



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