Clinical trial results:
A Phase II Open-Label, Randomized Study of Immunoconjugate L-DOS47 in Combination with Vinorelbine/Cisplatin Versus Vinorelbine/Cisplatin Alone in Patients with Lung Adenocarcinoma

Summary

EudraCT number	2016-003015-34
Trial protocol	PL HU
Global end of trial date	06 May 2020

Results information

Result version number	v1 (current)
This version publication date	28 August 2024
First version publication date	28 August 2024
Summary attachment (see zip file)	LDOS003 (CSR Synopsis.pdf)

Trial information

Trial identification

Sponsor protocol code	LDOS003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03891173
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Helix BioPharma Corp.
Sponsor organisation address	Bay Adelaide Centre - North Tower, 40 Temperance Street, Suite 2700, Toronto, Canada, M5H 0B4
Public contact	Chief Executive Officer, Helix BioPharma Corp., 1 6046842181, jantas@helixbiopharma.com
Scientific contact	Clinical Operations, Helix BioPharma Corp., 1 4168092101, blee@helixbiopharma.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	28 September 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 May 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To determine:
• Safety and tolerability of L-DOS47 in combination treatment with vinorelbine/cisplatin
• Dose limiting toxicities (DLTs) of L-DOS47 in combination treatment with vinorelbine/cisplatin
• Maximum tolerated dose (MTD) and recommended Part 2 dose of L-DOS47 in combination treatment with vinorelbine/cisplatin
• Preliminary efficacy of L-DOS47 by comparing the time to disease progression (TTP) of L-DOS47 in combination with vinorelbine/cisplatin to vinorelbine/cisplatin alone in patients with lung adenocarcinoma

Protection of trial subjects:

In the dose escalation portion of the trial, patients were recruited into cohorts, with a minimum of three and a maximum of six patients per cohort. Decision on whether to escalate to the next dose level was made only after all the subjects in the cohort had completed the dose limiting toxicity evaluation period and the safety data were reviewed by the Trial Steering Committee. In order to monitor and assess for possible infusion reactions and/or allergic reactions, patients remained on site for a minimum of two hours from the start of the L-DOS47 infusion. Only when the maximum tolerated dose was determined could the study proceed to the randomised portion of the study.

Background therapy:

N/A

Evidence for comparator:

N/A

Actual start date of recruitment	19 February 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	Ukraine: 9
Worldwide total number of subjects	9
EEA total number of subjects	0

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)	7
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

During the dose escalation portion of the study, patients were recruited at three different sites in Ukraine between February and December 2019. Due to restrictions related to the COVID 19 pandemic, recruitment for the final cohort could not be completed and a decision was made not to proceed to the randomised portion of the study.

Pre-assignment

Screening details:

≥ 18y; histologically confirmed metastatic lung adenocarcinoma; Eastern Cooperative Oncology Group performance status 0–1; life expectancy ≥3 months; not receiving radiotherapy (except symptomatic treatment of bone metastases), targeted therapy, hormonal therapy or immunotherapy, major surgery or other study drugs within 4 weeks of study treatment

Period 1

Period 1 title	Treatment Period (dose escalation) (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	L-DOS47 6 µg/kg

Arm description:

Patients were recruited into cohorts, minimum of three and a maximum of 6 patients per cohort.

Arm type	Experimental
Investigational medicinal product name	L-DOS47
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

For each 21-day treatment cycle, L-DOS47 was administered by IV infusion on days 1 and 8, in combination vinorelbine (30 mg/m2) on days 1 and 8, and cisplatin (80 mg/m2) on day 1, for a total of four treatment cycles.

Arm title	L-DOS47 9 µg/kg

Arm description:

Patients were recruited into cohorts, with a minimum of three and a maximum of six patients per cohort.

Arm type	Experimental
Investigational medicinal product name	L-DOS47
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

For each 21-day treatment cycle, L-DOS47 was administered by IV infusion on days 1 and 8, in combination vinorelbine (30 mg/m2) on days 1 and 8, and cisplatin (80 mg/m2) on day 1, for a total of four treatment cycles.

Arm title	L-DOS47 12 µg/kg

Arm description:

Patients were recruited into cohorts, with a minimum of three and a maximum of six patients per cohort.

Arm type	Experimental
Investigational medicinal product name	L-DOS47
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

For each 21-day treatment cycle, L-DOS47 was administered by IV infusion on days 1 and 8, in combination vinorelbine (30 mg/m2) on days 1 and 8, and cisplatin (80 mg/m2) on day 1, for a total of four treatment cycles.

Number of subjects in period 1	L-DOS47 6 µg/kg	L-DOS47 9 µg/kg	L-DOS47 12 µg/kg
Started	3	3	3
Completed	3	3	2
Not completed	0	0	1
Adverse event, non-fatal	-	-	1

Baseline characteristics

Reporting groups	
Reporting group title	L-DOS47 6 µg/kg
Reporting group description:	
Patients were recruited into cohorts, minimum of three and a maximum of 6 patients per cohort.	
Reporting group title	L-DOS47 9 µg/kg
Reporting group description:	
Patients were recruited into cohorts, with a minimum of three and a maximum of six patients per cohort.	
Reporting group title	L-DOS47 12 µg/kg
Reporting group description:	
Patients were recruited into cohorts, with a minimum of three and a maximum of six patients per cohort.	

Reporting group values	L-DOS47 6 µg/kg	L-DOS47 9 µg/kg	L-DOS47 12 µg/kg
Number of subjects	3	3	3
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	62.7	59.0	58.7
standard deviation	± 1.15	± 9.54	± 8.50
Gender categorical Units: Subjects			
Female	0	0	1
Male	3	3	2
Race Units: Subjects			
caucasian	3	3	3
ECOG Score			
Eastern Cooperative Oncology Group (ECOG) Performance Status Scale			
Units: Subjects			
ECOG 0	0	0	1
ECOG 1	3	3	2
Body Surface Area Units: m2			
arithmetic mean	1.78	1.76	1.83
standard deviation	± 0.121	± 0.136	± 0.171

Reporting group values	Total		
Number of subjects	9		
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean			

standard deviation	-		

Gender categorical Units: Subjects			
Female	1		
Male	8		
Race Units: Subjects			
caucasian	9		
ECOG Score			
Eastern Cooperative Oncology Group (ECOG) Performance Status Scale			
Units: Subjects			
ECOG 0	1		
ECOG 1	8		
Body Surface Area Units: m2 arithmetic mean standard deviation	- -		

Subject analysis sets

Subject analysis set title	Safety Evaluable Group
Subject analysis set type	Safety analysis

Subject analysis set description:

Comprises all subjects who receive at least one study drug dose (partial or complete).

Subject analysis set title	Response Evaluable Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Consists of all subjects who enrol in the study and receive at least one dose of study drug (partial or complete) and have at least one post-baseline response assessment.

Reporting group values	Safety Evaluable Group	Response Evaluable Group	
Number of subjects	9	8	
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	60.1	59.5	
standard deviation	± 6.70	± 6.89	
Gender categorical Units: Subjects			
Female	1	0	
Male	8	8	
Race Units: Subjects			
caucasian	9	8	
ECOG Score			
Eastern Cooperative Oncology Group (ECOG) Performance Status Scale			
Units: Subjects			

ECOG 0	1	0	
ECOG 1	8	8	

Body Surface Area			
Units: m2			
arithmetic mean	1.79	1.80	
standard deviation	± 0.142	± 0.146	

End points

End points reporting groups

Reporting group title	L-DOS47 6 µg/kg

Reporting group description:

Patients were recruited into cohorts, minimum of three and a maximum of 6 patients per cohort.

Reporting group title	L-DOS47 9 µg/kg

Reporting group description:

Patients were recruited into cohorts, with a minimum of three and a maximum of six patients per cohort.

Reporting group title	L-DOS47 12 µg/kg

Reporting group description:

Patients were recruited into cohorts, with a minimum of three and a maximum of six patients per cohort.

Subject analysis set title	Safety Evaluable Group
Subject analysis set type	Safety analysis

Subject analysis set description:

Comprises all subjects who receive at least one study drug dose (partial or complete).

Subject analysis set title	Response Evaluable Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Consists of all subjects who enrol in the study and receive at least one dose of study drug (partial or complete) and have at least one post-baseline response assessment.

Primary: Incidence drug-related adverse events as per dose-limiting toxicity definition

End point title	Incidence drug-related adverse events as per dose-limiting toxicity definition[1]

End point description:

Dose-limiting toxicity was defined as any NCI CTCAE v.4.0 ≥ Grade 3 non-haematologic and any ≥ Grade 4 haematologic adverse event that is at least possibly related to the study drug occurring ≤ 3 weeks after commencing L-DOS47 treatment.

End point type	Primary

End point timeframe:

Observations period for dose-limiting toxicities was 21 days, the length of one complete treatment cycle.

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 statistical analyses was done, as this endpoint is simply a count for adverse events meeting definition for dose-limiting toxicity in order to establish a maximum tolerated dose (MTD).

End point values	L-DOS47 6 µg/kg	L-DOS47 9 µg/kg	L-DOS47 12 µg/kg	Safety Evaluable Group
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	3	3	2[2]	8
Units: Number of Patients	0	0	0	0

Notes:

[2] - Third patient in cohort did not complete 21-day observation period.

Statistical analyses

No statistical analyses for this end point

Primary: Time to Disease Progression

End point title	Time to Disease Progression[3]

End point description:

Preliminary efficacy assessment of L-DOS47 in combination with cisplatin and vinorelbine.

End point type	Primary

End point timeframe:

From time of first study drug administration until time of documented disease progression.

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: No statistical analyses was performed, as the study was halted in the early (non-randomized) dose escalation phase with only 8 patients evaluable for time-to-disease progression.

End point values	Response Evaluable Group			
Subject group type	Subject analysis set			
Number of subjects analysed	8			
Units: Days				
median (full range (min-max))	169.5 (93 to 303)			

Statistical analyses

No statistical analyses for this end point

Secondary: Best Objective Response Rate (BORR) as per RECIST

End point title	Best Objective Response Rate (BORR) as per RECIST

End point description:

Best objective response rate is the sum of complete and partial responders divided by the number of patients included in the response evaluable population.

End point type	Secondary

End point timeframe:

From time of first study drug administration up to 12 weeks.

End point values	L-DOS47 6 µg/kg	L-DOS47 9 µg/kg	L-DOS47 12 µg/kg	Response Evaluable Group
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	3	3	2	8
Units: Number of Patients				
Complete Response	0	0	0	0
Partial response	1	0	1	2
Stable disease	1	3	0	4
Progressive disease	1	0	1	2
Objective response rate	1	0	1	2
Clinical benefit rate	2	3	1	6

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

End point title	Overall survival

End point description:

Preliminary assessment of overall survival with L-DOS47 treatment in combination with cisplatin and vinorelbine.

End point type	Secondary

End point timeframe:

From time of first study drug administration until documented death due to any cause.

End point values	Safety Evaluable Group			
Subject group type	Subject analysis set			
Number of subjects analysed	9			
Units: Days				
median (full range (min-max))	275 (131 to 303)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From time of enrolment until 30 days after the last study drug dose.	
Adverse event reporting additional description:	
Any untoward medical occurrence whether or not related to study treatment.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups	
Reporting group title	L-DOS47 6 µg/kg
Reporting group description:	
Patients were recruited into cohorts, minimum of three and a maximum of 6 patients per cohort.	
Reporting group title	L-DOS47 9 µg/kg
Reporting group description:	
Patients were recruited into cohorts, with a minimum of three and a maximum of six patients per cohort.	
Reporting group title	L-DOS47 12 µg/kg
Reporting group description:	
Patients were recruited into cohorts, with a minimum of three and a maximum of six patients per cohort.	
Reporting group title	Overall
Reporting group description:	
All L-DOS47 doses (6, 9, 12 µg/kg) combined.	

Serious adverse events	L-DOS47 6 µg/kg	L-DOS47 9 µg/kg	L-DOS47 12 µg/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Psychiatric disorders			
Acute stress disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Overall		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 9 (11.11%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Psychiatric disorders			
Acute stress disorder			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	L-DOS47 6 µg/kg	L-DOS47 9 µg/kg	L-DOS47 12 µg/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	3 / 3 (100.00%)	3 / 3 (100.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
General disorders and administration site conditions			
Chills			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Body temperature increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Neutrophil count decreased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Platelet count increased			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Electrocardiogram repolarization abnormality			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Bundle branch block right			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Left ventricular hypertrophy			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 3 (66.67%)	1 / 3 (33.33%)	2 / 3 (66.67%)
occurrences (all)	2	1	4
Leukopenia			
subjects affected / exposed	2 / 3 (66.67%)	3 / 3 (100.00%)	1 / 3 (33.33%)
occurrences (all)	2	4	1
Neutropenia			
subjects affected / exposed	3 / 3 (100.00%)	3 / 3 (100.00%)	1 / 3 (33.33%)
occurrences (all)	3	7	1
Thrombocytopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1

Faecaloma			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	3 / 3 (100.00%)	2 / 3 (66.67%)	2 / 3 (66.67%)
occurrences (all)	5	3	2
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 3 (66.67%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Skin and subcutaneous tissue disorders			
Subcutaneous emphysema			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Proteinuria			
subjects affected / exposed	0 / 3 (0.00%)	2 / 3 (66.67%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Urinary retention			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Infections and infestations			
Severe acute respiratory syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			

Hypoalbuminaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Hypocalcaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Overall		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 9 (100.00%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
General disorders and administration site conditions			
Chills			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Body temperature increased			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Neutrophil count decreased			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Platelet count increased			

subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Electrocardiogram repolarization abnormality			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Cardiac disorders			
Bundle branch block right			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Left ventricular hypertrophy			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 9 (55.56%)		
occurrences (all)	7		
Leukopenia			
subjects affected / exposed	6 / 9 (66.67%)		
occurrences (all)	7		
Neutropenia			
subjects affected / exposed	7 / 9 (77.78%)		
occurrences (all)	11		
Thrombocytopenia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		

Faecaloma subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1 7 / 9 (77.78%) 10 2 / 9 (22.22%) 2		
Hepatobiliary disorders Hyperbilirubinaemia subjects affected / exposed occurrences (all)	2 / 9 (22.22%) 3		
Skin and subcutaneous tissue disorders Subcutaneous emphysema subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Renal and urinary disorders Haematuria subjects affected / exposed occurrences (all) Proteinuria subjects affected / exposed occurrences (all) Urinary retention subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1 2 / 9 (22.22%) 2 1 / 9 (11.11%) 1		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Infections and infestations Severe acute respiratory syndrome subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Metabolism and nutrition disorders			

Hypoalbuminaemia subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Hypocalcaemia subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 December 2018	Additional text to clarify that historical biopsy samples collected at screening may be used for potential future analysis to identify the presence and density of tumour antigen and potential correlation of drug efficacy with this density. Also, remnants from centrally analysed samples may also be anonymized and pooled together for use in L-DOS47-related assay development and validation to avoid unnecessary additional blood sample collections.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
28 April 2020	Enrolment was halted due to lockdowns related to COVID pandemic.	-

Notes:

Limitations and caveats

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

Due to the study being halted during the lead-in dose escalation portion of the study, only 9 patients were treated in total, instead of the additional 118 patients intended in the randomized portion of the study.

Notes: