



Clinical trial results:

A Phase 2, Randomized, Active Comparator-Controlled, Open-Label, Adaptive Design Study to Assess the Safety and Efficacy of Intravenously-Administered SelK2 in Patients Undergoing Total Knee Arthroplasty

Summary

EudraCT number	2018-003122-88
Trial protocol	LV BG LT PL
Global end of trial date	14 November 2019

Results information

Result version number	v1 (current)
This version publication date	30 November 2020
First version publication date	30 November 2020

Trial information

Trial identification

Sponsor protocol code	SELK2-00005
-----------------------	-------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03812328
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Tetherex Pharmaceuticals Corporation
Sponsor organisation address	840 Research Parkway, Suite 516, Oklahoma City, United States, OK 73104
Public contact	Executive Director, Tetherex Pharmaceuticals Corporation, jstocker@tetherex.com
Scientific contact	Executive Director, Tetherex Pharmaceuticals Corporation, jstocker@tetherex.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	14 November 2019
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	14 November 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To investigate the efficacy of SelK2 as monotherapy for the prevention of total venous thromboembolism (VTE) in patients undergoing primary unilateral total knee arthroplasty (TKA).
- To assess the incidence of bleeding events in patients administered SelK2 and undergoing primary unilateral TKA.
- To assess the overall safety and tolerability of SelK2 in this patient population.

The study protocol was designed with an adaptive group (SelK2 plus enoxaparin) that could be initiated if the Steering and Safety Committee determined that preliminary data suggested the potential for an additive effect in VTE reduction and that the combination did not pose an additional safety risk. The objectives of the adaptive group were to assess the efficacy and safety of SelK2 when given together with standard of care enoxaparin for the prevention of VTE in patients undergoing primary unilateral TKA.

Protection of trial subjects:

The study was conducted in accordance with the protocol, the ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences International Ethical Guidelines, applicable International Council for Harmonisation Good Clinical Practice Guidelines, and applicable laws and regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 February 2019
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	Bulgaria: 8
Country: Number of subjects enrolled	Latvia: 72
Country: Number of subjects enrolled	Lithuania: 44
Country: Number of subjects enrolled	Poland: 22
Country: Number of subjects enrolled	Ukraine: 61
Worldwide total number of subjects	207
EEA total number of subjects	146

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)	78
From 65 to 84 years	129
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This Phase 2, multicenter, randomized, active comparator-controlled, open-label, adaptive design study assessed efficacy and safety of intravenous (IV) administration of SelK2 in patients undergoing TKA.

Pre-assignment

Screening details:

The study consisted of up to a 30-day Screening Phase, an 11-day ($\pm$ 2 days) Treatment Phase and a 45-day Follow-up Phase. Patients were initially randomized 1:1 to SelK2 alone or enoxaparin. When the adaptive group was activated, the SelK2 alone group was discontinued. Patients were then randomized 2:1 to SelK2 plus enoxaparin or enoxaparin only.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	SelK2

Arm description:

On Day 1, patients received a single dose of SelK2 at 7.5 milligrams/kilogram (mg/kg), IV, administered 12 to 24 hours prior to TKA. On Day 2, TKA surgery was performed. Venography of the operated leg was performed on Day 11 ($\pm$ 2 days).

Arm type	Experimental
Investigational medicinal product name	SelK2
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

SelK2 was administered as an IV infusion over 30 minutes.

Arm title	SelK2 plus Enoxaparin (adaptive group)
------------------	--

Arm description:

On Day 1, patients received a single dose of SelK2 at 7.5 mg/kg, IV, administered 12 to 24 hours prior to TKA. On Day 2, TKA surgery was performed and patients received enoxaparin at 40 mg, subcutaneous (SC), administered 12 hours post-TKA. Patients then continued to receive enoxaparin at 40 mg, SC, once daily (QD) on Days 3 to 11. Venography of the operated leg was performed on Day 11 ($\pm$ 2 days).

Arm type	Experimental
Investigational medicinal product name	SelK2
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

SelK2 was administered as an IV infusion over 30 minutes.

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: Commercially available enoxaparin (40 mg in 0.4 milliliter [mL] water in pre-filled disposable syringes for SC administration) was provided to the study site pharmacies for use in this study, in accordance with local regulatory requirements.	
Arm title	Enoxaparin
Arm description: On Day 1, patients received an optional dose of enoxaparin at 40 mg, SC, administered at least 12 hours pre-TKA. On Day 2, TKA surgery was performed and patients received enoxaparin at 40 mg, SC, administered 12 hours post-TKA. Patients then continued to receive enoxaparin at 40 mg, SC, QD on Days 3 to 11. Venography of the operated leg was performed on Day 11 ($\pm$ 2 days).	
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:

Commercially available enoxaparin (40 mg in 0.4 mL water in pre-filled disposable syringes for SC administration) was provided to the study site pharmacies for use in this study, in accordance with local regulatory requirements.

Number of subjects in period 1	SelK2	SelK2 plus Enoxaparin (adaptive group)	Enoxaparin
Started	55	63	89
Completed	55	60	88
Not completed	0	3	1
Consent withdrawn by subject	-	3	-
Did not receive treatment because surgery delayed	-	-	1

Baseline characteristics

Reporting groups

Reporting group title	SelK2
-----------------------	-------

Reporting group description:

On Day 1, patients received a single dose of SelK2 at 7.5 milligrams/kilogram (mg/kg), IV, administered 12 to 24 hours prior to TKA. On Day 2, TKA surgery was performed. Venography of the operated leg was performed on Day 11 ($\pm$ 2 days).

Reporting group title	SelK2 plus Enoxaparin (adaptive group)
-----------------------	--

Reporting group description:

On Day 1, patients received a single dose of SelK2 at 7.5 mg/kg, IV, administered 12 to 24 hours prior to TKA. On Day 2, TKA surgery was performed and patients received enoxaparin at 40 mg, subcutaneous (SC), administered 12 hours post-TKA. Patients then continued to receive enoxaparin at 40 mg, SC, once daily (QD) on Days 3 to 11. Venography of the operated leg was performed on Day 11 ($\pm$ 2 days).

Reporting group title	Enoxaparin
-----------------------	------------

Reporting group description:

On Day 1, patients received an optional dose of enoxaparin at 40 mg, SC, administered at least 12 hours pre-TKA. On Day 2, TKA surgery was performed and patients received enoxaparin at 40 mg, SC, administered 12 hours post-TKA. Patients then continued to receive enoxaparin at 40 mg, SC, QD on Days 3 to 11. Venography of the operated leg was performed on Day 11 ($\pm$ 2 days).

Reporting group values	SelK2	SelK2 plus Enoxaparin (adaptive group)	Enoxaparin
Number of subjects	55	63	89
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	66.3	66.3	65.6
standard deviation	$\pm$ 6.35	$\pm$ 7.54	$\pm$ 7.30
Gender categorical Units: Subjects			
Female	42	52	68
Male	13	11	21

Reporting group values	Total		
Number of subjects	207		

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			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	162		
Male	45		

End points

End points reporting groups

Reporting group title	SelK2
Reporting group description: On Day 1, patients received a single dose of SelK2 at 7.5 milligrams/kilogram (mg/kg), IV, administered 12 to 24 hours prior to TKA. On Day 2, TKA surgery was performed. Venography of the operated leg was performed on Day 11 ($\pm$ 2 days).	
Reporting group title	SelK2 plus Enoxaparin (adaptive group)
Reporting group description: On Day 1, patients received a single dose of SelK2 at 7.5 mg/kg, IV, administered 12 to 24 hours prior to TKA. On Day 2, TKA surgery was performed and patients received enoxaparin at 40 mg, subcutaneous (SC), administered 12 hours post-TKA. Patients then continued to receive enoxaparin at 40 mg, SC, once daily (QD) on Days 3 to 11. Venography of the operated leg was performed on Day 11 ($\pm$ 2 days).	
Reporting group title	Enoxaparin
Reporting group description: On Day 1, patients received an optional dose of enoxaparin at 40 mg, SC, administered at least 12 hours pre-TKA. On Day 2, TKA surgery was performed and patients received enoxaparin at 40 mg, SC, administered 12 hours post-TKA. Patients then continued to receive enoxaparin at 40 mg, SC, QD on Days 3 to 11. Venography of the operated leg was performed on Day 11 ($\pm$ 2 days).	

Primary: Incidence of Total VTE Through Venography Day (Day 11)

End point title	Incidence of Total VTE Through Venography Day (Day 11)
End point description: The primary efficacy endpoint was incidence of total VTE (reported as a percentage of patients) during the Treatment Phase up to venography day (Day 11 $\pm$ 2 days). Incidence of total VTE consisted of a composite of: • Asymptomatic deep vein thrombosis (DVT) detected by mandatory unilateral venography of the operated leg; • Confirmed symptomatic DVT of the leg(s); • Confirmed symptomatic pulmonary embolism (PE); or • Unexplained death for which PE could not be ruled out. VTE incidence = presence of any 1 of the 4 composite components. All efficacy endpoint data was adjudicated by the blinded Central Independent Adjudication Committee (CIAC). Analysis was performed on the modified intent-to-treat (mITT) population consisting of all randomized patients who also had a successful venogram or symptomatic VTE event, which allowed for assessment of the primary efficacy outcome.	
End point type	Primary
End point timeframe: Day 1 up to Day 11 (venography day)	

End point values	SelK2	SelK2 plus Enoxaparin (adaptive group)	Enoxaparin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	61	84	
Units: percentage of patients				
number (not applicable)	39.6	47.5	20.2	

Statistical analyses

Statistical analysis title	Comparison of SelK2 vs Enoxaparin
Statistical analysis description:	
Analysis was performed using the Farrington-Manning test with the non-inferiority margin of 15%. The 1-sided upper 90% confidence interval (CI) of the difference between SelK2 alone and enoxaparin alone was calculated and non-inferiority concluded if the upper limit of the 90% CI was $\leq 15\%$.	
Comparison groups	SelK2 v Enoxaparin
Number of subjects included in analysis	132
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.7
Method	Farrington-Manning test
Parameter estimate	Treatment Difference (%)
Point estimate	19.3
Confidence interval	
level	90 %
sides	1-sided
upper limit	32.2

Statistical analysis title	Comparison of SelK2 plus Enoxaparin vs Enoxaparin
Statistical analysis description:	
Analysis was performed using the Farrington-Manning test with the non-inferiority margin of 15%. The 1-sided upper 90% CI of the difference between SelK2 plus enoxaparin (adaptive group) and enoxaparin alone was calculated and non-inferiority concluded if the upper limit of the 90% CI was $\leq 15\%$.	
Comparison groups	SelK2 plus Enoxaparin (adaptive group) v Enoxaparin
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.942
Method	Farrington-Manning test
Parameter estimate	Treatment Difference (%)
Point estimate	27.3
Confidence interval	
level	90 %
sides	1-sided
upper limit	40

Secondary: Incidence of Total VTE Through Day 57

End point title	Incidence of Total VTE Through Day 57
-----------------	---------------------------------------

End point description:

The incidence of total VTE (reported as a percentage of patients) was assessed during the 11-day (± 2 days) Treatment Phase and 45-day Follow-up Phase up to Day 57. Incidence of total VTE consisted of a composite of:

- Asymptomatic DVT detected by mandatory unilateral venography of the operated leg;
- Confirmed symptomatic DVT of the leg(s);
- Confirmed symptomatic PE; or
- Unexplained death for which PE could not be ruled out.

VTE incidence = presence of any 1 of the 4 composite components. All efficacy endpoint data was adjudicated by the blinded CIAC. Analysis was performed on the mITT population consisting of all randomized patients who also had a successful venogram or symptomatic VTE event, which allowed for assessment of the primary efficacy outcome.

End point type	Secondary
End point timeframe:	
Day 1 up to Day 57	

End point values	SelK2	SelK2 plus Enoxaparin (adaptive group)	Enoxaparin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	61	84	
Units: percentage of patients				
number (not applicable)	39.6	47.5	20.2	

Statistical analyses

No statistical analyses for this end point

Secondary: Incidences of Asymptomatic DVT, Symptomatic DVT, Symptomatic PE, and Unexplained Deaths Through Venography Day (Day 11)

End point title	Incidences of Asymptomatic DVT, Symptomatic DVT, Symptomatic PE, and Unexplained Deaths Through Venography Day (Day 11)
-----------------	---

End point description:

The incidences of asymptomatic DVT, symptomatic DVT, symptomatic PE, and unexplained deaths (ie, individual composite components of the primary efficacy endpoint and reported as percentages of patients) were assessed during the Treatment Phase up to venography day (Day 11 ± 2 days). All efficacy endpoint data was adjudicated by the blinded CIAC. Analysis was performed on the mITT population consisting of all randomized patients who also had a successful venogram or symptomatic VTE event, which allowed for assessment of the primary efficacy outcome.

End point type	Secondary
End point timeframe:	
Day 1 up to Day 11 (venography day)	

End point values	SelK2	SelK2 plus Enoxaparin (adaptive group)	Enoxaparin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	61	84	
Units: percentage of patients				
number (not applicable)				
Asymptomatic DVT	35.4	45.9	20.2	
Symptomatic DVT	2.1	0.0	0.0	
Symptomatic PE	2.1	1.6	0.0	
Unexplained Death	0.0	0.0	0.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Incidences of Asymptomatic DVT, Symptomatic DVT, Symptomatic PE, and Unexplained Deaths Through Day 57

End point title	Incidences of Asymptomatic DVT, Symptomatic DVT, Symptomatic PE, and Unexplained Deaths Through Day 57
-----------------	--

End point description:

The incidences of asymptomatic DVT, symptomatic DVT, symptomatic PE, and unexplained deaths (ie, individual composite components of the primary efficacy endpoint and reported as percentages of patients) were assessed during the 11-day ($\pm$ 2 days) Treatment Phase and 45-day Follow-up Phase up to Day 57. All efficacy endpoint data was adjudicated by the blinded CIAC. Analysis was performed on the mITT population consisting of all randomized patients who also had a successful venogram or symptomatic VTE event, which allowed for assessment of the primary efficacy outcome.

End point type	Secondary
----------------	-----------

End point timeframe:

Day 1 up to Day 57

End point values	SelK2	SelK2 plus Enoxaparin (adaptive group)	Enoxaparin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	61	84	
Units: percentage of patients				
number (not applicable)				
Asymptomatic DVT	35.4	45.9	20.2	
Symptomatic DVT	2.1	0.0	0.0	
Symptomatic PE	2.1	1.6	0.0	
Unexplained Death	0.0	0.0	0.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Patients with Treatment-emergent Bleeding Events

End point title	Number of Patients with Treatment-emergent Bleeding Events
End point description: All suspected bleeding events were reviewed by the CIAC in a blinded fashion and were adjudicated for categorization as Major Bleeding (MB), Clinically Relevant Non-Major Bleeding (CRNMB), Minor Bleeding, or combination of MB and CRNMB. The number of patients in each of the indicated categories is reported. Analysis was performed on the safety population consisting of all patients who received at least 1 dose of study drug, analyzed by actual treatment received.	
End point type	Secondary
End point timeframe: Day 1 up to Day 57	

End point values	SelK2	SelK2 plus Enoxaparin (adaptive group)	Enoxaparin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	55	63	88	
Units: number of patients				
Any Bleeding Event	3	1	0	
MB Event	0	0	0	
CRNMB Event	2	1	0	
Minor Bleeding Event	2	0	0	
Combination of MB and CRNMB Events	2	1	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 up to Day 57.

Adverse event reporting additional description:

Treatment-emergent adverse events were defined as adverse events that started or worsened in severity on or after the randomization day (Day 1) through completion of the final Follow-up Phase visit (Day 57). The safety population consisted of all patients who received at least 1 dose of study drug, analyzed by actual treatment received.

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	21.1
--------------------	------

Reporting groups

Reporting group title	SelK2
-----------------------	-------

Reporting group description:

On Day 1, patients received a single dose of SelK2 at 7.5 mg/kg, IV, administered 12 to 24 hours prior to TKA. On Day 2, TKA surgery was performed. Venography of the operated leg was performed on Day 11 ($\pm$ 2 days).

Reporting group title	SelK2 plus Enoxaparin (adaptive group)
-----------------------	--

Reporting group description:

On Day 1, patients received a single dose of SelK2 at 7.5 mg/kg, IV, administered 12 to 24 hours prior to TKA. On Day 2, TKA surgery was performed and patients received enoxaparin at 40 mg, SC, administered 12 hours post-TKA. Patients then continued to receive enoxaparin at 40 mg, SC, QD on Days 3 to 11. Venography of the operated leg was performed on Day 11 ($\pm$ 2 days).

Reporting group title	Enoxaparin
-----------------------	------------

Reporting group description:

On Day 1, patients received an optional dose of enoxaparin at 40 mg, SC, administered at least 12 hours pre-TKA. On Day 2, TKA surgery was performed and patients received enoxaparin at 40 mg, SC, administered 12 hours post-TKA. Patients then continued to receive enoxaparin at 40 mg, SC, QD on Days 3 to 11. Venography of the operated leg was performed on Day 11 ($\pm$ 2 days).

Serious adverse events	SelK2	SelK2 plus Enoxaparin (adaptive group)	Enoxaparin
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 55 (3.64%)	3 / 63 (4.76%)	2 / 88 (2.27%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	0 / 55 (0.00%)	1 / 63 (1.59%)	0 / 88 (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
Cardiac disorders			
Myocardial ischaemia			

subjects affected / exposed	0 / 55 (0.00%)	0 / 63 (0.00%)	1 / 88 (1.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Transient ischaemic attack			
subjects affected / exposed	1 / 55 (1.82%)	0 / 63 (0.00%)	0 / 88 (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
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 55 (0.00%)	0 / 63 (0.00%)	1 / 88 (1.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	1 / 55 (1.82%)	1 / 63 (1.59%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Post procedural infection			
subjects affected / exposed	0 / 55 (0.00%)	1 / 63 (1.59%)	0 / 88 (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

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	SelK2	SelK2 plus Enoxaparin (adaptive group)	Enoxaparin
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 55 (16.36%)	6 / 63 (9.52%)	10 / 88 (11.36%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 55 (0.00%)	1 / 63 (1.59%)	2 / 88 (2.27%)
occurrences (all)	0	1	2
Aspartate aminotransferase increased			

subjects affected / exposed	0 / 55 (0.00%)	2 / 63 (3.17%)	1 / 88 (1.14%)
occurrences (all)	0	2	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	3 / 55 (5.45%)	4 / 63 (6.35%)	6 / 88 (6.82%)
occurrences (all)	3	4	6
Injury, poisoning and procedural complications			
Procedural haemorrhage			
subjects affected / exposed	3 / 55 (5.45%)	0 / 63 (0.00%)	1 / 88 (1.14%)
occurrences (all)	3	0	1
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	2 / 55 (3.64%)	0 / 63 (0.00%)	2 / 88 (2.27%)
occurrences (all)	2	0	2
Hypertension			
subjects affected / exposed	2 / 55 (3.64%)	0 / 63 (0.00%)	1 / 88 (1.14%)
occurrences (all)	2	0	1
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	2 / 55 (3.64%)	1 / 63 (1.59%)	0 / 88 (0.00%)
occurrences (all)	2	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 May 2019	• Updated adaptive design to initiate a prespecified adaptive group of the study and added text to reflect the discontinuation of the SelK2 alone group of the study. • Added clarification on specifics of dosing of SelK2 plus enoxaparin group (newly added adaptive group). • Modified the randomization procedures to accommodate the activation of the adaptive group and the discontinuation of the SelK2 alone group. • Added text to allow sites flexibility in the method of measuring body temperature and added text to clarify that the serum pregnancy test was only required for women of childbearing potential. • Added text to clarify that in the adaptive group, SelK2 should be administered the night prior to surgery and that enoxaparin should be administered approximately 12 hours after surgery, while the option to dose enoxaparin 12 hours prior to surgery was eliminated. • Added text to clarify that the planned primary and secondary analyses included the adaptive group.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported