



## Clinical trial results:

### A Randomised, Double-Blind, Placebo-Controlled, Phase II Study to Assess the Efficacy and Safety of Orally Administered DS102 in Patients with Severe Acute Decompensated Alcoholic Hepatitis.

#### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2018-000819-25  |
| Trial protocol           | BE FR DE LV GB  |
| Global end of trial date | 07 October 2019 |

#### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 20 July 2022 |
| First version publication date | 20 July 2022 |

#### Trial information

##### Trial identification

|                       |               |
|-----------------------|---------------|
| Sponsor protocol code | DS102A-05-AH1 |
|-----------------------|---------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03452540 |
| WHO universal trial number (UTN)   | -           |

Notes:

##### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Afimmune   |
| Sponsor organisation address | Trintech Building, South County Business Park, Dublin 18, Ireland, Dublin 18 |
| Public contact               | Study Director, Afimmune, +353 1 2946380, regulatory.afimmune@afimmune.com   |
| Scientific contact           | Study Director, Afimmune, +353 1 2946380, regulatory.afimmune@afimmune.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                       | 31 March 2020   |
| Is this the analysis of the primary completion data? | Yes             |
| Primary completion date                              | 19 June 2019    |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 07 October 2019 |
| Was the trial ended prematurely?                     | Yes             |

Notes:

## General information about the trial

Main objective of the trial:

The objectives for the pilot phase were:

Safety: To compare the safety of orally administered DS102 capsules versus placebo in the treatment of adult patients with severe acute decompensated Alcoholic Hepatitis (AH).

Pharmacokinetics: To evaluate the PK of 15(S)-HEPE EE following orally administration of DS102 capsules in 6 adult patients with severe acute decompensated AH.

Protection of trial subjects:

The study was managed and conducted according to the latest International Council for Harmonisation (ICH) guidelines for Good Clinical Practice (GCP) and applicable regulatory requirements (specifically the principles of GCP in ICH topic E6, as laid down by the Commission Directive 2005/28/EC and in accordance with applicable local laws and guidelines).

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 28 November 2018 |
| Long term follow-up planned                               | No               |
| Independent data monitoring committee (IDMC) involvement? | Yes              |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                  |
|--------------------------------------|------------------|
| Country: Number of subjects enrolled | United States: 6 |
| Country: Number of subjects enrolled | Georgia: 3       |
| 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:

The study was conducted in 3 countries at 10 sites.

### Pre-assignment

Screening details:

A total of 126 participants were planned with actual enrolment in the study at 9 participants before the study was ended prematurely due to futility purposes. The pilot phase of the study was completed, and treatment duration was 28 days with a follow up period to 90 days.

### Period 1

|                              |                              |
|------------------------------|------------------------------|
| Period 1 title               | Pilot Phase (overall period) |
| Is this the baseline period? | Yes                          |
| Allocation method            | Non-randomised - controlled  |
| Blinding used                | Not blinded                  |

### Arms

|                  |              |
|------------------|--------------|
| <b>Arm title</b> | DS102 2000mg |
|------------------|--------------|

Arm description:

2 x DS102 500mg capsules orally administered BID (four capsules daily) for 28 days

|  |                |
|--|----------------|
| Arm type                               | Experimental   |
| Investigational medicinal product name | DS102 Capsules |
| Investigational medicinal product code |                |
| Other name                             |                |
| Pharmaceutical forms                   | Capsule        |
| Routes of administration               | Oral use       |

Dosage and administration details:

2 x DS102 500mg capsules orally administered BID (four capsules daily) for 28 days

| Number of subjects in period 1 | DS102 2000mg |
|--------------------------------|--------------|
| Started                        | 9            |
| Completed                      | 5            |
| Not completed                  | 4            |
| Adverse Event                  | 1            |
| Other                          | 2            |
| Subject Withdrawal of Consent  | 1            |

## Baseline characteristics

### Reporting groups

|                       |              |
|-----------------------|--------------|
| Reporting group title | DS102 2000mg |
|-----------------------|--------------|

Reporting group description:

2 x DS102 500mg capsules orally administered BID (four capsules daily) for 28 days

| Reporting group values                             | DS102 2000mg | Total |  |
|--|--------------|-------|--|
| Number of subjects                                 | 9            | 9     |  |
| 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)                               |              | 0     |  |
| From 65-84 years                                   |              | 0     |  |
| 85 years and over                                  |              | 0     |  |
| Age continuous                                     |              |       |  |
| Units: years                                       |              |       |  |
| arithmetic mean                                    | 53.2         |       |  |
| standard deviation                                 | ± 12.94      | -     |  |
| Gender categorical                                 |              |       |  |
| Units: Subjects                                    |              |       |  |
| Female   | 3            | 3     |  |
| Male   | 6            | 6     |  |
| Ethnicity  |              |       |  |
| Units: Subjects                                    |              |       |  |
| Hispanic or Latino                                 | 2            | 2     |  |
| Not Hispanic or Latino                             | 6            | 6     |  |
| Not reported                                       | 1            | 1     |  |
| Race   |              |       |  |
| Units: Subjects                                    |              |       |  |
| Black or African American                          | 1            | 1     |  |
| American Indian/Alaska Native                      | 0            | 0     |  |
| Asian  | 0            | 0     |  |
| Native Hawaiian or Other Pacific Islander          | 0            | 0     |  |
| White  | 8            | 8     |  |
| Other  | 0            | 0     |  |

## End points

### End points reporting groups

|  |              |
|--|--------------|
| Reporting group title  | DS102 2000mg |
| Reporting group description:<br>2 x DS102 500mg capsules orally administered BID (four capsules daily) for 28 days |              |

### Primary: Treatment-emergent adverse events (TEAEs), serious TEAEs, and SUSARs.

|   |  |
|---|--|
| End point title   | Treatment-emergent adverse events (TEAEs), serious TEAEs, and SUSARs. <sup>[1]</sup> |
| End point description:<br>Treatment-emergent adverse events (TEAEs), serious TEAEs, and SUSARs. |  |
| End point type  | Primary  |
| End point timeframe:<br>Up to 90 days   |  |

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 analysis was carried out for this endpoint.

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| <b>End point values</b>                         | DS102 2000mg    |  |  |  |
| Subject group type                              | Reporting group |  |  |  |
| Number of subjects analysed                     | 9               |  |  |  |
| Units: Number of Events                         |                 |  |  |  |
| Total number of TEAEs                           | 7               |  |  |  |
| Total Number of Serious TEAEs                   | 4               |  |  |  |
| Total Number of Serious Treatment Related TEAEs | 1               |  |  |  |
| Total Number of Treatment related TEAEs         | 1               |  |  |  |
| Total Number of TEAEs not treatment related     | 6               |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Primary: Descriptive Statistics for Plasma Total 15(S)-HEPE and Unesterified 15(S)-HEPE Pharmacokinetic Results for 1000 mg BD DS102 Administered Orally Twice-daily to Patients with Alcoholic Hepatitis

|  |   |
|--|---|
| End point title  | Descriptive Statistics for Plasma Total 15(S)-HEPE and Unesterified 15(S)-HEPE Pharmacokinetic Results for 1000 mg BD DS102 Administered Orally Twice-daily to Patients with Alcoholic Hepatitis <sup>[2]</sup> |
| End point description:<br>Descriptive Statistics for Plasma Total 15(S)-HEPE and Unesterified 15(S)-HEPE Pharmacokinetic Results for 1000 mg BD DS102 Administered Orally Twice-daily to Patients with Alcoholic Hepatitis |   |
| End point type   | Primary   |

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End point timeframe:

Up to 7 days

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Notes:

[2] - 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 analysis was carried out for this endpoint.

|                                      |                 |  |  |  |
|--------------------------------------|-----------------|--|--|--|
| <b>End point values</b>              | DS102 2000mg    |  |  |  |
| Subject group type                   | Reporting group |  |  |  |
| Number of subjects analysed          | 9               |  |  |  |
| Units: ng/mL                         |                 |  |  |  |
| arithmetic mean (standard deviation) |                 |  |  |  |
| Day 0 Unesterified 15(S)-HEPE        | 542 (± 399.4)   |  |  |  |
| Day 7 Unesterified 15(S)-HEPE        | 1060 (± 1073)   |  |  |  |
| Day 0 Total 15(S)-HEPE               | 3110 (± 3721)   |  |  |  |
| Day 7 Total 15(S)-HEPE               | 4470 (± 3601)   |  |  |  |

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### Statistical analyses

No statistical analyses for this end point

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## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to 90 days

Adverse event reporting additional description:

An AE was defined as any undesirable experience occurring to a patient who had signed the ICF and who had taken their first dose of the investigational product, whether or not considered related to the investigational product. All AEs were recorded on the eCRF, defining relationship to investigational product and severity.

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

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 21.1 |
|--------------------|------|

### Reporting groups

|                       |              |
|-----------------------|--------------|
| Reporting group title | DS102 2000mg |
|-----------------------|--------------|

Reporting group description:

2 x DS102 500mg capsules orally administered BID (four capsules daily) for 28 days

| Serious adverse events                            | DS102 2000mg   |  |  |
|---|----------------|--|--|
| Total subjects affected by serious adverse events |                |  |  |
| subjects affected / exposed                       | 4 / 9 (44.44%) |  |  |
| number of deaths (all causes)                     | 2              |  |  |
| number of deaths resulting from adverse events    | 2              |  |  |
| Vascular disorders                                |                |  |  |
| Hypovolaemic shock                                |                |  |  |
| subjects affected / exposed                       | 1 / 9 (11.11%) |  |  |
| occurrences causally related to treatment / all   | 0 / 1          |  |  |
| deaths causally related to treatment / all        | 0 / 1          |  |  |
| Cardiac disorders                                 |                |  |  |
| Cardiac arrest                                    |                |  |  |
| subjects affected / exposed                       | 1 / 9 (11.11%) |  |  |
| occurrences causally related to treatment / all   | 0 / 1          |  |  |
| deaths causally related to treatment / all        | 0 / 0          |  |  |
| Nervous system disorders                          |                |  |  |
| Metabolic encephalopathy                          |                |  |  |
| subjects affected / exposed                       | 1 / 9 (11.11%) |  |  |
| occurrences causally related to treatment / all   | 0 / 1          |  |  |
| deaths causally related to treatment / all        | 0 / 0          |  |  |
| General disorders and administration              |                |  |  |

|   |                |  |  |
|---|----------------|--|--|
| site conditions                                 |                |  |  |
| Multiple organ dysfunction syndrome             |                |  |  |
| subjects affected / exposed                     | 1 / 9 (11.11%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Respiratory, thoracic and mediastinal disorders |                |  |  |
| Pulmonary oedema                                |                |  |  |
| subjects affected / exposed                     | 1 / 9 (11.11%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 1          |  |  |
| Psychiatric disorders                           |                |  |  |
| Mental status changes                           |                |  |  |
| subjects affected / exposed                     | 1 / 9 (11.11%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Renal and urinary disorders                     |                |  |  |
| Renal failure                                   |                |  |  |
| subjects affected / exposed                     | 1 / 9 (11.11%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Infections and infestations                     |                |  |  |
| Septic shock                                    |                |  |  |
| 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: 0 %

|   |                |  |  |
|---|----------------|--|--|
| <b>Non-serious adverse events</b>                     | DS102 2000mg   |  |  |
| Total subjects affected by non-serious adverse events |                |  |  |
| subjects affected / exposed                           | 7 / 9 (77.78%) |  |  |
| Investigations  |                |  |  |
| Aspartate aminotransferase increased                  |                |  |  |
| subjects affected / exposed                           | 2 / 9 (22.22%) |  |  |
| occurrences (all)                                     | 2              |  |  |

|   |   |  |  |
|---|---|--|--|
| Alanine aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)  | 1 / 9 (11.11%)<br>1   |  |  |
| Blood alkaline phosphatase increased<br>subjects affected / exposed<br>occurrences (all)  | 1 / 9 (11.11%)<br>1   |  |  |
| Paracentesis<br>subjects affected / exposed<br>occurrences (all)  | 1 / 9 (11.11%)<br>1   |  |  |
| Injury, poisoning and procedural complications<br>Fall<br>subjects affected / exposed<br>occurrences (all)<br><br>Head injury<br>subjects affected / exposed<br>occurrences (all)   | 2 / 9 (22.22%)<br>2<br><br>1 / 9 (11.11%)<br>1                            |  |  |
| Vascular disorders<br>Hypotension<br>subjects affected / exposed<br>occurrences (all)   | 1 / 9 (11.11%)<br>1   |  |  |
| Cardiac disorders<br>Palpitations<br>subjects affected / exposed<br>occurrences (all)   | 1 / 9 (11.11%)<br>1   |  |  |
| Nervous system disorders<br>Dizziness<br>subjects affected / exposed<br>occurrences (all)<br><br>Encephalopathy<br>subjects affected / exposed<br>occurrences (all)<br><br>Headache<br>subjects affected / exposed<br>occurrences (all)<br><br>Metabolic encephalopathy | 1 / 9 (11.11%)<br>1<br><br>1 / 9 (11.11%)<br>1<br><br>1 / 9 (11.11%)<br>1 |  |  |

|  |                |  |  |
|--|----------------|--|--|
| subjects affected / exposed                          | 1 / 9 (11.11%) |  |  |
| occurrences (all)                                    | 1              |  |  |
| General disorders and administration site conditions |                |  |  |
| Asthenia   |                |  |  |
| subjects affected / exposed                          | 1 / 9 (11.11%) |  |  |
| occurrences (all)                                    | 1              |  |  |
| Localised oedema                                     |                |  |  |
| subjects affected / exposed                          | 1 / 9 (11.11%) |  |  |
| occurrences (all)                                    | 1              |  |  |
| Oedema   |                |  |  |
| subjects affected / exposed                          | 1 / 9 (11.11%) |  |  |
| occurrences (all)                                    | 1              |  |  |
| Oedema peripheral                                    |                |  |  |
| subjects affected / exposed                          | 1 / 9 (11.11%) |  |  |
| occurrences (all)                                    | 2              |  |  |
| Gastrointestinal disorders                           |                |  |  |
| Abdominal distension                                 |                |  |  |
| subjects affected / exposed                          | 2 / 9 (22.22%) |  |  |
| occurrences (all)                                    | 2              |  |  |
| Abdominal pain                                       |                |  |  |
| subjects affected / exposed                          | 1 / 9 (11.11%) |  |  |
| occurrences (all)                                    | 1              |  |  |
| Diarrhoea  |                |  |  |
| subjects affected / exposed                          | 1 / 9 (11.11%) |  |  |
| occurrences (all)                                    | 1              |  |  |
| Flatulence   |                |  |  |
| subjects affected / exposed                          | 1 / 9 (11.11%) |  |  |
| occurrences (all)                                    | 1              |  |  |
| Glossitis  |                |  |  |
| subjects affected / exposed                          | 1 / 9 (11.11%) |  |  |
| occurrences (all)                                    | 1              |  |  |
| Vomiting   |                |  |  |
| subjects affected / exposed                          | 1 / 9 (11.11%) |  |  |
| occurrences (all)                                    | 1              |  |  |
| Respiratory, thoracic and mediastinal disorders      |                |  |  |

|  |                     |  |  |
|--|---------------------|--|--|
| Dyspnoea<br>subjects affected / exposed<br>occurrences (all)                                       | 1 / 9 (11.11%)<br>1 |  |  |
| Skin and subcutaneous tissue disorders<br>Rash<br>subjects affected / exposed<br>occurrences (all) | 1 / 9 (11.11%)<br>1 |  |  |
| Skin lesion<br>subjects affected / exposed<br>occurrences (all)                                    | 1 / 9 (11.11%)<br>1 |  |  |
| Psychiatric disorders<br>Confusional state<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? No

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### 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.

|  |
|--|
| Early termination - The study was stopped at the end of the pilot phase (n=9), so no patients were enrolled in the double-blind phase. |
|--|

Notes: