# 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<br>Units: Subjects | | | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 62.7 | 59.0 | 58.7 |
| standard deviation | ± 1.15 | ± 9.54 | ± 8.50 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 0 | 0 | 1 |
| Male | 3 | 3 | 2 |
| Race<br>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<br>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<br>Units: Subjects | | | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | | | |

| | | | |
|---|---|---|---|
| standard deviation | - | | |

| | | | |
|---|---|---|---|
| Gender categorical<br>Units: Subjects | | | |
| Female | 1 | | |
| Male | 8 | | |
| Race<br>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<br>Units: m2<br>arithmetic mean<br>standard deviation | -<br>- | | |

**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<br>Units: Subjects | | | |

| | | | |
|---|---|---|---|
| Age continuous<br>Units: years | | | |
| arithmetic mean | 60.1 | 59.5 | |
| standard deviation | ± 6.70 | ± 6.89 | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 1 | 0 | |
| Male | 8 | 8 | |
| Race<br>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<br>subjects affected / exposed<br>occurrences (all)<br><br>Nausea<br>subjects affected / exposed<br>occurrences (all)<br><br>Vomiting<br>subjects affected / exposed<br>occurrences (all) | 1 / 9 (11.11%)<br>1<br><br>7 / 9 (77.78%)<br>10<br><br>2 / 9 (22.22%)<br>2 | | |
| Hepatobiliary disorders<br>Hyperbilirubinaemia<br>subjects affected / exposed<br>occurrences (all) | 2 / 9 (22.22%)<br>3 | | |
| Skin and subcutaneous tissue disorders<br>Subcutaneous emphysema<br>subjects affected / exposed<br>occurrences (all) | 1 / 9 (11.11%)<br>1 | | |
| Renal and urinary disorders<br>Haematuria<br>subjects affected / exposed<br>occurrences (all)<br><br>Proteinuria<br>subjects affected / exposed<br>occurrences (all)<br><br>Urinary retention<br>subjects affected / exposed<br>occurrences (all) | 1 / 9 (11.11%)<br>1<br><br>2 / 9 (22.22%)<br>2<br><br>1 / 9 (11.11%)<br>1 | | |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all) | 1 / 9 (11.11%)<br>1 | | |
| Infections and infestations<br>Severe acute respiratory syndrome<br>subjects affected / exposed<br>occurrences (all) | 1 / 9 (11.11%)<br>1 | | |
| Metabolism and nutrition disorders | | | |

| | | | |
|---|---|---|---|
| Hypoalbuminaemia<br>subjects affected / exposed<br>occurrences (all) | 1 / 9 (11.11%)<br>1 | | |
| Hypocalcaemia<br>subjects affected / exposed<br>occurrences (all) | 1 / 9 (11.11%)<br>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: