Clinical trial results:
AURORA: A Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Cenicriviroc for the Treatment of Liver Fibrosis in Adult Subjects With Nonalcoholic Steatohepatitis

Summary

EudraCT number	2016-004566-26
Trial protocol	BE PT AT ES HU GB PL SI GR LV IT RO
Global end of trial date	09 March 2021

Results information

Result version number	v1
This version publication date	20 January 2022
First version publication date	20 January 2022

Trial information

Trial identification

Sponsor protocol code	3152-301-002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03028740
WHO universal trial number (UTN)	-
Other trial identifiers	Registro Nacional Estudios Clinicos (RNEC): 1001

Notes:

Sponsors

Sponsor organisation name	Tobira Therapeutics, a subsidiary of Allergan plc
Sponsor organisation address	701 Gateway Blvd, Suite 300, South San Francisco, United States, CA 94080
Public contact	Therapeutic Area, Head, Allergan, 001 714-246-4500, IR-CTRegistration@Allergan.com
Scientific contact	Therapeutic Area, Head, Allergan, 001 714-246-4500, IR-CTRegistration@Allergan.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	09 March 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 March 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The AURORA study was conducted to confirm the efficacy and safety of cenicriviroc (CVC) for the treatment of liver fibrosis in adult participants with Nonalcoholic Steatohepatitis (NASH).

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	05 April 2017
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	Norway: 4
Country: Number of subjects enrolled	Poland: 101
Country: Number of subjects enrolled	Portugal: 7
Country: Number of subjects enrolled	Spain: 35
Country: Number of subjects enrolled	United Kingdom: 42
Country: Number of subjects enrolled	Austria: 8
Country: Number of subjects enrolled	Belgium: 16
Country: Number of subjects enrolled	France: 48
Country: Number of subjects enrolled	Germany: 30
Country: Number of subjects enrolled	Greece: 3
Country: Number of subjects enrolled	Hungary: 8
Country: Number of subjects enrolled	Italy: 16
Country: Number of subjects enrolled	Latvia: 1
Country: Number of subjects enrolled	Romania: 2
Country: Number of subjects enrolled	Australia: 28
Country: Number of subjects enrolled	Brazil: 22
Country: Number of subjects enrolled	Canada: 27
Country: Number of subjects enrolled	Chile: 3
Country: Number of subjects enrolled	Hong Kong: 13
Country: Number of subjects enrolled	Israel: 29
Country: Number of subjects enrolled	Mexico: 25
Country: Number of subjects enrolled	New Zealand: 7

Country: Number of subjects enrolled	Russian Federation: 5
Country: Number of subjects enrolled	Singapore: 1
Country: Number of subjects enrolled	Switzerland: 6
Country: Number of subjects enrolled	Taiwan: 6
Country: Number of subjects enrolled	United States: 1285
Worldwide total number of subjects	1778
EEA total number of subjects	279

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)	1373
From 65 to 84 years	405
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

1778 participants were randomized of which 1769 received treatment; 1293 participated in Part 1. The study was terminated early, and Part 2 did not enroll the planned number of participants. Therefore, Part 1 and Part 2 data were combined and reported as the Full Study Cohort for reporting of the Part 2 efficacy endpoints and the safety endpoints.

Pre-assignment period milestones

Number of subjects started	1778
Number of subjects completed	1769

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Did Not Receive Study Drug: 9

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received cenicriviroc placebo-matching, tablet, orally, once daily for up to approximately 40 months.

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:

Cenicriviroc placebo-matching, tablet, orally, once daily for up to approximately 40 months.

Arm title	Cenicriviroc 150 mg

Arm description:

Participants received cenicriviroc, 150 milligrams (mg), tablet, orally, once daily for up to approximately 40 months.

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

Dosage and administration details:

Cenicriviroc, 150 mg, tablet, orally, once daily for up to approximately 40 months.

Number of subjects in period 1[1]	Placebo	Cenicriviroc 150 mg
Started	589	1180
Participated in Part 1	432	861
Part 1: Received Study Drug	429	859
Completed	0	0
Not completed	589	1180
Physician decision	4	11
Non-compliance with Study Drug	-	2
Adverse Event	8	26
Protocol-specified Withdrawal Criteria Met	27	55
Withdrawal by Subject	48	101
Protocol Violation	4	8
Study Terminated by Sponsor	467	917
Lost to follow-up	30	54
Reason not Specified	1	5
Lack of efficacy	-	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Baseline measures are based on the Safety Population.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received cenicriviroc placebo-matching, tablet, orally, once daily for up to approximately 40 months.	
Reporting group title	Cenicriviroc 150 mg
Reporting group description:	
Participants received cenicriviroc, 150 milligrams (mg), tablet, orally, once daily for up to approximately 40 months.	

Reporting group values	Placebo	Cenicriviroc 150 mg	Total
Number of subjects	589	1180	1769
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	447	918	1365
From 65-84 years	142	262	404
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	55.8	55.2	
standard deviation	± 11.04	± 10.76	-
Gender categorical Units: Subjects			
Female	354	749	1103
Male	235	431	666
Race Units: Subjects			
White	539	1075	1614
Black or African American	14	38	52
Asian	22	45	67
American Indian or Alaska Native	7	8	15
Native Hawaiian or Other Pacific Islander	2	7	9
More than one race	3	6	9
Unknown or Not Reported	2	1	3
Ethnicity Units: Subjects			
Hispanic or Latino	172	315	487
Not Hispanic or Latino	417	865	1282

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received cenicriviroc placebo-matching, tablet, orally, once daily for up to approximately 40 months.	
Reporting group title	Cenicriviroc 150 mg
Reporting group description:	
Participants received cenicriviroc, 150 milligrams (mg), tablet, orally, once daily for up to approximately 40 months.	

Primary: Percentage of Participants With Improvement in Fibrosis by at Least 2 Stages and No Worsening of Steatohepatitis on Liver Biopsy at Month 12 in the Full Study Cohort

End point title	Percentage of Participants With Improvement in Fibrosis by at Least 2 Stages and No Worsening of Steatohepatitis on Liver Biopsy at Month 12 in the Full Study Cohort[1]

End point description:

Fibrosis stage was evaluated using the NASH CRN Fibrosis Staging System with stages: 0=none; 1=perisinusoidal or periportal; 1A=mild, zone 3, perisinusoidal; 1B=moderate, zone 3, perisinusoidal; 1C=portal/periportal; 2=perisinusoidal and portal/periportal; 3=bridging fibrosis; 4=cirrhosis. No worsening of steatohepatitis was defined as no worsening of lobular inflammation or hepatocellular ballooning grade as per scoring in relevant NAS categories. NAS is a semiquantitative scoring system based on the unweighted sum of: steatosis (0=<5% to 3=>66%), lobular inflammation (0=no foci to 3=>4 foci/200x), and hepatocellular ballooning (0=none to 2=many cells/prominent ballooning) scores. Improvement in fibrosis is a decrease in the NASH CRN fibrosis stage. mITT Population for the full study cohort included participants randomly assigned to a treatment group who received at least one dose of study drug for Parts 1 and 2 of the study combined.

End point type	Primary

End point timeframe:

Month 12

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistical analysis was planned to be reported for this endpoint.

End point values	Placebo	Cenicriviroc 150 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	589	1180		
Units: percentage of participants				
number (confidence interval 95%)	8.3 (5.9 to 11.1)	6.8 (5.2 to 8.6)		

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Percentage of Participants With Improvement in Fibrosis by at Least 2 Stages and No Worsening of Steatohepatitis on Liver Histology at Month 12

End point title	Part 1: Percentage of Participants With Improvement in Fibrosis by at Least 2 Stages and No Worsening of Steatohepatitis on Liver Histology at Month 12

End point description:

Fibrosis stage was evaluated using the NASH CRN Fibrosis Staging System with stages: 0=none; 1=perisinusoidal or periportal; 1A=mild, zone 3, perisinusoidal; 1B=moderate, zone 3, perisinusoidal; 1C=portal/periportal; 2=perisinusoidal and portal/periportal; 3=bridging fibrosis; 4=cirrhosis. No worsening of steatohepatitis was defined as no worsening of lobular inflammation or hepatocellular ballooning grade as per scoring in relevant NAS categories. NAS is a semiquantitative scoring system based on the unweighted sum of: steatosis (0=<5% to 3=>66%), lobular inflammation (0=no foci to 3=>4 foci/200x), and hepatocellular ballooning (0=none to 2=many cells/prominent ballooning) scores. Improvement in fibrosis is a decrease in the NASH CRN fibrosis stage. mITT Population for Part 1 included participants randomly assigned to a treatment group who received at least one dose of study drug in Part 1.

End point type	Primary

End point timeframe:

Month 12

End point values	Placebo	Cenicriviroc 150 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	429	859		
Units: percentage of participants				
number (confidence interval 95%)	8.3 (6.0 to 11.3)	6.6 (5.1 to 8.5)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Cenicriviroc 150 mg
Number of subjects included in analysis	1288
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2827 [2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference
Point estimate	-1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.8
upper limit	1.5

Notes:

[2] - P-value was based on Cochran-Mantel-Haenszel general association test comparing Cenicriviroc vs Placebo, controlling for factors (randomization strata: fibrosis stage [2 vs 3] and presence or absence of T2DM at Baseline).

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Cenicriviroc 150 mg

Number of subjects included in analysis	1288
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.7844
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5032
upper limit	1.2229

Secondary: Part 1: Percentage of Participants With Improvement in Fibrosis by at Least 1 Stage and No Worsening of Steatohepatitis on Liver Histology at Month 12

End point title	Part 1: Percentage of Participants With Improvement in Fibrosis by at Least 1 Stage and No Worsening of Steatohepatitis on Liver Histology at Month 12

End point description:

Fibrosis stage was evaluated using the Nonalcoholic Steatohepatitis Clinical Research Network (NASH CRN) Fibrosis Staging System with stages: 0=none; 1=perisinusoidal or periportal;1A=mild, zone 3, perisinusoidal;1B=moderate, zone 3, perisinusoidal;1C=portal/periportal; 2=perisinusoidal and portal/periportal; 3=bridging fibrosis; 4=cirrhosis. No worsening of steatohepatitis=no worsening of lobular inflammation or hepatocellular ballooning grade as per scoring in relevant nonalcoholic fatty liver disease activity score (NAS) categories. NAS is a semiquantitative scoring system based on the unweighted sum of: steatosis (0=<5% to 3=>66%), lobular inflammation (0=no foci to 3=>4 foci/200x), and hepatocellular ballooning (0=none to 2=many cells/prominent ballooning) scores. Improvement in fibrosis is a decrease in the NASH CRN fibrosis stage. mITT Population for Part 1 included participants randomly assigned to a treatment group who received at least one dose of study drug in Part 1.

End point type	Secondary

End point timeframe:

Month 12

End point values	Placebo	Cenicriviroc 150 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	429	859		
Units: percentage of participants				
number (confidence interval 95%)	25.5 (21.5 to 29.9)	22.3 (19.6 to 25.2)		

Statistical analyses

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

Number of subjects included in analysis	1288
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2067 [3]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference
Point estimate	-3.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.2
upper limit	1.9

Notes:

[3] - P-value was based on Cochran-Mantel-Haenszel general association test comparing Cenicriviroc vs Placebo, controlling for factors (randomization strata: fibrosis stage [2 vs 3] and presence or absence of Type 2 diabetes mellitus (T2DM) at Baseline).

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Cenicriviroc 150 mg
Number of subjects included in analysis	1288
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.8369
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6341
upper limit	1.1044

Secondary: Time to First Occurrence of Adjudicated Events in the Full Study Cohort

End point title	Time to First Occurrence of Adjudicated Events in the Full Study Cohort

End point description:

Time to first occurrence from Baseline=number of days from first dose of randomized investigational product to onset of first occurrence of any of following adjudicated events:death(all cause),histopathologic progression to cirrhosis,liver transplant,model for end stage liver disease(MELD)score≥15,ascites,hospitalization for onset of:variceal bleed,hepatic encephalopathy,spontaneous bacterial peritonitis.MELD:scoring system for assessing severity of chronic liver disease and uses participant’s values for total bilirubin,serum creatinine,international normalized ratio for prothrombin time to predict survival.MELD score ranges from 6(less ill) to 40(gravely ill)where score 40=71.3% mortality,9 or less=1.9% mortality. mITT Population for full study cohort: participants randomly assigned to a treatment group who received >=1 dose of study drug in Parts 1 and 2 of study combined. 99999=Median, lower and upper limit of 95% CI were not estimable due to low number of participants with events.

End point type	Secondary

End point timeframe:

From first dose of study drug to onset of first occurrence of the event (Up to approximately 42 months)

End point values	Placebo	Cenicriviroc 150 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	589	1180		
Units: days				
median (confidence interval 95%)	99999 (99999 to 99999)	99999 (99999 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Percentage of Participants With Improvement in Fibrosis by at Least 1 Stage Regardless of Effect on Steatohepatitis at Month 12

End point title	Part 1: Percentage of Participants With Improvement in Fibrosis by at Least 1 Stage Regardless of Effect on Steatohepatitis at Month 12

End point description:

Fibrosis stage was evaluated using the NASH CRN Fibrosis Staging System with stages 0=none, 1=perisinusoidal or periportal, 1A=mild, zone 3, perisinusoidal, 1B=moderate, zone 3, perisinusoidal, 1C=portal/periportal, 2=perisinusoidal and portal/periportal, 3=bridging fibrosis, 4=cirrhosis. mITT Population for Part 1 included participants randomly assigned to a treatment group who received at least one dose of study drug in Part 1. Overall number analyzed is the number of participants with data available for analyses.

End point type	Secondary

End point timeframe:

Month 12

End point values	Placebo	Cenicriviroc 150 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	348	692		
Units: percentage of participants				
number (confidence interval 95%)	33.3 (28.6 to 38.4)	30.6 (27.3 to 34.2)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Cenicriviroc 150 mg
Number of subjects included in analysis	1040
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4054 [4]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference
Point estimate	-2.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.7
upper limit	3.3

Notes:

[4] - P-value was based on Cochran-Mantel-Haenszel general association test comparing Cenicriviroc vs Placebo, controlling for factors (randomization strata: fibrosis stage [2 vs 3] and presence or absence of T2DM at Baseline).

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Cenicriviroc 150 mg
Number of subjects included in analysis	1040
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.8877
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6709
upper limit	1.1744

Secondary: Part 1: Percentage of Participants With Improvement in Fibrosis by at Least 2 Stages Regardless of Effect on Steatohepatitis at Month 12

End point title	Part 1: Percentage of Participants With Improvement in Fibrosis by at Least 2 Stages Regardless of Effect on Steatohepatitis at Month 12

End point description:

Fibrosis stage was evaluated using the NASH CRN Fibrosis Staging System with stages 0=none, 1=perisinusoidal or periportal, 1A=mild, zone 3, perisinusoidal, 1B=moderate, zone 3, perisinusoidal, 1C=portal/periportal, 2=perisinusoidal and portal/periportal, 3=bridging fibrosis, 4=cirrhosis. mITT Population for Part 1 included participants randomly assigned to a treatment group who received at least one dose of study drug in Part 1.

End point type	Secondary

End point timeframe:

Month 12

End point values	Placebo	Cenicriviroc 150 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[5]	0[6]		
Units: percentage of participants				
number (confidence interval 95%)	(to)	(to)		

Notes:

[5] - Analyses were not conducted as primary and 2-stage change endpoints failed;no tables were generated.

[6] - Analyses were not conducted as primary and 2-stage change endpoints failed;no tables were generated.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Improvement in Fibrosis by at Least 1 Stage and No Worsening of Steatohepatitis on Liver Biopsy at Month 12 in the Full Study Cohort

End point title	Percentage of Participants With Improvement in Fibrosis by at Least 1 Stage and No Worsening of Steatohepatitis on Liver Biopsy at Month 12 in the Full Study Cohort

End point description:

Fibrosis stage was evaluated using the NASH CRN Fibrosis Staging System with stages: 0=none; 1=perisinusoidal or periportal; 1A=mild, zone 3, perisinusoidal; 1B=moderate, zone 3, perisinusoidal; 1C=portal/periportal; 2=perisinusoidal and portal/periportal; 3=bridging fibrosis; 4=cirrhosis. No worsening of steatohepatitis was defined as no worsening of lobular inflammation or hepatocellular ballooning grade as per scoring in relevant NAS categories. NAS is a semiquantitative scoring system based on the unweighted sum of: steatosis (0=<5% to 3=>66%), lobular inflammation (0=no foci to 3=>4 foci/200x), and hepatocellular ballooning (0=none to 2=many cells/prominent ballooning) scores. Improvement in fibrosis is a decrease in the NASH CRN fibrosis stage. mITT Population for the full study cohort included participants randomly assigned to a treatment group who received at least one dose of study drug in Parts 1 and 2 of the study combined.

End point type	Secondary

End point timeframe:

Month 12

End point values	Placebo	Cenicriviroc 150 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	589	1180		
Units: percentage of participants				
number (confidence interval 95%)	25.0 (21.2 to 29.2)	22.0 (19.4 to 24.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Improvement in Fibrosis by at Least 1 Stage Regardless of Effect on Steatohepatitis on Liver Biopsy at Month 12 in the Full Study Cohort

End point title	Percentage of Participants With Improvement in Fibrosis by at Least 1 Stage Regardless of Effect on Steatohepatitis on Liver Biopsy at Month 12 in the Full Study Cohort

End point description:

Fibrosis stage was evaluated using the NASH CRN Fibrosis Staging System with stages 0=none, 1=perisinusoidal or periportal, 1A=mild, zone 3, perisinusoidal, 1B=moderate, zone 3, perisinusoidal, 1C=portal/periportal, 2=perisinusoidal and portal/periportal, 3=bridging fibrosis, 4=cirrhosis. mITT Population for the full study cohort included participants randomly assigned to a treatment group who received at least one dose of study drug in Parts 1 and 2 of the study combined. Overall number analyzed is the number of participants with data available for analyses.

End point type	Secondary

End point timeframe:

Month 12

End point values	Placebo	Cenicriviroc 150 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	373	741		
Units: percentage of participants				
number (confidence interval 95%)	33.2 (28.7 to 38.2)	30.5 (27.3 to 33.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Improvement in Fibrosis by at Least 2 Stages Regardless of Effect on Steatohepatitis on Liver Biopsy at Month 12

End point title	Percentage of Participants With Improvement in Fibrosis by at Least 2 Stages Regardless of Effect on Steatohepatitis on Liver Biopsy at Month 12

End point description:

Fibrosis stage was evaluated using the NASH CRN Fibrosis Staging System with stages 0=none, 1=perisinusoidal or periportal, 1A=mild, zone 3, perisinusoidal, 1B=moderate, zone 3, perisinusoidal, 1C=portal/periportal, 2=perisinusoidal and portal/periportal, 3=bridging fibrosis, 4=cirrhosis.

End point type	Secondary

End point timeframe:

Month 12

End point values	Placebo	Cenicriviroc 150 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[7]	0[8]		
Units: percentage of participants				
number (confidence interval 95%)	(to)	(to)		

Notes:

[7] - Analyses were not conducted as primary and 2-stage change endpoints failed;no tables were generated.

[8] - Analyses were not conducted as primary and 2-stage change endpoints failed;no tables were generated.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Improvement in Fibrosis by at Least 1 Stage and No Worsening of Steatohepatitis on Liver Biopsy at Month 60 in the Full Study Cohort

End point title	Percentage of Participants With Improvement in Fibrosis by at Least 1 Stage and No Worsening of Steatohepatitis on Liver Biopsy at Month 60 in the Full Study Cohort

End point description:

Fibrosis stage was evaluated using the NASH CRN Fibrosis Staging System with stages: 0=none; 1=perisinusoidal or periportal; 1A=mild, zone 3, perisinusoidal; 1B=moderate, zone 3, perisinusoidal; 1C=portal/periportal; 2=perisinusoidal and portal/periportal; 3=bridging fibrosis; 4=cirrhosis. No worsening of steatohepatitis was defined as no worsening of lobular inflammation or hepatocellular ballooning grade as per scoring in relevant NAS categories. NAS is a semiquantitative scoring system based on the unweighted sum of: steatosis (0=<5% to 3=>66%), lobular inflammation (0=no foci to 3=>4 foci/200x), and hepatocellular ballooning (0=none to 2=many cells/prominent ballooning) scores. Improvement in fibrosis is a decrease in the NASH CRN fibrosis stage. No data was collected as the study was terminated and no participants reached the Month 60 timepoint.

End point type	Secondary

End point timeframe:

Month 60

End point values	Placebo	Cenicriviroc 150 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[9]	0[10]		
Units: percentage of participants				
number (confidence interval 95%)	(to)	(to)		

Notes:

[9] - No data was collected as study was terminated and no participants reached the Month 60 timepoint.
[10] - No data was collected as study was terminated and no participants reached the Month 60 timepoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Improvement in Fibrosis by at Least 1 Stage Regardless of Effect on Steatohepatitis on Liver Biopsy at Month 60 in the Full Study Cohort

End point title	Percentage of Participants With Improvement in Fibrosis by at Least 1 Stage Regardless of Effect on Steatohepatitis on Liver Biopsy at Month 60 in the Full Study Cohort

End point description:

Fibrosis stage was evaluated using the NASH CRN Fibrosis Staging System with stages 0=none, 1=perisinusoidal or periportal, 1A=mild, zone 3, perisinusoidal, 1B=moderate, zone 3, perisinusoidal, 1C=portal/periportal, 2=perisinusoidal and portal/periportal, 3=bridging fibrosis, 4=cirrhosis. No data was collected as the study was terminated and no participants reached the Month 60 timepoint.

End point type	Secondary

End point timeframe:

Month 60

End point values	Placebo	Cenicriviroc 150 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[11]	0[12]		
Units: percentage of participants				
number (confidence interval 95%)	(to)	(to)		

Notes:

[11] - No data was collected as study was terminated and no participants reached the Month 60 timepoint.
[12] - No data was collected as study was terminated and no participants reached the Month 60 timepoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Improvement in Fibrosis by at Least 2 Stages and No Worsening of Steatohepatitis on Liver Biopsy at Month 60 in the Full Study Cohort

End point title	Percentage of Participants With Improvement in Fibrosis by at Least 2 Stages and No Worsening of Steatohepatitis on Liver Biopsy at Month 60 in the Full Study Cohort

End point description:

Fibrosis stage was evaluated using the NASH CRN Fibrosis Staging System with stages: 0=none; 1=perisinusoidal or periportal; 1A=mild, zone 3, perisinusoidal; 1B=moderate, zone 3, perisinusoidal; 1C=portal/periportal; 2=perisinusoidal and portal/periportal; 3=bridging fibrosis; 4=cirrhosis. No worsening of steatohepatitis was defined as no worsening of lobular inflammation or hepatocellular ballooning grade as per scoring in relevant NAS categories. NAS is a semiquantitative scoring system based on the unweighted sum of: steatosis (0=<5% to 3=>66%), lobular inflammation (0=no foci to 3=>4 foci/200x), and hepatocellular ballooning (0=none to 2=many cells/prominent ballooning) scores. Improvement in fibrosis is a decrease in the NASH CRN fibrosis stage. No data was collected as the study was terminated and no participants reached the Month 60 timepoint.

End point type	Secondary

End point timeframe:

Month 60

End point values	Placebo	Cenicriviroc 150 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[13]	0[14]		
Units: percentage of participants				
number (confidence interval 95%)	(to)	(to)		

Notes:

[13] - No data was collected as study was terminated and no participants reached the Month 60 timepoint.
[14] - No data was collected as study was terminated and no participants reached the Month 60 timepoint

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Improvement in Fibrosis by at Least 2 Stages Regardless of Effect on Steatohepatitis on Liver Biopsy at Month 60 in the Full Study Cohort

End point title	Percentage of Participants With Improvement in Fibrosis by at Least 2 Stages Regardless of Effect on Steatohepatitis on Liver Biopsy at Month 60 in the Full Study Cohort

End point description:

Fibrosis stage was evaluated using NASH CRN Fibrosis Staging System with stages 0=None,

1=Perisinusoidal or periportal, 1A=Mild, zone 3, perisinusoidal, 1B=Moderate, zone 3, perisinusoidal, 1C=Portal/periportal, 2=Perisinusoidal and portal/periportal, 3=Bridging fibrosis, 4=Cirrhosis. No data was collected as the study was terminated and no participants reached the Month 60 timepoint.

End point type	Secondary

End point timeframe:

Month 60

End point values	Placebo	Cenicriviroc 150 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[15]	0[16]		
Units: percentage of participants				
number (confidence interval 95%)	(to)	(to)		

Notes:

[15] - No data was collected as study was terminated and no participants reached the Month 60 timepoint.
[16] - No data was collected as study was terminated and no participants reached the Month 60 timepoint.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose through 30 days after the last dose of study drug (Up to approximately 42 months)

Adverse event reporting additional description:

All-cause Mortality: All enrolled participants. Serious Adverse Events and Other Adverse Events: Safety Population for the full study cohort included participants who received at least one dose of study drug in Parts 1 and 2 of the study combined.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	Placebo

Reporting group description:

Participants received cenicriviroc placebo-matching, tablet, orally, once daily for up to approximately 40 months.

Reporting group title	Cenicriviroc 150 mg

Reporting group description:

Participants received cenicriviroc, 150 milligrams (mg), tablet, orally, once daily for up to approximately 40 months.

Serious adverse events	Placebo	Cenicriviroc 150 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	70 / 589 (11.88%)	159 / 1180 (13.47%)	
number of deaths (all causes)	2	6	
number of deaths resulting from adverse events	2	4	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 589 (0.00%)	3 / 1180 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal cell carcinoma			
subjects affected / exposed	0 / 589 (0.00%)	2 / 1180 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer	Additional description: Number of participants at risk (exposed) in each arm is based on the male population.		

subjects affected / exposed[1]	0 / 235 (0.00%)	2 / 431 (0.46%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acoustic neuroma			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma pancreas			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basosquamous carcinoma			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct cancer			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder transitional cell carcinoma			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bowen's disease			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain neoplasm benign			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial neoplasm	Additional description: Number of participants at risk (exposed) in each arm is based on the female population.		

subjects affected / exposed[2]	0 / 354 (0.00%)	1 / 749 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cancer			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intraductal proliferative breast lesion			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leiomyosarcoma			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma of eyelid			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-small cell lung cancer			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic neuroendocrine tumour			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Papillary thyroid cancer			

subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pituitary tumour benign			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasma cell myeloma			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cancer			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatocellular carcinoma			
subjects affected / exposed	2 / 589 (0.34%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma			
subjects affected / exposed	2 / 589 (0.34%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Brain neoplasm			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial cancer	Additional description: Number of participants at risk (exposed) in each arm is based on the female population.		

subjects affected / exposed[3]	1 / 354 (0.28%)	0 / 749 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour of ampulla of Vater			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic stenosis			
subjects affected / exposed	1 / 589 (0.17%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Phlebolith			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Ruptured ectopic pregnancy	Additional description: Number of participants at risk (exposed) in each arm is based on the female population.		
subjects affected / exposed[4]	1 / 534 (0.19%)	0 / 749 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	2 / 589 (0.34%)	4 / 1180 (0.34%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	0 / 589 (0.00%)	2 / 1180 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	1 / 589 (0.17%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Generalised oedema			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Reproductive system and breast disorders			
Benign prostatic hyperplasia	Additional description: Number of participants at risk (exposed) in each arm is based on the male population.		
subjects affected / exposed[5]	1 / 235 (0.43%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metrorrhagia	Additional description: Number of participants at risk (exposed) in each arm is based on the female population.		
subjects affected / exposed[6]	0 / 354 (0.00%)	1 / 749 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polycystic ovaries	Additional description: Number of participants at risk (exposed) in each arm is based on the female population.		
subjects affected / exposed[7]	0 / 354 (0.00%)	1 / 749 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial hyperplasia	Additional description: Number of participants at risk (exposed) in each arm is based on the female population.		
subjects affected / exposed[8]	1 / 354 (0.28%)	0 / 749 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 589 (0.00%)	3 / 1180 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	0 / 589 (0.00%)	2 / 1180 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 589 (0.17%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory distress syndrome			

subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sleep apnoea syndrome			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemothorax			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			

subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 589 (0.17%)	2 / 1180 (0.17%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			
subjects affected / exposed	1 / 589 (0.17%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric decompensation			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device dislocation			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Serum ferritin increased			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood uric acid increased			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transaminases increased			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	5 / 589 (0.85%)	2 / 1180 (0.17%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haematoma			
subjects affected / exposed	2 / 589 (0.34%)	2 / 1180 (0.17%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural pain			
subjects affected / exposed	1 / 589 (0.17%)	2 / 1180 (0.17%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	1 / 589 (0.17%)	2 / 1180 (0.17%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple injuries			
subjects affected / exposed	0 / 589 (0.00%)	2 / 1180 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Road traffic accident			
subjects affected / exposed	1 / 589 (0.17%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Animal bite			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Craniocerebral injury			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula fracture			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb injury			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural contusion			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural hypotension			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			

subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic vertebral fracture			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist fracture			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			
subjects affected / exposed	3 / 589 (0.51%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	2 / 589 (0.34%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia postoperative			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural complication			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural discomfort			

subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Snake bite			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Phimosis	Additional description: Number of participants at risk (exposed) in each arm is based on the male population.		
subjects affected / exposed[9]	0 / 235 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	2 / 589 (0.34%)	4 / 1180 (0.34%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	0 / 589 (0.00%)	4 / 1180 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	0 / 589 (0.00%)	3 / 1180 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 589 (0.00%)	3 / 1180 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	

Myocardial infarction			
subjects affected / exposed	1 / 589 (0.17%)	2 / 1180 (0.17%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute coronary syndrome			
subjects affected / exposed	0 / 589 (0.00%)	2 / 1180 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve incompetence			
subjects affected / exposed	0 / 589 (0.00%)	2 / 1180 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve disease			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve disease mixed			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac failure congestive			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular hypertrophy			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve incompetence			

subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Palpitations			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulseless electrical activity			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Stress cardiomyopathy			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Coronary artery stenosis			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	2 / 589 (0.34%)	3 / 1180 (0.25%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			

subjects affected / exposed	1 / 589 (0.17%)	3 / 1180 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraesthesia			
subjects affected / exposed	0 / 589 (0.00%)	2 / 1180 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	1 / 589 (0.17%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loss of consciousness			
subjects affected / exposed	1 / 589 (0.17%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain stem infarction			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical radiculopathy			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paralysis			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radial nerve palsy			

subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coma			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersomnia			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lethargy			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Blood loss anaemia			
subjects affected / exposed	2 / 589 (0.34%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune thrombocytopenia			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenitis			

subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenopathy			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenomegaly			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 589 (0.17%)	4 / 1180 (0.34%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo positional			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Visual impairment			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Pancreatitis acute			
subjects affected / exposed	2 / 589 (0.34%)	6 / 1180 (0.51%)	
occurrences causally related to treatment / all	0 / 2	1 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	

Colitis			
subjects affected / exposed	1 / 589 (0.17%)	2 / 1180 (0.17%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 589 (0.00%)	2 / 1180 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	2 / 589 (0.34%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticular perforation			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal distension			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal hernia			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain lower			

subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcoholic pancreatitis			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hiatus hernia			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired gastric emptying			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mesenteric panniculitis			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			

subjects affected / exposed	2 / 589 (0.34%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cirrhosis			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-alcoholic steatohepatitis			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash erythematous			
subjects affected / exposed	1 / 589 (0.17%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic foot			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pruritus			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 589 (0.00%)	4 / 1180 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute kidney injury			
subjects affected / exposed	1 / 589 (0.17%)	3 / 1180 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			

subjects affected / exposed	0 / 589 (0.00%)	2 / 1180 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal colic			
subjects affected / exposed	0 / 589 (0.00%)	2 / 1180 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract obstruction			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Hypoparathyroidism			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypothyroidism			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroid mass			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			

Back pain			
subjects affected / exposed	0 / 589 (0.00%)	4 / 1180 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc degeneration			
subjects affected / exposed	0 / 589 (0.00%)	2 / 1180 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facet joint syndrome			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Flank pain			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc displacement			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar spinal stenosis			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mixed connective tissue disease			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myositis			

subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical spinal stenosis			
subjects affected / exposed	2 / 589 (0.34%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	2 / 589 (0.34%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest wall haematoma			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Exostosis			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic lupus erythematosus			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendonitis			

subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	2 / 589 (0.34%)	6 / 1180 (0.51%)	
occurrences causally related to treatment / all	0 / 2	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonia			
subjects affected / exposed	4 / 589 (0.68%)	5 / 1180 (0.42%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	2 / 589 (0.34%)	5 / 1180 (0.42%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	2 / 589 (0.34%)	4 / 1180 (0.34%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	5 / 589 (0.85%)	2 / 1180 (0.17%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	2 / 589 (0.34%)	2 / 1180 (0.17%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	2 / 589 (0.34%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			

subjects affected / exposed	2 / 589 (0.34%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	1 / 589 (0.17%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute sinusitis			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder empyema			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gangrene			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney infection			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural infection			

subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative abscess			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary sepsis			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhinovirus infection			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal sepsis			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth abscess			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			

subjects affected / exposed	2 / 589 (0.34%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal infection			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical pneumonia			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis infective			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Empyema			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster oticus			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perineal abscess			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vulval cellulitis	Additional description: Number of participants at risk (exposed) in each arm is based on the female population.		
subjects affected / exposed[10]	1 / 354 (0.28%)	0 / 749 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyponatraemia			

subjects affected / exposed	0 / 589 (0.00%)	2 / 1180 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alkalosis hypochloraemic			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alkalosis hypokalaemic			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypomagnesaemia			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 589 (0.00%)	1 / 1180 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			

subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypocalcaemia			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obesity			
subjects affected / exposed	1 / 589 (0.17%)	0 / 1180 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Notes:

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

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

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

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

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Number of participants exposed in each arm is based on the male population.

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

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

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

[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Number of participants exposed in each arm is based on the male population.

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

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

Non-serious adverse events	Placebo	Cenicriviroc 150 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	218 / 589 (37.01%)	425 / 1180 (36.02%)	
Nervous system disorders			
Headache			
subjects affected / exposed	30 / 589 (5.09%)	64 / 1180 (5.42%)	
occurrences (all)	33	68	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	33 / 589 (5.60%)	74 / 1180 (6.27%)	
occurrences (all)	34	83	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	39 / 589 (6.62%)	104 / 1180 (8.81%)	
occurrences (all)	44	119	
Diarrhoea			
subjects affected / exposed	56 / 589 (9.51%)	92 / 1180 (7.80%)	
occurrences (all)	66	121	
Abdominal pain upper			
subjects affected / exposed	26 / 589 (4.41%)	64 / 1180 (5.42%)	
occurrences (all)	27	69	
Abdominal pain			

subjects affected / exposed	30 / 589 (5.09%)	56 / 1180 (4.75%)	
occurrences (all)	32	71	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	35 / 589 (5.94%)	68 / 1180 (5.76%)	
occurrences (all)	45	84	
Back pain			
subjects affected / exposed	36 / 589 (6.11%)	54 / 1180 (4.58%)	
occurrences (all)	39	55	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	33 / 589 (5.60%)	57 / 1180 (4.83%)	
occurrences (all)	42	64	
Upper respiratory tract infection			
subjects affected / exposed	39 / 589 (6.62%)	41 / 1180 (3.47%)	
occurrences (all)	43	45	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 May 2017	The following changes were implemented with Amendment 1: Revised program name from STELLARIS to AURORA. Modified Exclusion Criterion (aspartate aminotransferase [AST] criterion). Modified Exclusion Criterion (alanine aminotransferase [ALT] criterion). Revised timing of the Screening Visit relative to the Baseline Visit. Added hemoglobin A1c assessment to Screening Visit (Part 1 and Part 2). Added storage of plasma and serum samples to Screening Visit (Part 1 and Part 2). Added to study procedures the Short Form Healthy Survey—Version 2 (SF-36v2) questionnaire and its associated quality of life (QoL) evaluation. Removed from study procedures the Modified Medication Adherence Self-report Inventory (M-MASRI) questionnaire and clarified assessment of treatment adherence. Added fasting requirement prior to assessment of liver stiffness. Updated the number of subjects exposed to cenicriviroc (CVC). Modified concomitant use of p-glycoprotein (P-gp) inhibitors. Updated the list of allowed and disallowed concomitant medications. Updated the total blood volume collection. Clarified instructions for completion of all other study visits for subjects who permanently discontinue study drug. Clarified timing of study drug dosing. Added serum hepatic fibrosis indices and moderate end stage liver disease (MELD) score details to Appendix—Clinical Laboratory Tests. Added text for clarification and content-oriented changes were made.
29 June 2017	The following changes were implemented with Amendment 2: Correction made to disallowed supplementation with high-dose vitamin E. Removed requirement pertaining to counseling regarding prolonged ultraviolet (UV) exposure. Removed hepatitis B core antibody test from screening assessments. Added estimated glomerular filtration rate (eGFR) determinations to specified blood draw determinations. Revised Day 1 blood draw determinations to include hepatitis B core antibody (HBcAb) and hepatitis B surface antibody (HBsAb) titer. Clarified use of antiviral medications, opioids, and sedatives/hypnotics for disallowed medications. Provided updated version of the Work Productivity and Activity Impairment Questionnaire: Nonalcoholic Steatohepatitis for Fatty Liver questionnaire. Added text for clarification and content-oriented changes were made.
10 April 2018	The following changes were implemented with Amendment 3: Added adverse events of special interest (AESI) to types of reportable events. Added key secondary objective, secondary objectives, and exploratory objectives for Part 1. Revised the approximate number of participants to be randomized in Part 1 and participants randomized in Part 1 that will be included in Part 2 from 1000 participants to 1200. Increased the number of unique participants across Parts 1 and 2 from which adjudicated events were to be accrued before study termination from 240 to 367. Revised the number of participants to be randomized into Arms A and B of Part 1 from 667 to 800 and from 333 to 400, respectively and the number of participants to be newly randomized into Arms A and B of Part 2 from 667 to 534 and from 333 to 266, respectively. Increased the number of study centers from approximately 300 to up to 425. Revised the text to indicate that study drug (CVC or placebo) must be taken once daily with food. Added key secondary efficacy endpoint, secondary efficacy endpoint and exploratory efficacy endpoint for Part 1. Removed time to first occurrence of hepatocellular carcinoma (HCC) as a primary endpoint for Part 2. Safety analysis was updated to include major adverse cardiovascular events and new-onset type 2 diabetes mellitus (T2DM). Revised the definitions for intent-to-treat (ITT) and modified ITT (mITT) analysis sets. Revised the timing for the primary analysis of Part 1 to occur when approximately 1200 randomized participants had been followed for at least 12 months. Statistical significance levels for testing of the primary endpoints in Part 1 and 2 were updated. Statistical analysis was updated to reflect the testing hierarchy for the newly added key secondary endpoint. Testing methodology for the key secondary endpoint in Part 1 was added.

10 April 2018	Updated the number of participants exposed to CVC in the clinical development program. Added summaries of pharmacokinetic (PK) and safety data from studies 3152-101-002 and 3152-107-002. Updated the summary of data from the Phase 2b study (CENTAUR; Study 652-2-203 (NCT03059446)) based on the final Year 2 results. Added the definitions for treatment-emergent adverse events and for AESI. Changed the timing for collection of one sample for population PK analysis at Month 6 in Part 1. Revised the list of disallowed medications to allow for coadministration of P-gp inhibitors with CVC. Added text for clarification and content-oriented changes were made.
25 April 2019	The following changes were implemented with Amendment 4: Increased duration of 8 weeks for timing of Screening visit to 3 months to facilitate enrolment and all instances of "weeks" was changed to "months". Updated emergency contact and serious adverse event (SAE) reporting information. Increased number of sites from 425 up to 600. Updated exposure data. Added details regarding Study 652-1-121 (NCT02120547) and 3152-102-002 (NCT03376841). Updated results for year 2 CENTAUR study 652-2-203 (NCT03059446) based on final clinical study report (CSR). Added details regarding newly randomized Stage 3 participants in Part 2. Redefined primary efficacy objective and endpoint for Part 1. Reorganized secondary efficacy objectives for Part 2. Modified inclusion/exclusion criterias. Added details regarding disallowed medication use and antidiabetic agents and washout period. Added details regarding newly randomized participants in Part 1 and 2. Added description of patient-reported outcomes (PRO) assessment via electronic tablet. Added subgroup analysis text regarding change from Baseline to Month 12 in Enhanced Liver Fibrosis (ELF) score. Added text relevant to European Union (EU) requirement: ...European Union Data Protection Directive 95/46/EC). Added text regarding role and responsibilities of the study monitor. Text was revised to address concerns from specific country health authorities but which the sponsor determined could be applicable to all countries. Added text for clarification and content-oriented changes were made.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
09 March 2021	This study was terminated early due to lack of efficacy based on the results of the planned interim analysis of Part 1 data.	-

Notes:

Limitations and caveats

None reported