due to technical reason (e.g. change of needle), a re-start of dosing was allowed within 30 minutes.

Arm title	Placebo

Arm description:

Patients were allocated to receive a single dose of placebo at Visit 1.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

The placebo was a sterile sodium chloride 0.9% solution for infusion in 10 mL clear type 1 glass vials filled with 5 mL. The reference product was stored at 2-8 °C.
If a patient experienced an AE assessed as related to the IMP during the slow injection, the dosing was to be immediately stopped. If the dosing was stopped due to technical reason (e.g. change of needle), a re-start of dosing was allowed within 30 minutes.

Number of subjects in period 6	ATH3G10	Placebo
Started	41	36
Completed	41	36

Baseline characteristics

Reporting groups	
Reporting group title	ATH3G10
Reporting group description:	
Patients were allocated to the ATH3G10 group.	
Reporting group title	Placebo
Reporting group description:	
Patients were allocated to the placebo group.	

Reporting group values	ATH3G10	Placebo	Total
Number of subjects	43	39	82
Age categorical Units: Subjects			
Adults 40-85 years old	43	39	82
Age continuous Units: years			
arithmetic mean	64.6	64.8	
standard deviation	± 10.4	± 8.7	-
Gender categorical Units: Subjects			
Female	6	9	15
Male	37	30	67
Body weight Units: kg			
arithmetic mean	84.36	84.34	
standard deviation	± 12.23	± 11.72	-
Body mass index (BMI) Units: kg/x2			
arithmetic mean	27.34	27.19	
standard deviation	± 3.45	± 3.22	-

End points

End points reporting groups

Reporting group title	ATH3G10

Reporting group description:

Patients were allocated to the ATH3G10 group.

Reporting group title	Placebo

Reporting group description:

Patients were allocated to the placebo group.

Reporting group title	ATH3G10

Reporting group description:

Patients were allocated to receive a single dose of 250 mg of ATH3G10 at Visit 1.

Reporting group title	Placebo

Reporting group description:

Patients were allocated to receive a single dose of placebo at Visit 1.

Reporting group title	ATH3G10

Reporting group description:

Patients were allocated to receive a single dose of 250 mg of ATH3G10 at Visit 1.

Reporting group title	Placebo

Reporting group description: -

Reporting group title	ATH3G10

Reporting group description:

Patients were allocated to receive a single dose of 250 mg of ATH3G10 at Visit 1.

Reporting group title	Placebo

Reporting group description:

Patients were allocated to receive a single dose of placebo at Visit 1.

Reporting group title	ATH3G10

Reporting group description:

Patients were allocated to receive a single dose of 250 mg of ATH3G10 at Visit 1.

Reporting group title	Placebo

Reporting group description:

Patients were allocated to receive a single dose of placebo at Visit 1.

Reporting group title	ATH3G10

Reporting group description:

Patients were allocated to receive a single dose of 250 mg of ATH3G10 at Visit 1.

Reporting group title	Placebo

Reporting group description:

Patients were allocated to receive a single dose of placebo at Visit 1.

Subject analysis set title	ATH3G10- FAS
Subject analysis set type	Full analysis

Subject analysis set description:

The full analysis set (FAS) was defined as all randomised patients who received 1 dose of IMP and for whom at least 1 post-baseline efficacy assessment was made.
The FAS included 78 patients (41 patients in the ATH3G10 group and 37 patients in the placebo group).
There were 4 patients (2 in the ATH3G10 group and 2 in the placebo group) that were excluded from the FAS because they had no post-baseline efficacy data, due to early withdrawal.

Subject analysis set title	Placebo- FAS
Subject analysis set type	Full analysis

Subject analysis set description:

The full analysis set (FAS) was defined as all randomised patients who received 1 dose of IMP and for whom at least 1 post-baseline efficacy assessment was made.
The FAS included 78 patients (41 patients in the ATH3G10 group and 37 patients in the placebo group).

There were 4 patients (2 in the ATH3G10 group and 2 in the placebo group) that were excluded from the FAS because they had no post-baseline efficacy data, due to early withdrawal.

Primary: Left ventricular end-diastolic volume index (LV EDVi) Least squares (LS) mean

End point title	Left ventricular end-diastolic volume index (LV EDVi) Least squares (LS) mean

End point description:

The primary objective was to investigate effects on left ventricular remodelling as change in end diastolic volume measured by MRI.
The primary endpoint, change in LV EDVi from Visit 2 to Visit 3, was analysed using an analysis of covariance (ANCOVA) model to test for the difference between treatment with ATH3G10 and placebo. The model included the treatment group as fixed effect and LV EDVi at Visit 2 as covariate. The model included the change from Visit 2 to Visit 3 as dependent variable. The active treatment group was tested against the placebo group and the null hypothesis that the mean difference in change in LV EDVi is equal to zero was tested against the two-sided alternative hypothesis that the difference is not equal to zero.

End point type	Primary

End point timeframe:

The primary endpoint was the comparison of the change in LV EDVi between Visit 2 (Day 2 to 4 after IMP administration) and Visit 3 (Day 60 to 180 after IMP administration).

End point values	ATH3G10- FAS	Placebo- FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	41	37		
Units: mL/m2				
least squares mean (confidence interval 95%)				
Change in LV EDVi from Visit 2 to Visit 3	3.69 (-0.61 to 7.99)	7.17 (2.81 to 11.53)		

Statistical analyses

Statistical analysis title	Difference in LV EDVi change from V2 to V3

Statistical analysis description:

The primary endpoint was the comparison of the change in left ventricular end-diastolic volume index (LV EDVi) between Visit 2 (V2, i.e., Day 2 to 4 after IMP administration) and Visit 3 (V3, i.e., Day 60 to 180 after IMP administration).

Comparison groups	ATH3G10- FAS v Placebo- FAS
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.05 [1]
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-3.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.63
upper limit	2.67

Variability estimate	Standard deviation

Notes:

[1] - Difference in LS Means (95% CI): -3.48 (-9.63, 2.67)
p-value = 0.263

Primary: LV EDVi arithmetic mean

End point title	LV EDVi arithmetic mean[2]

End point description:

The primary objective was to investigate effects on left ventricular remodelling as change in end diastolic volume measured by MRI.
The primary endpoint, change in LV EDVi from Visit 2 to Visit 3, was analysed using an analysis of covariance (ANCOVA) model to test for the difference between treatment with ATH3G10 and placebo. The model included the treatment group as fixed effect and LV EDVi at Visit 2 as covariate. The model included the change from Visit 2 to Visit 3 as dependent variable. The active treatment group was tested against the placebo group and the null hypothesis that the mean difference in change in LV EDVi is equal to zero was tested against the two-sided alternative hypothesis that the difference is not equal to zero.

End point type	Primary

End point timeframe:

The primary endpoint was the comparison of the change in left ventricular end-diastolic volume index (LV EDVi) between Visit 2 (Day 2 to 4 after IMP administration) and Visit 3 (Day 60 to 180 after IMP administration).

Notes:

[2] - 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: The statistical analysis "Difference in LV EDVi change from V2 to V3" applies also to this primary endpoint.

End point values	ATH3G10- FAS	Placebo- FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	41	37		
Units: mL/m2				
arithmetic mean (standard deviation)				
LV EDVi at Visit 2	85.89 (± 14.37)	89.28 (± 11.85)		
LV EDVi at Visit 3	89.60 (± 17.95)	96.27 (± 18.67)		
Change in LV EDVi from Visit 2 to Visit 3	3.71 (± 10.97)	7.15 (± 14.43)		

Statistical analyses

No statistical analyses for this end point

Secondary: Myocardial Salvage index (MSi) at Visit 2- LS mean

End point title	Myocardial Salvage index (MSi) at Visit 2- LS mean

End point description:

The secondary objective was to investigate effects on MSi measured by MRI.
The secondary efficacy variable, MSi at Visit 2, was analysed using an analysis of variance (ANOVA) model to test for the difference between treatment with ATH3G10 and placebo. The model included the treatment group as fixed effect.
The active treatment group was tested against the placebo group and the null hypothesis that the mean difference in MSi is equal to zero was tested against the two-sided alternative hypothesis that the difference is not equal to zero.

End point type	Secondary

End point timeframe:

The secondary endpoint was the comparison of MSi at Visit 2 (Day 2 to 4 after IMP administration).

End point values	ATH3G10- FAS	Placebo- FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	41	37		
Units: percentage				
least squares mean (confidence interval 95%)				
MSi LS mean at Visit 2 (%)	39.77 (32.24 to 47.29)	39.90 (32.81 to 46.99)		

Statistical analyses

Statistical analysis title	Difference in MSi at Visit 2

Statistical analysis description:

The secondary endpoint was the comparison of MSi at Visit 2 (Day 2 to 4 after IMP administration).

Comparison groups	ATH3G10- FAS v Placebo- FAS
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.05 [3]
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.47
upper limit	10.21
Variability estimate	Standard deviation

Notes:

[3] - Difference in LS Means (95% CI) at Visit 2: -0.13 (-10.47, 10.21)
p-value = 0.980

Secondary: MSi at Visit 2- arithmetic mean

End point title	MSi at Visit 2- arithmetic mean

End point description:

The secondary objective was to investigate effects on MSi measured by MRI.
The secondary efficacy variable, MSi at Visit 2, was analysed using an analysis of variance (ANOVA) model to test for the difference between treatment with ATH3G10 and placebo. The model included the treatment group as fixed effect.

End point type	Secondary

End point timeframe:

The secondary endpoint was the comparison of MSi at Visit 2 (Day 2 to 4 after IMP administration).

End point values	ATH3G10- FAS	Placebo- FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	41	37		
Units: percentage				
arithmetic mean (standard deviation)				
MSi at Visit 2	39.77 (± 19.40)	39.90 (± 22.87)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were reproted from the time of IMP administration and until the end of the study (i.e., Visit 1- treatment to Visit 5- 12 month follow-up).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	ATH3G10

Reporting group description:

Patients were allocated to the ATH3G10 group.

Reporting group title	Placebo

Reporting group description:

Patients were allocated to the placebo group.

Serious adverse events	ATH3G10	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 43 (16.28%)	10 / 39 (25.64%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon adenoma			
subjects affected / exposed	1 / 43 (2.33%)	0 / 39 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Colectomy			
subjects affected / exposed	1 / 43 (2.33%)	0 / 39 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 43 (2.33%)	2 / 39 (5.13%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 43 (0.00%)	1 / 39 (2.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 43 (0.00%)	1 / 39 (2.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	1 / 43 (2.33%)	0 / 39 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Post procedural haemorrhage			
subjects affected / exposed	0 / 43 (0.00%)	1 / 39 (2.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	1 / 43 (2.33%)	1 / 39 (2.56%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular fibrillation			
subjects affected / exposed	2 / 43 (4.65%)	0 / 39 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac ventricular thrombosis			
subjects affected / exposed	1 / 43 (2.33%)	0 / 39 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			

subjects affected / exposed	1 / 43 (2.33%)	0 / 39 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 43 (2.33%)	1 / 39 (2.56%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	0 / 43 (0.00%)	1 / 39 (2.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine			
subjects affected / exposed	1 / 43 (2.33%)	0 / 39 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	1 / 43 (2.33%)	0 / 39 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 43 (2.33%)	0 / 39 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemolytic anaemia			
subjects affected / exposed	1 / 43 (2.33%)	0 / 39 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Melaena			
subjects affected / exposed	1 / 43 (2.33%)	0 / 39 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Rectal haemorrhage			
subjects affected / exposed	1 / 43 (2.33%)	0 / 39 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	0 / 43 (0.00%)	1 / 39 (2.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	0 / 43 (0.00%)	1 / 39 (2.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 43 (2.33%)	1 / 39 (2.56%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	1 / 43 (2.33%)	0 / 39 (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	ATH3G10	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 43 (62.79%)	22 / 39 (56.41%)	
Injury, poisoning and procedural complications			
Limb injury			
subjects affected / exposed	1 / 43 (2.33%)	2 / 39 (5.13%)	
occurrences (all)	1	2	
Vascular disorders			

Hypotension			
subjects affected / exposed	2 / 43 (4.65%)	2 / 39 (5.13%)	
occurrences (all)	2	2	
Hypertension			
subjects affected / exposed	1 / 43 (2.33%)	2 / 39 (5.13%)	
occurrences (all)	1	2	
Thrombosis			
subjects affected / exposed	0 / 43 (0.00%)	2 / 39 (5.13%)	
occurrences (all)	0	2	
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	6 / 43 (13.95%)	3 / 39 (7.69%)	
occurrences (all)	6	3	
Atrial fibrillation			
subjects affected / exposed	2 / 43 (4.65%)	3 / 39 (7.69%)	
occurrences (all)	2	3	
Ventricular tachycardia			
subjects affected / exposed	1 / 43 (2.33%)	3 / 39 (7.69%)	
occurrences (all)	1	3	
Cardiac ventricular thrombosis			
subjects affected / exposed	1 / 43 (2.33%)	2 / 39 (5.13%)	
occurrences (all)	1	2	
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 43 (9.30%)	3 / 39 (7.69%)	
occurrences (all)	4	3	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	4 / 43 (9.30%)	5 / 39 (12.82%)	
occurrences (all)	4	5	
Pyrexia			
subjects affected / exposed	4 / 43 (9.30%)	2 / 39 (5.13%)	
occurrences (all)	5	2	
Fatigue			
subjects affected / exposed	3 / 43 (6.98%)	1 / 39 (2.56%)	
occurrences (all)	3	1	

Oedema peripheral			
subjects affected / exposed	0 / 43 (0.00%)	2 / 39 (5.13%)	
occurrences (all)	0	2	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	4 / 43 (9.30%)	4 / 39 (10.26%)	
occurrences (all)	4	4	
Diarrhoea			
subjects affected / exposed	3 / 43 (6.98%)	3 / 39 (7.69%)	
occurrences (all)	3	3	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	4 / 43 (9.30%)	6 / 39 (15.38%)	
occurrences (all)	4	6	
Cough			
subjects affected / exposed	1 / 43 (2.33%)	2 / 39 (5.13%)	
occurrences (all)	1	2	
Epistaxis			
subjects affected / exposed	0 / 43 (0.00%)	2 / 39 (5.13%)	
occurrences (all)	0	3	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 43 (0.00%)	2 / 39 (5.13%)	
occurrences (all)	0	2	
Musculoskeletal stiffness			
subjects affected / exposed	0 / 43 (0.00%)	2 / 39 (5.13%)	
occurrences (all)	0	2	
Pain in extremity			
subjects affected / exposed	0 / 43 (0.00%)	2 / 39 (5.13%)	
occurrences (all)	0	2	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 43 (0.00%)	2 / 39 (5.13%)	
occurrences (all)	0	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 April 2019	The first clinical study protocol (CSP) version used for patient enrolment in Sweden was CSP Version 2.0, dated 2019-01-07. Substantial amendment 2.0 led to CSP Version 3.0, dated 2019-04-04. The CSP version used for patient enrolment in Denmark was CSP Version 4.0, while CSP Version 3.0 was used in The Netherlands. Substantial amendment 2.0 included: 1) clarification of the defiinition of the percutaneous coronary intervention (PCI) start. "PCI less than 4 hours after symptom onset" was replaced by "Start of PCI, defined as when the guide wire is passed through the stenosis, less than 4 hours after symptom onset" 2) clarification of the allowed time window of the IMP administration. "IMP will be administered as soon as possible after randomization and within 120 minutes of performed PCI procedure." was replaced by "IMP will be administered as soon as possible after randomization and within 120 minutes of start of the PCI procedure, defined as when the guide wire is passed through the stenosis." 3) Addition/update of assesements. "12-lead ECG" was replaced by "ECG monitoring at visit 1 and 2" and "Blood sampling for other biomarkers related to cardiovascular disease" was added for visit 1 (baseline sample)."
23 October 2019	Substantial amendment 3.0 led to CSP Version 4.0, dated 2019-10-23 (first CSP verison used for enrollment in Denmark) and included: 1) The use of Gadolinium-based contrast agents has been associated with severe reactions (Nephrogenic Systemic Fibrosis, NSF) in patients with severely reduced renal function. Clinical use is therefore contraindicated below an eGFR of 30 mL/min/1.73 m2 for all Gadolinium based contrast agents. Since no direct clinical benefit is gained by the study patients from the examination a conservative limit for the use of contrast agents, eGFR 50 mLl/min/1.73 m2, was initially selected. An increasing amount of clinical evidence suggests that the above mentioned risk for NSF is very low, if at all present for macrocyclic chelate complex contrast agents. (Young et al., Eur Radiol. 2019). As a consequence, the lower eGFR limit was changed from 50 to 30 mL/min/1.73 m2. As a further safety precaution in the eGFR interval 30 to 50mL/min/1.73m2 half the dose of contrast (macrocyclic chelate complex agents) was employed. 2) There is no literature available showing the time course of very early changes in cardiac dimensions following a ST elevation infarction, but it is likely that the mechanisms driving these changes are in place early after reperfusion. Therefore, it was desirable that the initial measurement of cardiac dimensions was carried out as soon as it was clinically and logistically acceptable for the patients to undergo an MRI investigation, as the result wouls be used as the baseline dimensions. For patients admitted shortly before weekends it was not be possible to perform MRI within 72 hours, but 96 hours were possible. The visit window for MRI baseline examination was therefore changed to within 96 hours. 3) Requirement that physical examination, blood pressure and ECG assessments must be performed "before the MRI examination" was removed to facilitate MRI booking. 4) Additional sites were added to increase recruitment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported