ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 09/08/2014

ClinicalTrials.gov ID: NCT01180790

## Study Identification

| | |
|---|---|
| Unique Protocol ID: | ACH625-003 |
| Brief Title: | Safety, Tolerability and Antiviral Activity of ACH-0141625 or Placebo in Combination With Peginterferon and Ribavirin in HCV Positive Subjects |
| Official Title: | A Phase IIa, Randomized, Double-blind (Subject and Investigator Blind, Sponsor Open), Placebo-controlled Trial to Evaluate the Safety, Tolerability and Antiviral Activity of Oral ACH-0141625 in Combination With Pegylated Interferon Alpha-2a and Ribavirin in Two Segments, After 28 Days of Dosing and, Subsequently, After 12 Weeks of Dosing in Subjects With Chronic Hepatitis C Virus Genotype 1 |
| Secondary IDs: | 2010-022092-65 [EudraCT Number] |

## Study Status

| | |
|---|---|
| Record Verification: | September 2014 |
| Overall Status: | Completed |
| Study Start: | September 2010 |
| Primary Completion: | March 2012 [Actual] |
| Study Completion: | April 2013 [Actual] |

## Sponsor/Collaborators

| | |
|---|---|
| Sponsor: | Achillion Pharmaceuticals |
| Responsible Party: | Sponsor |
| Collaborators: | |

## Oversight

| | |
|---|---|
| FDA Regulated?: | Yes |
| Applicable Trial?: | Section 801 Clinical Trial? Yes<br>Delayed Posting? No |
| IND/IDE Protocol?: | Yes |
| IND/IDE Information: | Grantor: CDER<br>IND/IDE Number: IND 108487<br>Serial Number:<br>Has Expanded Access? No |
| Review Board: | Approval Status:<br>Board Name:<br>Board Affiliation:<br>Phone:<br>Email: |
| Data Monitoring?: | |
| Plan to Share Data?: | |
| Oversight Authorities: | United States: Food and Drug Administration |

## Study Description

| | |
|---|---|
| Brief Summary: | Evaluate safety, tolerability and antiviral response of ACH-0141625 compared to Standard of Care in HCV positive subjects. |
| Detailed Description: | |

## Conditions

| | |
|---|---|
| Conditions: | Hepatitis C |
| Keywords: | HCV<br>Hepatitis C Genotype 1 |

## Study Design

| | |
|---|---|
| Study Type: | Interventional |
| Primary Purpose: | Treatment |
| Study Phase: | Phase 2 |

| | |
|---|---|
| Intervention Model: | Parallel Assignment |
| Number of Arms: | 7 |
| Masking: | Double Blind (Subject, Investigator) |
| Allocation: | Randomized |
| Endpoint Classification: | Safety/Efficacy Study |
| Enrollment: | 122 [Actual] |

## Arms and Interventions

| Arms | Assigned Interventions |
|---|---|
| Experimental: Segment 1: 200 mg ACH-0141625<br>200 mg ACH-0141625 for 28 days plus Peg-IFN alpha-2a and ribavirin for 48 weeks | Drug: ACH-0141625 (Sovaprevir)<br>200 mg oral capsule once daily<br>Drug: Pegylated Interferon alpha-2a<br>180 ug once a week by subcutaneous injection<br>Other Names:<br>• Peg-INF<br>Drug: Ribavirin<br>400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily<br>Other Names:<br>• Ribasphere<br>• Copegus |
| Experimental: Segment 1: 400 mg ACH-0141625<br>400 mg ACH-0141625 for 28 days plus Peg-IFN alpha-2a plus ribavirin for 48 weeks | Drug: ACH-0141625 (Sovaprevir)<br>400 mg oral capsule once daily<br>Drug: Pegylated Interferon alpha-2a<br>180 ug once a week by subcutaneous injection<br>Other Names:<br>• Peg-INF<br>Drug: Ribavirin<br>400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily<br>Other Names:<br>• Ribasphere<br>• Copegus |
| Experimental: Segment 1: 800 mg ACH-0141625<br>800 mg ACH-0141625 for 28 days plus Peg-IFN alpha-2a plus ribavirin for 48 weeks | Drug: ACH-0141625 (Sovaprevir)<br>800 mg oral capsule once daily<br>Drug: Pegylated Interferon alpha-2a<br>180 ug once a week by subcutaneous injection |

| Arms | Assigned Interventions |
| --- | --- |
| | Other Names:<br>• Peg-INF<br>Drug: Ribavirin<br>400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily<br>Other Names:<br>• Ribasphere<br>• Copegus |
| Placebo Comparator: Segment 1: Placebo<br>Placebo for 28 days plus Peg-IFN alpha-2a plus ribavirin for 48 weeks | Drug: Placebo<br>Powder in capsule once daily<br>Drug: Pegylated Interferon alpha-2a<br>180 ug once a week by subcutaneous injection<br>Other Names:<br>• Peg-INF<br>Drug: Ribavirin<br>400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily<br>Other Names:<br>• Ribasphere<br>• Copegus |
| Experimental: Segment 2: 200 mg ACH-0141625<br>200 mg ACH-0141625 for 12 weeks plus Peg-IFN and ribavirin for up to a total of 24 or 48 weeks | Drug: ACH-0141625 (Sovaprevir)<br>200 mg oral capsule once daily<br>Drug: Pegylated Interferon alpha-2a<br>180 ug once a week by subcutaneous injection<br>Other Names:<br>• Peg-INF<br>Drug: Ribavirin<br>400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily<br>Other Names:<br>• Ribasphere<br>• Copegus |
| Experimental: Segment 2 : 400 mg ACH-0141625<br>400 mg ACH-0141625 for 12 weeks plus Peg-IFN and ribavirin for up to a total of 24 or 48 weeks | Drug: ACH-0141625 (Sovaprevir)<br>400 mg oral capsule once daily<br>Drug: Pegylated Interferon alpha-2a<br>180 ug once a week by subcutaneous injection<br>Other Names:<br>• Peg-INF<br>Drug: Ribavirin |

| Arms | Assigned Interventions |
|---|---|
| | 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily<br>Other Names:<br>• Ribasphere<br>• Copegus |
| Experimental: Segment 2 : 800 mg ACH-0141625<br>800 mg ACH-0141625 for 12 weeks plus Peg-IFN and ribavirin for up to a total of 24 or 48 weeks | Drug: ACH-0141625 (Sovaprevir)<br>800 mg oral capsule once daily<br>Drug: Pegylated Interferon alpha-2a<br>180 ug once a week by subcutaneous injection<br>Other Names:<br>• Peg-INF<br>Drug: Ribavirin<br>400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily<br>Other Names:<br>• Ribasphere<br>• Copegus |

## Outcome Measures

[See Results Section.]

## Eligibility

Minimum Age: 18 Years

Maximum Age:

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- Males and females 18 years and older
- Chronic hepatitis C Genotype 1 (as specified in the protocol)
- Treatment naive
- Females who are post-menopausal and amenorrheic must have a FSH at screening. Females of child bearing potential must have a negative pregnancy test at screening and baseline. Females must use a non hormonal method of contraception and must agree not to get pregnant during the study and for six months following the discontinuation of SOC.
- Fertile males must agree to use a condom and his female partner must agree to use one or more methods of contraception. Males must not donate sperm during the study and three months following the last exposure to RBV.

Exclusion Criteria:

- BMI >36 kg/m2
- Pregnant or nursing females: or females of childbearing potential not willing to comply with contraceptive measures per protocol. Men whose female partners are pregnant or contemplating pregnancy. - Coinfection with HBV and/or HIV
- Other significant disease including liver disease
- History of drug or alcohol dependence or addiction within the past 6 months
- History of participation in a clinical trial with a protease inhibitor or previous treatment with a protease inhibitor, where at least one dose of the protease inhibitor was consumed.
- Use of herbal or homeopathic products, illicit drugs, cytochrome P450 (CYP 3A4/5 substrates, inducers or inhibitors, hormonal methods of contraception, corticosteroids, immunosuppressive, or cytotoxic agents within 28 days of first dose of study drug.
- Have a clinically significant laboratory abnormality at screening (as specified in protocol).
- Segment 1: Subjects with any history of decompensated liver disease defined as cirrhotic subjects with a Child-Pugh score of > or = to 7. Segment 2: Subjects who have had a liver biopsy that shows bridging fibrosis or cirrhosis.
- Nonalcoholic steatohepatitis if ballooning degeneration or Mallory bodies are present on liver biopsy.
- Subjects, who prematurely discontinued, interrupted or dose reduced prior Peg-IFN and Ribavirin therapy, due to noncompliance or safety issues.
- Encephalopathy or altered mental status of any etiology.
- History of moderate, severe or uncontrolled psychiatric disease (as specified in protocol).
- History of malignancy of any organ system treated or untreated within the past 5 years.
- Use of colony stimulating factor agents within 90 days prior to baseline.
- History of seizure disorder.
- History of known coagulopathy including hemophilia.
- Clinically of significant findings on fundoscopic or retinal examination at screening
- History of immunologically mediate disease.
- History of clinical evidence of chronic cardiac disease (as specified in protocol)
- Received concomitant systemic antibiotic, antifungals or antivirals for the treatment of active infection within 14 days prior to the first dose of the study drug (as specified in protocol)

## Contacts/Locations

Study Officials: Hetal Kocinsky, MD
Study Director
Achillion Pharmaceuticals, Inc.

Locations: United States, Texas
Alamo Medical Research
San Antonio, Texas, United States, 78215

United States, Florida
Orlando Immunology Center
Orlando, Florida, United States, 32803

United States, Texas
North Texas Research Institute

Arlington, Texas, United States, 76012

United States, California
Axis Clinical Trials
Los Angeles, California, United States, 90036

United States, Kansas
Vince and Associates Clinical Research
Overland Park, Kansas, United States, 66211

United States, California
Quest Clinical Research
San Francisco, California, United States, 94115

United States, Pennsylvania
Albert Einstein Medical Center
Philadelphia, Pennsylvania, United States, 19141

United States, Illinois
Northwestern University
Chicago, Illinois, United States, 60611

United States, Nevada
Impact Clinical Trials
Las Vegas, Nevada, United States, 89106

United States, Florida
Pointe West Infectious Disease
Brandenton, Florida, United States, 34209

United States, California
Cedars-Sinai Medical Center
Los Angeles, California, United States, 90048

United States, New York
Weill Medical College of Cornell University
New York, New York, United States, 10065

United States, Missouri
St. Louis University
St. Louis, Missouri, United States, 63104

United States, Virginia
Bon Secours St. Mary's Hospital of Richmond
Newport News, Virginia, United States, 23602

Belgium
Universitair Ziekenhuis Gent
Gent, Oost-Vlaanderen, Belgium, 9000

Universitair Ziekenhuis Antwerpen
Edgem, Antwerp, Belgium, 2650

Centre Hospitalier de Jolimont-Lobbes
Haine-Saint-Paul, Hainaut, Belgium, 7100

United States, Virginia
Digestive and Liver Diseas Specialists
Norfolk, Virginia, United States, 23502

## References

Citations:

Links: URL: http://studyforhepc.com/
Description Recruitment site for potential subjects

Study Data/Documents:

---

# Study Results

## Participant Flow

| | |
|---|---|
| Recruitment Details | Participants were recruited from 15 sites in the United States and 3 sites in Belgium between September 30, 2010 and January 3, 2012. |
| Pre-Assignment Details | Participants screened within 4 weeks (Day -28 to -1) before administration of study drug. Subjects who meet all eligibility criteria were instructed to arrive at the study center on Baseline day for randomization to treatment assignment. |

Reporting Groups

| | Description |
|---|---|
| Segment 1: 200 mg ACH-0141625 for 28 Days | ACH-0141625: 200 mg oral capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection for 48 weeks<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily for 48 weeks |

| | Description |
|---|---|
| Segment 1: 400 mg ACH-0141625 for 28 Days | ACH-0141625: 400 mg oral capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection for 48 weeks<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily for 48 weeks |
| Segment 1: 800 mg ACH-0141625 for 28 Days | ACH-0141625: 800 mg oral capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection for 48 weeks<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily for 48 weeks |
| Segment 1: Placebo for 28 Days | Placebo: Powder in capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection for 48 weeks<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily for 48 weeks |
| Segment 2: 200 mg ACH-0141625 for 12 Weeks | ACH-0141625: 200 mg oral capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection for up to 24 or 48 weeks<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily for up to 24 or 48 weeks |
| Segment 2 - 400 mg ACH-0141625 for 12 Weeks | ACH-0141625: 400 mg oral capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection for up to 24 or 48 weeks<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily for up to 24 or 48 weeks |
| Segment 2 - 800 mg ACH-0141625 for 12 Weeks | ACH-0141625: 800 mg oral capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection for up to 24 or 48 weeks<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily for up to 24 or 48 weeks |

Overall Study

| | Segment 1: 200 mg ACH-0141625 for 28 Days | Segment 1: 400 mg ACH-0141625 for 28 Days | Segment 1: 800 mg ACH-0141625 for 28 Days | Segment 1: Placebo for 28 Days | Segment 2: 200 mg ACH-0141625 for 12 Weeks | Segment 2 - 400 mg ACH-0141625 for 12 Weeks |
|---|---|---|---|---|---|---|
| Started | 16 | 16 | 17 | 15 | 19 | 20 |
| Completed | 7 | 11 | 4 | 6 | 14 | 13 |
| Not Completed | 9 | 5 | 13 | 9 | 5 | 7 |
| Adverse Event | 1 | 1 | 2 | 0 | 1 | 3 |
| Withdrawal by Subject | 3 | 0 | 5 | 0 | 2 | 1 |

| | Segment 1: 200 mg ACH-0141625 for 28 Days | Segment 1: 400 mg ACH-0141625 for 28 Days | Segment 1: 800 mg ACH-0141625 for 28 Days | Segment 1: Placebo for 28 Days | Segment 2: 200 mg ACH-0141625 for 12 Weeks | Segment 2 - 400 mg ACH-0141625 for 12 Weeks |
|---|---|---|---|---|---|---|
| Lost to Follow-up | 3 | 1 | 0 | 2 | 1 | 0 |
| Physician Decision | 1 | 0 | 0 | 1 | 0 | 0 |
| Lack of Efficacy | 1 | 2 | 5 | 6 | 1 | 3 |
| compliance | 0 | 1 | 0 | 0 | 0 | 0 |
| Severe coronary atherosclerosis (death) | 0 | 0 | 1 | 0 | 0 | 0 |

| | Segment 2 - 800 mg ACH-0141625 for 12 Weeks |
|---|---|
| Started | 19 |
| Completed | 18 |
| Not Completed | 1 |
| Adverse Event | 0 |
| Withdrawal by Subject | 0 |
| Lost to Follow-up | 1 |
| Physician Decision | 0 |
| Lack of Efficacy | 0 |
| compliance | 0 |
| Severe coronary atherosclerosis (death) | 0 |

## Baseline Characteristics

Analysis Population Description

The intent-to-treat (ITT) population, which was defined as all subjects randomized and treated with at least one dose of ACH 0141625 or Placebo. Subjects were analyzed according to the randomized treatment.

Reporting Groups

| | Description |
|---|---|
| Segment 1: 200 mg ACH-0141625 | 200 mg ACH-0141625 for 28 days plus Peg-IFN alpha-2a and ribavirin for 48 weeks<br>ACH-0141625: 200 mg oral capsule once daily for 28 days or for 12 weeks<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection for 48 weeks<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily for 48 weeks |
| Segment 1: 400 mg ACH-0141625 | 400 mg ACH-0141625 for 28 days plus Peg-IFN alpha-2a plus ribavirin for 48 weeks<br>ACH-0141625: 400 mg oral capsule once daily for 28 days or for 12 weeks<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection for 48 weeks<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily for 48 weeks |
| Segment 1: 800 mg ACH-0141625 | 800 mg ACH-0141625 for 28 days plus Peg-IFN alpha-2a plus ribavirin for 48 weeks<br>ACH-0141625: 800 mg oral capsule once daily for 28 days or for 12 weeks<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection for 48 weeks<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily for 48 weeks |
| Segment 1: Placebo | Placebo for 28 days plus Peg-IFN alpha-2a plus ribavirin for 48 weeks<br>Placebo: Powder in capsule once daily for 28 days<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection for 48 weeks<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily for 48 weeks |
| Segment 2: 200 mg ACH-0141625 | 200 mg ACH-0141625 for 12 weeks plus Peg-IFN and ribavirin for up to a total of 48 weeks<br>ACH-0141625: 200 mg oral capsule once daily for 28 days or for 12 weeks<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection for 48 weeks<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily for 48 weeks |
| Segment 2 - 400 mg ACH-0141625 | 400 mg ACH-0141625 for 12 weeks plus Peg-IFN and ribavirin for up to a total of 48 weeks<br>ACH-0141625: 400 mg oral capsule once daily for 28 days or for 12 weeks<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection for 48 weeks<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily for 48 weeks |

| | Description |
|---|---|
| Segment 2 - 800 mg ACH-0141625 | 800 mg ACH-0141625 for 12 weeks plus Peg-IFN and ribavirin for up to a total of 48 weeks<br>ACH-0141625: 800 mg oral capsule once daily for 28 days or for 12 weeks<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection for 48 weeks<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily for 48 weeks |

Baseline Measures

| | Segment 1: 200 mg ACH-0141625 | Segment 1: 400 mg ACH-0141625 | Segment 1: 800 mg ACH-0141625 | Segment 1: Placebo | Segment 2: 200 mg ACH-0141625 | Segment 2 - 400 mg ACH-0141625 |
|---|---|---|---|---|---|---|
| Number of Participants | 16 | 16 | 17 | 15 | 19 | 20 |
| Age, Continuous<br>[units: years]<br>Mean (Standard Deviation) | 51 (7) | 51 (9) | 52 (13) | 47 (9) | 45 (11) | 48 (12) |
| Age, Categorical<br>[units: participants] | | | | | | |
| <=18 years | 0 | 0 | 0 | 0 | 0 | 0 |
| Between 18 and 65 years | 15 | 16 | 16 | 15 | 19 | 19 |
| >=65 years | 1 | 0 | 1 | 0 | 0 | 1 |
| Gender, Male/Female<br>[units: participants] | | | | | | |
| Female | 3 | 6 | 4 | 4 | 7 | 5 |
| Male | 13 | 10 | 13 | 11 | 12 | 15 |

| | Segment 2 - 800 mg ACH-0141625 |
|---|---|
| Number of Participants | 19 |
| Age, Continuous<br>[units: years]<br>Mean (Standard Deviation) | 42 (12) |
| Age, Categorical<br>[units: participants] | |
| <=18 years | 0 |

| | Segment 2 - 800 mg ACH-0141625 |
|---|---|
| Between 18 and 65 years | 19 |
| >=65 years | 0 |
| Gender, Male/Female [units: participants] | |
| Female | 9 |
| Male | 10 |

## Outcome Measures

1. Primary Outcome Measure:

| | |
|---|---|
| Measure Title | Segment 1: Safety |
| Measure Description | Segment 1: Percentage of subjects with the following: adverse events, abnormal laboratory safety tests, dose reductions, interruptions, and discontinuations. Criteria for abnormal laboratory safety tests: treatment-emergent worsening DAIDs graded laboratory tests. |
| Time Frame | 4 weeks |
| Safety Issue? | Yes |

Analysis Population Description

The safety population, which was defined as all subjects randomized and treated with at least one dose of ACH-0141625 or Placebo. Subjects were analyzed according to the randomized treatment.

Reporting Groups

| | Description |
|---|---|
| Segment 1: Placebo | Placebo for 28 days plus Peg-IFN alpha-2a plus ribavirin for 48 weeks<br>Placebo: Powder in capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily |

| | Description |
|---|---|
| Segment 1: 200 mg ACH-0141625 | 200 mg ACH-0141625 for 28 days plus Peg-IFN alpha-2a and ribavirin for 48 weeks<br>ACH-0141625: 200 mg oral capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection for<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily |
| Segment 1: 400 mg ACH-0141625 | 400 mg ACH-0141625 for 28 days plus Peg-IFN alpha-2a plus ribavirin for 48 weeks<br>ACH-0141625: 400 mg oral capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily |
| Segment 1: 800 mg ACH-0141625 | 800 mg ACH-0141625 for 28 days plus Peg-IFN alpha-2a plus ribavirin for 48 weeks<br>ACH-0141625: 800 mg oral capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily |

Measured Values

| | Segment 1: Placebo | Segment 1: 200 mg ACH-0141625 | Segment 1: 400 mg ACH-0141625 | Segment 1: 800 mg ACH-0141625 |
|---|---|---|---|---|
| Number of Participants Analyzed | 15 | 16 | 16 | 17 |
| Segment 1: Safety<br>[units: percentage of participants] | | | | |
| Adverse Events (%) | 93.3 | 100.0 | 93.8 | 100.0 |
| Abnormal Laboratories (%) | 100.0 | 100.0 | 100.0 | 94.0 |
| Dose Reductions (%) | 0 | 0 | 0 | 0 |
| Dose Interruptions (%) | 0 | 0 | 0 | 0 |
| Dose Discontinuations (%) | 0 | 6.0 | 0 | 6.0 |

2. Primary Outcome Measure:

| | |
|---|---|
| Measure Title | Segment 1 : Rapid Viral Response at Week 4 (RVR4) |

| | |
|---|---|
| Measure Description | The primary efficacy endpoint for Segment 1 of the study was the percentage of subjects in each treatment group achieving RVR at Week 4 (HCV RNA< or equal to LOQ at the Week 4 visit). |
| Time Frame | 4 weeks |
| Safety Issue? | No |

Analysis Population Description

Efficacy analysis was performed on the virology population (a subset of the ITT population) and included all subjects who had a baseline HCV RNA result and at least 1 post baseline HCV RNA result.

Reporting Groups

| | Description |
|---|---|
| Segment 1: Placebo | Placebo for 28 days plus Peg-IFN alpha-2a plus ribavirin for 48 weeks<br>Placebo: Powder in capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily |
| Segment 1: 200 mg ACH-0141625 | 200 mg ACH-0141625 for 28 days plus Peg-IFN alpha-2a and ribavirin for 48 weeks<br>ACH-0141625: 200 mg oral capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily |
| Segment 1: 400 mg ACH-0141625 | 400 mg ACH-0141625 for 28 days plus Peg-IFN alpha-2a plus ribavirin for 48 weeks<br>ACH-0141625: 400 mg oral capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily |
| Segment 1: 800 mg ACH-0141625 | 800 mg ACH-0141625 for 28 days plus Peg-IFN alpha-2a plus ribavirin for 48 weeks<br>ACH-0141625: 800 mg oral capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily |

Measured Values

| | Segment 1: Placebo | Segment 1: 200 mg ACH-0141625 | Segment 1: 400 mg ACH-0141625 | Segment 1: 800 mg ACH-0141625 |
|---|---|---|---|---|
| Number of Participants Analyzed | 15 | 16 | 16 | 17 |

| | Segment 1: Placebo | Segment 1: 200 mg ACH-0141625 | Segment 1: 400 mg ACH-0141625 | Segment 1: 800 mg ACH-0141625 |
|---|---|---|---|---|
| Segment 1 : Rapid Viral Response at Week 4 (RVR4)<br>[units: percentage of participants] | | | | |
| Rapid Virologic Response (%) | 20.0 | 75.0 | 75.0 | 76.5 |
| No Rapid Virologic Response (%) | 80.0 | 25.0 | 25.0 | 23.5 |

Statistical Analysis 1 for Segment 1 : Rapid Viral Response at Week 4 (RVR4)

| | | |
|---|---|---|
| Statistical Analysis Overview | Comparison Groups | Segment 1: Placebo, Segment 1: 200 mg ACH-0141625, Segment 1: 400 mg ACH-0141625, Segment 1: 800 mg ACH-0141625 |
| | Comments | The null hypothesis is no difference between proportions of subjects in each treatment group achieving RVR4 at Week 4 of the study, while the alternative hypothesis is that the proportion of subjects achieving RVR4 at Week 4 increases with increasing doses of ACH-0141625. |
| | Non-Inferiority or Equivalence Analysis? | No |
| | Comments | [Not specified] |

| | | |
|---|---|---|
| Statistical Test of Hypothesis | P-Value | 0.003 |
| | Comments | To control for multiplicity, proportion in each treatment group achieving RVR4 are analyzed using a Cochran–Armitage test for trend among the ordered groups: placebo (considered zero dose), 200 mg ACH-1625, 400 mg ACH-1625, and 800 mg ACH-1625. |
| | Method | Other [Exact Cohcran-Armitage test] |
| | Comments | Only if overall test for trend is significant are pairwise comparisons evaluated using p-values for the difference in proportions (placebo – active). |

Statistical Analysis 2 for Segment 1 : Rapid Viral Response at Week 4 (RVR4)

| | | |
|---|---|---|
| Statistical Analysis Overview | Comparison Groups | Segment 1: Placebo, Segment 1: 200 mg ACH-0141625 |
| | Comments | To control for multiplicity, proportion in each treatment group achieving RVR4 are analyzed using a Cochran-Armitage test for trend among the ordered groups: placebo (considered zero dose), 200 mg ACH-1625, 400 mg ACH-1625, and 800 mg ACH-1625. Only if overall test for trend is significant are pairwise comparisons evaluated using p-values for the difference in proportions (placebo - active). |
| | Non-Inferiority or Equivalence Analysis? | No |

| | | |
|---|---|---|
| | Comments | [Not specified] |

| | | |
|---|---|---|
| Statistical Test of Hypothesis | P-Value | 0.004 |
| | Comments | [Not specified] |
| | Method | Fisher Exact |
| | Comments | [Not specified] |

Statistical Analysis 3 for Segment 1 : Rapid Viral Response at Week 4 (RVR4)

| | | |
|---|---|---|
| Statistical Analysis Overview | Comparison Groups | Segment 1: Placebo, Segment 1: 400 mg ACH-0141625 |
| | Comments | To control for multiplicity, proportion in each treatment group achieving RVR4 are analyzed using a Cochran-Armitage test for trend among the ordered groups: placebo (considered zero dose), 200 mg ACH-1625, 400 mg ACH-1625, and 800 mg ACH-1625. Only if overall test for trend is significant are pairwise comparisons evaluated using p-values for the difference in proportions (placebo - active). |
| | Non-Inferiority or Equivalence Analysis? | No |
| | Comments | [Not specified] |

| | | |
|---|---|---|
| Statistical Test of Hypothesis | P-Value | 0.004 |
| | Comments | [Not specified] |
| | Method | Fisher Exact |
| | Comments | [Not specified] |

Statistical Analysis 4 for Segment 1 : Rapid Viral Response at Week 4 (RVR4)

| | | |
|---|---|---|
| Statistical Analysis Overview | Comparison Groups | Segment 1: Placebo, Segment 1: 800 mg ACH-0141625 |
| | Comments | To control for multiplicity, proportion in each treatment group achieving RVR4 are analyzed using a Cochran-Armitage test for trend among the ordered groups: placebo (considered zero dose), 200 mg ACH-1625, 400 mg ACH-1625, and 800 mg ACH-1625. Only if overall test for trend is significant are pairwise comparisons evaluated using p-values for the difference in proportions (placebo - active). |
| | Non-Inferiority or Equivalence Analysis? | No |
| | Comments | [Not specified] |

| | | |
|---|---|---|
| Statistical Test of Hypothesis | P-Value | 0.004 |
| | Comments | [Not specified] |

| | | |
|---|---|---|
| | Method | Fisher Exact |
| | Comments | [Not specified] |

3. Primary Outcome Measure:

| | |
|---|---|
| Measure Title | Segment 2: Safety |
| Measure Description | Segment 2: Percentage of Subjects with the following: adverse events, abnormal laboratory safety tests and dose reductions, interruptions and discontinuations. Criteria for abnormal laboratory safety tests: treatment-emergent worsening DAIDs graded laboratory tests. |
| Time Frame | 12 weeks |
| Safety Issue? | Yes |

Analysis Population Description

The safety population, which was defined as all subjects randomized and treated with at least one dose of ACH-0141625. Subjects were analyzed according to the randomized treatment.

Reporting Groups

| | Description |
|---|---|
| Segment 2: 200 mg ACH-0141625 | 200 mg ACH-0141625 for 12 weeks plus Peg-IFN alpha-2a and ribavirin for up to a total of 24 or 48 weeks<br>ACH-0141625: 200 mg oral capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily |
| Segment 2: 400 mg ACH-0141625 | 400 mg ACH-0141625 for 12 weeks plus Peg-IFN alpha-2a plus ribavirin for up to 24 or 48 weeks<br>ACH-0141625: 400 mg oral capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily |
| Segment 2: 800 mg ACH-0141625 | 800 mg ACH-0141625 for 12 weeks plus Peg-IFN alpha-2a plus ribavirin for up to 24 or 48 weeks<br>ACH-0141625: 800 mg oral capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily |

Measured Values

| | Segment 2: 200 mg ACH-0141625 | Segment 2: 400 mg ACH-0141625 | Segment 2: 800 mg ACH-0141625 |
|---|---|---|---|
| Number of Participants Analyzed | 19 | 20 | 19 |
| Segment 2: Safety<br>[units: percentage of participants] | | | |
| Adverse Events (%) | 94.7 | 85.0 | 100.0 |
| Abnormal Laboratories (%) | 100.0 | 95.0 | 100.0 |
| Dose Reductions (%) | 0 | 0 | 0 |
| Dose Interruptions (%) | 0 | 0 | 0 |
| Dose Discontinuations (%) | 6.0 | 20.0 | 0 |

4. Primary Outcome Measure:

| | |
|---|---|
| Measure Title | Segment 2: Complete Early Virologic Response (cEVR) |
| Measure Description | The primary efficacy endpoint for Segment 2 of the study was the percentage of subjects achieving cEVR (complete early virologic response), defined as undetectable HCV RNA at Week 12. |
| Time Frame | Week 12 |
| Safety Issue? | No |

Analysis Population Description

Per protocol virology population (a subset of the virology population) and included all randomized subjects who completed 12 weeks of ACH-0141625 dosing.

Reporting Groups

| | Description |
|---|---|
| Segment 2: 200 mg ACH-0141625 | 200 mg ACH-0141625 for 12 weeks plus Peg-IFN and ribavirin for up to a total of 24 or 48 weeks<br>ACH-0141625: 200 mg oral capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily |

| | Description |
|---|---|
| Segment 2 - 400 mg ACH-0141625 | 400 mg ACH-0141625 for 12 weeks plus Peg-IFN and ribavirin for up to a total of 24 or 48 weeks<br>ACH-0141625: 400 mg oral capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection<br>Ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily |
| Segment 2 - 800 mg ACH-0141625 | 800 mg ACH-0141625 for 12 weeks plus Peg-IFN and ribavirin for up to a total of 24 or 48 weeks<br>ACH-0141625: 800 mg oral capsule once daily for 28 days<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection<br>Ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily |

Measured Values

| | Segment 2: 200 mg ACH-0141625 | Segment 2 - 400 mg ACH-0141625 | Segment 2 - 800 mg ACH-0141625 |
|---|---|---|---|
| Number of Participants Analyzed | 18 | 16 | 19 |
| Segment 2: Complete Early Virologic Response (cEVR)<br>[units: percentage of participants] | 100.0 | 94.0 | 100.00 |

Statistical Analysis 1 for Segment 2: Complete Early Virologic Response (cEVR)

| | | |
|---|---|---|
| Statistical Analysis Overview | Comparison Groups | Segment 2: 200 mg ACH-0141625, Segment 2 - 400 mg ACH-0141625, Segment 2 - 800 mg ACH-0141625 |
| | Comments | The null hypothesis is no difference between proportions of subjects in each treatment group achieving cEVR at Week 12 of the study, while the alternative hypothesis is that the proportion of subjects achieving cEVR at Week 12 increases with increasing doses of ACH-0141625. |
| | Non-Inferiority or Equivalence Analysis? | No |
| | Comments | [Not specified] |

| | | |
|---|---|---|
| Statistical Test of Hypothesis | P-Value | 0.34 |
| | Comments | To control for multiplicity, proportion of subjects in each treatment group achieving cEVR are analyzed using a Cochran-Armitage test for trend among the ordered treatment groups: 200 mg ACH-1625, 400 mg ACH-1625, and 800 mg ACH-1625. |

| | | |
|---|---|---|
| | Method | Other [Exact Cochran-Armitage test] |
| | Comments | Only if overall test for trend is significant are pairwise comparisons evaluated using p-values for the difference in proportions (placebo - active). |

5. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Segment 1: Complete Early Virologic Response (cEVR) |
| Measure Description | For Segment 1, the percentage of subjects in the virology population that achieved cEVR (complete early virologic response), defined as undetectable HCV RNA at Week 12. |
| Time Frame | 12 weeks |
| Safety Issue? | No |

Analysis Population Description

Analysis for Segment 1 was performed on the virology population (which is the same as the ITT population) and included all subjects who had a baseline HCV RNA result and at least 1 post baseline HCV RNA result.

Reporting Groups

| | Description |
|---|---|
| Segment 1: 200 mg ACH-0141625 | 200 mg ACH-0141625 for 28 days plus Peg-IFN alpha-2a and ribavirin for 48 weeks<br>ACH-0141625: 200 mg oral capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily |
| Segment 1: 400 mg ACH-0141625 | 400 mg ACH-0141625 for 28 days plus Peg-IFN alpha-2a plus ribavirin for 48 weeks<br>ACH-0141625: 400 mg oral capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily |
| Segment 1: 800 mg ACH-0141625 | 800 mg ACH-0141625 for 28 days plus Peg-IFN alpha-2a plus ribavirin for 48 weeks<br>ACH-0141625: 800 mg oral capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily |

| | Description |
|---|---|
| Segment 1: Placebo | Placebo for 28 days plus Peg-IFN alpha-2a plus ribavirin for 48 weeks<br>Placebo: powder in capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily |

Measured Values

| | Segment 1: 200 mg ACH-0141625 | Segment 1: 400 mg ACH-0141625 | Segment 1: 800 mg ACH-0141625 | Segment 1: Placebo |
|---|---|---|---|---|
| Number of Participants Analyzed | 16 | 16 | 17 | 15 |
| Segment 1: Complete Early Virologic Response (cEVR)<br>[units: percentage of participants] | 62.5 | 75.0 | 70.6 | 33.3 |

6. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Segment 2: RVR4 (Rapid Viral Response at 4 Weeks) |
| Measure Description | For Segment 2, the percentage of subjects in the virology population that achieved RVR4, defined as HCV RNA< or equal to LOQ at the Week 4 visit. |
| Time Frame | 4 weeks |
| Safety Issue? | No |

Analysis Population Description

Per protocol virology population (a subset of the virology population) and included all randomized subjects who completed 4 weeks of ACH-0141625 dosing.

Reporting Groups

| | Description |
|---|---|
| Segment 2: 200 mg ACH-0141625 | 200 mg ACH-0141625 for 12 weeks plus Peg-IFN alpha-2a and ribavirin for 48 weeks<br>ACH-0141625: 200 mg oral capsule once daily for 28 days or for 12 weeks<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection for 48 weeks<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily for 48 weeks |

| | Description |
|---|---|
| Segment 2: 400 mg ACH-0141625 | 400 mg ACH-0141625 for 12 weeks plus Peg-IFN alpha-2a plus ribavirin for 48 weeks<br>ACH-0141625: 400 mg oral capsule once daily for 28 days or for 12 weeks<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection for 48 weeks<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily for 48 weeks |
| Segment 2: 800 mg ACH-0141625 | 800 mg ACH-0141625 for 12 weeks plus Peg-IFN alpha-2a plus ribavirin for 48 weeks<br>ACH-0141625: 800 mg oral capsule once daily for 28 days or for 12 weeks<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection for 48 weeks<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily for 48 weeks |

Measured Values

| | Segment 2: 200 mg ACH-0141625 | Segment 2: 400 mg ACH-0141625 | Segment 2: 800 mg ACH-0141625 |
|---|---|---|---|
| Number of Participants Analyzed | 19 | 18 | 19 |
| Segment 2: RVR4 (Rapid Viral Response at 4 Weeks)<br>[units: percentage of participants] | 78.9 | 88.8 | 89.5 |

7. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Segment 1 and Segment 2: End of Treatment Response |
| Measure Description | The percentage of the Virology Population subjects that were reported as undetectable HCV RNA at the completion of treatment. |
| Time Frame | Week 48 (Segment 1); Week 24 (Segment 2) |
| Safety Issue? | No |

Analysis Population Description

Segment 2 analyzed the Per Protocol Population, which includes all randomized subjects who completed 12 weeks of ACH-014625 dosing and an additional 12 weeks of Peg/Ribavirin dosing.

Reporting Groups

| | Description |
|---|---|
| Segment 1: 200 mg ACH-0141625 | 200 mg ACH-0141625 for 28 days plus Peg-IFN alpha-2a and ribavirin for 48 weeks<br>ACH-0141625: 200 mg oral capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily |
| Segment 1: 400 mg ACH-0141625 | 400 mg ACH-0141625 for 28 days plus Peg-IFN alpha-2a plus ribavirin for 48 weeks<br>ACH-0141625: 400 mg oral capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily |
| Segment 1: 800 mg ACH-0141625 | 800 mg ACH-0141625 for 28 days plus Peg-IFN alpha-2a plus ribavirin for 48 weeks<br>ACH-0141625: 800 mg oral capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily |
| Segment 1: Placebo | Placebo for 28 days plus Peg-IFN alpha-2a plus ribavirin for 48 weeks<br>Placebo: Powder in capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily |
| Segment 2: 200 mg ACH-0141625 | 200 mg ACH-0141625 for 12 weeks plus Peg-IFN and ribavirin for up to a total of 24 or 48 weeks<br>ACH-0141625: 200 mg oral capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily |
| Segment 2: 400 mg ACH-0141625 | 400 mg ACH-0141625 for 12 weeks plus Peg-IFN and ribavirin for up to a total of 24 or 48 weeks<br>ACH-0141625: 400 mg oral capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily |

| | Description |
|---|---|
| Segment 2: 800 mg ACH-0141625 | 800 mg ACH-0141625 for 12 weeks plus Peg-IFN and ribavirin for up to a total of 24 or 48 weeks<br>ACH-0141625: 800 mg oral capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily |

Measured Values

| | Segment 1: 200 mg ACH-0141625 | Segment 1: 400 mg ACH-0141625 | Segment 1: 800 mg ACH-0141625 | Segment 1: Placebo | Segment 2: 200 mg ACH-0141625 | Segment 2: 400 mg ACH-0141625 |
|---|---|---|---|---|---|---|
| Number of Participants Analyzed | 16 | 16 | 17 | 15 | 12 | 13 |
| Segment 1 and Segment 2: End of Treatment Response<br>[units: percentage of participants] | 75.0 | 75.0 | 64.7 | 53.3 | 100.0 | 92.3 |

| | Segment 2: 800 mg ACH-0141625 |
|---|---|
| Number of Participants Analyzed | 14 |
| Segment 1 and Segment 2: End of Treatment Response<br>[units: percentage of participants] | 100.0 |

8. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Segment 1 and Segment 2: Sustained Virologic Response 12 Weeks ( Three Months Post Dosing) (SVR12) |
| Measure Description | The percentage of the Virology Population subjects that achieved sustained virologic response, defined as HCV RNA < LOQ, at 12 weeks (three months) post dosing. |
| Time Frame | 3 months post dosing |
| Safety Issue? | No |

Analysis Population Description

Segment 2 analyzed the Per Protocol Population (PPP=all randomized subjects completing 12 wks of ACH-014625 + an extra 12 wks of Peg/RBV) who returned for SVR12.

Reporting Groups

| | Description |
|---|---|
| Segment 1: 200 mg ACH-0141625 | 200 mg ACH-0141625 for 28 days plus Peg-IFN alpha-2a and ribavirin for 48 weeks<br>ACH-0141625: 200 mg oral capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily |
| Segment 1: 400 mg ACH-0141625 | 400 mg ACH-0141625 for 28 days plus Peg-IFN alpha-2a plus ribavirin<br>ACH-0141625: 400 mg oral capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily |
| Segment 1: 800 mg ACH-0141625 | 800 mg ACH-0141625 for 28 days plus Peg-IFN alpha-2a plus ribavirin for 48 weeks<br>ACH-0141625: 800 mg oral capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily |
| Segment 1: Placebo | Placebo for 28 days plus Peg-IFN alpha-2a plus ribavirin for 48 weeks<br>Placebo: Powder in capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily |
| Segment 2: 200 mg ACH-0141625 | 200 mg ACH-0141625 for 12 weeks plus Peg-IFN and ribavirin for up to a total of 24 or 48 weeks<br>ACH-0141625: 200 mg oral capsule once daily for<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily |
| Segment 2 - 400 mg ACH-0141625 | 400 mg ACH-0141625 for 12 weeks plus Peg-IFN and ribavirin for up to a total of 24 or 48 weeks<br>ACH-0141625: 400 mg oral capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily |

| | Description |
|---|---|
| Segment 2 - 800 mg ACH-0141625 | 800 mg ACH-0141625 for 12 weeks plus Peg-IFN and ribavirin for up to a total of 24 or 48 weeks<br>ACH-0141625: 800 mg oral capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily |

Measured Values

| | Segment 1: 200 mg ACH-0141625 | Segment 1: 400 mg ACH-0141625 | Segment 1: 800 mg ACH-0141625 | Segment 1: Placebo | Segment 2: 200 mg ACH-0141625 | Segment 2 - 400 mg ACH-0141625 |
|---|---|---|---|---|---|---|
| Number of Participants Analyzed | 16 | 16 | 17 | 15 | 10 | 13 |
| Segment 1 and Segment 2: Sustained Virologic Response 12 Weeks ( Three Months Post Dosing) (SVR12)<br>[units: percentage of participants] | 56.3 | 56.3 | 35.3 | 40.0 | 80.0 | 76.9 |

| | Segment 2 - 800 mg ACH-0141625 |
|---|---|
| Number of Participants Analyzed | 13 |
| Segment 1 and Segment 2: Sustained Virologic Response 12 Weeks ( Three Months Post Dosing) (SVR12)<br>[units: percentage of participants] | 84.5 |

9. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Segment 1 and Segment 2: Sustained Virologic Response ( Six Months Post Dosing) (SVR24) |
| Measure Description | The percentage of the Virology Population subjects that achieved sustained virologic response, defined as HCV RNA < LOQ, six months post dosing. |
| Time Frame | 6 months post dosing |
| Safety Issue? | No |

Analysis Population Description

Segment 2 analyzed the Per Protocol Population (PPP=all randomized subjects completing 12 wks of ACH-014625 + an extra 12 wks of Peg/RBV) who returned for SVR24.

Reporting Groups

| | Description |
|---|---|
| Segment 1: 200 mg ACH-0141625 | 200 mg ACH-0141625 for 28 days plus Peg-IFN alpha-2a and ribavirin for 48 weeks<br>ACH-0141625: 200 mg oral capsule once daily for 28 days or for 12 weeks<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection for 48 weeks<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily for 48 weeks |
| Segment 1: 400 mg ACH-0141625 | 400 mg ACH-0141625 for 28 days plus Peg-IFN alpha-2a plus ribavirin for 48 weeks<br>ACH-0141625: 400 mg oral capsule once daily for 28 days or for 12 weeks<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection for 48 weeks<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily for 48 weeks |
| Segment 1: 800 mg ACH-0141625 | 800 mg ACH-0141625 for 28 days plus Peg-IFN alpha-2a plus ribavirin for 48 weeks<br>ACH-0141625: 800 mg oral capsule once daily for 28 days or for 12 weeks<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection for 48 weeks<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily for 48 weeks |
| Segment 1: Placebo | Placebo for 28 days plus Peg-IFN alpha-2a plus ribavirin for 48 weeks<br>Placebo: Powder in capsule once daily for 28 days<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection for 48 weeks<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily for 48 weeks |
| Segment 2: 200 mg ACH-0141625 | 200 mg ACH-0141625 for 12 weeks plus Peg-IFN and ribavirin for up to a total of 48 weeks<br>ACH-0141625: 200 mg oral capsule once daily for 28 days or for 12 weeks<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection for 48 weeks<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily for 48 weeks |
| Segment 2: 400 mg ACH-0141625 | 400 mg ACH-0141625 for 12 weeks plus Peg-IFN and ribavirin for up to a total of 48 weeks<br>ACH-0141625: 400 mg oral capsule once daily for 28 days or for 12 weeks<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection for 48 weeks<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily for 48 weeks |

| | Description |
|---|---|
| Segment 2 : 800 mg ACH-0141625 | 800 mg ACH-0141625 for 12 weeks plus Peg-IFN and ribavirin for up to a total of 48 weeks<br>ACH-0141625: 800 mg oral capsule once daily for 28 days or for 12 weeks<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection for 48 weeks<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily for 48 weeks |

Measured Values

| | Segment 1: 200 mg ACH-0141625 | Segment 1: 400 mg ACH-0141625 | Segment 1: 800 mg ACH-0141625 | Segment 1: Placebo | Segment 2: 200 mg ACH-0141625 | Segment 2: 400 mg ACH-0141625 |
|---|---|---|---|---|---|---|
| Number of Participants Analyzed | 16 | 16 | 17 | 15 | 10 | 13 |
| Segment 1 and Segment 2: Sustained Virologic Response ( Six Months Post Dosing) (SVR24)<br>[units: percentage of participants] | 62.5 | 56.3 | 35.3 | 40.0 | 70.0 | 76.9 |

| | Segment 2 : 800 mg ACH-0141625 |
|---|---|
| Number of Participants Analyzed | 12 |
| Segment 1 and Segment 2: Sustained Virologic Response ( Six Months Post Dosing) (SVR24)<br>[units: percentage of participants] | 83.3 |

10. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Segment 1 and Segment 2: HCV RNA Change From Baseline |
| Measure Description | The mean change from baseline in log10 HCV RNA level by visit for the virology population |
| Time Frame | Week 4 |
| Safety Issue? | No |

Analysis Population Description

Efficacy analysis was performed on the virology population, which was a subset of the ITT population and included all subjects who had a baseline HCV RNA result and at least 1 post baseline HCV RNA result

Reporting Groups

| | Description |
|---|---|
| Segment 1: 200 mg ACH-0141625 | 200 mg ACH-0141625 for 28 days plus Peg-IFN alpha-2a and ribavirin for 48 weeks<br>ACH-0141625: 200 mg oral capsule once daily for 28 days or for 12 weeks<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection for 48 weeks<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily for 48 weeks |
| Segment 1: 400 mg ACH-0141625 | 400 mg ACH-0141625 for 28 days plus Peg-IFN alpha-2a plus ribavirin for 48 weeks<br>ACH-0141625: 400 mg oral capsule once daily for 28 days or for 12 weeks<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection for 48 weeks<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily for 48 weeks |
| Segment 1: 800 mg ACH-0141625 | 800 mg ACH-0141625 for 28 days plus Peg-IFN alpha-2a plus ribavirin for 48 weeks<br>ACH-0141625: 800 mg oral capsule once daily for 28 days or for 12 weeks<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection for 48 weeks<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily for 48 weeks |
| Segment 1: Placebo | Placebo for 28 days plus Peg-IFN alpha-2a plus ribavirin for 48 weeks<br>Placebo: Powder in capsule once daily for 28 days<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection for 48 weeks<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily for 48 weeks |
| Segment 2: 200 mg ACH-0141625 | 200 mg ACH-0141625 for 12 weeks plus Peg-IFN and ribavirin for up to a total of 48 weeks<br>ACH-0141625: 200 mg oral capsule once daily for 28 days or for 12 weeks<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection for 48 weeks<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily for 48 weeks |
| Segment 2 - 400 mg ACH-0141625 | 400 mg ACH-0141625 for 12 weeks plus Peg-IFN and ribavirin for up to a total of 48 weeks<br>ACH-0141625: 400 mg oral capsule once daily for 28 days or for 12 weeks<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection for 48 weeks<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily for 48 weeks |

| | Description |
|---|---|
| Segment 2 - 800 mg ACH-0141625 | 800 mg ACH-0141625 for 12 weeks plus Peg-IFN and ribavirin for up to a total of 48 weeks<br>ACH-0141625: 800 mg oral capsule once daily for 28 days or for 12 weeks<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection for 48 weeks<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily for 48 weeks |

Measured Values

| | Segment 1: 200 mg ACH-0141625 | Segment 1: 400 mg ACH-0141625 | Segment 1: 800 mg ACH-0141625 | Segment 1: Placebo | Segment 2: 200 mg ACH-0141625 | Segment 2 - 400 mg ACH-0141625 |
|---|---|---|---|---|---|---|
| Number of Participants Analyzed | 13 | 15 | 16 | 15 | 19 | 18 |
| Segment 1 and Segment 2: HCV RNA Change From Baseline<br>[units: log10 HCV RNA Level]<br>Mean (Standard Deviation) | -4.94 (0.993) | -4.60 (1.462) | -4.94 (1.098) | -2.22 (1.447) | -4.74 (1.072) | -5.04 (0.738) |

| | Segment 2 - 800 mg ACH-0141625 |
|---|---|
| Number of Participants Analyzed | 19 |
| Segment 1 and Segment 2: HCV RNA Change From Baseline<br>[units: log10 HCV RNA Level]<br>Mean (Standard Deviation) | -4.51 (0.941) |

11. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Segment 1 and Segment 2: HCV RNA Change From Baseline |
| Measure Description | Change from baseline in log10 HCV RNA level by visit. |
| Time Frame | Week 12 |
| Safety Issue? | No |

Analysis Population Description

Efficacy analysis was performed on the virology population , which was a subset of the ITT population and included all subjects who had a baseline HCV RNA result and at least 1 post baseline HCV RNA result

Reporting Groups

| | Description |
|---|---|
| Segment 1: 200 mg ACH-0141625 | 200 mg ACH-0141625 for 28 days plus Peg-IFN alpha-2a and ribavirin for 48 weeks<br>ACH-0141625: 200 mg oral capsule once daily for 28 days or for 12 weeks<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection for 48 weeks<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily for 48 weeks |
| Segment 1: 400 mg ACH-0141625 | 400 mg ACH-0141625 for 28 days plus Peg-IFN alpha-2a plus ribavirin for 48 weeks<br>ACH-0141625: 400 mg oral capsule once daily for 28 days or for 12 weeks<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection for 48 weeks<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily for 48 weeks |
| Segment 1: 800 mg ACH-0141625 | 800 mg ACH-0141625 for 28 days plus Peg-IFN alpha-2a plus ribavirin for 48 weeks<br>ACH-0141625: 800 mg oral capsule once daily for 28 days or for 12 weeks<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection for 48 weeks<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily for 48 weeks |
| Segment 1: Placebo | Placebo for 28 days plus Peg-IFN alpha-2a plus ribavirin for 48 weeks<br>Placebo: Powder in capsule once daily for 28 days<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection for 48 weeks<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily for 48 weeks |
| Segment 2: 200 mg ACH-0141625 | 200 mg ACH-0141625 for 12 weeks plus Peg-IFN and ribavirin for up to a total of 48 weeks<br>ACH-0141625: 200 mg oral capsule once daily for 28 days or for 12 weeks<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection for 48 weeks<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily for 48 weeks |
| Segment 2 - 400 mg ACH-0141625 | 400 mg ACH-0141625 for 12 weeks plus Peg-IFN and ribavirin for up to a total of 48 weeks<br>ACH-0141625: 400 mg oral capsule once daily for 28 days or for 12 weeks<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection for 48 weeks<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily for 48 weeks |

| | Description |
|---|---|
| Segment 2 - 800 mg ACH-0141625 | 800 mg ACH-0141625 for 12 weeks plus Peg-IFN and ribavirin for up to a total of 48 weeks<br>ACH-0141625: 800 mg oral capsule once daily for 28 days or for 12 weeks<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection for 48 weeks<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily for 48 weeks |

Measured Values

| | Segment 1: 200 mg ACH-0141625 | Segment 1: 400 mg ACH-0141625 | Segment 1: 800 mg ACH-0141625 | Segment 1: Placebo | Segment 2: 200 mg ACH-0141625 | Segment 2 - 400 mg ACH-0141625 |
|---|---|---|---|---|---|---|
| Number of Participants Analyzed | 13 | 14 | 11 | 15 | 18 | 16 |
| Segment 1 and Segment 2: HCV RNA Change From Baseline<br>[units: log10 HCV RNA level]<br>Mean (Standard Deviation) | -5.13 (0.518) | -4.51 (1.467) | -4.67 (1.555) | -3.48 (1.753) | -4.90 (1.104) | -5.08 (0.770) |

| | Segment 2 - 800 mg ACH-0141625 |
|---|---|
| Number of Participants Analyzed | 18 |
| Segment 1 and Segment 2: HCV RNA Change From Baseline<br>[units: log10 HCV RNA level]<br>Mean (Standard Deviation) | -4.58 (0.946) |

## Reported Adverse Events

| | |
|---|---|
| Time Frame | Adverse events data collected through end of treatment plus 4 weeks. |
| Additional Description | Treatment-emergent AEs presented: Day 1 through end of ACH-0141625/placebo treatment period plus 14 days. All SAEs reported during the study period are presented. |

Reporting Groups

| | Description |
|---|---|
| Segment 1: 200 mg ACH-0141625 | 200 mg ACH-0141625 for 28 days plus Peg-IFN alpha-2a and ribavirin for 48 weeks<br>ACH-0141625: 200 mg oral capsule<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily |
| Segment 1: 400 mg ACH-0141625 | 400 mg ACH-0141625 for 28 days plus Peg-IFN alpha-2a plus ribavirin for 48 weeks<br>ACH-0141625: 400 mg oral capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily for 48 weeks |
| Segment 1: 800 mg ACH-0141625 | 800 mg ACH-0141625 for 28 days plus Peg-IFN alpha-2a plus ribavirin for 48 weeks<br>ACH-0141625: 800 mg oral capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily |
| Segment 2: 200 mg ACH-0141625 | 200 mg ACH-0141625 for 12 weeks plus Peg-IFN and ribavirin for up to a total of 24 or 48 weeks<br>ACH-0141625: 200 mg oral capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily |
| Segment 2 - 400 mg ACH-0141625 | 400 mg ACH-0141625 for 12 weeks plus Peg-IFN and ribavirin for up to a total of 24 or 48 weeks<br>ACH-0141625: 400 mg oral capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily |
| Segment 2 - 800 mg ACH-0141625 | 800 mg ACH-0141625 for 12 weeks plus Peg-IFN and ribavirin for up to a total of 24 or 48 weeks<br>ACH-0141625: 800 mg oral capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily |

| | Description |
|---|---|
| Segment 1 - Placebo | Placebo for 28 days plus Peg-IFN alpha-2a plus ribavirin for 48 weeks<br>Placebo: Powder in capsule once daily<br>Pegylated Interferon alpha-2a: 180 ug once a week by subcutaneous injection<br>ribavirin: 400 mg or 600 mg (am) and 600 mg (pm) capsules taken orally twice daily |

Serious Adverse Events

| | Segment 1: 200 mg ACH-0141625 | | Segment 1: 400 mg ACH-0141625 | | Segment 1: 800 mg ACH-0141625 | | Segment 2: 200 mg ACH-0141625 | | Segment 2 - 400 mg ACH-0141625 | | Segment 2 - 800 mg ACH-0141625 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events |
| Total | 2/16 (12.5%) | | 1/16 (6.25%) | | 5/17 (29.41%) | | 0/19 (0%) | | 2/20 (10%) | | 0/19 (0%) | |
| Cardiac disorders | | | | | | | | | | | | |
| Severe Coronary Atherosclerosis MI (death) [A] † | 0/16 (0%) | 0 | 0/16 (0%) | 0 | 1/17 (5.88%) | 1 | 0/19 (0%) | 0 | 0/20 (0%) | 0 | 0/19 (0%) | 0 |
| Gastrointestinal disorders | | | | | | | | | | | | |
| Ischemic Colitis [A] † | 1/16 (6.25%) | 1 | 0/16 (0%) | 0 | 0/17 (0%) | 0 | 0/19 (0%) | 0 | 0/20 (0%) | 0 | 0/19 (0%) | 0 |
| General disorders | | | | | | | | | | | | |
| Chest Pain [A] † | 0/16 (0%) | 0 | 1/16 (6.25%) | 1 | 0/17 (0%) | 0 | 0/19 (0%) | 0 | 0/20 (0%) | 0 | 0/19 (0%) | 0 |
| Infections and infestations | | | | | | | | | | | | |
| Bacteremia [A] † | 1/16 (6.25%) | 1 | 0/16 (0%) | 0 | 0/17 (0%) | 0 | 0/19 (0%) | 0 | 0/20 (0%) | 0 | 0/19 (0%) | 0 |
| Nervous system disorders | | | | | | | | | | | | |
| Syncope [A] † | 0/16 (0%) | 0 | 0/16 (0%) | 0 | 1/17 (5.88%) | 1 | 0/19 (0%) | 0 | 0/20 (0%) | 0 | 0/19 (0%) | 0 |
| Psychiatric disorders | | | | | | | | | | | | |
| Depression [A] † | 0/16 (0%) | 0 | 0/16 (0%) | 0 | 0/17 (0%) | 0 | 0/19 (0%) | 0 | 1/20 (5%) | 1 | 0/19 (0%) | 0 |

| | Segment 1: 200 mg ACH-0141625 | | Segment 1: 400 mg ACH-0141625 | | Segment 1: 800 mg ACH-0141625 | | Segment 2: 200 mg ACH-0141625 | | Segment 2 - 400 mg ACH-0141625 | | Segment 2 - 800 mg ACH-0141625 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events |
| Exacerbation of schizophrenia [A] † | 0/16 (0%) | 0 | 0/16 (0%) | 0 | 1/17 (5.88%) | 1 | 0/19 (0%) | 0 | 0/20 (0%) | 0 | 0/19 (0%) | 0 |
| Mania [A] * | 0/16 (0%) | 0 | 0/16 (0%) | 0 | 0/17 (0%) | 0 | 0/19 (0%) | 0 | 1/20 (5%) | 1 | 0/19 (0%) | 0 |
| Respiratory, thoracic and mediastinal disorders | | | | | | | | | | | | |
| Pulmonary Embolism [A] † | 0/16 (0%) | 0 | 0/16 (0%) | 0 | 1/17 (5.88%) | 1 | 0/19 (0%) | 0 | 0/20 (0%) | 0 | 0/19 (0%) | 0 |
| Vascular disorders | | | | | | | | | | | | |
| Left Lower Extremity Deep Vein Thrombosis [A] † | 0/16 (0%) | 0 | 0/16 (0%) | 0 | 1/17 (5.88%) | 1 | 0/19 (0%) | 0 | 0/20 (0%) | 0 | 0/19 (0%) | 0 |

† Indicates events were collected by systematic assessment.
* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA 12.1

| | Segment 1 - Placebo | |
|---|---|---|
| | Affected/At Risk (%) | # Events |
| Total | 0/15 (0%) | |
| Cardiac disorders | | |
| Severe Coronary Atherosclerosis MI (death) [A] † | 0/15 (0%) | 0 |
| Gastrointestinal disorders | | |
| Ischemic Colitis [A] † | 0/15 (0%) | 0 |
| General disorders | | |
| Chest Pain [A] † | 0/15 (0%) | 0 |
| Infections and infestations | | |
| Bacteremia [A] † | 0/15 (0%) | 0 |

| | Segment 1 - Placebo | |
|---|---|---|
| | Affected/At Risk (%) | # Events |
| Nervous system disorders | | |
| Syncope [A] † | 0/15 (0%) | 0 |
| Psychiatric disorders | | |
| Depression [A] † | 0/15 (0%) | 0 |
| Exacerbation of schizophrenia [A] † | 0/15 (0%) | 0 |
| Mania [A] * | 0/15 (0%) | 0 |
| Respiratory, thoracic and mediastinal disorders | | |
| Pulmonary Embolism [A] † | 0/15 (0%) | 0 |
| Vascular disorders | | |
| Left Lower Extremity Deep Vein Thrombosis [A] † | 0/15 (0%) | 0 |

† Indicates events were collected by systematic assessment.
* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA 12.1

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 0%

| | Segment 1: 200 mg ACH-0141625 | | Segment 1: 400 mg ACH-0141625 | | Segment 1: 800 mg ACH-0141625 | | Segment 2: 200 mg ACH-0141625 | | Segment 2 - 400 mg ACH-0141625 | | Segment 2 - 800 mg ACH-0141625 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events |
| Total | 16/16 (100%) | | 15/16 (93.75%) | | 17/17 (100%) | | 18/19 (94.74%) | | 17/20 (85%) | | 19/19 (100%) | |
| Blood and lymphatic system disorders | | | | | | | | | | | | |
| Anaemia [A] † | 0/16 (0%) | | 4/16 (25%) | | 3/17 (17.65%) | | 2/19 (10.53%) | | 1/20 (5%) | | 2/19 (10.53%) | |
| Haemoglobinaemia [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 1/19 (5.26%) | | 0/20 (0%) | | 0/19 (0%) | |
| Haemolytic anaemia [A] † | 0/16 (0%) | | 2/16 (12.5%) | | 1/17 (5.88%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |

| | Segment 1: 200 mg ACH-0141625 | | Segment 1: 400 mg ACH-0141625 | | Segment 1: 800 mg ACH-0141625 | | Segment 2: 200 mg ACH-0141625 | | Segment 2 - 400 mg ACH-0141625 | | Segment 2 - 800 mg ACH-0141625 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events |
| Leukopenia [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 1/19 (5.26%) | | 0/20 (0%) | | 2/19 (10.53%) | |
| Neutropenia [A] † | 1/16 (6.25%) | | 2/16 (12.5%) | | 3/17 (17.65%) | | 2/19 (10.53%) | | 5/20 (25%) | | 5/19 (26.32%) | |
| Thrombocytopenia [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 1/19 (5.26%) | | 0/20 (0%) | | 2/19 (10.53%) | |
| Cardiac disorders | | | | | | | | | | | | |
| Palpitations [A] † | 0/16 (0%) | | 0/16 (0%) | | 1/17 (5.88%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Ear and labyrinth disorders | | | | | | | | | | | | |
| Ear discomfort [A] † | 1/16 (6.25%) | | 1/16 (6.25%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Ear pain [A] † | 0/16 (0%) | | 1/16 (6.25%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 1/19 (5.26%) | |
| Tinnitus [A] † | 0/16 (0%) | | 0/16 (0%) | | 1/17 (5.88%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Vertigo [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 1/19 (5.26%) | |
| Endocrine disorders | | | | | | | | | | | | |
| Thyroid disorder [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 1/19 (5.26%) | | 0/20 (0%) | | 0/19 (0%) | |
| Eye disorders | | | | | | | | | | | | |
| Abnormal sensation in eye [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 1/20 (5%) | | 0/19 (0%) | |
| Conjunctivitis [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 1/20 (5%) | | 0/19 (0%) | |
| Dry eye [A] † | 0/16 (0%) | | 0/16 (0%) | | 1/17 (5.88%) | | 0/19 (0%) | | 1/20 (5%) | | 0/19 (0%) | |
| Eye irritation [A] † | 0/16 (0%) | | 0/16 (0%) | | 1/17 (5.88%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |

| | Segment 1: 200 mg ACH-0141625 | | Segment 1: 400 mg ACH-0141625 | | Segment 1: 800 mg ACH-0141625 | | Segment 2: 200 mg ACH-0141625 | | Segment 2 - 400 mg ACH-0141625 | | Segment 2 - 800 mg ACH-0141625 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events |
| Eye pain [A] † | 0/16 (0%) | | 0/16 (0%) | | 1/17 (5.88%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Eye pruritus [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 1/20 (5%) | | 0/19 (0%) | |
| Photophobia [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Vision blurred [A] † | 0/16 (0%) | | 2/16 (12.5%) | | 1/17 (5.88%) | | 0/19 (0%) | | 1/20 (5%) | | 0/19 (0%) | |
| Gastrointestinal disorders | | | | | | | | | | | | |
| Abdominal distension [A] † | 1/16 (6.25%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Abdominal pain [A] † | 1/16 (6.25%) | | 2/16 (12.5%) | | 2/17 (11.76%) | | 1/19 (5.26%) | | 0/20 (0%) | | 0/19 (0%) | |
| Abdominal pain upper [A] † | 2/16 (12.5%) | | 2/16 (12.5%) | | 1/17 (5.88%) | | 2/19 (10.53%) | | 1/20 (5%) | | 0/19 (0%) | |
| Abdominal tenderness [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 2/19 (10.53%) | |
| Anal fissure [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 1/19 (5.26%) | | 0/20 (0%) | | 0/19 (0%) | |
| Aphthous stomatitis [A] † | 0/16 (0%) | | 0/16 (0%) | | 2/17 (11.76%) | | 1/19 (5.26%) | | 0/20 (0%) | | 1/19 (5.26%) | |
| Breath odour [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 1/19 (5.26%) | |
| Constipation [A] † | 0/16 (0%) | | 0/16 (0%) | | 1/17 (5.88%) | | 2/19 (10.53%) | | 1/20 (5%) | | 1/19 (5.26%) | |
| Dental caries [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 1/20 (5%) | | 0/19 (0%) | |
| Diarrhoea [A] † | 5/16 (31.25%) | | 3/16 (18.75%) | | 4/17 (23.53%) | | 1/19 (5.26%) | | 2/20 (10%) | | 0/19 (0%) | |

| | Segment 1: 200 mg ACH-0141625 | | Segment 1: 400 mg ACH-0141625 | | Segment 1: 800 mg ACH-0141625 | | Segment 2: 200 mg ACH-0141625 | | Segment 2 - 400 mg ACH-0141625 | | Segment 2 - 800 mg ACH-0141625 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events |
| Dry mouth [A] † | 2/16 (12.5%) | | 2/16 (12.5%) | | 0/17 (0%) | | 0/19 (0%) | | 1/20 (5%) | | 1/19 (5.26%) | |
| Dyspepsia [A] † | 3/16 (18.75%) | | 1/16 (6.25%) | | 1/17 (5.88%) | | 3/19 (15.79%) | | 1/20 (5%) | | 1/19 (5.26%) | |
| Flatulence [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 1/19 (5.26%) | |
| Frequent bowel movements [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 1/20 (5%) | | 0/19 (0%) | |
| Gastrooesophageal reflux disease [A] † | 1/16 (6.25%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 2/20 (10%) | | 0/19 (0%) | |
| Gingival pain [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 1/19 (5.26%) | |
| Gingivitis [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Glossodynia [A] † | 0/16 (0%) | | 0/16 (0%) | | 1/17 (5.88%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Haemorrhoids [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 1/19 (5.26%) | |
| Lip ulceration [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 1/19 (5.26%) | | 0/20 (0%) | | 0/19 (0%) | |
| Nausea [A] † | 5/16 (31.25%) | | 5/16 (31.25%) | | 8/17 (47.06%) | | 5/19 (26.32%) | | 9/20 (45%) | | 12/19 (63.16%) | |
| Stomatitis [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 1/19 (5.26%) | | 0/20 (0%) | | 0/19 (0%) | |
| Toothache [A] † | 1/16 (6.25%) | | 0/16 (0%) | | 0/17 (0%) | | 1/19 (5.26%) | | 0/20 (0%) | | 1/19 (5.26%) | |
| Vomiting [A] † | 1/16 (6.25%) | | 2/16 (12.5%) | | 2/17 (11.76%) | | 2/19 (10.53%) | | 2/20 (10%) | | 1/19 (5.26%) | |
| General disorders | | | | | | | | | | | | |

| | Segment 1: 200 mg ACH-0141625 | | Segment 1: 400 mg ACH-0141625 | | Segment 1: 800 mg ACH-0141625 | | Segment 2: 200 mg ACH-0141625 | | Segment 2 - 400 mg ACH-0141625 | | Segment 2 - 800 mg ACH-0141625 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events |
| Application site erythema [A] † | 0/16 (0%) | | 1/16 (6.25%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Asthenia [A] † | 0/16 (0%) | | 1/16 (6.25%) | | 0/17 (0%) | | 0/19 (0%) | | 1/20 (5%) | | 0/19 (0%) | |
| Chest pain [A] † | 0/16 (0%) | | 1/16 (6.25%) | | 0/17 (0%) | | 1/19 (5.26%) | | 0/20 (0%) | | 2/19 (10.53%) | |
| Chills [A] † | 2/16 (12.5%) | | 2/16 (12.5%) | | 3/17 (17.65%) | | 1/19 (5.26%) | | 1/20 (5%) | | 0/19 (0%) | |
| Fatigue [A] † | 5/16 (31.25%) | | 7/16 (43.75%) | | 7/17 (41.18%) | | 9/19 (47.37%) | | 9/20 (45%) | | 10/19 (52.63%) | |
| Influenza like illness [A] † | 6/16 (37.5%) | | 2/16 (12.5%) | | 5/17 (29.41%) | | 4/19 (21.05%) | | 4/20 (20%) | | 3/19 (15.79%) | |
| Injection site erythema [A] † | 2/16 (12.5%) | | 2/16 (12.5%) | | 4/17 (23.53%) | | 1/19 (5.26%) | | 0/20 (0%) | | 0/19 (0%) | |
| Injection site haematoma [A] † | 0/16 (0%) | | 0/16 (0%) | | 1/17 (5.88%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Injection site irritation [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 1/19 (5.26%) | | 0/20 (0%) | | 0/19 (0%) | |
| Injection site pain [A] † | 1/16 (6.25%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Injection site pruritus [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Injection site rash [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Injection site reaction [A] † | 1/16 (6.25%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 1/19 (5.26%) | |
| Irritability [A] † | 3/16 (18.75%) | | 3/16 (18.75%) | | 2/17 (11.76%) | | 2/19 (10.53%) | | 2/20 (10%) | | 5/19 (26.32%) | |
| Pain [A] † | 3/16 (18.75%) | | 3/16 (18.75%) | | 4/17 (23.53%) | | 2/19 (10.53%) | | 3/20 (15%) | | 3/19 (15.79%) | |

| | Segment 1: 200 mg ACH-0141625 | | Segment 1: 400 mg ACH-0141625 | | Segment 1: 800 mg ACH-0141625 | | Segment 2: 200 mg ACH-0141625 | | Segment 2 - 400 mg ACH-0141625 | | Segment 2 - 800 mg ACH-0141625 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events |
| Pyrexia [A] † | 4/16 (25%) | | 3/16 (18.75%) | | 0/17 (0%) | | 2/19 (10.53%) | | 2/20 (10%) | | 4/19 (21.05%) | |
| Hepatobiliary disorders | | | | | | | | | | | | |
| Hyperbilirubinaemia [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 2/19 (10.53%) | |
| Jaundice [A] † | 0/16 (0%) | | 0/16 (0%) | | 1/17 (5.88%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Infections and infestations | | | | | | | | | | | | |
| Cellulitis [A] † | 0/16 (0%) | | 1/16 (6.25%) | | 1/17 (5.88%) | | 0/19 (0%) | | 1/20 (5%) | | 0/19 (0%) | |
| Folliculitis [A] † | 0/16 (0%) | | 0/16 (0%) | | 1/17 (5.88%) | | 0/19 (0%) | | 0/20 (0%) | | 1/19 (5.26%) | |
| Gastroenteritis [A] † | 0/16 (0%) | | 0/16 (0%) | | 1/17 (5.88%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Herpes virus infection [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 1/20 (5%) | | 0/19 (0%) | |
| Herpes zoster [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 1/19 (5.26%) | |
| Impetigo [A] † | 1/16 (6.25%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Nasopharyngitis [A] † | 0/16 (0%) | | 0/16 (0%) | | 1/17 (5.88%) | | 0/19 (0%) | | 1/20 (5%) | | 1/19 (5.26%) | |
| Oral herpes [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 1/20 (5%) | | 0/19 (0%) | |
| Otitis externa [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Pharyngitis [A] † | 0/16 (0%) | | 1/16 (6.25%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Pharyngitis streptococcal [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 2/19 (10.53%) | | 0/20 (0%) | | 0/19 (0%) | |

| | Segment 1: 200 mg ACH-0141625 | | Segment 1: 400 mg ACH-0141625 | | Segment 1: 800 mg ACH-0141625 | | Segment 2: 200 mg ACH-0141625 | | Segment 2 - 400 mg ACH-0141625 | | Segment 2 - 800 mg ACH-0141625 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events |
| Pneumonia [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 1/19 (5.26%) | | 0/20 (0%) | | 0/19 (0%) | |
| Rhinitis [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 1/20 (5%) | | 0/19 (0%) | |
| Sinusitis [A] † | 0/16 (0%) | | 1/16 (6.25%) | | 1/17 (5.88%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Tooth abscess [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 1/19 (5.26%) | | 0/20 (0%) | | 0/19 (0%) | |
| Upper respiratory tract infection [A] † | 0/16 (0%) | | 0/16 (0%) | | 2/17 (11.76%) | | 0/19 (0%) | | 0/20 (0%) | | 2/19 (10.53%) | |
| Urinary tract infection [A] † | 1/16 (6.25%) | | 0/16 (0%) | | 0/17 (0%) | | 1/19 (5.26%) | | 1/20 (5%) | | 0/19 (0%) | |
| Injury, poisoning and procedural complications | | | | | | | | | | | | |
| Animal scratch [A] † | 1/16 (6.25%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Contusion [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 1/19 (5.26%) | |
| Fall [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 1/19 (5.26%) | | 0/20 (0%) | | 0/19 (0%) | |
| Gun shot wound [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 1/19 (5.26%) | |
| Muscle strain [A] † | 1/16 (6.25%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 1/20 (5%) | | 0/19 (0%) | |
| Road traffic accident [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 1/19 (5.26%) | |
| Wound [A] † | 1/16 (6.25%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Investigations | | | | | | | | | | | | |

| | Segment 1: 200 mg ACH-0141625 | | Segment 1: 400 mg ACH-0141625 | | Segment 1: 800 mg ACH-0141625 | | Segment 2: 200 mg ACH-0141625 | | Segment 2 - 400 mg ACH-0141625 | | Segment 2 - 800 mg ACH-0141625 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events |
| Alanine aminotransferase increased [A] [1] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 1/20 (5%) | | 0/19 (0%) | |
| Blood alkaline phosphatase increased [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 1/19 (5.26%) | |
| Blood bilirubin increased [A] † | 0/16 (0%) | | 0/16 (0%) | | 1/17 (5.88%) | | 0/19 (0%) | | 0/20 (0%) | | 1/19 (5.26%) | |
| Blood triglycerides increased [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 1/19 (5.26%) | |
| Creatinine renal clearance decreased [A] † | 1/16 (6.25%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Haemoglobin decreased [A] † | 1/16 (6.25%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Neutrophil count decreased [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 1/19 (5.26%) | |
| Transaminases increased [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 1/19 (5.26%) | |
| White blood cell count decreased [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 1/19 (5.26%) | |
| Metabolism and nutrition disorders | | | | | | | | | | | | |
| Decreased appetite [A] † | 1/16 (6.25%) | | 3/16 (18.75%) | | 2/17 (11.76%) | | 5/19 (26.32%) | | 5/20 (25%) | | 4/19 (21.05%) | |
| Dehydration [A] † | 1/16 (6.25%) | | 0/16 (0%) | | 1/17 (5.88%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Hypokalaemia [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 1/19 (5.26%) | |
| Insulin resistance [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 1/20 (5%) | | 0/19 (0%) | |

| | Segment 1: 200 mg ACH-0141625 | | Segment 1: 400 mg ACH-0141625 | | Segment 1: 800 mg ACH-0141625 | | Segment 2: 200 mg ACH-0141625 | | Segment 2 - 400 mg ACH-0141625 | | Segment 2 - 800 mg ACH-0141625 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events |
| Polydipsia [A] † | 0/16 (0%) | | 1/16 (6.25%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Musculoskeletal and connective tissue disorders | | | | | | | | | | | | |
| Arthralgia [A] † | 4/16 (25%) | | 0/16 (0%) | | 2/17 (11.76%) | | 3/19 (15.79%) | | 2/20 (10%) | | 1/19 (5.26%) | |
| Back pain [A] † | 1/16 (6.25%) | | 0/16 (0%) | | 1/17 (5.88%) | | 0/19 (0%) | | 0/20 (0%) | | 3/19 (15.79%) | |
| Joint swelling [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 1/19 (5.26%) | |
| Muscle fatigue [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 1/19 (5.26%) | | 0/20 (0%) | | 0/19 (0%) | |
| Muscle spasms [A] † | 1/16 (6.25%) | | 0/16 (0%) | | 1/17 (5.88%) | | 0/19 (0%) | | 0/20 (0%) | | 1/19 (5.26%) | |
| Musculoskeletal pain [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 1/19 (5.26%) | | 1/20 (5%) | | 1/19 (5.26%) | |
| Musculoskeletal stiffness [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Myalgia [A] † | 4/16 (25%) | | 1/16 (6.25%) | | 1/17 (5.88%) | | 4/19 (21.05%) | | 4/20 (20%) | | 2/19 (10.53%) | |
| Neck mass [A] † | 0/16 (0%) | | 0/16 (0%) | | 1/17 (5.88%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Neck pain [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 1/19 (5.26%) | |
| Pain in extremity [A] † | 0/16 (0%) | | 0/16 (0%) | | 1/17 (5.88%) | | 0/19 (0%) | | 2/20 (10%) | | 0/19 (0%) | |
| Periarthritis [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 1/19 (5.26%) | | 0/20 (0%) | | 0/19 (0%) | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | | | | | | | | | | |
| Renal cell carcinoma [A] † | 0/16 (0%) | | 1/16 (6.25%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |

| | Segment 1: 200 mg ACH-0141625 | | Segment 1: 400 mg ACH-0141625 | | Segment 1: 800 mg ACH-0141625 | | Segment 2: 200 mg ACH-0141625 | | Segment 2 - 400 mg ACH-0141625 | | Segment 2 - 800 mg ACH-0141625 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events |
| Nervous system disorders | | | | | | | | | | | | |
| Disturbance in attention [A] † | 2/16 (12.5%) | | 1/16 (6.25%) | | 2/17 (11.76%) | | 1/19 (5.26%) | | 1/20 (5%) | | 0/19 (0%) | |
| Dizziness [A] † | 0/16 (0%) | | 2/16 (12.5%) | | 2/17 (11.76%) | | 0/19 (0%) | | 0/20 (0%) | | 2/19 (10.53%) | |
| Dizziness postural [A] † | 0/16 (0%) | | 1/16 (6.25%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Dysgeusia [A] † | 3/16 (18.75%) | | 2/16 (12.5%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 2/19 (10.53%) | |
| Headache [A] † | 8/16 (50%) | | 7/16 (43.75%) | | 5/17 (29.41%) | | 4/19 (21.05%) | | 6/20 (30%) | | 9/19 (47.37%) | |
| Hypoaesthesia [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 1/19 (5.26%) | | 1/20 (5%) | | 1/19 (5.26%) | |
| Loss of consciousness [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 1/20 (5%) | | 0/19 (0%) | |
| Mental impairment [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 1/20 (5%) | | 0/19 (0%) | |
| Migraine [A] † | 1/16 (6.25%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Poor quality sleep [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 1/20 (5%) | | 0/19 (0%) | |
| Presyncope [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Sciatica [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 1/19 (5.26%) | |
| Sinus headache [A] † | 0/16 (0%) | | 1/16 (6.25%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Syncope [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 1/19 (5.26%) | | 1/20 (5%) | | 1/19 (5.26%) | |
| Psychiatric disorders | | | | | | | | | | | | |

| | Segment 1: 200 mg ACH-0141625 | | Segment 1: 400 mg ACH-0141625 | | Segment 1: 800 mg ACH-0141625 | | Segment 2: 200 mg ACH-0141625 | | Segment 2 - 400 mg ACH-0141625 | | Segment 2 - 800 mg ACH-0141625 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events |
| Abnormal dreams [A] † | 0/16 (0%) | | 1/16 (6.25%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Affect lability [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 2/20 (10%) | | 0/19 (0%) | |
| Agitation [A] † | 1/16 (6.25%) | | 0/16 (0%) | | 3/17 (17.65%) | | 1/19 (5.26%) | | 4/20 (20%) | | 1/19 (5.26%) | |
| Alcohol abuse [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 1/20 (5%) | | 0/19 (0%) | |
| Anxiety [A] † | 1/16 (6.25%) | | 0/16 (0%) | | 1/17 (5.88%) | | 0/19 (0%) | | 2/20 (10%) | | 2/19 (10.53%) | |
| Delusion [A] † | 0/16 (0%) | | 0/16 (0%) | | 1/17 (5.88%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Depressed mood [A] † | 0/16 (0%) | | 1/16 (6.25%) | | 0/17 (0%) | | 2/19 (10.53%) | | 0/20 (0%) | | 2/19 (10.53%) | |
| Depression [A] † | 2/16 (12.5%) | | 2/16 (12.5%) | | 2/17 (11.76%) | | 0/19 (0%) | | 1/20 (5%) | | 2/19 (10.53%) | |
| Hallucination [A] † | 0/16 (0%) | | 0/16 (0%) | | 1/17 (5.88%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Insomnia [A] † | 4/16 (25%) | | 1/16 (6.25%) | | 2/17 (11.76%) | | 3/19 (15.79%) | | 5/20 (25%) | | 5/19 (26.32%) | |
| Libido decreased [A] † | 1/16 (6.25%) | | 0/16 (0%) | | 1/17 (5.88%) | | 0/19 (0%) | | 1/20 (5%) | | 0/19 (0%) | |
| Mania [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 1/20 (5%) | | 0/19 (0%) | |
| Mood swings [A] † | 1/16 (6.25%) | | 0/16 (0%) | | 0/17 (0%) | | 1/19 (5.26%) | | 1/20 (5%) | | 0/19 (0%) | |
| Nervousness [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 1/20 (5%) | | 0/19 (0%) | |
| Sleep disorder [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 1/20 (5%) | | 0/19 (0%) | |

| | Segment 1: 200 mg ACH-0141625 | | Segment 1: 400 mg ACH-0141625 | | Segment 1: 800 mg ACH-0141625 | | Segment 2: 200 mg ACH-0141625 | | Segment 2 - 400 mg ACH-0141625 | | Segment 2 - 800 mg ACH-0141625 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events |
| Sleep terror [A] † | 1/16 (6.25%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Tearfulness [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Renal and urinary disorders | | | | | | | | | | | | |
| Dysuria [A] † | 1/16 (6.25%) | | 0/16 (0%) | | 0/17 (0%) | | 1/19 (5.26%) | | 1/20 (5%) | | 0/19 (0%) | |
| Pollakiuria [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 1/19 (5.26%) | | 0/20 (0%) | | 0/19 (0%) | |
| Polyuria [A] † | 0/16 (0%) | | 1/16 (6.25%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Renal failure chronic [A] † | 0/16 (0%) | | 0/16 (0%) | | 1/17 (5.88%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Respiratory, thoracic and mediastinal disorders | | | | | | | | | | | | |
| Asthma [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 1/20 (5%) | | 0/19 (0%) | |
| Cough [A] † | 0/16 (0%) | | 3/16 (18.75%) | | 0/17 (0%) | | 2/19 (10.53%) | | 3/20 (15%) | | 2/19 (10.53%) | |
| Dyspnoea [A] † | 1/16 (6.25%) | | 1/16 (6.25%) | | 0/17 (0%) | | 0/19 (0%) | | 1/20 (5%) | | 0/19 (0%) | |
| Dyspnoea exertional [A] † | 1/16 (6.25%) | | 1/16 (6.25%) | | 1/17 (5.88%) | | 2/19 (10.53%) | | 1/20 (5%) | | 0/19 (0%) | |
| Epistaxis [A] † | 0/16 (0%) | | 0/16 (0%) | | 1/17 (5.88%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Nasal congestion [A] † | 0/16 (0%) | | 1/16 (6.25%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 1/19 (5.26%) | |
| Nasal dryness [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 2/19 (10.53%) | | 0/20 (0%) | | 0/19 (0%) | |
| Oropharyngeal pain [A] † | 1/16 (6.25%) | | 0/16 (0%) | | 0/17 (0%) | | 1/19 (5.26%) | | 1/20 (5%) | | 1/19 (5.26%) | |

| | Segment 1: 200 mg ACH-0141625 | | Segment 1: 400 mg ACH-0141625 | | Segment 1: 800 mg ACH-0141625 | | Segment 2: 200 mg ACH-0141625 | | Segment 2 - 400 mg ACH-0141625 | | Segment 2 - 800 mg ACH-0141625 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events |
| Respiratory tract congestion [A] † | 1/16 (6.25%) | | 0/16 (0%) | | 0/17 (0%) | | 1/19 (5.26%) | | 0/20 (0%) | | 0/19 (0%) | |
| Sinus congestion [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 1/19 (5.26%) | |
| Sneezing [A] † | 0/16 (0%) | | 1/16 (6.25%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Upper respiratory tract congestion [A] † | 0/16 (0%) | | 0/16 (0%) | | 1/17 (5.88%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Skin and subcutaneous tissue disorders | | | | | | | | | | | | |
| Alopecia [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 1/19 (5.26%) | | 0/20 (0%) | | 0/19 (0%) | |
| Dermatitis [A] † | 0/16 (0%) | | 1/16 (6.25%) | | 3/17 (17.65%) | | 0/19 (0%) | | 0/20 (0%) | | 1/19 (5.26%) | |
| Dry skin [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 4/20 (20%) | | 3/19 (15.79%) | |
| Eczema [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 1/19 (5.26%) | | 0/20 (0%) | | 1/19 (5.26%) | |
| Erythema [A] † | 0/16 (0%) | | 1/16 (6.25%) | | 0/17 (0%) | | 1/19 (5.26%) | | 0/20 (0%) | | 1/19 (5.26%) | |
| Hyperhidrosis [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 1/19 (5.26%) | | 1/20 (5%) | | 0/19 (0%) | |
| Night sweats [A] † | 1/16 (6.25%) | | 1/16 (6.25%) | | 1/17 (5.88%) | | 1/19 (5.26%) | | 1/20 (5%) | | 0/19 (0%) | |
| Photosensitivity reaction [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 1/19 (5.26%) | |
| Pruritus [A] † | 0/16 (0%) | | 1/16 (6.25%) | | 1/17 (5.88%) | | 1/19 (5.26%) | | 2/20 (10%) | | 2/19 (10.53%) | |
| Pruritus generalised [A] † | 1/16 (6.25%) | | 1/16 (6.25%) | | 1/17 (5.88%) | | 2/19 (10.53%) | | 1/20 (5%) | | 0/19 (0%) | |

| | Segment 1: 200 mg ACH-0141625 | | Segment 1: 400 mg ACH-0141625 | | Segment 1: 800 mg ACH-0141625 | | Segment 2: 200 mg ACH-0141625 | | Segment 2 - 400 mg ACH-0141625 | | Segment 2 - 800 mg ACH-0141625 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events | Affected/ At Risk (%) | # Events |
| Psoriasis [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 1/20 (5%) | | 0/19 (0%) | |
| Rash [A] † | 1/16 (6.25%) | | 2/16 (12.5%) | | 0/17 (0%) | | 2/19 (10.53%) | | 1/20 (5%) | | 3/19 (15.79%) | |
| Rash macular [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Rash papular [A] † | 0/16 (0%) | | 0/16 (0%) | | 1/17 (5.88%) | | 0/19 (0%) | | 1/20 (5%) | | 0/19 (0%) | |
| Rash pruritic [A] † | 1/16 (6.25%) | | 0/16 (0%) | | 0/17 (0%) | | 0/19 (0%) | | 0/20 (0%) | | 1/19 (5.26%) | |
| Seborrhoeic dermatitis [A] † | 0/16 (0%) | | 0/16 (0%) | | 0/17 (0%) | | 1/19 (5.26%) | | 0/20 (0%) | | 0/19 (0%) | |
| Skin chapped [A] † | 0/16 (0%) | | 0/16 (0%) | | 1/17 (5.88%) | | 0/19 (0%) | | 0/20 (0%) | | 0/19 (0%) | |
| Vascular disorders | | | | | | | | | | | | |
| Hot flush [A] † | 0/16 (0%) | | 1/16 (6.25%) | | 0/17 (0%) | | 1/19 (5.26%) | | 1/20 (5%) | | 0/19 (0%) | |

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 12.1

[1] Grade 3 ALT elevation occurred about Week 10. ACH-0141625 was held for four days, during which ALT decreased. Subject was re-challenged with ACH-0141625 for the remaining week of therapy, and ALT levels continued to improve, normalizing by Week 16.

| | Segment 1 - Placebo | |
|---|---|---|
| | Affected/At Risk (%) | # Events |
| Total | 14/15 (93.33%) | |
| Blood and lymphatic system disorders | | |
| Anaemia [A] † | 3/15 (20%) | |
| Haemoglobinaemia [A] † | 0/15 (0%) | |

| | Segment 1 - Placebo | |
|---|---|---|
| | Affected/At Risk (%) | # Events |
| Haemolytic anaemia [A] † | 0/15 (0%) | |
| Leukopenia [A] † | 0/15 (0%) | |
| Neutropenia [A] † | 4/15 (26.67%) | |
| Thrombocytopenia [A] † | 0/15 (0%) | |
| Cardiac disorders | | |
| Palpitations [A] † | 0/15 (0%) | |
| Ear and labyrinth disorders | | |
| Ear discomfort [A] † | 0/15 (0%) | |
| Ear pain [A] † | 0/15 (0%) | |
| Tinnitus [A] † | 0/15 (0%) | |
| Vertigo [A] † | 0/15 (0%) | |
| Endocrine disorders | | |
| Thyroid disorder [A] † | 0/15 (0%) | |
| Eye disorders | | |
| Abnormal sensation in eye [A] † | 0/15 (0%) | |
| Conjunctivitis [A] † | 0/15 (0%) | |
| Dry eye [A] † | 0/15 (0%) | |
| Eye irritation [A] † | 0/15 (0%) | |
| Eye pain [A] † | 0/15 (0%) | |
| Eye pruritus [A] † | 0/15 (0%) | |
| Photophobia [A] † | 1/15 (6.67%) | |
| Vision blurred [A] † | 0/15 (0%) | |
| Gastrointestinal disorders | | |

| | Segment 1 - Placebo | |
|---|---|---|
| | Affected/At Risk (%) | # Events |
| Abdominal distension [A] † | 0/15 (0%) | |
| Abdominal pain [A] † | 2/15 (13.33%) | |
| Abdominal pain upper [A] † | 0/15 (0%) | |
| Abdominal tenderness [A] † | 1/15 (6.67%) | |
| Anal fissure [A] † | 0/15 (0%) | |
| Aphthous stomatitis [A] † | 0/15 (0%) | |
| Breath odour [A] † | 0/15 (0%) | |
| Constipation [A] † | 2/15 (13.33%) | |
| Dental caries [A] † | 0/15 (0%) | |
| Diarrhoea [A] † | 2/15 (13.33%) | |
| Dry mouth [A] † | 0/15 (0%) | |
| Dyspepsia [A] † | 0/15 (0%) | |
| Flatulence [A] † | 0/15 (0%) | |
| Frequent bowel movements [A] † | 0/15 (0%) | |
| Gastrooesophageal reflux disease [A] † | 1/15 (6.67%) | |
| Gingival pain [A] † | 0/15 (0%) | |
| Gingivitis [A] † | 1/15 (6.67%) | |
| Glossodynia [A] † | 0/15 (0%) | |
| Haemorrhoids [A] † | 0/15 (0%) | |
| Lip ulceration [A] † | 0/15 (0%) | |
| Nausea [A] † | 4/15 (26.67%) | |
| Stomatitis [A] † | 0/15 (0%) | |

| | Segment 1 - Placebo | |
|---|---|---|
| | Affected/At Risk (%) | # Events |
| Toothache [A] † | 0/15 (0%) | |
| Vomiting [A] † | 1/15 (6.67%) | |
| General disorders | | |
| Application site erythema [A] † | 0/15 (0%) | |
| Asthenia [A] † | 0/15 (0%) | |
| Chest pain [A] † | 0/15 (0%) | |
| Chills [A] † | 2/15 (13.33%) | |
| Fatigue [A] † | 5/15 (33.33%) | |
| Influenza like illness [A] † | 1/15 (6.67%) | |
| Injection site erythema [A] † | 3/15 (20%) | |
| Injection site haematoma [A] † | 0/15 (0%) | |
| Injection site irritation [A] † | 0/15 (0%) | |
| Injection site pain [A] † | 0/15 (0%) | |
| Injection site pruritus [A] † | 1/15 (6.67%) | |
| Injection site rash [A] † | 1/15 (6.67%) | |
| Injection site reaction [A] † | 0/15 (0%) | |
| Irritability [A] † | 1/15 (6.67%) | |
| Pain [A] † | 1/15 (6.67%) | |
| Pyrexia [A] † | 0/15 (0%) | |
| Hepatobiliary disorders | | |
| Hyperbilirubinaemia [A] † | 0/15 (0%) | |
| Jaundice [A] † | 0/15 (0%) | |

| | Segment 1 - Placebo | |
|---|---|---|
| | Affected/At Risk (%) | # Events |
| Infections and infestations | | |
| Cellulitis [A] † | 0/15 (0%) | |
| Folliculitis [A] † | 0/15 (0%) | |
| Gastroenteritis [A] † | 0/15 (0%) | |
| Herpes virus infection [A] † | 0/15 (0%) | |
| Herpes zoster [A] † | 0/15 (0%) | |
| Impetigo [A] † | 0/15 (0%) | |
| Nasopharyngitis [A] † | 0/15 (0%) | |
| Oral herpes [A] † | 1/15 (6.67%) | |
| Otitis externa [A] † | 1/15 (6.67%) | |
| Pharyngitis [A] † | 0/15 (0%) | |
| Pharyngitis streptococcal [A] † | 0/15 (0%) | |
| Pneumonia [A] † | 0/15 (0%) | |
| Rhinitis [A] † | 0/15 (0%) | |
| Sinusitis [A] † | 0/15 (0%) | |
| Tooth abscess [A] † | 0/15 (0%) | |
| Upper respiratory tract infection [A] † | 0/15 (0%) | |
| Urinary tract infection [A] † | 0/15 (0%) | |
| Injury, poisoning and procedural complications | | |
| Animal scratch [A] † | 0/15 (0%) | |
| Contusion [A] † | 0/15 (0%) | |
| Fall [A] † | 0/15 (0%) | |

| | Segment 1 - Placebo | |
|---|---|---|
| | Affected/At Risk (%) | # Events |
| Gun shot wound [A] † | 0/15 (0%) | |
| Muscle strain [A] † | 0/15 (0%) | |
| Road traffic accident [A] † | 0/15 (0%) | |
| Wound [A] † | 0/15 (0%) | |
| Investigations | | |
| Alanine aminotransferase increased [A] [1] † | 0/15 (0%) | |
| Blood alkaline phosphatase increased [A] † | 0/15 (0%) | |
| Blood bilirubin increased [A] † | 0/15 (0%) | |
| Blood triglycerides increased [A] † | 0/15 (0%) | |
| Creatinine renal clearance decreased [A] † | 0/15 (0%) | |
| Haemoglobin decreased [A] † | 0/15 (0%) | |
| Neutrophil count decreased [A] † | 0/15 (0%) | |
| Transaminases increased [A] † | 0/15 (0%) | |
| White blood cell count decreased [A] † | 0/15 (0%) | |
| Metabolism and nutrition disorders | | |
| Decreased appetite [A] † | 0/15 (0%) | |
| Dehydration [A] † | 0/15 (0%) | |
| Hypokalaemia [A] † | 0/15 (0%) | |
| Insulin resistance [A] † | 0/15 (0%) | |
| Polydipsia [A] † | 0/15 (0%) | |
| Musculoskeletal and connective tissue disorders | | |
| Arthralgia [A] † | 2/15 (13.33%) | |

| | Segment 1 - Placebo | |
|---|---|---|
| | Affected/At Risk (%) | # Events |
| Back pain [A] † | 0/15 (0%) | |
| Joint swelling [A] † | 0/15 (0%) | |
| Muscle fatigue [A] † | 0/15 (0%) | |
| Muscle spasms [A] † | 0/15 (0%) | |
| Musculoskeletal pain [A] † | 0/15 (0%) | |
| Musculoskeletal stiffness [A] † | 1/15 (6.67%) | |
| Myalgia [A] † | 2/15 (13.33%) | |
| Neck mass [A] † | 0/15 (0%) | |
| Neck pain [A] † | 0/15 (0%) | |
| Pain in extremity [A] † | 0/15 (0%) | |
| Periarthritis [A] † | 0/15 (0%) | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | |
| Renal cell carcinoma [A] † | 0/15 (0%) | |
| Nervous system disorders | | |
| Disturbance in attention [A] † | 1/15 (6.67%) | |
| Dizziness [A] † | 0/15 (0%) | |
| Dizziness postural [A] † | 0/15 (0%) | |
| Dysgeusia [A] † | 1/15 (6.67%) | |
| Headache [A] † | 5/15 (33.33%) | |
| Hypoaesthesia [A] † | 0/15 (0%) | |
| Loss of consciousness [A] † | 0/15 (0%) | |
| Mental impairment [A] † | 0/15 (0%) | |

| | Segment 1 - Placebo | |
|---|---|---|
| | Affected/At Risk (%) | # Events |
| Migraine [A] † | 0/15 (0%) | |
| Poor quality sleep [A] † | 0/15 (0%) | |
| Presyncope [A] † | 1/15 (6.67%) | |
| Sciatica [A] † | 0/15 (0%) | |
| Sinus headache [A] † | 0/15 (0%) | |
| Syncope [A] † | 0/15 (0%) | |
| Psychiatric disorders | | |
| Abnormal dreams [A] † | 0/15 (0%) | |
| Affect lability [A] † | 0/15 (0%) | |
| Agitation [A] † | 1/15 (6.67%) | |
| Alcohol abuse [A] † | 0/15 (0%) | |
| Anxiety [A] † | 0/15 (0%) | |
| Delusion [A] † | 0/15 (0%) | |
| Depressed mood [A] † | 0/15 (0%) | |
| Depression [A] † | 0/15 (0%) | |
| Hallucination [A] † | 0/15 (0%) | |
| Insomnia [A] † | 3/15 (20%) | |
| Libido decreased [A] † | 0/15 (0%) | |
| Mania [A] † | 0/15 (0%) | |
| Mood swings [A] † | 0/15 (0%) | |
| Nervousness [A] † | 0/15 (0%) | |
| Sleep disorder [A] † | 0/15 (0%) | |

| | Segment 1 - Placebo | |
|---|---|---|
| | Affected/At Risk (%) | # Events |
| Sleep terror [A] † | 0/15 (0%) | |
| Tearfulness [A] † | 1/15 (6.67%) | |
| Renal and urinary disorders | | |
| Dysuria [A] † | 0/15 (0%) | |
| Pollakiuria [A] † | 0/15 (0%) | |
| Polyuria [A] † | 0/15 (0%) | |
| Renal failure chronic [A] † | 0/15 (0%) | |
| Respiratory, thoracic and mediastinal disorders | | |
| Asthma [A] † | 0/15 (0%) | |
| Cough [A] † | 2/15 (13.33%) | |
| Dyspnoea [A] † | 1/15 (6.67%) | |
| Dyspnoea exertional [A] † | 0/15 (0%) | |
| Epistaxis [A] † | 0/15 (0%) | |
| Nasal congestion [A] † | 1/15 (6.67%) | |
| Nasal dryness [A] † | 0/15 (0%) | |
| Oropharyngeal pain [A] † | 0/15 (0%) | |
| Respiratory tract congestion [A] † | 1/15 (6.67%) | |
| Sinus congestion [A] † | 0/15 (0%) | |
| Sneezing [A] † | 0/15 (0%) | |
| Upper respiratory tract congestion [A] † | 0/15 (0%) | |
| Skin and subcutaneous tissue disorders | | |
| Alopecia [A] † | 0/15 (0%) | |

| | Segment 1 - Placebo | |
|---|---|---|
| | Affected/At Risk (%) | # Events |
| Dermatitis [A] † | 0/15 (0%) | |
| Dry skin [A] † | 0/15 (0%) | |
| Eczema [A] † | 0/15 (0%) | |
| Erythema [A] † | 0/15 (0%) | |
| Hyperhidrosis [A] † | 1/15 (6.67%) | |
| Night sweats [A] † | 0/15 (0%) | |
| Photosensitivity reaction [A] † | 0/15 (0%) | |
| Pruritus [A] † | 0/15 (0%) | |
| Pruritus generalised [A] † | 1/15 (6.67%) | |
| Psoriasis [A] † | 0/15 (0%) | |
| Rash [A] † | 2/15 (13.33%) | |
| Rash macular [A] † | 1/15 (6.67%) | |
| Rash papular [A] † | 0/15 (0%) | |
| Rash pruritic [A] † | 0/15 (0%) | |
| Seborrhoeic dermatitis [A] † | 0/15 (0%) | |
| Skin chapped [A] † | 0/15 (0%) | |
| Vascular disorders | | |
| Hot flush [A] † | 2/15 (13.33%) | |

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 12.1

[1] Grade 3 ALT elevation occurred about Week 10. ACH-0141625 was held for four days, during which ALT decreased. Subject was re-challenged with ACH-0141625 for the remaining week of therapy, and ALT levels continued to improve, normalizing by Week 16.

## Limitations and Caveats

[Not specified]

## More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

Prior to submitting/presenting a manuscript or materials relating to a Study to a publisher, reviewer, or outside person, the Institution shall provide to Achillion a copy of all such manuscripts or materials, and Achillion shall have sixty (60) days to review and comment. The Institution shall, upon Achillion's request, further delay publication or presentation for a period of up to one hundred twenty (120) days to allow Achillion to protect its interests in any Achillion Inventions.

Results Point of Contact:

Name/Official Title: Kevin Kucharski, VP Clinical Operations
Organization: Achillion Pharmaceuticals, Inc.
Phone: 203-624-7000
Email: Kkucharski@achillion.com