



Clinical trial results:

A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Proof of Concept

Study (section A) with a conditional dose finding follow up (Section B) to Evaluate the

Efficacy on Cervical ripening, Safety, Tolerability and dose response of Subcutaneously

Administered Tafoxiparin in Term Pregnant, Nulliparous Women with an unripe cervix

undergoing Labor Induction.

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2019-000620-17 |
| Trial protocol | SE FI |
| Global end of trial date | 31 December 2022 |

Results information

| | |
|--------------------------------|-------------------|
| Result version number | v1 (current) |
| This version publication date | 20 September 2024 |
| First version publication date | 20 September 2024 |

Trial information

Trial identification

| | |
|-----------------------|-------|
| Sponsor protocol code | PPL17 |
|-----------------------|-------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04000438 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|-----------------------------------------------------------------------------------------------------------|
| Sponsor organisation name | Dilafor AB |
| Sponsor organisation address | Fogdevreten 2A, Solna, Sweden, SE-171 65 |
| Public contact | Gunvor Ekman-Ordeberg, Chief Medical Officer, Dilafor AB, 46 706083111, Gunvor.ekman-ordeberg@dilafor.com |
| Scientific contact | Gunvor Ekman-Ordeberg, Chief Medical Officer, Dilafor AB, 46 706083111, Gunvor.ekman-ordeberg@dilafor.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 | 29 February 2024 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 31 December 2022 |
| Global end of trial reached? | Yes |
| Global end of trial date | 31 December 2022 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To assess the Efficacy of tafoxiparin on cervical ripening

Protection of trial subjects:

The study was performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki (Ethical principles for Medical Research Involving Human Subjects, revised by the World Medical Association's (WMA) General Assembly, Fortaleza, Brazil, October 2013), 21 CFR - Part 50 (Protection of human subjects), 21 CFR - Part 54 (Financial Disclosure by Clinical Investigator) and 21 CFR - Part 312 (Investigational New Drug), and are consistent with the International Conference of Harmonization of Good Clinical Practice (ICH-GCP) (E6-R2, Step 4) guidelines.

Informed consent was obtained from all healthy volunteers prior to initiation of the study. All subjects participating in the study were thoroughly informed about the study during Screening, given the opportunity to ask study-related questions to the Investigator and given sufficient time to review the patient information sheet. Following this procedure, all subjects wishing to participate in the study were asked to sign and date the ICF. The Investigator did also sign and date the ICF to confirm that the subject has been thoroughly informed about the study.

Background therapy: -

Evidence for comparator: -

| | |
|-----------------------------------------------------------|-------------|
| Actual start date of recruitment | 01 May 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 | Sweden: 127 |
| Country: Number of subjects enrolled | Finland: 238 |
| Worldwide total number of subjects | 365 |
| EEA total number of subjects | 365 |

Notes:

Subjects enrolled per age group

| | |
|----------------------------------------|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 | 0 |

| | |
|------------------------------------------|-----|
| wk | |
| 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) | 365 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

As the participating clinics will consist of maternity wards, potential subjects will present to the clinic as a part of standard clinical practice. All women must be examined to check the cervical state before information. After having had time to review the nature of the study, they will have the opportunity to ask questions.

Pre-assignment

Screening details: -

Pre-assignment period milestones

| | |
|------------------------------|-----|
| Number of subjects started | 365 |
| Number of subjects completed | 348 |

Pre-assignment subject non-completion reasons

| | |
|----------------------------|--------------------------------------|
| Reason: Number of subjects | Did not pass inclusion/exclusion: 17 |
|----------------------------|--------------------------------------|

Period 1

| | |
|------------------------------|---------------------------------------------|
| Period 1 title | Overall trial - Part A & B (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor |

Arms

| | |
|------------------------------|-----------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Cohort 1 - IMP 300 mg |

Arm description:

IMP tafoxiparin 300 mg: 150 mg/ml of tafoxiparin in 0.015 M phosphate buffer. 1ml each from two vials injected as separate SC injections in the abdominal or hip region.

| | |
|----------------------------------------|--------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | tafoxiparin |
| Investigational medicinal product code | PPL17 |
| Other name | |
| Pharmaceutical forms | Solution for injection in vial |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

IMP tafoxiparin 300 mg: 150 mg/ml of tafoxiparin in 0.015 M phosphate buffer.
1ml each from two vials injected as separate SC injections in the abdominal or hip region.

| | |
|------------------|--------------------|
| Arm title | Cohort 2 - Placebo |
|------------------|--------------------|

Arm description:

Placebo: 9 mg/ml of NaCl solution. 1.0 ml each from two vials injected as separate SC injections in the abdominal or hip region. The placebo saline solution was indistinguishable from the active solutions in appearance, smell and packaging.

| | |
|----------------------------------------|--------------------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | Placebo |
| Other name | |
| Pharmaceutical forms | Solution for injection in vial |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Placebo: 9 mg/ml of NaCl solution. 1.0 ml each from two vials injected as separate SC injections in the abdominal or hip region.

The placebo saline solution was indistinguishable from the active solutions in appearance, smell and packaging.

| | |
|------------------|-----------------------|
| Arm title | Cohort 3 - IMP 150 mg |
|------------------|-----------------------|

Arm description:

IMP tafoxiparin 150 mg: 150 mg/ml of tafoxiparin in 0.015 M phosphate buffer. 0.5ml each from two vials injected as separate SC injections in the abdominal or hip region.

| | |
|----------------------------------------|--------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | tafoxiparin |
| Investigational medicinal product code | PPL17 |
| Other name | |
| Pharmaceutical forms | Solution for injection in vial |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

IMP tafoxiparin 150 mg: 150 mg/ml of tafoxiparin in 0.015 M phosphate buffer. 0.5ml each from two vials injected as separate SC injections in the abdominal or hip region.

| | |
|------------------|----------------------|
| Arm title | Cohort 4 - IMP 75 mg |
|------------------|----------------------|

Arm description:

IMP tafoxiparin 75 mg: 150 mg/ml of tafoxiparin in 0.015 M phosphate buffer and placebo solution 9 mg/ml of sodium chloride (NaCl) solution. 0.5ml each from one vial containing 150 mg/ml of tafoxiparin and one vial containing placebo, injected as separate SC injections in the abdominal or hip region.

| | |
|----------------------------------------|--------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | tafoxiparin |
| Investigational medicinal product code | PPL17 |
| Other name | |
| Pharmaceutical forms | Solution for injection in vial |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

IMP tafoxiparin 75 mg: 150 mg/ml of tafoxiparin in 0.015 M phosphate buffer and placebo solution 9 mg/ml of sodium chloride (NaCl) solution. 0.5ml each from one vial containing 150 mg/ml of tafoxiparin and one vial containing placebo, injected as separate SC injections in the abdominal or hip region.

| Number of subjects in period 1^[1] | Cohort 1 - IMP 300 mg | Cohort 2 - Placebo | Cohort 3 - IMP 150 mg |
|-----------------------------------------------------|-----------------------|--------------------|-----------------------|
| Started | 91 | 89 | 85 |
| Completed | 90 | 86 | 85 |
| Not completed | 1 | 3 | 0 |
| Consent withdrawn by subject | - | 2 | - |
| Reluctance to continue with the study drug | - | 1 | - |
| None stated | - | - | - |
| Hyponatremia, gestational hyperlipidemia | 1 | - | - |

| Number of subjects in period 1^[1] | Cohort 4 - IMP 75 mg |
|-----------------------------------------------------|----------------------|
| Started | 83 |

| | |
|--------------------------------------------|----|
| Completed | 82 |
| Not completed | 1 |
| Consent withdrawn by subject | - |
| Reluctance to continue with the study drug | - |
| None stated | 1 |
| Hyponatremia, gestational hyperlipidemia | - |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: As per protocol the sponsor had the option to replace subjects who were withdrawn from study prior receiving IMP. See study report section 9.3.3

Baseline characteristics

Reporting groups

| | |
|-----------------------|-----------------------|
| Reporting group title | Cohort 1 - IMP 300 mg |
|-----------------------|-----------------------|

Reporting group description:

IMP tafoxiparin 300 mg: 150 mg/ml of tafoxiparin in 0.015 M phosphate buffer. 1ml each from two vials injected as separate SC injections in the abdominal or hip region.

| | |
|-----------------------|--------------------|
| Reporting group title | Cohort 2 - Placebo |
|-----------------------|--------------------|

Reporting group description:

Placebo: 9 mg/ml of NaCl solution. 1.0 ml each from two vials injected as separate SC injections in the abdominal or hip region. The placebo saline solution was indistinguishable from the active solutions in appearance, smell and packaging.

| | |
|-----------------------|-----------------------|
| Reporting group title | Cohort 3 - IMP 150 mg |
|-----------------------|-----------------------|

Reporting group description:

IMP tafoxiparin 150 mg: 150 mg/ml of tafoxiparin in 0.015 M phosphate buffer. 0.5ml each from two vials injected as separate SC injections in the abdominal or hip region.

| | |
|-----------------------|----------------------|
| Reporting group title | Cohort 4 - IMP 75 mg |
|-----------------------|----------------------|

Reporting group description:

IMP tafoxiparin 75 mg: 150 mg/ml of tafoxiparin in 0.015 M phosphate buffer and placebo solution 9 mg/ml of sodium chloride (NaCl) solution. 0.5ml each from one vial containing 150 mg/ml of tafoxiparin and one vial containing placebo, injected as separate SC injections in the abdominal or hip region.

| Reporting group values | Cohort 1 - IMP 300 mg | Cohort 2 - Placebo | Cohort 3 - IMP 150 mg |
|------------------------|-----------------------|--------------------|-----------------------|
| Number of subjects | 91 | 89 | 85 |
| Age categorical | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 91 | 89 | 85 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 31.2 | 31.3 | 31.4 |
| standard deviation | ± 4.34 | ± 5.07 | ± 4.22 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 91 | 89 | 85 |
| Male | 0 | 0 | 0 |

| Reporting group values | Cohort 4 - IMP 75 mg | Total | |
|------------------------|----------------------|-------|--|
| Number of subjects | 83 | 348 | |
| Age categorical | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 83 | 348 | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 31.6 | - | |
| standard deviation | ± 5.28 | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 83 | 348 | |
| Male | 0 | 0 | |

End points

End points reporting groups

| | |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| Reporting group title | Cohort 1 - IMP 300 mg |
| Reporting group description: IMP tafoxiparin 300 mg: 150 mg/ml of tafoxiparin in 0.015 M phosphate buffer. 1ml each from two vials injected as separate SC injections in the abdominal or hip region. | |
| Reporting group title | Cohort 2 - Placebo |
| Reporting group description: Placebo: 9 mg/ml of NaCl solution. 1.0 ml each from two vials injected as separate SC injections in the abdominal or hip region. The placebo saline solution was indistinguishable from the active solutions in appearance, smell and packaging. | |
| Reporting group title | Cohort 3 - IMP 150 mg |
| Reporting group description: IMP tafoxiparin 150 mg: 150 mg/ml of tafoxiparin in 0.015 M phosphate buffer. 0.5ml each from two vials injected as separate SC injections in the abdominal or hip region. | |
| Reporting group title | Cohort 4 - IMP 75 mg |
| Reporting group description: IMP tafoxiparin 75 mg: 150 mg/ml of tafoxiparin in 0.015 M phosphate buffer and placebo solution 9 mg/ml of sodium chloride (NaCl) solution. 0.5ml each from one vial containing 150 mg/ml of tafoxiparin and one vial containing placebo, injected as separate SC injections in the abdominal or hip region. | |

Primary: Cervical ripening rate during up to the first seven days of treatment, measured by Bishop Score - Intercept

| | |
|---------------------------------------|-------------------------------------------------------------------------------------------------------------|
| End point title | Cervical ripening rate during up to the first seven days of treatment, measured by Bishop Score - Intercept |
| End point description: | |
| End point type | Primary |
| End point timeframe: Up to 7 days. | |

| End point values | Cohort 1 - IMP 300 mg | Cohort 2 - Placebo | Cohort 3 - IMP 150 mg | Cohort 4 - IMP 75 mg |
|--------------------------------------|-----------------------|--------------------|-----------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 91 | 88 | 85 | 83 |
| Units: Bishop Score | | | | |
| arithmetic mean (standard deviation) | 2.61 (± 0.299) | 2.42 (± 0.305) | 2.34 (± 0.295) | 2.14 (± 0.309) |

Statistical analyses

| | |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------|
| Statistical analysis title | Primary endpoint - Main statistical analyses |
| Statistical analysis description: Main statistical analyses used for the evaluation of primary and secondary efficacy endpoints, including Linear Mixed Model, ANCOVA, Logistic regression, Weibull models and Cox regression was performed with center and treatment included as covariates. Hence the evaluation of treatment effect was adjusted for center. | |

| | |
|-----------------------------------------|-------------------------------------------------------------------------------------------|
| Comparison groups | Cohort 2 - Placebo v Cohort 1 - IMP 300 mg v Cohort 3 - IMP 150 mg v Cohort 4 - IMP 75 mg |
| Number of subjects included in analysis | 347 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.05 |
| Method | ANCOVA |

Primary: Cervical ripening rate during up to the first seven days of treatment, measured by Bishop Score - Slope

| | |
|---------------------------------------|---------------------------------------------------------------------------------------------------------|
| End point title | Cervical ripening rate during up to the first seven days of treatment, measured by Bishop Score - Slope |
| End point description: | |
| End point type | Primary |
| End point timeframe: up to 7 days. | |

| End point values | Cohort 1 - IMP 300 mg | Cohort 2 - Placebo | Cohort 3 - IMP 150 mg | Cohort 4 - IMP 75 mg |
|--------------------------------------|-----------------------|--------------------|-----------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 91 | 89 | 85 | 83 |
| Units: Bishop Score | | | | |
| arithmetic mean (standard deviation) | 0.86 (± 0.062) | 0.62 (± 0.060) | 0.81 (± 0.062) | 0.78 (± 0.061) |

Statistical analyses

| | |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------|
| Statistical analysis title | Primary endpoint - Main statistical analyses |
| Statistical analysis description: | |
| Main statistical analyses used for the evaluation of primary and secondary efficacy endpoints, including Linear Mixed Model, ANCOVA, Logistic regression, Weibull models and Cox regression was performed with center and treatment included as covariates. Hence the evaluation of treatment effect was adjusted for center. | |
| Comparison groups | Cohort 1 - IMP 300 mg v Cohort 2 - Placebo v Cohort 3 - IMP 150 mg v Cohort 4 - IMP 75 mg |
| Number of subjects included in analysis | 348 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.05 |
| Method | ANCOVA |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose to until discharge from hospital.

Adverse event reporting additional description:

During labor and post-partum, this definition is also applicable for the infant child.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 25.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-----------------------|
| Reporting group title | Cohort 1 - IMP 300 mg |
|-----------------------|-----------------------|

Reporting group description:

IMP tafoxiparin 300 mg: 150 mg/ml of tafoxiparin in 0.015 M phosphate buffer. 1ml each from two vials injected as separate SC injections in the abdominal or hip region.

| | |
|-----------------------|--------------------|
| Reporting group title | Cohort 2 - Placebo |
|-----------------------|--------------------|

Reporting group description:

Placebo: 9 mg/ml of NaCl solution. 1.0 ml each from two vials injected as separate SC injections in the abdominal or hip region. The placebo saline solution was indistinguishable from the active solutions in appearance, smell and packaging.

| | |
|-----------------------|-----------------------|
| Reporting group title | Cohort 3 - IMP 150 mg |
|-----------------------|-----------------------|

Reporting group description:

IMP tafoxiparin 150 mg: 150 mg/ml of tafoxiparin in 0.015 M phosphate buffer. 0.5ml each from two vials injected as separate SC injections in the abdominal or hip region.

| | |
|-----------------------|----------------------|
| Reporting group title | Cohort 4 - IMP 75 mg |
|-----------------------|----------------------|

Reporting group description:

IMP tafoxiparin 75 mg: 150 mg/ml of tafoxiparin in 0.015 M phosphate buffer and placebo solution 9 mg/ml of sodium chloride (NaCl) solution. 0.5ml each from one vial containing 150 mg/ml of tafoxiparin and one vial containing placebo, injected as separate SC injections in the abdominal or hip region.

| Serious adverse events | Cohort 1 - IMP 300 mg | Cohort 2 - Placebo | Cohort 3 - IMP 150 mg |
|---------------------------------------------------|-----------------------|--------------------|-----------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 6 / 91 (6.59%) | 2 / 88 (2.27%) | 7 / 85 (8.24%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Investigations | | | |
| Total bile acids increased | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 1 / 88 (1.14%) | 0 / 85 (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 |
| Hepatic enzyme increased | | | |

| | | | |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 1 / 85 (1.18%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Procedural hemorrhage | | | |
| subjects affected / exposed | 1 / 91 (1.10%) | 0 / 88 (0.00%) | 0 / 85 (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 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 91 (1.10%) | 0 / 88 (0.00%) | 0 / 85 (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 |
| Pregnancy, puerperium and perinatal conditions | | | |
| Postpartum haemorrhage | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 1 / 85 (1.18%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| bradycardia fetal | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 1 / 85 (1.18%) |
| 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 | | | |
| Procedural headache | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 0 / 85 (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 |
| Blood and lymphatic system disorders | | | |
| Heparin-induced thrombocytopenia | | | |
| subjects affected / exposed | 2 / 91 (2.20%) | 0 / 88 (0.00%) | 1 / 85 (1.18%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombocytopenia | | | |

| | | | |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 1 / 85 (1.18%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 1 / 85 (1.18%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Amniotic cavity infection | | | |
| subjects affected / exposed | 2 / 91 (2.20%) | 0 / 88 (0.00%) | 1 / 85 (1.18%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 1 / 85 (1.18%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Postpartum sepsis | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 1 / 88 (1.14%) | 0 / 85 (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 |

| | | | |
|---------------------------------------------------|----------------------|--|--|
| Serious adverse events | Cohort 4 - IMP 75 mg | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 83 (2.41%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | | | |
| Investigations | | | |
| Total bile acids increased | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatic enzyme increased | | | |

| | | | |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Procedural hemorrhage | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pregnancy, puerperium and perinatal conditions | | | |
| Postpartum haemorrhage | | | |
| subjects affected / exposed | 1 / 83 (1.20%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| bradycardia fetal | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Procedural headache | | | |
| subjects affected / exposed | 1 / 83 (1.20%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Heparin-induced thrombocytopenia | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Thrombocytopenia | | | |

| | | | |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Amniotic cavity infection | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sepsis | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Postpartum sepsis | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Cohort 1 - IMP 300 mg | Cohort 2 - Placebo | Cohort 3 - IMP 150 mg |
|---------------------------------------------------------------------|-----------------------|--------------------|-----------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 52 / 91 (57.14%) | 47 / 88 (53.41%) | 54 / 85 (63.53%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Uterine leiomyoma | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 1 / 88 (1.14%) | 1 / 85 (1.18%) |
| occurrences (all) | 0 | 1 | 1 |
| Mesothelioma malignant | | | |
| subjects affected / exposed | 1 / 91 (1.10%) | 0 / 88 (0.00%) | 0 / 85 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|------------------------------------------------|----------------|----------------|------------------|
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 3 / 91 (3.30%) | 1 / 88 (1.14%) | 0 / 85 (0.00%) |
| occurrences (all) | 3 | 1 | 0 |
| Haemorrhage | | | |
| subjects affected / exposed | 2 / 91 (2.20%) | 3 / 88 (3.41%) | 0 / 85 (0.00%) |
| occurrences (all) | 2 | 3 | 0 |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 1 / 85 (1.18%) |
| occurrences (all) | 0 | 0 | 1 |
| Superficial vein thrombosis | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 1 / 85 (1.18%) |
| occurrences (all) | 0 | 0 | 1 |
| Haematoma | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 0 / 85 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vulval haematoma | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 0 / 85 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Surgical and medical procedures | | | |
| Bladder catheterisation | | | |
| subjects affected / exposed | 6 / 91 (6.59%) | 3 / 88 (3.41%) | 0 / 85 (0.00%) |
| occurrences (all) | 6 | 3 | 0 |
| Caesarean section | | | |
| subjects affected / exposed | 1 / 91 (1.10%) | 0 / 88 (0.00%) | 0 / 85 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Episiotomy | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 1 / 85 (1.18%) |
| occurrences (all) | 0 | 0 | 1 |
| Epidural anaesthesia | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 1 / 88 (1.14%) | 0 / 85 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pregnancy, puerperium and perinatal conditions | | | |
| Perineal injury | | | |
| subjects affected / exposed | 2 / 91 (2.20%) | 4 / 88 (4.55%) | 17 / 85 (20.00%) |
| occurrences (all) | 2 | 4 | 17 |

| | | | |
|--------------------------------|----------------|----------------|----------------|
| Bradycardia foetal | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 6 / 85 (7.06%) |
| occurrences (all) | 0 | 0 | 6 |
| Tachycardia foetal | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 3 / 85 (3.53%) |
| occurrences (all) | 0 | 0 | 3 |
| Postpartum haemorrhage | | | |
| subjects affected / exposed | 1 / 91 (1.10%) | 0 / 88 (0.00%) | 2 / 85 (2.35%) |
| occurrences (all) | 1 | 0 | 2 |
| Gestational hypertension | | | |
| subjects affected / exposed | 1 / 91 (1.10%) | 3 / 88 (3.41%) | 1 / 85 (1.18%) |
| occurrences (all) | 1 | 3 | 1 |
| Uterine atony | | | |
| subjects affected / exposed | 3 / 91 (3.30%) | 0 / 88 (0.00%) | 1 / 85 (1.18%) |
| occurrences (all) | 3 | 0 | 1 |
| Retained placenta or membranes | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 1 / 88 (1.14%) | 0 / 85 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Oligohydramnios | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 1 / 88 (1.14%) | 1 / 85 (1.18%) |
| occurrences (all) | 0 | 1 | 1 |
| Foetal distress syndrome | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 3 / 88 (3.41%) | 0 / 85 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Labour pain | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 2 / 85 (2.35%) |
| occurrences (all) | 0 | 0 | 2 |
| Inferior vena cava syndrome | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 1 / 85 (1.18%) |
| occurrences (all) | 0 | 0 | 1 |
| Symphysiolysis | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 1 / 85 (1.18%) |
| occurrences (all) | 0 | 0 | 1 |
| Foetal hypokinesia | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 1 / 88 (1.14%) | 1 / 85 (1.18%) |
| occurrences (all) | 0 | 1 | 1 |

| | | | |
|-----------------------------------------------------------------------------------------|----------------------|---------------------|----------------------|
| Transient tachypnoea of the newborn subjects affected / exposed occurrences (all) | 0 / 91 (0.00%) 0 | 0 / 88 (0.00%) 0 | 1 / 85 (1.18%) 1 |
| Prolonged labour subjects affected / exposed occurrences (all) | 0 / 91 (0.00%) 0 | 0 / 88 (0.00%) 0 | 0 / 85 (0.00%) 0 |
| Placental calcification subjects affected / exposed occurrences (all) | 0 / 91 (0.00%) 0 | 0 / 88 (0.00%) 0 | 1 / 85 (1.18%) 1 |
| Pelvic haematoma obstetric subjects affected / exposed occurrences (all) | 1 / 91 (1.10%) 1 | 0 / 88 (0.00%) 0 | 0 / 85 (0.00%) 0 |
| Uterine hyperstimulation subjects affected / exposed occurrences (all) | 0 / 91 (0.00%) 0 | 0 / 88 (0.00%) 0 | 0 / 85 (0.00%) 0 |
| Uterine contractions abnormal subjects affected / exposed occurrences (all) | 0 / 91 (0.00%) 0 | 1 / 88 (1.14%) 1 | 0 / 85 (0.00%) 0 |
| General disorders and administration site conditions | | | |
| Pyrexia subjects affected / exposed occurrences (all) | 8 / 91 (8.79%) 8 | 7 / 88 (7.95%) 7 | 9 / 85 (10.59%) 9 |
| Injection site pain subjects affected / exposed occurrences (all) | 8 / 91 (8.79%) 14 | 1 / 88 (1.14%) 1 | 2 / 85 (2.35%) 2 |
| Fatigue subjects affected / exposed occurrences (all) | 1 / 91 (1.10%) 1 | 0 / 88 (0.00%) 0 | 4 / 85 (4.71%) 4 |
| Injection site pruritus subjects affected / exposed occurrences (all) | 1 / 91 (1.10%) 5 | 0 / 88 (0.00%) 0 | 1 / 85 (1.18%) 1 |
| Injection site bruising subjects affected / exposed occurrences (all) | 1 / 91 (1.10%) 1 | 0 / 88 (0.00%) 0 | 3 / 85 (3.53%) 3 |
| Injection site discolouration | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 3 / 91 (3.30%) | 0 / 88 (0.00%) | 1 / 85 (1.18%) |
| occurrences (all) | 3 | 0 | 1 |
| Chills | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 1 / 88 (1.14%) | 1 / 85 (1.18%) |
| occurrences (all) | 0 | 2 | 1 |
| Injection site swelling | | | |
| subjects affected / exposed | 2 / 91 (2.20%) | 0 / 88 (0.00%) | 2 / 85 (2.35%) |
| occurrences (all) | 3 | 0 | 2 |
| Peripheral swelling | | | |
| subjects affected / exposed | 1 / 91 (1.10%) | 1 / 88 (1.14%) | 2 / 85 (2.35%) |
| occurrences (all) | 1 | 1 | 2 |
| Feeling hot | | | |
| subjects affected / exposed | 1 / 91 (1.10%) | 0 / 88 (0.00%) | 1 / 85 (1.18%) |
| occurrences (all) | 1 | 0 | 2 |
| Injection site erythema | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 2 / 85 (2.35%) |
| occurrences (all) | 0 | 0 | 2 |
| Pain | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 1 / 85 (1.18%) |
| occurrences (all) | 0 | 0 | 1 |
| Malaise | | | |
| subjects affected / exposed | 2 / 91 (2.20%) | 0 / 88 (0.00%) | 0 / 85 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Puncture site haemorrhage | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 1 / 85 (1.18%) |
| occurrences (all) | 0 | 0 | 2 |
| Injection site warmth | | | |
| subjects affected / exposed | 2 / 91 (2.20%) | 0 / 88 (0.00%) | 0 / 85 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Hyperhidrosis | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 0 / 85 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chest discomfort | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 1 / 88 (1.14%) | 0 / 85 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Asthenia | | | |

| | | | |
|-----------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 91 (0.00%) 0 | 1 / 88 (1.14%) 1 | 0 / 85 (0.00%) 0 |
| Injection site reaction subjects affected / exposed occurrences (all) | 0 / 91 (0.00%) 0 | 0 / 88 (0.00%) 0 | 1 / 85 (1.18%) 1 |
| Reproductive system and breast disorders | | | |
| Vulvovaginal injury subjects affected / exposed occurrences (all) | 2 / 91 (2.20%) 2 | 5 / 88 (5.68%) 5 | 1 / 85 (1.18%) 1 |
| Cervical discharge subjects affected / exposed occurrences (all) | 0 / 91 (0.00%) 0 | 0 / 88 (0.00%) 0 | 2 / 85 (2.35%) 3 |
| Vaginal haemorrhage subjects affected / exposed occurrences (all) | 0 / 91 (0.00%) 0 | 1 / 88 (1.14%) 1 | 0 / 85 (0.00%) 0 |
| Endometriosis subjects affected / exposed occurrences (all) | 1 / 91 (1.10%) 1 | 0 / 88 (0.00%) 0 | 0 / 85 (0.00%) 0 |
| Vaginal haematoma subjects affected / exposed occurrences (all) | 2 / 91 (2.20%) 2 | 0 / 88 (0.00%) 0 | 0 / 85 (0.00%) 0 |
| Pelvic pain subjects affected / exposed occurrences (all) | 0 / 91 (0.00%) 0 | 0 / 88 (0.00%) 0 | 1 / 85 (1.18%) 1 |
| Vaginal discharge subjects affected / exposed occurrences (all) | 0 / 91 (0.00%) 0 | 1 / 88 (1.14%) 1 | 0 / 85 (0.00%) 0 |
| Uterine haemorrhage subjects affected / exposed occurrences (all) | 0 / 91 (0.00%) 0 | 0 / 88 (0.00%) 0 | 1 / 85 (1.18%) 1 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 1 / 91 (1.10%) 1 | 0 / 88 (0.00%) 0 | 1 / 85 (1.18%) 1 |
| Nasal congestion | | | |

| | | | |
|--------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 1 / 85 (1.18%) |
| occurrences (all) | 0 | 0 | 1 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 1 / 88 (1.14%) | 0 / 85 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Tachypnoea | | | |
| subjects affected / exposed | 1 / 91 (1.10%) | 0 / 88 (0.00%) | 0 / 85 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Cough | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 1 / 88 (1.14%) | 0 / 85 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Investigations | | | |
| Haemoglobin decreased | | | |
| subjects affected / exposed | 6 / 91 (6.59%) | 3 / 88 (3.41%) | 2 / 85 (2.35%) |
| occurrences (all) | 6 | 3 | 3 |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 1 / 91 (1.10%) | 0 / 88 (0.00%) | 2 / 85 (2.35%) |
| occurrences (all) | 1 | 0 | 2 |
| Foetal monitoring abnormal | | | |
| subjects affected / exposed | 2 / 91 (2.20%) | 1 / 88 (1.14%) | 0 / 85 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Blood lactic acid increased | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 2 / 88 (2.27%) | 0 / 85 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Blood lactate dehydrogenase abnormal | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 0 / 85 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood creatine increased | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 1 / 85 (1.18%) |
| occurrences (all) | 0 | 0 | 1 |
| Protein urine present | | | |
| subjects affected / exposed | 1 / 91 (1.10%) | 0 / 88 (0.00%) | 0 / 85 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Cardiac murmur | | | |

| | | | |
|--------------------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 91 (0.00%) 0 | 1 / 88 (1.14%) 1 | 0 / 85 (0.00%) 0 |
| Visual analogue scale subjects affected / exposed occurrences (all) | 0 / 91 (0.00%) 0 | 1 / 88 (1.14%) 1 | 0 / 85 (0.00%) 0 |
| Injury, poisoning and procedural complications | | | |
| Anal sphincter injury subjects affected / exposed occurrences (all) | 2 / 91 (2.20%) 2 | 2 / 88 (2.27%) 2 | 0 / 85 (0.00%) 0 |
| Wound dehiscence subjects affected / exposed occurrences (all) | 0 / 91 (0.00%) 0 | 0 / 88 (0.00%) 0 | 2 / 85 (2.35%) 2 |
| Contusion subjects affected / exposed occurrences (all) | 0 / 91 (0.00%) 0 | 0 / 88 (0.00%) 0 | 1 / 85 (1.18%) 1 |
| Anaesthetic complication subjects affected / exposed occurrences (all) | 0 / 91 (0.00%) 0 | 1 / 88 (1.14%) 1 | 0 / 85 (0.00%) 0 |
| Procedural haemorrhagee subjects affected / exposed occurrences (all) | 0 / 91 (0.00%) 0 | 0 / 88 (0.00%) 0 | 1 / 85 (1.18%) 1 |
| Obstetric procedure complication subjects affected / exposed occurrences (all) | 0 / 91 (0.00%) 0 | 1 / 88 (1.14%) 1 | 0 / 85 (0.00%) 0 |
| Fall subjects affected / exposed occurrences (all) | 0 / 91 (0.00%) 0 | 0 / 88 (0.00%) 0 | 1 / 85 (1.18%) 1 |
| Cardiac disorders | | | |
| Extrasystoles subjects affected / exposed occurrences (all) | 0 / 91 (0.00%) 0 | 0 / 88 (0.00%) 0 | 1 / 85 (1.18%) 1 |
| Sinus tachycardia subjects affected / exposed occurrences (all) | 0 / 91 (0.00%) 0 | 1 / 88 (1.14%) 1 | 0 / 85 (0.00%) 0 |
| Nervous system disorders | | | |

| | | | |
|--------------------------------------|----------------|----------------|----------------|
| Headache | | | |
| subjects affected / exposed | 6 / 91 (6.59%) | 5 / 88 (5.68%) | 7 / 85 (8.24%) |
| occurrences (all) | 6 | 5 | 7 |
| Dizziness | | | |
| subjects affected / exposed | 1 / 91 (1.10%) | 3 / 88 (3.41%) | 0 / 85 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 1 / 91 (1.10%) | 0 / 88 (0.00%) | 0 / 85 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Tremor | | | |
| subjects affected / exposed | 1 / 91 (1.10%) | 1 / 88 (1.14%) | 1 / 85 (1.18%) |
| occurrences (all) | 1 | 1 | 1 |
| Post lumbar puncture syndrome | | | |
| subjects affected / exposed | 1 / 91 (1.10%) | 1 / 88 (1.14%) | 0 / 85 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Head discomfort | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 1 / 88 (1.14%) | 0 / 85 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Aura | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 1 / 85 (1.18%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 91 (1.10%) | 0 / 88 (0.00%) | 6 / 85 (7.06%) |
| occurrences (all) | 1 | 0 | 6 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 91 (1.10%) | 1 / 88 (1.14%) | 0 / 85 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Thymus enlargement | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 1 / 88 (1.14%) | 0 / 85 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Leukocytosis | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 1 / 85 (1.18%) |
| occurrences (all) | 0 | 0 | 1 |
| Ear and labyrinth disorders | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| Vertigo | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 0 / 85 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tinnitus | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 1 / 85 (1.18%) |
| occurrences (all) | 0 | 0 | 1 |
| Eye disorders | | | |
| Abnormal sensation in eye | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 1 / 85 (1.18%) |
| occurrences (all) | 0 | 0 | 1 |
| Visual impairment | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 1 / 85 (1.18%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed | 2 / 91 (2.20%) | 6 / 88 (6.82%) | 6 / 85 (7.06%) |
| occurrences (all) | 3 | 6 | 7 |
| Vomiting | | | |
| subjects affected / exposed | 2 / 91 (2.20%) | 3 / 88 (3.41%) | 6 / 85 (7.06%) |
| occurrences (all) | 2 | 3 | 6 |
| Dyspepsia | | | |
| subjects affected / exposed | 2 / 91 (2.20%) | 4 / 88 (4.55%) | 0 / 85 (0.00%) |
| occurrences (all) | 2 | 4 | 0 |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 0 / 85 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 1 / 85 (1.18%) |
| occurrences (all) | 0 | 0 | 1 |
| Abdominal pain lower | | | |
| subjects affected / exposed | 1 / 91 (1.10%) | 0 / 88 (0.00%) | 0 / 85 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 0 / 85 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Salivary hypersecretion | | | |

| | | | |
|----------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 1 / 85 (1.18%) |
| occurrences (all) | 0 | 0 | 1 |
| Toothache | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 0 / 85 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Constipation | | | |
| subjects affected / exposed | 1 / 91 (1.10%) | 0 / 88 (0.00%) | 0 / 85 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Pruritus | | | |
| subjects affected / exposed | 1 / 91 (1.10%) | 2 / 88 (2.27%) | 0 / 85 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Skin discolouration | | | |
| subjects affected / exposed | 2 / 91 (2.20%) | 0 / 88 (0.00%) | 0 / 85 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Rash erythematous | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 1 / 85 (1.18%) |
| occurrences (all) | 0 | 0 | 1 |
| Urticaria | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 0 / 85 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dry skin | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 0 / 85 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Subcutaneous emphysema | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 1 / 88 (1.14%) | 0 / 85 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Skin burning sensation | | | |
| subjects affected / exposed | 1 / 91 (1.10%) | 0 / 88 (0.00%) | 0 / 85 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Erythema | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 1 / 85 (1.18%) |
| occurrences (all) | 0 | 0 | 1 |
| Renal and urinary disorders | | | |
| Urinary retention | | | |

| | | | |
|-------------------------------------------------|----------------|----------------|------------------|
| subjects affected / exposed | 6 / 91 (6.59%) | 7 / 88 (7.95%) | 10 / 85 (11.76%) |
| occurrences (all) | 6 | 8 | 10 |
| Dysuria | | | |
| subjects affected / exposed | 2 / 91 (2.20%) | 1 / 88 (1.14%) | 0 / 85 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Proteinuria | | | |
| subjects affected / exposed | 1 / 91 (1.10%) | 0 / 88 (0.00%) | 0 / 85 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Glycosuria | | | |
| subjects affected / exposed | 1 / 91 (1.10%) | 0 / 88 (0.00%) | 0 / 85 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pollakiuria | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 1 / 85 (1.18%) |
| occurrences (all) | 0 | 0 | 1 |
| Oliguria | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 1 / 85 (1.18%) |
| occurrences (all) | 0 | 0 | 1 |
| Leukocyturia | | | |
| subjects affected / exposed | 1 / 91 (1.10%) | 0 / 88 (0.00%) | 0 / 85 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 1 / 91 (1.10%) | 0 / 88 (0.00%) | 4 / 85 (4.71%) |
| occurrences (all) | 1 | 0 | 4 |
| Neck pain | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 1 / 85 (1.18%) |
| occurrences (all) | 0 | 0 | 1 |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 1 / 88 (1.14%) | 0 / 85 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 1 / 88 (1.14%) | 0 / 85 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Musculoskeletal pain | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 1 / 85 (1.18%) |
| occurrences (all) | 0 | 0 | 1 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 0 / 85 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 1 / 88 (1.14%) | 0 / 85 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 1 / 85 (1.18%) |
| occurrences (all) | 0 | 0 | 1 |
| Bone pain | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 0 / 85 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Amniotic cavity infection | | | |
| subjects affected / exposed | 1 / 91 (1.10%) | 1 / 88 (1.14%) | 1 / 85 (1.18%) |
| occurrences (all) | 1 | 1 | 1 |
| COVID-19 | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 1 / 85 (1.18%) |
| occurrences (all) | 0 | 0 | 1 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 0 / 85 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infection | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 1 / 88 (1.14%) | 0 / 85 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Bacterial vaginosis | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 0 / 88 (0.00%) | 1 / 85 (1.18%) |
| occurrences (all) | 0 | 0 | 1 |
| Rhinitis | | | |
| subjects affected / exposed | 1 / 91 (1.10%) | 0 / 88 (0.00%) | 0 / 85 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Genital herpes simplex | | | |
| subjects affected / exposed | 0 / 91 (0.00%) | 1 / 88 (1.14%) | 0 / 85 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|---------------------------------------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| Herpes virus infection subjects affected / exposed occurrences (all) | 0 / 91 (0.00%) 0 | 0 / 88 (0.00%) 0 | 0 / 85 (0.00%) 0 |
| Streptococcal sepsis subjects affected / exposed occurrences (all) | 0 / 91 (0.00%) 0 | 1 / 88 (1.14%) 1 | 0 / 85 (0.00%) 0 |
| Metabolism and nutrition disorders Hyponatraemia subjects affected / exposed occurrences (all) | 0 / 91 (0.00%) 0 | 0 / 88 (0.00%) 0 | 1 / 85 (1.18%) 1 |

| | | | |
|----------------------------------------------------------------------------------------------------------------------------------------------|----------------------|--|--|
| Non-serious adverse events | Cohort 4 - IMP 75 mg | | |
| Total subjects affected by non-serious adverse events subjects affected / exposed | 54 / 83 (65.06%) | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) Uterine leiomyoma subjects affected / exposed occurrences (all) | 0 / 83 (0.00%) 0 | | |
| Mesothelioma malignant subjects affected / exposed occurrences (all) | 0 / 83 (0.00%) 0 | | |
| Vascular disorders Hypertension subjects affected / exposed occurrences (all) | 1 / 83 (1.20%) 1 | | |
| Haemorrhage subjects affected / exposed occurrences (all) | 0 / 83 (0.00%) 0 | | |
| Epistaxis subjects affected / exposed occurrences (all) | 1 / 83 (1.20%) 1 | | |
| Superficial vein thrombosis subjects affected / exposed occurrences (all) | 0 / 83 (0.00%) 0 | | |
| Haematoma | | | |

| | | | |
|------------------------------------------------|------------------|--|--|
| subjects affected / exposed | 1 / 83 (1.20%) | | |
| occurrences (all) | 1 | | |
| Vulval haematoma | | | |
| subjects affected / exposed | 1 / 83 (1.20%) | | |
| occurrences (all) | 1 | | |
| Surgical and medical procedures | | | |
| Bladder catheterisation | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Caesarean section | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Episiotomy | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Epidural anaesthesia | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pregnancy, puerperium and perinatal conditions | | | |
| Perineal injury | | | |
| subjects affected / exposed | 21 / 83 (25.30%) | | |
| occurrences (all) | 21 | | |
| Bradycardia foetal | | | |
| subjects affected / exposed | 1 / 83 (1.20%) | | |
| occurrences (all) | 3 | | |
| Tachycardia foetal | | | |
| subjects affected / exposed | 3 / 83 (3.61%) | | |
| occurrences (all) | 3 | | |
| Postpartum haemorrhage | | | |
| subjects affected / exposed | 3 / 83 (3.61%) | | |
| occurrences (all) | 3 | | |
| Gestational hypertension | | | |
| subjects affected / exposed | 1 / 83 (1.20%) | | |
| occurrences (all) | 1 | | |
| Uterine atony | | | |

| | | | |
|-------------------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Retained placenta or membranes | | | |
| subjects affected / exposed | 3 / 83 (3.61%) | | |
| occurrences (all) | 3 | | |
| Oligohydramnios | | | |
| subjects affected / exposed | 2 / 83 (2.41%) | | |
| occurrences (all) | 2 | | |
| Foetal distress syndrome | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Labour pain | | | |
| subjects affected / exposed | 1 / 83 (1.20%) | | |
| occurrences (all) | 1 | | |
| Inferior vena cava syndrome | | | |
| subjects affected / exposed | 1 / 83 (1.20%) | | |
| occurrences (all) | 1 | | |
| Symphysiolysis | | | |
| subjects affected / exposed | 1 / 83 (1.20%) | | |
| occurrences (all) | 1 | | |
| Foetal hypokinesia | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Transient tachypnoea of the newborn | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Prolonged labour | | | |
| subjects affected / exposed | 1 / 83 (1.20%) | | |
| occurrences (all) | 1 | | |
| Placental calcification | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pelvic haematoma obstetric | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Uterine hyperstimulation | | | |

| | | | |
|------------------------------------------------------|------------------|--|--|
| subjects affected / exposed | 1 / 83 (1.20%) | | |
| occurrences (all) | 1 | | |
| Uterine contractions abnormal | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 11 / 83 (13.25%) | | |
| occurrences (all) | 11 | | |
| Injection site pain | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Fatigue | | | |
| subjects affected / exposed | 5 / 83 (6.02%) | | |
| occurrences (all) | 6 | | |
| Injection site pruritus | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Injection site bruising | | | |
| subjects affected / exposed | 1 / 83 (1.20%) | | |
| occurrences (all) | 1 | | |
| Injection site discolouration | | | |
| subjects affected / exposed | 1 / 83 (1.20%) | | |
| occurrences (all) | 1 | | |
| Chills | | | |
| subjects affected / exposed | 1 / 83 (1.20%) | | |
| occurrences (all) | 2 | | |
| Injection site swelling | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Peripheral swelling | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Feeling hot | | | |

| | | | |
|------------------------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Injection site erythema | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pain | | | |
| subjects affected / exposed | 1 / 83 (1.20%) | | |
| occurrences (all) | 1 | | |
| Malaise | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Puncture site haemorrhage | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Injection site warmth | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hyperhidrosis | | | |
| subjects affected / exposed | 1 / 83 (1.20%) | | |
| occurrences (all) | 1 | | |
| Chest discomfort | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Injection site reaction | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Reproductive system and breast disorders | | | |
| Vulvovaginal injury | | | |
| subjects affected / exposed | 1 / 83 (1.20%) | | |
| occurrences (all) | 1 | | |
| Cervical discharge | | | |

| | | | |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed | 1 / 83 (1.20%) | | |
| occurrences (all) | 1 | | |
| Vaginal haemorrhage | | | |
| subjects affected / exposed | 2 / 83 (2.41%) | | |
| occurrences (all) | 3 | | |
| Endometriosis | | | |
| subjects affected / exposed | 1 / 83 (1.20%) | | |
| occurrences (all) | 1 | | |
| Vaginal haematoma | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pelvic pain | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Vaginal discharge | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Uterine haemorrhage | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nasal congestion | | | |
| subjects affected / exposed | 1 / 83 (1.20%) | | |
| occurrences (all) | 1 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Tachypnoea | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Cough | | | |

| | | | |
|---------------------------------------------------------------------------------------------|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 0 / 83 (0.00%) 0 | | |
| Investigations | | | |
| Haemoglobin decreased subjects affected / exposed occurrences (all) | 4 / 83 (4.82%) 4 | | |
| Hepatic enzyme increased subjects affected / exposed occurrences (all) | 0 / 83 (0.00%) 0 | | |
| Foetal monitoring abnormal subjects affected / exposed occurrences (all) | 0 / 83 (0.00%) 0 | | |
| Blood lactic acid increased subjects affected / exposed occurrences (all) | 0 / 83 (0.00%) 0 | | |
| Blood lactate dehydrogenase abnormal subjects affected / exposed occurrences (all) | 1 / 83 (1.20%) 1 | | |
| Blood creatine increased subjects affected / exposed occurrences (all) | 0 / 83 (0.00%) 0 | | |
| Protein urine present subjects affected / exposed occurrences (all) | 0 / 83 (0.00%) 0 | | |
| Cardiac murmur subjects affected / exposed occurrences (all) | 0 / 83 (0.00%) 0 | | |
| Visual analogue scale subjects affected / exposed occurrences (all) | 0 / 83 (0.00%) 0 | | |
| Injury, poisoning and procedural complications | | | |
| Anal sphincter injury subjects affected / exposed occurrences (all) | 0 / 83 (0.00%) 0 | | |
| Wound dehiscence | | | |

| | | | |
|----------------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Contusion | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Anaesthetic complication | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Procedural haemorrhage | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Obstetric procedure complication | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Fall | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Cardiac disorders | | | |
| Extrasystoles | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Sinus tachycardia | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 8 / 83 (9.64%) | | |
| occurrences (all) | 10 | | |
| Dizziness | | | |
| subjects affected / exposed | 2 / 83 (2.41%) | | |
| occurrences (all) | 2 | | |
| Insomnia | | | |
| subjects affected / exposed | 2 / 83 (2.41%) | | |
| occurrences (all) | 2 | | |
| Tremor | | | |

| | | | |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|--|--|
| <p>subjects affected / exposed</p> <p>0 / 83 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> | | | |
| <p>Post lumbar puncture syndrome</p> <p>subjects affected / exposed</p> <p>0 / 83 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> | | | |
| <p>Head discomfort</p> <p>subjects affected / exposed</p> <p>0 / 83 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> | | | |
| <p>Aura</p> <p>subjects affected / exposed</p> <p>0 / 83 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> | | | |
| <p>Blood and lymphatic system disorders</p> <p>Anaemia</p> <p>subjects affected / exposed</p> <p>3 / 83 (3.61%)</p> <p>occurrences (all)</p> <p>3</p> <p>Thrombocytopenia</p> <p>subjects affected / exposed</p> <p>0 / 83 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> <p>Thymus enlargement</p> <p>subjects affected / exposed</p> <p>0 / 83 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> <p>Leukocytosis</p> <p>subjects affected / exposed</p> <p>0 / 83 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> | | | |
| <p>Ear and labyrinth disorders</p> <p>Vertigo</p> <p>subjects affected / exposed</p> <p>1 / 83 (1.20%)</p> <p>occurrences (all)</p> <p>1</p> <p>Tinnitus</p> <p>subjects affected / exposed</p> <p>0 / 83 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> | | | |
| <p>Eye disorders</p> <p>Abnormal sensation in eye</p> <p>subjects affected / exposed</p> <p>0 / 83 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> <p>Visual impairment</p> | | | |

| | | | |
|--------------------------------------------------|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 0 / 83 (0.00%) 0 | | |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed | 2 / 83 (2.41%) | | |
| occurrences (all) | 2 | | |
| Vomiting | | | |
| subjects affected / exposed | 5 / 83 (6.02%) | | |
| occurrences (all) | 5 | | |
| Dyspepsia | | | |
| subjects affected / exposed | 3 / 83 (3.61%) | | |
| occurrences (all) | 3 | | |
| Haemorrhoids | | | |
| subjects affected / exposed | 3 / 83 (3.61%) | | |
| occurrences (all) | 3 | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 83 (1.20%) | | |
| occurrences (all) | 1 | | |
| Abdominal pain lower | | | |
| subjects affected / exposed | 1 / 83 (1.20%) | | |
| occurrences (all) | 1 | | |
| Gastritis | | | |
| subjects affected / exposed | 1 / 83 (1.20%) | | |
| occurrences (all) | 1 | | |
| Salivary hypersecretion | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Toothache | | | |
| subjects affected / exposed | 1 / 83 (1.20%) | | |
| occurrences (all) | 1 | | |
| Constipation | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Pruritus | | | |

| | | | |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Skin discolouration | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rash erythematous | | | |
| subjects affected / exposed | 1 / 83 (1.20%) | | |
| occurrences (all) | 1 | | |
| Urticaria | | | |
| subjects affected / exposed | 1 / 83 (1.20%) | | |
| occurrences (all) | 1 | | |
| Dry skin | | | |
| subjects affected / exposed | 1 / 83 (1.20%) | | |
| occurrences (all) | 1 | | |
| Subcutaneous emphysema | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Skin burning sensation | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Erythema | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Renal and urinary disorders | | | |
| Urinary retention | | | |
| subjects affected / exposed | 6 / 83 (7.23%) | | |
| occurrences (all) | 6 | | |
| Dysuria | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Proteinuria | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Glycosuria | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|-------------------------------------------------|----------------|--|--|
| Pollakiuria | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Oliguria | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Leukocyturia | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 1 / 83 (1.20%) | | |
| occurrences (all) | 1 | | |
| Neck pain | | | |
| subjects affected / exposed | 1 / 83 (1.20%) | | |
| occurrences (all) | 1 | | |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Myalgia | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 1 / 83 (1.20%) | | |
| occurrences (all) | 1 | | |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Bone pain | | | |

| | | | |
|--------------------------------------------------|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 1 / 83 (1.20%) 1 | | |
| Infections and infestations | | | |
| Amniotic cavity infection | | | |
| subjects affected / exposed | 1 / 83 (1.20%) | | |
| occurrences (all) | 1 | | |
| COVID-19 | | | |
| subjects affected / exposed | 2 / 83 (2.41%) | | |
| occurrences (all) | 2 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 2 / 83 (2.41%) | | |
| occurrences (all) | 2 | | |
| Infection | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Bacterial vaginosis | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rhinitis | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Genital herpes simplex | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Herpes virus infection | | | |
| subjects affected / exposed | 1 / 83 (1.20%) | | |
| occurrences (all) | 1 | | |
| Streptococcal sepsis | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |
| Metabolism and nutrition disorders | | | |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 83 (0.00%) | | |
| occurrences (all) | 0 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 15 May 2019 | Updates were made to Inclusion and Exclusion criteria as well as corresponding examinations performed during screening and baseline. Ripe cervix was defined as: "Bishop score ≥ 6 ". Additional reasons for exceptions from reporting of SAEs during prolongation of hospitalization were updated. |
| 18 December 2020 | The following was added under section 7.2 Exclusion criteria "Any relevant condition, laboratory value or concomitant medication which, in the opinion of the investigator, makes the subject unsuitable for entry into the study." The following was added under section 7.4 Subject Withdrawal "Any subject who represents a protocol deviation may be replaced at the discretion of the Sponsor." |
| 15 January 2021 | Updates were made to the Risk-Benefit Assessment section in the protocol to include more information on the ability of treatment with tafoxiparin inducing thrombocytopenia. Additionally, blood tests were added after the fifth dose of IMP and before discharge to detect cases of thrombocytopenia. |
| 01 July 2021 | The Risk Benefit assessment and Sample Size estimation was updated following completion of Part A of the study. |
| 15 January 2022 | The use of the term "Section" was changed to the term "Part" in order to avoid confusion with the protocol sections 1, 2, 3, 4, 5, 5.1, 5.2 etc. throughout the protocol. The change was administrative and effective throughout the protocol. Additionally, blood tests were added prior to labor induction and immediately prior to any epidural anesthesia, to detect cases of thrombocytopenia. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported