Clinical trial results:
Open-label Rollover Study of Cenicriviroc for the Treatment of Liver Fibrosis in Adult Subjects with Nonalcoholic Steatohepatitis (NASH)

Summary

EudraCT number	2016-004754-15
Trial protocol	GB DE BE ES HU AT IT
Global end of trial date	05 January 2021

Results information

Result version number	v1 (current)
This version publication date	03 November 2021
First version publication date	03 November 2021

Trial information

Trial identification

Sponsor protocol code	3152-201-002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03059446
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Allergan
Sponsor organisation address	1st Floor, Marlow International, The Parkway, Marlow Buckinghamshire, United Kingdom, SL7 1YL
Public contact	Therapeutic Area, Head, Allergan, 001 714-246-4500, IR-CTRegistration@Allergan.com
Scientific contact	Therapeutic Area, Head, Allergan, 001 714-246-4500, IR-CTRegistration@Allergan.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	05 January 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 January 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

This rollover study provided open-label treatment with cenicriviroc and assessed the long-term safety of continued treatment with cenicriviroc in participants who participated in either the CENTAUR study 652-2-203 [NCT02217475] or the AURORA study [NCT03028740].

Protection of trial subjects:

All study participants were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 February 2017
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	Belgium: 8
Country: Number of subjects enrolled	Germany: 8
Country: Number of subjects enrolled	Spain: 8
Country: Number of subjects enrolled	France: 7
Country: Number of subjects enrolled	Italy: 7
Country: Number of subjects enrolled	Poland: 4
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	United States: 108
Country: Number of subjects enrolled	Australia: 8
Country: Number of subjects enrolled	Hong Kong: 6
Worldwide total number of subjects	167
EEA total number of subjects	42

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)	121
From 65 to 84 years	46
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants who completed the CENTAUR study [NCT02217475] or the AURORA study [NCT03028740] were eligible for enrollment in this rollover study.

Period 1

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

Arms

Arm title	Cenicriviroc (CVC) 150 mg

Arm description:

Cenicriviroc 150 mg tablet once daily in the morning with food until the study was terminated (up to approximately 4 years).

Arm type	Experimental
Investigational medicinal product name	Cenicriviroc
Investigational medicinal product code	
Other name	CVC
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Cenicriviroc 150 mg immediate release tablet once daily in the morning with food.

Number of subjects in period 1	Cenicriviroc (CVC) 150 mg
Started	167
Completed	0
Not completed	167
Adverse event, serious fatal	1
Withdrawal of Consent	16
Adverse event, non-fatal	10
Study Terminated by Sponsor	131
Lost to follow-up	3
Reason not Specified	5
Protocol deviation	1

Baseline characteristics

Reporting groups	
Reporting group title	Cenicriviroc (CVC) 150 mg
Reporting group description:	
Cenicriviroc 150 mg tablet once daily in the morning with food until the study was terminated (up to approximately 4 years).	

Reporting group values	Cenicriviroc (CVC) 150 mg	Total	
Number of subjects	167	167	
Age categorical Units: Subjects			
Adults (18-64 years)	121	121	
From 65-84 years	46	46	
Age Continuous Units: years			
arithmetic mean	56.8		
standard deviation	± 10.41	-	
Sex: Female, Male Units: participants			
Female	88	88	
Male	79	79	
Race Units: Subjects			
American Indian or Alaska Native	1	1	
Asian	9	9	
Native Hawaiian or Other Pacific Islander	2	2	
Black or African American	4	4	
White	150	150	
More than one race	0	0	
Unknown or Not Reported	1	1	
Ethnicity Units: Subjects			
Hispanic or Latino	24	24	
Not Hispanic or Latino	143	143	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	Cenicriviroc (CVC) 150 mg

Reporting group description:

Cenicriviroc 150 mg tablet once daily in the morning with food until the study was terminated (up to approximately 4 years).

Primary: Number of Participants With Treatment-emergent Adverse Events (AE)

End point title	Number of Participants With Treatment-emergent Adverse Events (AE)[1]

End point description:

An AE is any untoward medical occurrence in a participant or clinical investigation participant administered a pharmaceutical product and which does not necessarily have a causal relationship with the treatment. A treatment-emergent AE is an AE that occurs after a participant receives study drug. Safety Population included all participants who received at least one dose of study drug.

End point type	Primary

End point timeframe:

Day 1 until the study was terminated (up to approximately 4 years)

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 are reported for this endpoint.

End point values	Cenicriviroc (CVC) 150 mg			
Subject group type	Reporting group			
Number of subjects analysed	167			
Units: participants	140			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Day 1 until the study was terminated (Up to approximately 4 years)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups	
Reporting group title	Cenicriviroc 150 mg
Reporting group description:	
Cenicriviroc 150 mg tablet once daily in the morning with food until the study was terminated (up to approximately 4 years).	

Serious adverse events	Cenicriviroc 150 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	40 / 167 (23.95%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	2 / 167 (1.20%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Bowen’s disease			
subjects affected / exposed	2 / 167 (1.20%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hepatocellular carcinoma			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Invasive lobular breast carcinoma			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Ovarian cancer	Additional description: Number of participants at risk is based on the female population.		
subjects affected / exposed[1]	1 / 88 (1.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Papillary thyroid cancer			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal cancer			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal cell carcinoma			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Squamous cell carcinoma of skin			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lymphatic fistula			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Asthenia			

subjects affected / exposed	1 / 167 (0.60%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Chronic obstructive pulmonary disease				
subjects affected / exposed	1 / 167 (0.60%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
Weight decreased				
subjects affected / exposed	1 / 167 (0.60%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Contusion				
subjects affected / exposed	1 / 167 (0.60%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Post procedural fever				
subjects affected / exposed	1 / 167 (0.60%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Road traffic accident				
subjects affected / exposed	1 / 167 (0.60%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Post procedural haemorrhage				
subjects affected / exposed	1 / 167 (0.60%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Toxicity to various agents				

subjects affected / exposed	1 / 167 (0.60%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal compression fracture			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	3 / 167 (1.80%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Acute coronary syndrome			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Angina unstable			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Coronary artery occlusion			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tachycardia			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			

Cerebrovascular accident			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dizziness			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Migraine with aura			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Headache			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Uraemic encephalopathy			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vertebral artery stenosis			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			

Retinal artery occlusion				
subjects affected / exposed	1 / 167 (0.60%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal pain upper				
subjects affected / exposed	1 / 167 (0.60%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Food poisoning				
subjects affected / exposed	1 / 167 (0.60%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pancreatitis				
subjects affected / exposed	1 / 167 (0.60%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	1 / 167 (0.60%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Salivary gland calculus				
subjects affected / exposed	1 / 167 (0.60%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholecystitis acute				
subjects affected / exposed	2 / 167 (1.20%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Cholecystitis				
subjects affected / exposed	1 / 167 (0.60%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	3 / 167 (1.80%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Cellulitis			
subjects affected / exposed	3 / 167 (1.80%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Pneumonia legionella			
subjects affected / exposed	2 / 167 (1.20%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Bone abscess			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	2 / 167 (1.20%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
COVID-19 pneumonia			
subjects affected / exposed	1 / 167 (0.60%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Carbuncle			

subjects affected / exposed	1 / 167 (0.60%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Empyema				
subjects affected / exposed	1 / 167 (0.60%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	1 / 167 (0.60%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Liver abscess				
subjects affected / exposed	1 / 167 (0.60%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	1 / 167 (0.60%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Q fever				
subjects affected / exposed	1 / 167 (0.60%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Gout				
subjects affected / exposed	1 / 167 (0.60%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dehydration				
subjects affected / exposed	3 / 167 (1.80%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Hypoglycaemia				

subjects affected / exposed	1 / 167 (0.60%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Number of participants at risk is based on the female population.

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

Non-serious adverse events	Cenicriviroc 150 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	98 / 167 (58.68%)		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	10 / 167 (5.99%)		
occurrences (all)	11		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	10 / 167 (5.99%)		
occurrences (all)	11		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	20 / 167 (11.98%)		
occurrences (all)	27		
Abdominal pain upper			
subjects affected / exposed	12 / 167 (7.19%)		
occurrences (all)	13		
Abdominal pain			
subjects affected / exposed	12 / 167 (7.19%)		
occurrences (all)	14		
Nausea			
subjects affected / exposed	13 / 167 (7.78%)		
occurrences (all)	19		
Constipation			
subjects affected / exposed	12 / 167 (7.19%)		
occurrences (all)	13		
Respiratory, thoracic and mediastinal disorders			

Cough subjects affected / exposed occurrences (all)	9 / 167 (5.39%) 9		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	13 / 167 (7.78%) 18		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	22 / 167 (13.17%) 29		
Infections and infestations Influenza subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) Sinusitis subjects affected / exposed occurrences (all) Bronchitis subjects affected / exposed occurrences (all)	14 / 167 (8.38%) 14 17 / 167 (10.18%) 21 9 / 167 (5.39%) 10 9 / 167 (5.39%) 13 12 / 167 (7.19%) 14		
Metabolism and nutrition disorders Diabetes mellitus subjects affected / exposed occurrences (all)	12 / 167 (7.19%) 12		

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? Yes

Date	Interruption	Restart date
05 January 2021	This study was terminated early due to lack of efficacy based on the results of Part I of the AURORA study.	-

Notes:

Limitations and caveats

None reported