



Clinical trial results:

A Randomized, Open-Label, Study Drug-Dose Blind, Multicenter Study to Evaluate the Efficacy and Safety of JNJ-70033093 (BMS-986177), an Oral Factor Xla Inhibitor, Versus Subcutaneous Enoxaparin in Subjects Undergoing Elective Total Knee Replacement Surgery

Summary

EudraCT number	2018-004237-32
Trial protocol	BE HU PL PT BG ES GR LT IT
Global end of trial date	06 April 2021

Results information

Result version number	v1 (current)
This version publication date	22 April 2022
First version publication date	22 April 2022

Trial information

Trial identification

Sponsor protocol code	70033093THR2001
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03891524
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Research & Development, LLC
Sponsor organisation address	920 Route 202, South Raritan, United States, 08869
Public contact	Clinical Registry Group, Janssen Research & Development, LLC, clinicaltrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen Research & Development, LLC, clinicaltrialsEU@its.jnj.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	06 April 2021
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	06 April 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to determine the efficacy of JNJ-70033093 in preventing total venous thromboembolism (VTE) events (proximal and/or distal deep vein thrombosis (DVT) [asymptomatic confirmed by venography assessment or objectively confirmed symptomatic], nonfatal pulmonary embolism (PE), or any death) during the treatment period.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices and applicable regulatory requirements. The safety evaluations included adverse events, including non-serious adverse events, serious adverse events, adverse events of interest (that is, bleeding events, liver enzyme elevations and clinical liver events, and wound or joint complications), clinical laboratory tests (that is, hematology, clinical chemistry, urinalysis), and physical examinations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 June 2019
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	Argentina: 47
Country: Number of subjects enrolled	Belgium: 49
Country: Number of subjects enrolled	Bulgaria: 77
Country: Number of subjects enrolled	Brazil: 8
Country: Number of subjects enrolled	Canada: 5
Country: Number of subjects enrolled	Spain: 87
Country: Number of subjects enrolled	Greece: 81
Country: Number of subjects enrolled	Hungary: 107
Country: Number of subjects enrolled	Israel: 59
Country: Number of subjects enrolled	Italy: 10
Country: Number of subjects enrolled	Japan: 134
Country: Number of subjects enrolled	Poland: 217
Country: Number of subjects enrolled	Portugal: 79
Country: Number of subjects enrolled	Russian Federation: 20
Country: Number of subjects enrolled	Turkey: 23
Country: Number of subjects enrolled	Ukraine: 84
Country: Number of subjects enrolled	United States: 155

Worldwide total number of subjects	1242
EEA total number of subjects	707

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)	409
From 65 to 84 years	817
85 years and over	16

Subject disposition

Recruitment

Recruitment details:

No text entered

Pre-assignment

Screening details:

A total of 1,242 subjects were randomized and included in the ITT population.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	JNJ-70033093 25 mg Once Daily + Placebo

Arm description:

Subjects received JNJ-70033093 25 mg (1*25 milligrams [mg] capsule) once daily and 1 placebo capsule in the morning and 2 placebo capsules in the evening, orally for 10 to 14 postoperative days.

Arm type	Experimental
Investigational medicinal product name	JNJ-70033093 25 mg
Investigational medicinal product code	
Other name	BMS-986177
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received JNJ-70033093 25 mg (1*25 mg capsule) once daily.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	BMS-986177
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received 1 placebo capsule orally in the morning and 2 placebo capsules in the evening.

Arm title	JNJ-70033093 50 mg once daily + Placebo
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Arm description:

Subjects received JNJ-70033093 50 mg (2*25 mg capsules in the morning) once daily and 2 placebo capsules in the evening, orally for 10 to 14 postoperative days.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	BMS-986177
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received 2 matching placebo capsules orally.

Investigational medicinal product name	JNJ-70033093 50 mg
Investigational medicinal product code	
Other name	BMS-986177
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
Subjects received JNJ-70033093 50 mg (2*25 mg capsules orally in the morning) once daily.	
Arm title	JNJ-70033093 25 mg + Placebo Twice daily (BID)
Arm description:	
Subjects received JNJ-70033093 25 mg (1*25 mg capsule) and 1 placebo capsule twice daily (BID), orally for 10 to 14 postoperative days.	
Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	BMS-986177
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
Subjects received 1 matching placebo capsule orally, twice daily.	
Investigational medicinal product name	JNJ-70033093 25 mg
Investigational medicinal product code	
Other name	BMS-986177
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
Subjects received JNJ-70033093 25 mg (1*25 mg capsule) orally twice daily.	
Arm title	JNJ-70033093 50 mg BID
Arm description:	
Subjects received JNJ-70033093 50 mg (2*25 mg capsules) BID orally for 10 to 14 postoperative days.	
Arm type	Experimental
Investigational medicinal product name	JNJ-70033093 50 mg
Investigational medicinal product code	
Other name	BMS-986177
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
Subjects received JNJ-70033093 50 mg (2*25 mg capsules) BID orally.	
Arm title	JNJ-70033093 200 mg Once Daily + Placebo
Arm description:	
Subjects received JNJ-70033093 200 mg (2*100 mg capsules in the morning) once daily and 2 placebo capsules in the evening, orally for 10 to 14 postoperative days.	
Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	BMS-986177
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
Subjects received 2 matching placebo capsules orally, in the evening.	

Investigational medicinal product name	JNJ-70033093 200 mg
Investigational medicinal product code	
Other name	BMS-986177
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received JNJ-70033093 200 mg (2*100 mg capsules in the morning) orally once daily.

Arm title	JNJ-70033093 100 mg + Placebo BID
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Arm description:

Subjects received JNJ-70033093 100 mg (1*100 mg capsule) and 1 placebo capsule BID orally for 10 to 14 postoperative days.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	BMS-986177
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received 1 matching placebo capsule BID orally.

Investigational medicinal product name	JNJ-70033093 100 mg
Investigational medicinal product code	
Other name	BMS-986177
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received JNJ-70033093 100 mg (1*100 mg capsule) BID orally.

Arm title	JNJ-70033093 200 mg BID
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Arm description:

Subjects received JNJ-70033093 200 mg (2*100 mg capsules) BID orally for 10 to 14 postoperative days.

Arm type	Experimental
Investigational medicinal product name	JNJ-70033093 200 mg
Investigational medicinal product code	
Other name	BMS-986177
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received JNJ-70033093 200 mg (2*100 mg capsules) BID orally.

Arm title	Enoxaparin 40 mg Once Daily
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Arm description:

Subjects received enoxaparin 40 mg once daily subcutaneously for 10 to 14 postoperative days.

Arm type	Active comparator
Investigational medicinal product name	Enoxaparin 40 mg
Investigational medicinal product code	
Other name	BMS-986177
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received enoxaparin 40 mg once daily subcutaneously.

Number of subjects in period 1	JNJ-70033093 25 mg Once Daily + Placebo	JNJ-70033093 50 mg once daily + Placebo	JNJ-70033093 25 mg + Placebo Twice daily (BID)
Started	34	150	153
Safety analysis set	33 ^[1]	150	148 ^[2]
Completed	34	149	151
Not completed	0	1	2
Adverse event, serious fatal	-	-	-
Consent withdrawn by subject	-	1	2

Number of subjects in period 1	JNJ-70033093 50 mg BID	JNJ-70033093 200 mg Once Daily + Placebo	JNJ-70033093 100 mg + Placebo BID
Started	150	149	152
Safety analysis set	148 ^[3]	147	149 ^[4]
Completed	149	147	150
Not completed	1	2	2
Adverse event, serious fatal	-	-	-
Consent withdrawn by subject	1	2	2

Number of subjects in period 1	JNJ-70033093 200 mg BID	Enoxaparin 40 mg Once Daily
Started	153	301
Safety analysis set	148 ^[5]	296 ^[6]
Completed	151	299
Not completed	2	2
Adverse event, serious fatal	-	1
Consent withdrawn by subject	2	1

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Among 1242 intent to treat (ITT) subjects, 1,219 subjects received at least one dose of study drug and were included in the safety analysis set.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Among 1242 intent to treat (ITT) subjects, 1,219 subjects received at least one dose of study drug and were included in the safety analysis set.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Among 1242 intent to treat (ITT) subjects, 1,219 subjects received at least one dose of study drug and were included in the safety analysis set.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Among 1242 intent to treat (ITT) subjects, 1,219 subjects received at least one dose of study drug and were included in the safety analysis set.

[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Among 1242 intent to treat (ITT) subjects, 1,219 subjects received at least one dose of study drug and were included in the safety analysis set.

[6] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Among 1242 intent to treat (ITT) subjects, 1,219 subjects received at least one dose of study drug and were included in the safety analysis set.

Baseline characteristics

Reporting groups	
Reporting group title	JNJ-70033093 25 mg Once Daily + Placebo
Reporting group description: Subjects received JNJ-70033093 25 mg (1*25 milligrams [mg] capsule) once daily and 1 placebo capsule in the morning and 2 placebo capsules in the evening, orally for 10 to 14 postoperative days.	
Reporting group title	JNJ-70033093 50 mg once daily + Placebo
Reporting group description: Subjects received JNJ-70033093 50 mg (2*25 mg capsules in the morning) once daily and 2 placebo capsules in the evening, orally for 10 to 14 postoperative days.	
Reporting group title	JNJ-70033093 25 mg + Placebo Twice daily (BID)
Reporting group description: Subjects received JNJ-70033093 25 mg (1*25 mg capsule) and 1 placebo capsule twice daily (BID), orally for 10 to 14 postoperative days.	
Reporting group title	JNJ-70033093 50 mg BID
Reporting group description: Subjects received JNJ-70033093 50 mg (2*25 mg capsules) BID orally for 10 to 14 postoperative days.	
Reporting group title	JNJ-70033093 200 mg Once Daily + Placebo
Reporting group description: Subjects received JNJ-70033093 200 mg (2*100 mg capsules in the morning) once daily and 2 placebo capsules in the evening, orally for 10 to 14 postoperative days.	
Reporting group title	JNJ-70033093 100 mg + Placebo BID
Reporting group description: Subjects received JNJ-70033093 100 mg (1*100 mg capsule) and 1 placebo capsule BID orally for 10 to 14 postoperative days.	
Reporting group title	JNJ-70033093 200 mg BID
Reporting group description: Subjects received JNJ-70033093 200 mg (2*100 mg capsules) BID orally for 10 to 14 postoperative days.	
Reporting group title	Enoxaparin 40 mg Once Daily
Reporting group description: Subjects received enoxaparin 40 mg once daily subcutaneously for 10 to 14 postoperative days.	

Reporting group values	JNJ-70033093 25 mg Once Daily + Placebo	JNJ-70033093 50 mg once daily + Placebo	JNJ-70033093 25 mg + Placebo Twice daily (BID)
Number of subjects	34	150	153
Age categorical Units: Subjects			
From 50-64 years	9	51	47
65 years and over	25	99	106
Age continuous Units: years			
arithmetic mean	68.1	67.9	68.4
standard deviation	± 5.74	± 8.03	± 8.49
Sex: Female, Male Units: subjects			
Female	24	107	113
Male	10	43	40

Reporting group values	JNJ-70033093 50	JNJ-70033093 200	JNJ-70033093 100
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	mg BID	mg Once Daily + Placebo	mg + Placebo BID
Number of subjects	150	149	152
Age categorical Units: Subjects			
From 50-64 years	43	51	55
65 years and over	107	98	97
Age continuous Units: years			
arithmetic mean	68.8	68	67
standard deviation	± 8.17	± 8.25	± 8
Sex: Female, Male Units: subjects			
Female	108	108	102
Male	42	41	50

Reporting group values	JNJ-70033093 200 mg BID	Enoxaparin 40 mg Once Daily	Total
Number of subjects	153	301	1242
Age categorical Units: Subjects			
From 50-64 years	49	104	409
65 years and over	104	197	833
Age continuous Units: years			
arithmetic mean	68.6	67.8	
standard deviation	± 7.76	± 7.97	-
Sex: Female, Male Units: subjects			
Female	106	208	876
Male	47	93	366

End points

End points reporting groups

Reporting group title	JNJ-70033093 25 mg Once Daily + Placebo
Reporting group description: Subjects received JNJ-70033093 25 mg (1*25 milligrams [mg] capsule) once daily and 1 placebo capsule in the morning and 2 placebo capsules in the evening, orally for 10 to 14 postoperative days.	
Reporting group title	JNJ-70033093 50 mg once daily + Placebo
Reporting group description: Subjects received JNJ-70033093 50 mg (2*25 mg capsules in the morning) once daily and 2 placebo capsules in the evening, orally for 10 to 14 postoperative days.	
Reporting group title	JNJ-70033093 25 mg + Placebo Twice daily (BID)
Reporting group description: Subjects received JNJ-70033093 25 mg (1*25 mg capsule) and 1 placebo capsule twice daily (BID), orally for 10 to 14 postoperative days.	
Reporting group title	JNJ-70033093 50 mg BID
Reporting group description: Subjects received JNJ-70033093 50 mg (2*25 mg capsules) BID orally for 10 to 14 postoperative days.	
Reporting group title	JNJ-70033093 200 mg Once Daily + Placebo
Reporting group description: Subjects received JNJ-70033093 200 mg (2*100 mg capsules in the morning) once daily and 2 placebo capsules in the evening, orally for 10 to 14 postoperative days.	
Reporting group title	JNJ-70033093 100 mg + Placebo BID
Reporting group description: Subjects received JNJ-70033093 100 mg (1*100 mg capsule) and 1 placebo capsule BID orally for 10 to 14 postoperative days.	
Reporting group title	JNJ-70033093 200 mg BID
Reporting group description: Subjects received JNJ-70033093 200 mg (2*100 mg capsules) BID orally for 10 to 14 postoperative days.	
Reporting group title	Enoxaparin 40 mg Once Daily
Reporting group description: Subjects received enoxaparin 40 mg once daily subcutaneously for 10 to 14 postoperative days.	
Subject analysis set title	Female
Subject analysis set type	Intention-to-treat
Subject analysis set description: Participants received JNJ-70033093 (either 25 mg, 50 mg, 100 mg or 200 mg) once daily or twice daily orally for 10 to 14 postoperative days.	
Subject analysis set title	Male
Subject analysis set type	Intention-to-treat
Subject analysis set description: Participants received JNJ-70033093 (either 25 mg, 50 mg, 100 mg or 200 mg) once daily or twice daily orally for 10 to 14 postoperative days.	
Subject analysis set title	Age: Less than or Equal to ($\leq$) 68 years
Subject analysis set type	Intention-to-treat
Subject analysis set description: Subjects received JNJ-70033093 (either 25 mg, 50 mg, 100 mg or 200 mg) once daily or twice daily orally for 10 to 14 postoperative days.	
Subject analysis set title	Age: Greater than ($>$) 68 years
Subject analysis set type	Intention-to-treat
Subject analysis set description: Subjects received JNJ-70033093 (either 25 mg, 50 mg, 100 mg or 200 mg) once daily or twice daily orally for 10 to 14 postoperative days.	
Subject analysis set title	Weight: Less than or Equal to ($\leq$) 82 kilograms (kg)

Subject analysis set type	Intention-to-treat
Subject analysis set description: Subjects received JNJ-70033093 (either 25 mg, 50 mg, 100 mg or 200 mg) once daily or twice daily orally for 10 to 14 postoperative days.	
Subject analysis set title	Weight: Greater than (>) 82 kg
Subject analysis set type	Intention-to-treat
Subject analysis set description: Subjects received JNJ-70033093 (either 25 mg, 50 mg, 100 mg or 200 mg) once daily or twice daily orally for 10 to 14 postoperative days.	
Subject analysis set title	Creatinine clearance (CRCL): Less than (<) 90
Subject analysis set type	Intention-to-treat
Subject analysis set description: Subjects received JNJ-70033093 (either 25 mg, 50 mg, 100 mg or 200 mg) once daily or twice daily orally for 10 to 14 postoperative days.	
Subject analysis set title	CRCL: Greater than or equal to (>=) 90
Subject analysis set type	Intention-to-treat
Subject analysis set description: Subjects received JNJ-70033093 (either 25 mg, 50 mg, 100 mg or 200 mg) once daily or twice daily orally for 10 to 14 postoperative days.	
Subject analysis set title	Overall
Subject analysis set type	Intention-to-treat
Subject analysis set description: Subjects received JNJ-70033093 (either 25 mg, 50 mg, 100 mg or 200 mg) once daily or twice daily orally for 10 to 14 postoperative days.	

Primary: Number of Subjects with Total Venous Thromboembolism (VTE) (CEC-adjudicated)

End point title	Number of Subjects with Total Venous Thromboembolism (VTE) (CEC-adjudicated) ^[1]
End point description: Total VTE was defined as the composite of clinical events committee (CEC)-adjudicated proximal and/or distal Deep Vein Thrombosis (DVT) (asymptomatic confirmed by venography assessment of the operated leg or objectively confirmed symptomatic), nonfatal pulmonary embolism (PE), or any death. The modified Intent-to-treat (mITT) analysis set included all intent-to-treat (ITT) subjects who received at least 1 dose of study drug with an evaluable venography assessment or a confirmed symptomatic proximal DVT, PE or death as adjudicated by the CEC.	
End point type	Primary
End point timeframe: Up to Day 14	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics was done, no inferential statistical analysis was performed.

End point values	JNJ-70033093 25 mg Once Daily + Placebo	JNJ-70033093 50 mg once daily + Placebo	JNJ-70033093 25 mg + Placebo Twice daily (BID)	JNJ-70033093 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	127	129	124
Units: subjects	7	30	27	14

End point values	JNJ-70033093 200 mg Once	JNJ-70033093 100 mg +	JNJ-70033093 200 mg BID	Enoxaparin 40 mg Once Daily
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	Daily + Placebo	Placebo BID		
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	123	134	131	252
Units: subjects	8	12	10	54

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with any Bleeding Event (CEC-adjudicated)

End point title	Number of Subjects with any Bleeding Event (CEC-adjudicated)
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End point description:

Any bleeding was defined as the composite of major bleeding according to the International Society on Thrombosis and Haemostasis (ISTH) criteria modified for the surgical setting, clinically relevant nonmajor bleeding events, or minimal bleeding events as assessed by the CEC. The safety analysis set was a subset of the intent to treat (ITT) analysis set, consisting of all ITT subjects who received at least 1 dose (partial or complete) of study drug.

End point type	Secondary
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End point timeframe:

Up to Day 14; Up to Day 52

End point values	JNJ-70033093 25 mg Once Daily + Placebo	JNJ-70033093 50 mg once daily + Placebo	JNJ-70033093 25 mg + Placebo Twice daily (BID)	JNJ-70033093 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	150	148	148
Units: subjects				
Up to Day 14	0	8	2	7
Up to Day 52	0	8	2	7

End point values	JNJ-70033093 200 mg Once Daily + Placebo	JNJ-70033093 100 mg + Placebo BID	JNJ-70033093 200 mg BID	Enoxaparin 40 mg Once Daily
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	147	149	148	296
Units: subjects				
Up to Day 14	11	7	6	12
Up to Day 52	11	7	6	12

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Total VTE (CEC-adjudicated) Up to Day 52

End point title	Number of Subjects with Total VTE (CEC-adjudicated) Up to Day 52
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End point description:

Total VTE was defined as the composite of CEC-adjudicated proximal and/or DVT (asymptomatic confirmed by venography assessment of the operated leg or objectively confirmed symptomatic), nonfatal PE, or any death. The mITT analysis set included all the subjects in mITT at Day 14 plus the subjects who had symptomatic/asymptomatic VTE events (DVT, non-fatal PE or any death) after day 17 through day 52. Here, 'N' (number of subjects analyzed) signifies those subjects who were evaluable for this endpoint.

End point type	Secondary
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End point timeframe:

Up to Day 52

End point values	JNJ-70033093 25 mg Once Daily + Placebo	JNJ-70033093 50 mg once daily + Placebo	JNJ-70033093 25 mg + Placebo Twice daily (BID)	JNJ-70033093 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	128	129	124
Units: subjects	7	30	27	14

End point values	JNJ-70033093 200 mg Once Daily + Placebo	JNJ-70033093 100 mg + Placebo BID	JNJ-70033093 200 mg BID	Enoxaparin 40 mg Once Daily
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	123	135	131	253
Units: subjects	8	12	10	54

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Composite of Major and Clinically Relevant Non-Major CRNM Bleeding Events (CEC-adjudicated)

End point title	Number of Subjects With Composite of Major and Clinically Relevant Non-Major CRNM Bleeding Events (CEC-adjudicated)
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End point description:

Composite of Major BE: Fatal bleeding; bleeding that is symptomatic and occurs in critical area/organ and/or; extrasurgical site bleeding causing fall in Hb level of 20 g/L or more, or leading to transfusion of 2 or more units of whole blood or red cells with temporal association within 24-48 hours to bleeding, and/or; surgical site bleeding that requires second intervention open, arthroscopic, endovascular, or hemarthrosis resulting in prolonged hospitalization, deep wound infection and/or either unexpected and prolonged and/or sufficiently large to cause hemodynamic instability. CRNM bleeding: acute clinically overt bleeding that does not satisfy additional criteria required for bleeding event to be defined as major BE is still considered clinically relevant for example: Epistaxis, Gastrointestinal bleed, Hematuria, Bruising/ecchymosis, Hemoptysis, Hematoma. The analysis set: safety set. Here, 'N' (number of subjects analyzed) signifies those subjects who were evaluable for this endpoint.

End point type	Secondary
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End point timeframe:

Up to Day 14, Up to Day 52

End point values	JNJ-70033093 25 mg Once Daily + Placebo	JNJ-70033093 50 mg once daily + Placebo	JNJ-70033093 25 mg + Placebo Twice daily (BID)	JNJ-70033093 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	150	148	148
Units: subjects				
Up to Day 14	0	2	0	2
Up to Day 52	0	2	0	2

End point values	JNJ-70033093 200 mg Once Daily + Placebo	JNJ-70033093 100 mg + Placebo BID	JNJ-70033093 200 mg BID	Enoxaparin 40 mg Once Daily
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	147	149	148	296
Units: subjects				
Up to Day 14	1	1	1	5
Up to Day 52	2	1	1	5

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Major Bleeding Events (CEC-adjudicated)

End point title	Number of Subjects with Major Bleeding Events (CEC-adjudicated)
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End point description:

Number of subjects with major bleeding events (adjudicated by CEC) were reported. Major bleeding was defined as: Fatal bleeding; Bleeding that is symptomatic and occurs in critical area/organ and/or; Extrasurgical site bleeding causing fall in hemoglobin (Hb) level of 20 grams per liter (g/L) or more, or leading to transfusion of 2 or more units of whole blood or red cells with temporal association within 24-48 hours to bleeding, and/or; Surgical site bleeding that requires second intervention open, arthroscopic, endovascular, or hemarthrosis resulting in prolonged hospitalization or a deep wound infection and/or; Surgical site bleeding that is unexpected and prolonged and/or sufficiently large to cause hemodynamic instability. The safety analysis set was a subset of the ITT analysis set, consisting of all ITT subjects who received at least 1 dose (partial or complete) of study drug.

End point type	Secondary
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End point timeframe:

Up to Day 14; Up to Day 52

End point values	JNJ-70033093 25 mg Once Daily + Placebo	JNJ-70033093 50 mg once daily + Placebo	JNJ-70033093 25 mg + Placebo Twice daily (BID)	JNJ-70033093 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	150	148	148
Units: subjects				
Up to Day 14	0	0	0	0
Up to Day 52	0	0	0	0

End point values	JNJ-70033093 200 mg Once Daily + Placebo	JNJ-70033093 100 mg + Placebo BID	JNJ-70033093 200 mg BID	Enoxaparin 40 mg Once Daily
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	147	149	148	296
Units: subjects				
Up to Day 14	0	0	0	1
Up to Day 52	0	0	0	1

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with CRNM Bleeding Events (CEC-adjudicated)

End point title	Number of Subjects with CRNM Bleeding Events (CEC-adjudicated)
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End point description:

Number of subjects with CRNM bleeding events (adjudicated by CEC) were reported. CRNM bleeding events were defined as acute clinically overt bleeding that does not satisfy additional criteria required for bleeding event to be defined as major BE and meets and is still considered clinically relevant for example: Epistaxis, Gastrointestinal bleed, Hematuria, Bruising/ecchymosis, Hemoptysis, Hematoma. The safety analysis set was a subset of the ITT analysis set, consisting of all ITT subjects who received at least 1 dose (partial or complete) of study drug.

End point type	Secondary
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End point timeframe:

Up to Day 14; Up to Day 52

End point values	JNJ-70033093 25 mg Once Daily + Placebo	JNJ-70033093 50 mg once daily + Placebo	JNJ-70033093 25 mg + Placebo Twice daily (BID)	JNJ-70033093 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	150	148	148
Units: subjects				
Up to Day 14	0	2	0	2
Up to Day 52	0	2	0	2

End point values	JNJ-70033093 200 mg Once Daily + Placebo	JNJ-70033093 100 mg + Placebo BID	JNJ-70033093 200 mg BID	Enoxaparin 40 mg Once Daily
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	147	149	148	296
Units: subjects				
Up to Day 14	1	1	1	4
Up to Day 52	2	1	1	4

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Minimal Bleeding Events (CEC-adjudicated)

End point title	Number of Subjects with Minimal Bleeding Events (CEC-adjudicated)
End point description:	
Number of participants with minimal bleeding events (adjudicated by CEC) were reported. Minimal bleeding event was defined as any bleeding event not met major or CRNM criteria. The safety analysis set was a subset of the ITT analysis set, consisting of all ITT subjects who received at least 1 dose (partial or complete) of study drug.	
End point type	Secondary
End point timeframe:	
Up to Day 14; Up to Day 52	

End point values	JNJ-70033093 25 mg Once Daily + Placebo	JNJ-70033093 50 mg once daily + Placebo	JNJ-70033093 25 mg + Placebo Twice daily (BID)	JNJ-70033093 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	150	148	148
Units: subjects				
Up to Day 14	0	6	2	5
Up to Day 52	0	6	2	5

End point values	JNJ-70033093 200 mg Once Daily + Placebo	JNJ-70033093 100 mg + Placebo BID	JNJ-70033093 200 mg BID	Enoxaparin 40 mg Once Daily
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	147	149	148	296
Units: subjects				
Up to Day 14	8	7	4	8
Up to Day 52	9	7	5	8

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Major or CRNM Bleeding Events (CEC- adjudicated)

End point title	Number of Subjects with Major or CRNM Bleeding Events (CEC- adjudicated)
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End point description:

Major Bleeding: Fatal bleeding; That is symptomatic and occurs in critical area/organ and/or; Extrasurgical site bleeding causing fall in Hb level of 20 g/L or more, or leading to transfusion of 2 or more units of whole blood or red cells with temporal association within 24-48 hours to bleeding, and/or; Surgical site bleeding that requires second intervention open, arthroscopic, endovascular, or hemarthrosis resulting in prolonged hospitalization or deep wound infection and/or; Surgical site bleeding that is unexpected and prolonged and/or sufficiently large to cause hemodynamic instability. CRNM bleeding: acute clinically overt bleeding that does not satisfy additional criteria required for bleeding event to be defined as major BE, still considered clinically relevant for example: Epistaxis, Gastrointestinal

End point type	Secondary
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End point timeframe:

Up to Day 14; Up to Day 52

End point values	JNJ-70033093 25 mg Once Daily + Placebo	JNJ-70033093 50 mg once daily + Placebo	JNJ-70033093 25 mg + Placebo Twice daily (BID)	JNJ-70033093 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	150	148	148
Units: subjects				
Up to Day 14	0	2	0	2
Up to Day 52	0	0	0	0

End point values	JNJ-70033093 200 mg Once Daily + Placebo	JNJ-70033093 100 mg + Placebo BID	JNJ-70033093 200 mg BID	Enoxaparin 40 mg Once Daily
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	147	149	148	296
Units: subjects				
Up to Day 14	1	1	1	5
Up to Day 52	1	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Major VTE (CEC-adjudicated)

End point title	Number of Subjects with Major VTE (CEC-adjudicated)
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End point description:

Number of subjects with major VTE (adjudicated by CEC) were reported. Major VTE was defined as a composite of proximal DVT (asymptomatic confirmed by venography or objectively confirmed symptomatic), nonfatal PE, or any death. mITT at Day 14 included all ITT subjects who received at least 1 dose of study drug with an evaluable venography assessment or a confirmed symptomatic VTE event (DVT, non-fatal PE or any death). Here, 'N' (number of subjects analyzed) signifies those subjects who were evaluable for this endpoint.

End point type	Secondary
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End point timeframe:

Up to Day 14

End point values	JNJ-70033093 25 mg Once Daily + Placebo	JNJ-70033093 50 mg once daily + Placebo	JNJ-70033093 25 mg + Placebo Twice daily (BID)	JNJ-70033093 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	127	129	124
Units: subjects	0	2	1	1

End point values	JNJ-70033093 200 mg Once Daily + Placebo	JNJ-70033093 100 mg + Placebo BID	JNJ-70033093 200 mg BID	Enoxaparin 40 mg Once Daily
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	123	134	131	252
Units: subjects	0	2	0	4

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Major VTE (CEC-adjudicated) Up to Day 52

End point title	Number of Subjects with Major VTE (CEC-adjudicated) Up to Day 52
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End point description:

Number of subjects with major VTE (adjudicated by CEC) were reported. Major VTE was defined as a composite of proximal DVT (asymptomatic confirmed by venography or objectively confirmed symptomatic), nonfatal PE, or any death. The mITT analysis set included all the subjects in mITT at Day 14 plus the subjects who had symptomatic/asymptomatic VTE events (DVT, non-fatal PE or any death) after day 17 through day 52. Here, 'N' (number of subjects analyzed) signifies those subjects who were evaluable for this outcome measure.

End point type	Secondary
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End point timeframe:

Up to Day 52

End point values	JNJ-70033093 25 mg Once Daily + Placebo	JNJ-70033093 50 mg once daily + Placebo	JNJ-70033093 25 mg + Placebo Twice daily (BID)	JNJ-70033093 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	128	129	124
Units: subjects	0	2	1	1

End point values	JNJ-70033093 200 mg Once Daily + Placebo	JNJ-70033093 100 mg + Placebo BID	JNJ-70033093 200 mg BID	Enoxaparin 40 mg Once Daily
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	123	135	131	253
Units: subjects	0	2	0	4

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Proximal Deep Vein Thrombosis (DVT) (CEC- adjudicated)

End point title	Number of Subjects with Proximal Deep Vein Thrombosis (DVT) (CEC- adjudicated)
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End point description:

Number of subjects with proximal DVT (adjudicated by CEC) were reported. DVT asymptomatic confirmed by venography assessment of the operated leg or objectively confirmed symptomatic. The mITT analysis set at Day 14 includes all ITT subjects who received at least 1 dose of study drug with an evaluable venography assessment or a confirmed symptomatic VTE event (DVT, non-fatal PE or any death). The subjects whose venography result is not evaluable distal but no proximal clot.

End point type	Secondary
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End point timeframe:

Up to Day 14

End point values	JNJ-70033093 25 mg Once Daily + Placebo	JNJ-70033093 50 mg once daily + Placebo	JNJ-70033093 25 mg + Placebo Twice daily (BID)	JNJ-70033093 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	134	133	128
Units: subjects				
Asymptomatic	0	0	0	0
Symptomatic	0	0	0	0

End point values	JNJ-70033093 200 mg Once Daily + Placebo	JNJ-70033093 100 mg + Placebo BID	JNJ-70033093 200 mg BID	Enoxaparin 40 mg Once Daily
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	128	136	135	259
Units: subjects				
Asymptomatic	0	0	0	1
Symptomatic	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Proximal DVT (CEC-adjudicated) Up to Day 52

End point title	Number of Participants with Proximal DVT (CEC-adjudicated) Up to Day 52
End point description:	
Number of subjects with proximal DVT (CEC-adjudicated) were reported. DVT asymptomatic confirmed by venography assessment of the operated leg or objectively confirmed symptomatic. The mITT analysis set at Week 6 included all the subjects in mITT at Day 14 plus the subjects who had symptomatic/asymptomatic VTE events (DVT, non-fatal PE or any death) after day 17 through day 52. Also included the subjects whose venography result was not evaluable distal but no proximal clot.	
End point type	Secondary
End point timeframe:	
Up to Day 52	

End point values	JNJ-70033093 25 mg Once Daily + Placebo	JNJ-70033093 50 mg once daily + Placebo	JNJ-70033093 25 mg + Placebo Twice daily (BID)	JNJ-70033093 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	135	133	128
Units: subjects				
Asymptomatic	0	0	0	0
Symptomatic	0	0	0	0

End point values	JNJ-70033093 200 mg Once Daily + Placebo	JNJ-70033093 100 mg + Placebo BID	JNJ-70033093 200 mg BID	Enoxaparin 40 mg Once Daily
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	128	137	135	260
Units: subjects				
Asymptomatic	0	0	0	1

Symptomatic	0	0	0	0
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Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Distal DVT (CEC-adjudicated)

End point title	Number of Subjects with Distal DVT (CEC-adjudicated)
End point description: Number of subjects with distal DVT (CEC-adjudicated) were reported. DVT asymptomatic confirmed by venography assessment of the operated leg or objectively confirmed symptomatic. The mITT analysis set at Day 14 included all ITT subjects who received at least 1 dose of study drug with an evaluable venography assessment or a confirmed symptomatic VTE event (DVT, non-fatal PE or any death). Here, 'N' (number of subjects analyzed) signifies those participants who were evaluable for this endpoint.	
End point type	Secondary
End point timeframe: Up to Day 14	

End point values	JNJ-70033093 25 mg Once Daily + Placebo	JNJ-70033093 50 mg once daily + Placebo	JNJ-70033093 25 mg + Placebo Twice daily (BID)	JNJ-70033093 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	128	129	124
Units: subjects				
Asymptomatic	7	27	26	13
Symptomatic	0	2	0	0

End point values	JNJ-70033093 200 mg Once Daily + Placebo	JNJ-70033093 100 mg + Placebo BID	JNJ-70033093 200 mg BID	Enoxaparin 40 mg Once Daily
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	123	135	131	252
Units: subjects				
Asymptomatic	8	10	10	50
Symptomatic	0	1	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Distal DVT (CEC-adjudicated) Up to Day 52

End point title	Number of Subjects with Distal DVT (CEC-adjudicated) Up to Day 52
End point description: Number of subjects with distal DVT (adjudicated by CEC) were reported. DVT asymptomatic confirmed by venography assessment of the operated leg or objectively confirmed symptomatic. mITT included all the subjects in mITT at Day 14 plus the subjects who had symptomatic/asymptomatic VTE events (DVT, non-fatal PE or any death) after day 17 through day 52. Here, 'N' (number of subjects analyzed) signifies those subjects who were evaluable for this outcome measure.	
End point type	Secondary
End point timeframe: Up to Day 52	

End point values	JNJ-70033093 25 mg Once Daily + Placebo	JNJ-70033093 50 mg once daily + Placebo	JNJ-70033093 25 mg + Placebo Twice daily (BID)	JNJ-70033093 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	128	129	124
Units: subjects				
Asymptomatic (Up to Day 52)	7	27	26	13
Symptomatic (Up to Day 52)	0	2	2	0

End point values	JNJ-70033093 200 mg Once Daily + Placebo	JNJ-70033093 100 mg + Placebo BID	JNJ-70033093 200 mg BID	Enoxaparin 40 mg Once Daily
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	123	135	131	253
Units: subjects				
Asymptomatic (Up to Day 52)	8	10	10	50
Symptomatic (Up to Day 52)	0	1	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Nonfatal Pulmonary Embolism (PE) (CEC-adjudicated)

End point title	Number of Subjects with Nonfatal Pulmonary Embolism (PE) (CEC-adjudicated)
End point description: Number of subjects with nonfatal PE (adjudicated by CEC) were reported. mITT at Day 14 included all ITT subjects who received at least 1 dose of study drug with an evaluable venography assessment or a confirmed symptomatic VTE event (DVT, non-fatal PE or any death). Here, 'N' (number of subjects analyzed) signifies those subjects who were evaluable for this endpoint.	
End point type	Secondary
End point timeframe: Up to Day 14	

End point values	JNJ-70033093 25 mg Once Daily + Placebo	JNJ-70033093 50 mg once daily + Placebo	JNJ-70033093 25 mg + Placebo Twice daily (BID)	JNJ-70033093 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	127	129	124
Units: subjects	0	0	0	1

End point values	JNJ-70033093 200 mg Once Daily + Placebo	JNJ-70033093 100 mg + Placebo BID	JNJ-70033093 200 mg BID	Enoxaparin 40 mg Once Daily
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	123	134	131	252
Units: subjects	0	1	0	1

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Nonfatal PE (CEC-adjudicated) Up to Day 52

End point title	Number of Subjects with Nonfatal PE (CEC-adjudicated) Up to Day 52
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End point description:

Number of subjects with nonfatal PE (adjudicated by CEC) were reported. The mITT analysis set included all the participants in mITT at Day 14 plus the subjects who had symptomatic/asymptomatic VTE events (DVT, non-fatal PE or any death) after day 17 through day 52. Here, 'N' (number of subjects analyzed) signifies those subjects who were evaluable for this endpoint.

End point type	Secondary
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End point timeframe:

Up to Day 52

End point values	JNJ-70033093 25 mg Once Daily + Placebo	JNJ-70033093 50 mg once daily + Placebo	JNJ-70033093 25 mg + Placebo Twice daily (BID)	JNJ-70033093 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	128	129	124
Units: subjects	0	0	0	1

End point values	JNJ-70033093 200 mg Once	JNJ-70033093 100 mg +	JNJ-70033093 200 mg BID	Enoxaparin 40 mg Once Daily
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	Daily + Placebo	Placebo BID		
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	123	135	131	253
Units: subjects	0	1	0	1

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Deaths (CEC-adjudicated)

End point title	Number of Subjects with Deaths (CEC-adjudicated)
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End point description:

Number of subjects with deaths (CEC-adjudicated) were reported. mITT at Day 14 included all ITT subjects who received at least 1 dose of study drug with an evaluable venography assessment or a confirmed symptomatic VTE event (DVT, non-fatal PE or any death). Here, 'N' (number of subjects analyzed) signifies those subjects who were evaluable for this endpoint.

End point type	Secondary
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End point timeframe:

Up to Day 14

End point values	JNJ-70033093 25 mg Once Daily + Placebo	JNJ-70033093 50 mg once daily + Placebo	JNJ-70033093 25 mg + Placebo Twice daily (BID)	JNJ-70033093 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	127	129	124
Units: subjects	0	0	0	0

End point values	JNJ-70033093 200 mg Once Daily + Placebo	JNJ-70033093 100 mg + Placebo BID	JNJ-70033093 200 mg BID	Enoxaparin 40 mg Once Daily
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	123	134	131	252
Units: subjects	0	0	0	1

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Deaths (CEC-adjudicated) Up to Day 52

End point title	Number of Subjects with Deaths (CEC-adjudicated) Up to Day 52
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End point description:

Number of subjects with deaths (CEC-adjudicated) were reported. mITT at Week 6 included all the subjects in mITT at Day 14 plus the subjects who had symptomatic/asymptomatic VTE events (DVT, non-fatal PE or any death) after day 17 through day 52. Here, 'N' (number of subjects analyzed) signifies those subjects who were evaluable for this endpoint.

End point type	Secondary
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End point timeframe:

Up to Day 52

End point values	JNJ-70033093 25 mg Once Daily + Placebo	JNJ-70033093 50 mg once daily + Placebo	JNJ-70033093 25 mg + Placebo Twice daily (BID)	JNJ-70033093 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	128	129	124
Units: subjects	0	0	0	0

End point values	JNJ-70033093 200 mg Once Daily + Placebo	JNJ-70033093 100 mg + Placebo BID	JNJ-70033093 200 mg BID	Enoxaparin 40 mg Once Daily
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	123	135	131	253
Units: subjects	0	0	0	1

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Volume of Distribution (V/F) of JNJ-70033093

End point title	Apparent Volume of Distribution (V/F) of JNJ-70033093
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End point description:

V/F was defined as the theoretical volume in which the total amount of drug would need to be uniformly distributed to produce the desired serum concentration of a drug. Here, 'N' (number of subjects analyzed) signifies those subjects who were evaluable for this endpoint. This endpoint was planned to be analyzed for overall subjects and not group wise.

End point type	Secondary
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End point timeframe:

Up to Day 14

End point values	Overall			
Subject group type	Subject analysis set			
Number of subjects analysed	921			
Units: Liter				
geometric mean (geometric coefficient of variation)	148 ($\pm$ 77.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Clearance (CL/F) of JNJ-70033093

End point title	Apparent Clearance (CL/F) of JNJ-70033093
End point description:	
Apparent clearance of a drug was defined as a measure of the rate at which a drug got metabolized or eliminated by normal biological processes. Clearance obtained after oral dose (apparent oral clearance) is influenced by the fraction of the dose absorbed. Here, 'N' (number of subjects analyzed) signifies those subjects who were evaluable for this outcome measure. This outcome measure was planned to be analyzed for overall subjects and not group wise.	
End point type	Secondary
End point timeframe:	
Up to Day 14	

End point values	Overall			
Subject group type	Subject analysis set			
Number of subjects analysed	921			
Units: Liter per hour (L/h)				
geometric mean (geometric coefficient of variation)	8.33 ($\pm$ 45.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Impact of Selected Demographics: Sex on CL/F

End point title	Impact of Selected Demographics: Sex on CL/F
End point description:	
Impact of sex on CL/F was assessed. The PK analysis set consisted of subjects who received at least 1 dose of milvexian and had at least one valid blood sample drawn for PK analysis. Arms are created based on sex (male and female) to report the effect of sex on CL/F. Here, 'N' (number of subjects analyzed) signifies those subjects who were evaluable for this endpoint.	
End point type	Secondary
End point timeframe:	
Up to Day 14	

End point values	Female	Male		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	653	268		
Units: Litres per hour (L/h)				
geometric mean (geometric coefficient of variation)	7.70 ($\pm$ 48.4)	9.87 ($\pm$ 36.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Impact of Selected Demographic: Age on CL/F

End point title	Impact of Selected Demographic: Age on CL/F
End point description:	
Impact of age CL/F was assessed. The PK analysis set consisted of subjects who received at least 1 dose of milvexian and had at least one valid blood sample drawn for PK analysis. Here, 'N' (number of subjects analyzed) signifies those subjects who were evaluable for this endpoint. Arms are created based on age to report the effect of age on CL/F.	
End point type	Secondary
End point timeframe:	
Up to Day 14	

End point values	Age: Less than or Equal to ($\leq$) 68 years	Age: Greater than ($>$) 68 years		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	464	457		
Units: L/h				
geometric mean (geometric coefficient of variation)	9.33 ($\pm$ 45.5)	7.32 ($\pm$ 41.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Impact of Selected Demographic: Weight on CL/F

End point title	Impact of Selected Demographic: Weight on CL/F
End point description:	
Impact of weight) on CL/F was assessed. The PK analysis set consisted of subjects who received at least 1 dose of milvexian and had at least one valid blood sample drawn for PK analysis. Here, 'N' (number of subjects analyzed) signifies those subjects who were evaluable for this endpoints. Arms are created based on weight to report the effect of weight on CL/F.	
End point type	Secondary

End point timeframe:

Up to Day 14

End point values	Weight: Less than or Equal to ($\leq$) 82 kilograms (kg)	Weight: Greater than ($>$) 82 kg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	486	435		
Units: L/h				
geometric mean (geometric coefficient of variation)	7.56 ($\pm$ 41.2)	9.20 ($\pm$ 46.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Impact of Selected Laboratory Values: Renal Function on CL/F

End point title	Impact of Selected Laboratory Values: Renal Function on CL/F
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End point description:

Impact of renal function on V/F was assessed. The PK analysis set consisted of subjects who received at least 1 dose of milvexian and had at least one valid blood sample drawn for PK analysis. The outcome measure was reported based on CRCL. Here, 'N' (number of subjects analyzed) signifies those subjects who were evaluable for this outcome measure. Arms are created based on CRCL to report the effect of renal function on CL/F.

End point type	Secondary
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End point timeframe:

Up to Day 14

End point values	Creatinine clearance (CRCL): Less than ($<$) 90	CRCL: Greater than or equal to ($\geq$) 90		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	442	447		
Units: L/h				
geometric mean (geometric coefficient of variation)	7.21 ($\pm$ 43.4)	9.40 ($\pm$ 43.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Impact of Selected Demographics: Apparent Clearance (CL/F) Based on Sex

End point title	Impact of Selected Demographics: Apparent Clearance (CL/F) Based on Sex
End point description: Impact of sex on V/F was assessed. The PK analysis set consisted of subjects who received at least 1 dose of milvexian and had at least one valid blood sample drawn for PK analysis. Here, 'N' (number of subjects analyzed) signifies those subjects who were evaluable for this outcome measure. Arms are created based on sex (male and female) to report the effect of sex on V/F.	
End point type	Secondary
End point timeframe: Up to Day 14	

End point values	Female	Male		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	653	268		
Units: Liters				
geometric mean (geometric coefficient of variation)	140 ($\pm$ 81.2)	166 ($\pm$ 69.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Impact of Selected Demographics : Age on V/F

End point title	Impact of Selected Demographics : Age on V/F
End point description: Impact of age on V/F was assessed. The PK analysis set consisted of subjects who received at least 1 dose of milvexian and had at least one valid blood sample drawn for PK analysis. Here, 'N' (number of subjects analyzed) signifies those subjects who were evaluable for this outcome measure. Arms are created based on age to report the effect of sex on V/F.	
End point type	Secondary
End point timeframe: Up to Day 14	

End point values	Age: Less than or Equal to ($\leq$) 68 years	Age: Greater than ($>$) 68 years		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	464	457		
Units: Liters				
geometric mean (geometric coefficient of variation)	160 ($\pm$ 83.2)	135 ($\pm$ 66.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Impact of Selected Demographics : Weight on V/F

End point title	Impact of Selected Demographics : Weight on V/F
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End point description:

Impact of weight on V/F was assessed. The PK analysis set consisted of subjects who received at least 1 dose of milvexian and had at least one valid blood sample drawn for PK analysis. Here, 'N' (number of subjects analyzed) signifies those subjects who were evaluable for this endpoint. Arms are created based on weight to report the effect of weight on CV/F.

End point type	Secondary
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End point timeframe:

Up to Day 14

End point values	Weight: Less than or Equal to ($\leq$) 82 kilograms (kg)	Weight: Greater than ($>$) 82 kg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	486	435		
Units: Liters				
geometric mean (geometric coefficient of variation)	127 ($\pm$ 65.4)	171 ($\pm$ 80.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Impact of Selected Laboratory Values: Renal Function on V/F

End point title	Impact of Selected Laboratory Values: Renal Function on V/F
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End point description:

Impact of renal function on V/F was assessed. The PK analysis set consisted of subjects who received at least 1 dose of milvexian and had at least one valid blood sample drawn for PK analysis. The outcome measure was reported based on CRCL. Here, 'N' (number of subjects analyzed) signifies those subjects who were evaluable for this endpoint. Arms are created based on CRCL to report the effect of renal function on V/F.

End point type	Secondary
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End point timeframe:

Up to Day 14

End point values	Creatinine clearance (CRCL): Less than ($<$) 90	CRCL: Greater than or equal to ($\geq$) 90		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	442	447		
Units: Liters				
geometric mean (geometric coefficient	136 ($\pm$ 66.3)	160 ($\pm$ 84.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Relationship between JNJ-70033093 Dose Levels with Total VTE

End point title	Relationship between JNJ-70033093 Dose Levels with Total
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End point description:

Relationship between JNJ-70033093 dose levels with total VTE was determined using a multiple comparison procedures and modeling (MCP-Mod) approach. The mITT analysis set at Day 14 included all ITT participants who received at least 1 dose of study drug with an evaluable venography assessment or a confirmed symptomatic VTE event (DVT, non-fatal PE or any death). Here 'number' signifies the estimated response rate.

End point type	Secondary
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End point timeframe:

Up to 14 days

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Endpoint was planned to be analyzed for specified arms only.

End point values	JNJ-70033093 25 mg Once Daily + Placebo	JNJ-70033093 50 mg once daily + Placebo	JNJ-70033093 25 mg + Placebo Twice daily (BID)	JNJ-70033093 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	150	148	148
Units: percentage of subjects				
number (confidence interval 95%)	0.35 (0.17 to 0.52)	0.21 (0.16 to 0.25)	0.20 (0.15 to 0.24)	0.13 (0.10 to 0.16)

End point values	JNJ-70033093 200 mg Once Daily + Placebo	JNJ-70033093 100 mg + Placebo BID	JNJ-70033093 200 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	147	149	148	
Units: percentage of subjects				
number (confidence interval 95%)	0.09 (0.07 to 0.12)	0.09 (0.06 to 0.11)	0.07 (0.03 to 0.10)	

Statistical analyses

No statistical analyses for this end point

Secondary: Relationship Between JNJ-70033093 Dose Levels with Composite of Major or Clinically Relevant Nonmajor Bleeding Events

End point title	Relationship Between JNJ-70033093 Dose Levels with Composite of Major or Clinically Relevant Nonmajor Bleeding Events ^[3]
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End point description:

Relationship between JNJ-70033093 dose levels with composite of major or clinically relevant nonmajor bleeding events was determined using a MCP-Mod approach. The mITT analysis set at Day 14 included all ITT subjects who received at least 1 dose of study drug with an evaluable venography assessment or a confirmed symptomatic VTE event (DVT, non-fatal PE or any death). Here 'number' signifies the estimated response rate.

End point type	Secondary
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End point timeframe:

Up to 14 days

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Endpoint was planned to be analyzed for specified arms only.

End point values	JNJ-70033093 25 mg Once Daily + Placebo	JNJ-70033093 50 mg once daily + Placebo	JNJ-70033093 25 mg + Placebo Twice daily (BID)	JNJ-70033093 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	150	148	148
Units: percentage of subjects				
number (confidence interval 95%)	0.02 (0.00 to 0.17)	0.01 (0.00 to 0.03)	0.01 (0.00 to 0.04)	0.01 (0.00 to 0.02)

End point values	JNJ-70033093 200 mg Once Daily + Placebo	JNJ-70033093 100 mg + Placebo BID	JNJ-70033093 200 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	147	149	148	
Units: percentage of subjects				
number (confidence interval 95%)	0.01 (0.00 to 0.02)	0.01 (0.00 to 0.02)	0.01 (0.00 to 0.02)	

Statistical analyses

No statistical analyses for this end point

Secondary: Relationship between JNJ-70033093 Dose Levels with Major Bleeding Events

End point title	Relationship between JNJ-70033093 Dose Levels with Major Bleeding Events ^[4]
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End point description:

Relationship between JNJ-70033093 dose levels with major bleeding events was determined using a MCP-Mod approach. The PK analysis set consisted of subjects who received at least 1 dose of milvexian and had at least one valid blood sample drawn for PK analysis. Here "99999" indicates that data was not available as there were no major bleeding events.

End point type	Secondary
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End point timeframe:

Up to 14 days

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint was planned to be analyzed for specified arms only.

End point values	JNJ-70033093 25 mg Once Daily + Placebo	JNJ-70033093 50 mg once daily + Placebo	JNJ-70033093 25 mg + Placebo Twice daily (BID)	JNJ-70033093 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	150	148	148
Units: unitless				
geometric mean (geometric coefficient of variation)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)

End point values	JNJ-70033093 200 mg Once Daily + Placebo	JNJ-70033093 100 mg + Placebo BID	JNJ-70033093 200 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	147	149	148	
Units: unitless				
geometric mean (geometric coefficient of variation)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Relationship between JNJ-70033093 Dose Levels with Clinically Relevant Nonmajor Bleeding Events

End point title	Relationship between JNJ-70033093 Dose Levels with Clinically Relevant Nonmajor Bleeding Events ^[5]
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End point description:

Relationship between JNJ-70033093 dose levels with clinically relevant nonmajor bleeding events was determined using a MCP-Mod approach. The mITT analysis set at Day 14 included all ITT participants who received at least 1 dose of study drug with an evaluable venography assessment or a confirmed symptomatic VTE event (DVT, non-fatal PE or any death). Here '99999' indicates that data was not available as there were no clinically relevant nonmajor events.

End point type	Secondary
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End point timeframe:

Up to 14 days

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint was planned to be analyzed for specified arms only.

End point values	JNJ-70033093 25 mg Once Daily + Placebo	JNJ-70033093 50 mg once daily + Placebo	JNJ-70033093 25 mg + Placebo Twice daily (BID)	JNJ-70033093 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	150	148	148
Units: unitless				
geometric mean (geometric coefficient of variation)	99999 ($\pm$ 99999)	0.0133 ($\pm$ 863.1)	99999 ($\pm$ 99999)	0.0136 ($\pm$ 854.4)

End point values	JNJ-70033093 200 mg Once Daily + Placebo	JNJ-70033093 100 mg + Placebo BID	JNJ-70033093 200 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	147	149	148	
Units: unitless				
geometric mean (geometric coefficient of variation)	0.00680 ($\pm$ 1212.4)	0.00671 ($\pm$ 1220.7)	0.00676 ($\pm$ 0.00676)	

Statistical analyses

No statistical analyses for this end point

Secondary: Relationship between JNJ-70033093 Dose Levels with Minimal Bleeding Events

End point title	Relationship between JNJ-70033093 Dose Levels with Minimal Bleeding Events ^[6]
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End point description:

Relationship between JNJ-70033093 dose levels with minimal bleeding events was determined using a MCP-Mod approach. The PK analysis set consisted of subjects who received at least 1 dose of milvexian and had at least one valid blood sample drawn for PK analysis. Here "99999" indicates that data was not available as there were no minimal bleeding events.

End point type	Secondary
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End point timeframe:

Up to 14 days

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Endpoint was planned to be analyzed for specified arms only.

End point values	JNJ-70033093 25 mg Once Daily + Placebo	JNJ-70033093 50 mg once daily + Placebo	JNJ-70033093 25 mg + Placebo Twice daily (BID)	JNJ-70033093 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	150	150	148
Units: unitless				
geometric mean (geometric coefficient of variation)	99999 ($\pm$ 99999)	0.0533 ($\pm$ 422.7)	0.0135 ($\pm$ 857.3)	0.0476 ($\pm$ 448.7)

End point values	JNJ-70033093 200 mg Once Daily + Placebo	JNJ-70033093 100 mg + Placebo BID	JNJ-70033093 200 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	147	149	148	
Units: unitless				
geometric mean (geometric coefficient of variation)	0.0612 ($\pm$ 392.9)	0.0470 ($\pm$ 451.9)	0.0338 ($\pm$ 536.6)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 6 weeks

Adverse event reporting additional description:

The safety analysis set is a subset of the intent to treat (ITT) analysis set, consisting of all ITT participants who received at least 1 dose (partial or complete) of study drug.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.1
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Reporting groups

Reporting group title	JNJ-70033093 25 mg Once Daily + Placebo
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Reporting group description:

Subjects received JNJ-70033093 25 mg (1*25 mg capsule) once daily and 1 placebo capsule in the morning and 2 placebo capsules in the evening, orally for 10 to 14 postoperative days.

Reporting group title	JNJ-70033093 50 mg once daily + Placebo
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Reporting group description:

Subjects received JNJ-70033093 50 mg (2*25 mg capsules in the morning) once daily and 2 placebo capsules in the evening, orally for 10 to 14 postoperative days.

Reporting group title	JNJ-70033093 25 mg + Placebo Twice daily (BID)
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Reporting group description:

Subjects received JNJ-70033093 25 milligram (mg) (1*25 mg capsule) and 1 placebo capsule twice daily (BID), orally for 10 to 14 postoperative days.

Reporting group title	JNJ-70033093 50 mg BID
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Reporting group description:

Subjects received JNJ-70033093 50 mg (2*25 mg capsules) BID orally for 10 to 14 postoperative days.

Reporting group title	JNJ-70033093 200 mg Once Daily + Placebo
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Reporting group description:

Subjects received JNJ-70033093 200 mg (2*100 mg capsules in the morning) once daily and 2 placebo capsules in the evening, orally for 10 to 14 postoperative days.

Reporting group title	JNJ-70033093 100 mg + Placebo BID
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Reporting group description:

Subjects received JNJ-70033093 100 mg (1*100 mg capsule) and 1 placebo capsule BID orally for 10 to 14 postoperative days.

Reporting group title	JNJ-70033093 200 mg BID
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Reporting group description:

Subjects received JNJ-70033093 200 mg (2*100 mg capsules) BID orally for 10 to 14 postoperative days.

Reporting group title	Enoxaparin 40 mg Once Daily
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Reporting group description:

Subjects received enoxaparin 40 mg once daily subcutaneously for 10 to 14 postoperative days.

Serious adverse events	JNJ-70033093 25 mg Once Daily + Placebo	JNJ-70033093 50 mg once daily + Placebo	JNJ-70033093 25 mg + Placebo Twice daily (BID)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 33 (3.03%)	2 / 150 (1.33%)	5 / 148 (3.38%)
number of deaths (all causes)	0	0	0

number of deaths resulting from adverse events			
Investigations			
Cardiovascular Evaluation			
subjects affected / exposed	0 / 33 (0.00%)	0 / 150 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Full Blood Count Decreased			
subjects affected / exposed	0 / 33 (0.00%)	0 / 150 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoglobin Decreased			
subjects affected / exposed	0 / 33 (0.00%)	1 / 150 (0.67%)	0 / 148 (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
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 33 (0.00%)	0 / 150 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Craniocerebral Injury			
subjects affected / exposed	0 / 33 (0.00%)	0 / 150 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periprosthetic Fracture			
subjects affected / exposed	0 / 33 (0.00%)	0 / 150 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural Haemorrhage			
subjects affected / exposed	0 / 33 (0.00%)	0 / 150 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep Vein Thrombosis			

subjects affected / exposed	1 / 33 (3.03%)	1 / 150 (0.67%)	1 / 148 (0.68%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral Artery Embolism			
subjects affected / exposed	0 / 33 (0.00%)	0 / 150 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma			
subjects affected / exposed	0 / 33 (0.00%)	0 / 150 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 150 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial Fibrillation			
subjects affected / exposed	0 / 33 (0.00%)	0 / 150 (0.00%)	1 / 148 (0.68%)
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			
Ischaemic Stroke			
subjects affected / exposed	0 / 33 (0.00%)	0 / 150 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Non-Cardiac Chest Pain			
subjects affected / exposed	0 / 33 (0.00%)	0 / 150 (0.00%)	1 / 148 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			

subjects affected / exposed	0 / 33 (0.00%)	0 / 150 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 33 (0.00%)	0 / 150 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 33 (0.00%)	0 / 150 (0.00%)	1 / 148 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 150 (0.00%)	1 / 148 (0.68%)
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	0 / 33 (0.00%)	0 / 150 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory Failure			
subjects affected / exposed	0 / 33 (0.00%)	0 / 150 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 150 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Compartment Syndrome			
subjects affected / exposed	0 / 33 (0.00%)	0 / 150 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Rhabdomyolysis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 150 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Covid-19			
subjects affected / exposed	0 / 33 (0.00%)	0 / 150 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device Related Infection			
subjects affected / exposed	0 / 33 (0.00%)	0 / 150 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 150 (0.00%)	1 / 148 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound Infection			
subjects affected / exposed	0 / 33 (0.00%)	0 / 150 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 150 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electrolyte Imbalance			
subjects affected / exposed	0 / 33 (0.00%)	0 / 150 (0.00%)	0 / 148 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Serious adverse events			
	JNJ-70033093 50 mg BID	JNJ-70033093 200 mg Once Daily + Placebo	JNJ-70033093 100 mg + Placebo BID
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 148 (3.38%)	2 / 147 (1.36%)	5 / 149 (3.36%)

number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Investigations			
Cardiovascular Evaluation			
subjects affected / exposed	0 / 148 (0.00%)	1 / 147 (0.68%)	0 / 149 (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
Full Blood Count Decreased			
subjects affected / exposed	0 / 148 (0.00%)	0 / 147 (0.00%)	1 / 149 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoglobin Decreased			
subjects affected / exposed	0 / 148 (0.00%)	0 / 147 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 148 (0.68%)	0 / 147 (0.00%)	0 / 149 (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
Craniocerebral Injury			
subjects affected / exposed	0 / 148 (0.00%)	0 / 147 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periprosthetic Fracture			
subjects affected / exposed	1 / 148 (0.68%)	0 / 147 (0.00%)	0 / 149 (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
Subdural Haemorrhage			
subjects affected / exposed	0 / 148 (0.00%)	0 / 147 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep Vein Thrombosis			

subjects affected / exposed	1 / 148 (0.68%)	0 / 147 (0.00%)	2 / 149 (1.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral Artery Embolism			
subjects affected / exposed	1 / 148 (0.68%)	0 / 147 (0.00%)	0 / 149 (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
Haematoma			
subjects affected / exposed	0 / 148 (0.00%)	0 / 147 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	0 / 148 (0.00%)	0 / 147 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial Fibrillation			
subjects affected / exposed	0 / 148 (0.00%)	0 / 147 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Ischaemic Stroke			
subjects affected / exposed	0 / 148 (0.00%)	0 / 147 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Non-Cardiac Chest Pain			
subjects affected / exposed	0 / 148 (0.00%)	0 / 147 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			

subjects affected / exposed	0 / 148 (0.00%)	0 / 147 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 148 (0.00%)	1 / 147 (0.68%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 148 (0.00%)	0 / 147 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 148 (0.00%)	0 / 147 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary Embolism			
subjects affected / exposed	1 / 148 (0.68%)	0 / 147 (0.00%)	1 / 149 (0.67%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory Failure			
subjects affected / exposed	0 / 148 (0.00%)	0 / 147 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 148 (0.00%)	0 / 147 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Compartment Syndrome			
subjects affected / exposed	1 / 148 (0.68%)	0 / 147 (0.00%)	0 / 149 (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

Rhabdomyolysis			
subjects affected / exposed	1 / 148 (0.68%)	0 / 147 (0.00%)	0 / 149 (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
Infections and infestations			
Covid-19			
subjects affected / exposed	0 / 148 (0.00%)	0 / 147 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device Related Infection			
subjects affected / exposed	0 / 148 (0.00%)	0 / 147 (0.00%)	1 / 149 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 148 (0.00%)	0 / 147 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound Infection			
subjects affected / exposed	0 / 148 (0.00%)	0 / 147 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 148 (0.00%)	0 / 147 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electrolyte Imbalance			
subjects affected / exposed	0 / 148 (0.00%)	0 / 147 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Serious adverse events			
	JNJ-70033093 200 mg BID	Enoxaparin 40 mg Once Daily	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 148 (1.35%)	11 / 296 (3.72%)	
number of deaths (all causes)	0	1	

number of deaths resulting from adverse events			
Investigations			
Cardiovascular Evaluation			
subjects affected / exposed	0 / 148 (0.00%)	0 / 296 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Full Blood Count Decreased			
subjects affected / exposed	0 / 148 (0.00%)	0 / 296 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoglobin Decreased			
subjects affected / exposed	0 / 148 (0.00%)	0 / 296 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 148 (0.00%)	0 / 296 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Craniocerebral Injury			
subjects affected / exposed	0 / 148 (0.00%)	1 / 296 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Periprosthetic Fracture			
subjects affected / exposed	0 / 148 (0.00%)	0 / 296 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural Haemorrhage			
subjects affected / exposed	0 / 148 (0.00%)	1 / 296 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep Vein Thrombosis			

subjects affected / exposed	0 / 148 (0.00%)	0 / 296 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral Artery Embolism			
subjects affected / exposed	0 / 148 (0.00%)	0 / 296 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma			
subjects affected / exposed	0 / 148 (0.00%)	1 / 296 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			
subjects affected / exposed	0 / 148 (0.00%)	1 / 296 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial Fibrillation			
subjects affected / exposed	0 / 148 (0.00%)	0 / 296 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Ischaemic Stroke			
subjects affected / exposed	1 / 148 (0.68%)	0 / 296 (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			
Non-Cardiac Chest Pain			
subjects affected / exposed	0 / 148 (0.00%)	0 / 296 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			

subjects affected / exposed	0 / 148 (0.00%)	1 / 296 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 148 (0.00%)	0 / 296 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 148 (0.00%)	0 / 296 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	0 / 148 (0.00%)	0 / 296 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary Embolism			
subjects affected / exposed	0 / 148 (0.00%)	1 / 296 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory Failure			
subjects affected / exposed	0 / 148 (0.00%)	1 / 296 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 148 (0.68%)	0 / 296 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Compartment Syndrome			
subjects affected / exposed	0 / 148 (0.00%)	0 / 296 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Rhabdomyolysis			
subjects affected / exposed	0 / 148 (0.00%)	0 / 296 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Covid-19			
subjects affected / exposed	0 / 148 (0.00%)	1 / 296 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device Related Infection			
subjects affected / exposed	0 / 148 (0.00%)	0 / 296 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 148 (0.00%)	0 / 296 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound Infection			
subjects affected / exposed	0 / 148 (0.00%)	1 / 296 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 148 (0.00%)	1 / 296 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrolyte Imbalance			
subjects affected / exposed	0 / 148 (0.00%)	1 / 296 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	JNJ-70033093 25 mg Once Daily + Placebo	JNJ-70033093 50 mg once daily + Placebo	JNJ-70033093 25 mg + Placebo Twice daily (BID)
Total subjects affected by non-serious adverse events subjects affected / exposed	0 / 33 (0.00%)	6 / 150 (4.00%)	9 / 148 (6.08%)
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	6 / 150 (4.00%) 6	9 / 148 (6.08%) 9

Non-serious adverse events	JNJ-70033093 50 mg BID	JNJ-70033093 200 mg Once Daily + Placebo	JNJ-70033093 100 mg + Placebo BID
Total subjects affected by non-serious adverse events subjects affected / exposed	8 / 148 (5.41%)	3 / 147 (2.04%)	4 / 149 (2.68%)
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all)	8 / 148 (5.41%) 8	3 / 147 (2.04%) 3	4 / 149 (2.68%) 4

Non-serious adverse events	JNJ-70033093 200 mg BID	Enoxaparin 40 mg Once Daily	
Total subjects affected by non-serious adverse events subjects affected / exposed	3 / 148 (2.03%)	17 / 296 (5.74%)	
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all)	3 / 148 (2.03%) 3	17 / 296 (5.74%) 17	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 September 2019	The overall reasons for the amendment was to modify the study design with regards to the planned and optional doses and to remove the option for preoperative dosing and some minor editorial changes.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

No notable study limitations were identified by the sponsor.

Notes: