Clinical trial results:
A Phase 2 Study Assessing the Safety and Efficacy of AT-527 in Combination with Daclatasvir in Subjects with Chronic HCV Infection

Summary

EudraCT number	2019-001431-31
Trial protocol	BE
Global end of trial date	18 March 2020

Results information

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

Trial information

Trial identification

Sponsor protocol code	AT-01B-002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04019717
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Atea Pharmaceuticals, Inc.
Sponsor organisation address	125 Summer Street, Suite 1675, Boston, MA, United States, 02110
Public contact	Keith Pietropaolo, Atea Pharmaceuticals, Inc., +1 857284-8957, Pietropaolo.keith@ateapharma.com
Scientific contact	Keith Pietropaolo, Atea Pharmaceuticals, Inc., +1 857284-8957, Pietropaolo.keith@ateapharma.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	18 March 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 March 2020
Global end of trial reached?	Yes
Global end of trial date	18 March 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

•To evaluate the safety and tolerability of AT-527 in combination with daclatasvir
•To evaluate the efficacy of the combination of AT-527 and daclatasvir as measured by the proportion of subjects who achieve sustained virologic response (SVR12) (HCV ribonucleic acid (RNA) < lower limit of quantitation (LLOQ) at 12 weeks after end of treatment (EOT)) with 8 or 12 weeks of treatment.

Protection of trial subjects:

This study was conducted in compliance with the study protocol, the ethical principles in the latest version of the Declaration of Helsinki, the International Conference on Harmonisation (ICH) Guideline E6 for Good Clinical Practices (GCP) and local regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 June 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Moldova, Republic of: 4
Country: Number of subjects enrolled	Mauritius: 5
Worldwide total number of subjects	10
EEA total number of subjects	1

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)	10

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 3 clinical centers in 3 countries.

Pre-assignment

Screening details:

31 subjects were screened. Ten subjects were enrolled and were treated with AT-527 and daclatasvir. Nine subjects received AT-527 and daclatasvir for 8 weeks and 1 subject received AT-527 and daclatasvir for 12 weeks.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	AT-527 & daclatasvir - 8 weeks

Arm description:

Subjects took one (1) 550 mg tablet of AT-527 and one (1) 60 mg tablet of daclatasvir daily for 8 weeks

Arm type	Experimental & Commercial
Investigational medicinal product name	AT-527
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

One (1) 550 mg tablet of AT-527 daily for 8 weeks.
Tablets were taken orally each morning on an empty stomach.

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

Dosage and administration details:

One (1) 60 mg tablet of daclatasvir daily for 8 weeks.
Tablets were taken orally each morning on an empty stomach.

Arm title	AT-527 & daclatasvir - 12 weeks

Arm description:

Subjects took one (1) 550 mg tablet of AT-527 and one (1) 60 mg tablet of daclatasvir daily for 12 weeks.

Arm type	Experimental & Commercial
Investigational medicinal product name	AT-527
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

One (1) 550 mg tablet of AT-527 daily for 12 weeks.
Tablets were taken orally each morning on an empty stomach.

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

Dosage and administration details:

One (1) 60 mg tablet of daclatasvir daily for 12 weeks.
Tablets were taken orally each morning on an empty stomach.

Number of subjects in period 1	AT-527 & daclatasvir - 8 weeks	AT-527 & daclatasvir - 12 weeks
Started	9	1
Completed	9	1

Baseline characteristics

Reporting groups	
Reporting group title	AT-527 & daclatasvir - 8 weeks
Reporting group description:	
Subjects took one (1) 550 mg tablet of AT-527 and one (1) 60 mg tablet of daclatasvir daily for 8 weeks	
Reporting group title	AT-527 & daclatasvir - 12 weeks
Reporting group description:	
Subjects took one (1) 550 mg tablet of AT-527 and one (1) 60 mg tablet of daclatasvir daily for 12 weeks.	

Reporting group values	AT-527 & daclatasvir - 8 weeks	AT-527 & daclatasvir - 12 weeks	Total
Number of subjects	9	1	10
Age categorical Units: Subjects			
Adults (18-64 years)	9	1	10
Age continuous Units: years			
median	31.0	44.0	
full range (min-max)	26 to 57	44.0 to 44.0	-
Gender categorical Units: Subjects			
Female	2	0	2
Male	7	1	8

End points

End points reporting groups

Reporting group title	AT-527 & daclatasvir - 8 weeks
Reporting group description:	
Subjects took one (1) 550 mg tablet of AT-527 and one (1) 60 mg tablet of daclatasvir daily for 8 weeks	
Reporting group title	AT-527 & daclatasvir - 12 weeks
Reporting group description:	
Subjects took one (1) 550 mg tablet of AT-527 and one (1) 60 mg tablet of daclatasvir daily for 12 weeks.	
Subject analysis set title	AT-527 & daclatasvir
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Efficacy	

Primary: Safety: Treatment-Emergent Adverse Events

End point title	Safety: Treatment-Emergent Adverse Events[1]
End point description:	

End point type	Primary
End point timeframe:	
During treatment	

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

End point values	AT-527 & daclatasvir - 8 weeks	AT-527 & daclatasvir - 12 weeks	AT-527 & daclatasvir	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	9	1	10	
Units: subjects				
At least one TEAE	6	1	7	
At least one serious TEAE	0	0	0	
At least one grade ≥3 TEAE	1	0	1	
At least one fatal TEAE	0	0	0	
At least one TEAE related to AT-527	5	0	5	
At least one TEAE related to daclatasvir	4	1	5	
At least one TEAE leading to study withdrawal	0	0	0	

Statistical analyses

No statistical analyses for this end point

Primary: Efficacy: Sustained Virologic Response (SVR)

End point title	Efficacy: Sustained Virologic Response (SVR)[2]

End point description:

The proportion of subjects who achieved SVR12 (HCV RNA < LLOQ at 12 weeks after EOT) with 8 or 12 weeks of treatment

End point type	Primary

End point timeframe:

4, 12 and 24 weeks after end of treatment

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

End point values	AT-527 & daclatasvir - 8 weeks	AT-527 & daclatasvir - 12 weeks	AT-527 & daclatasvir	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	9	1	10	
Units: subjects				
SVR4	9	1	10	
SVR12	8	1	9	
SVR24	8	1	9	

Statistical analyses

No statistical analyses for this end point

Secondary: Efficacy: Virologic Response over time

End point title	Efficacy: Virologic Response over time

End point description:

(HCV RNA < LLOQ over time)

End point type	Secondary

End point timeframe:

W1 to FU W 24

End point values	AT-527 & daclatasvir - 8 weeks	AT-527 & daclatasvir - 12 weeks	AT-527 & daclatasvir	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	9[3]	1	10	
Units: subjects				
W1	1	0	1	
W2	7	0	7	
W4	9	0	9	
W6	9	0	9	
W8	9	1	10	
W12	0	1	1	
End of Treatment	9	1	10	
Follow Up W4	9	1	10	
Follow Up W12	8	1	9	

Follow Up W24	8	1	9	

Notes:

[3] - Week 12 no value as not applicable

Statistical analyses

No statistical analyses for this end point

Secondary: Efficacy: Resistance Analysis

End point title	Efficacy: Resistance Analysis

End point description:

No emerging NS5A or NS5B RAVs were observed in the subject experiencing virologic failure. This single subject who relapsed with GT 1b virus had the following RAVs/variants both at baseline and at the SVR12 time point: NS5A: R30Q NS5B: L159F/A218S/C316N.

End point type	Secondary

End point timeframe:

SVR4, SVR 12 and SVR24 (4,12 and 24 weeks after end of treatment)

End point values	AT-527 & daclatasvir - 8 weeks	AT-527 & daclatasvir - 12 weeks	AT-527 & daclatasvir	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	9[4]	1[5]	10[6]	
Units: subjects				
SVR4 without NS5B RAV at baseline	6	1	7	
SVR12 without NS5B RAV at baseline	6	1	7	
SVR24 without NS5B RAV at baseline	6	1	7	
SVR4 with NS5B RAV at baseline	3	0	3	
SVR12 with NS5B RAV at baseline	2	0	2	
SVR24 with NS5B RAV at baseline	2	0	2	

Notes:

[4] - Subjects without a NS5B RAV at baseline = 6
Subjects with a NS5B RAV at baseline = 3

[5] - Subjects without a NS5B RAV at baseline = 1
Subjects with a NS5B RAV at baseline = 0

[6] - Subjects without a NS5B RAV at baseline = 7
Subjects with a NS5B RAV at baseline = 3

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From informed consent until the end of the study	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups	
Reporting group title	AT-527 & daclatasvir - 8 weeks
Reporting group description:	
Subjects will take one (1) 550 mg tablet of AT-527 and one (1) 60 mg tablet of daclatasvir daily for 8 weeks	
Reporting group title	AT-527 & daclatasvir - 12 weeks
Reporting group description:	
Subjects will take one (1) 550 mg tablet of AT-527 and one (1) 60 mg tablet of daclatasvir daily for 12 weeks.	

Serious adverse events	AT-527 & daclatasvir - 8 weeks	AT-527 & daclatasvir - 12 weeks	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 9 (0.00%)	0 / 1 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	AT-527 & daclatasvir - 8 weeks	AT-527 & daclatasvir - 12 weeks	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 9 (66.67%)	1 / 1 (100.00%)	
Investigations			
Lipase increased			
subjects affected / exposed	2 / 9 (22.22%)	0 / 1 (0.00%)	
occurrences (all)	2	0	
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 9 (22.22%)	1 / 1 (100.00%)	
occurrences (all)	3	1	
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	1 / 9 (11.11%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Abdominal pain upper			
subjects affected / exposed	1 / 9 (11.11%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
nausea			
subjects affected / exposed	1 / 9 (11.11%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 9 (11.11%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Rhinorrhoea			
subjects affected / exposed	1 / 9 (11.11%)	0 / 1 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 September 2019	Update to Individual Safety Stopping Rules: Confirmed elevation of ALT and/or AST >5 x baseline or post-baseline nadir, and >5 x ULN To warrant treatment discontinuation, a grade 4 laboratory abnormality should have clinical findings expected to be associated with the laboratory abnormality. Subjects with isolated asymptomatic laboratory abnormalities, without any clinical correlations, are allowed to remain on treatment with continued monitoring according to the preference of the investigator.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported