



Clinical trial results:

A Single Blind, Two-Stage Dose Finding Study to Evaluate the Safety, Tolerability and Efficacy of a Single Liproca® Depot Injection into the Prostate in Patients with Localized Prostate Cancer, Assigned to Active Surveillance who are at High Risk for Disease Progression (followed by an Open Label Extension with a Repeat Injection (Optional)).

Summary

EudraCT number	2016-002504-43
Trial protocol	FI LT
Global end of trial date	06 July 2020

Results information

Result version number	v1 (current)
This version publication date	17 November 2021
First version publication date	17 November 2021

Trial information

Trial identification

Sponsor protocol code	LPC-004
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03348527
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	LIDDS AB
Sponsor organisation address	Virdings Alle 32b, Uppsala, Sweden, SE-75450
Public contact	Nina Herne, LIDDS AB, nina.herne@liddspharma.com
Scientific contact	Charlotta Gauffin, LIDDS AB, charlotta.gauffin@liddspharma.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	26 August 2020
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	06 July 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary objectives:

- To define the highest tolerable dose of Liproca®Depot for transrectal injection into the prostate
- To determine the level of Prostate Specific Antigen (PSA) reduction for the doses in Treatment groups 3 and 4

Protection of trial subjects:

Patients received prophylactic antibiotics prior to transrectal injection procedure.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 June 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Finland: 3
Country: Number of subjects enrolled	Lithuania: 24
Country: Number of subjects enrolled	Canada: 34
Worldwide total number of subjects	61
EEA total number of subjects	27

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0

Adults (18-64 years)	37
From 65 to 84 years	24
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

First patient in: 26 June 2017.

Last patient out: 06 July 2020

Pre-assignment

Screening details:

Men at 18 - 80 years of age and assigned to Active Surveillance

Histologically confirmed, localized prostate cancer with Gleason score 3+3 or 3+4 .

PSA must be below 20 ng/mL.

No previous or ongoing hormonal therapy for prostate cancer allowed.

Period 1

Period 1 title	Single dose
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment group 1

Arm description:

Dose: 35% of prostate volume

Arm type	Experimental
Investigational medicinal product name	Liproca Depot
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for suspension for injection
Routes of administration	Injection

Dosage and administration details:

Single dose, injection at baseline.

Intraprostatic injection of suspension.

Arm title	Treatment group 2
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Arm description:

Dose: 45% of prostate volume

Arm type	Experimental
Investigational medicinal product name	Liproca Depot
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for suspension for injection
Routes of administration	Injection

Dosage and administration details:

Single dose, injection at baseline.

Intraprostatic injection of suspension.

Arm title	Treatment group 3
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Arm description:

Dose: 16 mL

Arm type	Experimental
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Investigational medicinal product name	Liproca Depot
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for suspension for injection
Routes of administration	Injection

Dosage and administration details:
 Single dose, injection at baseline.
 Intraprostatic injection of suspension.

Arm title	Treatment group 4
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Arm description:

Dose: 20 mL

Arm type	Experimental
Investigational medicinal product name	Liproca Depot
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for suspension for injection
Routes of administration	Injection

Dosage and administration details:
 Single dose, injection at baseline.
 Intraprostatic injection of suspension.

Number of subjects in period 1	Treatment group 1	Treatment group 2	Treatment group 3
Started	10	10	21
Completed	10	10	21

Number of subjects in period 1	Treatment group 4
Started	20
Completed	20

Period 2

Period 2 title	Repeat dose
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Repeated dose
Arm description: Repeted injection of study drug	
Arm type	Experimental
Investigational medicinal product name	Liproca Depot
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for suspension for injection
Routes of administration	Injection

Dosage and administration details:

Repeted injection of study drug.
Intraprostatic injection of suspension.

Number of subjects in period 2^[1]	Repeated dose
Started	12
Completed	12

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Participation in Period 2 was voluntary

Baseline characteristics

Reporting groups

Reporting group title	Treatment group 1
Reporting group description: Dose: 35% of prostate volume	
Reporting group title	Treatment group 2
Reporting group description: Dose: 45% of prostate volume	
Reporting group title	Treatment group 3
Reporting group description: Dose: 16 mL	
Reporting group title	Treatment group 4
Reporting group description: Dose: 20 mL	

Reporting group values	Treatment group 1	Treatment group 2	Treatment group 3
Number of subjects	10	10	21
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	7	7	9
From 65-84 years	3	3	12
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	0	0	0
Male	10	10	21

Reporting group values	Treatment group 4	Total	
Number of subjects	20	61	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	14	37	
From 65-84 years	6	24	

85 years and over	0	0	
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Gender categorical Units: Subjects			
Female	0	0	
Male	20	61	

End points

End points reporting groups

Reporting group title	Treatment group 1
Reporting group description: Dose: 35% of prostate volume	
Reporting group title	Treatment group 2
Reporting group description: Dose: 45% of prostate volume	
Reporting group title	Treatment group 3
Reporting group description: Dose: 16 mL	
Reporting group title	Treatment group 4
Reporting group description: Dose: 20 mL	
Reporting group title	Repeated dose
Reporting group description: Repeated injection of study drug	

Primary: PSA responder rate

End point title	PSA responder rate ^{[1][2]}
End point description:	
End point type	Primary
End point timeframe: Week 20	

Notes:

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

Justification: Descriptive statistics.

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

Justification: All four arms were evaluated for safety, while only two arms were evaluated for efficacy in the primary objective and endpoint.

End point values	Treatment group 3	Treatment group 4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	20		
Units: Percentage	57	40		

Statistical analyses

No statistical analyses for this end point

Primary: Time to PSA recurrence

End point title	Time to PSA recurrence ^[3]
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End point description:

End point type	Primary
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End point timeframe:

24-48 weeks

Notes:

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

Justification: Descriptive statistics.

End point values	Repeated dose			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: week				
arithmetic mean (full range (min-max))	43 (32 to 48)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

24 weeks

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.1
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Reporting groups

Reporting group title	Treatment group 1
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Reporting group description: -

Reporting group title	Treatment group 2
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Reporting group description: -

Reporting group title	Treatment group 3
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Reporting group description: -

Reporting group title	Treatment group 4
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Reporting group description: -

Reporting group title	Repeated dose
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Reporting group description:

Repeated dose

Serious adverse events	Treatment group 1	Treatment group 2	Treatment group 3
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	1 / 21 (4.76%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 21 (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
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bacteraemia			

subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Treatment group 4	Repeated dose	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 20 (15.00%)	1 / 6 (16.67%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	2 / 20 (10.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	0 / 20 (0.00%)	1 / 6 (16.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bacteraemia			

subjects affected / exposed	0 / 20 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Treatment group 1	Treatment group 2	Treatment group 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 10 (60.00%)	5 / 10 (50.00%)	16 / 21 (76.19%)
Investigations			
Blood urine present			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	1 / 21 (4.76%)
occurrences (all)	0	1	1
Hepatic enzyme increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			

subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0	0 / 21 (0.00%) 0
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0	0 / 21 (0.00%) 0
General disorders and administration site conditions			
Pyrexia subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0	2 / 21 (9.52%) 2
Constipation subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 10 (10.00%) 1	0 / 21 (0.00%) 0
Injection site pain subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 10 (10.00%) 1	0 / 21 (0.00%) 0
Chills subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0	1 / 21 (4.76%) 1
Reproductive system and breast disorders			
Prostatitis subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0	2 / 21 (9.52%) 2
Prostatic pain subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0	0 / 21 (0.00%) 0
Gastrointestinal disorders			
Vomiting subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0	0 / 21 (0.00%) 0
Dyschezia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0	0 / 21 (0.00%) 0
Haematochezia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0	0 / 21 (0.00%) 0

Abdominal pain lower subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0	0 / 21 (0.00%) 0
Renal and urinary disorders			
Dysuria subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	2 / 10 (20.00%) 3	5 / 21 (23.81%) 6
Urinary retention subjects affected / exposed occurrences (all)	3 / 10 (30.00%) 3	2 / 10 (20.00%) 2	3 / 21 (14.29%) 4
Haematuria subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0	5 / 21 (23.81%) 6
Hypertonic bladder subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0	0 / 21 (0.00%) 0
Micturition urgency subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 10 (10.00%) 1	0 / 21 (0.00%) 0
Pollakiuria subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 10 (10.00%) 1	1 / 21 (4.76%) 1
Nocturia subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 2	0 / 10 (0.00%) 0	2 / 21 (9.52%) 2
Lower urinary tract symptoms subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0	3 / 21 (14.29%) 3
Urine flow decreased subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0	2 / 21 (9.52%) 2
Leukocyturia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0	1 / 21 (4.76%) 1
Infections and infestations			

Epididymitis subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0	0 / 21 (0.00%) 0
Metabolism and nutrition disorders Hyponatraemia subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0	0 / 21 (0.00%) 0
Hypokalaemia subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0	0 / 21 (0.00%) 0

Non-serious adverse events	Treatment group 4	Repeated dose	
Total subjects affected by non-serious adverse events subjects affected / exposed	15 / 20 (75.00%)	6 / 6 (100.00%)	
Investigations Blood urine present subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	1 / 6 (16.67%) 1	
Hepatic enzyme increased subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 6 (0.00%) 0	
C-reactive protein increased subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 6 (0.00%) 0	
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 6 (0.00%) 0	
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 6 (0.00%) 0	
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 6 (0.00%) 0	
General disorders and administration site conditions Pyrexia			

subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	1 / 6 (16.67%) 1	
Constipation subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 6 (16.67%) 1	
Injection site pain subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 6 (0.00%) 0	
Chills subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 2	1 / 6 (16.67%) 1	
Reproductive system and breast disorders Prostatitis subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 2	1 / 6 (16.67%) 1	
Prostatic pain subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 6 (0.00%) 0	
Gastrointestinal disorders Vomiting subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 6 (0.00%) 0	
Dyschezia subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 2	0 / 6 (0.00%) 0	
Haematochezia subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 6 (0.00%) 0	
Abdominal pain lower subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	1 / 6 (16.67%) 1	
Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all)	5 / 20 (25.00%) 5	1 / 6 (16.67%) 2	
Urinary retention			

subjects affected / exposed	5 / 20 (25.00%)	2 / 6 (33.33%)	
occurrences (all)	5	3	
Haematuria			
subjects affected / exposed	5 / 20 (25.00%)	1 / 6 (16.67%)	
occurrences (all)	5	2	
Hypertonic bladder			
subjects affected / exposed	0 / 20 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Micturition urgency			
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Pollakiuria			
subjects affected / exposed	2 / 20 (10.00%)	0 / 6 (0.00%)	
occurrences (all)	2	0	
Nocturia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	2	
Lower urinary tract symptoms			
subjects affected / exposed	0 / 20 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Urine flow decreased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Leukocyturia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Epididymitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Hypokalaemia			

subjects affected / exposed	0 / 20 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 March 2017	Upon request from Health Canada: I/E criteria clarified, increased number of MRI assessments.
19 July 2017	Upon request by Health Canada: I/E criteria #9: Creatinine less than 30 times ULN changed to eGF equal or more than 30 mL/min (by Cockcroft-Gault)
11 June 2018	Following data safety monitoring board outcome: Change in injection procedure and dose levels for treatment arms 3 and 4.
06 October 2019	Upon Health Canada Request: Change in cut-off level for PSA-responder

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/33583762>