Clinical trial results:
A Multicenter, Randomized, Open-Label, Blinded Endpoint Evaluation, Active-Controlled, Dose-Ranging Study to Compare the Efficacy and Safety of i.v. MAA868 and s.c. Enoxaparin in Adult Patients Undergoing Elective Unilateral Total Knee Arthroplasty

Summary

EudraCT number	2019-003756-37
Trial protocol	LT BE LV BG
Global end of trial date	12 March 2021

Results information

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

Trial information

Trial identification

Sponsor protocol code	ANT-005

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	IND Number: : 129008

Notes:

Sponsors

Sponsor organisation name	Anthos Therapeutics
Sponsor organisation address	55 Cambridge Pkwy, Suite 103, Cambridge, United States, MA 02142
Public contact	Information Desk, Anthos Therapeutics, Inc., +1 617-430-6940, info@anthostherapeutics.com
Scientific contact	Information Desk, Anthos Therapeutics, Inc., +1 617-430-6940, info@anthostherapeutics.com

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	23 August 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 March 2021
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:

• To assess if at least one dose of MAA868 is non-inferior to enoxaparin 40 mg through Day 10 after randomization in terms of incidence of adjudicated total VTE in patients undergoing unilateral TKA.

Protection of trial subjects:

The protocol and amendments were reviewed and approved by the relevant Ethics Committees (ECs) or Institutional Review Boards (IRBs) for each study site.

The study was conducted in accordance with the Declaration of Helsinki and its most recent update, and the International Council for Harmonisation (ICH) E6 Good Clinical Practice (GCP) guideline. The study was also conducted in accordance with local legal and regulatory requirements of the country (or countries) involved, and with Standard Operating Procedures in place.

A Steering and Safety Committee (SSC) in collaboration with the sponsor (Anthos Therapeutics) was responsible for study design and oversight. The SSC was set up to review aggregated data for total VTE, total bleeding events, and other safety events unblinded to treatment assignment.

The Informed Consent Form (ICF) was approved by the Investigator's local IRB or EC before patients were enrolled and written informed consent for the study was obtained from all patients before protocol-specific procedures were carried out.

The Investigator (or designee) explained the nature of the study and its purpose, the procedures, expected duration, potential risks and benefits, potential alternative procedures, the action of the test product, and the extent of maintaining the confidentiality of the patient's records. Patients were informed that participation was voluntary and that they could withdraw from the study at any time. The informed consent process was documented by the use of a written ICF approved by the designated IRB or EC and was signed by the patient (or patient's legal representative, or legal guardian). The patient was given a copy of the signed ICF.

Background therapy: -

Evidence for comparator:

Enoxaparin sodium (40 mg s.c.) was used as comparator, in accordance with the local country requirements and regulations. Enoxaparin, a low-molecular-weight heparin, is commonly used for the prevention of VTE after TKA. Enoxaparin has a predictable pharmacokinetic (PK) profile and dose-response relationship, allowing simplified dosing without the need for monitoring.

Actual start date of recruitment	20 May 2020
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: 4
Country: Number of subjects enrolled	Latvia: 256

Country: Number of subjects enrolled	Lithuania: 92
Country: Number of subjects enrolled	Russian Federation: 1
Country: Number of subjects enrolled	Ukraine: 59
Worldwide total number of subjects	412
EEA total number of subjects	352

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)	156
From 65 to 84 years	256
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Male and female patients (≥18 and <80 years old) scheduled to undergo elective unilateral total knee arthroplasty with a body weight between 50 and 130 kg, inclusive.

Pre-assignment

Screening details:

Patients underwent screening assessments during the screening period (Day -30 to Day -1). The Investigator verified that they were eligible per criteria, patients who met the eligibility criteria were randomized to 1 of the 4 treatment groups.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

This study was open label with regard to MAA868 versus enoxaparin but blinded to the dose of MAA868. Blinded randomization schedule and procedures were used as outlined in the Statistical Analysis Plan (SAP).

Arms

Are arms mutually exclusive?	Yes
Arm title	MAA868 30 mg

Arm description:

MAA868 30 mg i.v.

Arm type	Experimental
Investigational medicinal product name	Abelacimab
Investigational medicinal product code	MAA868
Other name	MAA868
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

MAA868 as liquid in vial concentrate (150 mg/mL). Dose groups were administered as single i.v. administrations approximately 4 to 8 hours after surgical wound closure, but no less than 4 hours after the removal of an epidural catheter.

Arm title	MAA868 75 mg

Arm description:

MAA868 75 mg i.v.

Arm type	Experimental
Investigational medicinal product name	Abelacimab
Investigational medicinal product code	MAA868
Other name	MAA868
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

MAA868 as liquid in vial concentrate (150 mg/mL). Dose groups were administered as single i.v. administrations approximately 4 to 8 hours after surgical wound closure, but no less than 4 hours after the removal of an epidural catheter.

Arm title	MAA868 150 mg

Arm description:

MAA868 150 mg i.v.

Arm type	Experimental
Investigational medicinal product name	Abelacimab
Investigational medicinal product code	MAA868
Other name	MAA868
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

MAA868 as liquid in vial concentrate (150 mg/mL). Dose groups were administered as single i.v. administrations approximately 4 to 8 hours after surgical wound closure, but no less than 4 hours after the removal of an epidural catheter.

Arm title	Enoxaparin

Arm description:

Enoxaparin 40 mg s.c.

Arm type	Active comparator
Investigational medicinal product name	Enoxaparin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Enoxaparin 40 mg was administered subcutaneously starting approximately 12 hours after TKA surgery followed by daily s.c. injections of 40 mg enoxaparin up to the visit Day 10 venography. A single initial 40 mg s.c. enoxaparin dose prior to TKA surgery may have been given at the discretion of the Investigator per local guidelines.

Number of subjects in period 1	MAA868 30 mg	MAA868 75 mg	MAA868 150 mg
Started	104	105	100
Completed	103	102	99
Not completed	1	3	1
Consent withdrawn by subject	-	1	1
Physician decision	-	1	-
Adverse event, non-fatal	1	1	-

Number of subjects in period 1	Enoxaparin
Started	103
Completed	103
Not completed	0
Consent withdrawn by subject	-
Physician decision	-
Adverse event, non-fatal	-

Baseline characteristics

Reporting groups	
Reporting group title	MAA868 30 mg
Reporting group description: MAA868 30 mg i.v.	
Reporting group title	MAA868 75 mg
Reporting group description: MAA868 75 mg i.v.	
Reporting group title	MAA868 150 mg
Reporting group description: MAA868 150 mg i.v.	
Reporting group title	Enoxaparin
Reporting group description: Enoxaparin 40 mg s.c.	

Reporting group values	MAA868 30 mg	MAA868 75 mg	MAA868 150 mg
Number of subjects	104	105	100
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	40	43	32
From 65-84 years	64	62	68
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	66.5	66.5	67.7
standard deviation	± 7.41	± 7.96	± 6.69
Gender categorical Units: Subjects			
Female	90	85	78
Male	14	20	22
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	104	105	100
Unknown	0	0	0
Race Units: Subjects			
White	104	105	100
Black or African American	0	0	0
Asian	0	0	0

Native Hawaiian or Other Pacific Islander	0	0	0
American Indian or Alaska Native	0	0	0
Other	0	0	0
Height			
Units: cm			
arithmetic mean	164.35	164.90	165.17
standard deviation	± 7.913	± 9.053	± 8.284
Weight			
Units: kg			
arithmetic mean	91.810	89.686	89.995
standard deviation	± 17.4128	± 15.2486	± 14.7515
Body Mass Index			
Units: kg/m2			
arithmetic mean	33.952	33.062	33.039
standard deviation	± 5.8979	± 5.5630	± 5.2556

Reporting group values	Enoxaparin	Total	
Number of subjects	103	412	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	41	156	
From 65-84 years	62	256	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	65.9		
standard deviation	± 8.07	-	
Gender categorical			
Units: Subjects			
Female	82	335	
Male	21	77	
Ethnicity			
Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	103	412	
Unknown	0	0	
Race			
Units: Subjects			
White	103	412	
Black or African American	0	0	
Asian	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
American Indian or Alaska Native	0	0	

Other	0	0	

Height			
Units: cm			
arithmetic mean	164.67		
standard deviation	± 8.095	-	
Weight			
Units: kg			
arithmetic mean	93.956		
standard deviation	± 15.2836	-	
Body Mass Index			
Units: kg/m2			
arithmetic mean	34.651		
standard deviation	± 5.1765	-	

Subject analysis sets

Subject analysis set title	MAA868 30 mg Safety
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety Set included randomized patients who received at least one dose of study drug. Patients were analyzed based on the actual treatment taken.

Subject analysis set title	MAA868 75 mg Safety
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety Set included randomized patients who received at least one dose of study drug. Patients were analyzed based on the actual treatment taken.

Subject analysis set title	MAA868 150 mg Safety
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety Set included randomized patients who received at least one dose of study drug. Patients were analyzed based on the actual treatment taken.

Subject analysis set title	Enoxaparin 40 mg Safety
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety Set included randomized patients who received at least one dose of study drug. Patients were analyzed based on the actual treatment taken.

Subject analysis set title	MAA868 30 mg mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The Modified Intent-to-Treat (mITT) Population included all patients who were randomized and received at least 1 dose of the assigned study drug and were evaluable for the primary efficacy outcome (ie, the patient had either an evaluable venogram or had an objectively confirmed symptomatic VTE event, a VTE-related death, or a death for which PE could not be excluded). For all efficacy analyses, the main analysis was based on the mITT Population.

Subject analysis set title	MAA868 75 mg mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The Modified Intent-to-Treat (mITT) Population included all patients who were randomized and received at least 1 dose of the assigned study drug and were evaluable for the primary efficacy outcome (ie, the patient had either an evaluable venogram or had an objectively confirmed symptomatic VTE event, a VTE-related death, or a death for which PE could not be excluded). For all efficacy analyses, the main analysis was based on the mITT Population.

Subject analysis set title	MAA868 150 mg mITT

Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The Modified Intent-to-Treat (mITT) Population included all patients who were randomized and received at least 1 dose of the assigned study drug and were evaluable for the primary efficacy outcome (ie, the patient had either an evaluable venogram or had an objectively confirmed symptomatic VTE event, a VTE-related death, or a death for which PE could not be excluded). For all efficacy analyses, the main analysis was based on the mITT Population.

Subject analysis set title	Enoxaparin 40 mg mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The Modified Intent-to-Treat (mITT) Population included all patients who were randomized and received at least 1 dose of the assigned study drug and were evaluable for the primary efficacy outcome (ie, the patient had either an evaluable venogram or had an objectively confirmed symptomatic VTE event, a VTE-related death, or a death for which PE could not be excluded). For all efficacy analyses, the main analysis was based on the mITT Population.

Reporting group values	MAA868 30 mg Safety	MAA868 75 mg Safety	MAA868 150 mg Safety
Number of subjects	102	104	99
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	39	42	33
From 65-84 years	63	62	66
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	66.4	66.7	67.6
standard deviation	± 7.36	± 7.71	± 6.71
Gender categorical Units: Subjects			
Female	89	85	77
Male	13	19	22
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	102	104	99
Unknown	0	0	0
Race Units: Subjects			
White	102	104	99
Black or African American	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
American Indian or Alaska Native	0	0	0
Other	0	0	0

Height			
Units: cm			
arithmetic mean	164.20	164.76	165.12
standard deviation	± 7.897	± 8.973	± 8.312
Weight			
Units: kg			
arithmetic mean	91.628	89.644	90.376
standard deviation	± 17.4793	± 15.3165	± 14.8977
Body Mass Index			
Units: kg/m2			
arithmetic mean	33.950	33.101	33.184
standard deviation	± 5.9508	± 5.5755	± 5.2197

Reporting group values	Enoxaparin 40 mg Safety	MAA868 30 mg mITT	MAA868 75 mg mITT
Number of subjects	104	102	99
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	41	39	41
From 65-84 years	63	63	58
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	65.9	66.5	66.4
standard deviation	± 8.03	± 7.33	± 7.71
Gender categorical			
Units: Subjects			
Female	83	89	80
Male	21	13	19
Ethnicity			
Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	104	102	99
Unknown	0	0	0
Race			
Units: Subjects			
White	104	102	99
Black or African American	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
American Indian or Alaska Native	0	0	0
Other	0	0	0

Height			
Units: cm			
arithmetic mean	164.72	164.21	164.80
standard deviation	± 8.073	± 7.911	± 9.023
Weight			
Units: kg			
arithmetic mean	93.777	91.588	89.825
standard deviation	± 15.3188	± 17.4295	± 15.5015
Body Mass Index			
Units: kg/m2			
arithmetic mean	34.569	33.933	33.145
standard deviation	± 5.2198	± 5.9427	± 5.5983

Reporting group values	MAA868 150 mg mITT	Enoxaparin 40 mg mITT	
Number of subjects	98	101	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	32	40	
From 65-84 years	66	61	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	67.6	66.1	
standard deviation	± 6.71	± 7.91	
Gender categorical			
Units: Subjects			
Female	77	81	
Male	21	20	
Ethnicity			
Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	98	101	
Unknown	0	0	
Race			
Units: Subjects			
White	98	101	
Black or African American	0	0	
Asian	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
American Indian or Alaska Native	0	0	
Other	0	0	

Height			
Units: cm			
arithmetic mean	165.06	164.53	
standard deviation	± 8.296	± 8.115	
Weight			
Units: kg			
arithmetic mean	89.993	94.162	
standard deviation	± 14.8998	± 15.3368	
Body Mass Index			
Units: kg/m2			
arithmetic mean	33.078	34.774	
standard deviation	± 5.2878	± 5.1384	

End points

End points reporting groups

Reporting group title	MAA868 30 mg
Reporting group description: MAA868 30 mg i.v.	
Reporting group title	MAA868 75 mg
Reporting group description: MAA868 75 mg i.v.	
Reporting group title	MAA868 150 mg
Reporting group description: MAA868 150 mg i.v.	
Reporting group title	Enoxaparin
Reporting group description: Enoxaparin 40 mg s.c.	
Subject analysis set title	MAA868 30 mg Safety
Subject analysis set type	Safety analysis
Subject analysis set description: The Safety Set included randomized patients who received at least one dose of study drug. Patients were analyzed based on the actual treatment taken.	
Subject analysis set title	MAA868 75 mg Safety
Subject analysis set type	Safety analysis
Subject analysis set description: The Safety Set included randomized patients who received at least one dose of study drug. Patients were analyzed based on the actual treatment taken.	
Subject analysis set title	MAA868 150 mg Safety
Subject analysis set type	Safety analysis
Subject analysis set description: The Safety Set included randomized patients who received at least one dose of study drug. Patients were analyzed based on the actual treatment taken.	
Subject analysis set title	Enoxaparin 40 mg Safety
Subject analysis set type	Safety analysis
Subject analysis set description: The Safety Set included randomized patients who received at least one dose of study drug. Patients were analyzed based on the actual treatment taken.	
Subject analysis set title	MAA868 30 mg mITT
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: The Modified Intent-to-Treat (mITT) Population included all patients who were randomized and received at least 1 dose of the assigned study drug and were evaluable for the primary efficacy outcome (ie, the patient had either an evaluable venogram or had an objectively confirmed symptomatic VTE event, a VTE-related death, or a death for which PE could not be excluded). For all efficacy analyses, the main analysis was based on the mITT Population.	
Subject analysis set title	MAA868 75 mg mITT
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: The Modified Intent-to-Treat (mITT) Population included all patients who were randomized and received at least 1 dose of the assigned study drug and were evaluable for the primary efficacy outcome (ie, the patient had either an evaluable venogram or had an objectively confirmed symptomatic VTE event, a VTE-related death, or a death for which PE could not be excluded). For all efficacy analyses, the main analysis was based on the mITT Population.	
Subject analysis set title	MAA868 150 mg mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The Modified Intent-to-Treat (mITT) Population included all patients who were randomized and received at least 1 dose of the assigned study drug and were evaluable for the primary efficacy outcome (ie, the patient had either an evaluable venogram or had an objectively confirmed symptomatic VTE event, a VTE-related death, or a death for which PE could not be excluded). For all efficacy analyses, the main analysis was based on the mITT Population.

Subject analysis set title	Enoxaparin 40 mg mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The Modified Intent-to-Treat (mITT) Population included all patients who were randomized and received at least 1 dose of the assigned study drug and were evaluable for the primary efficacy outcome (ie, the patient had either an evaluable venogram or had an objectively confirmed symptomatic VTE event, a VTE-related death, or a death for which PE could not be excluded). For all efficacy analyses, the main analysis was based on the mITT Population.

Primary: Primary Endpoint

End point title	Primary Endpoint

End point description:

The primary efficacy endpoints included occurrence of confirmed composite endpoint of asymptomatic DVT on the protocol required venography, confirmed symptomatic VTE (including confirmed symptomatic DVT of the leg, fatal or non-fatal PE), or unexplained death for which PE could not be ruled out during treatment through Day 10.

End point type	Primary

End point timeframe:

During the treatment period (Days 0 through 10)

End point values	MAA868 30 mg mITT	MAA868 75 mg mITT	MAA868 150 mg mITT	Enoxaparin 40 mg mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	102	99	98	101
Units: number	13	5	4	22

Statistical analyses

Statistical analysis title	% Difference vs Enoxaparin(95% CI)- MAA868 30 mg

Statistical analysis description:

% Difference vs Enoxaparin (95% CI)

Comparison groups	Enoxaparin 40 mg mITT v MAA868 30 mg mITT
Number of subjects included in analysis	203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0843
Method	Cochran-Mantel-Haenszel
Parameter estimate	between treatment differences
Point estimate	-9.16

Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.41
upper limit	1.09

Statistical analysis title	% Difference vs Enoxaparin(95% CI) - MAA868 75 mg
Comparison groups	MAA868 75 mg mITT v Enoxaparin 40 mg mITT
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0006
Method	Cochran-Mantel-Haenszel
Parameter estimate	between-treatment differences
Point estimate	-16.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	-25.95
upper limit	-7.63

Statistical analysis title	% Difference vs Enoxaparin(95% CI)- MAA868 150 mg
Comparison groups	MAA868 150 mg mITT v Enoxaparin 40 mg mITT
Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0002
Method	Cochran-Mantel-Haenszel
Parameter estimate	between-treatment differences
Point estimate	-17.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	-26.72
upper limit	-8.81

Statistical analysis title	% Difference doses combined vs Enoxaparin (95% CI)
Statistical analysis description:	
% Difference (MAA868 150mg and 75mg doses combined) vs Enoxaparin (95% CI)	
Comparison groups	MAA868 75 mg mITT v MAA868 150 mg mITT v Enoxaparin 40 mg mITT

Number of subjects included in analysis	298
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	between-treatment differences
Point estimate	-17.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-25.83
upper limit	-8.69

Secondary: Secondary efficacy endpoint through Day 30 and 110.

End point title	Secondary efficacy endpoint through Day 30 and 110.

End point description:

Secondary efficacy endpoint is the proportion of patients with confirmed composite endpoint of adjudicated asymptomatic DVT, symptomatic DVT, fatal or non-fatal PE, or unexplained death for which PE could not be ruled out during treatment through Days 30 and 110.

End point type	Secondary

End point timeframe:

through Days 30 and 110

End point values	MAA868 30 mg mITT	MAA868 75 mg mITT	MAA868 150 mg mITT	Enoxaparin 40 mg mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	102	99	98	101
Units: number	13	5	4	22

Statistical analyses

Statistical analysis title	% Difference vs Enoxaparin (95% CI)- MAA868 30 mg
Comparison groups	MAA868 30 mg mITT v Enoxaparin 40 mg mITT
Number of subjects included in analysis	203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0843
Method	Cochran-Mantel-Haenszel
Parameter estimate	between-treatment differences
Point estimate	-9.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.41
upper limit	1.09

Statistical analysis title	% Difference vs Enoxaparin (95% CI)- MAA868 75 mg
Comparison groups	MAA868 75 mg mITT v Enoxaparin 40 mg mITT
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0006
Method	Cochran-Mantel-Haenszel
Parameter estimate	between-treatment differences
Point estimate	-16.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	-25.95
upper limit	-7.63

Statistical analysis title	% Difference vs Enoxaparin(95% CI)- MAA868 150 mg
Comparison groups	MAA868 150 mg mITT v Enoxaparin 40 mg mITT
Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0002
Method	Cochran-Mantel-Haenszel
Parameter estimate	between-treatment differences
Point estimate	-17.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	-26.72
upper limit	-8.81

Statistical analysis title	% Difference doses combined vs Enoxaparin (95% CI)
Statistical analysis description: % Difference (MAA868 150mg and 75mg doses combined) vs Enoxaparin (95% CI)	
Comparison groups	Enoxaparin 40 mg mITT v MAA868 150 mg mITT v MAA868 75 mg mITT
Number of subjects included in analysis	298
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	between-treatment differences
Point estimate	-17.26

Confidence interval	
level	95 %
sides	2-sided
lower limit	-25.83
upper limit	-8.69

Secondary: Secondary: composite endpoint of major bleeding and CRNM bleeding

End point title	Secondary: composite endpoint of major bleeding and CRNM bleeding

End point description:

Occurrence of confirmed composite endpoint of major bleeding and CRNM bleeding events through Days 10 and 30

End point type	Secondary

End point timeframe:

Through Days 10 and 30

End point values	MAA868 30 mg Safety	MAA868 75 mg Safety	MAA868 150 mg Safety	Enoxaparin 40 mg Safety
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	102	104	99	104
Units: number	2	2	0	0

Statistical analyses

Statistical analysis title	% Difference vs Enoxaparin - MAA868 30 mg

Statistical analysis description:

% Difference vs Enoxaparin (95% CI) - MAA868 30 mg i.v.

Comparison groups	MAA868 30 mg Safety v Enoxaparin 40 mg Safety
Number of subjects included in analysis	206
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1602
Method	Cochran-Mantel-Haenszel
Parameter estimate	% Difference
Point estimate	1.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.74
upper limit	4.6

Statistical analysis title	% Difference vs Enoxaparin - MAA868 75 mg
Statistical analysis description: % Difference vs Enoxaparin - MAA868 75 mg iv	
Comparison groups	MAA868 75 mg Safety v Enoxaparin 40 mg Safety
Number of subjects included in analysis	208
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1617
Method	Cochran-Mantel-Haenszel
Parameter estimate	% Difference
Point estimate	1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.72
upper limit	4.53

Other pre-specified: Exploratory efficacy endpoint : proportion of patients with symptomatic venous thromboembolism through the Day 110/EoS visit

End point title	Exploratory efficacy endpoint : proportion of patients with symptomatic venous thromboembolism through the Day 110/EoS visit
End point description: The exploratory efficacy endpoint is the proportion of patients with symptomatic venous thromboembolism (symptomatic deep vein thrombosis and symptomatic pulmonary embolism) through the Day 110/EoS visit	
End point type	Other pre-specified
End point timeframe: Through the Day 110/EoS visit	

End point values	MAA868 30 mg mITT	MAA868 75 mg mITT	MAA868 150 mg mITT	Enoxaparin 40 mg mITT
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	102	99	98	101
Units: percentages	0	0	0	1

Statistical analyses

Statistical analysis title	% Difference vs Enoxaparin (95% CI) - MAA868 30 mg
Comparison groups	MAA868 30 mg mITT v Enoxaparin 40 mg mITT

Number of subjects included in analysis	203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3211
Method	Cochran-Mantel-Haenszel
Parameter estimate	proportion of patients
Point estimate	-0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.9
upper limit	0.94

Statistical analysis title	% Difference vs Enoxaparin (95% CI) - MAA868 75 mg
Comparison groups	MAA868 75 mg mITT v Enoxaparin 40 mg mITT
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.325
Method	Cochran-Mantel-Haenszel
Parameter estimate	proportion of patients
Point estimate	-0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.91
upper limit	0.94

Statistical analysis title	% Difference vs Enoxaparin (95% CI)- MAA868 150 mg
Comparison groups	MAA868 150 mg mITT v Enoxaparin 40 mg mITT
Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3289
Method	Cochran-Mantel-Haenszel
Parameter estimate	proportion of patients
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.91
upper limit	0.94

Statistical analysis title	% Difference doses combined vs Enoxaparin

Statistical analysis description:	
% Difference (MAA868 150mg and 75mg doses combined) vs Enoxaparin (95% CI)	
Comparison groups	MAA868 150 mg mITT v MAA868 75 mg mITT
Number of subjects included in analysis	197
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1657
Method	Cochran-Mantel-Haenszel
Parameter estimate	proportion of patients
Point estimate	-0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.91
upper limit	0.94

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Duration of study	
Adverse event reporting additional description:	
A TEAE was defined as an adverse event that started during or after the start of the infusion or started prior to the start of the infusion and increased in severity after the start of the infusion.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups	
Reporting group title	MAA868 30 mg Safety
Reporting group description:	
MAA868 30 mg i.v.	
Reporting group title	MAA868 75 mg Safety
Reporting group description:	
MAA868 75 mg i.v.	
Reporting group title	MAA868 150 mg Safety
Reporting group description:	
MAA868 150 mg i.v.	
Reporting group title	Enoxaparin 40 mg Safety
Reporting group description:	
Enoxaparin 40 mg s.c.	

Serious adverse events	MAA868 30 mg Safety	MAA868 75 mg Safety	MAA868 150 mg Safety
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 102 (0.98%)	3 / 104 (2.88%)	1 / 99 (1.01%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Gastrointestinal disorders			
Ileus			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Ovarian cyst torsion			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Infections and infestations			
Medical device site joint infection			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	1 / 99 (1.01%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Corona virus infection			
subjects affected / exposed	1 / 102 (0.98%)	0 / 104 (0.00%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	1 / 102 (0.98%)	0 / 104 (0.00%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Enoxaparin 40 mg Safety		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 104 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Gastrointestinal disorders			
Ileus			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Ovarian cyst torsion			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Medical device site joint infection			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Corona virus infection			

subjects affected / exposed	0 / 104 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Wound infection			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	MAA868 30 mg Safety	MAA868 75 mg Safety	MAA868 150 mg Safety
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 102 (14.71%)	16 / 104 (15.38%)	15 / 99 (15.15%)
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 102 (0.00%)	2 / 104 (1.92%)	2 / 99 (2.02%)
occurrences (all)	0	2	2
Deep vein thrombosis			
subjects affected / exposed	0 / 102 (0.00%)	0 / 104 (0.00%)	0 / 99 (0.00%)
occurrences (all)	0	0	0
Peripheral venous disease			
subjects affected / exposed	0 / 102 (0.00%)	0 / 104 (0.00%)	1 / 99 (1.01%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Oedema			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	1 / 99 (1.01%)
occurrences (all)	0	1	1
Asthenia			
subjects affected / exposed	0 / 102 (0.00%)	0 / 104 (0.00%)	0 / 99 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	0 / 99 (0.00%)
occurrences (all)	0	1	0
Pyrexia			

subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	0 / 99 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Ovarian cyst torsion			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	0 / 99 (0.00%)
occurrences (all)	0	1	0
Investigations			
Liver function test abnormal			
subjects affected / exposed	0 / 102 (0.00%)	0 / 104 (0.00%)	2 / 99 (2.02%)
occurrences (all)	0	0	2
Haemoglobin decreased			
subjects affected / exposed	0 / 102 (0.00%)	0 / 104 (0.00%)	1 / 99 (1.01%)
occurrences (all)	0	0	1
Alanine aminotransferase increased			
subjects affected / exposed	0 / 102 (0.00%)	0 / 104 (0.00%)	1 / 99 (1.01%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 102 (0.98%)	0 / 104 (0.00%)	0 / 99 (0.00%)
occurrences (all)	1	0	0
Post procedural oedema			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	0 / 99 (0.00%)
occurrences (all)	0	1	0
Ligament injury			
subjects affected / exposed	1 / 102 (0.98%)	0 / 104 (0.00%)	0 / 99 (0.00%)
occurrences (all)	1	0	0
Post procedural inflammation			
subjects affected / exposed	0 / 102 (0.00%)	0 / 104 (0.00%)	0 / 99 (0.00%)
occurrences (all)	0	0	0
Post procedural swelling			
subjects affected / exposed	1 / 102 (0.98%)	0 / 104 (0.00%)	0 / 99 (0.00%)
occurrences (all)	1	0	0
Procedural haemorrhage			
subjects affected / exposed	1 / 102 (0.98%)	0 / 104 (0.00%)	0 / 99 (0.00%)
occurrences (all)	1	0	0
Seroma			

subjects affected / exposed	1 / 102 (0.98%)	0 / 104 (0.00%)	0 / 99 (0.00%)
occurrences (all)	1	0	0
Spinal compression fracture			
subjects affected / exposed	0 / 102 (0.00%)	0 / 104 (0.00%)	0 / 99 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 102 (0.98%)	1 / 104 (0.96%)	1 / 99 (1.01%)
occurrences (all)	1	1	1
Cardiac failure chronic			
subjects affected / exposed	0 / 102 (0.00%)	0 / 104 (0.00%)	1 / 99 (1.01%)
occurrences (all)	0	0	1
Sinus node dysfunction			
subjects affected / exposed	0 / 102 (0.00%)	0 / 104 (0.00%)	1 / 99 (1.01%)
occurrences (all)	0	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 102 (1.96%)	0 / 104 (0.00%)	0 / 99 (0.00%)
occurrences (all)	2	0	0
Blood and lymphatic system disorders			
Spontaneous haematoma			
subjects affected / exposed	0 / 102 (0.00%)	0 / 104 (0.00%)	0 / 99 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 102 (0.00%)	0 / 104 (0.00%)	1 / 99 (1.01%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 102 (0.98%)	1 / 104 (0.96%)	0 / 99 (0.00%)
occurrences (all)	1	1	0
Diarrhoea			
subjects affected / exposed	1 / 102 (0.98%)	0 / 104 (0.00%)	0 / 99 (0.00%)
occurrences (all)	1	0	0
Gastric ulcer			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	0 / 99 (0.00%)
occurrences (all)	0	1	0

Ileus			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	0 / 99 (0.00%)
occurrences (all)	0	1	0
Hepatobiliary disorders			
Cholecystitis chronic			
subjects affected / exposed	1 / 102 (0.98%)	0 / 104 (0.00%)	0 / 99 (0.00%)
occurrences (all)	1	0	0
Hepatitis toxic			
subjects affected / exposed	1 / 102 (0.98%)	0 / 104 (0.00%)	0 / 99 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 102 (0.98%)	0 / 104 (0.00%)	0 / 99 (0.00%)
occurrences (all)	1	0	0
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	0 / 99 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Ligament disorder			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	0 / 99 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Corona virus infection			
subjects affected / exposed	2 / 102 (1.96%)	1 / 104 (0.96%)	1 / 99 (1.01%)
occurrences (all)	2	1	1
Laryngitis			
subjects affected / exposed	1 / 102 (0.98%)	0 / 104 (0.00%)	1 / 99 (1.01%)
occurrences (all)	1	0	1
Medical device site joint infection			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	1 / 99 (1.01%)
occurrences (all)	0	1	1
Bronchitis			
subjects affected / exposed	1 / 102 (0.98%)	0 / 104 (0.00%)	0 / 99 (0.00%)
occurrences (all)	1	0	0
Pneumonia			

subjects affected / exposed	1 / 102 (0.98%)	0 / 104 (0.00%)	0 / 99 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	0 / 102 (0.00%)	0 / 104 (0.00%)	0 / 99 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	0 / 99 (0.00%)
occurrences (all)	0	1	0
Wound infection			
subjects affected / exposed	1 / 102 (0.98%)	0 / 104 (0.00%)	0 / 99 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Glucose tolerance impaired			
subjects affected / exposed	1 / 102 (0.98%)	1 / 104 (0.96%)	2 / 99 (2.02%)
occurrences (all)	1	1	2
Decreased appetite			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	1 / 99 (1.01%)
occurrences (all)	0	1	1
Cell death			
subjects affected / exposed	0 / 102 (0.00%)	0 / 104 (0.00%)	1 / 99 (1.01%)
occurrences (all)	0	0	1
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 102 (0.00%)	0 / 104 (0.00%)	1 / 99 (1.01%)
occurrences (all)	0	0	1
Platelet count decreased			
subjects affected / exposed	1 / 102 (0.98%)	0 / 104 (0.00%)	0 / 99 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Enoxaparin 40 mg Safety		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 104 (12.50%)		
Vascular disorders			
Haematoma			
subjects affected / exposed	2 / 104 (1.92%)		
occurrences (all)	2		
Deep vein thrombosis			

subjects affected / exposed occurrences (all) Peripheral venous disease subjects affected / exposed occurrences (all)	1 / 104 (0.96%) 1 0 / 104 (0.00%) 0		
General disorders and administration site conditions Oedema subjects affected / exposed occurrences (all) Asthenia subjects affected / exposed occurrences (all) Chest pain subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all)	 1 / 104 (0.96%) 1 1 / 104 (0.96%) 1 0 / 104 (0.00%) 0 0 / 104 (0.00%) 0		
Reproductive system and breast disorders Ovarian cyst torsion subjects affected / exposed occurrences (all)	 0 / 104 (0.00%) 0		
Investigations Liver function test abnormal subjects affected / exposed occurrences (all) Haemoglobin decreased subjects affected / exposed occurrences (all) Alanine aminotransferase increased subjects affected / exposed occurrences (all)	 2 / 104 (1.92%) 2 1 / 104 (0.96%) 1 0 / 104 (0.00%) 0		
Injury, poisoning and procedural complications Contusion			

subjects affected / exposed	2 / 104 (1.92%)		
occurrences (all)	2		
Post procedural oedema			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences (all)	1		
Ligament injury			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences (all)	0		
Post procedural inflammation			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences (all)	1		
Post procedural swelling			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences (all)	0		
Procedural haemorrhage			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences (all)	0		
Seroma			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences (all)	0		
Spinal compression fracture			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences (all)	1		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences (all)	0		
Cardiac failure chronic			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences (all)	0		
Sinus node dysfunction			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			

subjects affected / exposed occurrences (all)	0 / 104 (0.00%) 0		
Blood and lymphatic system disorders Spontaneous haematoma subjects affected / exposed occurrences (all)	 1 / 104 (0.96%) 1		
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	 0 / 104 (0.00%) 0		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Gastric ulcer subjects affected / exposed occurrences (all) Ileus subjects affected / exposed occurrences (all)	 0 / 104 (0.00%) 0 0 / 104 (0.00%) 0 0 / 104 (0.00%) 0 0 / 104 (0.00%) 0		
Hepatobiliary disorders Cholecystitis chronic subjects affected / exposed occurrences (all) Hepatitis toxic subjects affected / exposed occurrences (all)	 0 / 104 (0.00%) 0 0 / 104 (0.00%) 0		
Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all)	 0 / 104 (0.00%) 0		
Endocrine disorders Hyperthyroidism			

subjects affected / exposed	0 / 104 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Ligament disorder			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Corona virus infection			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences (all)	0		
Laryngitis			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences (all)	0		
Medical device site joint infection			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences (all)	0		
Bronchitis			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences (all)	0		
Pneumonia			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences (all)	1		
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences (all)	0		
Wound infection			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Glucose tolerance impaired			
subjects affected / exposed	2 / 104 (1.92%)		
occurrences (all)	2		
Decreased appetite			

subjects affected / exposed	0 / 104 (0.00%)		
occurrences (all)	0		
Cell death			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences (all)	0		
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences (all)	0		
Platelet count decreased			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 July 2020	Amendment Rationale This protocol was amended to minimize the impact of COVID-19 on the study and to incorporate changes requested by Health Authorities. These changes are intended to reduce the burden on patients participating in the study and to provide clarification and guidance to sites in response to restrictions that may be put in place due to COVID-19. In addition, the Sponsor is using this opportunity to incorporate changes to the protocol requested by the Latvian Health Authority.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported