



## Clinical trial results:

### Phase II Study of ADI-PEG 20 in Patients with Relapsed Sensitive or Refractory Small Cell Lung Cancer

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2009-017885-22 |
| Trial protocol           | BE DE GB       |
| Global end of trial date | 15 July 2013   |

#### Results information

|                                |               |
|--------------------------------|---------------|
| Result version number          | v1 (current)  |
| This version publication date  | 29 March 2020 |
| First version publication date | 29 March 2020 |

#### Trial information

##### Trial identification

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | LUD2009-007 |
|-----------------------|-------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01266018 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Ludwig Institute for Cancer Research   |
| Sponsor organisation address | 666 3rd Ave, New York, United States, 10017-4011   |
| Public contact               | Clinical Trial Information, Ludwig Institute for Cancer Research, 001 2124501515, <a href="mailto:clintrialinformation@licr.org">clintrialinformation@licr.org</a> |
| Scientific contact           | Clinical Trial Information, Ludwig Institute for Cancer Research, 001 2124501515, <a href="mailto:clintrialinformation@licr.org">clintrialinformation@licr.org</a> |

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:

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**Results analysis stage**

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|  |                  |
|--|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 19 December 2014 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 24 June 2013     |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 15 July 2013     |
| Was the trial ended prematurely?                     | Yes              |

Notes:

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**General information about the trial**

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Main objective of the trial:

The primary objective of this study was to assess the clinical efficacy of ADI-PEG 20, via the primary endpoint of tumor response by RECIST, in subjects with relapsed sensitive or refractory Small Cell Lung Cancer (SCLC).

Protection of trial subjects:

The study was conducted in full conformity with the current revision of the Declaration of Helsinki, International Conference on Harmonisation (ICH) Guidelines and applicable local laws and regulations, with the understanding that local laws and regulations took precedence over respective sections in the Declaration of Helsinki and/or the ICH Guidelines. Before study drug could be shipped and subjects could be entered into the study, the Institutional Review Board (IRB) or its equivalent must have approved the protocol and informed consent form in writing.

The investigator was to obtain witnessed written informed consent from each subject or the subject's legally authorized representative after adequate explanation of the aims, methods, anticipated benefits, and potential hazards of the study and before any study procedures were performed. Subjects were only to be identified by their initials, date of birth, and subject number on the case report forms (CRFs) or other documents submitted to the Sponsor.

Background therapy: -

Evidence for comparator: -

|   |                 |
|---|-----------------|
| Actual start date of recruitment                          | 04 January 2012 |
| Long term follow-up planned                               | No              |
| Independent data monitoring committee (IDMC) involvement? | No              |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |                   |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | United Kingdom: 3 |
| Country: Number of subjects enrolled | Belgium: 1        |
| Country: Number of subjects enrolled | Germany: 1        |
| Country: Number of subjects enrolled | United States: 11 |
| Country: Number of subjects enrolled | Taiwan: 6         |
| Worldwide total number of subjects   | 22                |
| EEA total number of subjects         | 5                 |

Notes:

| <b>Subjects enrolled per age group</b>    |    |
|---|----|
| 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)                      | 14 |
| From 65 to 84 years                       | 8  |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

This was a 2-arm, open-label, phase 2 study of pegylated arginine deiminase (ADI-PEG) 20 in subjects with relapsed sensitive or refractory small cell lung cancer (SCLC). ADI-PEG 20 was administered intramuscularly (IM) at a fixed dose of 320 IU/m<sup>2</sup> once weekly for a 4-week cycle.

### Pre-assignment

Screening details:

22 subjects were enrolled in the study and were treated.

### Period 1

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

Blinding implementation details:

none

### Arms

|                              |     |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

|                  |                            |
|------------------|----------------------------|
| <b>Arm title</b> | Cohort 1 Sensitive Disease |
|------------------|----------------------------|

Arm description:

Cohort 1 comprised subjects with "sensitive" disease, defined as subjects who were treated with 1 previous line of chemotherapy and maintained an appropriate response for 90 days or more. Subjects received 4 administrations of ADI-PEG 20 (320 IU/m<sup>2</sup>) followed by 1 week of follow-up in each treatment cycle.

|  |                              |
|--|------------------------------|
| Arm type                               | Experimental                 |
| Investigational medicinal product name | ADI-PEG 20                   |
| Investigational medicinal product code |                              |
| Other name                             | Arginine deiminase pegylated |
| Pharmaceutical forms                   | Solution for injection       |
| Routes of administration               | Intramuscular use            |

Dosage and administration details:

ADI-PEG 20 was administered intramuscularly (IM) at a fixed dose of 320 IU/m<sup>2</sup> (36.8 mg/m<sup>2</sup>) once weekly for 4 weeks followed by a 1-week follow-up (1 cycle).

|                  |                             |
|------------------|-----------------------------|
| <b>Arm title</b> | Cohort 2 Refractory Disease |
|------------------|-----------------------------|

Arm description:

Cohort 2 comprised subjects with "refractory" disease, defined as subjects who either (a) were treated with 1 previous line of chemotherapy and either had no response or progressed < 90 days after completing treatment or (b) required third-line therapy, i.e., had completed 2 previous lines of chemotherapy, regardless of response. Subjects received 4 administrations of ADI-PEG 20 (320 IU/m<sup>2</sup>) followed by 1 week of follow-up in each treatment cycle.

|  |                              |
|--|------------------------------|
| Arm type                               | Experimental                 |
| Investigational medicinal product name | ADI-PEG 20                   |
| Investigational medicinal product code |                              |
| Other name                             | Arginine deiminase pegylated |
| Pharmaceutical forms                   | Solution for injection       |
| Routes of administration               | Intramuscular use            |

Dosage and administration details:

ADI-PEG 20 was administered intramuscularly (IM) at a fixed dose of 320 IU/m<sup>2</sup> (36.8 mg/m<sup>2</sup>) once weekly for 4 weeks followed by a 1-week follow-up (1 cycle).

| <b>Number of subjects in period 1</b> | Cohort 1 Sensitive Disease | Cohort 2 Refractory Disease |
|---------------------------------------|----------------------------|-----------------------------|
| Started                               | 9                          | 13                          |
| Completed                             | 8                          | 13                          |
| Not completed                         | 1                          | 0                           |
| Physician decision                    | 1                          | -                           |

## Baseline characteristics

### Reporting groups

|                       |               |
|-----------------------|---------------|
| Reporting group title | overall study |
|-----------------------|---------------|

Reporting group description: -

| Reporting group values                             | overall study | Total |  |
|--|---------------|-------|--|
| Number of subjects                                 | 22            | 22    |  |
| Age categorical                                    |               |       |  |
| Units: Subjects                                    |               |       |  |
| In utero   | 0             | 0     |  |
| Preterm newborn infants (gestational age < 37 wks) | 0             | 0     |  |
| Newborns (0-27 days)                               | 0             | 0     |  |
| Infants and toddlers (28 days-23 months)           | 0             | 0     |  |
| Children (2-11 years)                              | 0             | 0     |  |
| Adolescents (12-17 years)                          | 0             | 0     |  |
| Adults (18-64 years)                               | 14            | 14    |  |
| From 65-84 years                                   | 8             | 8     |  |
| 85 years and over                                  | 0             | 0     |  |
| Age continuous                                     |               |       |  |
| Age at baseline                                    |               |       |  |
| Units: years                                       |               |       |  |
| arithmetic mean                                    | 63.4          |       |  |
| standard deviation                                 | ± 9.4         | -     |  |
| Gender categorical                                 |               |       |  |
| Units: Subjects                                    |               |       |  |
| Female   | 8             | 8     |  |
| Male   | 14            | 14    |  |

## End points

### End points reporting groups

|   |                             |
|---|-----------------------------|
| Reporting group title   | Cohort 1 Sensitive Disease  |
| Reporting group description:<br>Cohort 1 comprised subjects with "sensitive" disease, defined as subjects who were treated with 1 previous line of chemotherapy and maintained an appropriate response for 90 days or more. Subjects received 4 administrations of ADI-PEG 20 (320 IU/m <sup>2</sup> ) followed by 1 week of follow-up in each treatment cycle.   |                             |
| Reporting group title   | Cohort 2 Refractory Disease |
| Reporting group description:<br>Cohort 2 comprised subjects with "refractory" disease, defined as subjects who either (a) were treated with 1 previous line of chemotherapy and either had no response or progressed < 90 days after completing treatment or (b) required third-line therapy, i.e., had completed 2 previous lines of chemotherapy, regardless of response. Subjects received 4 administrations of ADI-PEG 20 (320 IU/m <sup>2</sup> ) followed by 1 week of follow-up in each treatment cycle. |                             |

### Primary: Best overall response

|   |                                      |
|---|--------------------------------------|
| End point title   | Best overall response <sup>[1]</sup> |
| End point description:<br>Tumor responses were evaluated using any appropriate imaging type and were categorized according to Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1. Per RECIST for target lesions and assessed by MRI:<br><br>Complete Response (CR): Disappearance of all target lesions [no evidence of disease]; Partial Response (PR): ≥ 30% decrease in the sum of the longest diameter of target lesions; Progressive Disease (PD): ≥ 20% increase in the sum of the longest diameter of target lesions; Stable Disease (SD): small changes that do not meet above criteria. |                                      |
| End point type  | Primary                              |
| End point timeframe:<br>Every 4 to 8 weeks for up to 16 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: Because no subject in the refractory disease cohort had a response, the study was terminated early and declared negative.

| End point values            | Cohort 1<br>Sensitive<br>Disease | Cohort 2<br>Refractory<br>Disease |  |  |
|-----------------------------|----------------------------------|-----------------------------------|--|--|
| Subject group type          | Reporting group                  | Reporting group                   |  |  |
| Number of subjects analysed | 8 <sup>[2]</sup>                 | 12 <sup>[3]</sup>                 |  |  |
| Units: number of subjects   |                                  |                                   |  |  |
| stable disease              | 2                                | 2                                 |  |  |
| progressive disease         | 6                                | 10                                |  |  |

Notes:

[2] - includes all subjects who were evaluable for tumor response

[3] - Includes all subjects who were evaluable for tumor response

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

All adverse events (AEs) occurring between the signing of informed consent and the off-study date were documented, regardless of the causal relationship to study drug. AEs occurring after the first dose of study drug were considered treatment emergent.

Adverse event reporting additional description:

Analysis of treatment-emergent adverse events (TEAEs) reported from clinical laboratory tests, physical examinations, and vital signs.

AE documentation included onset/resolution dates, severity using NCI CTCAE (v4.0), seriousness, study drug action taken, treatment, and outcome.

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 13.1   |

### Reporting groups

|                       |                                    |
|-----------------------|------------------------------------|
| Reporting group title | All Subjects (Safety Analysis Set) |
|-----------------------|------------------------------------|

Reporting group description:

Includes all subjects in Cohort 1 (n = 9) and Cohort 2 (n = 13) who received at least 1 dose of study drug.

| Serious adverse events  | All Subjects (Safety Analysis Set) |  |  |
|---|------------------------------------|--|--|
| Total subjects affected by serious adverse events                   |                                    |  |  |
| subjects affected / exposed   | 10 / 22 (45.45%)                   |  |  |
| number of deaths (all causes)                                       | 3                                  |  |  |
| number of deaths resulting from adverse events                      | 3                                  |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                    |  |  |
| Malignant neoplasm progression                                      |                                    |  |  |
| subjects affected / exposed   | 2 / 22 (9.09%)                     |  |  |
| occurrences causally related to treatment / all                     | 0 / 2                              |  |  |
| deaths causally related to treatment / all                          | 0 / 2                              |  |  |
| Cardiac disorders   |                                    |  |  |
| Cardiac arrest  |                                    |  |  |
| subjects affected / exposed   | 1 / 22 (4.55%)                     |  |  |
| occurrences causally related to treatment / all                     | 0 / 1                              |  |  |
| deaths causally related to treatment / all                          | 0 / 1                              |  |  |
| Nervous system disorders  |                                    |  |  |
| Hypoaesthesia   |                                    |  |  |



|  |                |  |  |
|--|----------------|--|--|
| subjects affected / exposed                          | 1 / 22 (4.55%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Paraesthesia   |                |  |  |
| subjects affected / exposed                          | 1 / 22 (4.55%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Somnolence   |                |  |  |
| subjects affected / exposed                          | 1 / 22 (4.55%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Blood and lymphatic system disorders                 |                |  |  |
| Febrile neutropenia                                  |                |  |  |
| subjects affected / exposed                          | 1 / 22 (4.55%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Leukopenia   |                |  |  |
| subjects affected / exposed                          | 1 / 22 (4.55%) |  |  |
| occurrences causally related to treatment / all      | 1 / 1          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Neutropenia  |                |  |  |
| subjects affected / exposed                          | 1 / 22 (4.55%) |  |  |
| occurrences causally related to treatment / all      | 1 / 1          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Lymphopenia  |                |  |  |
| subjects affected / exposed                          | 1 / 22 (4.55%) |  |  |
| occurrences causally related to treatment / all      | 1 / 1          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| General disorders and administration site conditions |                |  |  |
| Non-cardiac chest pain                               |                |  |  |
| subjects affected / exposed                          | 1 / 22 (4.55%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| Respiratory, thoracic and mediastinal disorders |                 |  |  |
| Dyspnoea  |                 |  |  |
| subjects affected / exposed                     | 3 / 22 (13.64%) |  |  |
| occurrences causally related to treatment / all | 0 / 3           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |

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

| <b>Non-serious adverse events</b>                     | All Subjects (Safety Analysis Set) |  |  |
|---|------------------------------------|--|--|
| Total subjects affected by non-serious adverse events |                                    |  |  |
| subjects affected / exposed                           | 21 / 22 (95.45%)                   |  |  |
| Investigations  |                                    |  |  |
| White blood cell count decreased                      |                                    |  |  |
| subjects affected / exposed                           | 4 / 22 (18.18%)                    |  |  |
| occurrences (all)                                     | 5                                  |  |  |
| Platelet count decreased                              |                                    |  |  |
| subjects affected / exposed                           | 3 / 22 (13.64%)                    |  |  |
| occurrences (all)                                     | 3                                  |  |  |
| Blood creatinine increased                            |                                    |  |  |
| subjects affected / exposed                           | 2 / 22 (9.09%)                     |  |  |
| occurrences (all)                                     | 2                                  |  |  |
| Haemoglobin decreased                                 |                                    |  |  |
| subjects affected / exposed                           | 2 / 22 (9.09%)                     |  |  |
| occurrences (all)                                     | 2                                  |  |  |
| Cardiac disorders                                     |                                    |  |  |
| Tachycardia   |                                    |  |  |
| subjects affected / exposed                           | 2 / 22 (9.09%)                     |  |  |
| occurrences (all)                                     | 2                                  |  |  |
| Nervous system disorders                              |                                    |  |  |
| Dysgeusia   |                                    |  |  |
| subjects affected / exposed                           | 2 / 22 (9.09%)                     |  |  |
| occurrences (all)                                     | 2                                  |  |  |
| Headache  |                                    |  |  |
| subjects affected / exposed                           | 2 / 22 (9.09%)                     |  |  |
| occurrences (all)                                     | 4                                  |  |  |
| General disorders and administration site conditions  |                                    |  |  |

|   |   |  |  |
|---|---|--|--|
| <p>Fatigue</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>  | <p>10 / 22 (45.45%)</p> <p>12</p>   |  |  |
| <p>Asthenia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>   | <p>4 / 22 (18.18%)</p> <p>5</p>   |  |  |
| <p>Chest discomfort</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>   | <p>2 / 22 (9.09%)</p> <p>2</p>  |  |  |
| <p>Gastrointestinal disorders</p> <p>Constipation</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Nausea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Vomiting</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Diarrhoea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                        | <p>4 / 22 (18.18%)</p> <p>4</p> <p>4 / 22 (18.18%)</p> <p>5</p> <p>4 / 22 (18.18%)</p> <p>4</p> <p>3 / 22 (13.64%)</p> <p>3</p> |  |  |
| <p>Respiratory, thoracic and mediastinal disorders</p> <p>Dyspnoea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Cough</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Wheezing</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Productive cough</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>2 / 22 (9.09%)</p> <p>3</p> <p>4 / 22 (18.18%)</p> <p>5</p> <p>3 / 22 (13.64%)</p> <p>3</p> <p>2 / 22 (9.09%)</p> <p>3</p>   |  |  |
| <p>Skin and subcutaneous tissue disorders</p>   |   |  |  |

|  |  |  |  |
|--|--|--|--|
| Pruritus<br>subjects affected / exposed<br>occurrences (all)   | 2 / 22 (9.09%)<br>2  |  |  |
| Psychiatric disorders<br>Insomnia<br>subjects affected / exposed<br>occurrences (all)  | 2 / 22 (9.09%)<br>2  |  |  |
| Musculoskeletal and connective tissue disorders<br>Back pain<br>subjects affected / exposed<br>occurrences (all)<br><br>Muscular weakness<br>subjects affected / exposed<br>occurrences (all)<br><br>Pain in extremity<br>subjects affected / exposed<br>occurrences (all) | 2 / 22 (9.09%)<br>2<br><br>2 / 22 (9.09%)<br>2<br><br>2 / 22 (9.09%)<br>2  |  |  |
| Infections and infestations<br>Lower respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)   | 2 / 22 (9.09%)<br>2  |  |  |
| Metabolism and nutrition disorders<br>Decreased appetite<br>subjects affected / exposed<br>occurrences (all)<br><br>Dehydration<br>subjects affected / exposed<br>occurrences (all)<br><br>Hyperglycaemia<br>subjects affected / exposed<br>occurrences (all)              | 7 / 22 (31.82%)<br>8<br><br>2 / 22 (9.09%)<br>2<br><br>2 / 22 (9.09%)<br>2 |  |  |

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported