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 fron 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	0 / 91 (0.00%)	0 / 88 (0.00%)	1 / 85 (1.18%)
occurrences (all)	0	0	1
Prolonged labour			
subjects affected / exposed	0 / 91 (0.00%)	0 / 88 (0.00%)	0 / 85 (0.00%)
occurrences (all)	0	0	0
Placental calcification			
subjects affected / exposed	0 / 91 (0.00%)	0 / 88 (0.00%)	1 / 85 (1.18%)
occurrences (all)	0	0	1
Pelvic haematoma obstetric			
subjects affected / exposed	1 / 91 (1.10%)	0 / 88 (0.00%)	0 / 85 (0.00%)
occurrences (all)	1	0	0
Uterine hyperstimulation			
subjects affected / exposed	0 / 91 (0.00%)	0 / 88 (0.00%)	0 / 85 (0.00%)
occurrences (all)	0	0	0
Uterine contractions abnormal			
subjects affected / exposed	0 / 91 (0.00%)	1 / 88 (1.14%)	0 / 85 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	8 / 91 (8.79%)	7 / 88 (7.95%)	9 / 85 (10.59%)
occurrences (all)	8	7	9
Injection site pain			
subjects affected / exposed	8 / 91 (8.79%)	1 / 88 (1.14%)	2 / 85 (2.35%)
occurrences (all)	14	1	2
Fatigue			
subjects affected / exposed	1 / 91 (1.10%)	0 / 88 (0.00%)	4 / 85 (4.71%)
occurrences (all)	1	0	4
Injection site pruritus			
subjects affected / exposed	1 / 91 (1.10%)	0 / 88 (0.00%)	1 / 85 (1.18%)
occurrences (all)	5	0	1
Injection site bruising			
subjects affected / exposed	1 / 91 (1.10%)	0 / 88 (0.00%)	3 / 85 (3.53%)
occurrences (all)	1	0	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	0 / 91 (0.00%)	1 / 88 (1.14%)	0 / 85 (0.00%)
occurrences (all)	0	1	0
Injection site reaction			
subjects affected / exposed	0 / 91 (0.00%)	0 / 88 (0.00%)	1 / 85 (1.18%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Vulvovaginal injury			
subjects affected / exposed	2 / 91 (2.20%)	5 / 88 (5.68%)	1 / 85 (1.18%)
occurrences (all)	2	5	1
Cervical discharge			
subjects affected / exposed	0 / 91 (0.00%)	0 / 88 (0.00%)	2 / 85 (2.35%)
occurrences (all)	0	0	3
Vaginal haemorrhage			
subjects affected / exposed	0 / 91 (0.00%)	1 / 88 (1.14%)	0 / 85 (0.00%)
occurrences (all)	0	1	0
Endometriosis			
subjects affected / exposed	1 / 91 (1.10%)	0 / 88 (0.00%)	0 / 85 (0.00%)
occurrences (all)	1	0	0
Vaginal haematoma			
subjects affected / exposed	2 / 91 (2.20%)	0 / 88 (0.00%)	0 / 85 (0.00%)
occurrences (all)	2	0	0
Pelvic pain			
subjects affected / exposed	0 / 91 (0.00%)	0 / 88 (0.00%)	1 / 85 (1.18%)
occurrences (all)	0	0	1
Vaginal discharge			
subjects affected / exposed	0 / 91 (0.00%)	1 / 88 (1.14%)	0 / 85 (0.00%)
occurrences (all)	0	1	0
Uterine haemorrhage			
subjects affected / exposed	0 / 91 (0.00%)	0 / 88 (0.00%)	1 / 85 (1.18%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 91 (1.10%)	0 / 88 (0.00%)	1 / 85 (1.18%)
occurrences (all)	1	0	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	0 / 91 (0.00%)	1 / 88 (1.14%)	0 / 85 (0.00%)
occurrences (all)	0	1	0
Visual analogue scale			
subjects affected / exposed	0 / 91 (0.00%)	1 / 88 (1.14%)	0 / 85 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Anal sphincter injury			
subjects affected / exposed	2 / 91 (2.20%)	2 / 88 (2.27%)	0 / 85 (0.00%)
occurrences (all)	2	2	0
Wound dehiscence			
subjects affected / exposed	0 / 91 (0.00%)	0 / 88 (0.00%)	2 / 85 (2.35%)
occurrences (all)	0	0	2
Contusion			
subjects affected / exposed	0 / 91 (0.00%)	0 / 88 (0.00%)	1 / 85 (1.18%)
occurrences (all)	0	0	1
Anaesthetic complication			
subjects affected / exposed	0 / 91 (0.00%)	1 / 88 (1.14%)	0 / 85 (0.00%)
occurrences (all)	0	1	0
Procedural haemorrhagee			
subjects affected / exposed	0 / 91 (0.00%)	0 / 88 (0.00%)	1 / 85 (1.18%)
occurrences (all)	0	0	1
Obstetric procedure complication			
subjects affected / exposed	0 / 91 (0.00%)	1 / 88 (1.14%)	0 / 85 (0.00%)
occurrences (all)	0	1	0
Fall			
subjects affected / exposed	0 / 91 (0.00%)	0 / 88 (0.00%)	1 / 85 (1.18%)
occurrences (all)	0	0	1
Cardiac disorders			
Extrasystoles			
subjects affected / exposed	0 / 91 (0.00%)	0 / 88 (0.00%)	1 / 85 (1.18%)
occurrences (all)	0	0	1
Sinus tachycardia			
subjects affected / exposed	0 / 91 (0.00%)	1 / 88 (1.14%)	0 / 85 (0.00%)
occurrences (all)	0	1	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	0 / 91 (0.00%)	0 / 88 (0.00%)	0 / 85 (0.00%)
occurrences (all)	0	0	0
Streptococcal sepsis			
subjects affected / exposed	0 / 91 (0.00%)	1 / 88 (1.14%)	0 / 85 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 91 (0.00%)	0 / 88 (0.00%)	1 / 85 (1.18%)
occurrences (all)	0	0	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	0 / 83 (0.00%)		
occurrences (all)	0		
Mesothelioma malignant			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 83 (1.20%)		
occurrences (all)	1		
Haemorrhage			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences (all)	0		
Epistaxis			
subjects affected / exposed	1 / 83 (1.20%)		
occurrences (all)	1		
Superficial vein thrombosis			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences (all)	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	0 / 83 (0.00%)		
occurrences (all)	0		
Investigations			
Haemoglobin decreased			
subjects affected / exposed	4 / 83 (4.82%)		
occurrences (all)	4		
Hepatic enzyme increased			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences (all)	0		
Foetal monitoring abnormal			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences (all)	0		
Blood lactic acid increased			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences (all)	0		
Blood lactate dehydrogenase abnormal			
subjects affected / exposed	1 / 83 (1.20%)		
occurrences (all)	1		
Blood creatine increased			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences (all)	0		
Protein urine present			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences (all)	0		
Cardiac murmur			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences (all)	0		
Visual analogue scale			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Anal sphincter injury			
subjects affected / exposed	0 / 83 (0.00%)		
occurrences (all)	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 haemorrhagee			
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			

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

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