



Clinical trial results: Phase I/II Trial Investigating an Immunostimulatory Oncolytic Adenovirus for Cancer Summary

EudraCT number	2017-002565-22
Trial protocol	SE
Global end of trial date	22 August 2023

Results information

Result version number	v1 (current)
This version publication date	04 September 2024
First version publication date	04 September 2024

Trial information

Trial identification

Sponsor protocol code	LOKON002
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03225989
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Lokon Pharma AB
Sponsor organisation address	Bredgrand 14, Uppsala, Sweden, 75320
Public contact	Angelica Loskog, Lokon Pharma AB, angelica.loskog@lokonpharma.com
Scientific contact	Angelica Loskog, Lokon Pharma AB, angelica.loskog@lokonpharma.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	22 August 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 August 2023
Global end of trial reached?	Yes
Global end of trial date	22 August 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to determine the tolerability of increasing doses of LOAd703 intratumoral injections during standard of care or added conditioning chemotherapy.

Protection of trial subjects:

The study was conducted in accordance to the protocol, applicable regulatory requirements, GCP and ethical principals of the latest version of the Declaration of Helsinki. The principal investigators were responsible for ensuring the protocol is followed. Safeguards to protect clinical research volunteers include Institutional Review Boards/Independent Ethics Committee, informed consent and cohort review safety meetings.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 April 2018
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: 42
Worldwide total number of subjects	42
EEA total number of subjects	42

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)	23
From 65 to 84 years	19

Subject disposition

Recruitment

Recruitment details:

Overall, a total of 47 subjects were screened, 42 subjects were enrolled in the study and 5 subjects were screening failures. One out of 42 enrolled did not received any LOAd703 treatment. The study enrollment was stopped after obtaining sufficient safety data, and subjects were followed until the End of Study was reached as per protocol.

Pre-assignment

Screening details:

Adult patients (≥ 18 years of age) with a pathological confirmation of colorectal carcinoma, pancreatic carcinoma, biliary cancer, or epithelial ovarian carcinoma (encompassed epithelial ovarian, fallopian tube or primary peritoneal carcinoma), have advanced disease (metastatic or locally advanced unresectable), were eligible for the study.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Treatment arm
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Arm description:

LOAD703 (Delolimogene mupadenorepvec) at three dose levels: 5x10e10 VP, 1x10e11 VP and 5x10e11 VP as add-on to standard-of care for each indication. Treatments of LOAd703 (up to 8 times) were delivered by intratumoral injection every 2 weeks.

Arm type	Experimental
Investigational medicinal product name	LOAd703
Investigational medicinal product code	
Other name	delolimogene mupadenorepvec
Pharmaceutical forms	Suspension for injection
Routes of administration	Intratumoral use

Dosage and administration details:

Modified adenovirus serotype 5/35 containing a CMV promoter-driven transgene cassette with human transgenes encoding membrane-bound CD40 ligand (TMZ-CD40L) and full-length 4-1BBL. LOAd703 was tested at three dose levels: 5x10e10VP, 1x10e11VP and 5x10e11VP. LOAd703 is delivered frozen in vials containing 650 μ l of virus in suspension. The frozen vial is thawed at the clinic on wet ice or in a refrigerator +4°C ($\pm 2^\circ$ C) according to the Sponsor's instructions.

The thawed LOAd703 virus is used directly or is diluted with physiological saline (0.9% NaCl) prior use depending on the patient dose and number of lesions to be injected. The Investigator and the radiologist assess together which lesion(s) are suitable for direct or image guided injection. The prescribed virus dose in suspension is administered by i.t. injections into ≤ 3 lesions per treatment occasion.

Number of subjects in period 1	Treatment arm
Started	42
Completed	4
Not completed	38
Clinical progression	1
Consent withdrawn by subject	1

Physician decision	1
Patient decision to stop treatment	1
Adverse event, non-fatal	3
Death	5
Progressive disease	25
LOAd703 treatment not started	1

Baseline characteristics

Reporting groups

Reporting group title	Overall trial
Reporting group description: -	

Reporting group values	Overall trial	Total	
Number of subjects	42	42	
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)	23	23	
From 65-84 years	19	19	
85 years and over	0	0	
Age continuous			
Units: years			
median	63.0		
full range (min-max)	33.0 to 77.0	-	
Gender categorical			
Units: Subjects			
Female	23	23	
Male	19	19	
Race			
Units: Subjects			
White	42	42	
Oncological disease at study entry			
Locally advanced cancer is cancer that has spread from where it started to nearby tissue or lymph nodes. Metastatic cancer is spread of cancer from the primary site to other places in the body.			
Units: Subjects			
Locally advanced	8	8	
Metastatic	34	34	

Subject analysis sets

Subject analysis set title	LOAD703 dose 5x10e10 VP
Subject analysis set type	Sub-group analysis
Subject analysis set description: LOAD703 dose is 5x10e10 VP as add-on to standard-of-care tailored to the indication.	
Subject analysis set title	LOAD703 dose 1x10e11 VP
Subject analysis set type	Sub-group analysis
Subject analysis set description: LOAD703 dose is 1x10e11 VP as add-on to standard-of-care tailored to the indication.	
Subject analysis set title	LOAD703 dose 5x10e11 VP

Subject analysis set type	Sub-group analysis
Subject analysis set description: LOAD703 dose is 5x10e11 VP as add-on to standard-of-care tailored to the indication.	
Subject analysis set title	Colorectal cancer
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subjects diagnosed with colorectal cancer	
Subject analysis set title	Biliary cancer
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subjects diagnosed with biliary cancer	
Subject analysis set title	Pancreatic cancer
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subjects diagnosed with pancreatic cancer	
Subject analysis set title	Ovarian cancer
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subjects diagnosed with ovarian cancer	

Reporting group values	LOAD703 dose 5x10e10 VP	LOAD703 dose 1x10e11 VP	LOAD703 dose 5x10e11 VP
Number of subjects	3	12	27
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)	2	5	16
From 65-84 years	1	7	11
85 years and over	0	0	0
Age continuous Units: years			
median	58.0	67.0	63.0
full range (min-max)	42.0 to 67.0	33.0 to 76.0	48.0 to 77.0
Gender categorical Units: Subjects			
Female	0	6	17
Male	3	6	10
Race Units: Subjects			
White	3	12	27
Oncological disease at study entry			
Locally advanced cancer is cancer that has spread from where it started to nearby tissue or lymph nodes. Metastatic cancer is spread of cancer from the primary site to other places in the body.			
Units: Subjects			
Locally advanced	0	4	4
Metastatic	3	8	23

Reporting group values	Colorectal cancer	Biliary cancer	Pancreatic cancer
Number of subjects	5	3	29
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)	3	1	16
From 65-84 years	2	2	13
85 years and over	0	0	0
Age continuous Units: years			
median	57.0	72.0	63.0
full range (min-max)	42.0 to 73.0	61.0 to 74.0	48.0 to 77.0
Gender categorical Units: Subjects			
Female	2	3	13
Male	3	0	16
Race Units: Subjects			
White	5	3	29
Oncological disease at study entry			
Locally advanced cancer is cancer that has spread from where it started to nearby tissue or lymph nodes. Metastatic cancer is spread of cancer from the primary site to other places in the body.			
Units: Subjects			
Locally advanced	0	0	8
Metastatic	5	3	21

Reporting group values	Ovarian cancer		
Number of subjects	5		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	3		
From 65-84 years	2		
85 years and over	0		
Age continuous Units: years			
median	52.0		
full range (min-max)	33.0 to 75.0		

Gender categorical			
Units: Subjects			
Female	5		
Male	0		
Race			
Units: Subjects			
White	5		
Oncological disease at study entry			
Locally advanced cancer is cancer that has spread from where it started to nearby tissue or lymph nodes. Metastatic cancer is spread of cancer from the primary site to other places in the body.			
Units: Subjects			
Locally advanced	0		
Metastatic	5		

End points

End points reporting groups

Reporting group title	Treatment arm
Reporting group description: LOAD703 (Delolimogene mupadenorepvec) at three dose levels: 5x10e10 VP, 1x10e11 VP and 5x10e11 VP as add-on to standard-of care for each indication. Treatments of LOAd703 (up to 8 times) were delivered by intratumoral injection every 2 weeks.	
Subject analysis set title	LOAD703 dose 5x10e10 VP
Subject analysis set type	Sub-group analysis
Subject analysis set description: LOAd703 dose is 5x10e10 VP as add-on to standard-of-care tailored to the indication.	
Subject analysis set title	LOAD703 dose 1x10e11 VP
Subject analysis set type	Sub-group analysis
Subject analysis set description: LOAd703 dose is 1x10e11 VP as add-on to standard-of-care tailored to the indication.	
Subject analysis set title	LOAd703 dose 5x10e11 VP
Subject analysis set type	Sub-group analysis
Subject analysis set description: LOAd703 dose is 5x10e11 VP as add-on to standard-of-care tailored to the indication.	
Subject analysis set title	Colorectal cancer
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subjects diagnosed with colorectal cancer	
Subject analysis set title	Biliary cancer
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subjects diagnosed with biliary cancer	
Subject analysis set title	Pancreatic cancer
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subjects diagnosed with pancreatic cancer	
Subject analysis set title	Ovarian cancer
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subjects diagnosed with ovarian cancer	

Primary: Safety determined by the NCI-CTCAE v4.03

End point title	Safety determined by the NCI-CTCAE v4.03 ^[1]
End point description:	
End point type	Primary
End point timeframe: 40 weeks	

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: No formal statistical analysis was performed to compare dose or cancer groups. Results are presented with descriptive statistics, are tabulated by groups and reviewed to evaluate the study endpoints.

End point values	LOAD703 dose 5x10e10 VP	LOAD703 dose 1x10e11 VP	LOAD703 dose 5x10e11 VP	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	3 ^[2]	12 ^[3]	26 ^[4]	
Units: Number of events				
All Adverse events (AEs)	61	139	411	
All Serious adverse events (SAEs)	7	31	63	
Serious adverse reactions related to LOAD703	3	4	21	
AE leading to LOAD703 discontinuation	0	2	6	
AE leading to withdrawal from the study	0	1	2	
AE leading to death	0	0	1	
AE related to LOAD703	29	33	169	
AE related to LOAD703 grade 1	15	29	111	
AE related to LOAD703 grade 2	14	3	52	
AE related to LOAD703 grade 3	0	0	6	
AE related to LOAD703 grade 4	0	1	0	
AE related to LOAD703 grade 5	0	0	0	
AE unrelated to LOAD703	32	106	242	

Notes:

[2] - Number of subjects based on safety evaluable population (at least one LOAD703 treatment received)

[3] - Number of subjects based on safety evaluable population (at least one LOAD703 treatment received)

[4] - Number of subjects based on safety evaluable population (at least one LOAD703 treatment received)

Statistical analyses

No statistical analyses for this end point

Secondary: Best overall tumor response according to RECIST 1.1

End point title	Best overall tumor response according to RECIST 1.1
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End point description:

Overall Response Rate is defined as proportion of subjects with the best overall response of complete response (CR) or partial response (PR). Clinical Benefit Rate is defined as proportion of subjects with the best overall response of complete response (CR) or partial response (PR) or stable disease (SD).

End point type	Secondary
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End point timeframe:

40 weeks

End point values	LOAD703 dose 5x10e10 VP	LOAD703 dose 1x10e11 VP	LOAD703 dose 5x10e11 VP	Colorectal cancer
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3 ^[5]	10 ^[6]	22 ^[7]	5 ^[8]
Units: Number of subjects				
Complete response	0	0	0	0
Partial response	0	3	3	0
Stable disease	1	4	11	2
Progressive disease	2	3	8	3
Not evaluable	0	0	0	0
Overall response rate (CR or PR)	0	3	3	0

Clinical benefit rate (CR, PR or SD)	1	7	14	2
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Notes:

[5] - Number of subjects based on efficacy evaluable population (at least 3 LOAd703 inj+CT evaluation)

[6] - Number of subjects based on efficacy evaluable population (at least 3 LOAd703 inj+CT evaluation)

[7] - Number of subjects based on efficacy evaluable population (at least 3 LOAd703 inj+CT evaluation)

[8] - Number of subjects based on efficacy evaluable population (at least 3 LOAd703 inj+CT evaluation)

End point values	Biliary cancer	Pancreatic cancer	Ovarian cancer	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	3 ^[9]	24 ^[10]	3 ^[11]	
Units: Number of subjects				
Complete response	0	0	0	
Partial response	0	6	0	
Stable disease	1	11	2	
Progressive disease	2	7	1	
Not evaluable	0	0	0	
Overall response rate (CR or PR)	0	6	0	
Clinical benefit rate (CR, PR or SD)	1	17	2	

Notes:

[9] - Number of subjects based on efficacy evaluable population (at least 3 LOAd703 inj+CT evaluation)

[10] - Number of subjects based on efficacy evaluable population (at least 3 LOAd703 inj+CT evaluation)

[11] - Number of subjects based on efficacy evaluable population (at least 3 LOAd703 inj+CT evaluation)

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

End point title	Overall survival
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End point description:

Overall survival is defined as the time from the first dose of LOAd703 treatment until death.

End point type	Secondary
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End point timeframe:

up to 72 months

End point values	Treatment arm	LOAD703 dose 5x10e10 VP	LOAD703 dose 1x10e11 VP	LOAD703 dose 5x10e11 VP
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	35 ^[12]	3 ^[13]	10 ^[14]	22 ^[15]
Units: months				
median (confidence interval 95%)	7.46 (5.49 to 10.48)	4.40 (3.02 to 12.85)	8.44 (2.66 to 40.54)	7.38 (5.39 to 10.71)

Notes:

[12] - Number of subjects based on efficacy evaluable population (at least 3 LOAd703 inj+CT evaluation)

[13] - Number of subjects based on efficacy evaluable population (at least 3 LOAd703 inj+CT evaluation)

[14] - Number of subjects based on efficacy evaluable population (at least 3 LOAd703 inj+CT evaluation)

evaluation)

[15] - Number of subjects based on efficacy evaluable population (at least 3 LOAd703 inj+CT evaluation)

End point values	Colorectal cancer	Biliary cancer	Pancreatic cancer	Ovarian cancer
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5 ^[16]	3 ^[17]	24 ^[18]	3 ^[19]
Units: months				
median (confidence interval 95%)	5.36 (3.02 to 8.44)	6.64 (5.26 to 7.46)	7.29 (5.39 to 12.85)	40.54 (9.69 to 40.54)

Notes:

[16] - Number of subjects based on efficacy evaluable population (at least 3 LOAd703 inj+CT evaluation)

[17] - Number of subjects based on efficacy evaluable population (at least 3 LOAd703 inj+CT evaluation)

[18] - Number of subjects based on efficacy evaluable population (at least 3 LOAd703 inj+CT evaluation)

[19] - Number of subjects based on efficacy evaluable population (at least 3 LOAd703 inj+CT evaluation)

Statistical analyses

No statistical analyses for this end point

Secondary: Progression free survival

End point title	Progression free survival
End point description:	Progression free survival is defined as the time from the first dose of LOAd703 treatment until progression according to RECIST1.1 or death (whichever occurred first).
End point type	Secondary
End point timeframe:	up to 72 months

End point values	Treatment arm	LOAD703 dose 5x10e10 VP	LOAD703 dose 1x10e11 VP	LOAD703 dose 5x10e11 VP
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	35 ^[20]	3 ^[21]	10 ^[22]	22 ^[23]
Units: months				
median (confidence interval 95%)	3.75 (2.27 to 5.49)	2.40 (1.74 to 3.68)	3.79 (1.81 to 5.49)	4.32 (1.87 to 5.72)

Notes:

[20] - Number of subjects based on efficacy evaluable population (at least 3 LOAd703 inj+CT evaluation)

[21] - Number of subjects based on efficacy evaluable population (at least 3 LOAd703 inj+CT evaluation)

[22] - Number of subjects based on efficacy evaluable population (at least 3 LOAd703 inj+CT evaluation)

[23] - Number of subjects based on efficacy evaluable population (at least 3 LOAd703 inj+CT evaluation)

End point values	Colorectal cancer	Biliary cancer	Pancreatic cancer	Ovarian cancer
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5 ^[24]	3 ^[25]	24 ^[26]	3 ^[27]

Units: months				
median (confidence interval 95%)	2.40 (1.74 to 5.36)	1.81 (1.58 to 4.76)	4.62 (2.27 to 5.72)	3.88 (1.87 to 20.07)

Notes:

[24] - Number of subjects based on efficacy evaluable population (at least 3 LOAd703 inj+CT evaluation)

[25] - Number of subjects based on efficacy evaluable population (at least 3 LOAd703 inj+CT evaluation)

[26] - Number of subjects based on efficacy evaluable population (at least 3 LOAd703 inj+CT evaluation)

[27] - Number of subjects based on efficacy evaluable population (at least 3 LOAd703 inj+CT evaluation)

Statistical analyses

No statistical analyses for this end point

Secondary: Time to progression

End point title	Time to progression
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End point description:

Time to progression (TTP) defined as the time from first dose of LOAd703 treatment until progression according to RECIST v1.1.

End point type	Secondary
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End point timeframe:

up to 72 months

End point values	Treatment arm	LOAD703 dose 5x10e10 VP	LOAD703 dose 1x10e11 VP	LOAD703 dose 5x10e11 VP
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	35 ^[28]	3 ^[29]	10 ^[30]	22 ^[31]
Units: months				
median (confidence interval 95%)	3.71 (2.10 to 5.49)	2.40 (1.74 to 3.68)	3.79 (1.81 to 5.49)	3.88 (1.87 to 5.72)

Notes:

[28] - Number of subjects based on efficacy evaluable population (at least 3 LOAd703 inj+CT evaluation)

[29] - Number of subjects based on efficacy evaluable population (at least 3 LOAd703 inj+CT evaluation)

[30] - Number of subjects based on efficacy evaluable population (at least 3 LOAd703 inj+CT evaluation)

[31] - Number of subjects based on efficacy evaluable population (at least 3 LOAd703 inj+CT evaluation)

End point values	Colorectal cancer	Biliary cancer	Pancreatic cancer	Ovarian cancer
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5 ^[32]	3 ^[33]	24 ^[34]	3 ^[35]
Units: months				
median (confidence interval 95%)	2.40 (1.74 to 3.84)	1.81 (1.58 to 4.76)	3.75 (2.27 to 5.72)	3.88 (1.87 to 20.07)

Notes:

[32] - Number of subjects based on efficacy evaluable population (at least 3 LOAd703 inj+CT evaluation)

[33] - Number of subjects based on efficacy evaluable population (at least 3 LOAd703 inj+CT evaluation)

[34] - Number of subjects based on efficacy evaluable population (at least 3 LOAd703 inj+CT evaluation)

[35] - Number of subjects based on efficacy evaluable population (at least 3 LOAd703 inj+CT evaluation)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

40 weeks

Adverse event reporting additional description:

The AE reporting period for this study begins upon receiving the first LOAd703 treatment and continues until final visit at week 40. If a patient experiences an AE after signing the informed consent but before the first treatment, the event may be recorded as medical condition.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.0
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Reporting groups

Reporting group title	LOAd703 dose 5x10e10VP
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Reporting group description: -

Reporting group title	LOAd703 dose 1x10e11VP
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Reporting group description: -

Reporting group title	LOAd703 dose 5x10e11VP
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Reporting group description: -

Serious adverse events	LOAd703 dose 5x10e10VP	LOAd703 dose 1x10e11VP	LOAd703 dose 5x10e11VP
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	12 / 12 (100.00%)	20 / 26 (76.92%)
number of deaths (all causes)	3	10	23
number of deaths resulting from adverse events	0	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 3 (33.33%)	2 / 12 (16.67%)	11 / 26 (42.31%)
occurrences causally related to treatment / all	3 / 3	1 / 3	10 / 18
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			

subjects affected / exposed	1 / 3 (33.33%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	1 / 3 (33.33%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chills			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	3 / 26 (11.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	0 / 26 (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
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	4 / 26 (15.38%)
occurrences causally related to treatment / all	0 / 0	1 / 1	6 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary oedema			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	2 / 26 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pleural effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device dislocation	Additional description: NP-catheter dislocation		
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood creatine increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic enzyme increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	0 / 26 (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
Nervous system disorders			
Seizure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	0 / 26 (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
Febrile neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	0 / 26 (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
Neutropenia			

subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	0 / 26 (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
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	0 / 3 (0.00%)	2 / 12 (16.67%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer perforation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	0 / 26 (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
Ileus			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			

Cholangitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	0 / 26 (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
Cholecystitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperbilirubinaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	2 / 26 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash	Additional description: Rash generalized		
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	0 / 26 (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
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glomerulonephritis membranoproliferative			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	0 / 26 (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
Renal colic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Renal failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	2 / 26 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 12 (0.00%)	0 / 26 (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
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
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			
Clostridial infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	0 / 26 (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
Erysipelas			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	0 / 26 (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
Infection			
subjects affected / exposed	0 / 3 (0.00%)	2 / 12 (16.67%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver abscess			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	0 / 26 (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
Sepsis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	4 / 26 (15.38%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Septic shock			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	0 / 26 (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
Hyperkalaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	LOAd703 dose 5x10e10VP	LOAd703 dose 1x10e11VP	LOAd703 dose 5x10e11VP
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	11 / 12 (91.67%)	26 / 26 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 12 (0.00%) 0	2 / 26 (7.69%) 3
Tumour pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 12 (0.00%) 0	2 / 26 (7.69%) 2
Tumour thrombosis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 12 (0.00%) 0	1 / 26 (3.85%) 1
Vascular disorders			
Hypertension subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 4	2 / 12 (16.67%) 2	4 / 26 (15.38%) 4
Hypotension subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	2 / 12 (16.67%) 2	3 / 26 (11.54%) 6
Deep vein thrombosis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 12 (0.00%) 0	2 / 26 (7.69%) 2
Embolism subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 12 (0.00%) 0	1 / 26 (3.85%) 1
General disorders and administration site conditions			
Chills subjects affected / exposed occurrences (all)	3 / 3 (100.00%) 7	3 / 12 (25.00%) 3	11 / 26 (42.31%) 25
Fatigue subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 5	7 / 12 (58.33%) 9	16 / 26 (61.54%) 19
General physical health deterioration subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 12 (0.00%) 0	2 / 26 (7.69%) 2
Malaise subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 12 (0.00%) 0	1 / 26 (3.85%) 1
Oedema peripheral			

subjects affected / exposed	2 / 3 (66.67%)	5 / 12 (41.67%)	6 / 26 (23.08%)
occurrences (all)	2	7	7
Pyrexia			
subjects affected / exposed	3 / 3 (100.00%)	8 / 12 (66.67%)	24 / 26 (92.31%)
occurrences (all)	9	10	66
Discomfort			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	0 / 26 (0.00%)
occurrences (all)	0	2	0
Gastroenteritis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Injection site oedema			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Localised oedema			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	1 / 26 (3.85%)
occurrences (all)	0	1	1
Face oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Feeling cold			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Generalised oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Influenza like illness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Injection site inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Injection site pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	2 / 26 (7.69%)
occurrences (all)	0	0	2
Mucosal inflammation			

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 12 (0.00%) 0	2 / 26 (7.69%) 3
Pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 12 (0.00%) 0	1 / 26 (3.85%) 1
Swelling subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 12 (0.00%) 0	1 / 26 (3.85%) 1
Immune system disorders Cytokine release syndrome subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 12 (0.00%) 0	2 / 26 (7.69%) 2
Respiratory, thoracic and mediastinal disorders			
Dyspnoea subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 2	2 / 12 (16.67%) 2	2 / 26 (7.69%) 2
Lung infiltration subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	1 / 12 (8.33%) 1	2 / 26 (7.69%) 2
Hypoxia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 12 (8.33%) 1	0 / 26 (0.00%) 0
Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 12 (8.33%) 1	0 / 26 (0.00%) 0
Cough subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 12 (0.00%) 0	2 / 26 (7.69%) 3
Epistaxis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 12 (0.00%) 0	2 / 26 (7.69%) 2
Pleural effusion subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 12 (0.00%) 0	2 / 26 (7.69%) 2
Pulmonary embolism			

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 12 (0.00%) 0	2 / 26 (7.69%) 2
Respiratory failure subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 12 (0.00%) 0	1 / 26 (3.85%) 1
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 12 (0.00%) 0	2 / 26 (7.69%) 2
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 12 (8.33%) 1	4 / 26 (15.38%) 4
Blood bilirubin increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 12 (8.33%) 1	0 / 26 (0.00%) 0
Blood creatinine increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 12 (8.33%) 1	2 / 26 (7.69%) 2
C-reactive protein increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	2 / 12 (16.67%) 2	6 / 26 (23.08%) 6
Cardiac murmur subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 12 (8.33%) 1	0 / 26 (0.00%) 0
Electrocardiogram abnormal subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 12 (8.33%) 1	0 / 26 (0.00%) 0
Heart rate irregular subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 12 (8.33%) 1	0 / 26 (0.00%) 0
Hepatic enzyme increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 12 (8.33%) 1	2 / 26 (7.69%) 2
Neutrophil count decreased			

subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	5 / 26 (19.23%)
occurrences (all)	0	1	5
Weight decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	3 / 26 (11.54%)
occurrences (all)	0	1	3
White blood cell count decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	5 / 26 (19.23%)
occurrences (all)	0	1	6
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	3 / 26 (11.54%)
occurrences (all)	0	0	3
Blood albumin decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	2 / 26 (7.69%)
occurrences (all)	0	0	2
Blood pressure decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Platelet count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	2
Transaminases increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Weight increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			

Incisional hernia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 12 (0.00%) 0	1 / 26 (3.85%) 1
Muscle strain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 12 (0.00%) 0	1 / 26 (3.85%) 1
Peripancreatic fluid collection subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 12 (0.00%) 0	1 / 26 (3.85%) 1
Cardiac disorders			
Cardiac failure subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	2 / 12 (16.67%) 2	0 / 26 (0.00%) 0
Palpitations subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 12 (0.00%) 0	0 / 26 (0.00%) 0
Sinus tachycardia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 12 (8.33%) 1	0 / 26 (0.00%) 0
Atrial fibrillation subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 12 (0.00%) 0	1 / 26 (3.85%) 1
Pericardial effusion subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 12 (0.00%) 0	1 / 26 (3.85%) 1
Nervous system disorders			
Headache subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	2 / 12 (16.67%) 7	6 / 26 (23.08%) 11
Neuropathy peripheral subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 12 (8.33%) 1	3 / 26 (11.54%) 3
Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 12 (8.33%) 1	0 / 26 (0.00%) 0
Syncope			

subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Dysgeusia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	2 / 26 (7.69%)
occurrences (all)	0	0	2
Paraesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Posterior reversible encephalopathy syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Tremor			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 3 (33.33%)	4 / 12 (33.33%)	8 / 26 (30.77%)
occurrences (all)	1	5	11
Leukopenia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	1 / 26 (3.85%)
occurrences (all)	0	1	1
Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	3 / 12 (25.00%)	2 / 26 (7.69%)
occurrences (all)	0	3	2
Thrombocytopenia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	1 / 26 (3.85%)
occurrences (all)	0	2	1
Thrombocytosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Eye disorders			

Periorbital oedema subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 12 (0.00%) 0	1 / 26 (3.85%) 1
Gastrointestinal disorders			
Constipation subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 12 (0.00%) 0	4 / 26 (15.38%) 5
Nausea subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 2	5 / 12 (41.67%) 6	16 / 26 (61.54%) 18
Proctalgia subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 12 (0.00%) 0	0 / 26 (0.00%) 0
Stomatitis subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	1 / 12 (8.33%) 1	0 / 26 (0.00%) 0
Vomiting subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 7	2 / 12 (16.67%) 2	10 / 26 (38.46%) 17
Abdominal pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	2 / 12 (16.67%) 2	5 / 26 (19.23%) 6
Ascites subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 12 (8.33%) 1	1 / 26 (3.85%) 1
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 12 (0.00%) 0	2 / 26 (7.69%) 2
Diarrhoea subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	2 / 12 (16.67%) 2	6 / 26 (23.08%) 6
Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 12 (8.33%) 1	1 / 26 (3.85%) 1
Change of bowel habit			

subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	2 / 26 (7.69%)
occurrences (all)	0	0	2
Colitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Faeces discoloured			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Gastritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	2 / 26 (7.69%)
occurrences (all)	0	0	2
Gingival blister			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Mesenteric vein thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Rash			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	2 / 26 (7.69%)
occurrences (all)	0	2	2
Alopecia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Eczema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Pain of skin			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Urticaria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	2 / 26 (7.69%)
occurrences (all)	0	0	2

Renal and urinary disorders			
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	3 / 12 (25.00%)	3 / 26 (11.54%)
occurrences (all)	0	3	3
Glomerulonephritis membranoproliferative			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Urinary retention			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 12 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Back pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences (all)	2	0	1
Myalgia			
subjects affected / exposed	2 / 3 (66.67%)	1 / 12 (8.33%)	4 / 26 (15.38%)
occurrences (all)	3	1	4
Groin pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	3 / 26 (11.54%)
occurrences (all)	0	0	4
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Clostridial infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Erysipelas			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	1 / 26 (3.85%)
occurrences (all)	0	1	1

Infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	2 / 12 (16.67%)	2 / 26 (7.69%)
occurrences (all)	0	3	3
Oral candidiasis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Oral fungal infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Cystitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Device related infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Groin infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Infusion related reaction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 3 (33.33%)	1 / 12 (8.33%)	3 / 26 (11.54%)
occurrences (all)	1	1	3
Hypokalaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 12 (8.33%)	2 / 26 (7.69%)
occurrences (all)	0	1	2
Hyponatraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 12 (0.00%)	2 / 26 (7.69%)
occurrences (all)	0	0	2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 April 2019	<p>Substantial changes:</p> <p>Platinum-resistance disease has been added to the definition of the ovarian cancer population (section 2.7.4 and 4.1)</p> <p>Continuation criteria to consider when assessing the patient prior to next LOAD703 injection, has been added, (section 5.1, 5.2)</p> <p>Follow-up of patients after injection has been extended: overnight stays, vital signs, (section 5.1, 5.2)</p> <p>Information on immediate reactions to the LOAd703 virus particle cytokine release syndrome and their handling plans, has been added (section 9.4.1 and 9.4.3).</p> <p>The use of corticosteroids during study has been added to as the pre-medication list under certain conditions (section 5.11)</p> <p>Information on DLT assessment and dose adjustments, has been added (section 4.4, 5.1, 5.6 and 5.7)</p> <p>INR/PT and aPTT/PTT are added to the lab list before injections/biopsy (section 7.2.8)</p> <p>Administrative changes.</p>
15 November 2019	<p>Substantial changes:</p> <p>Exclusion criteria nr 4: "patients on warfarin (or other anti-coagulants) are not eligible" has been changed to not exclude patients on other anti-coagulants than warfarin since the hospital guidelines regarding such patients has been changed. They are now eligible for injections and biopsy and can therefore be enrolled in this trial. Synopsis, section 4.2 and 6.3 are updated accordingly.</p> <p>Karolinska Hospital is included as a new site and the trial is therefore not single center but multi center. Patient samples from patients enrolled at Karolinska Hospital will be temporarily stored in their biobank. Synopsis, 1.4-6, 1.10.2, 3.3, 4, 5.4.1, 5.4.3, 7.1.1, 12.2 and 14.5 are updated accordingly.</p> <p>Administrative changes.</p>
02 January 2020	<p>Substantial change:</p> <p>Sections 5.5.3 and 5.5.5 are modified to allow storage of an unopened, thawed virus vial up to 24 hours in refrigerator and to change dilution buffer to physiological saline in accordance with the approved IMPD (version 5) and IB (version 6).</p>

06 December 2021	<p>Substantial changes:</p> <p>Phase II is divided in phase IIa and phase IIb. In phase IIb additional pancreas cancer (PC) and ovarian cancer patients (EOC) are enrolled. Enrolment of biliary cancer and colorectal cancer patients is stopped (synopsis, section 3.3 and 10.2.2)</p> <p>Inclusion of two dose levels (1x1011 VP and 5x1011VP) in Phase IIb (synopsis, section 3.3, 5.2 and 10.2.2)</p> <p>Expansion of total accrual in phase II to achieve up to 53 efficacy evaluable patients (phase IIa: 18, phase IIb: up to 35) (synopsis, section 3.3, and 10.2.2, 10.4). The total number of patients to be enrolled in the study is 80.</p> <p>Extension of study duration to 72 months (synopsis, section 3.4)</p> <p>Update of inclusion criteria for PC patients (no. 3bi): LOAd703 is an add-on to SoC treatment at first and second line. (synopsis, section 2.7.2 and 4.1)</p> <p>Update of inclusion criteria for EOC patients. Inclusion criterion no. 3di was removed and inclusion criteria no.3dii-iv) were updated to include:</p> <ul style="list-style-type: none"> - patients with platinum-sensitive relapse that previously received at least one line of chemotherapy and not eligible for PARP-inhibitor maintenance; - patients with platinum-resistant relapse, who have not received more than two lines of appropriate standard of care and not eligible for bevacizumab. Maintenance treatment does not count as a line of therapy; - patients that have received appropriate therapy with PARP inhibitors if eligible (synopsis, section 2.7.4 and 4.1). <p>Update regarding chemotherapy schedule for EOC patients in the extended phase IIb (section 5.10.4)</p> <p>Addition of exclusion criteria no. 12 and 13 to exclude patients having received adenovirus based gene therapy and adenovirus-based vaccine prior to LOAd703 treatment (synopsis, section 4.2)</p> <p>Addition of severe (grade 3) cytokine release syndrome (CRS) as condition for dose reduction</p> <p>Update regarding reporting of chemotherapy-induced bone marrow toxicities</p> <p>Administrative changes</p>
21 December 2022	Non-substantial amendment. Administrative changes only.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Exploratory analysis for shedding, anti-adenovirus immunity, PK atezolizumab, immunity to atezolizumab, immune and protein profile was done. Results are summarized per individual subjects or over time without statistical analysis. Data not submitted.

Notes: