



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 |
|-----------------------|-----------------|

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 |
|------------------|---|

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 |
|------------------|-----------------------------------|

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 |
|------------------|-------------------------|

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 |
|------------------|-----------------------------|

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 |
|------------------------|-----------------|------------------|------------------|
|------------------------|-----------------|------------------|------------------|

| | 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 |
|-------------------------|-----------------------------|--------------------------|----------------------------|--------------------------------|
|-------------------------|-----------------------------|--------------------------|----------------------------|--------------------------------|

| | 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) |
|-----------------|--|

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 |
|----------------|-----------|

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 |
|-----------------|--|

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 |
|----------------|-----------|

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) |
|-----------------|---|

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 |
|----------------|-----------|

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) |
|-----------------|---|

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 |
|----------------|-----------|

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) |
|-----------------|--|

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 |
|----------------|-----------|

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) |
|-----------------|--|

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 |
|----------------|-----------|

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) |
|-----------------|---|

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 |
|----------------|-----------|

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 |
|-----------------|--|

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 |
|----------------|-----------|

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) |
|-----------------|--|

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 |
|----------------|-----------|

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 |
|-------------|---|---|---|---|

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 |
|-----------------|--|

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 |
|----------------|-----------|

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 |
|------------------|-----------------------------|--------------------------|----------------------------|--------------------------------|
|------------------|-----------------------------|--------------------------|----------------------------|--------------------------------|

| | 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) |
|-----------------|--|

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 |
|----------------|-----------|

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 |
|-----------------|---|

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 |
|----------------|-----------|

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 |
|-----------------|---|

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 |
|----------------|-----------|

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 |
|-----------------|--|

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 |
|----------------|-----------|

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 |
| 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 |
| 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 |
| 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 |
| 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 |
|-----------------|--|

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 |
|----------------|-----------|

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] |
|-----------------|--|

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 |
|----------------|-----------|

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] |
|-----------------|---|

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 |
|----------------|-----------|

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] |
|-----------------|--|

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 |
|----------------|-----------|

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] |
|-----------------|---|

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 |
|----------------|-----------|

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 |
|-----------------|----------------|

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 23.1 |
|--------------------|------|

Reporting groups

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

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 |
|-----------------------|---|

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 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 |
|-----------------------|------------------------|

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.

| 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: