Clinical trial results:
A Study to Evaluate the Safety, Pharmacokinetics and Efficacy of the Combination of AL-335, ACH-3102, and Simeprevir

Summary

EudraCT number	2016-002845-46
Trial protocol	GB
Global end of trial date	11 May 2018

Results information

Result version number	v1 (current)
This version publication date	26 May 2019
First version publication date	26 May 2019

Trial information

Trial identification

Sponsor protocol code	AL-335-604

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02569710
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Alios BioPharm
Sponsor organisation address	260 E. Grand Ave, South San Francisco CA, United States, 94080
Public contact	Clinical Registry group, Alios BioPharma, swang162@ITS.JNJ.com
Scientific contact	Clinical Registry group, Alios BioPharma, swang162@ITS.JNJ.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	11 May 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 May 2018
Global end of trial reached?	Yes
Global end of trial date	11 May 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary purpose of the study is to evaluate the safety and tolerability of AL-335 in combination with Odalasvir (ODV) with or without Simeprevir (SMV) in subjects with chronic Genotype (GT)1 or GT2 or GT3 Hepatitis C virus (HCV) infection.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with good clinical practices and applicable regulatory requirements. Safety was evaluated throughout the study and included adverse events (AEs), vital signs, laboratory assessments (chemistry, hematology, urinalysis, and pregnancy tests), 12-lead electrocardiogram (ECG), and physical examination.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 October 2015
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	Moldova, Republic of: 16
Country: Number of subjects enrolled	Mauritius: 8
Country: Number of subjects enrolled	New Zealand: 134
Country: Number of subjects enrolled	United Kingdom: 3
Worldwide total number of subjects	161
EEA total number of subjects	3

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)	154
From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

No subjects were recruited for Cohorts 10 and 12, hence no data is reported here for these two cohorts.

Pre-assignment

Screening details:

A total of 161 subjects were randomized, 112 in subjects without cirrhosis and 49 in subjects with cirrhosis.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1 (8 Weeks Genotype [GT1])

Arm description:

Cohort 1 (Subjects without Cirrhosis) received single dose of AL-335 400 milligrams (mg) tablets once daily (QD), odalasvir (ODV) 50 mg tablet and simeprevir 100 mg tablet QD for 8 weeks.

Arm type	Experimental
Investigational medicinal product name	AL-335
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received AL-335 400 mg tablets QD.

Investigational medicinal product name	Simeprevir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received Simeprevir tablets 100 mg QD.

Investigational medicinal product name	Odalasvir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received Odalasvir 50 mg tablets QD.

Arm title	Cohort 1b + Cohort 4 (8 Weeks GT1)

Arm description:

Cohort 1b (Subjects without Cirrhosis) received single dose of AL-335 800 mg tablets QD and ODV 50 mg tablets every other day (QOD) for 8 weeks; Cohort 4 (Subjects without Cirrhosis) received single dose of AL-335 800 mg tablets QD and ODV 50 mg tablets QOD for 8 weeks.

Arm type	Experimental

Investigational medicinal product name	AL-335
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received AL-335 800 mg tablets QD.

Investigational medicinal product name	Odalasvir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received Odalasvir 50 mg tablets QOD.

Arm title	Cohort 2 (8 Weeks GT1)

Arm description:

Cohort 2 (Subjects without Cirrhosis) received single dose of AL-335 800 mg tablets QD, ODV 50 mg tablets QOD and SMV 75 mg tablets QD for 8 weeks.

Arm type	Experimental
Investigational medicinal product name	Al-335
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received AL-335 800 mg tablets QD.

Investigational medicinal product name	Odalasvir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received Odalasvir 50 mg tablets QOD.

Investigational medicinal product name	Simeprevir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received Simeprevir 75 mg tablets QD.

Arm title	Cohort 3 (Subjects with Cirrhosis)

Arm description:

Cohort 3 (Subjects with Cirrhosis) received single dose of AL-335 800 mg QD, ODV 50 mg QOD and SMV 75 mg QD for 8 weeks.

Arm type	Experimental
Investigational medicinal product name	AL-335
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received AL-335 800 mg tablets QD.

Investigational medicinal product name	Odalasvir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received Odalasvir 50 mg tablets QOD.

Investigational medicinal product name	Simeprevir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received Simeprevir 75 mg tablets QD.

Arm title	Cohort 4 (12 Weeks GT1)

Arm description:

Cohort 4 (Subjects without Cirrhosis) received single dose of AL-335 800 mg tablets QD and ODV 50 mg tablets QOD for 12 weeks.

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

Dosage and administration details:

Subjects received Odalasvir 50 mg tablets QOD.

Investigational medicinal product name	AL-335
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received AL-335 800 mg tablets QD.

Arm title	Cohort 5a (8 Weeks GT3)

Arm description:

Cohort 5a (Subjects without Cirrhosis) received single dose of AL-335 800 mg tablets QD, ODV 50 mg tablets QOD and SMV 75 mg tablets QD for 8 weeks.

Arm type	Experimental
Investigational medicinal product name	AL-335
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received AL-335 800 mg tablets QD.

Investigational medicinal product name	Odalasvir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received Odalasvir 50 mg tablets QOD.

Investigational medicinal product name	Simeprevir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received Simeprevir 75 mg tablets QD.

Arm title	Cohort 5b (12 Weeks GT3)

Arm description:

Cohort 5b (Subjects without Cirrhosis) received single dose of AL-335 800 mg tablets QD, ODV 50 mg tablets QOD and SMV 75 mg tablets QD for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	AL-335
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received AL-335 800 mg tablets QD.

Investigational medicinal product name	Odalasvir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received Odalasvir 50 mg tablets QOD.

Investigational medicinal product name	Simeprevir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received Simeprevir 75 mg tablets QD.

Arm title	Cohort 6,7,8 (8 Weeks GT1 F4)

Arm description:

Cohort 6 (Subjects with Cirrhosis) received single dose of AL-335 800 mg tablets QD, ODV 50 mg tablets QOD and SMV 75 mg tablets QD for 8 weeks; Cohort 7 and Cohort 8 (Subjects with Cirrhosis) received single dose of AL-335 800 mg tablets QD, ODV 25 mg tablets QD and SMV 75 mg tablets QD for 8 weeks.

Arm type	Experimental
Investigational medicinal product name	AL-335
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received AL-335 800 mg tablets QD.

Investigational medicinal product name	Simeprevir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received Simeprevir 75 mg tablets QD.

Investigational medicinal product name	Odalasvir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received Odalasvir 50 mg tablets QOD.

Arm title	Cohort 9 (12 Weeks GT1 F4)

Arm description:

Cohort 9 (Subjects with Cirrhosis) received single dose of AL-335 800 mg tablets QD, ODV 25 mg tablets QD and SMV 75 mg tablets QD for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	AL-335
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received AL-335 800 mg tablets QD.

Investigational medicinal product name	Simeprevir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received Simeprevir tablets 75 mg QD.

Investigational medicinal product name	Odalasvir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received Odalasvir 25 mg tablets QD.

Arm title	Cohort 11 (12 Weeks GT2 F4)

Arm description:

Cohort 11 (Subjects with Cirrhosis) received single dose of AL-335 800 mg tablets QD, ODV 25 mg tablets QD and SMV 75 mg tablets QD for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	Al-335
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received AL-335 800 mg tablets QD.

Investigational medicinal product name	Simeprevir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details: Subjects received Simeprevir 75 mg tablets QD.	
Investigational medicinal product name	Odalasvir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Subjects received Odalasvir 25 mg tablets QD.	

Number of subjects in period 1	Cohort 1 (8 Weeks Genotype [GT1])	Cohort 1b + Cohort 4 (8 Weeks GT1)	Cohort 2 (8 Weeks GT1)
Started	20	25	20
Completed	19	25	20
Not completed	1	0	0
Consent withdrawn by subject	-	-	-
Adverse event, non-fatal	1	-	-
Other	-	-	-
Lost to follow-up	-	-	-

Number of subjects in period 1	Cohort 3 (Subjects with Cirrhosis)	Cohort 4 (12 Weeks GT1)	Cohort 5a (8 Weeks GT3)
Started	20	8	5
Completed	20	7	4
Not completed	0	1	1
Consent withdrawn by subject	-	-	1
Adverse event, non-fatal	-	-	-
Other	-	1	-
Lost to follow-up	-	-	-

Number of subjects in period 1	Cohort 5b (12 Weeks GT3)	Cohort 6,7,8 (8 Weeks GT1 F4)	Cohort 9 (12 Weeks GT1 F4)
Started	14	30	15
Completed	12	29	14
Not completed	2	1	1
Consent withdrawn by subject	-	-	-
Adverse event, non-fatal	-	-	-
Other	1	1	-
Lost to follow-up	1	-	1

Number of subjects in period 1	Cohort 11 (12 Weeks GT2 F4)
Started	4
Completed	4
Not completed	0
Consent withdrawn by subject	-

Adverse event, non-fatal	-
Other	-
Lost to follow-up	-

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1 (8 Weeks Genotype [GT1])
Reporting group description:	
Cohort 1 (Subjects without Cirrhosis) received single dose of AL-335 400 milligrams (mg) tablets once daily (QD), odalasvir (ODV) 50 mg tablet and simeprevir 100 mg tablet QD for 8 weeks.	
Reporting group title	Cohort 1b + Cohort 4 (8 Weeks GT1)
Reporting group description:	
Cohort 1b (Subjects without Cirrhosis) received single dose of AL-335 800 mg tablets QD and ODV 50 mg tablets every other day (QOD) for 8 weeks; Cohort 4 (Subjects without Cirrhosis) received single dose of AL-335 800 mg tablets QD and ODV 50 mg tablets QOD for 8 weeks.	
Reporting group title	Cohort 2 (8 Weeks GT1)
Reporting group description:	
Cohort 2 (Subjects without Cirrhosis) received single dose of AL-335 800 mg tablets QD, ODV 50 mg tablets QOD and SMV 75 mg tablets QD for 8 weeks.	
Reporting group title	Cohort 3 (Subjects with Cirrhosis)
Reporting group description:	
Cohort 3 (Subjects with Cirrhosis) received single dose of AL-335 800 mg QD, ODV 50 mg QOD and SMV 75 mg QD for 8 weeks.	
Reporting group title	Cohort 4 (12 Weeks GT1)
Reporting group description:	
Cohort 4 (Subjects without Cirrhosis) received single dose of AL-335 800 mg tablets QD and ODV 50 mg tablets QOD for 12 weeks.	
Reporting group title	Cohort 5a (8 Weeks GT3)
Reporting group description:	
Cohort 5a (Subjects without Cirrhosis) received single dose of AL-335 800 mg tablets QD, ODV 50 mg tablets QOD and SMV 75 mg tablets QD for 8 weeks.	
Reporting group title	Cohort 5b (12 Weeks GT3)
Reporting group description:	
Cohort 5b (Subjects without Cirrhosis) received single dose of AL-335 800 mg tablets QD, ODV 50 mg tablets QOD and SMV 75 mg tablets QD for 12 weeks.	
Reporting group title	Cohort 6,7,8 (8 Weeks GT1 F4)
Reporting group description:	
Cohort 6 (Subjects with Cirrhosis) received single dose of AL-335 800 mg tablets QD, ODV 50 mg tablets QOD and SMV 75 mg tablets QD for 8 weeks; Cohort 7 and Cohort 8 (Subjects with Cirrhosis) received single dose of AL-335 800 mg tablets QD, ODV 25 mg tablets QD and SMV 75 mg tablets QD for 8 weeks.	
Reporting group title	Cohort 9 (12 Weeks GT1 F4)
Reporting group description:	
Cohort 9 (Subjects with Cirrhosis) received single dose of AL-335 800 mg tablets QD, ODV 25 mg tablets QD and SMV 75 mg tablets QD for 12 weeks.	
Reporting group title	Cohort 11 (12 Weeks GT2 F4)
Reporting group description:	
Cohort 11 (Subjects with Cirrhosis) received single dose of AL-335 800 mg tablets QD, ODV 25 mg tablets QD and SMV 75 mg tablets QD for 12 weeks.	

Reporting group values	Cohort 1 (8 Weeks Genotype [GT1])	Cohort 1b + Cohort 4 (8 Weeks GT1)	Cohort 2 (8 Weeks GT1)
Number of subjects	20	25	20
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0

Adults (18-64 years)	20	25	20
From 65 to 84 years	0	0	0
85 years and over	0	0	0
Title for AgeContinuous Units: years			
median	56	55	56
full range (min-max)	30 to 61	29 to 64	36 to 62
Title for Gender Units: subjects			
Female	7	8	6
Male	13	17	14

Reporting group values	Cohort 3 (Subjects with Cirrhosis)	Cohort 4 (12 Weeks GT1)	Cohort 5a (8 Weeks GT3)
Number of subjects	20	8	5
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	20	8	5
From 65 to 84 years	0	0	0
85 years and over	0	0	0
Title for AgeContinuous Units: years			
median	55.5	55	54
full range (min-max)	30 to 64	41 to 60	38 to 64
Title for Gender Units: subjects			
Female	8	5	0
Male	12	3	5

Reporting group values	Cohort 5b (12 Weeks GT3)	Cohort 6,7,8 (8 Weeks GT1 F4)	Cohort 9 (12 Weeks GT1 F4)
Number of subjects	14	30	15
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	13	27	14
From 65 to 84 years	1	3	1
85 years and over	0	0	0
Title for AgeContinuous Units: years			
median	44.5	56.5	52
full range (min-max)	18 to 65	37 to 68	36 to 67
Title for Gender Units: subjects			
Female	1	16	2
Male	13	14	13

Reporting group values	Cohort 11 (12 Weeks GT2 F4)	Total	
Number of subjects	4	161	

Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	2	154	
From 65 to 84 years	2	7	
85 years and over	0	0	
Title for AgeContinuous Units: years			
median	63.5		
full range (min-max)	61 to 69	-	
Title for Gender Units: subjects			
Female	1	54	
Male	3	107	

End points

End points reporting groups

Reporting group title	Cohort 1 (8 Weeks Genotype [GT1])
Reporting group description:	
Cohort 1 (Subjects without Cirrhosis) received single dose of AL-335 400 milligrams (mg) tablets once daily (QD), odalasvir (ODV) 50 mg tablet and simeprevir 100 mg tablet QD for 8 weeks.	
Reporting group title	Cohort 1b + Cohort 4 (8 Weeks GT1)
Reporting group description:	
Cohort 1b (Subjects without Cirrhosis) received single dose of AL-335 800 mg tablets QD and ODV 50 mg tablets every other day (QOD) for 8 weeks; Cohort 4 (Subjects without Cirrhosis) received single dose of AL-335 800 mg tablets QD and ODV 50 mg tablets QOD for 8 weeks.	
Reporting group title	Cohort 2 (8 Weeks GT1)
Reporting group description:	
Cohort 2 (Subjects without Cirrhosis) received single dose of AL-335 800 mg tablets QD, ODV 50 mg tablets QOD and SMV 75 mg tablets QD for 8 weeks.	
Reporting group title	Cohort 3 (Subjects with Cirrhosis)
Reporting group description:	
Cohort 3 (Subjects with Cirrhosis) received single dose of AL-335 800 mg QD, ODV 50 mg QOD and SMV 75 mg QD for 8 weeks.	
Reporting group title	Cohort 4 (12 Weeks GT1)
Reporting group description:	
Cohort 4 (Subjects without Cirrhosis) received single dose of AL-335 800 mg tablets QD and ODV 50 mg tablets QOD for 12 weeks.	
Reporting group title	Cohort 5a (8 Weeks GT3)
Reporting group description:	
Cohort 5a (Subjects without Cirrhosis) received single dose of AL-335 800 mg tablets QD, ODV 50 mg tablets QOD and SMV 75 mg tablets QD for 8 weeks.	
Reporting group title	Cohort 5b (12 Weeks GT3)
Reporting group description:	
Cohort 5b (Subjects without Cirrhosis) received single dose of AL-335 800 mg tablets QD, ODV 50 mg tablets QOD and SMV 75 mg tablets QD for 12 weeks.	
Reporting group title	Cohort 6,7,8 (8 Weeks GT1 F4)
Reporting group description:	
Cohort 6 (Subjects with Cirrhosis) received single dose of AL-335 800 mg tablets QD, ODV 50 mg tablets QOD and SMV 75 mg tablets QD for 8 weeks; Cohort 7 and Cohort 8 (Subjects with Cirrhosis) received single dose of AL-335 800 mg tablets QD, ODV 25 mg tablets QD and SMV 75 mg tablets QD for 8 weeks.	
Reporting group title	Cohort 9 (12 Weeks GT1 F4)
Reporting group description:	
Cohort 9 (Subjects with Cirrhosis) received single dose of AL-335 800 mg tablets QD, ODV 25 mg tablets QD and SMV 75 mg tablets QD for 12 weeks.	
Reporting group title	Cohort 11 (12 Weeks GT2 F4)
Reporting group description:	
Cohort 11 (Subjects with Cirrhosis) received single dose of AL-335 800 mg tablets QD, ODV 25 mg tablets QD and SMV 75 mg tablets QD for 12 weeks.	
Subject analysis set title	Cohort 1
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Cohort 1 (Subjects without Cirrhosis) received single dose of AL-335 400 milligrams (mg) tablets once daily (QD), odalasvir (ODV) 50 mg tablet and simeprevir 100 mg tablet QD for 8 weeks.	
Subject analysis set title	Cohort 1b + Cohort 4
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Cohort 1b (Subjects without Cirrhosis) received single dose of AL- 335 800 mg tablets QD and ODV 50	

mg tablets every other day (QOD) for 8 weeks; Cohort 4 (Participants without Cirrhosis) received single dose of AL- 335 800 mg tablets QD and ODV 50 mg tablets QOD for 8 weeks.

Subject analysis set title	Cohort 2 + Cohort 3 + Cohort 5
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Cohort 2+3+5 (Subjects with Cirrhosis) received single dose of AL-335 800 mg QD, ODV 50 mg QOD and SMV 75 mg QD.

Subject analysis set title	Cohort 6
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Cohort 6 (Subjects with Cirrhosis) received single dose of AL-335 800 mg QD, ODV 50 mg QOD and SMV 75 mg QD for 8 weeks.

Subject analysis set title	Cohort 7 + Cohort 8 + Cohort 9 + Cohort 11
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Cohort 7+8 +9+11 (Subjects with Cirrhosis) received single dose of AL-335 800 mg QD, ODV 25 mg QD and SMV 75 mg QD.

Primary: Number of Subjects with Treatment-Emergent Adverse Event (TEAE)

End point title	Number of Subjects with Treatment-Emergent Adverse Event (TEAE)[1]

End point description:

An adverse event (AE) was any untoward medical occurrence in a subject who received study drug without regard to the possibility of a causal relationship. A serious adverse event (SAE) was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Treatment-emergent were events between administration of study drug and up to 43 weeks that were absent before treatment or that worsened relative to pre-treatment state. Safety set included all subjects enrolled in the study who had received at least 1 dose of any study drug, whether prematurely withdrawn from the study or not.

End point type	Primary

End point timeframe:

Approximately 2.6 years

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Cohort 1 (8 Weeks Genotype [GT1])	Cohort 1b + Cohort 4 (8 Weeks GT1)	Cohort 2 (8 Weeks GT1)	Cohort 3 (Subjects with Cirrhosis)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	25	20	20
Units: Subjects	17	19	14	13

End point values	Cohort 4 (12 Weeks GT1)	Cohort 5a (8 Weeks GT3)	Cohort 5b (12 Weeks GT3)	Cohort 6,7,8 (8 Weeks GT1 F4)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	5	14	30
Units: Subjects	7	4	13	17

End point values	Cohort 9 (12 Weeks GT1 F4)	Cohort 11 (12 Weeks GT2 F4)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	4		
Units: Subjects	10	4		

Statistical analyses

No statistical analyses for this end point

Primary: Body Weight at End of Treatment

End point title	Body Weight at End of Treatment[2]

End point description:

Body weight (measured using a calibrated scale) at end of treatment was reported. Safety set included all subjects enrolled into the study who had received at least 1 dose of any study drug, whether prematurely withdrawn from the study or not. Safety set included all subjects enrolled in the study who had received at least 1 dose of any study drug, whether prematurely withdrawn from the study or not. Here, N (number of subjects analyzed) signifies number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

End of treatment (Cohort 3: 6 weeks; Cohort 1, Cohort 1b+ Cohort 4, Cohort 2, Cohort 5a, and Cohort 6, 7, 8: 8 weeks; Cohort 4, Cohort 5b, Cohort 9 and Cohort 11: 12 weeks)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Cohort 1 (8 Weeks Genotype [GT1])	Cohort 1b + Cohort 4 (8 Weeks GT1)	Cohort 2 (8 Weeks GT1)	Cohort 3 (Subjects with Cirrhosis)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	25	20	20
Units: Kilograms (kg)				
arithmetic mean (standard deviation)	76.02 (± 15.13)	84.58 (± 15.09)	80.19 (± 17.79)	74.07 (± 12.78)

End point values	Cohort 4 (12 Weeks GT1)	Cohort 5a (8 Weeks GT3)	Cohort 5b (12 Weeks GT3)	Cohort 6,7,8 (8 Weeks GT1 F4)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	5	14	30
Units: Kilograms (kg)				
arithmetic mean (standard deviation)	73.09 (± 8.62)	81.30 (± 13.82)	81.83 (± 13.67)	80.15 (± 17.92)

End point values	Cohort 9 (12 Weeks GT1 F4)	Cohort 11 (12 Weeks GT2 F4)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	4		
Units: Kilograms (kg)				
arithmetic mean (standard deviation)	86.02 (± 15.56)	69.90 (± 11.55)		

Statistical analyses

No statistical analyses for this end point

Primary: Body Mass Index (BMI) at End of Treatment

End point title	Body Mass Index (BMI) at End of Treatment[3]

End point description:

BMI was calculated by dividing the body weight (in kilogram) by the square of height (in meters). BMI at the end of treatment was reported. Safety set included all subjects enrolled in the study who had received at least 1 dose of any study drug, whether prematurely withdrawn from the study or not. Here, N (number of subjects analyzed) signifies number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

End of treatment (Cohort 3: 6 weeks; Cohort 1, Cohort 1b+ Cohort 4, Cohort 2, Cohort 5a, and Cohort 6, 7, 8: 8 weeks; Cohort 4, Cohort 5b, Cohort 9 and Cohort 11: 12 weeks)

Notes:

[3] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Cohort 1 (8 Weeks Genotype [GT1])	Cohort 1b + Cohort 4 (8 Weeks GT1)	Cohort 2 (8 Weeks GT1)	Cohort 3 (Subjects with Cirrhosis)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	25	20	20
Units: Kilograms per square meter (Kg/m^2)				
arithmetic mean (standard deviation)	25.89 (± 4.63)	28.43 (± 4.26)	26.45 (± 5.53)	25.46 (± 3.53)

End point values	Cohort 4 (12 Weeks GT1)	Cohort 5a (8 Weeks GT3)	Cohort 5b (12 Weeks GT3)	Cohort 6,7,8 (8 Weeks GT1 F4)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	5	14	30
Units: Kilograms per square meter (Kg/m^2)				
arithmetic mean (standard deviation)	25.60 (± 3.21)	25.60 (± 2.82)	26.17 (± 4.20)	27.69 (± 5.28)

End point values	Cohort 9 (12 Weeks GT1 F4)	Cohort 11 (12 Weeks GT2 F4)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	4		
Units: Kilograms per square meter (Kg/m^2)				
arithmetic mean (standard deviation)	27.98 (± 4.37)	23.64 (± 4.50)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Worst Post-Baseline Values of Vital Signs

End point title	Percentage of Subjects with Worst Post-Baseline Values of Vital Signs[4]

End point description:

Percentage of subjects with the worst post-baseline values of vital signs (Systolic blood pressure [sBP], Diastolic blood pressure [dBP], and Heart rate) were reported. For sBP, abnormally low: less than or equal to [<=] 90 millimeters mercury [mmHg]; Grade 1 or mild: greater than [>] 140 to less than [<] 160 mmHg; Grade 2 or moderate: >=160 to <180 and Grade 3 or severe: >=180 mmHg. For dBP, abnormally low: <=50 mmHg; Grade 1 or mild: >90 to <100 mmHg; Grade 2 or moderate: >=100 to <110 mmHg and Grade 3 or severe: >=110 mmHg. For Heart Rate, abnormally low: <=50 beats per minute [bpm] and abnormally high: >=120 bpm) were reported. Safety set included all subjects enrolled in the study who had received at least 1 dose of any study drug, whether prematurely withdrawn from the study or not.

End point type	Primary

End point timeframe:

Up to 43 weeks

Notes:

[4] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Cohort 1 (8 Weeks Genotype [GT1])	Cohort 1b + Cohort 4 (8 Weeks GT1)	Cohort 2 (8 Weeks GT1)	Cohort 3 (Subjects with Cirrhosis)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	25	20	20
Units: Percentage of subjects				
number (not applicable)				
sBP: Abnormally low	0	0	0	0
sBP: Grade 1 or mild	20.0	32.0	35.0	25.0
sBP: Grade 2 or moderate	10.0	8.0	0	5.0
sBP: Grade 3 or severe	0	4.0	5.0	0
dBP: Abnormally low	0	4.0	0	0
dBP: Grade 1 or mild	5.0	20.0	35.0	20.0
dBP: Grade 2 or moderate	5.0	12.0	0	0
dBP: Grade 3 or severe	0	0	0	0
Heart Rate: Abnormally low	35.0	32.0	35.0	30.0

Heart Rate: Abnormally high	0	0	0	0

End point values	Cohort 4 (12 Weeks GT1)	Cohort 5a (8 Weeks GT3)	Cohort 5b (12 Weeks GT3)	Cohort 6,7,8 (8 Weeks GT1 F4)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	5	14	30
Units: Percentage of subjects				
number (not applicable)				
sBP: Abnormally low	0	0	0	3.3
sBP: Grade 1 or mild	37.5	60.0	57.1	26.7
sBP: Grade 2 or moderate	37.5	0	7.1	20.0
sBP: Grade 3 or severe	0	0	0	3.3
dBP: Abnormally low	12.5	0	0	0
dBP: Grade 1 or mild	0	60.0	21.4	10.0
dBP: Grade 2 or moderate	0	0	14.3	13.3
dBP: Grade 3 or severe	25.0	0	7.1	3.3
Heart Rate: Abnormally low	50.0	20.0	21.4	13.3
Heart Rate: Abnormally high	12.5	0	0	0

End point values	Cohort 9 (12 Weeks GT1 F4)	Cohort 11 (12 Weeks GT2 F4)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	4		
Units: Percentage of subjects				
number (not applicable)				
sBP: Abnormally low	0	0		
sBP: Grade 1 or mild	46.7	25.0		
sBP: Grade 2 or moderate	13.3	50.0		
sBP: Grade 3 or severe	13.3	0		
dBP: Abnormally low	0	0		
dBP: Grade 1 or mild	26.7	0		
dBP: Grade 2 or moderate	6.7	25.0		
dBP: Grade 3 or severe	6.7	0		
Heart Rate: Abnormally low	13.3	0		
Heart Rate: Abnormally high	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Maximum Decrease from Baseline in Mean Ejection Fraction

End point title	Percentage of Subjects with Maximum Decrease from Baseline in Mean Ejection Fraction[5]

End point description:

Percentage of subjects with maximum decrease from baseline in mean ejection fraction was reported. Percentages are based on the number of subjects with available data. Safety set included all subjects enrolled into the study who had received at least 1 dose of any study drug, whether prematurely withdrawn from the study or not.

End point type	Primary

End point timeframe:

Baseline up to End of treatment (up to 43 weeks)

Notes:

[5] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Cohort 1 (8 Weeks Genotype [GT1])	Cohort 1b + Cohort 4 (8 Weeks GT1)	Cohort 2 (8 Weeks GT1)	Cohort 3 (Subjects with Cirrhosis)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	25	20	20
Units: Percentage of subjects				
number (not applicable)				
Decline of > 10%	0.0	0.0	0.0	0.0
Decline of >5-<=10%	0.0	4.0	10.0	10.0
Decline of >0-<=5%	65.0	48.0	60.0	50.0

End point values	Cohort 4 (12 Weeks GT1)	Cohort 5a (8 Weeks GT3)	Cohort 5b (12 Weeks GT3)	Cohort 6,7,8 (8 Weeks GT1 F4)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	5	14	30
Units: Percentage of subjects				
number (not applicable)				
Decline of > 10%	0.0	0.0	0.0	0.0
Decline of >5-<=10%	12.5	0.0	21.4	3.3
Decline of >0-<=5%	50.0	20.0	64.3	80.0

End point values	Cohort 9 (12 Weeks GT1 F4)	Cohort 11 (12 Weeks GT2 F4)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	4		
Units: Percentage of subjects				
number (not applicable)				
Decline of > 10%	0.0	0.0		
Decline of >5-<=10%	6.7	0.0		
Decline of >0-<=5%	46.7	50.0		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects by Treatment-Emergent Toxicity Grade - Hematology Parameters

End point title	Percentage of Subjects by Treatment-Emergent Toxicity Grade - Hematology Parameters[6]

End point description:

Percentage of subjects by treatment-emergent toxicity grade (1, 2, 3, 4 and 3+4) for Hematology parameters (hemoglobin, lymphocytes, neutrophils, leukocytes, platelets) were reported. Toxicity grades were defined as Grade 1: Mild; Grade 2: Moderate; Grade 3: Severe and Grade 4: potentially life-threatening. Toxicity is treatment-emergent if it is worse than the baseline or if the baseline is missing. Safety set included all subjects enrolled in the study who had received at least 1 dose of any study drug, whether prematurely withdrawn from the study or not.

End point type	Primary

End point timeframe:

Up to 43 weeks

Notes:

[6] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Cohort 1 (8 Weeks Genotype [GT1])	Cohort 1b + Cohort 4 (8 Weeks GT1)	Cohort 2 (8 Weeks GT1)	Cohort 3 (Subjects with Cirrhosis)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	25	20	20
Units: Percentage of subjects				
number (not applicable)				
Hemoglobin: Grade 1	5.0	0.0	0.0	5.0
Hemoglobin: Grade 2	0.0	0.0	0.0	0.0
Hemoglobin: Grade 3	0.0	0.0	0.0	0.0
Hemoglobin: Grade 4	0.0	0.0	0.0	0.0
Hemoglobin: Grade 3+4	0.0	0.0	0.0	0.0
Lymphocytes: Grade 1	0.0	0.0	0.0	0.0
Lymphocytes: Grade 2	0.0	0.0	0.0	0.0
Lymphocytes: Grade 3	0.0	0.0	0.0	0.0
Lymphocytes: Grade 4	0.0	0.0	0.0	0.0
Lymphocytes: Grade 3+4	0.0	0.0	0.0	0.0
Neutrophils: Grade 1	0.0	0.0	0.0	0.0
Neutrophils: Grade 2	0.0	0.0	0.0	0.0
Neutrophils: Grade 3	0.0	0.0	0.0	0.0
Neutrophils: Grade 4	0.0	0.0	0.0	0.0
Neutrophils: Grade 3+4	0.0	0.0	0.0	0.0
Leukocytes: Grade 1	0.0	0.0	0.0	0.0
Leukocytes: Grade 2	0.0	0.0	0.0	0.0
Leukocytes: Grade 3	0.0	0.0	0.0	0.0
Leukocytes: Grade 4	0.0	0.0	0.0	0.0
Leukocytes: Grade 3+4	0.0	0.0	0.0	0.0
Platelets: Grade 1	5.0	0.0	5.0	5.0
Platelets: Grade 2	0.0	0.0	0.0	0.0
Platelets: Grade 3	0.0	0.0	0.0	0.0
Platelets: Grade 4	0.0	0.0	0.0	0.0
Platelets: Grade 3+4	0.0	0.0	0.0	0.0

End point values	Cohort 4 (12 Weeks GT1)	Cohort 5a (8 Weeks GT3)	Cohort 5b (12 Weeks GT3)	Cohort 6,7,8 (8 Weeks GT1 F4)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	5	14	30
Units: Percentage of subjects				
number (not applicable)				
Hemoglobin: Grade 1	0.0	0.0	0.0	0.0
Hemoglobin: Grade 2	0.0	0.0	0.0	0.0
Hemoglobin: Grade 3	0.0	0.0	0.0	0.0
Hemoglobin: Grade 4	0.0	0.0	0.0	0.0
Hemoglobin: Grade 3+4	0.0	0.0	0.0	0.0
Lymphocytes: Grade 1	0.0	0.0	0.0	6.7
Lymphocytes: Grade 2	0.0	0.0	7.1	10.0
Lymphocytes: Grade 3	0.0	0.0	0.0	0.0
Lymphocytes: Grade 4	0.0	0.0	0.0	0.0
Lymphocytes: Grade 3+4	0.0	0.0	0.0	0.0
Neutrophils: Grade 1	0.0	0.0	0.0	0.0
Neutrophils: Grade 2	0.0	0.0	0.0	0.0
Neutrophils: Grade 3	0.0	0.0	0.0	0.0
Neutrophils: Grade 4	0.0	0.0	0.0	0.0
Neutrophils: Grade 3+4	0.0	0.0	0.0	0.0
Leukocytes: Grade 1	0.0	0.0	0.0	10.0
Leukocytes: Grade 2	0.0	0.0	0.0	0.0
Leukocytes: Grade 3	0.0	0.0	0.0	0.0
Leukocytes: Grade 4	0.0	0.0	0.0	0.0
Leukocytes: Grade 3+4	0.0	0.0	0.0	0.0
Platelets: Grade 1	0.0	0.0	7.1	6.7
Platelets: Grade 2	0.0	0.0	0.0	16.7
Platelets: Grade 3	0.0	0.0	0.0	0.0
Platelets: Grade 4	0.0	0.0	0.0	0.0
Platelets: Grade 3+4	0.0	0.0	0.0	0.0

End point values	Cohort 9 (12 Weeks GT1 F4)	Cohort 11 (12 Weeks GT2 F4)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	4		
Units: Percentage of subjects				
number (not applicable)				
Hemoglobin: Grade 1	0.0	0.0		
Hemoglobin: Grade 2	0.0	0.0		
Hemoglobin: Grade 3	0.0	0.0		
Hemoglobin: Grade 4	0.0	0.0		
Hemoglobin: Grade 3+4	0.0	0.0		
Lymphocytes: Grade 1	0.0	0.0		
Lymphocytes: Grade 2	0.0	0.0		
Lymphocytes: Grade 3	0.0	0.0		

Lymphocytes: Grade 4	0.0	0.0		
Lymphocytes: Grade 3+4	0.0	0.0		
Neutrophils: Grade 1	0.0	0.0		
Neutrophils: Grade 2	0.0	0.0		
Neutrophils: Grade 3	0.0	0.0		
Neutrophils: Grade 4	0.0	0.0		
Neutrophils: Grade 3+4	0.0	0.0		
Leukocytes: Grade 1	0.0	0.0		
Leukocytes: Grade 2	0.0	0.0		
Leukocytes: Grade 3	0.0	0.0		
Leukocytes: Grade 4	0.0	0.0		
Leukocytes: Grade 3+4	0.0	0.0		
Platelets: Grade 1	13.3	25.0		
Platelets: Grade 2	0.0	0.0		
Platelets: Grade 3	0.0	0.0		
Platelets: Grade 4	0.0	0.0		
Platelets: Grade 3+4	0.0	0.0		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects by Treatment-Emergent Toxicity Grade - Blood Chemistry Parameters

End point title	Percentage of Subjects by Treatment-Emergent Toxicity Grade - Blood Chemistry Parameters[7]

End point description:

Percentage of subjects by treatment-emergent toxicity grade (Grade 1,2,3,4,3+4) for Blood Chemistry (Calcium, Phosphate, Potassium, Sodium, Bicarbonate, Alanine aminotransferase, Alkaline phosphatase, Aspartate aminotransferase, Bilirubin, Direct Bilirubin, Glucose, Cholesterol, Triglycerides, Urate, Triacylglycerol lipase, Creatinine, Creatinine clearance, Albumin, and Creatine kinase) were reported. Toxicity grades were
defined as Grade 1: Mild; Grade 2: Moderate; Grade 3: Severe and Grade 4: potentially life-threatening. Toxicity is treatment-emergent if it is worse than the baseline or if the baseline is missing. Safety set included all subjects enrolled in the study who had received at least 1 dose of any study drug, whether prematurely withdrawn from the study or not.

End point type	Primary

End point timeframe:

Up to 43 weeks

Notes:

[7] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Cohort 1 (8 Weeks Genotype [GT1])	Cohort 1b + Cohort 4 (8 Weeks GT1)	Cohort 2 (8 Weeks GT1)	Cohort 3 (Subjects with Cirrhosis)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	25	20	20
Units: Percentage of subjects				
number (not applicable)				
Calcium: Grade 1	0.0	0.0	0.0	0.0

Calcium: Grade 2	0.0	0.0	0.0	0.0
Calcium: Grade 3	0.0	0.0	0.0	0.0
Calcium: Grade 4	0.0	0.0	0.0	0.0
Calcium: Grade 3+4	0.0	0.0	0.0	0.0
Phosphate: Grade 1	0.0	0.0	0.0	0.0
Phosphate: Grade 2	10.0	20.0	25.0	15.0
Phosphate: Grade 3	0.0	0.0	0.0	0.0
Phosphate: Grade 4	0.0	0.0	0.0	0.0
Phosphate: Grade 3+4	0.0	0.0	0.0	0.0
Potassium: Grade 1	0.0	4.0	0.0	0.0
Potassium: Grade 2	0.0	0.0	0.0	0.0
Potassium: Grade 3	0.0	0.0	0.0	0.0
Potassium: Grade 4	0.0	0.0	0.0	0.0
Potassium: Grade 3+4	0.0	0.0	0.0	0.0
Sodium: Grade 1	0.0	8.0	5.0	0.0
Sodium: Grade 2	0.0	0.0	0.0	0.0
Sodium: Grade 3	0.0	0.0	0.0	0.0
Sodium: Grade 4	0.0	0.0	0.0	0.0
Sodium: Grade 3+4	0.0	0.0	0.0	0.0
Bicarbonate: Grade 1	0.0	16.0	15.0	5.0
Bicarbonate: Grade 2	0.0	0.0	0.0	0.0
Bicarbonate: Grade 3	0.0	0.0	0.0	0.0
Bicarbonate: Grade 4	0.0	0.0	0.0	0.0
Bicarbonate: Grade 3+4	0.0	0.0	0.0	0.0
Alanine aminotransferase: Grade 1	0.0	0.0	0.0	0.0
Alanine aminotransferase: Grade 2	0.0	0.0	0.0	0.0
Alanine aminotransferase: Grade 3	0.0	0.0	0.0	0.0
Alanine aminotransferase: Grade 4	0.0	0.0	0.0	0.0
Alanine aminotransferase: Grade 3+4	0.0	0.0	0.0	0.0
Alkaline phosphatase: Grade 1	0.0	0.0	0.0	0.0
Alkaline phosphatase: Grade 2	0.0	0.0	0.0	0.0
Alkaline phosphatase: Grade 3	0.0	0.0	0.0	0.0
Alkaline phosphatase: Grade 4	0.0	0.0	0.0	0.0
Alkaline phosphatase: Grade 3+4	0.0	0.0	0.0	0.0
Aspartate aminotransferase: Grade: 1	0.0	0.0	0.0	0.0
Aspartate aminotransferase: Grade: 2	0.0	0.0	0.0	0.0
Aspartate aminotransferase: Grade: 3	0.0	0.0	0.0	0.0
Aspartate aminotransferase: Grade: 4	0.0	0.0	0.0	0.0
Aspartate aminotransferase: Grade: 3+4	0.0	0.0	0.0	0.0
Bilirubin: Grade 1	0.0	0.0	10.0	10.0
Bilirubin: Grade 2	5.0	0.0	0.0	0.0
Bilirubin: Grade 3	0.0	0.0	0.0	0.0
Bilirubin: Grade 4	0.0	0.0	0.0	0.0
Bilirubin: Grade 3+4	0.0	0.0	0.0	0.0
Direct bilirubin: Grade 1	0.0	0.0	0.0	0.0
Direct bilirubin: Grade 2	0.0	0.0	0.0	0.0
Direct bilirubin: Grade 3	0.0	0.0	0.0	0.0
Direct bilirubin: Grade 4	0.0	0.0	0.0	0.0
Direct bilirubin: Grade 3+4	0.0	0.0	0.0	0.0
Glucose: Grade 1	15.0	4.0	10.0	5.0
Glucose: Grade 2	0.0	4.0	5.0	0.0

Glucose: Grade 3	0.0	0.0	0.0	0.0
Glucose: Grade 4	0.0	0.0	0.0	0.0
Glucose: Grade 3+4	0.0	0.0	0.0	0.0
Cholesterol: Grade 1	20.0	24.0	30.0	35.0
Cholesterol: Grade 2	15.0	8.0	5.0	5.0
Cholesterol: Grade 3	0.0	0.0	5.0	0.0
Cholesterol: Grade 4	0.0	0.0	0.0	0.0
Cholesterol: Grade 3+4	0.0	0.0	5.0	0.0
Triglycerides: Grade 1	5.0	16.0	10.0	15.0
Triglycerides: Grade 2	0.0	0.0	0.0	0.0
Triglycerides: Grade 3	0.0	0.0	0.0	0.0
Triglycerides: Grade 4	0.0	0.0	0.0	0.0
Triglycerides: Grade 3+4	0.0	0.0	0.0	0.0
Urate: Grade 1	5.0	12.0	5.0	0.0
Urate: Grade 2	0.0	4.0	0.0	5.0
Urate: Grade 3	0.0	0.0	0.0	0.0
Urate: Grade 4	0.0	0.0	0.0	0.0
Urate: Grade 3+4	0.0	0.0	0.0	0.0
Triacylglycerol lipase: Grade 1	5.0	12.0	5.0	0.0
Triacylglycerol lipase: Grade 2	15.0	4.0	10.0	0.0
Triacylglycerol lipase: Grade 3	5.0	8.0	0.0	0.0
Triacylglycerol lipase: Grade 4	0.0	0.0	5.0	0.0
Triacylglycerol lipase: Grade 3+4	5.0	8.0	5.0	0.0
Creatinine: Grade 1	0.0	0.0	0.0	0.0
Creatinine: Grade 2	0.0	0.0	0.0	0.0
Creatinine: Grade 3	0.0	0.0	0.0	0.0
Creatinine: Grade 4	0.0	0.0	0.0	0.0
Creatinine: Grade 3+4	0.0	0.0	0.0	0.0
Creatinine clearance: Grade 1	0.0	0.0	0.0	0.0
Creatinine clearance: Grade 2	0.0	0.0	0.0	0.0
Creatinine clearance: Grade 3	0.0	0.0	0.0	0.0
Creatinine clearance: Grade 4	0.0	0.0	0.0	0.0
Creatinine clearance: Grade 3+4	0.0	0.0	0.0	0.0
Albumin: Grade 1	5.0	4.0	0.0	0.0
Albumin: Grade 2	0.0	0.0	0.0	0.0
Albumin: Grade 3	0.0	0.0	0.0	0.0
Albumin: Grade 4	0.0	0.0	0.0	0.0
Albumin: Grade 3+4	0.0	0.0	0.0	0.0
Creatine kinase: Grade 1	0.0	0.0	0.0	0.0
Creatine kinase: Grade 2	0.0	0.0	0.0	0.0
Creatine kinase: Grade 3	0.0	0.0	0.0	0.0
Creatine kinase: Grade 4	0.0	0.0	0.0	0.0
Creatine kinase: Grade 3+4	0.0	0.0	0.0	0.0

End point values	Cohort 4 (12 Weeks GT1)	Cohort 5a (8 Weeks GT3)	Cohort 5b (12 Weeks GT3)	Cohort 6,7,8 (8 Weeks GT1 F4)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	5	14	30
Units: Percentage of subjects				

number (not applicable)				
Calcium: Grade 1	0.0	0.0	3.3	13.3
Calcium: Grade 2	0.0	0.0	0.0	0.0
Calcium: Grade 3	0.0	0.0	0.0	0.0
Calcium: Grade 4	0.0	0.0	0.0	0.0
Calcium: Grade 3+4	0.0	0.0	0.0	0.0
Phosphate: Grade 1	0.0	0.0	0.0	0.0
Phosphate: Grade 2	12.5	0.0	14.3	13.3
Phosphate: Grade 3	0.0	0.0	21.4	3.3
Phosphate: Grade 4	0.0	0.0	0.0	0.0
Phosphate: Grade 3+4	0.0	0.0	21.4	3.3
Potassium: Grade 1	0.0	0.0	0.0	6.7
Potassium: Grade 2	0.0	0.0	0.0	0.0
Potassium: Grade 3	0.0	0.0	0.0	0.0
Potassium: Grade 4	0.0	0.0	0.0	0.0
Potassium: Grade 3+4	0.0	0.0	0.0	0.0
Sodium: Grade 1	12.5	20.0	0.0	3.3
Sodium: Grade 2	0.0	0.0	0.0	0.0
Sodium: Grade 3	0.0	0.0	0.0	0.0
Sodium: Grade 4	0.0	0.0	0.0	0.0
Sodium: Grade 3+4	0.0	0.0	0.0	0.0
Bicarbonate: Grade 1	12.5	20.0	7.1	0.0
Bicarbonate: Grade 2	0.0	0.0	0.0	6.7
Bicarbonate: Grade 3	0.0	0.0	0.0	0.0
Bicarbonate: Grade 4	0.0	0.0	0.0	0.0
Bicarbonate: Grade 3+4	0.0	0.0	0.0	0.0
Alanine aminotransferase: Grade 1	0.0	0.0	0.0	3.3
Alanine aminotransferase: Grade 2	0.0	0.0	0.0	0.0
Alanine aminotransferase: Grade 3	0.0	0.0	0.0	0.0
Alanine aminotransferase: Grade 4	0.0	0.0	0.0	6.7
Alanine aminotransferase: Grade 3+4	0.0	0.0	0.0	6.7
Alkaline phosphatase: Grade 1	0.0	0.0	0.0	6.7
Alkaline phosphatase: Grade 2	0.0	0.0	0.0	0.0
Alkaline phosphatase: Grade 3	0.0	0.0	0.0	0.0
Alkaline phosphatase: Grade 4	0.0	0.0	0.0	0.0
Alkaline phosphatase: Grade 3+4	0.0	0.0	0.0	0.0
Aspartate aminotransferase: Grade: 1	0.0	0.0	0.0	0.0
Aspartate aminotransferase: Grade: 2	0.0	0.0	0.0	3.3
Aspartate aminotransferase: Grade: 3	0.0	0.0	0.0	0.0
Aspartate aminotransferase: Grade: 4	0.0	0.0	0.0	0.0
Aspartate aminotransferase: Grade: 3+4	0.0	0.0	0.0	0.0
Bilirubin: Grade 1	0.0	0.0	0.0	3.3
Bilirubin: Grade 2	0.0	0.0	0.0	3.3
Bilirubin: Grade 3	0.0	0.0	0.0	3.3
Bilirubin: Grade 4	0.0	0.0	0.0	0.0
Bilirubin: Grade 3+4	0.0	0.0	0.0	3.3
Direct bilirubin: Grade 1	0.0	0.0	0.0	0.0
Direct bilirubin: Grade 2	0.0	0.0	0.0	0.0
Direct bilirubin: Grade 3	0.0	0.0	0.0	3.3
Direct bilirubin: Grade 4	0.0	0.0	0.0	0.0
Direct bilirubin: Grade 3+4	0.0	0.0	0.0	3.3

Glucose: Grade 1	25.0	0.0	35.7	10.0
Glucose: Grade 2	12.5	0.0	14.3	13.3
Glucose: Grade 3	0.0	0.0	0.0	3.3
Glucose: Grade 4	0.0	0.0	0.0	0.0
Glucose: Grade 3+4	0.0	0.0	0.0	3.3
Cholesterol: Grade 1	12.5	0.0	42.9	3.3
Cholesterol: Grade 2	37.5	0.0	0.0	6.7
Cholesterol: Grade 3	0.0	0.0	0.0	3.3
Cholesterol: Grade 4	0.0	0.0	0.0	0.0
Cholesterol: Grade 3+4	0.0	0.0	0.0	3.3
Triglycerides: Grade 1	50.0	20.0	28.6	16.7
Triglycerides: Grade 2	0.0	0.0	14.3	0.0
Triglycerides: Grade 3	0.0	0.0	0.0	0.0
Triglycerides: Grade 4	0.0	0.0	0.0	0.0
Triglycerides: Grade 3+4	0.0	0.0	0.0	0.0
Urate: Grade 1	12.5	0.0	28.6	10.0
Urate: Grade 2	0.0	0.0	0.0	3.3
Urate: Grade 3	0.0	0.0	0.0	0.0
Urate: Grade 4	0.0	0.0	0.0	0.0
Urate: Grade 3+4	0.0	0.0	0.0	0.0
Triacylglycerol lipase: Grade 1	12.5	20.0	7.1	13.3
Triacylglycerol lipase: Grade 2	12.5	0.0	7.1	3.3
Triacylglycerol lipase: Grade 3	0.0	0.0	0.0	0.0
Triacylglycerol lipase: Grade 4	0.0	0.0	0.0	0.0
Triacylglycerol lipase: Grade 3+4	0.0	0.0	0.0	0.0
Creatinine: Grade 1	0.0	0.0	0.0	0.0
Creatinine: Grade 2	0.0	0.0	7.1	0.0
Creatinine: Grade 3	12.5	0.0	0.0	3.3
Creatinine: Grade 4	0.0	0.0	0.0	0.0
Creatinine: Grade 3+4	12.5	0.0	0.0	3.3
Creatinine clearance: Grade 1	0.0	0.0	0.0	0.0
Creatinine clearance: Grade 2	0.0	0.0	0.0	0.0
Creatinine clearance: Grade 3	0.0	0.0	0.0	0.0
Creatinine clearance: Grade 4	0.0	0.0	0.0	0.0
Creatinine clearance: Grade 3+4	0.0	0.0	0.0	0.0
Albumin: Grade 1	25.0	0.0	0.0	0.0
Albumin: Grade 2	0.0	0.0	0.0	0.0
Albumin: Grade 3	0.0	0.0	0.0	0.0
Albumin: Grade 4	0.0	0.0	0.0	0.0
Albumin: Grade 3+4	0.0	0.0	0.0	0.0
Creatine kinase: Grade 1	0.0	0.0	7.1	0.0
Creatine kinase: Grade 2	0.0	0.0	0.0	0.0
Creatine kinase: Grade 3	0.0	0.0	0.0	0.0
Creatine kinase: Grade 4	0.0	0.0	0.0	0.0
Creatine kinase: Grade 3+4	0.0	0.0	0.0	0.0

End point values	Cohort 9 (12 Weeks GT1 F4)	Cohort 11 (12 Weeks GT2 F4)		

Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	4		
Units: Percentage of subjects				
number (not applicable)				
Calcium: Grade 1	0.0	0.0		
Calcium: Grade 2	0.0	0.0		
Calcium: Grade 3	0.0	0.0		
Calcium: Grade 4	0.0	0.0		
Calcium: Grade 3+4	0.0	0.0		
Phosphate: Grade 1	0.0	0.0		
Phosphate: Grade 2	6.7	0.0		
Phosphate: Grade 3	0.0	0.0		
Phosphate: Grade 4	0.0	0.0		
Phosphate: Grade 3+4	0.0	0.0		
Potassium: Grade 1	0.0	0.0		
Potassium: Grade 2	0.0	0.0		
Potassium: Grade 3	0.0	0.0		
Potassium: Grade 4	0.0	0.0		
Potassium: Grade 3+4	0.0	0.0		
Sodium: Grade 1	20.0	0.0		
Sodium: Grade 2	0.0	0.0		
Sodium: Grade 3	0.0	0.0		
Sodium: Grade 4	0.0	0.0		
Sodium: Grade 3+4	0.0	0.0		
Bicarbonate: Grade 1	0.0	0.0		
Bicarbonate: Grade 2	0.0	0.0		
Bicarbonate: Grade 3	0.0	0.0		
Bicarbonate: Grade 4	0.0	0.0		
Bicarbonate: Grade 3+4	0.0	0.0		
Alanine aminotransferase: Grade 1	0.0	0.0		
Alanine aminotransferase: Grade 2	0.0	0.0		
Alanine aminotransferase: Grade 3	0.0	0.0		
Alanine aminotransferase: Grade 4	0.0	0.0		
Alanine aminotransferase: Grade 3+4	0.0	0.0		
Alkaline phosphatase: Grade 1	0.0	0.0		
Alkaline phosphatase: Grade 2	0.0	0.0		
Alkaline phosphatase: Grade 3	0.0	0.0		
Alkaline phosphatase: Grade 4	0.0	0.0		
Alkaline phosphatase: Grade 3+4	0.0	0.0		
Aspartate aminotransferase: Grade: 1	0.0	25.0		
Aspartate aminotransferase: Grade: 2	0.0	0.0		
Aspartate aminotransferase: Grade: 3	6.7	0.0		
Aspartate aminotransferase: Grade: 4	0.0	0.0		
Aspartate aminotransferase: Grade: 3+4	6.7	0.0		
Bilirubin: Grade 1	0.0	0.0		
Bilirubin: Grade 2	0.0	25.0		
Bilirubin: Grade 3	0.0	0.0		
Bilirubin: Grade 4	0.0	0.0		
Bilirubin: Grade 3+4	0.0	0.0		
Direct bilirubin: Grade 1	0.0	0.0		
Direct bilirubin: Grade 2	0.0	0.0		

Direct bilirubin: Grade 3	6.7	0.0		
Direct bilirubin: Grade 4	0.0	0.0		
Direct bilirubin: Grade 3+4	6.7	0.0		
Glucose: Grade 1	13.3	0.0		
Glucose: Grade 2	13.3	25.0		
Glucose: Grade 3	0.0	0.0		
Glucose: Grade 4	0.0	0.0		
Glucose: Grade 3+4	0.0	0.0		
Cholesterol: Grade 1	20.0	50.0		
Cholesterol: Grade 2	6.7	0.0		
Cholesterol: Grade 3	0.0	0.0		
Cholesterol: Grade 4	0.0	0.0		
Cholesterol: Grade 3+4	0.0	0.0		
Triglycerides: Grade 1	33.3	25.0		
Triglycerides: Grade 2	0.0	0.0		
Triglycerides: Grade 3	0.0	0.0		
Triglycerides: Grade 4	0.0	0.0		
Triglycerides: Grade 3+4	0.0	0.0		
Urate: Grade 1	26.7	0.0		
Urate: Grade 2	0.0	0.0		
Urate: Grade 3	0.0	0.0		
Urate: Grade 4	0.0	0.0		
Urate: Grade 3+4	0.0	0.0		
Triacylglycerol lipase: Grade 1	0.0	0.0		
Triacylglycerol lipase: Grade 2	0.0	0.0		
Triacylglycerol lipase: Grade 3	0.0	0.0		
Triacylglycerol lipase: Grade 4	0.0	0.0		
Triacylglycerol lipase: Grade 3+4	0.0	0.0		
Creatinine: Grade 1	0.0	0.0		
Creatinine: Grade 2	0.0	0.0		
Creatinine: Grade 3	0.0	0.0		
Creatinine: Grade 4	0.0	0.0		
Creatinine: Grade 3+4	0.0	0.0		
Creatinine clearance: Grade 1	0.0	0.0		
Creatinine clearance: Grade 2	0.0	0.0		
Creatinine clearance: Grade 3	0.0	0.0		
Creatinine clearance: Grade 4	0.0	0.0		
Creatinine clearance: Grade 3+4	0.0	0.0		
Albumin: Grade 1	0.0	0.0		
Albumin: Grade 2	0.0	0.0		
Albumin: Grade 3	0.0	0.0		
Albumin: Grade 4	0.0	0.0		
Albumin: Grade 3+4	0.0	0.0		
Creatine kinase: Grade 1	0.0	0.0		
Creatine kinase: Grade 2	6.7	0.0		
Creatine kinase: Grade 3	0.0	0.0		
Creatine kinase: Grade 4	0.0	0.0		
Creatine kinase: Grade 3+4	0.0	0.0		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects by Treatment Emergent Toxicity Grade - Prothrombin International Normalized Ratio (INR)

End point title	Percentage of Subjects by Treatment Emergent Toxicity Grade - Prothrombin International Normalized Ratio (INR)[8]

End point description:

Percentage of subjects by treatment-emergent toxicity grade for coagulation parameter (Prothrombin International Normalized Ratio) were reported. Toxicity grades were defined as Grade 1: Mild; Grade 2: Moderate; Grade 3: Severe and Grade 4: potentially life-threatening. Toxicity is treatment-emergent if it is worse than the baseline or if the baseline is missing. Safety set included all subjects enrolled in the study who had received at least 1 dose of any study drug, whether prematurely withdrawn from the study or not.

End point type	Primary

End point timeframe:

Up to 43 weeks

Notes:

[8] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Cohort 1 (8 Weeks Genotype [GT1])	Cohort 1b + Cohort 4 (8 Weeks GT1)	Cohort 2 (8 Weeks GT1)	Cohort 3 (Subjects with Cirrhosis)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	25	20	20
Units: Percentage of subject				
number (not applicable)				
Prothrombin INR: Grade 1	0.0	0.0	0.0	0.0
Prothrombin INR: Grade 2	0.0	0.0	0.0	0.0
Prothrombin INR: Grade 3	0.0	0.0	0.0	0.0
Prothrombin INR: Grade 4	0.0	0.0	0.0	0.0
Prothrombin INR: Grade 3+4	0.0	4.0	0.0	0.0

End point values	Cohort 4 (12 Weeks GT1)	Cohort 5a (8 Weeks GT3)	Cohort 5b (12 Weeks GT3)	Cohort 6,7,8 (8 Weeks GT1 F4)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	5	14	30
Units: Percentage of subject				
number (not applicable)				
Prothrombin INR: Grade 1	0.0	0.0	0.0	0.0
Prothrombin INR: Grade 2	0.0	0.0	0.0	0.0
Prothrombin INR: Grade 3	0.0	0.0	0.0	0.0
Prothrombin INR: Grade 4	0.0	0.0	0.0	0.0
Prothrombin INR: Grade 3+4	0.0	0.0	0.0	0.0

End point values	Cohort 9 (12	Cohort 11 (12		

	Weeks GT1 F4)	Weeks GT2 F4)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	4		
Units: Percentage of subject				
number (not applicable)				
Prothrombin INR: Grade 1	0.0	0.0		
Prothrombin INR: Grade 2	0.0	0.0		
Prothrombin INR: Grade 3	0.0	0.0		
Prothrombin INR: Grade 4	0.0	0.0		
Prothrombin INR: Grade 3+4	0.0	0.0		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subject by Treatment-Emergent Toxicity Grade - Urinalysis Parameter - Protien

End point title	Percentage of Subject by Treatment-Emergent Toxicity Grade - Urinalysis Parameter - Protien[9]

End point description:

Percentage of subjects by treatment-emergent toxicity grade (Grade 1, 2, 3, 4, 3+4) for urinalysis parameter (protein) was reported. Toxicity grades were defined as Grade 1: Mild; Grade 2: Moderate; Grade 3: Severe and Grade 4: potentially life-threatening. Toxicity is treatment-emergent if it is worse than the baseline or if the baseline is missing. Safety set included all subject enrolled in the study who had received at least 1 dose of any study drug, whether prematurely withdrawn from the study or not.

End point type	Primary

End point timeframe:

Up to 43 weeks

Notes:

[9] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Cohort 1 (8 Weeks Genotype [GT1])	Cohort 1b + Cohort 4 (8 Weeks GT1)	Cohort 2 (8 Weeks GT1)	Cohort 3 (Subjects with Cirrhosis)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	25	20	20
Units: Percentage of subject				
number (not applicable)				
Protein: Grade 1	0.0	4.0	0.0	0.0
Protein: Grade 2	0.0	0.0	0.0	0.0
Protein: Grade 3	0.0	0.0	0.0	0.0
Protein: Grade 4	0.0	0.0	0.0	0.0
Protein: Grade 3+4	0.0	0.0	0.0	0.0

End point values	Cohort 4 (12 Weeks GT1)	Cohort 5a (8 Weeks GT3)	Cohort 5b (12 Weeks GT3)	Cohort 6,7,8 (8 Weeks GT1 F4)

Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	5	14	30
Units: Percentage of subject				
number (not applicable)				
Protein: Grade 1	0.0	0.0	7.1	3.3
Protein: Grade 2	0.0	0.0	0.0	0.0
Protein: Grade 3	0.0	0.0	0.0	3.3
Protein: Grade 4	0.0	0.0	0.0	0.0
Protein: Grade 3+4	0.0	0.0	0.0	3.3

End point values	Cohort 9 (12 Weeks GT1 F4)	Cohort 11 (12 Weeks GT2 F4)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	4		
Units: Percentage of subject				
number (not applicable)				
Protein: Grade 1	26.7	50.0		
Protein: Grade 2	13.3	0.0		
Protein: Grade 3	0.0	25.0		
Protein: Grade 4	0.0	0.0		
Protein: Grade 3+4	0.0	25.0		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Worst Treatment-Emergent Abnormalities of Electrocardiogram (ECG) Parameters

End point title	Percentage of Subjects with Worst Treatment-Emergent Abnormalities of Electrocardiogram (ECG) Parameters[10]

End point description:

Percentage of subjects with worst treatment-emergent abnormalities of ECG parameters (Fridericia Corrected QT interval [QTcF], Bazett Corrected QT interval [QTcB], Heart rate, QRS and PR, was reported. For QTcF abnormality was defined as 30 milliseconds (ms) less than or equal to (<=) QTcF increase from baseline <= 60 ms; for QTcB abnormality was defined as 30 ms <= QTcB increase from baseline <= 60 ms; for heart rate - abnormal low: <= 50 beats per minute (bpm) and abnormal high: >= 120 bpm; for QRS – abnormal high: >120 ms; for PR - abnormally low: PR < 120 ms; abnormally high - 200 ms < PR <= 240 ms and 240 ms < PR <= 300 ms. Safety set included all subjects enrolled into the study who had received at least 1 dose of any study drug, whether prematurely withdrawn from the study or not.

End point type	Primary

End point timeframe:

Up to 43 weeks

Notes:

[10] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Cohort 1 (8 Weeks Genotype [GT1])	Cohort 1b + Cohort 4 (8 Weeks GT1)	Cohort 2 (8 Weeks GT1)	Cohort 3 (Subjects with Cirrhosis)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	25	20	20
Units: Percentage of subject				
number (not applicable)				
QTcF: Abnormal	5.0	0.0	5.0	0.0
QTcB: Abnormal	5.0	8.0	10.0	0.0
Heart rate: Abnormal low	25.0	16.0	10.0	15.0
Heart rate: Abnormal high	0.0	0.0	0.0	0.0
QRS: Abnormal high	0.0	0.0	0.0	0.0
PR: Abnormally low (PR<120 ms)	0.0	0.0	0.0	0.0
PR: Abnormally high (200 ms<PR<= 240 ms)	5.0	8.0	15.0	10.0
PR: Abnormal high (240 ms<PR<=300 ms)	10.0	0.0	0.0	0.0

End point values	Cohort 4 (12 Weeks GT1)	Cohort 5a (8 Weeks GT3)	Cohort 5b (12 Weeks GT3)	Cohort 6,7,8 (8 Weeks GT1 F4)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	5	14	30
Units: Percentage of subject				
number (not applicable)				
QTcF: Abnormal	0.0	0.0	7.1	3.3
QTcB: Abnormal	0.0	0.0	28.6	3.3
Heart rate: Abnormal low	25.0	20.0	14.3	13.3
Heart rate: Abnormal high	12.5	0.0	0.0	0.0
QRS: Abnormal high	0.0	0.0	0.0	0.0
PR: Abnormally low (PR<120 ms)	0.0	0.0	7.1	3.3
PR: Abnormally high (200 ms<PR<= 240 ms)	0.0	0.0	0.0	6.7
PR: Abnormal high (240 ms<PR<=300 ms)	0.0	0.0	7.1	0.0

End point values	Cohort 9 (12 Weeks GT1 F4)	Cohort 11 (12 Weeks GT2 F4)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	4		
Units: Percentage of subject				
number (not applicable)				
QTcF: Abnormal	0.0	0.0		
QTcB: Abnormal	6.7	0.0		
Heart rate: Abnormal low	0.0	25.0		
Heart rate: Abnormal high	0.0	0.0		
QRS: Abnormal high	0.0	0.0		
PR: Abnormally low (PR<120 ms)	0.0	0.0		
PR: Abnormally high (200 ms<PR<= 240 ms)	13.3	0.0		

PR: Abnormal high (240 ms<PR<=300 ms)	0.0	0.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Sustained Virologic Response (SVR) at week 4, 12 and 24 After end of Treatment

End point title	Percentage of Subjects with Sustained Virologic Response (SVR) at week 4, 12 and 24 After end of Treatment

End point description:

Subjects were considered to have achieved SVR if the Hepatitis C virus (HCV) Ribonucleic acid (RNA) less than (<) Lower limit of quantification (LLOQ) (<15 international unit per milliliter [IU/mL]) detectable or undetectable at Week 4, 12 and 24 after the actual end of study drug treatment. Safety set included all subjects enrolled in the study who had received at least 1 dose of any study drug, whether prematurely withdrawn from the study or not. Here '99999' indicates that the upper and lower limit of CI was not estimable as no subject achieved SVR at specified timepoint.

End point type	Secondary

End point timeframe:

At Week 4, 12 and Week 24 after end of treatment (Cohort 3: 6 weeks; Cohort 1, Cohort 1b+ Cohort 4, Cohort 2, Cohort 5a, and Cohort 6, 7, 8: 8 weeks; Cohort 4, Cohort 5b, Cohort 9 and Cohort 11: 12 weeks)

End point values	Cohort 1 (8 Weeks Genotype [GT1])	Cohort 1b + Cohort 4 (8 Weeks GT1)	Cohort 2 (8 Weeks GT1)	Cohort 3 (Subjects with Cirrhosis)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	25	20	20
Units: Percentage of Subjects				
number (confidence interval 95%)				
4 weeks after end of treatment	100 (83.2 to 100)	96.0 (79.6 to 99.9)	100 (83.2 to 100)	100 (83.2 to 100)
12 weeks after end of treatment	100 (83.2 to 100)	84.0 (63.9 to 95.5)	100 (83.2 to 100)	100 (83.2 to 100)
24 weeks after end of treatment	100 (83.2 to 100)	84.0 (63.9 to 95.5)	100 (83.2 to 100)	100 (83.2 to 100)

End point values	Cohort 4 (12 Weeks GT1)	Cohort 5a (8 Weeks GT3)	Cohort 5b (12 Weeks GT3)	Cohort 6,7,8 (8 Weeks GT1 F4)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	5	14	30
Units: Percentage of Subjects				
number (confidence interval 95%)				
4 weeks after end of treatment	87.5 (47.3 to 99.7)	0 (-99999 to 99999)	71.4 (41.9 to 91.6)	100 (88.4 to 100)

12 weeks after end of treatment	87.5 (47.3 to 99.7)	0 (-99999 to 99999)	71.4 (41.9 to 91.6)	96.7 (82.8 to 99.9)
24 weeks after end of treatment	87.5 (47.3 to 99.7)	0 (-99999 to 99999)	71.4 (41.9 to 91.6)	96.7 (82.3 to 99.9)

End point values	Cohort 9 (12 Weeks GT1 F4)	Cohort 11 (12 Weeks GT2 F4)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	4		
Units: Percentage of Subjects				
number (confidence interval 95%)				
4 weeks after end of treatment	93.3 (68.1 to 99.8)	100 (39.8 to 100)		
12 weeks after end of treatment	93.3 (68.1 to 99.8)	100 (39.8 to 100)		
24 weeks after end of treatment	93.3 (68.1 to 99.8)	100 (39.8 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum Observed Plasma Concentration (Cmin) of AL-335 and its metabolites (ALS-022399 and ALS-022227)

End point title	Minimum Observed Plasma Concentration (Cmin) of AL-335 and its metabolites (ALS-022399 and ALS-022227)

End point description:

Cmin is the minimum observed plasma concentration of AL-335 and its metabolites (ALS-022399, and ALS-022227). For Pharmacokinetic (PK) analyses, cohorts were grouped by treatment dosage (not the duration of treatment) for subjects without cirrhosis (Cohort 1; Cohort 1b+4; Cohort 2+3+5) and for subjects with cirrhosis (Cohort 6; Cohort 7+8+9+11). PK set: all safety set subjects except those who violated inclusion/exclusion criteria, deviated from protocol, or if data were unavailable/incomplete which influenced PK analysis.

End point type	Secondary

End point timeframe:

Predose, 0.5, 1, 2, 3, 4, 6, 9, and 24 hours postdose (Week 2), 2-4 hours postdose (Weeks 3 and 6), 6-8 hours postdose (Weeks 4 and 8)

End point values	Cohort 1	Cohort 1b + Cohort 4	Cohort 2 + Cohort 3 + Cohort 5	Cohort 6
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	11	16	6
Units: nanogram per milliliter (ng/ml)				
arithmetic mean (standard deviation)				
AL-335	0.0 (± 0.0)	0.0 (± 0.0)	0.0 (± 0.0)	0.0 (± 0.0)
ALS-022399	0.000 (± 0.000)	0.000 (± 0.000)	0.308 (± 1.233)	0.000 (± 0.000)

ALS-022227	35.73 (± 13.61)	35.80 (± 11.15)	57.25 (± 31.63)	68.30 (± 38.33)

End point values	Cohort 7 + Cohort 8 + Cohort 9 + Cohort 11			
Subject group type	Subject analysis set			
Number of subjects analysed	27			
Units: nanogram per milliliter (ng/ml)				
arithmetic mean (standard deviation)				
AL-335	0.0 (± 0.0)			
ALS-022399	0.280 (± 0.814)			
ALS-022227	64.96 (± 28.63)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Plasma Concentration (Cmax) of AL-335 and its Metabolite (ALS-022399 and ALS-022227)

End point title	Maximum Observed Plasma Concentration (Cmax) of AL-335 and its Metabolite (ALS-022399 and ALS-022227)

End point description:

Cmax is the maximum observed plasma concentration of AL-335 and its metabolite (ALS-022227). For PK analyses, cohorts were grouped by treatment dosage (not the duration of treatment) for subjects without cirrhosis (Cohort 1; Cohort 1b+4; Cohort 2+3+5) and for subjects with cirrhosis (Cohort 6; Cohort 7+8+9+11). PK set: all safety set subjects except those who violated inclusion/exclusion criteria, deviated from protocol, or if data were unavailable/incomplete which influenced PK analysis.

End point type	Secondary

End point timeframe:

Predose, 0.5, 1, 2, 3, 4, 6, 9, and 24 hours postdose (Week 2), 2-4 hours postdose (Weeks 3 and 6), 6-8 hours postdose (Weeks 4 and 8)

End point values	Cohort 1	Cohort 1b + Cohort 4	Cohort 2 + Cohort 3 + Cohort 5	Cohort 6
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	11	16	6
Units: ng/mL				
arithmetic mean (standard deviation)				
AL-335	414.79 (± 317.93)	547.36 (± 226.06)	563.04 (± 423.53)	529.17 (± 265.17)
ALS-022399	103.57 (± 52.25)	148.89 (± 48.77)	174.89 (± 87.05)	158.80 (± 55.97)
ALS-022227	364.4 (± 129.1)	392.6 (± 144.2)	658.0 (± 275.1)	643.2 (± 318.4)

End point values	Cohort 7 + Cohort 8 + Cohort 9 + Cohort 11			
Subject group type	Subject analysis set			
Number of subjects analysed	27			
Units: ng/mL				
arithmetic mean (standard deviation)				
AL-335	677.59 (± 554.83)			
ALS-022399	186.28 (± 113.18)			
ALS-022227	619.7 (± 224.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Trough Plasma Concentration (Ctrough) for AL-335 and its metabolites (ALS-022399 and ALS-022227)

End point title	Trough Plasma Concentration (Ctrough) for AL-335 and its metabolites (ALS-022399 and ALS-022227)

End point description:

Ctrough is the trough plasma concentration for AL-335, ALS-022399, and ALS-022227. For PK analyses, cohorts were grouped by treatment dosage (not the duration of treatment) for subjects without cirrhosis (Cohort 1; Cohort 1b+4; Cohort 2+3+5) and for subjects with cirrhosis (Cohort 6; Cohort 7+8+9+11). PK set: all safety set participants except those who violated inclusion/exclusion criteria, deviated from protocol, or if data were unavailable/incomplete which influenced PK analysis. Here '99999' indicates that the data was not evaluated as there were no subjects analyzed at specified timepoint. Here 'n' signifies the number of subjects analyzed at this time point.

End point type	Secondary

End point timeframe:

Predose, 0.5, 1, 2, 3, 4, 6, 9, and 24 hours postdose (Week 2), 2-4 hours postdose (Weeks 3 and 6), 6-8 hours postdose (Weeks 4 and 8)

End point values	Cohort 1	Cohort 1b + Cohort 4	Cohort 2 + Cohort 3 + Cohort 5	Cohort 6
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	11	16	6
Units: ng/ml				
arithmetic mean (standard deviation)				
AL-335 (n=0, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
ALS-022399 (n=0, 0, 6, 2, 8)	99999 (± 99999)	99999 (± 99999)	4.640 (± 4.018)	4.570 (± 2.899)
ALS-022227 (n=11, 11, 6, 27)	42.74 (± 19.26)	36.77 (± 10.42)	61.82 (± 35.47)	86.20 (± 56.31)

End point values	Cohort 7 + Cohort 8 + Cohort 9 + Cohort 11			
Subject group type	Subject analysis set			
Number of subjects analysed	27			
Units: ng/ml				
arithmetic mean (standard deviation)				
AL-335 (n=0, 0, 0, 0)	99999 (± 99999)			
ALS-022399 (n=0, 0, 6, 2, 8)	4.400 (± 2.560)			
ALS-022227 (n=11, 11, 6, 27)	73.85 (± 35.15)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach the Maximum Plasma Concentration (Tmax) of AL-335 and its metabolites (ALS-022399 and ALS-022227)

End point title	Time to Reach the Maximum Plasma Concentration (Tmax) of AL-335 and its metabolites (ALS-022399 and ALS-022227)

End point description:

Tmax is the time to reach the maximum plasma concentration of AL-335, ALS-022399, and ALS-022227. For PK analyses, cohorts were grouped by treatment dosage (not the duration of treatment) for subjects without cirrhosis (Cohort 1; Cohort 1b+4; Cohort 2+3+5) and for subjects with cirrhosis (Cohort 6; Cohort 7+8+9+11). PK set: all safety set subjects except those who violated inclusion/exclusion criteria, deviated from protocol, or if data were unavailable/incomplete which influenced PK analysis.

End point type	Secondary

End point timeframe:

Predose, 0.5, 1, 2, 3, 4, 6, 9, and 24 hours postdose (Week 2), 2-4 hours postdose (Weeks 3 and 6), 6-8 hours postdose (Weeks 4 and 8)

End point values	Cohort 1	Cohort 1b + Cohort 4	Cohort 2 + Cohort 3 + Cohort 5	Cohort 6
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	11	16	6
Units: Hours				
median (full range (min-max))				
AL-335	2.000 (0.50 to 4.00)	2.000 (1.00 to 4.00)	1.500 (1.00 to 4.00)	1.000 (1.00 to 2.00)
ALS-022399	4.000 (1.00 to 6.00)	3.000 (2.00 to 4.00)	3.000 (1.00 to 4.00)	2.000 (1.00 to 4.00)
ALS-022227	4.000 (2.00 to 4.60)	4.000 (3.00 to 6.00)	3.500 (2.00 to 6.00)	3.500 (2.00 to 6.00)

End point values	Cohort 7 + Cohort 8 + Cohort 9 + Cohort 11			
Subject group type	Subject analysis set			
Number of subjects analysed	27			
Units: Hours				
median (full range (min-max))				
AL-335	2.000 (0.50 to 4.00)			
ALS-022399	3.000 (2.00 to 6.00)			
ALS-022227	4.000 (2.00 to 6.00)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-Time Curve From Time 0 to Last Measurable Plasma Concentration (AUC [0-last]) of AL-335 and its metabolites (ALS-022399 and ALS-022227)

End point title	Area Under the Plasma Concentration-Time Curve From Time 0 to Last Measurable Plasma Concentration (AUC [0-last]) of AL-335 and its metabolites (ALS-022399 and ALS-022227)

End point description:

AUC(0-last) is the area under the plasma concentration-time curve from time 0 to last measurable plasma concentration of AL-335 and its metabolites (ALS-022399, and ALS-022227). For PK analyses, cohorts were grouped by treatment dosage (not the duration of treatment) for subjects without cirrhosis (Cohort 1; Cohort 1b+4; Cohort 2+3+5) and for subjects with cirrhosis (Cohort 6; Cohort 7+8+9+11). PK set: all safety set subjects except those who violated inclusion/exclusion criteria, deviated from protocol, or if data were unavailable/incomplete which influenced PK analysis.

End point type	Secondary

End point timeframe:

Predose, 0.5, 1, 2, 3, 4, 6, 9, and 24 hours postdose (Week 2), 2-4 hours postdose (Weeks 3 and 6), 6-8 hours postdose (Weeks 4 and 8)

End point values	Cohort 1	Cohort 1b + Cohort 4	Cohort 2 + Cohort 3 + Cohort 5	Cohort 6
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	11	16	6
Units: nanogram*hours per milliliters (ng*h/mL)				
arithmetic mean (standard deviation)				
AL-335	1049.3 (± 890.0)	1185.8 (± 502.8)	1526.3 (± 1328.9)	1178.5 (± 594.0)
ALS-022399	469.3 (± 224.0)	660.7 (± 211.5)	945.2 (± 551.1)	844.2 (± 287.9)

ALS-022227	2920.0 (± 1029.1)	3238.2 (± 972.8)	5258.1 (± 1969.4)	5218.3 (± 2011.9)

End point values	Cohort 7 + Cohort 8 + Cohort 9 + Cohort 11			
Subject group type	Subject analysis set			
Number of subjects analysed	27			
Units: nanogram*hours per milliliters (ng*h/mL)				
arithmetic mean (standard deviation)				
AL-335	1774.8 (± 1348.5)			
ALS-022399	933.3 (± 544.3)			
ALS-022227	5425.2 (± 1878.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration Time-Curve at 24 hours (AUC0-24) for AL-335 and its Metabolites (ALS-022399 and ALS-022227)

End point title	Area Under the Plasma Concentration Time-Curve at 24 hours (AUC0-24) for AL-335 and its Metabolites (ALS-022399 and ALS-022227)

End point description:

AUC(0-24) is the area under the plasma concentration-time curve from time zero to time 24 hours for AL-335, ALS-022399, and ALS-022227. For PK analyses, cohorts were grouped by treatment dosage (not the duration of treatment) for subjects without cirrhosis (Cohort 1; Cohort 1b+4; Cohort 2+3+5) and for subjects with cirrhosis (Cohort 6; Cohort 7+8+9+11). PK set: all safety set subjects except those who violated inclusion/exclusion criteria, deviated from protocol, or if data were unavailable/incomplete which influenced PK analysis.

End point type	Secondary

End point timeframe:

Predose, 0.5, 1, 2, 3, 4, 6, 9, and 24 hours postdose

End point values	Cohort 1	Cohort 1b + Cohort 4	Cohort 2 + Cohort 3 + Cohort 5	Cohort 6
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	11	16	6
Units: ng*h/mL				
arithmetic mean (standard deviation)				
AL-335	1058.0 (± 886.9)	1197.2 (± 507.7)	1532.7 (± 1329.5)	1187.3 (± 600.9)
ALS-022399	500.5 (± 230.8)	718.0 (± 240.7)	1009.7 (± 599.4)	932.7 (± 330.1)

ALS-022227	2897.0 (± 1081.8)	3238.2 (± 972.8)	5258.1 (± 1969.4)	4806.0 (± 1945.4)

End point values	Cohort 7 + Cohort 8 + Cohort 9 + Cohort 11			
Subject group type	Subject analysis set			
Number of subjects analysed	27			
Units: ng*h/mL				
arithmetic mean (standard deviation)				
AL-335	1792.2 (± 1350.9)			
ALS-022399	1044.7 (± 561.1)			
ALS-022227	5425.2 (± 1878.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Last Measurable Plasma Concentration (Clast) of AL-335 and its Metabolite (ALS-022399 and ALS-022227)

End point title	Last Measurable Plasma Concentration (Clast) of AL-335 and its Metabolite (ALS-022399 and ALS-022227)

End point description:

Clast is the last measurable plasma concentration (Clast) of AL-335, ALS-022399, and ALS-022227. For PK analyses, cohorts were grouped by treatment dosage (not the duration of treatment) for subjects without cirrhosis (Cohort 1; Cohort 1b+4; Cohort 2+3+5) and for subjects with cirrhosis (Cohort 6; Cohort 7+8+9+11). PK set: all safety set subjects except those who violated inclusion/exclusion criteria, deviated from protocol, or if data were unavailable/incomplete which influenced PK analysis.

End point type	Secondary

End point timeframe:

Predose, 0.5, 1, 2, 3, 4, 6, 9, and 24 hours postdose (Week 2), 2-4 hours postdose (Weeks 3 and 6), 6-8 hours postdose (Weeks 4 and 8)

End point values	Cohort 1	Cohort 1b + Cohort 4	Cohort 2 + Cohort 3 + Cohort 5	Cohort 6
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	11	16	6
Units: ng/ml				
arithmetic mean (standard deviation)				
AL-335	5.931 (± 4.752)	7.077 (± 4.676)	4.983 (± 3.339)	5.698 (± 5.620)
ALS-022399	5.995 (± 1.649)	10.335 (± 5.558)	14.591 (± 10.741)	14.793 (± 8.738)

ALS-022227	38.28 (± 12.20)	47.26 (± 10.68)	67.08 (± 40.66)	69.18 (± 38.01)

End point values	Cohort 7 + Cohort 8 + Cohort 9 + Cohort 11			
Subject group type	Subject analysis set			
Number of subjects analysed	27			
Units: ng/ml				
arithmetic mean (standard deviation)				
AL-335	5.811 (± 8.622)			
ALS-022399	17.520 (± 10.972)			
ALS-022227	72.14 (± 29.23)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time Corresponding to Last Measurable Plasma Concentration (Tlast) for AL-335 and its Metabolites (ALS-022399 and ALS-022227)

End point title	Time Corresponding to Last Measurable Plasma Concentration (Tlast) for AL-335 and its Metabolites (ALS-022399 and ALS-022227)

End point description:

Tlast is the time corresponding to last measurable plasma concentration for AL-335, ALS-022399 and ALS-022227. For PK analyses, cohorts were grouped by treatment dosage (not duration of treatment) for subjects without cirrhosis (Cohort 1; Cohort 1b+4; Cohort 2+3+5) and for subjects with cirrhosis (Cohort 6; Cohort 7+8+9+11). PK set: all safety set subjects except those who violated inclusion/exclusion criteria, deviated from protocol, or if data were unavailable/incomplete which influenced PK analysis.

End point type	Secondary

End point timeframe:

Predose, 0.5, 1, 2, 3, 4, 6, 9, and 24 hours postdose (Week 2), 2-4 hours postdose (Weeks 3 and 6), 6-8 hours postdose (Weeks 4 and 8)

End point values	Cohort 1	Cohort 1b + Cohort 4	Cohort 2 + Cohort 3 + Cohort 5	Cohort 6
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	11	16	6
Units: Hours				
median (full range (min-max))				
AL-335	6.000 (6.00 to 9.00)	6.000 (6.00 to 9.00)	6.000 (4.00 to 24.10)	6.025 (1.01 to 9.00)
ALS-022399	12.000 (9.00 to 12.00)	12.000 (12.00 to 12.00)	12.000 (9.00 to 24.10)	12.000 (12.00 to 12.00)

ALS-022227	24.00 (24.0 to 24.1)	24.00 (23.7 to 24.1)	24.00 (24.0 to 24.1)	24.00 (24.0 to 24.2)

End point values	Cohort 7 + Cohort 8 + Cohort 9 + Cohort 11			
Subject group type	Subject analysis set			
Number of subjects analysed	27			
Units: Hours				
median (full range (min-max))				
AL-335 ALS-022399 ALS-022227	8.670 (5.98 to 12.00) 12.000 (8.50 to 24.00) 23.90 (23.5 to 24.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Average Plasma Concentration at Steady State (Css.avg) of ALS-022227

End point title	Average Plasma Concentration at Steady State (Css.avg) of ALS-022227

End point description:

Css.avg is the average plasma concentration at the steady state of ALS-022227. For PK analyses, cohorts were grouped by treatment dosage (not the duration of treatment) for subjects without cirrhosis (Cohort 1; Cohort 1b+4; Cohort 2+3+5) and for subjects with cirrhosis (Cohort 6; Cohort 7+8+9+11). PK set: all safety set subjects except those who violated inclusion/exclusion criteria, deviated from protocol, or if data were unavailable/incomplete which influenced PK analysis.

End point type	Secondary

End point timeframe:

Predose, 0.5, 1, 2, 3, 4, 6, 9, and 24 hours postdose (Week 2), 2-4 hours postdose (Weeks 3 and 6), 6-8 hours postdose (Weeks 4 and 8)

End point values	Cohort 1	Cohort 1b + Cohort 4	Cohort 2 + Cohort 3 + Cohort 5	Cohort 6
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	11	16	6
Units: ng/ml				
arithmetic mean (standard deviation)	121.49 (± 42.81)	135.20 (± 41.16)	218.88 (± 81.80)	217.17 (± 83.26)

End point values	Cohort 7 +			

	Cohort 8 + Cohort 9 + Cohort 11			
Subject group type	Subject analysis set			
Number of subjects analysed	27			
Units: ng/ml				
arithmetic mean (standard deviation)	227.37 (± 78.46)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cmin of Simeprevir

End point title	Cmin of Simeprevir

End point description:

Cmin is the minimum measured plasma concentration of simeprevir. For PK analyses, cohorts were grouped by treatment dosage (not the duration of treatment) for subjects without cirrhosis (Cohort 1; Cohort 1b+4; Cohort 2+3+5) and for subjects with cirrhosis (Cohort 6; Cohort 7+8+9+11). PK set: all safety set subjects except those who violated inclusion/exclusion criteria, deviated from protocol, or if data were unavailable/incomplete which influenced PK analysis.

End point type	Secondary

End point timeframe:

Predose, 0.5, 1, 2, 3, 4, 6, 9, and 24 hours postdose (Week 2), 2-4 hours postdose (Weeks 3 and 6), 6-8 hours postdose (Weeks 4 and 8)

End point values	Cohort 1	Cohort 2 + Cohort 3 + Cohort 5	Cohort 6	Cohort 7 + Cohort 8 + Cohort 9 + Cohort 11
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	16	6	27
Units: ng/ml				
arithmetic mean (standard deviation)	379.75 (± 247.02)	452.65 (± 641.99)	517.00 (± 416.45)	561.19 (± 424.71)

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax of Simeprevir

End point title	Cmax of Simeprevir

End point description:

Cmax is the maximum measured plasma concentration of simeprevir. For PK analyses, cohorts were grouped by treatment dosage (not the duration of treatment) for subjects without cirrhosis (Cohort 1; Cohort 1b+4; Cohort 2+3+5) and for subjects with cirrhosis (Cohort 6; Cohort 7+8+9+11). PK set: all safety set subjects except those who violated inclusion/exclusion criteria, deviated from protocol, or if data were unavailable/incomplete which influenced PK analysis.

End point type	Secondary

End point timeframe:

Predose, 0.5, 1, 2, 3, 4, 6, 9, and 24 hours postdose (Week 2), 2-4 hours postdose (Weeks 3 and 6), 6-8 hours postdose (Weeks 4 and 8)

End point values	Cohort 1	Cohort 2 + Cohort 3 + Cohort 5	Cohort 6	Cohort 7 + Cohort 8 + Cohort 9 + Cohort 11
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	16	6	27
Units: ng/ml				
arithmetic mean (standard deviation)	1927.7 (± 1205.3)	1537.6 (± 1325.2)	1769.3 (± 881.6)	1925.1 (± 1034.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Ctrough of Simeprevir

End point title	Ctrough of Simeprevir

End point description:

Ctrough is the trough plasma concentration of Simeprevir. For PK analyses, cohorts were grouped by treatment dosage (not the duration of treatment) for subjects without cirrhosis (Cohort 1; Cohort 1b+4; Cohort 2+3+5) and for subjects with cirrhosis (Cohort 6; Cohort 7+8+9+11). PK set: all safety set subjects except those who violated inclusion/exclusion criteria, deviated from protocol, or if data were unavailable/incomplete which influenced PK analysis.

End point type	Secondary

End point timeframe:

Predose, 0.5, 1, 2, 3, 4, 6, 9, and 24 hours postdose (Week 2), 2-4 hours postdose (Weeks 3 and 6), 6-8 hours postdose (Weeks 4 and 8)

End point values	Cohort 1	Cohort 2 + Cohort 3 + Cohort 5	Cohort 6	Cohort 7 + Cohort 8 + Cohort 9 + Cohort 11
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	16	6	27
Units: ng/ml				
arithmetic mean (standard deviation)	475.42 (± 317.63)	570.64 (± 816.36)	669.00 (± 442.50)	636.88 (± 455.94)

Statistical analyses

No statistical analyses for this end point

Secondary: Tmax of Simeprevir

End point title	Tmax of Simeprevir

End point description:

Tmax is the Time to reach the maximum plasma concentration of simeprevir. For PK analyses, cohorts were grouped by treatment dosage (not duration of treatment) for subjects without cirrhosis (Cohort 1; Cohort 1b+4; Cohort 2+3+5) and for subjects with cirrhosis (Cohort 6; Cohort 7+8+9+11). PK set: all safety set subjects except those who violated inclusion/exclusion criteria, deviated from protocol, or if data were unavailable/incomplete which influenced PK analysis.

End point type	Secondary

End point timeframe:

Predose, 0.5, 1, 2, 3, 4, 6, 9, and 24 hours postdose (Week 2), 2-4 hours postdose (Weeks 3 and 6), 6-8 hours postdose (Weeks 4 and 8)

End point values	Cohort 1	Cohort 2 + Cohort 3 + Cohort 5	Cohort 6	Cohort 7 + Cohort 8 + Cohort 9 + Cohort 11
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	16	6	27
Units: Hours				
median (full range (min-max))	6.000 (4.00 to 12.00)	6.000 (4.00 to 9.00)	6.000 (4.00 to 6.05)	6.000 (3.00 to 8.50)

Statistical analyses

No statistical analyses for this end point

Secondary: AUC (0-last) of Simeprevir

End point title	AUC (0-last) of Simeprevir

End point description:

AUC (0-last) is the area under the plasma concentration-time curve from time 0 to last measurable plasma concentration of simeprevir. For PK analyses, cohorts were grouped by treatment dosage (not the duration of treatment) for subjects without cirrhosis (Cohort 1; Cohort 1b+4; Cohort 2+3+5) and for subjects with cirrhosis (Cohort 6; Cohort 7+8+9+11). PK set: all safety set subjects except those who violated inclusion/exclusion criteria, deviated from protocol, or if data were unavailable/incomplete which influenced PK analysis.

End point type	Secondary

End point timeframe:

Predose, 0.5, 1, 2, 3, 4, 6, 9, and 24 hours postdose (Week 2), 2-4 hours postdose (Weeks 3 and 6), 6-8 hours postdose (Weeks 4 and 8)

End point values	Cohort 1	Cohort 2 + Cohort 3 + Cohort 5	Cohort 6	Cohort 7 + Cohort 8 + Cohort 9 + Cohort 11
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	16	6	27
Units: ng*h/ml				
arithmetic mean (standard deviation)	25018.2 (± 15248.7)	23061.3 (± 24724.4)	25266.7 (± 15523.4)	27070.7 (± 15895.7)

Statistical analyses

No statistical analyses for this end point

Secondary: AUC (0-24) of Simeprevir

End point title	AUC (0-24) of Simeprevir

End point description:

AUC (0-24) is the area under the plasma concentration-time curve from time 0 to 24 hours of simeprevir. For PK analyses, cohorts were grouped by treatment dosage (not duration of treatment) for subjects without cirrhosis (Cohort 1; Cohort 1b+4; Cohort 2+3+5) and for subjects with cirrhosis (Cohort 6; Cohort 7+8+9+11). PK set: all safety set subjects except those who violated inclusion/exclusion criteria, deviated from protocol, or if data were unavailable/incomplete which influenced PK analysis.

End point type	Secondary

End point timeframe:

Predose, 0.5, 1, 2, 3, 4, 6, 9, and 24 hours postdose

End point values	Cohort 1	Cohort 2 + Cohort 3 + Cohort 5	Cohort 6	Cohort 7 + Cohort 8 + Cohort 9 + Cohort 11
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	16	6	27
Units: ng*h/ml				
arithmetic mean (standard deviation)	25018.2 (± 15248.7)	23061.3 (± 24724.4)	25266.7 (± 15523.4)	27070.7 (± 15895.7)

Statistical analyses

No statistical analyses for this end point

Secondary: Clast of Simeprevir

End point title	Clast of Simeprevir

End point description:

Clast is the maximum measured plasma concentration of simeprevir. For PK analyses, cohorts were grouped by treatment dosage (not duration of treatment) for subjects without cirrhosis (Cohort 1; Cohort 1b+4; Cohort 2+3+5) and for subjects with cirrhosis (Cohort 6; Cohort 7+8+9+11). PK set: all safety set subjects except those who violated inclusion/exclusion criteria, deviated from protocol, or if data were unavailable/incomplete which influenced PK analysis.

End point type	Secondary

End point timeframe:

Predose, 0.5, 1, 2, 3, 4, 6, 9, and 24 hours postdose (Week 2), 2-4 hours postdose (Weeks 3 and 6), 6-8 hours postdose (Weeks 4 and 8)

End point values	Cohort 1	Cohort 2 + Cohort 3 + Cohort 5	Cohort 6	Cohort 7 + Cohort 8 + Cohort 9 + Cohort 11
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	16	6	27
Units: ng/ml				
arithmetic mean (standard deviation)	402.55 (± 244.20)	481.76 (± 644.76)	538.67 (± 456.21)	602.60 (± 453.12)

Statistical analyses

No statistical analyses for this end point

Secondary: Tlast of Simeprevir

End point title	Tlast of Simeprevir

End point description:

Tlast is the time corresponding to last measurable plasma concentration of simeprevir. For PK analyses, cohorts were grouped by treatment dosage (not duration of treatment) for subjects without cirrhosis (Cohort 1; Cohort 1b+4; Cohort 2+3+5) and for subjects with cirrhosis (Cohort 6; Cohort 7+8+9+11). PK set: all safety set subjects except those who violated inclusion/exclusion criteria, deviated from protocol, or if data were unavailable/incomplete which influenced PK analysis.

End point type	Secondary

End point timeframe:

Predose, 0.5, 1, 2, 3, 4, 6, 9, and 24 hours postdose (Week 2), 2-4 hours postdose (Weeks 3 and 6), 6-8 hours postdose (Weeks 4 and 8)

End point values	Cohort 1	Cohort 2 + Cohort 3 + Cohort 5	Cohort 6	Cohort 7 + Cohort 8 + Cohort 9 + Cohort 11
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	16	6	27
Units: ng/ml				
median (full range (min-max))	24.00 (24.0 to 24.1)	24.00 (24.0 to 24.1)	24.00 (24.0 to 24.2)	23.90 (23.5 to 24.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Average Plasma Concentration at Steady State (Css,avg) of Simeprevir

End point title	Average Plasma Concentration at Steady State (Css,avg) of Simeprevir

End point description:

Css,avg is the average plasma concentration at steady state of simeprevir. For PK analyses, cohorts were grouped by treatment dosage (not duration of treatment) for subjects without cirrhosis (Cohort 1; Cohort 1b+4; Cohort 2+3+5) and for subjects with cirrhosis (Cohort 6; Cohort 7+8+9+11). PK set: all safety set subjects except those who violated inclusion/exclusion criteria, deviated from protocol, or if data were unavailable/incomplete which influenced PK analysis.

End point type	Secondary

End point timeframe:

Predose, 0.5, 1, 2, 3, 4, 6, 9, and 24 hours postdose (Week 2), 2-4 hours postdose (Weeks 3 and 6), 6-8 hours postdose (Weeks 4 and 8)

End point values	Cohort 1	Cohort 2 + Cohort 3 + Cohort 5	Cohort 6	Cohort 7 + Cohort 8 + Cohort 9 + Cohort 11
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	16	6	27
Units: ng/ml				
arithmetic mean (standard deviation)	1042.8 (± 0.03)	960.5 (± 1030.7)	1053.8 (± 1053.8)	1134.6 (± 666.6)

Statistical analyses

No statistical analyses for this end point

Secondary: Cmin of Odalasvir

End point title	Cmin of Odalasvir

End point description:

Cmin is the minimum observed plasma concentration of odalasvir. For PK analyses, cohorts were grouped by treatment dosage (not duration of treatment) for subjects without cirrhosis (Cohort 1; Cohort 1b+4; Cohort 2+3+5) and for subjects with cirrhosis (Cohort 6; Cohort 7+8+9+11). PK set: all safety set subjects except those who violated inclusion/exclusion criteria, deviated from protocol, or if data were unavailable/incomplete which influenced PK analysis.

End point type	Secondary

End point timeframe:

Predose, 0.5, 1, 2, 3, 4, 6, 9, and 24 hours postdose

End point values	Cohort 1	Cohort 1b + Cohort 4	Cohort 2 + Cohort 3 + Cohort 5	Cohort 6
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	11	16	6
Units: ng/ml				
arithmetic mean (standard deviation)	322.45 (± 139.21)	97.21 (± 58.62)	107.90 (± 49.46)	102.73 (± 47.08)

End point values	Cohort 7 + Cohort 8 + Cohort 9 + Cohort 11			
Subject group type	Subject analysis set			
Number of subjects analysed	27			
Units: ng/ml				
arithmetic mean (standard deviation)	131.31 (± 62.31)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax of Odalasvir

End point title	Cmax of Odalasvir

End point description:

Cmin is the maximum observed plasma concentration of odalasvir. For PK analyses, cohorts were grouped by treatment dosage (not duration of treatment) for subjects without cirrhosis (Cohort 1; Cohort 1b+4; Cohort 2+3+5) and for subjects with cirrhosis (Cohort 6; Cohort 7+8+9+11). PK set: all safety set subjects except those who violated inclusion/exclusion criteria, deviated from protocol, or if data were unavailable/incomplete which influenced PK analysis.

End point type	Secondary

End point timeframe:

Predose, 0.5, 1, 2, 3, 4, 6, 9, and 24 hours postdose

End point values	Cohort 1	Cohort 1b + Cohort 4	Cohort 2 + Cohort 3 + Cohort 5	Cohort 6
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	11	16	6
Units: ng/ml				
arithmetic mean (standard deviation)	634.27 (± 257.29)	363.36 (± 184.48)	322.46 (± 167.29)	232.85 (± 187.53)

End point values	Cohort 7 + Cohort 8 +			

	Cohort 9 + Cohort 11			
Subject group type	Subject analysis set			
Number of subjects analysed	27			
Units: ng/ml				
arithmetic mean (standard deviation)	298.67 (± 133.99)			

Statistical analyses

No statistical analyses for this end point

Secondary: Ctrough of Odalasvir

End point title	Ctrough of Odalasvir

End point description:

Ctrough is the trough plasma concentration of odalasvir. For PK analyses, cohorts were grouped by treatment dosage (not duration of treatment) for subjects without cirrhosis (Cohort 1; Cohort 1b+4; Cohort 2+3+5) and for subjects with cirrhosis (Cohort 6; Cohort 7+8+9+11). PK set: all safety set subjects except those who violated inclusion/exclusion criteria, deviated from protocol, or if data were unavailable/incomplete which influenced PK analysis.

End point type	Secondary

End point timeframe:

Predose, 0.5, 1, 2, 3, 4, 6, 9, and 24 hours postdose (Week 2), 2-4 hours postdose (Weeks 3 and 6), 6-8 hours postdose (Weeks 4 and 8)

End point values	Cohort 1	Cohort 1b + Cohort 4	Cohort 2 + Cohort 3 + Cohort 5	Cohort 6
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	11	16	6
Units: ng/ml				
arithmetic mean (standard deviation)	335.18 (± 146.14)	100.98 (± 61.90)	112.44 (± 51.53)	119.82 (± 58.87)

End point values	Cohort 7 + Cohort 8 + Cohort 9 + Cohort 11			
Subject group type	Subject analysis set			
Number of subjects analysed	27			
Units: ng/ml				
arithmetic mean (standard deviation)	141.56 (± 64.81)			

Statistical analyses

No statistical analyses for this end point

Secondary: Tmax of Odalasvir

End point title	Tmax of Odalasvir

End point description:

Tmax is the time to reach the maximum plasma concentration of odalasvir. For PK analyses, cohorts were grouped by treatment dosage (not duration of treatment) for subjects without cirrhosis (Cohort 1; Cohort 1b+4; Cohort 2+3+5) and for subjects with cirrhosis (Cohort 6; Cohort 7+8+9+11). PK set: all safety set subjects except those who violated inclusion/exclusion criteria, deviated from protocol, or if data were unavailable/incomplete which influenced PK analysis.

End point type	Secondary

End point timeframe:

Predose, 0.5, 1, 2, 3, 4, 6, 9, and 24 hours postdose (Week 2), 2-4 hours postdose (Weeks 3 and 6), 6-8 hours postdose (Weeks 4 and 8)

End point values	Cohort 1	Cohort 1b + Cohort 4	Cohort 2 + Cohort 3 + Cohort 5	Cohort 6
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	11	16	6
Units: Hours				
median (full range (min-max))	6.000 (4.00 to 12.00)	6.000 (4.00 to 12.00)	6.000 (3.00 to 9.00)	4.500 (0.00 to 9.00)

End point values	Cohort 7 + Cohort 8 + Cohort 9 + Cohort 11			
Subject group type	Subject analysis set			
Number of subjects analysed	27			
Units: Hours				
median (full range (min-max))	6.000 (3.98 to 9.00)			

Statistical analyses

No statistical analyses for this end point

Secondary: AUC (0-last) of Odalasvir

End point title	AUC (0-last) of Odalasvir

End point description:

AUC(0-last) is the area under the plasma concentration-time curve from time 0 to last measurable plasma concentration of odalasvir. For PK analyses, cohorts were grouped by treatment dosage (not duration of treatment) for subjects without cirrhosis (Cohort 1; Cohort 1b+4; Cohort 2+3+5) and for subjects with cirrhosis (Cohort 6; Cohort 7+8+9+11). PK set: all safety set subjects except those who violated inclusion/exclusion criteria, deviated from protocol, or if data were unavailable/incomplete which influenced PK analysis.

End point type	Secondary

End point timeframe:

Predose, 0.5, 1, 2, 3, 4, 6, 9, and 24 hours postdose (Week 2), 2-4 hours postdose (Weeks 3 and 6), 6-8 hours postdose (Weeks 4 and 8)

End point values	Cohort 1	Cohort 1b + Cohort 4	Cohort 2 + Cohort 3 + Cohort 5	Cohort 6
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	11	16	6
Units: ng*h/ml				
arithmetic mean (standard deviation)	11805.5 (± 4902.6)	8635.5 (± 4656.7)	8648.1 (± 4161.1)	7050.0 (± 4001.4)

End point values	Cohort 7 + Cohort 8 + Cohort 9 + Cohort 11			
Subject group type	Subject analysis set			
Number of subjects analysed	27			
Units: ng*h/ml				
arithmetic mean (standard deviation)	8422.2 (± 3617.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: AUC (0-24) for Odalasvir

End point title	AUC (0-24) for Odalasvir

End point description:

AUC(0-24) is the area under the plasma concentration-time curve from time zero to time 24 hours for odalasvir. For PK analyses, cohorts were grouped by treatment dosage (not duration of treatment) for subjects without cirrhosis (Cohort 1; Cohort 1b+4; Cohort 2+3+5) and for subjects with cirrhosis (Cohort 6; Cohort 7+8+9+11). PK set: all safety set subjects except those who violated inclusion/exclusion criteria, deviated from protocol, or if data were unavailable/incomplete which influenced PK analysis.

End point type	Secondary

End point timeframe:

Predose, 0.5, 1, 2, 3, 4, 6, 9, and 24 hours postdose (Week 2), 2-4 hours postdose (Weeks 3 and 6), 6-8 hours postdose (Weeks 4 and 8)

End point values	Cohort 1	Cohort 1b + Cohort 4	Cohort 2 + Cohort 3 + Cohort 5	Cohort 6
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	11	16	6
Units: ng*h/mL				
arithmetic mean (standard deviation)	11805.5 (± 4902.6)	5530.0 (± 2930.3)	5393.8 (± 2695.4)	4048.3 (± 2727.8)

End point values	Cohort 7 + Cohort 8 + Cohort 9 + Cohort 11			
Subject group type	Subject analysis set			
Number of subjects analysed	27			
Units: ng*h/mL				
arithmetic mean (standard deviation)	4924.1 (± 2122.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Clast of Odalasvir

End point title	Clast of Odalasvir

End point description:

Clast is the last measurable plasma concentration (Clast) of odalasvir. For PK analyses, cohorts were grouped by treatment dosage (not duration of treatment) for subjects without cirrhosis (Cohort 1; Cohort 1b+4; Cohort 2+3+5) and for subjects with cirrhosis (Cohort 6; Cohort 7+8+9+11). PK set: all safety set subjects except those who violated inclusion/exclusion criteria, deviated from protocol, or if data were unavailable/incomplete which influenced PK analysis.

End point type	Secondary

End point timeframe:

Predose, 0.5, 1, 2, 3, 4, 6, 9, and 24 hours postdose (Week 2), 2-4 hours postdose (Weeks 3 and 6), 6-8 hours postdose (Weeks 4 and 8)

End point values	Cohort 1	Cohort 1b + Cohort 4	Cohort 2 + Cohort 3 + Cohort 5	Cohort 6
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	11	16	6
Units: ng/ml				
arithmetic mean (standard deviation)	384.09 (± 172.29)	162.65 (± 87.39)	163.54 (± 78.10)	131.92 (± 74.01)

End point values	Cohort 7 + Cohort 8 + Cohort 9 + Cohort 11			
Subject group type	Subject analysis set			
Number of subjects analysed	27			
Units: ng/ml				
arithmetic mean (standard deviation)	152.47 (± 66.50)			

Statistical analyses

No statistical analyses for this end point

Secondary: Tlast of Odalasvir

End point title	Tlast of Odalasvir

End point description:

Tlast is the time corresponding to last measurable plasma concentration of odalasvir. For PK analyses, cohorts were grouped by treatment dosage (not duration of treatment) for subjects without cirrhosis (Cohort 1; Cohort 1b+4; Cohort 2+3+5) and for subjects with cirrhosis (Cohort 6; Cohort 7+8+9+11). PK set: all safety set subjects except those who violated inclusion/exclusion criteria, deviated from protocol, or if data were unavailable/incomplete which influenced PK analysis.

End point type	Secondary

End point timeframe:

Predose, 0.5, 1, 2, 3, 4, 6, 9, and 24 hours postdose (Week 2), 2-4 hours postdose (Weeks 3 and 6), 6-8 hours postdose (Weeks 4 and 8)

End point values	Cohort 1	Cohort 1b + Cohort 4	Cohort 2 + Cohort 3 + Cohort 5	Cohort 6
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	11	16	6
Units: Hours				
median (full range (min-max))	24.00 (24.0 to 24.1)	47.60 (47.5 to 47.7)	47.50 (47.4 to 47.9)	47.80 (47.4 to 48.0)

End point values	Cohort 7 + Cohort 8 + Cohort 9 + Cohort 11			
Subject group type	Subject analysis set			
Number of subjects analysed	27			
Units: Hours				
median (full range (min-max))	47.50 (47.5 to 47.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Average Plasma Concentration at Steady State (Css,avg) of Odalasvir

End point title	Average Plasma Concentration at Steady State (Css,avg) of Odalasvir

End point description:

Css,avg is average plasma concentration at steady state of odalasvir. For PK analyses, cohorts were grouped by treatment dosage (not duration of treatment) for subjects without cirrhosis (Cohort 1; Cohort 1b+4; Cohort 2+3+5) and for subjects with cirrhosis (Cohort 6; Cohort 7+8+9+11). PK set: all safety set subjects except those who violated inclusion/exclusion criteria, deviated from protocol, or if data were unavailable/incomplete which influenced PK analysis.

End point type	Secondary

End point timeframe:

Predose, 0.5, 1, 2, 3, 4, 6, 9, and 24 hours postdose (Week 2), 2-4 hours postdose (Weeks 3 and 6), 6-8 hours postdose (Weeks 4 and 8)

End point values	Cohort 1	Cohort 1b + Cohort 4	Cohort 2 + Cohort 3 + Cohort 5	Cohort 6
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	11	16	6
Units: ng/ml				
arithmetic mean (standard deviation)	491.55 (± 203.85)	181.60 (± 97.99)	181.58 (± 87.25)	147.40 (± 83.86)

End point values	Cohort 7 + Cohort 8 + Cohort 9 + Cohort 11			
Subject group type	Subject analysis set			
Number of subjects analysed	27			
Units: ng/ml				
arithmetic mean (standard deviation)	176.86 (± 75.91)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Virologic Relapse During the Follow-up Period

End point title	Percentage of Subjects with Virologic Relapse During the Follow-up Period

End point description:

Viral relapse is defined as subjects SVR12, with HCV RNA <LLOQ at the actual end of study drug treatment and confirmed HCV RNA greater than or equal to (>=) LLOQ during follow up. Safety set included all subjects enrolled in the study who had received at least 1 dose of any study drug, whether

prematurely withdrawn from the study or not.

End point type	Secondary

End point timeframe:

Follow up period (Up to Week 12 after end of treatment)

End point values	Cohort 1 (8 Weeks Genotype [GT1])	Cohort 1b + Cohort 4 (8 Weeks GT1)	Cohort 2 (8 Weeks GT1)	Cohort 3 (Subjects with Cirrhosis)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	25	20	20
Units: Percentage of subjects				
number (not applicable)	0	16.0	0	0

End point values	Cohort 4 (12 Weeks GT1)	Cohort 5a (8 Weeks GT3)	Cohort 5b (12 Weeks GT3)	Cohort 6,7,8 (8 Weeks GT1 F4)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	5	14	30
Units: Percentage of subjects				
number (not applicable)	0	100.0	14.3	3.3

End point values	Cohort 9 (12 Weeks GT1 F4)	Cohort 11 (12 Weeks GT2 F4)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	4		
Units: Percentage of subjects				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with On-treatment Failure

End point title	Percentage of Subjects with On-treatment Failure

End point description:

On-treatment failure was defined by subjects who did not achieve SVR12 and with confirmed HCV RNA >= LLOQ at the actual end of study drug treatment. Safety set included all subjects enrolled into the study who had received at least 1 dose of any study drug, whether prematurely withdrawn from the study or not.

End point type	Secondary

End point timeframe:

Up to 12 weeks

End point values	Cohort 1 (8 Weeks Genotype [GT1])	Cohort 1b + Cohort 4 (8 Weeks GT1)	Cohort 2 (8 Weeks GT1)	Cohort 3 (Subjects with Cirrhosis)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	25	20	20
Units: Percentage of subjects				
number (not applicable)	0	0	0	0

End point values	Cohort 4 (12 Weeks GT1)	Cohort 5a (8 Weeks GT3)	Cohort 5b (12 Weeks GT3)	Cohort 6,7,8 (8 Weeks GT1 F4)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	5	14	30
Units: Percentage of subjects				
number (not applicable)	12.5	0	7.1	0

End point values	Cohort 9 (12 Weeks GT1 F4)	Cohort 11 (12 Weeks GT2 F4)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	4		
Units: Percentage of subjects				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects who Acheived HCV RNA less then (<) LLOQ Undetectable

End point title	Percentage of Subjects who Acheived HCV RNA less then (<) LLOQ Undetectable

End point description:

Percentage of subjects who acheived HCV RNA less then (<) LLOQ undetectable was reported. Safety set included all subjects enrolled into the study who had received at least 1 dose of any study drug, whether prematurely withdrawn from the study or not. Here '99999' indicates that the data was not evaluated as subjects ended the treatment at the specified timepoint.

End point type	Secondary

End point timeframe:

Day 2, 3, Week 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 and End of treatment (Cohort 3: 6 weeks; Cohort 1, Cohort 1b+ Cohort 4, Cohort 2, Cohort 5a, and Cohort 6, 7, 8: 8 weeks; Cohort 4, Cohort 5b, Cohort 9 and Cohort 11: 12 weeks)

End point values	Cohort 1 (8 Weeks Genotype [GT1])	Cohort 1b + Cohort 4 (8 Weeks GT1)	Cohort 2 (8 Weeks GT1)	Cohort 3 (Subjects with Cirrhosis)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	25	20	20
Units: Percentage of subjects				
number (not applicable)				
Day 2	0	0	0	0
Day 3	0	0	0	5.0
Week 1	5.0	20.0	0	30.0
Week 2	35.0	44.0	45.0	70.0
Week 3	70.0	76.0	75.0	80.0
Week 4	80.0	92.0	90.0	85.0
Week 5	100	96.0	100	90.0
Week 6	90.0	100	85.0	90.0
Week 7	90.0	96.0	95.0	99999
Week 8	95.0	100	100	99999
Week 9	99999	99999	99999	99999
Week 10	99999	99999	99999	99999
Week 11	99999	99999	99999	99999
Week 12	99999	99999	99999	99999
End of treatment	95.0	100	100	90.0

End point values	Cohort 4 (12 Weeks GT1)	Cohort 5a (8 Weeks GT3)	Cohort 5b (12 Weeks GT3)	Cohort 6,7,8 (8 Weeks GT1 F4)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	5	14	30
Units: Percentage of subjects				
number (not applicable)				
Day 2	0	0	0	0
Day 3	0	0	0	0
Week 1	12.5	20.0	35.7	16.7
Week 2	25.0	40.0	64.3	50.0
Week 3	62.5	60.0	85.7	73.3
Week 4	87.5	60.0	92.9	80.0
Week 5	100	80.0	92.9	90.0
Week 6	100	100	92.9	96.7
Week 7	100	80.0	85.7	100
Week 8	87.5	100	85.7	100
Week 9	87.5	99999	92.9	99999
Week 10	87.5	99999	92.9	99999
Week 11	87.5	99999	92.9	99999
Week 12	100	99999	85.7	99999
End of treatment	87.5	100	85.7	100

End point values	Cohort 9 (12 Weeks GT1 F4)	Cohort 11 (12 Weeks GT2 F4)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	4		
Units: Percentage of subjects				
number (not applicable)				
Day 2	0	0		
Day 3	6.7	0		
Week 1	13.3	25.0		
Week 2	66.7	75.0		
Week 3	86.7	100		
Week 4	86.7	100		
Week 5	100	100		
Week 6	100	100		
Week 7	100	100		
Week 8	93.3	100		
Week 9	93.3	100		
Week 10	93.3	100		
Week 11	86.7	100		
Week 12	93.3	100		
End of treatment	93.3	100		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects who Achieved HCV RNA <LLOQ

End point title	Percentage of Subjects who Achieved HCV RNA <LLOQ

End point description:

Percentage of subjects who achieved HCV RNA <LLOQ was reported. Safety set included all subjects enrolled into the study who had received at least 1 dose of any study drug, whether prematurely withdrawn from the study or not. Here '99999' indicates that the data was not evaluated as subjects ended the treatment at the specified timepoint.

End point type	Secondary

End point timeframe:

Day 2, 3, Week 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 and End of treatment (Cohort 3: 6 weeks; Cohort 1, Cohort 1b+ Cohort 4, Cohort 2, Cohort 5a, and Cohort 6, 7, 8: 8 weeks; Cohort 4, Cohort 5b, Cohort 9 and Cohort 11: 12 weeks)

End point values	Cohort 1 (8 Weeks Genotype [GT1])	Cohort 1b + Cohort 4 (8 Weeks GT1)	Cohort 2 (8 Weeks GT1)	Cohort 3 (Subjects with Cirrhosis)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	25	20	20
Units: Percentage of subjects				
number (not applicable)				
Day 2	0	0	0	0
Day 3	0	0	0	0
Week 1	0	8.0	0	10.0
Week 2	20.0	20.0	15.0	40.0
Week 3	40.0	40.0	45.0	65.0
Week 4	55.0	52.0	60.0	80.0
Week 5	75.0	96.0	85.0	85.0
Week 6	80.0	88.0	85.0	80.0
Week 7	80.0	92.0	95.0	99999
Week 8	85.0	96.0	100	99999
Week 9	99999	99999	99999	99999
Week 10	99999	99999	99999	99999
Week 11	99999	99999	99999	99999
Week 12	99999	99999	99999	99999
End of treatment	85.0	96.0	100	80.0

End point values	Cohort 4 (12 Weeks GT1)	Cohort 5a (8 Weeks GT3)	Cohort 5b (12 Weeks GT3)	Cohort 6,7,8 (8 Weeks GT1 F4)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	5	14	30
Units: Percentage of subjects				
number (not applicable)				
Day 2	0	0	0	0
Day 3	0	0	0	0
Week 1	0	0	14.3	16.7
Week 2	0	20.0	42.9	50.0
Week 3	37.5	60.0	50.0	73.3
Week 4	62.5	40.0	78.6	80.0
Week 5	75.0	80.0	85.7	90.0
Week 6	87.5	80.0	92.9	96.7
Week 7	87.5	80.0	85.7	100
Week 8	87.5	100	85.7	100
Week 9	87.5	99999	92.9	99999
Week 10	87.5	99999	92.9	99999
Week 11	87.5	99999	92.9	99999
Week 12	87.5	99999	78.6	99999
End of treatment	87.5	100	78.6	100

End point values	Cohort 9 (12 Weeks GT1 F4)	Cohort 11 (12 Weeks GT2 F4)		

Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	4		
Units: Percentage of subjects				
number (not applicable)				
Day 2	0	0		
Day 3	0	0		
Week 1	13.3	25.0		
Week 2	66.7	75.0		
Week 3	86.7	100		
Week 4	86.7	100		
Week 5	100	100		
Week 6	100	100		
Week 7	100	100		
Week 8	93.3	100		
Week 9	93.3	100		
Week 10	93.3	100		
Week 11	86.7	100		
Week 12	93.3	100		
End of treatment	93.3	100		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Achieve Undetectable HCV RNA or < LLOQ HCV RNA

End point title	Time to Achieve Undetectable HCV RNA or < LLOQ HCV RNA

End point description:

Time to achieve undetectable HCV RNA or < LLOQ HCV RNA was reported. Safety set included all subjects enrolled into the study who had received at least 1 dose of any study drug, whether prematurely withdrawn from the study or not.

End point type	Secondary

End point timeframe:

Up to Week 24 (follow up visit)

End point values	Cohort 1 (8 Weeks Genotype [GT1])	Cohort 1b + Cohort 4 (8 Weeks GT1)	Cohort 2 (8 Weeks GT1)	Cohort 3 (Subjects with Cirrhosis)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[11]	0[12]	0[13]	0[14]
Units: Hours				
median (full range (min-max))	(to)	(to)	(to)	(to)

Notes:

[11] - The endpoint was not analyzed as per the change in planned analysis

[12] - The endpoint was not analyzed as per the change in planned analysis

[13] - The endpoint was not analyzed as per the change in planned analysis

[14] - The endpoint was not analyzed as per the change in planned analysis

End point values	Cohort 4 (12 Weeks GT1)	Cohort 5a (8 Weeks GT3)	Cohort 5b (12 Weeks GT3)	Cohort 6,7,8 (8 Weeks GT1 F4)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[15]	0[16]	0[17]	0[18]
Units: Hours				
median (full range (min-max))	(to)	(to)	(to)	(to)

Notes:

[15] - The endpoint was not analyzed as per the change in planned analysis

[16] - The endpoint was not analyzed as per the change in planned analysis

[17] - The endpoint was not analyzed as per the change in planned analysis

[18] - The endpoint was not analyzed as per the change in planned analysis

End point values	Cohort 9 (12 Weeks GT1 F4)	Cohort 11 (12 Weeks GT2 F4)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[19]	0[20]		
Units: Hours				
median (full range (min-max))	(to)	(to)		

Notes:

[19] - The endpoint was not analyzed as per the change in planned analysis

[20] - The endpoint was not analyzed as per the change in planned analysis

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With HCV Nonstructural Protein NS5A, NS5B, and NS3/4A Sequence in Subjects with Virologic Failure

End point title	Number of Subjects With HCV Nonstructural Protein NS5A, NS5B, and NS3/4A Sequence in Subjects with Virologic Failure

End point description:

Sequencing of the HCV nonstructural protein 3/4A (NS3/4A), nonstructural protein 5A (NS5A) and nonstructural protein 5B (NS5B) genes was done to identify pre-existing sequence polymorphisms and characterize emerging HCV viral variants in subjects with virologic failure. Safety set included all subjects enrolled in the study who had received at least 1 dose of any study drug, whether prematurely withdrawn from the study or not. Subjects who had virologic failure were included in this outcome measure.

End point type	Secondary

End point timeframe:

Up to Week 24 (Follow up visit)

End point values	Cohort 1 (8 Weeks Genotype [GT1])	Cohort 1b + Cohort 4 (8 Weeks GT1)	Cohort 2 (8 Weeks GT1)	Cohort 3 (Subjects with Cirrhosis)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[21]	4	0[22]	0[23]
Units: Subjects				
number (not applicable)		4		

Notes:

[21] - No subject had virologic failure.

[22] - No subject had virologic failure.

[23] - No subject had virologic failure.

End point values	Cohort 4 (12 Weeks GT1)	Cohort 5a (8 Weeks GT3)	Cohort 5b (12 Weeks GT3)	Cohort 6,7,8 (8 Weeks GT1 F4)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	5	3	1
Units: Subjects				
number (not applicable)	1	0	2	1

End point values	Cohort 9 (12 Weeks GT1 F4)	Cohort 11 (12 Weeks GT2 F4)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[24]	0[25]		
Units: Subjects				
number (not applicable)				

Notes:

[24] - No subject had virologic failure.

[25] - No subject had virologic failure.

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

Up to 43 weeks

Adverse event reporting additional description:

Safety set included all subjects enrolled in the study who had received at least 1 dose of any study drug, whether prematurely withdrawn from the study or not.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	Cohort 1 (8 Weeks Genotype [GT1])

Reporting group description:

Cohort 1 (Subjects without Cirrhosis) received single dose of AL-335 400 milligrams (mg) tablets once daily (QD), odalasvir (ODV) 50 mg tablet and simeprevir 100 mg tablet QD for 8 weeks.

Reporting group title	Cohort 1b + Cohort 4 (8 Weeks GT1)

Reporting group description:

Cohort 1b (Subjects without Cirrhosis) received single dose of AL-335 800 mg tablets QD and ODV 50 mg tablets every other day (QOD) for 8 weeks; Cohort 4 (Subjects without Cirrhosis) received single dose of AL-335 800 mg tablets QD and ODV 50 mg tablets QOD for 8 weeks.

Reporting group title	Cohort 2 (8 Weeks GT1)

Reporting group description:

Cohort 2 (Subjects without Cirrhosis) received single dose of AL-335 800 mg tablets QD, ODV 50 mg tablets QOD and SMV 75 mg tablets QD for 8 weeks.

Reporting group title	Cohort 3 (Subjects with Cirrhosis)

Reporting group description:

Cohort 3 (Subjects with Cirrhosis) received single dose of AL-335 800 mg QD, ODV 50 mg QOD and SMV 75 mg QD for 8 weeks.

Reporting group title	Cohort 4 (12 Weeks GT1)

Reporting group description:

Cohort 4 (Subjects without Cirrhosis) received single dose of AL-335 800 mg tablets QD and ODV 50 mg tablets QOD for 12 weeks.

Reporting group title	Cohort 5a (8 Weeks GT3)

Reporting group description:

Cohort 5a (Subjects without Cirrhosis) received single dose of AL-335 800 mg tablets QD, ODV 50 mg tablets QOD and SMV 75 mg tablets QD for 8 weeks.

Reporting group title	Cohort 5b (12 Weeks GT3)

Reporting group description:

Cohort 5b (Subjects without Cirrhosis) received single dose of AL-335 800 mg tablets QD, ODV 50 mg tablets QOD and SMV 75 mg tablets QD for 12 weeks.

Reporting group title	Cohort 6,7,8 (8 Weeks GT1 F4)

Reporting group description:

Cohort 6 (Subjects with Cirrhosis) received single dose of AL-335 800 mg tablets QD, ODV 50 mg tablets QOD and SMV 75 mg tablets QD for 8 weeks; Cohort 7 and Cohort 8 (Subjects with Cirrhosis) received single dose of AL-335 800 mg tablets QD, ODV 25 mg tablets QOD and SMV 75 mg tablets QD for 8 weeks.

Reporting group title	Cohort 9 (12 Weeks GT1 F4)

Reporting group description:

Cohort 9 (Subjects with Cirrhosis) received single dose of AL-335 800 mg tablets QD, ODV 25 mg tablets QOD and SMV 75 mg tablets QD for 12 weeks.

Reporting group title	Cohort 11 (12 Weeks GT2 F4)

Reporting group description:

Cohort 11 (Subjects with Cirrhosis) received single dose of AL-335 800 mg tablets QD, ODV 25 mg tablets QOD and SMV 75 mg tablets QD for 12 weeks.

Serious adverse events	Cohort 1 (8 Weeks Genotype [GT1])	Cohort 1b + Cohort 4 (8 Weeks GT1)	Cohort 2 (8 Weeks GT1)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 20 (5.00%)	2 / 25 (8.00%)	0 / 20 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate Aminotransferase Increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Transitional Cell Carcinoma Urethra			
subjects affected / exposed	0 / 20 (0.00%)	1 / 25 (4.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrioventricular Block			
subjects affected / exposed	1 / 20 (5.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			

Pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 25 (4.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort 3 (Subjects with Cirrhosis)	Cohort 4 (12 Weeks GT1)	Cohort 5a (8 Weeks GT3)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate Aminotransferase Increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Transitional Cell Carcinoma Urethra			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			

Fall			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrioventricular Block			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort 5b (12 Weeks GT3)	Cohort 6,7,8 (8 Weeks GT1 F4)	Cohort 9 (12 Weeks GT1 F4)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 14 (0.00%)	1 / 30 (3.33%)	2 / 15 (13.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate Aminotransferase Increased			

subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Transitional Cell Carcinoma Urethra			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrioventricular Block			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pain			
subjects affected / exposed	0 / 14 (0.00%)	1 / 30 (3.33%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort 11 (12 Weeks GT2 F4)		

Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 4 (25.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Aspartate Aminotransferase Increased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Transitional Cell Carcinoma Urethra			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrioventricular Block			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			

Cellulitis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Cohort 1 (8 Weeks Genotype [GT1])	Cohort 1b + Cohort 4 (8 Weeks GT1)	Cohort 2 (8 Weeks GT1)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 20 (85.00%)	20 / 25 (80.00%)	14 / 20 (70.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal Cell Carcinoma			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Aortic Aneurysm			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Haematoma			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hot Flush			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Phlebitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			

Chest Discomfort			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Chest Pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	6 / 20 (30.00%)	4 / 25 (16.00%)	2 / 20 (10.00%)
occurrences (all)	6	4	2
Feeling Abnormal			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Peripheral Swelling			
subjects affected / exposed	0 / 20 (0.00%)	1 / 25 (4.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Swelling			
subjects affected / exposed	1 / 20 (5.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Vessel Puncture Site Bruise			
subjects affected / exposed	0 / 20 (0.00%)	1 / 25 (4.00%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
Vessel Puncture Site Haematoma			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Vessel Puncture Site Phlebitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			

Vaginal Discharge			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Chronic Obstructive Pulmonary Disease			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	1 / 20 (5.00%)	2 / 25 (8.00%)	1 / 20 (5.00%)
occurrences (all)	1	2	1
Dry Throat			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Dysphonia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Nasal Congestion			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal Pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 25 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Rhinorrhoea			
subjects affected / exposed	2 / 20 (10.00%)	1 / 25 (4.00%)	0 / 20 (0.00%)
occurrences (all)	2	1	0
Sinus Congestion			
subjects affected / exposed	1 / 20 (5.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Sneezing			

subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Throat Irritation			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Upper-Airway Cough Syndrome			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Psychiatric disorders			
Abnormal Dreams			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	2 / 20 (10.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Depressed Mood			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Dysphoria			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Flat Affect			
subjects affected / exposed	0 / 20 (0.00%)	1 / 25 (4.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Insomnia			
subjects affected / exposed	1 / 20 (5.00%)	1 / 25 (4.00%)	3 / 20 (15.00%)
occurrences (all)	1	1	3
Irritability			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Libido Decreased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Nightmare			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0

Panic Attack			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Sleep Disorder			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood Creatine Phosphokinase Increase			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blood Pressure Increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Ejection Fraction Decreased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram Pr Prolongation			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Lipase Increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Accidental Overdose			
subjects affected / exposed	1 / 20 (5.00%)	1 / 25 (4.00%)	1 / 20 (5.00%)
occurrences (all)	1	1	1
Chest Injury			
subjects affected / exposed	0 / 20 (0.00%)	1 / 25 (4.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Contusion			
subjects affected / exposed	2 / 20 (10.00%)	2 / 25 (8.00%)	1 / 20 (5.00%)
occurrences (all)	2	2	1
Epicondylitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Eye Contusion			

subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Joint Injury			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Laceration			
subjects affected / exposed	0 / 20 (0.00%)	1 / 25 (4.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Ligament Sprain			
subjects affected / exposed	0 / 20 (0.00%)	1 / 25 (4.00%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
Limb Injury			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Lip Injury			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Muscle Strain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Scratch			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Skin Abrasion			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Sunburn			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Thermal Burn			
subjects affected / exposed	1 / 20 (5.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Tooth Fracture			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Wound			

subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Congenital, familial and genetic disorders			
Porphyria Non-Acute			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Atrioventricular Block First Degree			
subjects affected / exposed	1 / 20 (5.00%)	1 / 25 (4.00%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
Palpitations			
subjects affected / exposed	1 / 20 (5.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Supraventricular Tachycardia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Burning Sensation			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Disturbance in Attention			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	1 / 20 (5.00%)	1 / 25 (4.00%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
Dysgeusia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	8 / 20 (40.00%)	5 / 25 (20.00%)	2 / 20 (10.00%)
occurrences (all)	9	5	2
Hypogeusia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hyposmia			

subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Lethargy			
subjects affected / exposed	0 / 20 (0.00%)	1 / 25 (4.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Memory Impairment			
subjects affected / exposed	1 / 20 (5.00%)	0 / 25 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Migraine			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 25 (4.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Presyncope			
subjects affected / exposed	0 / 20 (0.00%)	1 / 25 (4.00%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
Sensory Disturbance			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Tension Headache			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Lymphadenopathy			
subjects affected / exposed	1 / 20 (5.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Ear Discomfort			
subjects affected / exposed	1 / 20 (5.00%)	1 / 25 (4.00%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
Ear Pruritus			

subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Dry Eye			
subjects affected / exposed	0 / 20 (0.00%)	1 / 25 (4.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Erythema of Eyelid			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Eye Irritation			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
Eye Pruritus			
subjects affected / exposed	1 / 20 (5.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Vision Blurred			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Visual Impairment			
subjects affected / exposed	1 / 20 (5.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal Discomfort			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Abdominal Distension			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Abdominal Pain			
subjects affected / exposed	3 / 20 (15.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	3	0	0
Abdominal Pain Lower			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Abdominal Pain Upper			

subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	1 / 20 (5.00%)	1 / 25 (4.00%)	0 / 20 (0.00%)
occurrences (all)	2	1	0
Dental Caries			
subjects affected / exposed	1 / 20 (5.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	1 / 20 (5.00%)	2 / 25 (8.00%)	1 / 20 (5.00%)
occurrences (all)	1	2	1
Dry Mouth			
subjects affected / exposed	1 / 20 (5.00%)	1 / 25 (4.00%)	1 / 20 (5.00%)
occurrences (all)	1	1	1
Dyspepsia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 25 (4.00%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
Eructation			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Gastrooesophageal Reflux Disease			
subjects affected / exposed	1 / 20 (5.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Loose Tooth			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	2 / 20 (10.00%)	1 / 25 (4.00%)	0 / 20 (0.00%)
occurrences (all)	2	1	0
Noninfective Sialoadenitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Salivary Gland Calculus			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Toothache			

subjects affected / exposed	0 / 20 (0.00%)	1 / 25 (4.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	1 / 20 (5.00%)	1 / 25 (4.00%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Dermal Cyst			
subjects affected / exposed	0 / 20 (0.00%)	1 / 25 (4.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Dermatitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Dermatitis Atopic			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Dermatitis Contact			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	1 / 20 (5.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Hand Dermatitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Mechanical Urticaria			
subjects affected / exposed	0 / 20 (0.00%)	1 / 25 (4.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0

Night Sweats			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Photosensitivity Reaction			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	1 / 20 (5.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Rash			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Rash Papular			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Rash Pruritic			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Seborrhoeic Dermatitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Skin Fissures			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Micturition Urgency			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Polyuria			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Renal Colic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 25 (4.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Back Pain			
subjects affected / exposed	1 / 20 (5.00%)	1 / 25 (4.00%)	2 / 20 (10.00%)
occurrences (all)	1	1	2
Bursitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Joint Stiffness			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Muscle Tightness			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal Chest Pain			
subjects affected / exposed	0 / 20 (0.00%)	1 / 25 (4.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal Pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Musculoskeletal Stiffness			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	1 / 20 (5.00%)	1 / 25 (4.00%)	1 / 20 (5.00%)
occurrences (all)	1	1	1
Neck Pain			
subjects affected / exposed	0 / 20 (0.00%)	1 / 25 (4.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Pain in Extremity			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Rotator Cuff Syndrome			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0

Infections and infestations			
Angular Cheilitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis Viral			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Folliculitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Furuncle			
subjects affected / exposed	0 / 20 (0.00%)	1 / 25 (4.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Gingivitis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 25 (4.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Hordeolum			
subjects affected / exposed	0 / 20 (0.00%)	1 / 25 (4.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Influenza			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Laryngitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Lower Respiratory Tract Infection			

subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Rash Pustular			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Respiratory Tract Infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Respiratory Tract Infection Viral			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Skin Infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Tooth Abscess			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Tooth Infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Upper Respiratory Tract Infection			
subjects affected / exposed	6 / 20 (30.00%)	3 / 25 (12.00%)	1 / 20 (5.00%)
occurrences (all)	6	4	1
Urinary Tract Infection			

subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Viral Infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Wound Infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Appetite Disorder			
subjects affected / exposed	1 / 20 (5.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Decreased Appetite			
subjects affected / exposed	0 / 20 (0.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hyperphagia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 25 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Increased Appetite			
subjects affected / exposed	0 / 20 (0.00%)	1 / 25 (4.00%)	1 / 20 (5.00%)
occurrences (all)	0	1	1

Non-serious adverse events	Cohort 3 (Subjects with Cirrhosis)	Cohort 4 (12 Weeks GT1)	Cohort 5a (8 Weeks GT3)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 20 (70.00%)	7 / 8 (87.50%)	4 / 5 (80.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal Cell Carcinoma			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Aortic Aneurysm			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Haematoma			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Hot Flush			
subjects affected / exposed	1 / 20 (5.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Hypertension			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Phlebitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Chest Discomfort			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Chest Pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	3 / 20 (15.00%)	2 / 8 (25.00%)	0 / 5 (0.00%)
occurrences (all)	3	2	0
Feeling Abnormal			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Peripheral Swelling			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Swelling			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Vessel Puncture Site Bruise			

subjects affected / exposed	1 / 20 (5.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Vessel Puncture Site Haematoma			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Vessel Puncture Site Phlebitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Vaginal Discharge			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Chronic Obstructive Pulmonary Disease			
subjects affected / exposed	0 / 20 (0.00%)	1 / 8 (12.50%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Cough			
subjects affected / exposed	2 / 20 (10.00%)	1 / 8 (12.50%)	0 / 5 (0.00%)
occurrences (all)	2	1	0
Dry Throat			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dysphonia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Nasal Congestion			
subjects affected / exposed	0 / 20 (0.00%)	2 / 8 (25.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Oropharyngeal Pain			

subjects affected / exposed	0 / 20 (0.00%)	1 / 8 (12.50%)	1 / 5 (20.00%)
occurrences (all)	0	2	1
Rhinorrhoea			
subjects affected / exposed	0 / 20 (0.00%)	1 / 8 (12.50%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Sinus Congestion			
subjects affected / exposed	0 / 20 (0.00%)	1 / 8 (12.50%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Sneezing			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Throat Irritation			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Upper-Airway Cough Syndrome			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Abnormal Dreams			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Depressed Mood			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dysphoria			
subjects affected / exposed	0 / 20 (0.00%)	1 / 8 (12.50%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Flat Affect			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Irritability			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Libido Decreased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Nightmare			
subjects affected / exposed	0 / 20 (0.00%)	1 / 8 (12.50%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Panic Attack			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Sleep Disorder			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood Creatine Phosphokinase Increase			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood Pressure Increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Ejection Fraction Decreased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram Pr Prolongation			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Lipase Increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Accidental Overdose			
subjects affected / exposed	3 / 20 (15.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	3	0	0
Chest Injury			

subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	1 / 20 (5.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Epicondylitis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 8 (12.50%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Eye Contusion			
subjects affected / exposed	1 / 20 (5.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Joint Injury			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Laceration			
subjects affected / exposed	2 / 20 (10.00%)	0 / 8 (0.00%)	1 / 5 (20.00%)
occurrences (all)	2	0	1
Ligament Sprain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Limb Injury			
subjects affected / exposed	1 / 20 (5.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Lip Injury			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Muscle Strain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Scratch			
subjects affected / exposed	1 / 20 (5.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Skin Abrasion			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Sunburn			

subjects affected / exposed	0 / 20 (0.00%)	1 / 8 (12.50%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Thermal Burn			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Tooth Fracture			
subjects affected / exposed	1 / 20 (5.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Wound			
subjects affected / exposed	1 / 20 (5.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Congenital, familial and genetic disorders			
Porphyria Non-Acute			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Atrioventricular Block First Degree			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	0 / 20 (0.00%)	1 / 8 (12.50%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Supraventricular Tachycardia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 8 (12.50%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Burning Sensation			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Disturbance in Attention			
subjects affected / exposed	1 / 20 (5.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	1 / 20 (5.00%)	1 / 8 (12.50%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Dysgeusia			

subjects affected / exposed	1 / 20 (5.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	3 / 20 (15.00%)	4 / 8 (50.00%)	2 / 5 (40.00%)
occurrences (all)	3	6	2
Hypogeusia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hyposmia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Lethargy			
subjects affected / exposed	0 / 20 (0.00%)	2 / 8 (25.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Memory Impairment			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	1 / 20 (5.00%)	1 / 8 (12.50%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Presyncope			
subjects affected / exposed	0 / 20 (0.00%)	1 / 8 (12.50%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Sensory Disturbance			
subjects affected / exposed	0 / 20 (0.00%)	1 / 8 (12.50%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Tension Headache			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Lymphadenopathy			
subjects affected / exposed	1 / 20 (5.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Ear Discomfort			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Ear Pruritus			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Dry Eye			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Erythema of Eyelid			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Eye Irritation			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Eye Pruritus			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Vision Blurred			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Visual Impairment			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal Discomfort			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Abdominal Distension			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Abdominal Pain			

subjects affected / exposed	0 / 20 (0.00%)	1 / 8 (12.50%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Abdominal Pain Lower			
subjects affected / exposed	0 / 20 (0.00%)	1 / 8 (12.50%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Abdominal Pain Upper			
subjects affected / exposed	1 / 20 (5.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	0 / 20 (0.00%)	1 / 8 (12.50%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Dental Caries			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 20 (0.00%)	1 / 8 (12.50%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Dry Mouth			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 20 (0.00%)	2 / 8 (25.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Eructation			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal Reflux Disease			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Loose Tooth			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 20 (0.00%)	1 / 8 (12.50%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Noninfective Sialoadenitis			

subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Salivary Gland Calculus			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	1 / 20 (5.00%)	1 / 8 (12.50%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Vomiting			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 20 (0.00%)	1 / 8 (12.50%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Dermal Cyst			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dermatitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dermatitis Atopic			
subjects affected / exposed	1 / 20 (5.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Dermatitis Contact			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 20 (0.00%)	1 / 8 (12.50%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Erythema			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hand Dermatitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Hyperhidrosis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 8 (12.50%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Mechanical Urticaria			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Night Sweats			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Photosensitivity Reaction			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 20 (0.00%)	1 / 8 (12.50%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Rash Papular			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Rash Pruritic			
subjects affected / exposed	1 / 20 (5.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Seborrhoeic Dermatitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Skin Fissures			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Micturition Urgency			
subjects affected / exposed	1 / 20 (5.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Polyuria			

subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Renal Colic			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Back Pain			
subjects affected / exposed	1 / 20 (5.00%)	1 / 8 (12.50%)	0 / 5 (0.00%)
occurrences (all)	1	2	0
Bursitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Joint Stiffness			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Muscle Tightness			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal Chest Pain			
subjects affected / exposed	0 / 20 (0.00%)	1 / 8 (12.50%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal Pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal Stiffness			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Myalgia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 8 (12.50%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Neck Pain			

subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Pain in Extremity			
subjects affected / exposed	0 / 20 (0.00%)	1 / 8 (12.50%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Rotator Cuff Syndrome			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Angular Cheilitis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 8 (12.50%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Bronchitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis Viral			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Folliculitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Furuncle			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gingivitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hordeolum			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Influenza			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Laryngitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Lower Respiratory Tract Infection			
subjects affected / exposed	1 / 20 (5.00%)	0 / 8 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	1
Pharyngitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 8 (12.50%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Rash Pustular			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Respiratory Tract Infection			
subjects affected / exposed	1 / 20 (5.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Respiratory Tract Infection Viral			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Skin Infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Tooth Abscess			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Tooth Infection			
subjects affected / exposed	0 / 20 (0.00%)	1 / 8 (12.50%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 20 (5.00%)	3 / 8 (37.50%)	2 / 5 (40.00%)
occurrences (all)	1	3	2
Urinary Tract Infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Viral Infection			
subjects affected / exposed	1 / 20 (5.00%)	1 / 8 (12.50%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Wound Infection			
subjects affected / exposed	1 / 20 (5.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Appetite Disorder			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Decreased Appetite			
subjects affected / exposed	0 / 20 (0.00%)	1 / 8 (12.50%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Hyperphagia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Increased Appetite			
subjects affected / exposed	0 / 20 (0.00%)	0 / 8 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1

Non-serious adverse events	Cohort 5b (12 Weeks GT3)	Cohort 6,7,8 (8 Weeks GT1 F4)	Cohort 9 (12 Weeks GT1 F4)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 14 (92.86%)	18 / 30 (60.00%)	10 / 15 (66.67%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal Cell Carcinoma			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1

Vascular disorders			
Aortic Aneurysm			
subjects affected / exposed	0 / 14 (0.00%)	1 / 30 (3.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Haematoma			
subjects affected / exposed	0 / 14 (0.00%)	1 / 30 (3.33%)	0 / 15 (0.00%)
occurrences (all)	0	3	0
Hot Flush			
subjects affected / exposed	0 / 14 (0.00%)	1 / 30 (3.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Hypertension			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	2
Phlebitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Chest Discomfort			
subjects affected / exposed	1 / 14 (7.14%)	1 / 30 (3.33%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
Chest Pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	6 / 14 (42.86%)	3 / 30 (10.00%)	1 / 15 (6.67%)
occurrences (all)	6	3	1
Feeling Abnormal			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 14 (0.00%)	1 / 30 (3.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Peripheral Swelling			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Pyrexia			

subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Swelling			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Vessel Puncture Site Bruise			
subjects affected / exposed	1 / 14 (7.14%)	2 / 30 (6.67%)	0 / 15 (0.00%)
occurrences (all)	1	3	0
Vessel Puncture Site Haematoma			
subjects affected / exposed	0 / 14 (0.00%)	1 / 30 (3.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Vessel Puncture Site Phlebitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Vaginal Discharge			
subjects affected / exposed	0 / 14 (0.00%)	1 / 30 (3.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Chronic Obstructive Pulmonary Disease			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 14 (0.00%)	2 / 30 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Dry Throat			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Dysphonia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 14 (0.00%)	1 / 30 (3.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Epistaxis			

subjects affected / exposed	0 / 14 (0.00%)	1 / 30 (3.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Nasal Congestion			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Oropharyngeal Pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Sinus Congestion			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Sneezing			
subjects affected / exposed	0 / 14 (0.00%)	1 / 30 (3.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Throat Irritation			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Upper-Airway Cough Syndrome			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Abnormal Dreams			
subjects affected / exposed	1 / 14 (7.14%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Anxiety			
subjects affected / exposed	1 / 14 (7.14%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Depressed Mood			
subjects affected / exposed	1 / 14 (7.14%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Dysphoria			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0

Flat Affect			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 30 (3.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Irritability			
subjects affected / exposed	1 / 14 (7.14%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Libido Decreased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Nightmare			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Panic Attack			
subjects affected / exposed	1 / 14 (7.14%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Sleep Disorder			
subjects affected / exposed	0 / 14 (0.00%)	2 / 30 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Investigations			
Blood Creatine Phosphokinase Increase			
subjects affected / exposed	0 / 14 (0.00%)	2 / 30 (6.67%)	1 / 15 (6.67%)
occurrences (all)	0	3	1
Blood Pressure Increased			
subjects affected / exposed	0 / 14 (0.00%)	1 / 30 (3.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Ejection Fraction Decreased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Electrocardiogram Pr Prolongation			
subjects affected / exposed	0 / 14 (0.00%)	1 / 30 (3.33%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Lipase Increased			

subjects affected / exposed	0 / 14 (0.00%)	1 / 30 (3.33%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Injury, poisoning and procedural complications			
Accidental Overdose			
subjects affected / exposed	0 / 14 (0.00%)	1 / 30 (3.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Chest Injury			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 14 (0.00%)	4 / 30 (13.33%)	0 / 15 (0.00%)
occurrences (all)	0	4	0
Epicondylitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Eye Contusion			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Joint Injury			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Laceration			
subjects affected / exposed	1 / 14 (7.14%)	2 / 30 (6.67%)	0 / 15 (0.00%)
occurrences (all)	1	3	0
Ligament Sprain			
subjects affected / exposed	0 / 14 (0.00%)	1 / 30 (3.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Limb Injury			
subjects affected / exposed	1 / 14 (7.14%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Lip Injury			
subjects affected / exposed	1 / 14 (7.14%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Muscle Strain			

subjects affected / exposed	1 / 14 (7.14%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Scratch			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Skin Abrasion			
subjects affected / exposed	0 / 14 (0.00%)	1 / 30 (3.33%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Sunburn			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Thermal Burn			
subjects affected / exposed	1 / 14 (7.14%)	1 / 30 (3.33%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
Tooth Fracture			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Wound			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Congenital, familial and genetic disorders			
Porphyria Non-Acute			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Atrioventricular Block First Degree			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	0 / 14 (0.00%)	1 / 30 (3.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Supraventricular Tachycardia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			

Burning Sensation			
subjects affected / exposed	1 / 14 (7.14%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Disturbance in Attention			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	1 / 14 (7.14%)	0 / 30 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Dysgeusia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	3 / 14 (21.43%)	2 / 30 (6.67%)	2 / 15 (13.33%)
occurrences (all)	3	3	3
Hypogeusia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Hyposmia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Lethargy			
subjects affected / exposed	1 / 14 (7.14%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Memory Impairment			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 14 (0.00%)	1 / 30 (3.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Paraesthesia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Presyncope			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0

Sensory Disturbance			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Tension Headache			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Lymphadenopathy			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear Discomfort			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Ear Pruritus			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Dry Eye			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Erythema of Eyelid			
subjects affected / exposed	0 / 14 (0.00%)	1 / 30 (3.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Eye Irritation			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Eye Pruritus			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Vision Blurred			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Visual Impairment			

subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal Discomfort			
subjects affected / exposed	1 / 14 (7.14%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Abdominal Distension			
subjects affected / exposed	1 / 14 (7.14%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Abdominal Pain			
subjects affected / exposed	1 / 14 (7.14%)	1 / 30 (3.33%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
Abdominal Pain Lower			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Abdominal Pain Upper			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Dental Caries			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	1 / 14 (7.14%)	3 / 30 (10.00%)	1 / 15 (6.67%)
occurrences (all)	1	3	1
Dry Mouth			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Eructation			
subjects affected / exposed	0 / 14 (0.00%)	1 / 30 (3.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0

Gastrooesophageal Reflux Disease			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Loose Tooth			
subjects affected / exposed	0 / 14 (0.00%)	1 / 30 (3.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	0 / 14 (0.00%)	3 / 30 (10.00%)	0 / 15 (0.00%)
occurrences (all)	0	3	0
Noninfective Sialoadenitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Salivary Gland Calculus			
subjects affected / exposed	1 / 14 (7.14%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Toothache			
subjects affected / exposed	0 / 14 (0.00%)	1 / 30 (3.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	0 / 14 (0.00%)	1 / 30 (3.33%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Dermal Cyst			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Dermatitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Dermatitis Atopic			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Dermatitis Contact			

subjects affected / exposed	0 / 14 (0.00%)	1 / 30 (3.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Eczema			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Hand Dermatitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Mechanical Urticaria			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Night Sweats			
subjects affected / exposed	1 / 14 (7.14%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Photosensitivity Reaction			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	1 / 14 (7.14%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Rash			
subjects affected / exposed	0 / 14 (0.00%)	1 / 30 (3.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Rash Papular			
subjects affected / exposed	1 / 14 (7.14%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Rash Pruritic			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Seborrhoeic Dermatitis			

subjects affected / exposed	1 / 14 (7.14%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Skin Fissures			
subjects affected / exposed	1 / 14 (7.14%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Micturition Urgency			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Polyuria			
subjects affected / exposed	1 / 14 (7.14%)	1 / 30 (3.33%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
Renal Colic			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 30 (3.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Back Pain			
subjects affected / exposed	3 / 14 (21.43%)	1 / 30 (3.33%)	0 / 15 (0.00%)
occurrences (all)	3	1	0
Bursitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Joint Stiffness			
subjects affected / exposed	0 / 14 (0.00%)	1 / 30 (3.33%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Muscle Tightness			
subjects affected / exposed	1 / 14 (7.14%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal Chest Pain			
subjects affected / exposed	0 / 14 (0.00%)	1 / 30 (3.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal Pain			

subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal Stiffness			
subjects affected / exposed	0 / 14 (0.00%)	1 / 30 (3.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 30 (3.33%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Neck Pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 30 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Pain in Extremity			
subjects affected / exposed	1 / 14 (7.14%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Rotator Cuff Syndrome			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Infections and infestations			
Angular Cheilitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Bronchitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Conjunctivitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis Viral			
subjects affected / exposed	1 / 14 (7.14%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Folliculitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Furuncle			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0

Gastroenteritis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	2
Gingivitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Hordeolum			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Laryngitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Lower Respiratory Tract Infection			
subjects affected / exposed	1 / 14 (7.14%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Pharyngitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Rash Pustular			
subjects affected / exposed	1 / 14 (7.14%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Respiratory Tract Infection			
subjects affected / exposed	1 / 14 (7.14%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Respiratory Tract Infection Viral			
subjects affected / exposed	1 / 14 (7.14%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Rhinitis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 30 (3.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0

Skin Infection			
subjects affected / exposed	0 / 14 (0.00%)	1 / 30 (3.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Tonsillitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Tooth Abscess			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Tooth Infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Upper Respiratory Tract Infection			
subjects affected / exposed	4 / 14 (28.57%)	3 / 30 (10.00%)	0 / 15 (0.00%)
occurrences (all)	4	3	0
Urinary Tract Infection			
subjects affected / exposed	0 / 14 (0.00%)	2 / 30 (6.67%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Viral Infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Wound Infection			
subjects affected / exposed	0 / 14 (0.00%)	1 / 30 (3.33%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Appetite Disorder			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Decreased Appetite			
subjects affected / exposed	1 / 14 (7.14%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Hyperphagia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Increased Appetite			

subjects affected / exposed	0 / 14 (0.00%)	0 / 30 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Cohort 11 (12 Weeks GT2 F4)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal Cell Carcinoma			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Aortic Aneurysm			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Haematoma			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hot Flush			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Phlebitis			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
General disorders and administration site conditions			
Chest Discomfort			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Chest Pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	2 / 4 (50.00%)		
occurrences (all)	2		

Feeling Abnormal subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Pain subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Peripheral Swelling subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Pyrexia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Swelling subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Vessel Puncture Site Bruise subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Vessel Puncture Site Haematoma subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Vessel Puncture Site Phlebitis subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Reproductive system and breast disorders Vaginal Discharge subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Chronic Obstructive Pulmonary Disease subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Cough subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		

Dry Throat			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Dysphonia			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Dyspnoea			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Epistaxis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Nasal Congestion			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Oropharyngeal Pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Rhinorrhoea			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Sinus Congestion			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Sneezing			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Throat Irritation			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Upper-Airway Cough Syndrome			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Abnormal Dreams			

subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Anxiety			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Depressed Mood			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Dysphoria			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Flat Affect			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Irritability			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Libido Decreased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Nightmare			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Panic Attack			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Sleep Disorder			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Investigations			
Blood Creatine Phosphokinase Increase			

subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Blood Pressure Increased			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Ejection Fraction Decreased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Electrocardiogram Pr Prolongation			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Lipase Increased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Accidental Overdose			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Chest Injury			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Contusion			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Epicondylitis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Eye Contusion			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Joint Injury			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Laceration			

subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Ligament Sprain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Limb Injury			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Lip Injury			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Muscle Strain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Scratch			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Skin Abrasion			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Sunburn			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Thermal Burn			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Tooth Fracture			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Wound			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Congenital, familial and genetic disorders			
Porphyria Non-Acute			

subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Cardiac disorders			
Atrioventricular Block First Degree			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Palpitations			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Supraventricular Tachycardia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Burning Sensation			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Disturbance in Attention			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Dizziness			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Dysgeusia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Hypogeusia			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Hyposmia			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Lethargy			

subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Memory Impairment			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Migraine			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Paraesthesia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Presyncope			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Sensory Disturbance			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Tension Headache			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Lymphadenopathy			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Ear Discomfort			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Ear Pruritus			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Eye disorders			

Dry Eye				
subjects affected / exposed	1 / 4 (25.00%)			
occurrences (all)	1			
Erythema of Eyelid				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Eye Irritation				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Eye Pruritus				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Vision Blurred				
subjects affected / exposed	1 / 4 (25.00%)			
occurrences (all)	1			
Visual Impairment				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Gastrointestinal disorders				
Abdominal Discomfort				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Abdominal Distension				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Abdominal Pain				
subjects affected / exposed	1 / 4 (25.00%)			
occurrences (all)	1			
Abdominal Pain Lower				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Abdominal Pain Upper				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Constipation				

subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Dental Caries				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Diarrhoea				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Dry Mouth				
subjects affected / exposed	1 / 4 (25.00%)			
occurrences (all)	1			
Dyspepsia				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Eructation				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Gastrooesophageal Reflux Disease				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Loose Tooth				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Nausea				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Noninfective Sialoadenitis				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Salivary Gland Calculus				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Toothache				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Vomiting				

subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	3		
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Dermal Cyst			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Dermatitis			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Dermatitis Atopic			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Dermatitis Contact			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Eczema			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Erythema			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Hand Dermatitis			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Hyperhidrosis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Mechanical Urticaria			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Night Sweats			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		

Photosensitivity Reaction subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Pruritus subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Rash subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Rash Papular subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Rash Pruritic subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Seborrhoeic Dermatitis subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Skin Fissures subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Renal and urinary disorders Micturition Urgency subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Polyuria subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Renal Colic subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Back Pain			

subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Bursitis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Joint Stiffness			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Muscle Tightness			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Musculoskeletal Chest Pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Musculoskeletal Pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Musculoskeletal Stiffness			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Neck Pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Pain in Extremity			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Rotator Cuff Syndrome			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Angular Cheilitis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		

Bronchitis				
subjects affected / exposed	1 / 4 (25.00%)			
occurrences (all)	1			
Conjunctivitis				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Conjunctivitis Viral				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Folliculitis				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Furuncle				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Gastroenteritis				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Gingivitis				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Hordeolum				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Influenza				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Laryngitis				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Lower Respiratory Tract Infection				
subjects affected / exposed	2 / 4 (50.00%)			
occurrences (all)	2			
Pharyngitis				
subjects affected / exposed	1 / 4 (25.00%)			
occurrences (all)	1			

Pneumonia				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Rash Pustular				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Respiratory Tract Infection				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Respiratory Tract Infection Viral				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Rhinitis				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Skin Infection				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Tonsillitis				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Tooth Abscess				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Tooth Infection				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Upper Respiratory Tract Infection				
subjects affected / exposed	1 / 4 (25.00%)			
occurrences (all)	1			
Urinary Tract Infection				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			
Viral Infection				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences (all)	0			

Wound Infection subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Metabolism and nutrition disorders Appetite Disorder subjects affected / exposed occurrences (all) Decreased Appetite subjects affected / exposed occurrences (all) Hyperphagia subjects affected / exposed occurrences (all) Increased Appetite subjects affected / exposed occurrences (all)	 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 November 2015	Name of ACH-3102 was changed to ODV. Subjects with chronic GT3 HCV infection were also included in the study. Added text in the background section to clarify previous clinical experience of SMV. Added dosing regimens in subjects with chronic GT1 HCV infection (Cohort 4) and GT3 HCV infection (Cohort 5). Inclusion Criterion #7 changed to include the additional Cohorts 4 and 5. Added dose regimens for the additional cohorts. Inclusion Criterion #10 changed to clarify collection timeframe from FibroScans (within 6 months from baseline). Explained allocation in Cohorts 2 and 3, and stratification of subjects in Cohorts 2 to 4. Study duration increased from 36 weeks to 37 weeks. Sample size increased from 60 (up to 80) subjects to 100 (up to 120) subjects.
25 November 2015	Added text in the background section to include the current clinical experience of AL-335. Updated text in the study design section to clarify actions that might be taken as the study progresses. The amendment also assigned an identifying term to the optional cohort (Cohort 1b). Updated Exclusion Criterion #11 to clarify screening ECG parameter as PR >200 ms and exclusion due to evidence of heart block or bundle branch block. Changed the text in the dose regimen section to clarify that the dose level and frequency of dosing of the study drugs might be modified in the subsequent cohorts, and Cohorts 1b, 2, and 5 might or might not include SMV. Added an additional futility criterion: Any subject with a PR interval >240 ms while on therapy be discontinued from ODV. Updated the text to clarify the management of cardiotoxicity.
22 January 2016	Updated the specific elements of the study design (eg, treatment duration, doses, dosing frequency, population, number/size of cohorts) to permit evaluation of varying combinations, which was important to preliminarily determine the optimal dosing regimen(s) for different drug/subject population combinations prior to starting Phase 2b studies. The size of the intensive PK population was increased to reflect the increase in size of the overall study, in case of adding 3 more optional Cohorts 6 to 8. Updated the text in the primary and secondary objectives to reflect that SMV will not be assessed in all cohorts. Added a secondary endpoint: “Effect of various baseline and host disease related characteristics on treatment outcome”. Updated the duration of study period from 37 to 43 weeks, with screening period increased from 35 to 50 days (for maintaining the eligibility of subjects entitled to enroll but delayed due to delay in initiating next cohorts) and planned maximum treatment duration increased from 8 to 12 weeks (to reflect the revised study design elements). Sample size increased from 100 (up to 120) subjects to 120 (up to 180) subjects.

10 May 2016	Changed the eligible subject population to include treatment-experienced subjects. Added a study objective and endpoint to evaluate the effect of prior HCV treatment on efficacy. More cohorts were added to allow the enrollment of additional dosing regimen combinations, which were especially needed if the treatment-experienced subject population was to be explored. The target daily ODV dose was 25 mg/day. In the earlier protocol version, this was achieved by administering 50 mg qod. Updated text to note that when a 25 mg tablet of ODV would be available, this was to be administered daily, to optimize subject compliance and minimize confusion with respect to ODV dosing. Although the effective total daily dose was assumed to be 25 mg qd, lower ODV doses had not been explored; thus, it could not be ruled out that a lower total daily dose of ODV would be equally effective. The lowest available strength for this study was 25 mg; thus, dosing 25 mg qod would allow the Sponsor to explore ODV dosing as low as the equivalent of 12.5 mg qd. The total sample size of the PK population was increased to 250 to reflect the increase in the number of cohorts and to allow for as much of this data to be collected as was possible.
11 May 2016	Modified Inclusion Criterion #12 to avoid unnecessary repetition of FibroScan, as subjects with known cirrhosis based on a historical FibroScan result did not need to undergo a repeat FibroScan evaluation during screening. Added Exclusion Criterion #21 for liver ultrasound (within 6 months) of hepatic mass or lesion concerning for malignancy (subjects with cirrhosis only) to ensure cirrhotic subjects who were at enhanced risk of hepatocellular carcinoma were not inadvertently enrolled. All Schedule of Events tables were updated accordingly. Updated the laboratory evaluation section to collect an optional serum sample after additional subject consent. This sample could be used a backup sample for safety assessments or to measure explore subject characteristics and potential biomarkers.
14 July 2016	Updated protocol title to include subjects with chronic GT2 HCV infection with or without compensated Child-Pugh A cirrhosis to reflect the population planned to be studied in the study. Updated treatment in the protocol title to reflect that the subjects may or may not receive SMV. All other instances in the protocol were updated accordingly. Updated protocol title page to include the IND number and the EudraCT number. Updated contact information and the SAE reporting section to allow flexibility in the event that the CRO for pharmacovigilance was changed. Removed reference of treatment-experienced subjects throughout the protocol. Updated number of sites and location to reflect the need to have more subjects enrolled. Added a rationale section to justify inclusion of women of childbearing potential.
26 July 2016	IND number was removed. As this study is conducted outside the US, the study is non-IND. Updated the synopsis table to provide clarification of the cohorts. Revised the background section to include a treatment-emergent SAE that was likely unrecognized but present at baseline and inadvertently omitted from prior safety discussion.
13 September 2016	Updated definition of sustained virologic failure. Additional post-treatment follow-up was added at Week 18. Clarification added for increase in cohort size, if dosing regimen was modified due to insufficient efficacy or safety, to ensure 20 subjects in each cohort. Updated study design to include maximum VL in case of insufficient efficacy due to dosing regimens, to ensure an adequate risk-benefit profile. Updated status of completed, initiated, and planned cohorts. Study design was updated to reflect current study plan. Updated number of sites, as number of subjects to be enrolled was increased. Updated background section with all available PK, efficacy, and safety data. Updated list of prohibited medications to permit conditional use of QTc prolonging medications.
21 December 2016	Updated pharmacovigilance contact details. Updated protocol sections to confirm the status of cohort enrollment as well as confirm that cohort regimens would not change unless necessary for safety purposes. Replaced “randomized/randomization” with “enrolled/enrollment” to correctly reflect the study conduct.

24 February 2017	Updated pharmacovigilance contact details. Definition of on-treatment failure and viral relapse were updated for clarity. Study-specific safety, efficacy, and PK data updated to reflect available known information. Contraception-related language updated based on new information available. Exclusion criterion for HbA1c updated based on the central laboratory reporting method. Added study treatment stopping criteria for compliance with the US Food and Drug Administration requirements. All sections related to discontinuation updated accordingly. Schedule of Events tables were updated to reflect changes in liver ultrasound time points and to remove PK sample at 12 hours removed to avoid subject stay at a clinic so late in the night. Added information on analysis of hepatitis B infection in case of ALT flares. Added information related to viral sequencing in the efficacy analysis section.
03 May 2017	Updated study design to include treatment-experienced subjects. A case-by-case review of illicit drug use was added due to small target population. Exclusion criterion for platelet counts broadened to allow enrollment of subjects with cirrhosis. Clarified that the subjects could undergo rescreening to enroll subjects who were screen failures due to minor cutoffs. Missed dose window changed from 24 hours to 12 hours due to change in dose regimen of ODV. Window of 3 days for echocardiogram at the screening visit was removed, as echocardiogram was less likely to change during the screening period because the study drug was not administered.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported