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

Arm title	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:	
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.[1]
End point description:	
Treatment-emergent adverse events (TEAEs), serious TEAEs, and SUSARs.	
End point type	Primary
End point timeframe:	
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.

End point values	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[2]
End point description:	
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

End point timeframe:

Up to 7 days

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.

End point values	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)			

Statistical analyses

No statistical analyses for this end point

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 %

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

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

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: