



Clinical trial results:

CENTAUR: Efficacy and Safety Study of Cenicriviroc for the Treatment of Nonalcoholic Steatohepatitis (NASH) in Adult Subjects with Liver Fibrosis

Summary

EudraCT number	2014-003164-21
Trial protocol	BE GB IT DE ES FR
Global end of trial date	22 June 2017

Results information

Result version number	v1 (current)
This version publication date	31 May 2019
First version publication date	31 May 2019

Trial information

Trial identification

Sponsor protocol code	652-2-203
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02217475
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Tobira Therapeutics, Inc., an affiliate of Allergan plc
Sponsor organisation address	Clonsaugh Business and Technology Park, Coolock, Dublin, Ireland, D17 E400
Public contact	Clinical Trials Registry Team, Allergan plc, 001 8772778566, IR-CTRegistration@allergan.com
Scientific contact	Therapeutic Area, Head, Allergan plc, 001 862-261-7000, 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	22 June 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 June 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate hepatic histological improvement in nonalcoholic fatty liver disease (NAFLD) activity score (NAS) at Year 1, relative to the Screening biopsy, defined by a minimum 2-point improvement in NAS with at least a 1-point reduction in either lobular inflammation or hepatocellular ballooning AND with no concurrent worsening of fibrosis stage (worsening defined as progression of NASH Clinical Research Network [CRN] fibrosis stage) at Year 1.

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	18 September 2014
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: 166
Country: Number of subjects enrolled	Australia: 15
Country: Number of subjects enrolled	China: 14
Country: Number of subjects enrolled	France: 37
Country: Number of subjects enrolled	Belgium: 15
Country: Number of subjects enrolled	Germany: 12
Country: Number of subjects enrolled	Spain: 10
Country: Number of subjects enrolled	Italy: 8
Country: Number of subjects enrolled	United Kingdom: 7
Country: Number of subjects enrolled	Poland: 5
Worldwide total number of subjects	289
EEA total number of subjects	94

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)	236
From 65 to 84 years	53
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

In total, 812 participants were screened, and 289 participants were randomised to treatment period 1. Of the 289 participants randomised, 250 participants completed Treatment Period 1. A total of 242 participants entered Treatment Period 2 and 212 completed.

Period 1

Period 1 title	Treatment Period 1 (Year 1)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Carer, Assessor, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo/Placebo

Arm description:

Placebo-matching cenicriviroc (CVC) tablet in Years 1 and 2.

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

Dosage and administration details:

Placebo-matching cenicriviroc (CVC) tablet, once daily in the morning with food in Year 1.

Arm title	Placebo/Cenicriviroc (CVC) 150 mg
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Arm description:

Placebo-matching CVC tablet in Year 1 then CVC 150 mg tablet in Year 2.

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

Dosage and administration details:

Placebo-matching cenicriviroc (CVC) tablet, once daily in the morning with food in Year 1.

Arm title	CVC 150mg/CVC 150 mg
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Arm description:

CVC 150 mg tablet in Years 1 and 2.

Arm type	Experimental
Investigational medicinal product name	Cenicriviroc (CVC)
Investigational medicinal product code	TBR-652
Other name	Cenicriviroc mesylate
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

CVC 150 mg tablet, once daily in the morning with food in Year 1.

Number of subjects in period 1	Placebo/Placebo	Placebo/Cenicriviroc (CVC) 150 mg	CVC 150mg/CVC 150 mg
Started	72	72	145
Safety Analysis Set	72	72	144
Completed	62	64	124
Not completed	10	8	21
Subject Withdrew Consent	5	2	11
Adverse event, non-fatal	4	5	9
Lost to follow-up	1	-	-
Other Miscellaneous Reasons	-	-	1
Protocol Deviation (with non-compliance)	-	1	-

Period 2

Period 2 title	Discontinued After Period 1
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo/Placebo
Arm description:	
Placebo-matching cenicriviroc (CVC) tablet in Years 1 and 2.	
Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	Placebo/Cenicriviroc (CVC) 150 mg
Arm description:	
Placebo-matching CVC tablet in Year 1 then CVC 150 mg tablet in Year 2.	
Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	CVC 150mg/CVC 150 mg

Arm description:

CVC 150 mg tablet in Years 1 and 2.

Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 2	Placebo/Placebo	Placebo/Cenicriviroc (CVC) 150 mg	CVC 150mg/CVC 150 mg
Started	62	64	124
Completed	60	61	121
Not completed	2	3	3
Physician decision	-	-	1
Subject Withdrew Consent	1	1	2
Adverse event	1	2	-

Period 3

Period 3 title	Treatment Period 2 (Year 2)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo/Placebo

Arm description:

Placebo-matching cenicriviroc (CVC) tablet in Years 1 and 2.

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

Dosage and administration details:

Placebo-matching cenicriviroc (CVC) tablet, once daily in the morning with food in Year 2.

Arm title	Placebo/Cenicriviroc (CVC) 150 mg
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Arm description:

Placebo-matching CVC tablet in Year 1 then CVC 150 mg tablet in Year 2.

Arm type	Experimental
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Investigational medicinal product name	Cenicriviroc (CVC)
Investigational medicinal product code	TBR-652
Other name	Cenicriviroc mesylate
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

CVC 150 mg tablet, once daily in the morning with food in Year 2.

Arm title	CVC 150mg/CVC 150 mg
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Arm description:

CVC 150 mg tablet in Years 1 and 2.

Arm type	Experimental
Investigational medicinal product name	Cenicriviroc (CVC)
Investigational medicinal product code	TBR-652
Other name	Cenicriviroc mesylate
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

CVC 150 mg tablet, once daily in the morning with food in Year 2.

Number of subjects in period 3	Placebo/Placebo	Placebo/Cenicriviroc (CVC) 150 mg	CVC 150mg/CVC 150 mg
Started	60	61	121
Completed	58	59	109
Not completed	2	2	12
Physician decision	-	-	2
Subject Withdrew Consent	2	-	2
Adverse event, non-fatal	-	1	5
Lost to follow-up	-	1	2
Other Miscellaneous Reasons	-	-	1

Baseline characteristics

Reporting groups

Reporting group title	Placebo/Placebo
Reporting group description: Placebo-matching cenicriviroc (CVC) tablet in Years 1 and 2.	
Reporting group title	Placebo/Cenicriviroc (CVC) 150 mg
Reporting group description: Placebo-matching CVC tablet in Year 1 then CVC 150 mg tablet in Year 2.	
Reporting group title	CVC 150mg/CVC 150 mg
Reporting group description: CVC 150 mg tablet in Years 1 and 2.	

Reporting group values	Placebo/Placebo	Placebo/Cenicriviroc (CVC) 150 mg	CVC 150mg/CVC 150 mg
Number of subjects	72	72	145
Age categorical Units: Subjects			
Adults (18-64 years)	57	60	119
From 65-84 years	15	12	26
Age Continuous Units: years arithmetic mean standard deviation	52.1 ± 11.37	55.3 ± 10.38	54.6 ± 10.22
Sex: Female, Male Units: Subjects			
Female	40	39	73
Male	32	33	72
Race/Ethnicity, Customized Units: Subjects			
Hispanic or Latino	7	18	23
Not Hispanic or Latino	65	51	122
Not reported	0	2	0
Unknown	0	1	0
Race/Ethnicity, Customized Units: Subjects			
Asian	9	6	6
American Indian or Alaska Native	1	0	0
Black or African American	2	1	5
Native Hawaiian or Other Pacific Islander	0	0	3
White	58	63	129
Other	2	2	2

Reporting group values	Total		
Number of subjects	289		
Age categorical Units: Subjects			
Adults (18-64 years)	236		
From 65-84 years	53		

Age Continuous Units: years arithmetic mean standard deviation	-		
Sex: Female, Male Units: Subjects			
Female	152		
Male	137		
Race/Ethnicity, Customized Units: Subjects			
Hispanic or Latino	48		
Not Hispanic or Latino	238		
Not reported	2		
Unknown	1		
Race/Ethnicity, Customized Units: Subjects			
Asian	21		
American Indian or Alaska Native	1		
Black or African American	8		
Native Hawaiian or Other Pacific Islander	3		
White	250		
Other	6		

End points

End points reporting groups

Reporting group title	Placebo/Placebo
Reporting group description: Placebo-matching cenicriviroc (CVC) tablet in Years 1 and 2.	
Reporting group title	Placebo/Cenicriviroc (CVC) 150 mg
Reporting group description: Placebo-matching CVC tablet in Year 1 then CVC 150 mg tablet in Year 2.	
Reporting group title	CVC 150mg/CVC 150 mg
Reporting group description: CVC 150 mg tablet in Years 1 and 2.	
Reporting group title	Placebo/Placebo
Reporting group description: Placebo-matching cenicriviroc (CVC) tablet in Years 1 and 2.	
Reporting group title	Placebo/Cenicriviroc (CVC) 150 mg
Reporting group description: Placebo-matching CVC tablet in Year 1 then CVC 150 mg tablet in Year 2.	
Reporting group title	CVC 150mg/CVC 150 mg
Reporting group description: CVC 150 mg tablet in Years 1 and 2.	
Reporting group title	Placebo/Placebo
Reporting group description: Placebo-matching cenicriviroc (CVC) tablet in Years 1 and 2.	
Reporting group title	Placebo/Cenicriviroc (CVC) 150 mg
Reporting group description: Placebo-matching CVC tablet in Year 1 then CVC 150 mg tablet in Year 2.	
Reporting group title	CVC 150mg/CVC 150 mg
Reporting group description: CVC 150 mg tablet in Years 1 and 2.	
Reporting group title	Placebo/Placebo
Reporting group description: Placebo-matching cenicriviroc (CVC) tablet in Years 1 and 2.	
Reporting group title	Placebo/Cenicriviroc (CVC) 150 mg
Reporting group description: Placebo-matching CVC tablet in Year 1 then CVC 150 mg tablet in Year 2.	
Reporting group title	CVC 150mg/CVC 150 mg
Reporting group description: CVC 150 mg tablet in Years 1 and 2.	
Subject analysis set title	CVC 150 mg/CVC 150 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description: CVC 150 mg tablet, once daily in the morning with food in Years 1 and 2.	
Subject analysis set title	Placebo/CVC 150 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description: Placebo-matching CVC tablet, once daily in the morning with food in Year 1 then CVC 150 mg tablet, once daily in the morning with food in Year 2.	
Subject analysis set title	Placebo/Placebo
Subject analysis set type	Sub-group analysis
Subject analysis set description: Placebo-matching cenicriviroc (CVC) tablet, once daily in the morning with food in Years 1 and 2.	
Subject analysis set title	Placebo
Subject analysis set type	Sub-group analysis
Subject analysis set description: Placebo-matching cenicriviroc tablet, once daily in the morning with food in Year 1.	
Subject analysis set title	CVC 150 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description: Cenicriviroc 150 mg tablet, once daily in the morning with food in Year 1.	

Subject analysis set title	Placebo
Subject analysis set type	Sub-group analysis
Subject analysis set description: Placebo-matching cenicriviroc tablet, once daily in the morning with food in Years 1 and 2.	
Subject analysis set title	CVC 150 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description: Cenicriviroc 150 mg tablet or placebo-matching cenicriviroc tablet, once daily in the morning with food in Year 1 then cenicriviroc 150 mg tablet, once daily in the morning with food in Year 2.	
Subject analysis set title	CVC 150 mg (Year 1)
Subject analysis set type	Sub-group analysis
Subject analysis set description: CVC 150 mg tablet, once daily in the morning with food in Year 1.	
Subject analysis set title	Placebo (Year 1)
Subject analysis set type	Sub-group analysis
Subject analysis set description: Placebo-matching cenicriviroc tablet once daily in the morning with food in Year 1.	
Subject analysis set title	CVC 150 mg/CVC 150 mg (Year 2)
Subject analysis set type	Sub-group analysis
Subject analysis set description: Cenicriviroc 150 mg tablet, once daily in the morning with food in Years 1 and 2. Included AEs that occurred in Year 2.	
Subject analysis set title	Placebo/CVC 150 mg (Year 2)
Subject analysis set type	Sub-group analysis
Subject analysis set description: Placebo-matching cenicriviroc tablet, once daily in the morning with food in Year 1 then cenicriviroc 150 mg tablet, once daily in the morning with food in Year 2. Included AEs that occurred in Year 2.	
Subject analysis set title	Placebo/Placebo (Year 2)
Subject analysis set type	Sub-group analysis
Subject analysis set description: Placebo-matching cenicriviroc tablet, once daily in the morning with food in Years 1 and 2.Observed Clinically significant vital signs in Year 2.	
Subject analysis set title	CVC 150 mg/CVC 150 mg (Year 2)
Subject analysis set type	Sub-group analysis
Subject analysis set description: Cenicriviroc 150 mg tablet, once daily in the morning with food in Years 1 and 2. Observed clinically abnormal ECG findings in Year 2.	
Subject analysis set title	Placebo/CVC 150 mg (Year 2)
Subject analysis set type	Sub-group analysis
Subject analysis set description: Placebo-matching cenicriviroc tablet, once daily in the morning with food in Year 1 then Cenicriviroc 150 mg tablet, once daily in the morning with food in Year 2. Observed clinically abnormal ECG findings in Year 2.	
Subject analysis set title	Placebo/Placebo (Year 2)
Subject analysis set type	Sub-group analysis
Subject analysis set description: Placebo-matching cenicriviroc tablet, once daily in the morning with food in Years 1 and 2. Observed clinically abnormal ECG findings in Year 2.	
Subject analysis set title	Placebo
Subject analysis set type	Sub-group analysis
Subject analysis set description: Placebo-matching cenicriviroc tablet, once daily in the morning with food in Years 1 and 2.	
Subject analysis set title	CVC 150 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Cenicriviroc 150 mg tablet or placebo-matching cenicriviroc tablet, once daily in the morning with food in Year 1 then cenicriviroc 150 mg tablet, once daily in the morning with food in Year 2.

Subject analysis set title	Placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Placebo-matching cenicriviroc tablet, once daily in the morning with food in Year 1.

Subject analysis set title	CVC 150 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Cenicriviroc 150 mg tablet, once daily in the morning with food in Year 1.

Subject analysis set title	Placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Placebo-matching cenicriviroc tablet, once daily in the morning with food in Years 1 and 2.

Subject analysis set title	CVC 150 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Cenicriviroc 150 mg tablet or placebo-matching cenicriviroc tablet, once daily in the morning with food in Year 1 then cenicriviroc 150 mg tablet, once daily in the morning with food in Year 2.

Subject analysis set title	Placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Placebo-matching cenicriviroc tablet, once daily in the morning with food in Year 1.

Subject analysis set title	CVC 150 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Cenicriviroc 150 mg tablet, once daily in the morning with food in Year 1.

Subject analysis set title	Placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Placebo-matching cenicriviroc tablet, once daily in the morning with food in Year 1.

Subject analysis set title	CVC 150 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Cenicriviroc 150 mg tablet, once daily in the morning with food in Year 1.

Subject analysis set title	Placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Placebo-matching cenicriviroc tablet, once daily in the morning with food in Years 1 and 2.

Subject analysis set title	CVC 150 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Cenicriviroc 150 mg tablet or placebo-matching cenicriviroc tablet, once daily in the morning with food in Year 1 then cenicriviroc 150 mg tablet, once daily in the morning with food in Year 2.

Subject analysis set title	Placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Placebo-matching cenicriviroc tablet, once daily in the morning with food in Year 1.

Subject analysis set title	CVC 150 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Cenicriviroc 150 mg tablet, once daily in the morning with food in Year 1.

Subject analysis set title	Placebo
Subject analysis set type	Sub-group analysis
Subject analysis set description: Placebo-matching cenicriviroc tablet, once daily in the morning with food in Years 1 and 2.	
Subject analysis set title	CVC 150 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description: Cenicriviroc 150 mg tablet or placebo-matching cenicriviroc tablet, once daily in the morning with food in Year 1 then cenicriviroc 150 mg tablet, once daily in the morning with food in Year 2.	
Subject analysis set title	CVC 150 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description: Cenicriviroc 150 mg tablet, once daily in the morning with food in Year 1.	
Subject analysis set title	Placebo
Subject analysis set type	Sub-group analysis
Subject analysis set description: Placebo-matching cenicriviroc tablet, once daily in the morning with food in Years 1 and 2.	
Subject analysis set title	CVC 150 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description: Cenicriviroc 150 mg tablet or placebo-matching cenicriviroc tablet, once daily in the morning with food in Year 1 then cenicriviroc 150 mg tablet, once daily in the morning with food in Year 2.	
Subject analysis set title	CVC 150 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description: Cenicriviroc 150 mg tablet or placebo-matching cenicriviroc tablet, once daily in the morning with food in Year 1 then cenicriviroc 150 mg tablet, once daily in the morning with food in Year 2.	
Subject analysis set title	Placebo then CVC 150 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description: Placebo-matching cenicriviroc tablet, once daily in the morning with food in Year 1 then Cenicriviroc 150 mg tablet, once daily in the morning with food in Year 2. Includes AEs that occurred in Year 2.	
Subject analysis set title	Placebo then Placebo
Subject analysis set type	Sub-group analysis
Subject analysis set description: Placebo-matching cenicriviroc tablet, once daily in the morning with food in Years 1 and 2. Includes AEs that occurred in Year 2.	

Primary: Number of Participants with Hepatic Histological Improvement in NAS by ≥ 2 Points with at Least 1-Point Reduction in Either Lobular Inflammation or Hepatocellular Ballooning and no Concurrent Worsening of Fibrosis at Year 1

End point title	Number of Participants with Hepatic Histological Improvement in NAS by ≥ 2 Points with at Least 1-Point Reduction in Either Lobular Inflammation or Hepatocellular Ballooning and no Concurrent Worsening of Fibrosis at Year 1
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End point description:

Hepatic histological improvement in Nonalcoholic Fatty Liver Disease Activity Score (NAS) at Year 1 was defined as a decrease (improvement) in NAS by ≥ 2 with at least a 1-point reduction in either lobular inflammation or hepatocellular ballooning and with no concurrent worsening of fibrosis stage. The NAS was derived as the unweighted sum of steatosis (0 to 3), lobular inflammation (0 to 3), and hepatocellular ballooning (0 to 2) scores. The NAS ranges from 0-8 with the higher score indicating more aggressive disease. Evaluation of fibrosis stage was based on the nonalcoholic steatohepatitis clinical research network (NASH CRN) fibrosis staging system, which was scaled from 0 to 4 stages where 0=None to 4=Cirrhosis. Worsening of fibrosis stage was defined as progression of NASH CRN fibrosis stage. Intent-to-treat (ITT) population included all randomised participants regardless of starting treatment.

End point type	Primary
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End point timeframe:

Year 1

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	144	145		
Units: participants	27	23		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v CVC 150 mg
Number of subjects included in analysis	289
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5194
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.816
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.439
upper limit	1.516

Secondary: Number of Participants with Complete Resolution of Steatohepatitis with no Concurrent Worsening of Fibrosis Stage and Improvement in Fibrosis by at Least 1 Stage (NASH CRN system) and no Worsening of Steatohepatitis at Year 1

End point title	Number of Participants with Complete Resolution of Steatohepatitis with no Concurrent Worsening of Fibrosis Stage and Improvement in Fibrosis by at Least 1 Stage (NASH CRN system) and no Worsening of Steatohepatitis at Year 1
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End point description:

Complete resolution of steatohepatitis was defined as histopathologic interpretation of no fatty liver disease, or simple or isolated steatosis with no steatohepatitis. As per NASH CRN system, no worsening of steatohepatitis was defined as no worsening of lobular inflammation or hepatocellular ballooning grade. The evaluation of fibrosis stage associated with NASH was based on the NASH CRN fibrosis staging system which was scaled from 0 to 4 stages where, 0=None to 4=Cirrhosis. ITT population included all randomised participants regardless of starting treatment.

End point type	Secondary
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End point timeframe:

Year 1

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	144	145		
Units: participants	4	7		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v CVC 150 mg
Number of subjects included in analysis	289
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0388
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.934
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.035
upper limit	3.614

Secondary: Number of Participants with Complete Resolution of Steatohepatitis with no Concurrent Worsening of Fibrosis Stage and Improvement in Fibrosis by at Least 1 Stage (NASH CRN system) and no Worsening of Steatohepatitis at Year 2

End point title	Number of Participants with Complete Resolution of Steatohepatitis with no Concurrent Worsening of Fibrosis Stage and Improvement in Fibrosis by at Least 1 Stage (NASH CRN system) and no Worsening of Steatohepatitis at Year 2
End point description:	Complete resolution of steatohepatitis was defined as histopathologic interpretation of no fatty liver disease, or simple or isolated steatosis with no steatohepatitis. As per NASH CRN system, no worsening of steatohepatitis was defined as no worsening of lobular inflammation or hepatocellular ballooning grade. The evaluation of fibrosis stage associated with NASH was based on the NASH CRN fibrosis staging system which was scaled from 0 to 4 stages where, 0=None to 4=Cirrhosis. ITT population Year 2 included all participants who had an evaluable year 1 biopsy and received at least 1 dose of study drug during Year 2.
End point type	Secondary
End point timeframe:	
Year 2	

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	57	178		
Units: participants	2	5		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v CVC 150 mg
Number of subjects included in analysis	235
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.592
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.249
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.553
upper limit	2.821

Secondary: Number of Participants with Complete Resolution of Steatohepatitis with no Concurrent Worsening of Fibrosis Stage at Year 1

End point title	Number of Participants with Complete Resolution of Steatohepatitis with no Concurrent Worsening of Fibrosis Stage at Year 1
End point description:	Complete resolution of steatohepatitis was defined as histopathologic interpretation of no fatty liver disease, or simple or isolated steatosis with no steatohepatitis. As per NASH CRN system, no worsening of steatohepatitis was defined as no worsening of lobular inflammation or hepatocellular ballooning grade. The evaluation of fibrosis stage associated with NASH was based on the NASH CRN fibrosis staging system which was scaled from 0 to 4 stages where, 0=None to 4=Cirrhosis. ITT population included all randomised participants regardless of starting treatment.
End point type	Secondary
End point timeframe:	
Year 1	

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	144	145		
Units: participants	8	11		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v CVC 150 mg
Number of subjects included in analysis	289
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4941
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.396
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.537
upper limit	3.628

Secondary: Number of Participants with Complete Resolution of Steatohepatitis with no Concurrent Worsening of Fibrosis Stage at Year 2

End point title	Number of Participants with Complete Resolution of Steatohepatitis with no Concurrent Worsening of Fibrosis Stage at Year 2
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End point description:

Complete resolution of steatohepatitis was defined as histopathologic interpretation of no fatty liver disease, or simple or isolated steatosis with no steatohepatitis. As per NASH CRN system, no worsening of steatohepatitis was defined as no worsening of lobular inflammation or hepatocellular ballooning grade. The evaluation of fibrosis stage associated with NASH was based on the NASH CRN fibrosis staging system which was scaled from 0 to 4 stages where, 0=None to 4=Cirrhosis. ITT population Year 2 included all participants who had an evaluable Year 1 biopsy and received at least 1 dose of study drug during Year 2.

End point type	Secondary
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End point timeframe:

Year 2

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	57	178		
Units: participants	3	11		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v CVC 150 mg

Number of subjects included in analysis	235
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8434
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.142
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.305
upper limit	4.277

Secondary: Number of Participants with Improvement in Fibrosis by at Least 1 Stage (NASH CRN system) and no Worsening of Steatohepatitis at Year 1

End point title	Number of Participants with Improvement in Fibrosis by at Least 1 Stage (NASH CRN system) and no Worsening of Steatohepatitis at Year 1
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End point description:

The evaluation of fibrosis stage associated with NASH was based on the NASH CRN Fibrosis Staging System which was scaled from 0 to 4 stages where, 0=None to 4=Cirrhosis. As per NASH CRN system, no worsening of steatohepatitis was defined as no worsening of lobular inflammation or hepatocellular ballooning grade. ITT population included all randomised participants regardless of starting treatment.

End point type	Secondary
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End point timeframe:

Year 1

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	144	145		
Units: participants	15	29		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v CVC 150 mg
Number of subjects included in analysis	289
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0234
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.201

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.113
upper limit	4.352

Secondary: Number of Participants with Improvement in Fibrosis by at Least 1 Stage (NASH CRN system) and no Worsening of Steatohepatitis at Year 2

End point title	Number of Participants with Improvement in Fibrosis by at Least 1 Stage (NASH CRN system) and no Worsening of Steatohepatitis at Year 2
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End point description:

The evaluation of fibrosis stage associated with NASH was based on the NASH CRN Fibrosis Staging System which was scaled from 0 to 4 stages where, 0=None to 4=Cirrhosis. As per NASH CRN system, no worsening of steatohepatitis was defined as no worsening of lobular inflammation or hepatocellular ballooning grade. ITT analysis set Year 2 included all participants who have an evaluable Year 1 biopsy and who received at least one dose of study drug during Year 2 (after the 1 year biopsy).

End point type	Secondary
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End point timeframe:

Year 2

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	57	178		
Units: participants	8	27		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v CVC 150 mg
Number of subjects included in analysis	235
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7474
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.154
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.484
upper limit	2.752

Secondary: Number of Participants with Deaths, Treatment Emergent Adverse Events (TEAEs), Serious Adverse Events (SAEs), TEAEs Leading Study Drug to Discontinuation

End point title	Number of Participants with Deaths, Treatment Emergent Adverse Events (TEAEs), Serious Adverse Events (SAEs), TEAEs Leading Study Drug to Discontinuation
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End point description:

A TEAE was defined as any adverse event that started or worsened on or after the start of the study medication and up to 30 days after the discontinuation of the study medication. An SAE was defined as any untoward medical occurrence that, at any dose, results in death, was life threatening, requires hospitalisation or results in prolongation of existing hospitalisation, results in disability/incapacity, or was a congenital anomaly/birth defect. Safety Analysis Set Year 1 and Year 2 included all participants who received at least 1 dose of study drug.

End point type	Secondary
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End point timeframe:

Years 1 and 2

End point values	CVC 150 mg/CVC 150 mg	Placebo/CVC 150 mg	Placebo/Placebo	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	144	72	72	
Units: participants				
Deaths	0	0	0	
TEAEs	137	68	70	
SAEs	25	8	12	
TEAEs Leading Study Drug to Discontinuation	14	8	5	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Clinically Significant Changes in Vital Signs

End point title	Number of Participants with Clinically Significant Changes in Vital Signs
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End point description:

Vital signs included blood pressure, temperature, heart rate, and respiration rate. Vital signs were reviewed by the Investigator for clinically significant changes. Safety Analysis Set Year 1 and Year 2 included all participants who received at least 1 dose of study drug.

End point type	Secondary
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End point timeframe:

Years 1 and 2

End point values	CVC 150 mg/CVC 150 mg	Placebo/CVC 150 mg	Placebo/Placebo	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	144	72	72	
Units: participants	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Clinical Laboratory Abnormalities

End point title	Number of Participants with Clinical Laboratory Abnormalities
End point description:	
Grade 3-4 abnormal clinical laboratory values that occurred in $\geq 2\%$ participants were reported. Criteria used for various parameters was: Fasting glucose Grade3: $>250-500$ mg/dL and Grade4: >500 mg/dL; Alanine aminotransferase(ALT) Grade3: $>5.0-20.0 \times$ Upper Limit of Normal(ULN) and Grade4: $>20.0 \times$ ULN; Aspartate aminotransferase(AST) Grade3: $>5.0-20.0 \times$ ULN and Grade4: $>20.0 \times$ ULN; Activated partial thromboplastin(APT)/Partial thromboplastin time(PTT) Grade3: $>2.5 \times$ ULN; Triglycerides Grade3: $>500-1000$ mg/dL and Grade4: >1000 mg/dL; Gamma-glutamyl transferase(GGT) Grade3: $>5.0-20.0 \times$ ULN and Grade4: $>20.0 \times$ ULN; Creatine kinase Grade 3: $>5.0-10.0 \times$ ULN and Grade4: $>10.0 \times$ ULN; Uric acid Grade3: (ULN-10 mg/dL; ULN-0.59 mmol/L) and Grade4: >10 mg/dL; Amylase Grade3: $>2.0-5.0 \times$ ULN and Grade4: $>5.0 \times$ ULN; Lipase Grade3: $>2.0-5.0 \times$ ULN and Grade4: $>5.0 \times$ ULN; Phosphorus Grade3: $<2.0-1.0$ mg/dL and Grade4: <1.0 mg/dL and Absolute neutrophil Grade3: $<1.0-0.5 \times 10^9/L$ and Grade4: $<0.5 \times 10^9/L$. Safety Analysis Set Year 1 and	
End point type	Secondary
End point timeframe:	
Years 1 and 2	

End point values	CVC 150 mg (Year 1)	Placebo (Year 1)	CVC 150 mg	Placebo then CVC 150 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	144	144	121	61
Units: participants				
Fasting glucose (Grade 3)	17	13	10	6
Fasting glucose (Grade 4)	0	0	0	0
ALT (Grade 3)	17	17	4	3
ALT (Grade 4)	0	0	0	0
AST (Grade 3)	7	10	1	3
AST (Grade 4)	0	0	0	0
APT/PTT (Grade 3)	4	2	1	1
Triglycerides (Grade 3)	5	7	6	5
Triglycerides (Grade 4)	3	3	2	0
GGT (Grade 3)	8	7	8	2
GGT (Grade 4)	1	1	1	0
Creatine kinase (Grade 3)	6	7	1	2
Creatine kinase (Grade 4)	2	2	3	1
Uric acid (Grade 3)	9	8	4	3
Uric acid (Grade 4)	11	6	5	1
Amylase (Grade 3)	6	1	4	0

Amylase (Grade 4)	3	0	2	0
Lipase (Grade 3)	4	2	3	0
Lipase (Grade 4)	5	0	3	0
Phosphorus (Grade 3)	5	2	2	1
Phosphorus (Grade 4)	0	0	0	0
Absolute neutrophil (Grade 3)	2	3	3	0
Absolute neutrophil (Grade 4)	2	1	1	1

End point values	Placebo then Placebo			
Subject group type	Subject analysis set			
Number of subjects analysed	60			
Units: participants				
Fasting glucose (Grade 3)	5			
Fasting glucose (Grade 4)	0			
ALT (Grade 3)	2			
ALT (Grade 4)	0			
AST (Grade 3)	1			
AST (Grade 4)	0			
APT/PTT (Grade 3)	2			
Triglycerides (Grade 3)	2			
Triglycerides (Grade 4)	1			
GGT (Grade 3)	2			
GGT (Grade 4)	0			
Creatine kinase (Grade 3)	4			
Creatine kinase (Grade 4)	0			
Uric acid (Grade 3)	2			
Uric acid (Grade 4)	6			
Amylase (Grade 3)	1			
Amylase (Grade 4)	0			
Lipase (Grade 3)	1			
Lipase (Grade 4)	1			
Phosphorus (Grade 3)	1			
Phosphorus (Grade 4)	0			
Absolute neutrophil (Grade 3)	1			
Absolute neutrophil (Grade 4)	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Clinically Abnormal Electrocardiogram (ECG) Findings

End point title	Number of Participants with Clinically Abnormal Electrocardiogram (ECG) Findings
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End point description:

A 12-lead ECG was performed. ECG results were reviewed by the Investigator for clinically notable abnormalities. Safety Analysis Set Year 1 and Year 2 included all participants who received at least 1

dose of study drug.

End point type	Secondary
End point timeframe:	
Years 1 and 2	

End point values	CVC 150 mg/CVC 150 mg	Placebo/CVC 150 mg	Placebo/Placebo	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	144	72	72	
Units: participants	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Hepatic Histological Improvement in NAS at Year 2

End point title	Number of Participants with Hepatic Histological Improvement in NAS at Year 2
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End point description:

Hepatic histological improvement in NAS at Year 2 was defined as a decrease (improvement) in NAS by ≥ 2 with at least a 1-point reduction in either lobular inflammation or hepatocellular ballooning and with no concurrent worsening of fibrosis stage. The NAS was derived as the unweighted sum of steatosis (0 to 3), lobular inflammation (0 to 3), and hepatocellular ballooning (0 to 2) scores. The NAS ranges from 0-8 with the higher score indicating more aggressive disease. Full Analysis Set (FAS) in Year 2 included all participants who were randomised and received at least 1 dose of study drug, had a measurable Screening biopsy, and had no major eligibility violations.

End point type	Secondary
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End point timeframe:

Year 2

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	72	215		
Units: participants	7	24		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the 3 Categorical Features of NAS (Steatosis, Lobular Inflammation, Hepatocellular Ballooning) at Year 1

End point title	Change From Baseline in the 3 Categorical Features of NAS
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End point description:

NAS was calculated using the following 3 categorical features: steatosis which was scaled from 0-3 (steatosis score is defined as 0= <5%, 1= 5 – 33%, 2= >33 – 66%, and 3= >66%), lobular inflammation which was scaled from 0-3 (lobular inflammation score defined as 0= no foci, 1= < 2 foci/200x, 2= 2-4 foci/200x, and 3= > 4 foci/200x), and hepatocellular ballooning which was scaled from 0-2 (hepatocellular ballooning score is defined as 0=none, 1=few balloon cells, 2=many cells/prominent ballooning). A negative change from Baseline indicates improvement. FAS in Year 1 included all participants who were randomised and received at least 1 dose of study drug, had a measurable Screening biopsy, and had no major eligibility violations. Number analysed is the number of participants with data available for analysis at the given time-point.

End point type	Secondary
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End point timeframe:

Year 1

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	126	126		
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline (Steatosis)	1.4 (± 0.55)	1.3 (± 0.57)		
Change from Baseline (Steatosis)	-0.1 (± 0.66)	-0.2 (± 0.56)		
Baseline (Lobular Inflammation)	2.5 (± 0.56)	2.4 (± 0.58)		
Change from Baseline (Lobular Inflammation)	-0.1 (± 0.79)	-0.1 (± 0.88)		
Baseline (Hepatocellular Ballooning)	1.5 (± 0.50)	1.5 (± 0.50)		
Change from Baseline (Hepatocellular Ballooning)	-0.2 (± 0.75)	-0.1 (± 0.75)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the 3 Categorical Features of NAS (Steatosis, Lobular Inflammation, Hepatocellular Ballooning) at Year 2

End point title	Change From Baseline in the 3 Categorical Features of NAS (Steatosis, Lobular Inflammation, Hepatocellular Ballooning) at Year 2
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End point description:

NAS was calculated using the following 3 categorical features: steatosis which was scaled from 0-3 (steatosis score is defined as 0= <5%, 1= 5 – 33%, 2= >33 – 66%, and 3= >66%), lobular inflammation which was scaled from 0-3 (lobular inflammation score defined as 0= no foci, 1= < 2 foci/200x, 2= 2-4 foci/200x, and 3= > 4 foci/200x), and hepatocellular ballooning which was scaled from 0-2 (hepatocellular ballooning score is defined as 0=none, 1=few balloon cells, 2=many cells/prominent ballooning). A negative change from Baseline indicates improvement. FAS in Year 2 included all participants who were randomized and received at least 1 dose of study drug, had a measurable Screening biopsy, and had no major eligibility violations. Number analysed is the number of participants with data available for analysis at the given time-point.

End point type	Secondary
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End point timeframe:

Year 2

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	159		
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline (Steatosis)	1.5 (± 0.54)	1.3 (± 0.52)		
Change from Baseline (Steatosis)	-0.4 (± 0.56)	-0.2 (± 0.50)		
Baseline (Lobular Inflammation)	2.4 (± 0.63)	2.4 (± 0.54)		
Change from Baseline (Lobular Inflammation)	0.1 (± 0.72)	0.0 (± 0.84)		
Baseline (Hepatocellular Ballooning)	1.5 (± 0.50)	1.5 (± 0.50)		
Change from Baseline (Hepatocellular Ballooning)	-0.1 (± 0.68)	0.0 (± 0.83)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Hepatic Histological Improvement with a Minimum 2-Point Improvement in NAS with at Least a 1-Point Improvement in More Than 1 Categorical Features of NAS and no Concurrent Worsening of Fibrosis Stage at Year 1

End point title	Number of Participants with Hepatic Histological Improvement with a Minimum 2-Point Improvement in NAS with at Least a 1-Point Improvement in More Than 1 Categorical Features of NAS and no Concurrent Worsening of Fibrosis Stage at Year 1
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End point description:

Hepatic histological improvement in NAS was defined as a decrease (improvement) in NAS by ≥ 2 with at least a 1-point reduction in either steatosis, lobular inflammation or hepatocellular ballooning and with no concurrent worsening of fibrosis stage. The NAS was derived as the unweighted sum of steatosis (0 to 3), lobular inflammation (0 to 3), and hepatocellular ballooning (0 to 2) scores. The NAS ranges from 0-8 with the higher score indicating more aggressive disease. Worsening was defined as progression of NASH CRN fibrosis stage. FAS in Year 1 included all participants who were randomised and received at least 1 dose of study drug, had a measurable Screening biopsy, and had no major eligibility violations.

End point type	Secondary
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End point timeframe:

Year 1

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	143	144		
Units: participants	24	22		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Hepatic Histological Improvement with a Minimum 2-Point Improvement in NAS with at Least a 1-point Improvement in more than 1 Categorical Features of NAS and no Concurrent Worsening of Fibrosis Stage at Year 2

End point title	Number of Participants with Hepatic Histological Improvement with a Minimum 2-Point Improvement in NAS with at Least a 1-point Improvement in more than 1 Categorical Features of NAS and no Concurrent Worsening of Fibrosis Stage at Year 2
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End point description:

Hepatic histological improvement in NAS was defined as a decrease (improvement) in NAS by ≥ 2 with at least a 1-point reduction in either steatosis, lobular inflammation or hepatocellular ballooning and with no concurrent worsening of fibrosis stage. The NAS was derived as the unweighted sum of steatosis (0 to 3), lobular inflammation (0 to 3), and hepatocellular ballooning (0 to 2) scores. The NAS ranges from 0-8 with the higher score indicating more aggressive disease. Worsening was defined as progression of NASH CRN fibrosis stage. FAS in Year 2 included all participants who were randomised and received at least 1 dose of study drug, had a measurable Screening biopsy, and had no major eligibility violations.

End point type	Secondary
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End point timeframe:

Year 2

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	72	215		
Units: participants	6	20		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Resolution of NASH Using a Modified Definition Based on Categorical Features of NAS and no Concurrent Worsening of Fibrosis Stage at Year 1

End point title	Number of Participants with Resolution of NASH Using a Modified Definition Based on Categorical Features of NAS and no Concurrent Worsening of Fibrosis Stage at Year 1
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End point description:

Resolution of NASH was defined as having no hepatocellular ballooning (grade 0) and minimal to no lobular inflammation (grade 1 or 0) with no concurrent worsening of fibrosis stage (worsening defined as progression of NASH CRN fibrosis stage). FAS in Year 1 included all participants who were randomised and received at least 1 dose of study drug, had a measurable Screening biopsy, and had no major

eligibility violations.

End point type	Secondary
End point timeframe:	
Year 1	

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	143	144		
Units: participants	7	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Resolution of NASH using a Modified Definition Based on Categorical Features of NAS and no Concurrent Worsening of Fibrosis Stage at Year 2

End point title	Number of Participants with Resolution of NASH using a Modified Definition Based on Categorical Features of NAS and no Concurrent Worsening of Fibrosis Stage at Year 2
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End point description:

Resolution of NASH was defined as having no hepatocellular ballooning (grade 0) and minimal to no lobular inflammation (grade 1 or 0) with no concurrent worsening of fibrosis stage (worsening defined as progression of NASH CRN fibrosis stage). FAS in Year 2 included all participants who were randomised and received at least 1 dose of study drug, had a measurable Screening biopsy, and had no major eligibility violations.

End point type	Secondary
End point timeframe:	
Year 2	

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	72	215		
Units: participants	1	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Morphometric Quantitative Collagen on Liver Biopsy at Year 1

End point title	Change From Baseline in Morphometric Quantitative Collagen on Liver Biopsy at Year 1
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End point description:

The Morphometric Quantitative Collagen on Liver Biopsy was determined as percent collagen area (PCA) using Sirius red stain on liver biopsy at Year 1. A negative change from Baseline indicates improvement. FAS in Year 1 included all participants who were randomised and received at least 1 dose of study drug, had a measurable Screening biopsy, and had no major eligibility violations. Number analysed is the number of participants with data available for analysis at the given time-point.

End point type	Secondary
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End point timeframe:

Year 1

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	123	121		
Units: percent collagen area				
arithmetic mean (standard deviation)				
Baseline	2.49 (± 2.004)	2.37 (± 1.827)		
Change from Baseline to Year 1	-0.14 (± 2.389)	0.02 (± 2.357)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Morphometric Quantitative Collagen on Liver Biopsy at Year 2

End point title	Change From Baseline in Morphometric Quantitative Collagen on Liver Biopsy at Year 2
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End point description:

The Morphometric Quantitative Collagen on Liver Biopsy was determined as percent collagen area (PCA) using Sirius red stain on liver biopsy at Year 2. A negative change from Baseline indicates improvement. FAS in Year 2 included all participants who were randomised and received at least 1 dose of study drug, had a measurable Screening biopsy, and had no major eligibility violations. Number analysed is the number of participants with data available for analysis at the given time-point.

End point type	Secondary
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End point timeframe:

Year 2

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	51	150		
Units: percent collagen area				
arithmetic mean (standard deviation)				
Baseline	2.57 (± 2.156)	2.48 (± 1.892)		
Change from Baseline to Year 2	-0.17 (± 2.576)	-0.09 (± 2.160)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Hepatic Tissue Fibrogenic Protein Alpha-Smooth Muscle Actin (α -SMA) at Year 1

End point title	Change From Baseline in Hepatic Tissue Fibrogenic Protein Alpha-Smooth Muscle Actin (α -SMA) at Year 1
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End point description:

The hepatic tissue fibrogenic protein α -SMA level was determined as percent α -SMA + area using α -SMA stain on liver biopsy at Year 1. A positive change from Baseline indicates worsening. FAS in Year 1 included all participants who were randomised and received at least 1 dose of study drug, had a measurable Screening biopsy, and had no major eligibility violations. Number analysed is the number of participants with data available for analysis at the given time-point.

End point type	Secondary
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End point timeframe:

Baseline (Day 1) to Year 1

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	122	122		
Units: percentage of α -SMA positive cells/area				
arithmetic mean (standard deviation)				
Baseline	2.41 (\pm 2.264)	2.49 (\pm 2.885)		
Change from Baseline to Year 1	0.77 (\pm 3.529)	0.79 (\pm 3.861)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Hepatic Tissue Fibrogenic Protein Alpha-Smooth Muscle Actin (α -SMA) at Year 2

End point title	Change From Baseline in Hepatic Tissue Fibrogenic Protein Alpha-Smooth Muscle Actin (α -SMA) at Year 2
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End point description:

The hepatic tissue fibrogenic protein α -SMA level was determined as percent α -SMA + area using α -SMA stain on liver biopsy at Year 2. A positive change from Baseline indicates worsening. FAS in Year 2 included all participants who were randomised and received at least 1 dose of study drug, had a measurable Screening biopsy, and had no major eligibility violations. Number analysed is the number of participants with data available for analysis at the given time-point.

End point type	Secondary
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End point timeframe:

Baseline (Day 1) to Year 2

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	52	152		
Units: percentage of α -SMA positive cells/area				
arithmetic mean (standard deviation)				
Baseline	2.47 (\pm 2.679)	2.44 (\pm 2.505)		
Change from Baseline to Year 2	2.10 (\pm 4.533)	1.38 (\pm 3.793)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Morphometric Quantitative Fat Content on Liver Biopsy at Year 1

End point title	Change From Baseline in Morphometric Quantitative Fat Content on Liver Biopsy at Year 1
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End point description:

The morphometric quantitative fat content was done to find out the amount of fat accumulated in the liver. A liver biopsy was performed to determine percent fat area, at Year 1. A negative change from Baseline indicates improvement. FAS in Year 1 included all participants who were randomised and received at least 1 dose of study drug, had a measurable Screening biopsy, and had no major eligibility violations. Number analysed is the number of participants with data available for analysis at the given time-point.

End point type	Secondary
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End point timeframe:

Year 1

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	123	121		
Units: percent fat area				
arithmetic mean (standard deviation)				
Baseline	22.42 (\pm 10.016)	21.58 (\pm 8.740)		
Change from Baseline to Year 1	-3.39 (\pm 9.120)	-2.79 (\pm 8.127)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Morphometric Quantitative Fat Content on Liver Biopsy at Year 2

End point title	Change From Baseline in Morphometric Quantitative Fat Content on Liver Biopsy at Year 2
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End point description:

The morphometric quantitative fat content was done to find out the amount of fat accumulated in the liver. A liver biopsy was performed to determine percent fat area, at Year 2. A negative change from Baseline indicates improvement. FAS in Year 2 included all participants who were randomised and received at least 1 dose of study drug, had a measurable Screening biopsy, and had no major eligibility violations. Number analysed is the number of participants with data available for analysis at the given time-point.

End point type	Secondary
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End point timeframe:

Year 2

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50	150		
Units: percent fat area				
arithmetic mean (standard deviation)				
Baseline	23.30 (± 10.300)	21.62 (± 9.575)		
Change from Baseline to Year 2	-5.06 (± 9.739)	-2.96 (± 9.230)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Histologic Fibrosis Stage (NASH CRN System and Ishak Scale Score) at Year 1

End point title	Change From Baseline in Histologic Fibrosis Stage (NASH CRN System and Ishak Scale Score) at Year 1
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End point description:

The participant's histologic fibrosis stage was determined using the NASH CRN system and Ishak scale score assessment at Year 1. The evaluation of fibrosis stage associated with NASH was based on the NASH CRN Fibrosis Staging System which was scaled from 0 to 4 where, 0=None to 4=Cirrhosis. The histologic fibrosis stage based on the Ishak assessment was divided into 1 to 6 stages. Fibrosis was staged with the Ishak scale (ranging from 0=No fibrosis to 6=Cirrhosis). A positive change from Baseline indicates worsening. FAS in Year 1 included all participants who were randomised and received at least 1 dose of study drug, had a measurable Screening biopsy, and had no major eligibility violations. Number analysed is the number of participants with data available for analysis at the given time-point.

End point type	Secondary
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End point timeframe:

Baseline (Day 1) to Year 1

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	126	126		
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline (NASH CRN Fibrosis Stage)	2.1 (± 0.86)	2.0 (± 0.85)		
Change from Baseline (NASH CRN Fibrosis Stage)	0.2 (± 0.92)	0.0 (± 1.00)		
Baseline (Ishak Fibrosis Stage)	2.2 (± 1.00)	2.2 (± 1.05)		
Change from Baseline (Ishak Fibrosis Stage)	0.2 (± 1.10)	0.0 (± 1.20)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Histologic Fibrosis Stage (NASH CRN System and Ishak Scale Score) at Year 2

End point title	Change From Baseline in Histologic Fibrosis Stage (NASH CRN System and Ishak Scale Score) at Year 2
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End point description:

The participant's histologic fibrosis stage was determined using the NASH CRN system and Ishak scale score assessment at Year 1. The evaluation of fibrosis stage associated with NASH was based on the NASH CRN Fibrosis Staging System which was scaled from 0 to 4 where, 0=None to 4=Cirrhosis. The histologic fibrosis stage based on the Ishak assessment was divided into 1 to 6 stages. Fibrosis was staged with the Ishak scale (ranging from 0=No fibrosis to 6=Cirrhosis). A negative change from Baseline indicates improvement. FAS in Year 2 included all participants who were randomised and received at least 1 dose of study drug, had a measurable Screening biopsy, and had no major eligibility violations. Number analysed is the number of participants with data available for analysis at the given time-point.

End point type	Secondary
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End point timeframe:

Baseline (Day 1) to Year 2

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	159		
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline (NASH CRN Fibrosis Stage)	2.0 (± 0.88)	2.1 (± 0.85)		
Change from Baseline (NASH CRN Fibrosis Stage)	0.0 (± 0.89)	0.0 (± 1.08)		
Baseline (Ishak Fibrosis Stage)	2.1 (± 1.00)	2.2 (± 1.04)		
Change from Baseline (Ishak Fibrosis Stage)	0.1 (± 1.21)	0.0 (± 1.26)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Portal Inflammation Grade on Liver Biopsy at Year 1

End point title	Change From Baseline in Portal Inflammation Grade on Liver Biopsy at Year 1
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End point description:

Portal inflammation on liver biopsy was graded from 0 to 4 where 0= None, 1= Mild, 2= Moderate, and 3= Marked. A positive change from Baseline indicates worsening. FAS in Year 1 included all participants who were randomised and received at least 1 dose of study drug, had a measurable Screening biopsy, and had no major eligibility violations. Number analysed is the number of participants with data available for analysis at the given time-point.

End point type	Secondary
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End point timeframe:

Baseline (Day 1) to Year 1

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	126	124		
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline	1.6 (± 0.63)	1.5 (± 0.64)		
Change from Baseline to Year 1	0.0 (± 0.76)	0.2 (± 0.74)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Portal Inflammation Grade on Liver Biopsy at Year 2

End point title	Change From Baseline in Portal Inflammation Grade on Liver Biopsy at Year 2
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End point description:

Portal inflammation on liver biopsy was graded from 0 to 4 where 0= None, 1= Mild, 2= Moderate, and 3= Marked. A positive change from Baseline indicates worsening. FAS in Year 2 included all participants who were randomised and received at least 1 dose of study drug, had a measurable Screening biopsy, and had no major eligibility violations. Number analysed is the number of participants with data available for analysis at the given time-point.

End point type	Secondary
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End point timeframe:

Baseline (Day 1) to Year 2

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	159		
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline	1.5 (± 0.64)	1.6 (± 0.67)		
Change from Baseline to Year 1	0.1 (± 0.75)	0.2 (± 0.72)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Non-invasive Marker of Hepatic Fibrosis: Aspartate Aminotransferase to Platelet Count Ratio Index (APRI) at Months 3, 6 and 12

End point title	Change From Baseline in Non-invasive Marker of Hepatic Fibrosis: Aspartate Aminotransferase to Platelet Count Ratio Index (APRI) at Months 3, 6 and 12
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End point description:

APRI is the ratio of aspartate aminotransferase (AST) to platelet count. It is calculated using formula, $APRI = (AST \text{ level } [ULN] / \text{platelet counts } [10^9/L]) * 100$. An APRI index of ≤ 0.50 indicated the absence of significant fibrosis and an index of > 1.50 indicated the presence of significant fibrosis. A negative change from Baseline indicates decreased fibrosis. FAS in Year 1 included all participants who were randomised and received at least 1 dose of study drug, had a measurable Screening biopsy and had no major eligibility violations. 'n' is the number of participants with data available for analysis at both Baseline and the given time-point.

End point type	Secondary
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End point timeframe:

Baseline (Month 0) to Months 3, 6 and 12

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	143	144		
Units: ratio				
arithmetic mean (standard deviation)				
Baseline (Month 3) (n=127,133)	0.649 (± 0.3661)	0.596 (± 0.4089)		
Change from Baseline to Month 3 (n=127,133)	-0.005 (± 0.3012)	0.065 (± 0.3152)		
Baseline (Month 6) (n=128,127)	0.663 (± 0.3811)	0.578 (± 0.3794)		
Change from Baseline to Month 6 (n=128,127)	0.009 (± 0.3968)	0.102 (± 0.4536)		
Baseline (Month 12) (n=117,117)	0.662 (± 0.3915)	0.580 (± 0.3939)		

Change from Baseline to Month 12 (n=117,117)	0.066 (± 0.5572)	0.093 (± 0.3852)		
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Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Non-invasive Marker of Hepatic Fibrosis: Aspartate Aminotransferase to Platelet Count Ratio Index (APRI) at Months 15, 18 and 24

End point title	Change From Baseline in Non-invasive Marker of Hepatic Fibrosis: Aspartate Aminotransferase to Platelet Count Ratio Index (APRI) at Months 15, 18 and 24
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End point description:

APRI is the ratio of aspartate aminotransferase (AST) to platelet count. It is calculated using formula, $APRI = (AST \text{ level } [ULN] / \text{platelet counts } [10^9/L]) * 100$. An APRI index of ≤ 0.50 indicated the absence of significant fibrosis and an index of > 1.50 indicated the presence of significant fibrosis. A negative change from Baseline indicates decreased fibrosis. FAS in Year 2 included all participants who were randomised and received at least 1 dose of study drug, had a measurable Screening biopsy, and had no major eligibility violations. 'n' is the number of participants with data available for analysis at both Baseline and the given time-point.

End point type	Secondary
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End point timeframe:

Baseline (Month 0) to Months 15, 18 and 24

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	72	215		
Units: ratio				
arithmetic mean (standard deviation)				
Baseline (Month 15) (n=59, 167)	0.619 (± 0.3157)	0.584 (± 0.3572)		
Change from Baseline to Month 15 (n=59, 167)	0.002 (± 0.3422)	0.118 (± 0.4095)		
Baseline (Month 18) (n=53, 167)	0.620 (± 0.3305)	0.586 (± 0.3612)		
Change from Baseline to Month 18 (n=53, 167)	0.038 (± 0.4033)	0.133 (± 0.4269)		
Baseline (Month 24) (n=56, 158)	0.633 (± 0.3156)	0.584 (± 0.3617)		
Change from Baseline to Month 24 (n=56, 158)	-0.020 (± 0.4721)	0.086 (± 0.4153)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Non-invasive Marker of Hepatic Fibrosis: Fibrosis-4 (FIB-4) at Months 3, 6 and 12

End point title	Change From Baseline in Non-invasive Marker of Hepatic Fibrosis: Fibrosis-4 (FIB-4) at Months 3, 6 and 12
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End point description:

Fibrosis-4 is the ratio of age in years and aminotransferase to platelet count. It is a non-invasive hepatic fibrosis index score combining standard biochemical values, platelets, alanine aminotransferase (ALT), AST and age that is calculated using formula: $FIB-4 = (Age [years] \times AST [U/L]) / (platelets [10^9/L] \times (\text{square root of } ALT [U/L]))$. A FIB-4 index of < 1.45 indicated no or moderate fibrosis and an index of > 3.25 indicated extensive fibrosis/cirrhosis. A positive change from Baseline indicates increased fibrosis. FAS in Year 1 included all participants who were randomised and received at least 1 dose of study drug, had a measurable Screening biopsy, and had no major eligibility violations. 'n' is the number of participants with data available for analysis at both Baseline and the given time-point.

End point type	Secondary
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End point timeframe:

Baseline (Month 0) to Months 3, 6 and 12

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	143	144		
Units: ratio				
arithmetic mean (standard deviation)				
Baseline (Month 3) (n=127, 133)	1.444 (± 0.6753)	1.417 (± 0.6893)		
Change from Baseline to Month 3 (n=127, 133)	0.021 (± 0.4236)	0.071 (± 0.4209)		
Baseline (Month 6) (n=128, 127)	1.500 (± 0.7268)	1.388 (± 0.6771)		
Change from Baseline to Month 6 (n=128, 127)	0.015 (± 0.4591)	0.099 (± 0.5246)		
Baseline (Month 12) (n=117, 117)	1.503 (± 0.7442)	1.398 (± 0.6834)		
Change from Baseline to Month 12 (n=117, 117)	0.106 (± 0.6876)	0.117 (± 0.5069)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Non-invasive Marker of Hepatic Fibrosis: Fibrosis-4 (FIB-4) at Months 15, 18 and 24

End point title	Change From Baseline in Non-invasive Marker of Hepatic Fibrosis: Fibrosis-4 (FIB-4) at Months 15, 18 and 24
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End point description:

Fibrosis-4 is the ratio of age in years and aminotransferase to platelet count. It is a non-invasive hepatic fibrosis index score combining standard biochemical values, platelets, alanine aminotransferase (ALT), AST and age that is calculated using formula: $FIB-4 = (Age [years] \times AST [U/L]) / (platelets [10^9/L] \times (\text{square root of } ALT [U/L]))$. A FIB-4 index of < 1.45 indicated no or moderate fibrosis and an index of > 3.25 indicated extensive fibrosis/cirrhosis. A positive change from Baseline indicates increased fibrosis. FAS in Year 2 included all participants who were randomised and received at least 1 dose of study drug, had a measurable Screening biopsy, and had no major eligibility violations. 'n' is the number of participants with data available for analysis at both Baseline and the given time-point.

End point type	Secondary
End point timeframe:	
Baseline (Month 0) to Months 15, 18 and 24	

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	72	215		
Units: ratio				
arithmetic mean (standard deviation)				
Baseline (Month 15) (n=59, 167)	1.409 (± 0.6706)	1.440 (± 0.6714)		
Change from Baseline to Month 15 (n=59, 167)	0.075 (± 0.5982)	0.213 (± 0.6462)		
Baseline (Month 18) (n=53, 167)	1.389 (± 0.6699)	1.440 (± 0.6895)		
Change from Baseline to Month 18 (n=53, 167)	0.094 (± 0.5891)	0.219 (± 0.5559)		
Baseline (Month 24) (n=56, 158)	1.426 (± 0.6841)	1.444 (± 0.6838)		
Change from Baseline to Month 24 (n=56, 158)	0.064 (± 0.8103)	0.166 (± 0.6086)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Non-invasive Marker of Hepatic Fibrosis: Hyaluronic Acid at Months 6 and 12

End point title	Change From Baseline in Non-invasive Marker of Hepatic Fibrosis: Hyaluronic Acid at Months 6 and 12
End point description:	
Hyaluronic acid is a non-invasive hepatic fibrosis marker. A negative change from Baseline indicates decreased fibrosis. FAS in Year 1 included all participants who were randomised and received at least 1 dose of study drug, had a measurable Screening biopsy, and had no major eligibility violations. 'n' is the number of participants with data available for analysis at both Baseline and the given time-point.	
End point type	Secondary
End point timeframe:	
Baseline (Month 0) to Months 6 and 12	

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	143	144		
Units: ng/mL				
arithmetic mean (standard deviation)				
Baseline (Month 6) (n=128, 128)	68.7 (± 107.63)	68.2 (± 78.88)		

Change from Baseline to Month 6 (n=128, 128)	-2.4 (± 75.03)	10.7 (± 79.58)		
Baseline (Month 12) (n=122, 121)	70.7 (± 110.49)	69.5 (± 80.56)		
Change from Baseline to Month 12 (n=122, 121)	-0.2 (± 81.30)	10.9 (± 58.46)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Non-invasive Marker of Hepatic Fibrosis: Hyaluronic Acid at Months 18 and 24

End point title	Change From Baseline in Non-invasive Marker of Hepatic Fibrosis: Hyaluronic Acid at Months 18 and 24
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End point description:

Hyaluronic acid is a non-invasive hepatic fibrosis marker. A positive change from Baseline indicates increased fibrosis. FAS in Year 2 included all participants who were randomised and received at least 1 dose of study drug, had a measurable Screening biopsy and had no major eligibility violations. 'n' is the number of participants with data available for analysis at both Baseline and the given time-point.

End point type	Secondary
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End point timeframe:

Baseline (Month 0) to Months 18 and 24

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	72	215		
Units: ng/mL				
arithmetic mean (standard deviation)				
Baseline (Month 18) (n=58, 170)	46.4 (± 32.67)	79.6 (± 111.36)		
Change from Baseline to Month 18 (n=58, 170)	5.7 (± 34.66)	1.4 (± 81.20)		
Baseline (Month 24) (n=57, 164)	46.6 (± 32.91)	79.7 (± 112.46)		
Change from Baseline to Month 24 (n=57, 164)	19.3 (± 70.64)	13.0 (± 95.00)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Non-invasive Markers of Hepatic Fibrosis: Nonalcoholic Fatty Liver Disease (NAFLD) Fibrosis Score (NFS) at Months 3, 6 and 12

End point title	Change From Baseline in Non-invasive Markers of Hepatic Fibrosis: Nonalcoholic Fatty Liver Disease (NAFLD) Fibrosis Score (NFS) at Months 3, 6 and 12
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End point description:

NFS is calculated using formula: $NFS = -1.675 + 0.037 * \text{age (years)} + 0.094 * \text{Body mass index (BMI)} (\text{kg/m}^2) + 1.13 * \text{Impaired fasting glucose (IFG)/diabetes (yes = 1, no = 0)} + 0.99 * \text{Aspartate aminotransferase (AST)/ Alanine aminotransferase (ALT) ratio} - 0.013 \times \text{platelet} (*10^9/\text{L}) - 0.66 * \text{albumin (g/dL)}$. A negative change from Baseline indicates decreased fibrosis. FAS in Year 1 included all participants who were randomised and received at least 1 dose of study drug, had a measurable Screening biopsy, and had no major eligibility violations. 'n' is the number of participants with data available for analysis at both Baseline and the given time-point.

End point type	Secondary
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End point timeframe:

Baseline (Month 0) to Months 3, 6 and 12

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	143	144		
Units: ng/mL				
arithmetic mean (standard deviation)				
Baseline (Month 3) (n=125, 125)	-1.227 (± 1.5255)	-1.012 (± 1.2558)		
Change from Baseline to Month 3 (n=125, 125)	0.029 (± 0.5150)	0.087 (± 0.4608)		
Baseline (Month 6) (n=125, 119)	-1.119 (± 1.4935)	-1.064 (± 1.2403)		
Change from Baseline to Month 6 (n=125, 119)	0.051 (± 0.4747)	0.094 (± 0.5460)		
Baseline (Month 12) (n=115, 108)	-1.132 (± 1.4609)	-1.040 (± 1.1393)		
Change from Baseline to Month 12 (n=115, 108)	0.121 (± 0.5117)	0.139 (± 0.5016)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Non-invasive Markers of Hepatic Fibrosis: NAFLD Fibrosis Score (NFS) at Months 15, 18 and 24

End point title	Change From Baseline in Non-invasive Markers of Hepatic Fibrosis: NAFLD Fibrosis Score (NFS) at Months 15, 18 and 24
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End point description:

NFS is calculated using formula: $NFS = -1.675 + 0.037 * \text{age (years)} + 0.094 * \text{Body mass index (BMI)} (\text{kg/m}^2) + 1.13 * \text{Impaired fasting glucose (IFG)/diabetes (yes = 1, no = 0)} + 0.99 * \text{Aspartate aminotransferase (AST)/ Alanine aminotransferase (ALT) ratio} - 0.013 \times \text{platelet} (*10^9/\text{L}) - 0.66 * \text{albumin (g/dL)}$. A negative change from Baseline indicates decreased fibrosis. FAS in Year 2 included all participants who were randomised and received at least 1 dose of study drug, had a measurable Screening biopsy, and had no major eligibility violations. 'n' is the number of participants with data available for analysis at both Baseline and the given time-point.

End point type	Secondary
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End point timeframe:

Baseline (Month 0) to Months 15, 18 and 24

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	72	215		
Units: ng/mL				
arithmetic mean (standard deviation)				
Baseline (Month 15) (n=59, 158)	-1.252 (± 1.4602)	-1.051 (± 1.3410)		
Change from Baseline to Month 15 (n=59, 158)	0.057 (± 0.5981)	0.225 (± 0.5654)		
Baseline (Month 18) (n=53, 158)	-1.284 (± 1.4910)	-1.057 (± 1.3309)		
Change from Baseline to Month 18 (n=53, 158)	0.046 (± 0.5809)	0.196 (± 0.5583)		
Baseline (Month 24) (n=54, 147)	-1.245 (± 1.4778)	-1.100 (± 1.3228)		
Change from Baseline to Month 24 (n=54, 147)	0.046 (± 0.6188)	0.185 (± 0.6184)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Non-invasive Markers of Hepatic Fibrosis: Enhanced Liver Fibrosis Test (ELF) Score at Months 6 and 12

End point title	Change From Baseline in Non-invasive Markers of Hepatic Fibrosis: Enhanced Liver Fibrosis Test (ELF) Score at Months 6 and 12
End point description:	
<p>The markers of fibrosis assessed in this test comprised hyaluronic acid (CHA), tissue inhibitor of metalloproteinase (CTIMP1) and procollagen III N-terminal peptide (CP3NP); these are components of the extracellular matrix and basement sinusoidal membrane of the liver and are elevated during activation of the stellate cell. The ELF tests were performed on Centaur device and the composite score was calculated as follows: $\text{ELF score} = 2.278 + 0.851 \ln(\text{CHA}) + 0.751 \ln(\text{CP3NP}) + 0.394 \ln(\text{CTIMP1})$. ELF score < 7.7: no to mild fibrosis; $\geq 7.7 - < 9.8$: Moderate fibrosis; $\geq 9.8 - < 11.3$: Severe fibrosis; ≥ 11.3: Cirrhosis. A negative change from Baseline indicates decreased fibrosis. FAS in Year 1 included all participants who were randomised and received at least 1 dose of study drug, had a measurable Screening biopsy, and had no major eligibility violations. 'n' is the number of participants with data available for analysis at both Baseline and the given time-point.</p>	
End point type	Secondary
End point timeframe:	
Baseline (Month 0) to Months 6 and 12	

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	143	144		
Units: ng/mL				
arithmetic mean (standard deviation)				
Baseline (Month 6) (n=125, 125)	-0.786 (± 0.7179)	-0.837 (± 0.7238)		
Change from Baseline to Month 6 (n=125, 125)	-0.022 (± 0.4901)	0.060 (± 0.5228)		
Baseline (Month 12) (n=116, 118)	-0.795 (± 0.7435)	-0.801 (± 0.7162)		
Change from Baseline to Month 12 (n=116, 118)	-0.064 (± 0.5602)	0.041 (± 0.5727)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Non-invasive Markers of Hepatic Fibrosis: Enhanced Liver Fibrosis Test (ELF) Score at Months 18 and 24

End point title	Change From Baseline in Non-invasive Markers of Hepatic Fibrosis: Enhanced Liver Fibrosis Test (ELF) Score at Months 18 and 24
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End point description:

The markers of fibrosis assessed in this test comprised hyaluronic acid (CHA), tissue inhibitor of metalloproteinase (CTIMP1) and procollagen III N-terminal peptide (CP3NP); these are components of the extracellular matrix and basement sinusoidal membrane of the liver and are elevated during activation of the stellate cell. The ELF tests were performed on Centaur device and the composite score was calculated as follows: ELF score = 2.278 + 0.851 ln(CHA) + 0.751 ln (CP3NP) + 0.394 ln(CTIMP1). ELF score < 7.7: no to mild fibrosis; ≥ 7.7 - < 9.8: Moderate fibrosis; ≥ 9.8 - < 11.3: Severe fibrosis; ≥ 11.3: Cirrhosis. A negative change from Baseline indicates decreased fibrosis. FAS in Year 2 included all participants who were randomised and received at least 1 dose of study drug, had a measurable Screening biopsy, and had no major eligibility violations. 'n' is the number of participants with data available for analysis at both Baseline and the given time-point.

End point type	Secondary
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End point timeframe:

Baseline (Month 0) to Months 18 and 24

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	72	215		
Units: ng/mL				
arithmetic mean (standard deviation)				
Baseline (Month 18) (n=57,164)	-0.931 (± 0.6387)	-0.758 (± 0.7307)		
Change from Baseline to Month 18 (n=57,164)	-0.129 (± 0.6606)	-0.087 (± 0.6113)		
Baseline (Month 24) (n=56,157)	-0.940 (± 0.6587)	-0.765 (± 0.7127)		
Change from Baseline to Month 24 (n=56,157)	-0.024 (± 0.7375)	0.096 (± 0.6437)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Biomarkers of Hepatocyte Apoptosis: Caspase Cleaved (CK-18 [M-30]) Levels and Total M-65 (CK-18 [M-65]) Levels at Months 3, 6 and 12

End point title	Change From Baseline in Biomarkers of Hepatocyte Apoptosis: Caspase Cleaved (CK-18 [M-30]) Levels and Total M-65 (CK-18 [M-65]) Levels at Months 3, 6 and 12
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End point description:

Caspase-cleaved cytokeratin levels (CK18M30) and total M-65 (CK-18 [M-65]) were measured as biomarkers of hepatocyte apoptosis. A negative change from Baseline indicates decreased hepatocyte apoptosis. FAS in Year 1 included all participants who were randomised and received at least 1 dose of study drug, had a measurable Screening biopsy, and had no major eligibility violations. 'n' is the number of participants with data available for analysis at both Baseline and the given time-point.

End point type	Secondary
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End point timeframe:

Baseline (Month 0) to Months 3, 6 and 12

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	143	144		
Units: U/L				
arithmetic mean (standard deviation)				
Baseline (Month 3) (n=115, 119)	601.6 (± 431.77)	594.2 (± 554.20)		
Change from Baseline to Month 3 (n=115, 119)	-56.4 (± 451.14)	-59.0 (± 485.76)		
Baseline (Month 6) (n=105, 107)	550.3 (± 360.64)	552.9 (± 393.92)		
Change from Baseline to Month 6 (n=105, 107)	10.6 (± 461.98)	-26.1 (± 512.88)		
Baseline (Month 12) (n=107, 101)	555.3 (± 356.28)	567.9 (± 500.53)		
Change from Baseline to Month 12 (n=107, 101)	99.7 (± 824.50)	107.8 (± 830.28)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Biomarkers of Hepatocyte Apoptosis: Caspase Cleaved (CK-18 [M-30]) Levels and Total M-65 (CK-18 [M-65]) Levels at Months 15,

18 and 24

End point title	Change From Baseline in Biomarkers of Hepatocyte Apoptosis: Caspase Cleaved (CK-18 [M-30]) Levels and Total M-65 (CK-18 [M-65]) Levels at Months 15, 18 and 24
End point description:	
Caspase-cleaved cytokeratin levels (CK18M30) and total M-65 (CK-18 [M-65]) were measured as biomarkers of hepatocyte apoptosis. A negative change from Baseline indicates decreased hepatocyte apoptosis. FAS in Year 2 included all participants who were randomised and received at least 1 dose of study drug, had a measurable Screening biopsy, and had no major eligibility violations. 'n' is the number of participants with data available for analysis at both Baseline and the given time-point.	
End point type	Secondary
End point timeframe:	
Baseline (Month 0) to Months 15, 18 and 24	

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	72	215		
Units: U/L				
arithmetic mean (standard deviation)				
CK18M30, Baseline (Month 15)(n=51,145)	570.8 (± 297.42)	536.4 (± 459.06)		
CK18M30,Change from Baseline to Month 15(n=51,145)	-39.6 (± 287.44)	-13.3 (± 450.16)		
CK18M30, Baseline (Month 18)(n=51,149)	578.8 (± 293.93)	540.9 (± 453.90)		
CK18M30,Change from Baseline to Month 18(n=51,149)	23.8 (± 402.98)	57.3 (± 476.92)		
CK18M30, Baseline (Month 24)(n=50,143)	575.4 (± 293.64)	541.8 (± 462.29)		
CK18M30,Change from Baseline to Month 24(n=50,143)	-30.0 (± 369.60)	39.7 (± 437.60)		
CK18M65, Baseline (Month 15)(n=51,145)	772.7 (± 337.24)	687.4 (± 404.83)		
CK18M65,Change from Baseline to Month 15(n=51,145)	134.7 (± 534.46)	88.6 (± 559.11)		
CK18M65, Baseline (Month 18)(n=51,149)	777.8 (± 344.07)	694.8 (± 401.88)		
CK18M65,Change from Baseline to Month 18(n=51,149)	158.0 (± 732.63)	181.5 (± 620.57)		
CK18M65, Baseline (Month 24)(n=50,143)	770.2 (± 335.05)	693.9 (± 409.88)		
CK18M65,Change from Baseline to Month 24(n=50,143)	7.4 (± 570.92)	124.9 (± 522.08)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Weight at Months 3, 6 and 12

End point title	Change From Baseline in Weight at Months 3, 6 and 12
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End point description:

A negative change from Baseline represents decreased weight. Safety Analysis Set Year 1 included all participants who received at least 1 dose of study drug. 'n' is the number of participants with data available for analysis at both Baseline and the given time-point.

End point type	Secondary
End point timeframe:	
Baseline (Day 1) to Months 3, 6 and 12	

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	144	144		
Units: kg				
arithmetic mean (standard deviation)				
Baseline (Month 3) (n=133,138)	97.21 (± 22.368)	95.59 (± 20.590)		
Change from Baseline to Month 3 (n=133,138)	-0.50 (± 2.652)	-0.63 (± 2.632)		
Baseline (Month 6) (n=130,132)	97.18 (± 22.224)	95.18 (± 20.386)		
Change from Baseline to Month 6 (n=130,132)	-0.55 (± 3.319)	-0.47 (± 3.466)		
Baseline (Month 12) (n=126,122)	96.63 (± 22.139)	95.06 (± 20.651)		
Change from Baseline to Month 12 (n=126,122)	-0.08 (± 4.301)	-0.28 (± 4.166)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Weight at Months 15, 18 and 24

End point title	Change From Baseline in Weight at Months 15, 18 and 24
End point description:	
A negative change from Baseline represents decreased weight. Safety Analysis Set Year 2 included all participants who received at least 1 dose of study drug. 'n' is the number of participants with data available for analysis at both Baseline and the given time-point.	
End point type	Secondary
End point timeframe:	
Baseline (Day 1) to Months 15, 18 and 24	

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	60	182		
Units: kg				
arithmetic mean (standard deviation)				

Baseline (Month 15) (n=59,174)	98.25 (± 24.087)	95.32 (± 20.749)		
Change from Baseline to Month 15 (n=59,174)	0.15 (± 3.448)	-0.44 (± 4.257)		
Baseline (Month 18) (n=58,173)	96.98 (± 22.210)	95.23 (± 20.823)		
Change from Baseline to Month 18 (n=58,173)	0.05 (± 4.194)	-0.16 (± 4.458)		
Baseline (Month 24) (n=58,166)	96.98 (± 22.210)	95.19 (± 20.972)		
Change from Baseline to Month 24 (n=58,166)	-0.91 (± 5.649)	-0.56 (± 5.081)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Body Mass Index (BMI) at Months 3, 6 and 12

End point title	Change From Baseline in Body Mass Index (BMI) at Months 3, 6 and 12
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End point description:

The body mass index is a value derived from the mass (weight in kgs) and height (in centimetres) of an individual and is calculated as the body mass divided by the square of the body height. A negative change from Baseline represents decreased BMI. Safety Analysis Set Year 1 included all participants who received at least 1 dose of study drug. 'n' is the number of participants with data available for analysis at both Baseline and the given time-point.

End point type	Secondary
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End point timeframe:

Baseline (Day 1) to Months 3, 6 and 12

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	144	144		
Units: kg/m ²				
arithmetic mean (standard deviation)				
Baseline (Month 3) (n=133,135)	34.129 (± 7.2492)	33.706 (± 5.7812)		
Change from Baseline to Month 3 (n=133,135)	-0.172 (± 0.9200)	-0.232 (± 0.9500)		
Baseline (Month 6) (n=130,129)	34.196 (± 7.3086)	33.547 (± 5.6037)		
Change from Baseline to Month 6 (n=130,129)	-0.182 (± 1.1558)	-0.196 (± 1.2500)		
Baseline (Month 12) (n=126,119)	34.029 (± 7.1358)	33.374 (± 5.6631)		
Change from Baseline to Month 12 (n=126,119)	-0.013 (± 1.7507)	-0.145 (± 1.4891)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Body Mass Index (BMI) at Months 15, 18 and 24

End point title	Change From Baseline in Body Mass Index (BMI) at Months 15, 18 and 24
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End point description:

The body mass index is a value derived from the mass (weight in kgs) and height (in centimetres) of an individual and is calculated as the body mass divided by the square of the body height. A negative change from Baseline represents decreased BMI. Safety Analysis Set Year 2 included all participants who received at least 1 dose of study drug. 'n' is the number of participants with data available for analysis at both Baseline and the given time-point.

End point type	Secondary
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End point timeframe:

Baseline (Day 1) to Months 15, 18 and 24

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	60	182		
Units: kg/m ²				
arithmetic mean (standard deviation)				
Baseline (Month 15) (n=59,171)	34.713 (± 8.0431)	33.392 (± 5.9669)		
Change from Baseline to Month 15 (n=59,171)	-0.006 (± 1.2799)	-0.113 (± 1.6311)		
Baseline (Month 18) (n=58,170)	34.473 (± 7.8964)	33.345 (± 5.9443)		
Change from Baseline to Month 18 (n=58,170)	-0.039 (± 1.5931)	-0.040 (± 1.7153)		
Baseline (Month 24) (n=58,163)	34.473 (± 7.8964)	33.278 (± 6.0012)		
Change from Baseline to Month 24 (n=58,163)	-0.393 (± 2.0613)	-0.178 (± 1.8515)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Waist Circumference at Months 3, 6 and 12

End point title	Change From Baseline in Waist Circumference at Months 3, 6 and 12
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End point description:

A negative change from Baseline represents decreased in waist circumference. Safety Analysis Set Year 1 included all participants who received at least 1 dose of study drug. 'n' is the number of participants with data available for analysis at both Baseline and the given time-point.

End point type	Secondary
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End point timeframe:

Baseline (Day 1) to Months 3, 6 and 12

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	144	144		
Units: cm				
arithmetic mean (standard deviation)				
Baseline (Month 3) (n=131,135)	110.35 (± 14.866)	110.25 (± 13.406)		
Change from Baseline to Month 3 (n=131,135)	0.07 (± 5.147)	0.05 (± 5.396)		
Baseline (Month 6) (n=129,129)	110.42 (± 14.986)	110.12 (± 13.561)		
Change from Baseline to Month 6 (n=129,129)	0.42 (± 8.827)	-0.54 (± 5.876)		
Baseline (Month 12) (n=123,118)	109.77 (± 14.617)	110.02 (± 13.711)		
Change from Baseline to Month 12 (n=123,118)	0.44 (± 6.584)	-1.10 (± 6.255)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Waist Circumference at Months 15, 18 and 24

End point title	Change From Baseline in Waist Circumference at Months 15, 18 and 24
End point description:	
A negative change from Baseline represents decreased in waist circumference. Safety Analysis Set Year 2 included all participants who received at least 1 dose of study drug. 'n' is the number of participants with data available for analysis at both Baseline and the given time-point.	
End point type	Secondary
End point timeframe:	
Baseline (Day 1) to Months 15, 18 and 24	

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	60	182		
Units: cm				
arithmetic mean (standard deviation)				
Baseline (Month 15) (n=57,172)	110.19 (± 14.360)	110.26 (± 14.486)		
Change from Baseline to Month 15 (n=57,172)	0.52 (± 5.520)	-0.18 (± 6.280)		
Baseline (Month 18) (n=56,170)	109.48 (± 12.703)	110.25 (± 14.517)		
Change from Baseline to Month 18 (n=56,170)	1.36 (± 7.966)	-0.21 (± 6.578)		

Baseline (Month 24) (n=58,163)	109.36 (\pm 12.608)	110.08 (\pm 14.606)		
Change from Baseline to Month 24 (n=58,163)	0.11 (\pm 7.907)	-1.00 (\pm 6.503)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Hip Circumference at Months 3, 6 and 12

End point title	Change From Baseline in Hip Circumference at Months 3, 6 and 12
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End point description:

A negative change from Baseline represents decreased hip circumference. Safety Analysis Set Year 1 included all participants who received at least 1 dose of study drug. 'n' is the number of participants with data available for analysis at both Baseline and the given time-point.

End point type	Secondary
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End point timeframe:

Baseline (Day 1) to Months 3, 6 and 12

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	144	144		
Units: cm				
arithmetic mean (standard deviation)				
Baseline (Month 3) (n=129,130)	114.92 (\pm 16.150)	112.35 (\pm 13.802)		
Change from Baseline to Month 3 (n=129,130)	-0.30 (\pm 4.921)	-0.11 (\pm 6.475)		
Baseline (Month 6) (n=127,124)	115.09 (\pm 16.270)	112.16 (\pm 13.320)		
Change from Baseline to Month 6 (n=127,124)	-0.84 (\pm 4.396)	-0.18 (\pm 5.715)		
Baseline (Month 12) (n=121,113)	114.46 (\pm 15.970)	111.66 (\pm 13.376)		
Change from Baseline to Month 12 (n=121,113)	-0.25 (\pm 5.876)	-0.08 (\pm 7.474)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Hip Circumference at Months 15, 18 and 24

End point title	Change From Baseline in Hip Circumference at Months 15, 18 and 24
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End point description:

A negative change from Baseline represents decreased hip circumference. Safety Analysis Set Year 2 included all participants who received at least 1 dose of study drug. 'n' is the number of participants

with data available for analysis at both Baseline and the given time-point.

End point type	Secondary
End point timeframe:	
Baseline (Day 1) to Months 15, 18 and 24	

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	60	182		
Units: cm				
arithmetic mean (standard deviation)				
Baseline (Month 15) (n=58,165)	114.56 (± 17.500)	113.00 (± 14.183)		
Change from Baseline to Month 15 (n=58,165)	-0.06 (± 5.361)	-0.83 (± 7.050)		
Baseline (Month 18) (n=55,162)	114.28 (± 17.871)	112.70 (± 14.168)		
Change from Baseline to Month 18 (n=55,162)	0.55 (± 7.791)	-0.90 (± 6.066)		
Baseline (Month 24) (n=58,157)	114.34 (± 17.408)	112.88 (± 14.225)		
Change from Baseline to Month 24 (n=58,157)	-0.95 (± 7.700)	-1.21 (± 6.677)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Forearm Circumference at Months 3, 6 and 12

End point title	Change From Baseline in Forearm Circumference at Months 3, 6 and 12
End point description:	
A negative change from Baseline represents decreased forearm circumference. Safety Analysis Set Year 1 included all participants who received at least 1 dose of study drug. 'n' is the number of participants with data available for analysis at both Baseline and the given time-point.	
End point type	Secondary
End point timeframe:	
Baseline (Day 1) to Months 3, 6 and 12	

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	144	144		
Units: cm				
arithmetic mean (standard deviation)				
Baseline (Month 3) (n=127,132)	32.95 (± 7.346)	33.38 (± 4.835)		

Change from Baseline to Month 3 (n=127,132)	0.97 (± 6.023)	0.10 (± 6.486)		
Baseline (Month 6) (n=126,126)	32.70 (± 7.290)	33.25 (± 4.734)		
Change from Baseline to Month 6 (n=126,126)	0.82 (± 6.748)	-0.01 (± 3.447)		
Baseline (Month 12) (n=120,115)	32.51 (± 7.277)	33.09 (± 4.771)		
Change from Baseline to Month 12 (n=120,115)	0.83 (± 6.656)	-0.43 (± 3.516)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Forearm Circumference at Months 15, 18 and 24

End point title	Change From Baseline in Forearm Circumference at Months 15, 18 and 24
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End point description:

A negative change from Baseline represents decreased forearm circumference. Safety Analysis Set Year 2 included all participants who received at least 1 dose of study drug. 'n' is the number of participants with data available for analysis at both Baseline and the given time-point.

End point type	Secondary
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End point timeframe:

Baseline (Day 1) to Months 15, 18 and 24

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	60	182		
Units: cm				
arithmetic mean (standard deviation)				
Baseline (Month 15) (n=57,168)	32.88 (± 7.783)	32.91 (± 5.662)		
Change from Baseline to Month 15 (n=57,168)	1.61 (± 6.534)	0.01 (± 5.052)		
Baseline (Month 18) (n=55,166)	32.63 (± 7.718)	32.87 (± 5.696)		
Change from Baseline to Month 18 (n=55,166)	1.79 (± 6.715)	0.02 (± 4.709)		
Baseline (Month 24) (n=57,159)	32.79 (± 7.660)	33.02 (± 5.561)		
Change from Baseline to Month 24 (n=57,159)	0.78 (± 6.124)	-0.64 (± 4.408)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Tricep Skinfold Thickness at Months 3, 6 and 12

End point title	Change From Baseline in Tricep Skinfold Thickness at Months 3, 6 and 12
End point description: A negative change from Baseline represents decreased tricep skinfold thickness. Safety Analysis Set Year 1 included all participants who received at least 1 dose of study drug. 'n' is the number of participants with data available for analysis at both Baseline and the given time-point.	
End point type	Secondary
End point timeframe: Baseline (Day 1) to Months 3, 6 and 12	

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	144	144		
Units: mm				
arithmetic mean (standard deviation)				
Baseline (Month 3) (n=127,131)	28.32 (± 13.677)	25.41 (± 12.593)		
Change from Baseline to Month 3 (n=127,131)	-1.21 (± 6.548)	-0.62 (± 8.704)		
Baseline (Month 6) (n=128,125)	28.53 (± 13.763)	25.38 (± 12.769)		
Change from Baseline to Month 6 (n=128,125)	-2.72 (± 8.091)	-1.52 (± 9.287)		
Baseline (Month 12) (n=122,115)	28.54 (± 13.981)	25.14 (± 12.969)		
Change from Baseline to Month 12 (n=122,115)	-1.34 (± 9.389)	-0.26 (± 10.653)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Tricep Skinfold Thickness at Months 15, 18 and 24

End point title	Change From Baseline in Tricep Skinfold Thickness at Months 15, 18 and 24
End point description: A negative change from Baseline represents decreased tricep skinfold thickness. Safety Analysis Set Year 2 included all participants who received at least 1 dose of study drug. 'n' is the number of participants with data available for analysis at both Baseline and the given time-point.	
End point type	Secondary
End point timeframe: Baseline (Day 1) to Months 15, 18 and 24	

End point values	Placebo	CVC 150 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	60	182		
Units: mm				
arithmetic mean (standard deviation)				
Baseline (Month 15) (n=57,170)	29.84 (± 14.422)	25.41 (± 13.212)		
Change from Baseline to Month 15 (n=57,170)	-1.45 (± 9.364)	-1.59 (± 8.918)		
Baseline (Month 18) (n=55,168)	29.84 (± 14.655)	25.07 (± 12.856)		
Change from Baseline to Month 18 (n=55,168)	-2.27 (± 8.854)	-2.64 (± 8.864)		
Baseline (Month 24) (n=56,160)	29.91 (± 14.532)	24.82 (± 13.025)		
Change from Baseline to Month 24 (n=56,160)	-3.11 (± 8.553)	-1.33 (± 10.521)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline to Year 2

Adverse event reporting additional description:

Safety Analysis Set Year 1 and Year 2 included all participants who received at least 1 dose of study drug.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.1
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Reporting groups

Reporting group title	CVC 150mg/CVC 150 mg
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Reporting group description:

CVC 150 mg tablet, once daily in the morning with food in Years 1 and 2.

Reporting group title	Placebo/Cenicriviroc (CVC) 150 mg
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Reporting group description:

Placebo-matching CVC tablet, once daily in the morning with food in Year 1 then CVC 150 mg tablet, once daily in the morning with food in Year 2.

Reporting group title	Placebo/Placebo
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Reporting group description:

Placebo-matching cenicriviroc (CVC) tablet, once daily in the morning with food in Years 1 and 2.

Serious adverse events	CVC 150mg/CVC 150 mg	Placebo/Cenicriviroc (CVC) 150 mg	Placebo/Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	25 / 144 (17.36%)	8 / 72 (11.11%)	12 / 72 (16.67%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Pancreatic neoplasm			
subjects affected / exposed	0 / 144 (0.00%)	1 / 72 (1.39%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral nerve sheath tumour malignant			
subjects affected / exposed	0 / 144 (0.00%)	1 / 72 (1.39%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemangioma of skin			

subjects affected / exposed	0 / 144 (0.00%)	1 / 72 (1.39%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 144 (0.00%)	0 / 72 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 144 (0.69%)	0 / 72 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	2 / 144 (1.39%)	0 / 72 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 144 (0.69%)	0 / 72 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung disorder			
subjects affected / exposed	1 / 144 (0.69%)	0 / 72 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	0 / 144 (0.00%)	0 / 72 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Bipolar disorder			

subjects affected / exposed	0 / 144 (0.00%)	0 / 72 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood triglycerides increased			
subjects affected / exposed	0 / 144 (0.00%)	0 / 72 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	1 / 144 (0.69%)	0 / 72 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle fracture			
subjects affected / exposed	1 / 144 (0.69%)	0 / 72 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			
subjects affected / exposed	1 / 144 (0.69%)	0 / 72 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial bones fracture			
subjects affected / exposed	1 / 144 (0.69%)	0 / 72 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint injury			
subjects affected / exposed	0 / 144 (0.00%)	1 / 72 (1.39%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laceration			
subjects affected / exposed	1 / 144 (0.69%)	0 / 72 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Lumbar vertebral fracture			
subjects affected / exposed	1 / 144 (0.69%)	0 / 72 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meniscus injury			
subjects affected / exposed	0 / 144 (0.00%)	1 / 72 (1.39%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Traumatic haemothorax			
subjects affected / exposed	1 / 144 (0.69%)	0 / 72 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	1 / 144 (0.69%)	0 / 72 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	1 / 144 (0.69%)	0 / 72 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural pain			
subjects affected / exposed	0 / 144 (0.00%)	1 / 72 (1.39%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wrist fracture			
subjects affected / exposed	0 / 144 (0.00%)	0 / 72 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 144 (0.69%)	0 / 72 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			

subjects affected / exposed	1 / 144 (0.69%)	0 / 72 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arrhythmia			
subjects affected / exposed	1 / 144 (0.69%)	0 / 72 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	1 / 144 (0.69%)	0 / 72 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery occlusion			
subjects affected / exposed	1 / 144 (0.69%)	0 / 72 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
subjects affected / exposed	1 / 144 (0.69%)	0 / 72 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Convulsion			
subjects affected / exposed	1 / 144 (0.69%)	0 / 72 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	1 / 144 (0.69%)	0 / 72 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised tonic-clonic seizure			
subjects affected / exposed	1 / 144 (0.69%)	0 / 72 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Loss of consciousness			

subjects affected / exposed	1 / 144 (0.69%)	0 / 72 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraesthesia			
subjects affected / exposed	1 / 144 (0.69%)	0 / 72 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VIIth nerve paralysis			
subjects affected / exposed	0 / 144 (0.00%)	0 / 72 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 144 (0.69%)	0 / 72 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Inguinal hernia			
subjects affected / exposed	1 / 144 (0.69%)	0 / 72 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 144 (0.00%)	0 / 72 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	0 / 144 (0.00%)	1 / 72 (1.39%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ischaemic			
subjects affected / exposed	0 / 144 (0.00%)	0 / 72 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine polyp			

subjects affected / exposed	0 / 144 (0.00%)	0 / 72 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritoneal haemorrhage			
subjects affected / exposed	0 / 144 (0.00%)	0 / 72 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vasculitis gastrointestinal			
subjects affected / exposed	1 / 144 (0.69%)	0 / 72 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 144 (0.69%)	0 / 72 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 144 (0.00%)	1 / 72 (1.39%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	1 / 144 (0.69%)	0 / 72 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure acute			
subjects affected / exposed	0 / 144 (0.00%)	1 / 72 (1.39%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder dysplasia			
subjects affected / exposed	1 / 144 (0.69%)	0 / 72 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue			

disorders			
Back pain			
subjects affected / exposed	0 / 144 (0.00%)	0 / 72 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal osteoarthritis			
subjects affected / exposed	0 / 144 (0.00%)	0 / 72 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	2 / 144 (1.39%)	0 / 72 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 144 (0.00%)	0 / 72 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar spinal stenosis			
subjects affected / exposed	0 / 144 (0.00%)	0 / 72 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psoriatic arthropathy			
subjects affected / exposed	1 / 144 (0.69%)	0 / 72 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 144 (0.00%)	1 / 72 (1.39%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 144 (0.69%)	0 / 72 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Diverticulitis			
subjects affected / exposed	1 / 144 (0.69%)	0 / 72 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 144 (0.00%)	0 / 72 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 144 (0.69%)	0 / 72 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 144 (0.69%)	0 / 72 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	1 / 144 (0.69%)	0 / 72 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	0 / 144 (0.00%)	0 / 72 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	1 / 144 (0.69%)	0 / 72 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 144 (0.69%)	0 / 72 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 2 diabetes mellitus			

subjects affected / exposed	1 / 144 (0.69%)	0 / 72 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypovolaemia			
subjects affected / exposed	0 / 144 (0.00%)	0 / 72 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	CVC 150mg/CVC 150 mg	Placebo/Cenicriviroc (CVC) 150 mg	Placebo/Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	127 / 144 (88.19%)	59 / 72 (81.94%)	60 / 72 (83.33%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	15 / 144 (10.42%)	9 / 72 (12.50%)	5 / 72 (6.94%)
occurrences (all)	24	11	7
Blood creatine phosphokinase increased			
subjects affected / exposed	3 / 144 (2.08%)	5 / 72 (6.94%)	0 / 72 (0.00%)
occurrences (all)	3	5	0
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	5 / 144 (3.47%)	2 / 72 (2.78%)	9 / 72 (12.50%)
occurrences (all)	7	2	11
Vascular disorders			
Hypertension			
subjects affected / exposed	10 / 144 (6.94%)	4 / 72 (5.56%)	3 / 72 (4.17%)
occurrences (all)	10	4	3
Nervous system disorders			
Headache			
subjects affected / exposed	24 / 144 (16.67%)	15 / 72 (20.83%)	9 / 72 (12.50%)
occurrences (all)	28	18	9
Dizziness			
subjects affected / exposed	13 / 144 (9.03%)	0 / 72 (0.00%)	5 / 72 (6.94%)
occurrences (all)	16	0	6

General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	24 / 144 (16.67%)	10 / 72 (13.89%)	13 / 72 (18.06%)
occurrences (all)	35	12	16
Oedema peripheral			
subjects affected / exposed	5 / 144 (3.47%)	5 / 72 (6.94%)	3 / 72 (4.17%)
occurrences (all)	6	5	3
Pyrexia			
subjects affected / exposed	8 / 144 (5.56%)	4 / 72 (5.56%)	1 / 72 (1.39%)
occurrences (all)	8	4	1
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	16 / 144 (11.11%)	12 / 72 (16.67%)	10 / 72 (13.89%)
occurrences (all)	22	17	11
Diarrhoea			
subjects affected / exposed	32 / 144 (22.22%)	14 / 72 (19.44%)	15 / 72 (20.83%)
occurrences (all)	38	19	17
Abdominal pain			
subjects affected / exposed	18 / 144 (12.50%)	6 / 72 (8.33%)	11 / 72 (15.28%)
occurrences (all)	20	9	11
Nausea			
subjects affected / exposed	28 / 144 (19.44%)	6 / 72 (8.33%)	8 / 72 (11.11%)
occurrences (all)	41	7	11
Abdominal distension			
subjects affected / exposed	13 / 144 (9.03%)	4 / 72 (5.56%)	0 / 72 (0.00%)
occurrences (all)	15	4	0
Constipation			
subjects affected / exposed	13 / 144 (9.03%)	4 / 72 (5.56%)	6 / 72 (8.33%)
occurrences (all)	16	4	6
Flatulence			
subjects affected / exposed	9 / 144 (6.25%)	3 / 72 (4.17%)	2 / 72 (2.78%)
occurrences (all)	10	3	2
Gastrooesophageal reflux disease			
subjects affected / exposed	6 / 144 (4.17%)	3 / 72 (4.17%)	4 / 72 (5.56%)
occurrences (all)	6	3	4
Vomiting			

subjects affected / exposed occurrences (all)	18 / 144 (12.50%) 20	3 / 72 (4.17%) 3	5 / 72 (6.94%) 5
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	16 / 144 (11.11%)	5 / 72 (6.94%)	6 / 72 (8.33%)
occurrences (all)	21	7	6
Oropharyngeal pain			
subjects affected / exposed	13 / 144 (9.03%)	3 / 72 (4.17%)	4 / 72 (5.56%)
occurrences (all)	14	3	5
Nasal congestion			
subjects affected / exposed	8 / 144 (5.56%)	0 / 72 (0.00%)	2 / 72 (2.78%)
occurrences (all)	8	0	2
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	10 / 144 (6.94%)	3 / 72 (4.17%)	5 / 72 (6.94%)
occurrences (all)	14	3	7
Rash			
subjects affected / exposed	12 / 144 (8.33%)	3 / 72 (4.17%)	8 / 72 (11.11%)
occurrences (all)	14	5	8
Psychiatric disorders			
Insomnia			
subjects affected / exposed	10 / 144 (6.94%)	2 / 72 (2.78%)	2 / 72 (2.78%)
occurrences (all)	10	2	2
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	11 / 144 (7.64%)	11 / 72 (15.28%)	12 / 72 (16.67%)
occurrences (all)	13	12	13
Myalgia			
subjects affected / exposed	11 / 144 (7.64%)	5 / 72 (6.94%)	3 / 72 (4.17%)
occurrences (all)	13	5	4
Muscle spasms			
subjects affected / exposed	15 / 144 (10.42%)	4 / 72 (5.56%)	2 / 72 (2.78%)
occurrences (all)	16	4	2
Arthralgia			
subjects affected / exposed	23 / 144 (15.97%)	4 / 72 (5.56%)	4 / 72 (5.56%)
occurrences (all)	30	4	4

Pain in extremity subjects affected / exposed occurrences (all)	14 / 144 (9.72%) 17	1 / 72 (1.39%) 1	6 / 72 (8.33%) 6
Infections and infestations			
Urinary tract infection subjects affected / exposed occurrences (all)	17 / 144 (11.81%) 24	10 / 72 (13.89%) 12	4 / 72 (5.56%) 4
Nasopharyngitis subjects affected / exposed occurrences (all)	21 / 144 (14.58%) 25	9 / 72 (12.50%) 11	7 / 72 (9.72%) 9
Upper respiratory tract infection subjects affected / exposed occurrences (all)	18 / 144 (12.50%) 24	9 / 72 (12.50%) 10	8 / 72 (11.11%) 8
Influenza subjects affected / exposed occurrences (all)	11 / 144 (7.64%) 12	3 / 72 (4.17%) 3	3 / 72 (4.17%) 4
Sinusitis subjects affected / exposed occurrences (all)	18 / 144 (12.50%) 22	3 / 72 (4.17%) 5	9 / 72 (12.50%) 12
Bronchitis subjects affected / exposed occurrences (all)	10 / 144 (6.94%) 12	1 / 72 (1.39%) 1	7 / 72 (9.72%) 10
Ear infection subjects affected / exposed occurrences (all)	5 / 144 (3.47%) 5	2 / 72 (2.78%) 2	4 / 72 (5.56%) 4
Gastroenteritis subjects affected / exposed occurrences (all)	3 / 144 (2.08%) 3	1 / 72 (1.39%) 1	4 / 72 (5.56%) 5
Metabolism and nutrition disorders			
Type 2 diabetes mellitus subjects affected / exposed occurrences (all)	6 / 144 (4.17%) 7	5 / 72 (6.94%) 6	4 / 72 (5.56%) 4
Hyperglycaemia subjects affected / exposed occurrences (all)	0 / 144 (0.00%) 0	4 / 72 (5.56%) 4	2 / 72 (2.78%) 2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 December 2014	Increase in no. of study centres, inclusion criteria changes to increase age range, clarify, or correct typographical errors.
15 June 2016	Updated the study objectives and endpoints.
06 June 2017	Added additional secondary and tertiary objectives and efficacy endpoints. Added summary of additional efficacy analyses to be performed at Year 2.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported