# Clinical trial results:
# FLUTicasone in Eosinophilic esophagitis (FLUTE): A Randomized, Double-blind, Placebo-controlled, Dose-ranging, and Maintenance Study of APT-1011 in Subjects with Eosinophilic Esophagitis

## Summary

| | |
|---|---|
| EudraCT number | 2016-004749-10 |
| Trial protocol | BE DE ES |
| Global end of trial date | 23 October 2019 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 03 April 2022 |
| First version publication date | 03 April 2022 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | SP-1011-002 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03191864 |
| WHO universal trial number (UTN) | - |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Adare Pharmaceuticals US, LP |
| Sponsor organisation address | 1200 Lenox Drive, Suite 100, Lawrenceville, United States, 08648 |
| Public contact | Project Management, IQVIA, Inc. (formerly QuintilesIMS), +34 934894035, ensayosclinicos@quintiles.com |
| Scientific contact | Project Management, IQVIA, Inc. (formerly QuintilesIMS), +34 934894035, ensayosclinicos@quintiles.com |

Notes:

### Paediatric regulatory details

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

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 23 October 2019 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 03 January 2019 |
| Global end of trial reached? | Yes |
| Global end of trial date | 23 October 2019 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of the study is to evaluate the efficacy (histological response) of APT-1011 in adults with eosinophilic esophagitis (EoE).

Protection of trial subjects:

FLUTE was conducted according to the principles of the Declaration of Helsinki (Seoul, October 2008), and the ICH guidelines for GCP. The Sponsor ensured that the study complies with all local, federal, or country regulatory requirements as applicable.

Background therapy:

Not applicable.

Evidence for comparator:

Not applicable.

| | |
|---|---|
| Actual start date of recruitment | 22 June 2017 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Belgium: 1 |
| Country: Number of subjects enrolled | Spain: 35 |
| Country: Number of subjects enrolled | Germany: 9 |
| Country: Number of subjects enrolled | Canada: 12 |
| Country: Number of subjects enrolled | United States: 249 |
| Country: Number of subjects enrolled | Switzerland: 2 |
| Worldwide total number of subjects | 308 |
| EEA total number of subjects | 45 |

Notes:

### Subjects enrolled per age group

| | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |

| | |
|---|---|
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 296 |
| From 65 to 84 years | 12 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Recruitment in 6 countries (United States, Canada, Belgium, Germany, Spain, and Switzerland) took place between 22-Jun-2017 (First Subject Enrolled) until 23-Aug-2018 (Last Subject Enrolled).

### Pre-assignment

Screening details:

The Screening Period was 4 weeks (28 days). Along with the reports confirming the subject's primary diagnosis of EoE, the Investigator assessed eligibility criteria of the subject based on screening results. The Global EoE Symptom Score had to be >3 for the subject to continue in the study.

### Period 1

| | |
|---|---|
| Period 1 title | Baseline Symptom Assessment |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

### Arms

| | |
|---|---|
| **Arm title** | Placebo Run-in |

Arm description:

Due to the high placebo response rates, the study utilized a 4-week single-blind placebo run-in period to not only establish the baseline symptoms for the study, but also to ensure that all subjects enrolled had sufficient severity of EoE to warrant inclusion in the study.

| | |
|---|---|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

All subjects received placebo 30 minutes after breakfast and HS (at bedtime) daily.

| **Number of subjects in period 1** | Placebo Run-in |
|---|---|
| Started | 308 |
| Completed | 106 |
| Not completed | 202 |
| Consent withdrawn by subject | 19 |
| Violation of inclusion/exclusion criteria | 179 |
| Adverse event, non-fatal | 2 |
| Other | 2 |

## Period 2

| | |
|---|---|
| Period 2 title | Part 1 - Induction |
| Is this the baseline period? | Yes[1] |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

## Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | APT-1011 1.5 mg HS |

Arm description:

Subjects received placebo 30 minutes after breakfast and 1.5 mg APT-1011 HS (at bedtime) daily

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | APT-1011 |
| Investigational medicinal product code | |
| Other name | fluticasone propionate |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received 1.5 mg APT-1011 HS (at bedtime) daily

| | |
|---|---|
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received placebo 30 minutes after breakfast daily

| | |
|---|---|
| **Arm title** | APT-1011 1.5 mg BID |

Arm description:

Subjects received 1.5 mg APT-1011 30 minutes after breakfast and at bedtime daily for a total daily dose of 3.0 mg

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | APT-1011 |
| Investigational medicinal product code | |
| Other name | fluticasone propionate |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received 1.5 mg APT-1011 30 minutes after breakfast and at bedtime daily for a total daily dose of 3.0 mg

| | |
|---|---|
| **Arm title** | APT-1011 3 mg HS |

Arm description:

Subjects received placebo 30 minutes after breakfast and 3.0 mg APT-1011 at bedtime daily

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | APT-1011 |
| Investigational medicinal product code | |
| Other name | fluticasone propionate |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received 3.0 mg APT-1011 at bedtime daily

| | |
|---|---|
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received placebo 30 minutes after breakfast daily

| | |
|---|---|
| **Arm title** | APT-1011 3 mg BID |

Arm description:

Subjects received 3 mg APT-1011 30 minutes after breakfast and at bedtime daily for a total daily dose of 6.0 mg

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | APT-1011 |
| Investigational medicinal product code | |
| Other name | fluticasone propionate |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received 3 mg APT-1011 30 minutes after breakfast and at bedtime daily for a total daily dose of 6.0 mg

| | |
|---|---|
| **Arm title** | Placebo |

Arm description:

Subjects received placebo 30 minutes after breakfast and HS (at bedtime) daily

| | |
|---|---|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received placebo 30 minutes after breakfast and HS (at bedtime) daily

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: Period 1 is the Placebo Run-in period where a 4-week baseline symptom assessment has been completed. 308 subjects entered this period but only 106 completed, the majority due to the fact that there was a violation of inclusion/exclusion criteria in the study. For that reason, we believe it is most appropriate to count Period 2 as the baseline period and to report the baseline characteristics for those participants who were randomized into the study and comprise the FAS, as presented in the CSR.

| **Number of subjects in period 2[2][3]** | APT-1011 1.5 mg HS | APT-1011 1.5 mg BID | APT-1011 3 mg HS |
|---|---|---|---|
| Started | 21 | 22 | 21 |
| Completed | 17 | 20 | 19 |
| Not completed | 4 | 2 | 2 |
| Consent withdrawn by subject | 3 | 1 | 1 |
| Adverse event, non-fatal | - | 1 | - |
| Other | 1 | - | 1 |

| **Number of subjects in period 2[2][3]** | APT-1011 3 mg BID | Placebo |
|---|---|---|
| Started | 20 | 19 |

| | | |
|---|---|---|
| Completed | 19 | 17 |
| Not completed | 1 | 2 |
| Consent withdrawn by subject | - | 1 |
| Adverse event, non-fatal | 1 | 1 |
| Other | - | - |

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Period 1 is the Placebo Run-in period where a 4-week baseline symptom assessment has been completed. 308 subjects entered this period but only 106 completed, the majority due to the fact that there was a violation of inclusion/exclusion criteria in the study. For that reason, we believe it is most appropriate to count Period 2 as the baseline period and to report the baseline characteristics for those participants who were randomized into the study and comprise the FAS, as presented in the CSR.

[3] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Period 1 is the Placebo Run-in period where a 4-week baseline symptom assessment has been completed. 308 subjects entered this period but only 106 completed, the majority due to the fact that there was a violation of inclusion/exclusion criteria in the study. For that reason, we believe it is most appropriate to count Period 2 as the baseline period and to report the baseline characteristics for those participants who were randomized into the study and comprise the FAS, as presented in the CSR.

## Period 3

| | |
|---|---|
| Period 3 title | Part 2 - Maintenance |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Single blind |
| Roles blinded | Subject |

Blinding implementation details:

Note that those subjects that were non-responders at Week 12 were switched from another arm to the Single-blind APT-1011 3 mg BID arm. This arm was a single-blinded arm for the subjects only.

## Arms

| | |
|---|---|
| Are arms mutually exclusive? | No |
| **Arm title** | APT-1011 1.5 mg HS |

Arm description:

Subjects received placebo 30 minutes after breakfast and 1.5 mg APT-1011 HS (at bedtime) daily

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | APT-1011 |
| Investigational medicinal product code | |
| Other name | fluticasone propionate |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received 1.5 mg APT-1011 HS (at bedtime) daily

| | |
|---|---|
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received placebo 30 minutes after breakfast daily

| | |
|---|---|
| **Arm title** | APT-1011 1.5 mg BID |

Arm description:

Subjects received 1.5 mg APT-1011 30 minutes after breakfast and at bedtime daily for a total daily dose of 3.0 mg

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | APT-1011 |
| Investigational medicinal product code | |
| Other name | fluticasone propionate |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received 1.5 mg APT-1011 30 minutes after breakfast and at bedtime daily for a total daily dose of 3.0 mg

| | |
|---|---|
| **Arm title** | APT-1011 3 mg HS |

Arm description:

Subjects received placebo 30 minutes after breakfast and 3.0 mg APT-1011 at bedtime daily

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | APT-1011 |
| Investigational medicinal product code | |
| Other name | fluticasone propionate |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received 3.0 mg APT-1011 at bedtime daily

| | |
|---|---|
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received placebo 30 minutes after breakfast daily

| | |
|---|---|
| **Arm title** | APT-1011 3 mg BID |

Arm description:

Subjects received 3 mg APT-1011 30 minutes after breakfast and at bedtime daily for a total daily dose of 6.0 mg

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | APT-1011 |
| Investigational medicinal product code | |
| Other name | fluticasone propionate |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received 3 mg APT-1011 30 minutes after breakfast and at bedtime daily for a total daily dose of 6.0 mg

| | |
|---|---|
| **Arm title** | Single-Blind APT-1011 3 mg BID |

Arm description:

Subjects received 3 mg APT-1011 30 minutes after breakfast and at bedtime daily for a total daily dose of 6.0 mg

| | |
|---|---|
| Arm type | Experimental |

| | |
|---|---|
| Investigational medicinal product name | APT-1011 |
| Investigational medicinal product code | |
| Other name | fluticasone propionate |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received 3 mg APT-1011 30 minutes after breakfast and at bedtime daily for a total daily dose of 6.0 mg

| **Number of subjects in period 3** | APT-1011 1.5 mg HS | APT-1011 1.5 mg BID | APT-1011 3 mg HS |
|---|---|---|---|
| Started | 10 | 19 | 14 |
| Completed | 5 | 17 | 11 |
| Not completed | 5 | 2 | 3 |
| Consent withdrawn by subject | 2 | - | - |
| Physician decision | 1 | - | - |
| Adverse event, non-fatal | - | - | - |
| Other | 1 | - | 1 |
| Lack of efficacy | 1 | 2 | 2 |

| **Number of subjects in period 3** | APT-1011 3 mg BID | Single-Blind APT-1011 3 mg BID |
|---|---|---|
| Started | 16 | 34 |
| Completed | 14 | 19 |
| Not completed | 2 | 15 |
| Consent withdrawn by subject | - | 3 |
| Physician decision | - | - |
| Adverse event, non-fatal | - | 1 |
| Other | - | 1 |
| Lack of efficacy | 2 | 10 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | APT-1011 1.5 mg HS |
| Reporting group description: | |
| Subjects received placebo 30 minutes after breakfast and 1.5 mg APT-1011 HS (at bedtime) daily | |
| Reporting group title | APT-1011 1.5 mg BID |
| Reporting group description: | |
| Subjects received 1.5 mg APT-1011 30 minutes after breakfast and at bedtime daily for a total daily dose of 3.0 mg | |
| Reporting group title | APT-1011 3 mg HS |
| Reporting group description: | |
| Subjects received placebo 30 minutes after breakfast and 3.0 mg APT-1011 at bedtime daily | |
| Reporting group title | APT-1011 3 mg BID |
| Reporting group description: | |
| Subjects received 3 mg APT-1011 30 minutes after breakfast and at bedtime daily for a total daily dose of 6.0 mg | |
| Reporting group title | Placebo |
| Reporting group description: | |
| Subjects received placebo 30 minutes after breakfast and HS (at bedtime) daily | |

| Reporting group values | APT-1011 1.5 mg HS | APT-1011 1.5 mg BID | APT-1011 3 mg HS |
|---|---|---|---|
| Number of subjects | 21 | 22 | 21 |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 21 | 21 | 20 |
| From 65-84 years | 0 | 1 | 1 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 36.8 | 41.3 | 42.9 |
| standard deviation | ± 11.65 | ± 12.24 | ± 11.52 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 7 | 7 | 10 |
| Male | 14 | 15 | 11 |
| Race<br>Units: Subjects | | | |
| White | 21 | 22 | 20 |
| Black or African American | 0 | 0 | 1 |
| Asian | 0 | 0 | 0 |
| American Indian or Alaska Native | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Missing | 0 | 0 | 0 |
| Ethnicity<br>Units: Subjects | | | |
| Hispanic or Latino | 4 | 5 | 2 |
| Not Hispanic or Latino | 17 | 17 | 19 |
| Other | 0 | 0 | 0 |
| Missing | 0 | 0 | 0 |
| Geographic Region<br>Units: Subjects | | | |
| North America | 15 | 16 | 17 |
| Western Europe | 6 | 6 | 4 |
| Smoking status<br>Units: Subjects | | | |
| Never | 18 | 17 | 18 |
| Former | 2 | 3 | 3 |
| Current | 1 | 2 | 0 |
| Missing | 0 | 0 | 0 |
| History of esophageal stricture(s)<br>Units: Subjects | | | |
| Yes | 11 | 10 | 8 |
| No | 10 | 12 | 13 |
| Missing | 0 | 0 | 0 |
| Current esophageal stricture(s) based on the study EGD<br>Units: Subjects | | | |
| Yes | 4 | 5 | 5 |
| No | 17 | 17 | 16 |
| Missing | 0 | 0 | 0 |
| History of positive steroid Response to EoE<br>Units: Subjects | | | |
| Yes | 3 | 5 | 4 |
| No | 18 | 17 | 17 |
| Missing | 0 | 0 | 0 |
| Proton pump inhibitor status<br>Units: Subjects | | | |
| Continuing into study | 12 | 18 | 12 |
| Not continuing into study | 9 | 4 | 9 |
| Missing | 0 | 0 | 0 |
| Height<br>Units: cm | | | |
| arithmetic mean | 175.4 | 173.0 | 170.9 |
| standard deviation | ± 8.55 | ± 8.56 | ± 9.85 |
| Weight<br>Units: kg | | | |
| arithmetic mean | 87.4 | 83.7 | 83.6 |
| standard deviation | ± 17.69 | ± 14.72 | ± 18.89 |
| BMI<br>Units: kg/m2 | | | |
| arithmetic mean | 28.3 | 27.4 | 28.8 |
| standard deviation | ± 5.19 | ± 4.34 | ± 6.90 |
| Global EoE Symptom Score prior to | | | |

| | | | |
|---|---|---|---|
| randomization | | | |
| Units: EoE Symptom Score | | | |
| arithmetic mean | 5.1 | 4.5 | 5.1 |
| standard deviation | ± 1.62 | ± 2.13 | ± 1.95 |

| **Reporting group values** | APT-1011 3 mg BID | Placebo | Total |
|---|---|---|---|
| Number of subjects | 20 | 19 | 103 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 20 | 19 | 101 |
| From 65-84 years | 0 | 0 | 2 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 36.8 | 38.6 | |
| standard deviation | ± 9.19 | ± 14.70 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 4 | 5 | 33 |
| Male | 16 | 14 | 70 |
| Race | | | |
| Units: Subjects | | | |
| White | 19 | 18 | 100 |
| Black or African American | 1 | 1 | 3 |
| Asian | 0 | 0 | 0 |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Missing | 0 | 0 | 0 |
| Ethnicity | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 2 | 3 | 16 |
| Not Hispanic or Latino | 16 | 16 | 85 |
| Other | 2 | 0 | 2 |
| Missing | 0 | 0 | 0 |
| Geographic Region | | | |
| Units: Subjects | | | |
| North America | 13 | 16 | 77 |
| Western Europe | 7 | 3 | 26 |
| Smoking status | | | |
| Units: Subjects | | | |
| Never | 16 | 15 | 84 |
| Former | 4 | 4 | 16 |
| Current | 0 | 0 | 3 |
| Missing | 0 | 0 | 0 |
| History of esophageal stricture(s) | | | |

| | | | |
|---|---|---|---|
| Units: Subjects | | | |
| Yes | 8 | 9 | 46 |
| No | 12 | 10 | 57 |
| Missing | 0 | 0 | 0 |
| Current esophageal stricture(s) based on the study EGD<br>Units: Subjects | | | |
| Yes | 4 | 5 | 23 |
| No | 16 | 14 | 80 |
| Missing | 0 | 0 | 0 |
| History of positive steroid Response to EoE<br>Units: Subjects | | | |
| Yes | 4 | 3 | 19 |
| No | 16 | 16 | 84 |
| Missing | 0 | 0 | 0 |
| Proton pump inhibitor status<br>Units: Subjects | | | |
| Continuing into study | 13 | 14 | 69 |
| Not continuing into study | 7 | 5 | 34 |
| Missing | 0 | 0 | 0 |
| Height<br>Units: cm | | | |
| arithmetic mean | 176.7 | 174.3 | |
| standard deviation | ± 8.61 | ± 7.40 | - |
| Weight<br>Units: kg | | | |
| arithmetic mean | 79.7 | 84.1 | |
| standard deviation | ± 14.93 | ± 17.26 | - |
| BMI<br>Units: kg/m2 | | | |
| arithmetic mean | 25.5 | 28.4 | |
| standard deviation | ± 4.45 | ± 6.71 | - |
| Global EoE Symptom Score prior to randomization<br>Units: EoE Symptom Score | | | |
| arithmetic mean | 4.3 | 5.1 | |
| standard deviation | ± 1.94 | ± 1.68 | - |

## Subject analysis sets

| | |
|---|---|
| Subject analysis set title | Intent-to-Treat Analysis Population |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

The Intent-To-Treat (ITT) analysis population contained all subjects enrolled (All Subjects Enrolled Population) who were randomized. Subjects were classified according to randomized treatment.

| | |
|---|---|
| Subject analysis set title | Full Analysis Set Population |
| Subject analysis set type | Full analysis |

Subject analysis set description:

The Full Analysis Set (FAS) analysis population contained all subjects in the ITT population who did not meet any of the following criteria:
1. Subjects who did not receive any study drug
2. Subjects given wrong drug
3. Subjects mis-randomized

Subjects were classified according to randomized treatment.

| | |
|---|---|
| Subject analysis set title | Per-Protocol Analysis Population |
| Subject analysis set type | Per protocol |

Subject analysis set description:

The Per-Protocol (PP) analysis population contained all subjects in the ITT analysis set who did not experience any reason for exclusion. It was used for sensitivity analysis of the primary efficacy parameter. Subjects were classified according to randomized treatment.

| | |
|---|---|
| Subject analysis set title | Safety Analysis Population |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

The Safety Analysis Set (SAF) population contains all subjects who received at least one dose of study drug. Subjects are classified according to treatment received. If there was any doubt whether a subject was treated or not, they were assumed treated for the purposes of analysis.

| | |
|---|---|
| Subject analysis set title | All Subjects Enrolled Population |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

The All Subjects Enrolled (ENR) population contained all subjects who signed an ICF.

| **Reporting group values** | Intent-to-Treat Analysis Population | Full Analysis Set Population | Per-Protocol Analysis Population |
|---|---|---|---|
| Number of subjects | 106 | 103 | 96 |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 104 | 101 | 94 |
| From 65-84 years | 2 | 2 | 2 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 39.2 | 39.3 | 39.0 |
| standard deviation | ± 11.92 | ± 11.98 | ± 11.75 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 33 | 33 | 64 |
| Male | 73 | 70 | 32 |
| Race<br>Units: Subjects | | | |
| White | 103 | 100 | 93 |
| Black or African American | 3 | 3 | 3 |
| Asian | 0 | 0 | 0 |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Missing | 0 | 0 | 0 |
| Ethnicity<br>Units: Subjects | | | |
| Hispanic or Latino | 16 | 16 | 13 |
| Not Hispanic or Latino | 87 | 85 | 81 |
| Other | 3 | 2 | 2 |

| | | | |
|---|---|---|---|
| Missing | 0 | 0 | 0 |
| Geographic Region<br>Units: Subjects | | | |
| North America | 79 | 77 | 73 |
| Western Europe | 27 | 26 | 23 |
| Smoking status<br>Units: Subjects | | | |
| Never | 87 | 84 | 77 |
| Former | 16 | 16 | 16 |
| Current | 3 | 3 | 3 |
| Missing | 0 | 0 | 0 |
| History of esophageal stricture(s)<br>Units: Subjects | | | |
| Yes | 46 | 46 | 43 |
| No | 60 | 57 | 53 |
| Missing | 0 | 0 | 0 |
| Current esophageal stricture(s) based on the study EGD<br>Units: Subjects | | | |
| Yes | 23 | 23 | 22 |
| No | 83 | 80 | 74 |
| Missing | 0 | 0 | 0 |
| History of positive steroid Response to EoE<br>Units: Subjects | | | |
| Yes | 21 | 19 | 18 |
| No | 85 | 84 | 78 |
| Missing | 0 | 0 | 0 |
| Proton pump inhibitor status<br>Units: Subjects | | | |
| Continuing into study | 71 | 69 | 64 |
| Not continuing into study | 35 | 34 | 32 |
| Missing | 0 | 0 | 0 |
| Height<br>Units: cm | | | |
| arithmetic mean | 174.1 | 174.0 | 174.1 |
| standard deviation | ± 8.63 | ± 8.72 | ± 8.58 |
| Weight<br>Units: kg | | | |
| arithmetic mean | 84.0 | 84.1 | 84.3 |
| standard deviation | ± 17.09 | ± 17.26 | ± 17.28 |
| BMI<br>Units: kg/m2 | | | |
| arithmetic mean | 27.6 | 27.7 | 27.7 |
| standard deviation | ± 5.57 | ± 5.62 | ± 5.69 |
| Global EoE Symptom Score prior to randomization<br>Units: EoE Symptom Score | | | |
| arithmetic mean | 4.8 | 4.8 | 4.7 |
| standard deviation | ± 1.87 | ± 1.88 | ± 1.85 |

| **Reporting group values** | Safety Analysis Population | All Subjects Enrolled Population | |
|---|---|---|---|

| | | | |
|---|---|---|---|
| Number of subjects | 104 | 308 | |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 102 | 296 | |
| From 65-84 years | 2 | 12 | |
| 85 years and over | 0 | 0 | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 39.3 | 41.2 | |
| standard deviation | ± 11.92 | ± 12.98 | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 33 | 121 | |
| Male | 71 | 187 | |
| Race<br>Units: Subjects | | | |
| White | 101 | 284 | |
| Black or African American | 3 | 18 | |
| Asian | 0 | 4 | |
| American Indian or Alaska Native | 0 | 1 | |
| Missing | 0 | 1 | |
| Ethnicity<br>Units: Subjects | | | |
| Hispanic or Latino | 16 | 42 | |
| Not Hispanic or Latino | 85 | 259 | |
| Other | 3 | 6 | |
| Missing | 0 | 1 | |
| Geographic Region<br>Units: Subjects | | | |
| North America | 77 | 261 | |
| Western Europe | 27 | 47 | |
| Smoking status<br>Units: Subjects | | | |
| Never | 85 | 244 | |
| Former | 16 | 48 | |
| Current | 3 | 15 | |
| Missing | 0 | 1 | |
| History of esophageal stricture(s)<br>Units: Subjects | | | |
| Yes | 46 | 113 | |
| No | 58 | 184 | |
| Missing | 0 | 11 | |
| Current esophageal stricture(s) based on the study EGD | | | |

| | | | |
|---|---|---|---|
| Units: Subjects | | | |
| Yes | 23 | 54 | |
| No | 81 | 236 | |
| Missing | 0 | 18 | |
| History of positive steroid Response to EoE<br>Units: Subjects | | | |
| Yes | 19 | 53 | |
| No | 85 | 241 | |
| Missing | 0 | 14 | |
| Proton pump inhibitor status<br>Units: Subjects | | | |
| Continuing into study | 69 | 71 | |
| Not continuing into study | 35 | 35 | |
| Missing | 0 | 202 | |
| Height<br>Units: cm | | | |
| arithmetic mean | 174.1 | 172.6 | |
| standard deviation | ± 8.69 | ± 9.47 | |
| Weight<br>Units: kg | | | |
| arithmetic mean | 83.9 | 85.1 | |
| standard deviation | ± 17.24 | ± 19.76 | |
| BMI<br>Units: kg/m2 | | | |
| arithmetic mean | 27.6 | 28.5 | |
| standard deviation | ± 5.63 | ± 6.54 | |
| Global EoE Symptom Score prior to randomization<br>Units: EoE Symptom Score | | | |
| arithmetic mean | 4.8 | 4.2 | |
| standard deviation | ± 1.87 | ± 2.20 | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Placebo Run-in |
| Reporting group description: | |
| Due to the high placebo response rates, the study utilized a 4-week single-blind placebo run-in period to not only establish the baseline symptoms for the study, but also to ensure that all subjects enrolled had sufficient severity of EoE to warrant inclusion in the study. | |
| Reporting group title | APT-1011 1.5 mg HS |
| Reporting group description: | |
| Subjects received placebo 30 minutes after breakfast and 1.5 mg APT-1011 HS (at bedtime) daily | |
| Reporting group title | APT-1011 1.5 mg BID |
| Reporting group description: | |
| Subjects received 1.5 mg APT-1011 30 minutes after breakfast and at bedtime daily for a total daily dose of 3.0 mg | |
| Reporting group title | APT-1011 3 mg HS |
| Reporting group description: | |
| Subjects received placebo 30 minutes after breakfast and 3.0 mg APT-1011 at bedtime daily | |
| Reporting group title | APT-1011 3 mg BID |
| Reporting group description: | |
| Subjects received 3 mg APT-1011 30 minutes after breakfast and at bedtime daily for a total daily dose of 6.0 mg | |
| Reporting group title | Placebo |
| Reporting group description: | |
| Subjects received placebo 30 minutes after breakfast and HS (at bedtime) daily | |
| Reporting group title | APT-1011 1.5 mg HS |
| Reporting group description: | |
| Subjects received placebo 30 minutes after breakfast and 1.5 mg APT-1011 HS (at bedtime) daily | |
| Reporting group title | APT-1011 1.5 mg BID |
| Reporting group description: | |
| Subjects received 1.5 mg APT-1011 30 minutes after breakfast and at bedtime daily for a total daily dose of 3.0 mg | |
| Reporting group title | APT-1011 3 mg HS |
| Reporting group description: | |
| Subjects received placebo 30 minutes after breakfast and 3.0 mg APT-1011 at bedtime daily | |
| Reporting group title | APT-1011 3 mg BID |
| Reporting group description: | |
| Subjects received 3 mg APT-1011 30 minutes after breakfast and at bedtime daily for a total daily dose of 6.0 mg | |
| Reporting group title | Single-Blind APT-1011 3 mg BID |
| Reporting group description: | |
| Subjects received 3 mg APT-1011 30 minutes after breakfast and at bedtime daily for a total daily dose of 6.0 mg | |
| Subject analysis set title | Intent-to-Treat Analysis Population |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: | |
| The Intent-To-Treat (ITT) analysis population contained all subjects enrolled (All Subjects Enrolled Population) who were randomized. Subjects were classified according to randomized treatment. | |
| Subject analysis set title | Full Analysis Set Population |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| The Full Analysis Set (FAS) analysis population contained all subjects in the ITT population who did not meet any of the following criteria:<br>1. Subjects who did not receive any study drug | |

2. Subjects given wrong drug
3. Subjects mis-randomized
Subjects were classified according to randomized treatment.

| | |
|---|---|
| Subject analysis set title | Per-Protocol Analysis Population |
| Subject analysis set type | Per protocol |

Subject analysis set description:

The Per-Protocol (PP) analysis population contained all subjects in the ITT analysis set who did not experience any reason for exclusion. It was used for sensitivity analysis of the primary efficacy parameter. Subjects were classified according to randomized treatment.

| | |
|---|---|
| Subject analysis set title | Safety Analysis Population |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

The Safety Analysis Set (SAF) population contains all subjects who received at least one dose of study drug. Subjects are classified according to treatment received. If there was any doubt whether a subject was treated or not, they were assumed treated for the purposes of analysis.

| | |
|---|---|
| Subject analysis set title | All Subjects Enrolled Population |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

The All Subjects Enrolled (ENR) population contained all subjects who signed an ICF.

## Primary: Percentage of subjects with ≤6 peak eos/HPF

| | |
|---|---|
| End point title | Percentage of subjects with ≤6 peak eos/HPF |

End point description:

Percentage of subjects with ≤6 peak eosinophils (eos)/high-power field (HPF) after assessing at least 5 to 6 biopsies from the proximal and distal esophagus (approximately 3 each) where the HPF area was 235 square microns (40 magnification lens with a 22 mm ocular)

| | |
|---|---|
| End point type | Primary |

End point timeframe:

Week 12

| End point values | APT-1011 1.5 mg HS | APT-1011 1.5 mg BID | APT-1011 3 mg HS | APT-1011 3 mg BID |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 21 | 22 | 21 | 20 |
| Units: Number of Patients | | | | |
| Responder | 10 | 19 | 14 | 16 |
| Non-Responder | 11 | 3 | 7 | 4 |

| End point values | Placebo | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 19 | | | |
| Units: Number of Patients | | | | |
| Responder | 0 | | | |
| Non-Responder | 19 | | | |

**Statistical analyses**

| **Statistical analysis title** | Histology: 1.5 mg HS to Placebo |
|---|---|
| Comparison groups | APT-1011 1.5 mg HS v Placebo |
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.001 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Odds ratio (OR) |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| Variability estimate | Standard deviation |

| **Statistical analysis title** | Histology: 1.5 mg BID to Placebo |
|---|---|
| Comparison groups | APT-1011 1.5 mg BID v Placebo |
| Number of subjects included in analysis | 41 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Odds ratio (OR) |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| Variability estimate | Standard deviation |

| **Statistical analysis title** | Histology: 3 mg HS to Placebo |
|---|---|
| Comparison groups | APT-1011 3 mg HS v Placebo |
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Odds ratio (OR) |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| Variability estimate | Standard deviation |

| **Statistical analysis title** | Histology: 3 mg BID to Placebo |
|---|---|
| Comparison groups | APT-1011 3 mg BID v Placebo |

| | |
|---|---|
| Number of subjects included in analysis | 39 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Odds ratio (OR) |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| Variability estimate | Standard deviation |

## Secondary: Percentage of Subjects Who Met the Primary Endpoint at Week 12 and Maintained the Primary Endpoint at Weeks 26 and 52

| | |
|---|---|
| End point title | Percentage of Subjects Who Met the Primary Endpoint at Week 12 and Maintained the Primary Endpoint at Weeks 26 and 52 |

End point description:

Percentage of subjects who met the primary endpoint (histology) at Week 12 and maintained the primary endpoint at Weeks 26 and 52
Note: Following Week 14, all patients in the placebo group were given APT-1011 3mg BID and results reflect percentage of subjects who met the primary endpoint following 12 or 38 weeks of treatment.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Week 26, and Week 52

| End point values | APT-1011 1.5 mg HS | APT-1011 1.5 mg BID | APT-1011 3 mg HS | APT-1011 3 mg BID |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 10 | 19 | 14 | 16 |
| Units: Percentage of particpants | | | | |
| Week 26 Responders | 7 | 17 | 11 | 14 |
| Week 52 Responders | 3 | 16 | 9 | 11 |

| End point values | Placebo | Single-Blind APT-1011 3 mg BID | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 18 | | |
| Units: Percentage of particpants | | | | |
| Week 26 Responders | 12 | 7 | | |
| Week 52 Responders | 10 | 5 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline Eosinophilic Esophagitis Endoscopic Reference Score (EREFs) at Weeks 12, 26, and 52

| End point title | Change from Baseline Eosinophilic Esophagitis Endoscopic Reference Score (EREFs) at Weeks 12, 26, and 52 |
|---|---|

End point description:

Endoscopic changes will be assessed as per the EREFs evaluation based on the following endoscopic features: edema, rings, exudates, furrows, stricture, and several miscellaneous features (crepe paper esophagus, narrow caliber esophagus, and esophageal erosions).
Note: Following Week 14, all patients in the placebo group were given APT-1011 3mg BID and results reflect EREF evaluation following 12 or 38 weeks of treatment.

| End point type | Secondary |
|---|---|

End point timeframe:

Week 12, Week 26, and Week 52

| End point values | APT-1011 1.5 mg HS | APT-1011 1.5 mg BID | APT-1011 3 mg HS | APT-1011 3 mg BID |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 21 | 22 | 21 | 20 |
| Units: mean change | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 12 (n=18, n=20, n=20, n=19, n=17) | -2.4 (± 2.04) | -2.7 (± 2.66) | -3.3 (± 2.36) | -2.2 (± 2.15) |
| Week 26 (n=8, n=19, n=13, n=16, n=0) | -3.1 (± 1.25) | -3.2 (± 2.77) | -4.2 (± 2.61) | -3.0 (± 1.67) |
| Week 52 (n=5, n=17, n=11, n=14, n=0) | -3.4 (± 1.82) | -3.5 (± 3.08) | -3.8 (± 3.19) | -2.9 (± 1.29) |

| End point values | Placebo | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 19 | | | |
| Units: mean change | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 12 (n=18, n=20, n=20, n=19, n=17) | -0.9 (± 1.63) | | | |
| Week 26 (n=8, n=19, n=13, n=16, n=0) | 0 (± 0) | | | |
| Week 52 (n=5, n=17, n=11, n=14, n=0) | 0 (± 0) | | | |

### Statistical analyses

| Statistical analysis title | Change from Baseline EREFs: 1.5 mg HS to Placebo |
|---|---|
| Comparison groups | APT-1011 1.5 mg HS v Placebo |

| | |
|---|---|
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.02 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -1.28 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -2.29 |
| upper limit | -0.26 |
| Variability estimate | Standard deviation |

| **Statistical analysis title** | Change from Baseline EREFs: 1.5 mg BID to Placebo |
|---|---|
| Comparison groups | APT-1011 1.5 mg BID v Placebo |
| Number of subjects included in analysis | 41 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -2.08 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -3.07 |
| upper limit | -1.1 |
| Variability estimate | Standard deviation |

| **Statistical analysis title** | Change from Baseline EREFs: 3.0 mg HS to Placebo |
|---|---|
| Comparison groups | APT-1011 3 mg HS v Placebo |
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -2.25 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -3.23 |
| upper limit | -1.26 |
| Variability estimate | Standard deviation |

| **Statistical analysis title** | Change from Baseline EREFs: 3 mg BID to Placebo |
|---|---|
| Comparison groups | APT-1011 3 mg BID v Placebo |
| Number of subjects included in analysis | 39 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.005 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -1.59 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -2.59 |
| upper limit | -0.59 |
| Variability estimate | Standard deviation |

## Secondary: Percentage of Subjects With a Peak Eosinophils/HPF Number <1 and <15

| End point title | Percentage of Subjects With a Peak Eosinophils/HPF Number <1 and <15 |
|---|---|

End point description:

Peak eosinophils/high power field (HPF) number <1 and <15 at Weeks 12, 26 and 52
Note: Following Week 14, all patients in the placebo group were given APT-1011 3mg BID and results reflect peak eosinophils/HPF following 12 or 38 weeks of treatment.

| End point type | Secondary |
|---|---|

End point timeframe:

Week 12, Week 26, Week 52

| **End point values** | APT-1011 1.5 mg HS | APT-1011 1.5 mg BID | APT-1011 3 mg HS | APT-1011 3 mg BID |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 21 | 22 | 21 | 20 |
| Units: Percentage of Participants | | | | |
| number (not applicable) | | | | |
| Week 12 <1/HPF | 38.9 | 70.0 | 60.0 | 78.9 |
| Week 12 <15 HPF | 66.7 | 95.0 | 75.0 | 84.2 |
| Week 26 <1/HPF | 50.0 | 78.9 | 69.2 | 81.3 |
| Week 26 <15/HPF | 100.0 | 94.7 | 92.3 | 87.5 |
| Week 52 <1/HPF | 20.0 | 70.6 | 63.6 | 71.4 |
| Week 52 <15/HPF | 60.0 | 100.0 | 90.9 | 85.7 |

| End point values | Placebo | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 19 | | | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | | | | |
| Week 12 <1/HPF | 0 | | | |
| Week 12 <15 HPF | 5.9 | | | |
| Week 26 <1/HPF | 0 | | | |
| Week 26 <15/HPF | 0 | | | |
| Week 52 <1/HPF | 0 | | | |
| Week 52 <15/HPF | 0 | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline Global EOE Symptom Score

| End point title | Change From Baseline Global EOE Symptom Score |
|---|---|

End point description:

Change from Baseline Global EOE Symptom Score Assessed Prior to Randomization
Note: Following Week 14, all patients in the placebo group were given APT-1011 3mg BID and results reflect change from baseline global EOE symptom score following 4, 8, 12, 14, 22, 30 or 38 weeks of treatment.

| End point type | Secondary |
|---|---|

End point timeframe:

Weeks 4, 8, 12, 14, 18, 22, 26, 28, 36, 44, 52

| End point values | APT-1011 1.5 mg HS | APT-1011 1.5 mg BID | APT-1011 3 mg HS | APT-1011 3 mg BID |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 21 | 22 | 21 | 20 |
| Units: Mean | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 4 (n=21, n=20, n=20, n=20, n=16) | -1.8 (± 2.64) | -1.3 (± 2.15) | -2.5 (± 3.12) | -1.6 (± 1.39) |
| Week 8 (n=18, n=22, n=19, n=20, n=17) | -2.6 (± 2.12) | -1.7 (± 1.94) | -3.1 (± 2.64) | -2.1 (± 1.92) |
| Week 12 (n=18, n=21, n=20, n=19, n=17) | -3.1 (± 2.17) | -1.5 (± 2.20) | -3.1 (± 2.74) | -1.7 (± 2.42) |
| Week 14 (n=10, n=18, n=13, n=16, n=0) | -2.7 (± 2.26) | -2.3 (± 2.45) | -3.9 (± 2.81) | -2.8 (± 1.77) |
| Week 18 (n=9, n=19, n=14, n=15, n=0) | -4.1 (± 1.36) | -2.7 (± 2.58) | -4.1 (± 2.92) | -3.1 (± 2.17) |
| Week 22 (n=8, n=19, n=14, n=16, n=0) | -4.0 (± 1.41) | -3.2 (± 2.46) | -3.8 (± 2.97) | -3.0 (± 2.76) |
| Week 26 (n=8, n=18, n=13, n=16, n=0) | -3.8 (± 1.39) | -3.1 (± 2.52) | -4.0 (± 2.68) | -3.8 (± 2.57) |
| Week 28 (n=7, n=18, n=10, n=14 n=0) | -4.3 (± 1.38) | -3.3 (± 2.42) | -4.8 (± 2.44) | -3.9 (± 2.09) |

| | | | | |
|---|---|---|---|---|
| Week 36 (n=6, n=16, n=11, n=14, n=0) | -4.2 (± 1.47) | -3.9 (± 2.25) | -4.8 (± 2.09) | -3.9 (± 2.07) |
| Week 44 (n=5, n=15, n=11, n=14, n=0) | -4.8 (± 2.39) | -3.7 (± 2.41) | -4.4 (± 3.20) | -4.4 (± 1.95) |
| Week 52 (n=4, n=14, n=10, n=14, n=0) | -3.3 (± 1.71) | -3.1 (± 2.40) | -4.2 (± 2.66) | -4.7 (± 2.27) |

| **End point values** | Placebo | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 19 | | | |
| Units: Mean | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 4 (n=21, n=20, n=20, n=20, n=16) | -1.0 (± 1.67) | | | |
| Week 8 (n=18, n=22, n=19, n=20, n=17) | -1.4 (± 2.21) | | | |
| Week 12 (n=18, n=21, n=20, n=19, n=17) | -1.7 (± 1.83) | | | |
| Week 14 (n=10, n=18, n=13, n=16, n=0) | 0 (± 0) | | | |
| Week 18 (n=9, n=19, n=14, n=15, n=0) | 0 (± 0) | | | |
| Week 22 (n=8, n=19, n=14, n=16, n=0) | 0 (± 0) | | | |
| Week 26 (n=8, n=18, n=13, n=16, n=0) | 0 (± 0) | | | |
| Week 28 (n=7, n=18, n=10, n=14 n=0) | 0 (± 0) | | | |
| Week 36 (n=6, n=16, n=11, n=14, n=0) | 0 (± 0) | | | |
| Week 44 (n=5, n=15, n=11, n=14, n=0) | 0 (± 0) | | | |
| Week 52 (n=4, n=14, n=10, n=14, n=0) | 0 (± 0) | | | |

**Statistical analyses**

| **Statistical analysis title** | CFB Week 12: 1.5 mg HS to Placebo |
|---|---|
| Comparison groups | APT-1011 1.5 mg HS v Placebo |
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.067 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -1.19 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -2.49 |
| upper limit | 0.12 |

| | |
|---|---|
| Variability estimate | Standard deviation |

| **Statistical analysis title** | CFB Week 12: 1.5 mg BID to Placebo |
|---|---|
| Comparison groups | APT-1011 1.5 mg BID v Placebo |
| Number of subjects included in analysis | 41 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.672 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.34 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -0.91 |
| upper limit | 1.59 |
| Variability estimate | Standard deviation |

| **Statistical analysis title** | CFB Week 12: 3 mg HS to Placebo |
|---|---|
| Comparison groups | Placebo v APT-1011 3 mg HS |
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.048 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -1.28 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -2.55 |
| upper limit | -0.01 |
| Variability estimate | Standard deviation |

| **Statistical analysis title** | CFB Week 12: 3 mg BID to Placebo |
|---|---|
| Comparison groups | Placebo v APT-1011 3 mg BID |
| Number of subjects included in analysis | 39 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.653 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.31 |

| | |
|---|---|
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -0.98 |
| upper limit | 1.59 |
| Variability estimate | Standard deviation |

## Secondary: Change in the Number of Dysphagia Episodes

| | |
|---|---|
| End point title | Change in the Number of Dysphagia Episodes |

End point description:

Change in the number of dysphagia episodes at baseline (14-day period prior to randomization) compared with the 14-day period prior to the timepoint of interest
Note: Following Week 14, all patients in the placebo group were given APT-1011 3mg BID and results reflect the change in the number of dysphagia episodes following 12 or 38 weeks of treatment.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Weeks, 12, 26 and 52

| End point values | APT-1011 1.5 mg HS | APT-1011 1.5 mg BID | APT-1011 3 mg HS | APT-1011 3 mg BID |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 21 | 22 | 21 | 20 |
| Units: mean change from baseline | | | | |
| arithmetic mean (standard deviation) | | | | |
| CFB Week 12 (n=18, n=21, n=20, n=19, n=17) | -8.2 (± 5.48) | -4.4 (± 9.41) | -9.3 (± 7.37) | -9.1 (± 11.01) |
| CFB Week 26 (n=8, n=19, n=13, n=15, n=0) | -12.8 (± 5.65) | -10.0 (± 10.97) | -9.8 (± 7.82) | -13.4 (± 11.78) |
| CFB Week 52 (n=5, n=16, n=10, n=14, n=0) | -11.2 (± 5.26) | -13.0 (± 10.79) | -9.5 (± 9.66) | -14.5 (± 11.68) |

| End point values | Placebo | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 19 | | | |
| Units: mean change from baseline | | | | |
| arithmetic mean (standard deviation) | | | | |
| CFB Week 12 (n=18, n=21, n=20, n=19, n=17) | -5.5 (± 7.89) | | | |
| CFB Week 26 (n=8, n=19, n=13, n=15, n=0) | 0 (± 0) | | | |
| CFB Week 52 (n=5, n=16, n=10, n=14, n=0) | 0 (± 0) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline 7-Day Eosinophilic Esophagitis Activity Index (EEsAI) Total Score

| End point title | Change from Baseline 7-Day Eosinophilic Esophagitis Activity Index (EEsAI) Total Score |
|---|---|

End point description:

Change from Baseline 7-Day 7-day Eosinophilic Esophagitis Activity Index (EEsAI) total score assessed prior to randomization and those assessed at Weeks 12, 26 and 52 (Total score 100)
Components of the EEsAI were also reported: Avoidance, Modifiacion and Slow Eating (AMS) Score, minimum 0, maximum 10; and Visual Dysphagia Question (VDQ) Score, minimum 0, maximum 10.
Higher score means a worse outcome
Note: Following Week 14, all patients in the placebo group were given APT-1011 3mg BID and results reflect the change from baseline 7-day EEsAI total score following 12 or 38 weeks of treatment.

| End point type | Secondary |
|---|---|

End point timeframe:

Weeks 12, 26 and 52

| End point values | APT-1011 1.5 mg HS | APT-1011 1.5 mg BID | APT-1011 3 mg HS | APT-1011 3 mg BID |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 21 | 22 | 21 | 20 |
| Units: Mean Change from Baseline | | | | |
| arithmetic mean (standard deviation) | | | | |
| EEsAI Week 12 (n=18, n=20, n=20, n=19, n=17) | -20.4 (± 15.90) | -15.6 (± 21.02) | -22.7 (± 16.60) | -22.6 (± 21.11) |
| EEsAI Week 26 (n=8, n=19, n=13, n=16, n=0) | -25.6 (± 21.11) | -29.6 (± 25.48) | -28.8 (± 21.10) | -34.6 (± 25.43) |
| EEsAI Week 52 (n=5, n=17, n=11, n=14, n=0) | -39.8 (± 28.42) | -37.4 (± 27.02) | -37.0 (± 23.72) | -41.1 (± 20.56) |

| End point values | Placebo | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 19 | | | |
| Units: Mean Change from Baseline | | | | |
| arithmetic mean (standard deviation) | | | | |
| EEsAI Week 12 (n=18, n=20, n=20, n=19, n=17) | -9.6 (± 14.07) | | | |
| EEsAI Week 26 (n=8, n=19, n=13, n=16, n=0) | 0 (± 0) | | | |
| EEsAI Week 52 (n=5, n=17, n=11, n=14, n=0) | 0 (± 0) | | | |

## Statistical analyses

| **Statistical analysis title** | EEsAI Total Score Change from Baseline Week 12 |
|---|---|
| Comparison groups | APT-1011 1.5 mg HS v Placebo |
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.071 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -8.81 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -19.36 |
| upper limit | 1.13 |
| Variability estimate | Standard deviation |

| **Statistical analysis title** | EEsAI Total Score Change from Baseline Week 12 |
|---|---|
| Comparison groups | APT-1011 1.5 mg BID v Placebo |
| Number of subjects included in analysis | 41 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.217 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -5.18 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -14.72 |
| upper limit | 5.28 |
| Variability estimate | Standard deviation |

| **Statistical analysis title** | EEsAI Total Score Change from Baseline Week 12 |
|---|---|
| Comparison groups | APT-1011 3 mg HS v Placebo |
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.016 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -12.56 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -23.04 |
| upper limit | -3.05 |

| | |
|---|---|
| Variability estimate | Standard deviation |

| **Statistical analysis title** | EEsAI Total Score Change from Baseline Week 12 |
|---|---|
| Comparison groups | Placebo v APT-1011 3 mg BID |
| Number of subjects included in analysis | 39 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.05 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -10.61 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -20.4 |
| upper limit | 0.02 |
| Variability estimate | Standard deviation |

**Secondary: Percentage of subjects with mean 7-day EEsAI total score <20**

| End point title | Percentage of subjects with mean 7-day EEsAI total score <20 |
|---|---|

End point description:

Percentage of subjects with mean 7-day EEsAI total score <20 to those assessed at Weeks 12, 26, and 52
Note: Following Week 14, all patients in the placebo group were given APT-1011 3mg BID and results reflect change from baseline global EOE symptom score following 12 or 38 weeks of treatment.

| End point type | Secondary |
|---|---|

End point timeframe:

Weeks 12, 26, and 52

| **End point values** | APT-1011 1.5 mg HS | APT-1011 1.5 mg BID | APT-1011 3 mg HS | APT-1011 3 mg BID |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 21 | 22 | 21 | 20 |
| Units: Percentage of Participants | | | | |
| number (not applicable) | | | | |
| Week 12 (n=18, n=20, n=20, n=19, n=17) | 22.2 | 5.0 | 30.0 | 26.3 |
| Week 26 (n=8, n=19, n=13, n=16, n=0) | 37.5 | 26.3 | 53.8 | 43.8 |
| Week 52 (n=5, n=17, n=11, n=14, n=0) | 60.0 | 41.2 | 63.6 | 71.4 |

| **End point values** | Placebo | | | |
|---|---|---|---|---|

| Subject group type | Reporting group | | | |
|---|---|---|---|---|
| Number of subjects analysed | 19 | | | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | | | | |
| Week 12 (n=18, n=20, n=20, n=19, n=17) | 11.8 | | | |
| Week 26 (n=8, n=19, n=13, n=16, n=0) | 0 | | | |
| Week 52 (n=5, n=17, n=11, n=14, n=0) | 0 | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change in Patient Global Impression of Severity (PGIS) for EoE Symptoms

| End point title | Change in Patient Global Impression of Severity (PGIS) for EoE Symptoms |
|---|---|

End point description:

Change From Baseline PGIS for EoE Symptoms as Assessed Prior to Randomization at Weeks 4, 8, 12, 14, 18, 22, 26, 28, 36, 44, and 52
Note: Following Week 14, all patients in the placebo group were given APT-1011 3mg BID and results reflect change from baseline global EOE symptom score following 4, 8, 12, 14, 22, 30 or 38 weeks of treatment.

| End point type | Secondary |
|---|---|

End point timeframe:

Weeks, 4, 8, 12, 14, 18, 22, 26, 28, 36, 44, and 52

| End point values | APT-1011 1.5 mg HS | APT-1011 1.5 mg BID | APT-1011 3 mg HS | APT-1011 3 mg BID |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 21 | 22 | 21 | 20 |
| Units: Percentage of participants | | | | |
| Week 4 Mild to None (n=20, n=19, n=20, n=19, n=15) | 1 | 0 | 0 | 0 |
| Week 4 Mild to Mild | 0 | 0 | 1 | 0 |
| Week 4 Mild to Moderate | 0 | 0 | 0 | 0 |
| Week 4 Mild to Severe | 1 | 0 | 0 | 0 |
| Week 4 Mild to Very Severe | 0 | 0 | 0 | 0 |
| Week 4 Moderate to None | 0 | 0 | 4 | 0 |
| Week 4 Moderate to Mild | 8 | 7 | 5 | 6 |
| Week 4 Moderate to Moderate | 5 | 5 | 4 | 7 |
| Week 4 Moderate to Severe | 0 | 0 | 0 | 1 |
| Week 4 Moderate to Very Severe | 0 | 0 | 0 | 0 |
| Week 4 Severe to None | 0 | 0 | 1 | 0 |
| Week 4 Severe to Mild | 3 | 1 | 1 | 1 |
| Week 4 Severe to Moderate | 1 | 3 | 3 | 4 |

| | | | | |
|---|---|---|---|---|
| Week 4 Severe to Severe | 0 | 3 | 1 | 0 |
| Week 4 Severe to Very Severe | 0 | 0 | 0 | 0 |
| Week 4 Very Severe to None | 0 | 0 | 0 | 0 |
| Week 4 Very Severe to Mild | 0 | 0 | 0 | 0 |
| Week 4 Very Severe to Moderate | 0 | 0 | 0 | 0 |
| Week 4 Very Severe to Severe | 0 | 0 | 0 | 0 |
| Week 4 Very Severe to Very Severe | 1 | 0 | 0 | 0 |
| Week 8 Mild to None (n=17, n=21, n=19, n=19, n=16) | 0 | 0 | 0 | 0 |
| Week 8 Mild to Mild | 0 | 0 | 1 | 0 |
| Week 8 Mild to Moderate | 1 | 0 | 0 | 0 |
| Week 8 Mild to Severe | 0 | 0 | 0 | 0 |
| Week 8 Mild to Very Severe | 0 | 0 | 0 | 0 |
| Week 8 Moderate to None | 1 | 1 | 4 | 2 |
| Week 8 Moderate to Mild | 8 | 6 | 5 | 6 |
| Week 8 Moderate to Moderate | 3 | 6 | 3 | 6 |
| Week 8 Moderate to Severe | 0 | 0 | 0 | 0 |
| Week 8 Moderate to Very Severe | 0 | 0 | 0 | 0 |
| Week 8 Severe to None | 1 | 0 | 1 | 1 |
| Week 8 Severe to Mild | 1 | 1 | 2 | 0 |
| Week 8 Severe to Moderate | 1 | 6 | 1 | 4 |
| Week 8 Severe to Severe | 0 | 1 | 2 | 0 |
| Week 8 Severe to Very Severe | 0 | 0 | 0 | 0 |
| Week 8 Very Severe to None | 0 | 0 | 0 | 0 |
| Week 8 Very Severe to Mild | 0 | 0 | 0 | 0 |
| Week 8 Very Severe to Moderate | 0 | 0 | 0 | 0 |
| Week 8 Very Severe to Severe | 1 | 0 | 0 | 0 |
| Week 8 Very Severe to Very Severe | 0 | 0 | 0 | 0 |
| Week 12 Mild to None (n=18, n=20, n=20, n=18,n=17) | 0 | 0 | 0 | 0 |
| Week 12 Mild to Mild | 1 | 0 | 1 | 0 |
| Week 12 Mild to Moderate | 0 | 0 | 0 | 0 |
| Week 12 Mild to Severe | 0 | 0 | 0 | 0 |
| Week 12 Mild to Very Severe | 0 | 0 | 0 | 0 |
| Week 12 Moderate to None | 1 | 0 | 5 | 2 |
| Week 12 Moderate to Mild | 10 | 7 | 5 | 6 |
| Week 12 Moderate to Moderate | 2 | 5 | 3 | 4 |
| Week 12 Moderate to Severe | 0 | 0 | 0 | 1 |
| Week 12 Moderate to Very Severe | 0 | 0 | 0 | 0 |
| Week 12 Severe to None | 2 | 0 | 1 | 1 |
| Week 12 Severe to Mild | 1 | 3 | 0 | 1 |
| Week 12 Severe to Moderate | 0 | 4 | 4 | 2 |
| Week 12 Severe to Severe | 0 | 1 | 1 | 1 |
| Week 12 Severe to Very Severe | 0 | 0 | 0 | 0 |
| Week 12 Very Severe to None | 0 | 0 | 0 | 0 |
| Week 12 Very Severe to Mild | 0 | 0 | 0 | 0 |
| Week 12 Very Severe to Moderate | 1 | 0 | 0 | 0 |
| Week 12 Very Severe to Severe | 0 | 0 | 0 | 0 |
| Week 12 Very Severe to Very Severe | 0 | 0 | 0 | 0 |
| Week 14 Mild to None (n=10, n=18, n=13, n=15, n=0) | 0 | 0 | 0 | 0 |
| Week 14 Mild to Mild | 1 | 0 | 1 | 0 |
| Week 14 Mild to Moderate | 0 | 0 | 0 | 0 |

| | | | | |
|---|---|---|---|---|
| Week 14 Mild to Severe | 0 | 0 | 0 | 0 |
| Week 14 Mild to Very Severe | 0 | 0 | 0 | 0 |
| Week 14 Moderate to None | 0 | 1 | 5 | 4 |
| Week 14 Moderate to Mild | 7 | 8 | 1 | 3 |
| Week 14 Moderate to Moderate | 0 | 2 | 1 | 4 |
| Week 14 Moderate to Severe | 0 | 0 | 0 | 0 |
| Week 14 Moderate to Very Severe | 0 | 0 | 0 | 0 |
| Week 14 Severe to None | 0 | 1 | 0 | 1 |
| Week 14 Severe to Mild | 1 | 1 | 3 | 1 |
| Week 14 Severe to Moderate | 0 | 5 | 1 | 2 |
| Week 14 Severe to Severe | 0 | 0 | 1 | 0 |
| Week 14 Severe to Very Severe | 0 | 0 | 0 | 0 |
| Week 14 Very Severe to None | 0 | 0 | 0 | 0 |
| Week 14 Very Severe to Mild | 0 | 0 | 0 | 0 |
| Week 14 Very Severe to Moderate | 0 | 0 | 0 | 0 |
| Week 14 Very Severe to Severe | 0 | 0 | 0 | 0 |
| Week 14 Very Severe to Very Severe | 1 | 0 | 0 | 0 |
| Week 18 Mild to None (n=9, n=18, n=14, n=14, n=0) | 0 | 0 | 0 | 0 |
| Week 18 Mild to Mild | 0 | 0 | 1 | 0 |
| Week 18 Mild to Moderate | 0 | 0 | 0 | 0 |
| Week 18 Mild to Severe | 0 | 0 | 0 | 0 |
| Week 18 Mild to Very Severe | 0 | 0 | 0 | 0 |
| Week 18 Moderate to None | 0 | 1 | 5 | 5 |
| Week 18 Moderate to Mild | 6 | 9 | 2 | 4 |
| Week 18 Moderate to Moderate | 1 | 1 | 1 | 2 |
| Week 18 Moderate to Severe | 0 | 0 | 0 | 0 |
| Week 18 Moderate to Very Severe | 0 | 0 | 0 | 0 |
| Week 18 Severe to None | 0 | 2 | 1 | 0 |
| Week 18 Severe to Mild | 1 | 2 | 2 | 1 |
| Week 18 Severe to Moderate | 0 | 3 | 1 | 2 |
| Week 18 Severe to Severe | 0 | 0 | 1 | 0 |
| Week 18 Severe to Very Severe | 0 | 0 | 0 | 0 |
| Week 18 Very Severe to None | 0 | 0 | 0 | 0 |
| Week 18 Very Severe to Mild | 0 | 0 | 0 | 0 |
| Week 18 Very Severe to Moderate | 1 | 0 | 0 | 0 |
| Week 18 Very Severe to Severe | 0 | 0 | 0 | 0 |
| Week 18 Very Severe to Very Severe | 0 | 0 | 0 | 0 |
| Week 22 Mild to None (n=8, n=18, n=13, n=16, n=0) | 0 | 0 | 0 | 0 |
| Week 22 Mild to Mild | 0 | 0 | 1 | 0 |
| Week 22 Mild to Moderate | 0 | 0 | 0 | 0 |
| Week 22 Mild to Severe | 0 | 0 | 0 | 0 |
| Week 22 Mild to Very Severe | 0 | 0 | 0 | 0 |
| Week 22 Moderate to None | 1 | 2 | 3 | 4 |
| Week 22 Moderate to Mild | 6 | 8 | 2 | 3 |
| Week 22 Moderate to Moderate | 0 | 1 | 2 | 5 |
| Week 22 Moderate to Severe | 0 | 0 | 0 | 0 |
| Week 22 Moderate to Very Severe | 0 | 0 | 0 | 0 |
| Week 22 Severe to None | 0 | 1 | 1 | 2 |
| Week 22 Severe to Mild | 1 | 3 | 1 | 0 |
| Week 22 Severe to Moderate | 0 | 2 | 2 | 2 |

| | | | | |
|---|---|---|---|---|
| Week 22 Severe to Severe | 0 | 1 | 0 | 0 |
| Week 22 Severe to Very Severe | 0 | 0 | 1 | 0 |
| Week 22 Very Severe to None | 0 | 0 | 0 | 0 |
| Week 22 Very Severe to Mild | 0 | 0 | 0 | 0 |
| Week 22 Very Severe to Moderate | 0 | 0 | 0 | 0 |
| Week 22 Very Severe to Severe | 0 | 0 | 0 | 0 |
| Week 22 Very Severe to Very Severe | 0 | 0 | 0 | 0 |
| Week 26 Mild to None (n=8, n=17, n=13, n=16, n=0) | 0 | 0 | 0 | 0 |
| Week 26 Mild to Mild | 0 | 0 | 1 | 0 |
| Week 26 Mild to Moderate | 0 | 0 | 0 | 0 |
| Week 26 Mild to Severe | 0 | 0 | 0 | 0 |
| Week 26 Mild to Very Severe | 0 | 0 | 0 | 0 |
| Week 26 Moderate to None | 2 | 1 | 4 | 5 |
| Week 26 Moderate to Mild | 2 | 8 | 2 | 5 |
| Week 26 Moderate to Moderate | 2 | 2 | 1 | 2 |
| Week 26 Moderate to Severe | 0 | 0 | 0 | 0 |
| Week 26 Moderate to Very Severe | 0 | 0 | 0 | 0 |
| Week 26 Severe to None | 0 | 2 | 2 | 1 |
| Week 26 Severe to Mild | 1 | 2 | 2 | 2 |
| Week 26 Severe to Moderate | 0 | 2 | 0 | 1 |
| Week 26 Severe to Severe | 0 | 0 | 1 | 0 |
| Week 26 Severe to Very Severe | 0 | 0 | 0 | 0 |
| Week 26 Very Severe to None | 0 | 0 | 0 | 0 |
| Week 26 Very Severe to Mild | 0 | 0 | 0 | 0 |
| Week 26 Very Severe to Moderate | 1 | 0 | 0 | 0 |
| Week 26 Very Severe to Severe | 0 | 0 | 0 | 0 |
| Week 26 Very Severe to Very Severe | 0 | 0 | 0 | 0 |
| Week 28 Mild to None (n=7, n=16, n=10, n=14, n=0) | 0 | 0 | 0 | 0 |
| Week 28 Mild to Mild | 0 | 0 | 1 | 0 |
| Week 28 Mild to Moderate | 0 | 0 | 0 | 0 |
| Week 28 Mild to Severe | 0 | 0 | 0 | 0 |
| Week 28 Mild to Very Severe | 0 | 0 | 0 | 0 |
| Week 28 Moderate to None | 2 | 1 | 4 | 4 |
| Week 28 Moderate to Mild | 3 | 7 | 1 | 5 |
| Week 28 Moderate to Moderate | 0 | 2 | 0 | 1 |
| Week 28 Moderate to Severe | 0 | 0 | 0 | 0 |
| Week 28 Moderate to Very Severe | 0 | 0 | 0 | 0 |
| Week 28 Severe to None | 0 | 2 | 2 | 1 |
| Week 28 Severe to Mild | 1 | 2 | 0 | 3 |
| Week 28 Severe to Moderate | 0 | 2 | 1 | 0 |
| Week 28 Severe to Severe | 0 | 0 | 1 | 0 |
| Week 28 Severe to Very Severe | 0 | 0 | 0 | 0 |
| Week 28 Very Severe to None | 0 | 0 | 0 | 0 |
| Week 28 Very Severe to Mild | 1 | 0 | 0 | 0 |
| Week 28 Very Severe to Moderate | 0 | 0 | 0 | 0 |
| Week 28 Very Severe to Severe | 0 | 0 | 0 | 0 |
| Week 28 Very Severe to Very Severe | 0 | 0 | 0 | 0 |
| Week 36 Mild to None (n=6, n=15, n=11, n=14, n=0) | 0 | 0 | 0 | 0 |
| Week 36 Mild to Mild | 0 | 0 | 1 | 0 |
| Week 36 Mild to Moderate | 0 | 0 | 0 | 0 |

| | | | | |
|---|---|---|---|---|
| Week 36 Mild to Severe | 0 | 0 | 0 | 0 |
| Week 36 Mild to Very Severe | 0 | 0 | 0 | 0 |
| Week 36 Moderate to None | 0 | 2 | 5 | 4 |
| Week 36 Moderate to Mild | 4 | 7 | 1 | 5 |
| Week 36 Moderate to Moderate | 0 | 1 | 0 | 1 |
| Week 36 Moderate to Severe | 0 | 0 | 0 | 0 |
| Week 36 Moderate to Very Severe | 0 | 0 | 0 | 0 |
| Week 36 Severe to None | 0 | 3 | 2 | 1 |
| Week 36 Severe to Mild | 1 | 2 | 1 | 2 |
| Week 36 Severe to Moderate | 0 | 0 | 0 | 1 |
| Week 36 Severe to Severe | 0 | 0 | 0 | 0 |
| Week 36 Severe to Very Severe | 0 | 0 | 1 | 0 |
| Week 36 Very Severe to None | 0 | 0 | 0 | 0 |
| Week 36 Very Severe to Mild | 0 | 0 | 0 | 0 |
| Week 36 Very Severe to Moderate | 1 | 0 | 0 | 0 |
| Week 36 Very Severe to Severe | 0 | 0 | 0 | 0 |
| Week 36 Very Severe to Very Severe | 0 | 0 | 0 | 0 |
| Week 44 Mild to None (n=5, n=15, n=10, n=14, n=0) | 0 | 0 | 0 | 0 |
| Week 44 Mild to Mild | 0 | 0 | 1 | 0 |
| Week 44 Mild to Moderate | 0 | 0 | 0 | 0 |
| Week 44 Mild to Severe | 0 | 0 | 0 | 0 |
| Week 44 Mild to Very Severe | 0 | 0 | 0 | 0 |
| Week 44 Moderate to None | 1 | 1 | 3 | 5 |
| Week 44 Moderate to Mild | 2 | 8 | 1 | 4 |
| Week 44 Moderate to Moderate | 0 | 1 | 1 | 1 |
| Week 44 Moderate to Severe | 0 | 0 | 0 | 0 |
| Week 44 Moderate to Very Severe | 0 | 0 | 0 | 0 |
| Week 44 Severe to None | 0 | 3 | 2 | 2 |
| Week 44 Severe to Mild | 1 | 2 | 1 | 1 |
| Week 44 Severe to Moderate | 0 | 0 | 0 | 1 |
| Week 44 Severe to Severe | 0 | 0 | 0 | 0 |
| Week 44 Severe to Very Severe | 0 | 0 | 1 | 0 |
| Week 44 Very Severe to None | 0 | 0 | 0 | 0 |
| Week 44 Very Severe to Mild | 1 | 0 | 0 | 0 |
| Week 44 Very Severe to Moderate | 0 | 0 | 0 | 0 |
| Week 44 Very Severe to Severe | 0 | 0 | 0 | 0 |
| Week 44 Very Severe to Very Severe | 0 | 0 | 0 | 0 |
| Week 52 Mild to None (n=4, n=14, n=10, n=14, n=0) | 0 | 0 | 1 | 0 |
| Week 52 Mild to Mild | 0 | 0 | 0 | 0 |
| Week 52 Mild to Moderate | 0 | 0 | 0 | 0 |
| Week 52 Mild to Severe | 0 | 0 | 0 | 0 |
| Week 52 Mild to Very Severe | 0 | 0 | 0 | 0 |
| Week 52 Moderate to None | 0 | 3 | 5 | 8 |
| Week 52 Moderate to Mild | 3 | 3 | 1 | 1 |
| Week 52 Moderate to Moderate | 0 | 4 | 0 | 1 |
| Week 52 Moderate to Severe | 0 | 0 | 0 | 0 |
| Week 52 Moderate to Very Severe | 0 | 0 | 0 | 0 |
| Week 52 Severe to None | 0 | 3 | 1 | 3 |
| Week 52 Severe to Mild | 0 | 1 | 1 | 0 |
| Week 52 Severe to Moderate | 1 | 0 | 0 | 1 |

| | | | | |
|---|---|---|---|---|
| Week 52 Severe to Severe | 0 | 0 | 0 | 0 |
| Week 52 Severe to Very Severe | 0 | 0 | 1 | 0 |
| Week 52 Very Severe to None | 0 | 0 | 0 | 0 |
| Week 52 Very Severe to Mild | 0 | 0 | 0 | 0 |
| Week 52 Very Severe to Moderate | 0 | 0 | 0 | 0 |
| Week 52 Very Severe to Severe | 0 | 0 | 0 | 0 |
| Week 52 Very Severe to Very Severe | 0 | 0 | 0 | 0 |

| **End point values** | Placebo | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 19 | | | |
| Units: Percentage of participants | | | | |
| Week 4 Mild to None (n=20, n=19, n=20, n=19, n=15) | 1 | | | |
| Week 4 Mild to Mild | 0 | | | |
| Week 4 Mild to Moderate | 0 | | | |
| Week 4 Mild to Severe | 0 | | | |
| Week 4 Mild to Very Severe | 0 | | | |
| Week 4 Moderate to None | 1 | | | |
| Week 4 Moderate to Mild | 5 | | | |
| Week 4 Moderate to Moderate | 3 | | | |
| Week 4 Moderate to Severe | 0 | | | |
| Week 4 Moderate to Very Severe | 0 | | | |
| Week 4 Severe to None | 0 | | | |
| Week 4 Severe to Mild | 0 | | | |
| Week 4 Severe to Moderate | 2 | | | |
| Week 4 Severe to Severe | 3 | | | |
| Week 4 Severe to Very Severe | 0 | | | |
| Week 4 Very Severe to None | 0 | | | |
| Week 4 Very Severe to Mild | 0 | | | |
| Week 4 Very Severe to Moderate | 0 | | | |
| Week 4 Very Severe to Severe | 0 | | | |
| Week 4 Very Severe to Very Severe | 0 | | | |
| Week 8 Mild to None (n=17, n=21, n=19, n=19, n=16) | 0 | | | |
| Week 8 Mild to Mild | 1 | | | |
| Week 8 Mild to Moderate | 0 | | | |
| Week 8 Mild to Severe | 0 | | | |
| Week 8 Mild to Very Severe | 0 | | | |
| Week 8 Moderate to None | 1 | | | |
| Week 8 Moderate to Mild | 7 | | | |
| Week 8 Moderate to Moderate | 2 | | | |
| Week 8 Moderate to Severe | 0 | | | |
| Week 8 Moderate to Very Severe | 0 | | | |
| Week 8 Severe to None | 0 | | | |
| Week 8 Severe to Mild | 0 | | | |
| Week 8 Severe to Moderate | 5 | | | |
| Week 8 Severe to Severe | 0 | | | |
| Week 8 Severe to Very Severe | 0 | | | |

| | | | | |
|---|---|---|---|---|
| Week 8 Very Severe to None | 0 | | | |
| Week 8 Very Severe to Mild | 0 | | | |
| Week 8 Very Severe to Moderate | 0 | | | |
| Week 8 Very Severe to Severe | 0 | | | |
| Week 8 Very Severe to Very Severe | 0 | | | |
| Week 12 Mild to None (n=18, n=20, n=20, n=18,n=17) | 1 | | | |
| Week 12 Mild to Mild | 0 | | | |
| Week 12 Mild to Moderate | 0 | | | |
| Week 12 Mild to Severe | 0 | | | |
| Week 12 Mild to Very Severe | 0 | | | |
| Week 12 Moderate to None | 1 | | | |
| Week 12 Moderate to Mild | 6 | | | |
| Week 12 Moderate to Moderate | 3 | | | |
| Week 12 Moderate to Severe | 0 | | | |
| Week 12 Moderate to Very Severe | 0 | | | |
| Week 12 Severe to None | 0 | | | |
| Week 12 Severe to Mild | 1 | | | |
| Week 12 Severe to Moderate | 4 | | | |
| Week 12 Severe to Severe | 1 | | | |
| Week 12 Severe to Very Severe | 0 | | | |
| Week 12 Very Severe to None | 0 | | | |
| Week 12 Very Severe to Mild | 0 | | | |
| Week 12 Very Severe to Moderate | 0 | | | |
| Week 12 Very Severe to Severe | 0 | | | |
| Week 12 Very Severe to Very Severe | 0 | | | |
| Week 14 Mild to None (n=10, n=18, n=13, n=15, n=0) | 0 | | | |
| Week 14 Mild to Mild | 0 | | | |
| Week 14 Mild to Moderate | 0 | | | |
| Week 14 Mild to Severe | 0 | | | |
| Week 14 Mild to Very Severe | 0 | | | |
| Week 14 Moderate to None | 0 | | | |
| Week 14 Moderate to Mild | 0 | | | |
| Week 14 Moderate to Moderate | 0 | | | |
| Week 14 Moderate to Severe | 0 | | | |
| Week 14 Moderate to Very Severe | 0 | | | |
| Week 14 Severe to None | 0 | | | |
| Week 14 Severe to Mild | 0 | | | |
| Week 14 Severe to Moderate | 0 | | | |
| Week 14 Severe to Severe | 0 | | | |
| Week 14 Severe to Very Severe | 0 | | | |
| Week 14 Very Severe to None | 0 | | | |
| Week 14 Very Severe to Mild | 0 | | | |
| Week 14 Very Severe to Moderate | 0 | | | |
| Week 14 Very Severe to Severe | 0 | | | |
| Week 14 Very Severe to Very Severe | 0 | | | |
| Week 18 Mild to None (n=9, n=18, n=14, n=14, n=0) | 0 | | | |
| Week 18 Mild to Mild | 0 | | | |
| Week 18 Mild to Moderate | 0 | | | |
| Week 18 Mild to Severe | 0 | | | |
| Week 18 Mild to Very Severe | 0 | | | |

| | | | | |
|---|---|---|---|---|
| Week 18 Moderate to None | 0 | | | |
| Week 18 Moderate to Mild | 0 | | | |
| Week 18 Moderate to Moderate | 0 | | | |
| Week 18 Moderate to Severe | 0 | | | |
| Week 18 Moderate to Very Severe | 0 | | | |
| Week 18 Severe to None | 0 | | | |
| Week 18 Severe to Mild | 0 | | | |
| Week 18 Severe to Moderate | 0 | | | |
| Week 18 Severe to Severe | 0 | | | |
| Week 18 Severe to Very Severe | 0 | | | |
| Week 18 Very Severe to None | 0 | | | |
| Week 18 Very Severe to Mild | 0 | | | |
| Week 18 Very Severe to Moderate | 0 | | | |
| Week 18 Very Severe to Severe | 0 | | | |
| Week 18 Very Severe to Very Severe | 0 | | | |
| Week 22 Mild to None (n=8, n=18, n=13, n=16, n=0) | 0 | | | |
| Week 22 Mild to Mild | 0 | | | |
| Week 22 Mild to Moderate | 0 | | | |
| Week 22 Mild to Severe | 0 | | | |
| Week 22 Mild to Very Severe | 0 | | | |
| Week 22 Moderate to None | 0 | | | |
| Week 22 Moderate to Mild | 0 | | | |
| Week 22 Moderate to Moderate | 0 | | | |
| Week 22 Moderate to Severe | 0 | | | |
| Week 22 Moderate to Very Severe | 0 | | | |
| Week 22 Severe to None | 0 | | | |
| Week 22 Severe to Mild | 0 | | | |
| Week 22 Severe to Moderate | 0 | | | |
| Week 22 Severe to Severe | 0 | | | |
| Week 22 Severe to Very Severe | 0 | | | |
| Week 22 Very Severe to None | 0 | | | |
| Week 22 Very Severe to Mild | 0 | | | |
| Week 22 Very Severe to Moderate | 0 | | | |
| Week 22 Very Severe to Severe | 0 | | | |
| Week 22 Very Severe to Very Severe | 0 | | | |
| Week 26 Mild to None (n=8, n=17, n=13, n=16, n=0) | 0 | | | |
| Week 26 Mild to Mild | 0 | | | |
| Week 26 Mild to Moderate | 0 | | | |
| Week 26 Mild to Severe | 0 | | | |
| Week 26 Mild to Very Severe | 0 | | | |
| Week 26 Moderate to None | 0 | | | |
| Week 26 Moderate to Mild | 0 | | | |
| Week 26 Moderate to Moderate | 0 | | | |
| Week 26 Moderate to Severe | 0 | | | |
| Week 26 Moderate to Very Severe | 0 | | | |
| Week 26 Severe to None | 0 | | | |
| Week 26 Severe to Mild | 0 | | | |
| Week 26 Severe to Moderate | 0 | | | |
| Week 26 Severe to Severe | 0 | | | |
| Week 26 Severe to Very Severe | 0 | | | |

| | | | | |
|---|---|---|---|---|
| Week 26 Very Severe to None | 0 | | | |
| Week 26 Very Severe to Mild | 0 | | | |
| Week 26 Very Severe to Moderate | 0 | | | |
| Week 26 Very Severe to Severe | 0 | | | |
| Week 26 Very Severe to Very Severe | 0 | | | |
| Week 28 Mild to None (n=7, n=16, n=10, n=14, n=0) | 0 | | | |
| Week 28 Mild to Mild | 0 | | | |
| Week 28 Mild to Moderate | 0 | | | |
| Week 28 Mild to Severe | 0 | | | |
| Week 28 Mild to Very Severe | 0 | | | |
| Week 28 Moderate to None | 0 | | | |
| Week 28 Moderate to Mild | 0 | | | |
| Week 28 Moderate to Moderate | 0 | | | |
| Week 28 Moderate to Severe | 0 | | | |
| Week 28 Moderate to Very Severe | 0 | | | |
| Week 28 Severe to None | 0 | | | |
| Week 28 Severe to Mild | 0 | | | |
| Week 28 Severe to Moderate | 0 | | | |
| Week 28 Severe to Severe | 0 | | | |
| Week 28 Severe to Very Severe | 0 | | | |
| Week 28 Very Severe to None | 0 | | | |
| Week 28 Very Severe to Mild | 0 | | | |
| Week 28 Very Severe to Moderate | 0 | | | |
| Week 28 Very Severe to Severe | 0 | | | |
| Week 28 Very Severe to Very Severe | 0 | | | |
| Week 36 Mild to None (n=6, n=15, n=11, n=14, n=0) | 0 | | | |
| Week 36 Mild to Mild | 0 | | | |
| Week 36 Mild to Moderate | 0 | | | |
| Week 36 Mild to Severe | 0 | | | |
| Week 36 Mild to Very Severe | 0 | | | |
| Week 36 Moderate to None | 0 | | | |
| Week 36 Moderate to Mild | 0 | | | |
| Week 36 Moderate to Moderate | 0 | | | |
| Week 36 Moderate to Severe | 0 | | | |
| Week 36 Moderate to Very Severe | 0 | | | |
| Week 36 Severe to None | 0 | | | |
| Week 36 Severe to Mild | 0 | | | |
| Week 36 Severe to Moderate | 0 | | | |
| Week 36 Severe to Severe | 0 | | | |
| Week 36 Severe to Very Severe | 0 | | | |
| Week 36 Very Severe to None | 0 | | | |
| Week 36 Very Severe to Mild | 0 | | | |
| Week 36 Very Severe to Moderate | 0 | | | |
| Week 36 Very Severe to Severe | 0 | | | |
| Week 36 Very Severe to Very Severe | 0 | | | |
| Week 44 Mild to None (n=5, n=15, n=10, n=14, n=0) | 0 | | | |
| Week 44 Mild to Mild | 0 | | | |
| Week 44 Mild to Moderate | 0 | | | |
| Week 44 Mild to Severe | 0 | | | |
| Week 44 Mild to Very Severe | 0 | | | |

| | | | | |
|---|---|---|---|---|
| Week 44 Moderate to None | 0 | | | |
| Week 44 Moderate to Mild | 0 | | | |
| Week 44 Moderate to Moderate | 0 | | | |
| Week 44 Moderate to Severe | 0 | | | |
| Week 44 Moderate to Very Severe | 0 | | | |
| Week 44 Severe to None | 0 | | | |
| Week 44 Severe to Mild | 0 | | | |
| Week 44 Severe to Moderate | 0 | | | |
| Week 44 Severe to Severe | 0 | | | |
| Week 44 Severe to Very Severe | 0 | | | |
| Week 44 Very Severe to None | 0 | | | |
| Week 44 Very Severe to Mild | 0 | | | |
| Week 44 Very Severe to Moderate | 0 | | | |
| Week 44 Very Severe to Severe | 0 | | | |
| Week 44 Very Severe to Very Severe | 0 | | | |
| Week 52 Mild to None (n=4, n=14, n=10, n=14, n=0) | 0 | | | |
| Week 52 Mild to Mild | 0 | | | |
| Week 52 Mild to Moderate | 0 | | | |
| Week 52 Mild to Severe | 0 | | | |
| Week 52 Mild to Very Severe | 0 | | | |
| Week 52 Moderate to None | 0 | | | |
| Week 52 Moderate to Mild | 0 | | | |
| Week 52 Moderate to Moderate | 0 | | | |
| Week 52 Moderate to Severe | 0 | | | |
| Week 52 Moderate to Very Severe | 0 | | | |
| Week 52 Severe to None | 0 | | | |
| Week 52 Severe to Mild | 0 | | | |
| Week 52 Severe to Moderate | 0 | | | |
| Week 52 Severe to Severe | 0 | | | |
| Week 52 Severe to Very Severe | 0 | | | |
| Week 52 Very Severe to None | 0 | | | |
| Week 52 Very Severe to Mild | 0 | | | |
| Week 52 Very Severe to Moderate | 0 | | | |
| Week 52 Very Severe to Severe | 0 | | | |
| Week 52 Very Severe to Very Severe | 0 | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Histologic Non-responders by Dose at Weeks 12, 26 and 52

| | |
|---|---|
| End point title | Percentage of Histologic Non-responders by Dose at Weeks 12, 26 and 52 |

End point description:

Percentage of histologic non-responders by dose at Weeks 12, 26 and 52
Note: Following Week 14, all patients in the placebo group were given APT-1011 3mg BID and results reflect non-response following 12 or 38 weeks of treatment.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Weeks 12, 26 and 52

| End point values | APT-1011 1.5 mg HS | APT-1011 1.5 mg BID | APT-1011 3 mg HS | APT-1011 3 mg BID |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 21 | 22 | 21 | 20 |
| Units: Percentage of Participants | | | | |
| number (not applicable) | | | | |
| Week 12 | 52.4 | 9.1 | 33.3 | 20.0 |
| Week 26 | 52.4 | 22.7 | 33.3 | 25.0 |
| Week 52 | 76.2 | 27.3 | 47.6 | 40.0 |

| End point values | Placebo | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 19 | | | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | | | | |
| Week 12 | 100.0 | | | |
| Week 26 | 36.8 | | | |
| Week 52 | 47.4 | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline 7-Day Eosinophilic Esophagitis Activity Index (EEsAI) Subscores

| End point title | Change From Baseline 7-Day Eosinophilic Esophagitis Activity Index (EEsAI) Subscores |
|---|---|

End point description:

Change from Baseline 7-Day Components of the Eosinophilic Esophagitis Activity Index (EEsAI): Avoidance, Modification and Slow Eating (AMS) Score, minimum 0, maximum 10; and Visual Dysphagia Question (VDQ) Score, minimum 0, maximum 10.
Higher score means a worse outcome
Note: Following Week 14, all patients in the placebo group were given APT-1011 3mg BID and results reflect change from baseline 7-day EEsAI subscores following 12 or 38 weeks of treatment.

| End point type | Secondary |
|---|---|

End point timeframe:

Weeks 12, 26 and 52

| End point values | APT-1011 1.5 mg HS | APT-1011 1.5 mg BID | APT-1011 3 mg HS | APT-1011 3 mg BID |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 21 | 22 | 21 | 20 |
| Units: Mean Change from Baseline | | | | |
| arithmetic mean (standard deviation) | | | | |
| VDQ Week 12 (n=18, n=19, n=20, n=19, n=17) | -3.9 (± 6.63) | -2.5 (± 3.24) | -5.0 (± 6.00) | -4.1 (± 8.03) |
| VDQ Week 26 (n=8, n=18, n=13, n=16, n=0) | -3.1 (± 4.36) | -6.8 (± 7.03) | -6.8 (± 6.46) | -7.7 (± 9.47) |
| VDQ Week 52 (n=5, n=16, n=11, n=14, n=0) | -9.4 (± 9.50) | -9.4 (± 8.25) | -12.6 (± 9.67) | -9.6 (± 7.27) |
| AMS Week 12 (n=18, n=20, n=20, n=19, n=17) | 0.0 (± 0.00) | -3.0 (± 7.80) | -1.4 (± 3.30) | -1.3 (± 6.47) |
| AMS Week 26 (n=8, n=19, n=13, n=15, n=0) | 0.0 (± 0.00) | -2.2 (± 8.31) | -0.7 (± 4.44) | -3.3 (± 7.54) |
| AMS Week 52 (n=5, n=17, n=11, n=13, n=0) | 0.0 (± 0.00) | -3.5 (± 8.39) | -0.8 (± 2.71) | -2.6 (± 7.17) |

| End point values | Placebo | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 19 | | | |
| Units: Mean Change from Baseline | | | | |
| arithmetic mean (standard deviation) | | | | |
| VDQ Week 12 (n=18, n=19, n=20, n=19, n=17) | -2.7 (± 3.41) | | | |
| VDQ Week 26 (n=8, n=18, n=13, n=16, n=0) | 0 (± 0) | | | |
| VDQ Week 52 (n=5, n=16, n=11, n=14, n=0) | 0 (± 0) | | | |
| AMS Week 12 (n=18, n=20, n=20, n=19, n=17) | 1.5 (± 6.85) | | | |
| AMS Week 26 (n=8, n=19, n=13, n=15, n=0) | 0 (± 0) | | | |
| AMS Week 52 (n=5, n=17, n=11, n=13, n=0) | 0 (± 0) | | | |

## Statistical analyses

| Statistical analysis title | VDQ Score Change from Baseline Week 12 |
|---|---|
| Comparison groups | APT-1011 1.5 mg HS v Placebo |
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.459 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.21 |

| | |
|---|---|
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -3.49 |
| upper limit | 3.08 |
| Variability estimate | Standard deviation |

| **Statistical analysis title** | VDQ Score Change from Baseline Week 12 |
|---|---|
| Comparison groups | APT-1011 1.5 mg BID v Placebo |
| Number of subjects included in analysis | 41 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.617 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.58 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -2.65 |
| upper limit | 3.8 |
| Variability estimate | Standard deviation |

| **Statistical analysis title** | VDQ Score Change from Baseline Week 12 |
|---|---|
| Comparison groups | APT-1011 3 mg HS v Placebo |
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.167 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -1.87 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -5.07 |
| upper limit | 1.33 |
| Variability estimate | Standard deviation |

| **Statistical analysis title** | VDQ Score Change from Baseline Week 12 |
|---|---|
| Comparison groups | APT-1011 3 mg BID v Placebo |

| | |
|---|---|
| Number of subjects included in analysis | 39 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.373 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.63 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -3.88 |
| upper limit | 2.61 |
| Variability estimate | Standard deviation |

| **Statistical analysis title** | AMS Score Change from Baseline Week 12 |
|---|---|
| Comparison groups | APT-1011 1.5 mg HS v Placebo |
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.203 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -1.66 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -4.96 |
| upper limit | 1.64 |
| Variability estimate | Standard deviation |

| **Statistical analysis title** | AMS Score Change from Baseline Week 12 |
|---|---|
| Comparison groups | APT-1011 1.5 mg BID v Placebo |
| Number of subjects included in analysis | 41 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.014 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -4.33 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -7.54 |
| upper limit | -1.13 |
| Variability estimate | Standard deviation |

| **Statistical analysis title** | AMS Score Change from Baseline Week 12 |
|---|---|
| Comparison groups | APT-1011 3 mg HS v Placebo |
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.061 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -3.02 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -6.23 |
| upper limit | 0.2 |
| Variability estimate | Standard deviation |

| **Statistical analysis title** | AMS Score Change from Baseline Week 12 |
|---|---|
| Comparison groups | APT-1011 3 mg BID v Placebo |
| Number of subjects included in analysis | 39 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.097 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -2.57 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -5.83 |
| upper limit | 0.69 |
| Variability estimate | Standard deviation |

## Secondary: Change from Baseline PGIS for Difficulty With Food or Pills Going Down as Assessed Prior to Randomization Post-Baseline Visit

| End point title | Change from Baseline PGIS for Difficulty With Food or Pills Going Down as Assessed Prior to Randomization Post-Baseline Visit |
|---|---|

End point description:

Change From Baseline PGIS for Difficulty with Food or Pills Going Down as Assessed Prior to Randomization at Weeks 4, 8, 12, 14, 18, 22, 26, 28, 36, 44, and 52
Note: Following Week 14, all patients in the placebo group were given APT-1011 3mg BID and results reflect change from baseline PGIS for difficulty with food or pills going down following 4, 8, 12, 14, 22, 30 or 38 weeks of treatment.

| End point type | Secondary |
|---|---|

End point timeframe:
Weeks 4, 8, 12, 14, 18, 22, 26, 28, 36, 44, and 52

| **End point values** | APT-1011 1.5 mg HS | APT-1011 1.5 mg BID | APT-1011 3 mg HS | APT-1011 3 mg BID |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 21 | 22 | 21 | 20 |
| Units: Percentage of particpants | | | | |
| Week 4 Mild to None (n=20, n=19, n=20, n=19, n=15) | 2 | 0 | 0 | 0 |
| Week 4 Mild to Mild | 1 | 1 | 1 | 1 |
| Week 4 Mild to Moderate | 0 | 0 | 1 | 1 |
| Week 4 Mild to Severe | 0 | 0 | 0 | 0 |
| Week 4 Mild to Very Severe | 0 | 0 | 0 | 0 |
| Week 4 Moderate to None | 0 | 0 | 6 | 0 |
| Week 4 Moderate to Mild | 6 | 6 | 4 | 7 |
| Week 4 Moderate to Moderate | 5 | 4 | 4 | 4 |
| Week 4 Moderate to Severe | 1 | 1 | 0 | 0 |
| Week 4 Moderate to Very Severe | 0 | 0 | 0 | 0 |
| Week 4 Severe to None | 0 | 0 | 1 | 1 |
| Week 4 Severe to Mild | 1 | 1 | 0 | 0 |
| Week 4 Severe to Moderate | 2 | 2 | 2 | 4 |
| Week 4 Severe to Severe | 1 | 4 | 0 | 1 |
| Week 4 Severe to Very Severe | 0 | 0 | 1 | 0 |
| Week 4 Very Severe to None | 0 | 0 | 0 | 0 |
| Week 4 Very Severe to Mild | 0 | 0 | 0 | 0 |
| Week 4 Very Severe to Moderate | 0 | 0 | 0 | 0 |
| Week 4 Very Severe to Severe | 0 | 0 | 0 | 0 |
| Week 4 Very Severe to Very Severe | 1 | 0 | 0 | 0 |
| Week 8 Mild to None (n=17, n=21, n=19, n=19, n=16) | 0 | 0 | 0 | 0 |
| Week 8 Mild to Mild | 2 | 1 | 2 | 1 |
| Week 8 Mild to Moderate | 1 | 0 | 0 | 1 |
| Week 8 Mild to Severe | 0 | 0 | 0 | 0 |
| Week 8 Mild to Very Severe | 0 | 0 | 0 | 0 |
| Week 8 Moderate to None | 1 | 1 | 4 | 2 |
| Week 8 Moderate to Mild | 8 | 5 | 5 | 5 |
| Week 8 Moderate to Moderate | 1 | 6 | 4 | 4 |
| Week 8 Moderate to Severe | 0 | 0 | 0 | 0 |
| Week 8 Moderate to Very Severe | 0 | 0 | 0 | 0 |
| Week 8 Severe to None | 1 | 0 | 1 | 1 |
| Week 8 Severe to Mild | 2 | 1 | 1 | 2 |
| Week 8 Severe to Moderate | 0 | 7 | 0 | 3 |
| Week 8 Severe to Severe | 0 | 0 | 1 | 0 |
| Week 8 Severe to Very Severe | 0 | 0 | 1 | 0 |
| Week 8 Very Severe to None | 0 | 0 | 0 | 0 |
| Week 8 Very Severe to Mild | 0 | 0 | 0 | 0 |
| Week 8 Very Severe to Moderate | 1 | 0 | 0 | 0 |
| Week 8 Very Severe to Severe | 0 | 0 | 0 | 0 |
| Week 8 Very Severe to Very Severe | 0 | 0 | 0 | 0 |

| | | | | |
|---|---|---|---|---|
| Week 12 Mild to None (n=18, n=20, n=20, n=18, n=17 | 1 | 0 | 0 | 0 |
| Week 12 Mild to Mild | 2 | 1 | 2 | 2 |
| Week 12 Mild to Moderate | 1 | 0 | 0 | 0 |
| Week 12 Mild to Severe | 0 | 0 | 0 | 0 |
| Week 12 Mild to Very Severe | 0 | 0 | 0 | 0 |
| Week 12 Moderate to None | 3 | 0 | 5 | 3 |
| Week 12 Moderate to Mild | 4 | 5 | 6 | 2 |
| Week 12 Moderate to Moderate | 3 | 6 | 3 | 5 |
| Week 12 Moderate to Severe | 0 | 0 | 0 | 0 |
| Week 12 Moderate to Very Severe | 0 | 0 | 0 | 0 |
| Week 12 Severe to None | 3 | 0 | 1 | 1 |
| Week 12 Severe to Mild | 0 | 4 | 0 | 1 |
| Week 12 Severe to Moderate | 0 | 3 | 2 | 2 |
| Week 12 Severe to Severe | 0 | 1 | 1 | 2 |
| Week 12 Severe to Very Severe | 0 | 0 | 0 | 0 |
| Week 12 Very Severe to None | 0 | 0 | 0 | 0 |
| Week 12 Very Severe to Mild | 0 | 0 | 0 | 0 |
| Week 12 Very Severe to Moderate | 1 | 0 | 0 | 0 |
| Week 12 Very Severe to Severe | 0 | 0 | 0 | 0 |
| Week 12 Very Severe to Very Severe | 0 | 0 | 0 | 0 |
| Week 14 Mild to None (n=10, n=18, n=13, n=15, n=0) | 0 | 0 | 1 | 0 |
| Week 14 Mild to Mild | 1 | 1 | 0 | 2 |
| Week 14 Mild to Moderate | 0 | 0 | 0 | 0 |
| Week 14 Mild to Severe | 0 | 0 | 0 | 0 |
| Week 14 Mild to Very Severe | 0 | 0 | 0 | 0 |
| Week 14 Moderate to None | 1 | 0 | 4 | 3 |
| Week 14 Moderate to Mild | 7 | 7 | 3 | 2 |
| Week 14 Moderate to Moderate | 0 | 2 | 1 | 3 |
| Week 14 Moderate to Severe | 0 | 1 | 0 | 0 |
| Week 14 Moderate to Very Severe | 0 | 0 | 0 | 0 |
| Week 14 Severe to None | 0 | 1 | 0 | 1 |
| Week 14 Severe to Mild | 0 | 2 | 2 | 2 |
| Week 14 Severe to Moderate | 0 | 4 | 1 | 2 |
| Week 14 Severe to Severe | 0 | 0 | 1 | 0 |
| Week 14 Severe to Very Severe | 0 | 0 | 0 | 0 |
| Week 14 Very Severe to None | 0 | 0 | 0 | 0 |
| Week 14 Very Severe to Mild | 0 | 0 | 0 | 0 |
| Week 14 Very Severe to Moderate | 0 | 0 | 0 | 0 |
| Week 14 Very Severe to Severe | 0 | 0 | 0 | 0 |
| Week 14 Very Severe to Very Severe | 1 | 0 | 0 | 0 |
| Week 18 Mild to None (n=9, n=18, n=14, n=14, n=0) | 0 | 0 | 1 | 0 |
| Week 18 Mild to Mild | 0 | 1 | 0 | 2 |
| Week 18 Mild to Moderate | 0 | 0 | 0 | 0 |
| Week 18 Mild to Severe | 0 | 0 | 0 | 0 |
| Week 18 Mild to Very Severe | 0 | 0 | 0 | 0 |
| Week 18 Moderate to None | 0 | 1 | 5 | 4 |
| Week 18 Moderate to Mild | 8 | 7 | 3 | 2 |
| Week 18 Moderate to Moderate | 0 | 2 | 1 | 2 |
| Week 18 Moderate to Severe | 0 | 0 | 0 | 0 |
| Week 18 Moderate to Very Severe | 0 | 0 | 0 | 0 |

| | | | | |
|---|---|---|---|---|
| Week 18 Severe to None | 0 | 2 | 1 | 1 |
| Week 18 Severe to Mild | 0 | 2 | 1 | 2 |
| Week 18 Severe to Moderate | 0 | 3 | 1 | 1 |
| Week 18 Severe to Severe | 0 | 0 | 1 | 0 |
| Week 18 Severe to Very Severe | 0 | 0 | 0 | 0 |
| Week 18 Very Severe to None | 0 | 0 | 0 | 0 |
| Week 18 Very Severe to Mild | 0 | 0 | 0 | 0 |
| Week 18 Very Severe to Moderate | 1 | 0 | 0 | 0 |
| Week 18 Very Severe to Severe | 0 | 0 | 0 | 0 |
| Week 18 Very Severe to Very Severe | 0 | 0 | 0 | 0 |
| Week 22 Mild to None (n=8, n=18, n=13, n=16, n=0) | 0 | 0 | 0 | 0 |
| Week 22 Mild to Mild | 0 | 1 | 1 | 2 |
| Week 22 Mild to Moderate | 0 | 0 | 0 | 0 |
| Week 22 Mild to Severe | 0 | 0 | 0 | 0 |
| Week 22 Mild to Very Severe | 0 | 0 | 0 | 0 |
| Week 22 Moderate to None | 2 | 1 | 3 | 4 |
| Week 22 Moderate to Mild | 6 | 7 | 3 | 3 |
| Week 22 Moderate to Moderate | 0 | 2 | 2 | 2 |
| Week 22 Moderate to Severe | 0 | 0 | 0 | 0 |
| Week 22 Moderate to Very Severe | 0 | 0 | 0 | 0 |
| Week 22 Severe to None | 0 | 2 | 1 | 2 |
| Week 22 Severe to Mild | 0 | 2 | 1 | 1 |
| Week 22 Severe to Moderate | 0 | 3 | 1 | 2 |
| Week 22 Severe to Severe | 0 | 0 | 0 | 0 |
| Week 22 Severe to Very Severe | 0 | 0 | 1 | 0 |
| Week 22 Very Severe to None | 0 | 0 | 0 | 0 |
| Week 22 Very Severe to Mild | 0 | 0 | 0 | 0 |
| Week 22 Very Severe to Moderate | 0 | 0 | 0 | 0 |
| Week 22 Very Severe to Severe | 0 | 0 | 0 | 0 |
| Week 22 Very Severe to Very Severe | 0 | 0 | 0 | 0 |
| Week 26 Mild to None (n=8, n=17, n=13, n=16, n=0) | 0 | 0 | 0 | 0 |
| Week 26 Mild to Mild | 0 | 1 | 1 | 2 |
| Week 26 Mild to Moderate | 0 | 0 | 0 | 0 |
| Week 26 Mild to Severe | 0 | 0 | 0 | 0 |
| Week 26 Mild to Very Severe | 0 | 0 | 0 | 0 |
| Week 26 Moderate to None | 3 | 0 | 4 | 5 |
| Week 26 Moderate to Mild | 3 | 7 | 3 | 2 |
| Week 26 Moderate to Moderate | 1 | 2 | 1 | 2 |
| Week 26 Moderate to Severe | 0 | 0 | 0 | 0 |
| Week 26 Moderate to Very Severe | 0 | 0 | 0 | 0 |
| Week 26 Severe to None | 0 | 3 | 2 | 2 |
| Week 26 Severe to Mild | 0 | 3 | 1 | 2 |
| Week 26 Severe to Moderate | 0 | 1 | 0 | 1 |
| Week 26 Severe to Severe | 0 | 0 | 1 | 0 |
| Week 26 Severe to Very Severe | 0 | 0 | 0 | 0 |
| Week 26 Very Severe to None | 0 | 0 | 0 | 0 |
| Week 26 Very Severe to Mild | 0 | 0 | 0 | 0 |
| Week 26 Very Severe to Moderate | 1 | 0 | 0 | 0 |
| Week 26 Very Severe to Severe | 0 | 0 | 0 | 0 |
| Week 26 Very Severe to Very Severe | 0 | 0 | 0 | 0 |

| | | | | |
|---|---|---|---|---|
| Week 28 Mild to None (n=7, n=16, n=10, n=14, n=0) | 0 | 0 | 1 | 1 |
| Week 28 Mild to Mild | 0 | 1 | 0 | 1 |
| Week 28 Mild to Moderate | 0 | 0 | 0 | 0 |
| Week 28 Mild to Severe | 0 | 0 | 0 | 0 |
| Week 28 Mild to Very Severe | 0 | 0 | 0 | 0 |
| Week 28 Moderate to None | 4 | 0 | 4 | 4 |
| Week 28 Moderate to Mild | 2 | 7 | 1 | 2 |
| Week 28 Moderate to Moderate | 0 | 1 | 0 | 1 |
| Week 28 Moderate to Severe | 0 | 0 | 0 | 0 |
| Week 28 Moderate to Very Severe | 0 | 0 | 0 | 0 |
| Week 28 Severe to None | 0 | 3 | 2 | 1 |
| Week 28 Severe to Mild | 0 | 2 | 0 | 4 |
| Week 28 Severe to Moderate | 0 | 2 | 1 | 0 |
| Week 28 Severe to Severe | 0 | 0 | 1 | 0 |
| Week 28 Severe to Very Severe | 0 | 0 | 0 | 0 |
| Week 28 Very Severe to None | 0 | 0 | 0 | 0 |
| Week 28 Very Severe to Mild | 1 | 0 | 0 | 0 |
| Week 28 Very Severe to Moderate | 0 | 0 | 0 | 0 |
| Week 28 Very Severe to Severe | 0 | 0 | 0 | 0 |
| Week 28 Very Severe to Very Severe | 0 | 0 | 0 | 0 |
| Week 36 Mild to None (n=6, n=15, n=11, n=14, n=0) | 0 | 0 | 0 | 2 |
| Week 36 Mild to Mild | 0 | 1 | 1 | 0 |
| Week 36 Mild to Moderate | 0 | 0 | 0 | 0 |
| Week 36 Mild to Severe | 0 | 0 | 0 | 0 |
| Week 36 Mild to Very Severe | 0 | 0 | 0 | 0 |
| Week 36 Moderate to None | 2 | 2 | 5 | 4 |
| Week 36 Moderate to Mild | 3 | 5 | 1 | 2 |
| Week 36 Moderate to Moderate | 0 | 1 | 0 | 1 |
| Week 36 Moderate to Severe | 0 | 0 | 0 | 0 |
| Week 36 Moderate to Very Severe | 0 | 0 | 0 | 0 |
| Week 36 Severe to None | 0 | 4 | 2 | 1 |
| Week 36 Severe to Mild | 0 | 1 | 1 | 3 |
| Week 36 Severe to Moderate | 0 | 1 | 0 | 1 |
| Week 36 Severe to Severe | 0 | 0 | 0 | 0 |
| Week 36 Severe to Very Severe | 0 | 0 | 1 | 0 |
| Week 36 Very Severe to None | 0 | 0 | 0 | 0 |
| Week 36 Very Severe to Mild | 0 | 0 | 0 | 0 |
| Week 36 Very Severe to Moderate | 0 | 0 | 0 | 0 |
| Week 36 Very Severe to Severe | 1 | 0 | 0 | 0 |
| Week 36 Very Severe to Very Severe | 0 | 0 | 0 | 0 |
| Week 44 Mild to None (n=5, n=15, n=10, n=14, n=0) | 0 | 0 | 0 | 1 |
| Week 44 Mild to Mild | 0 | 1 | 1 | 1 |
| Week 44 Mild to Moderate | 0 | 0 | 0 | 0 |
| Week 44 Mild to Severe | 0 | 0 | 0 | 0 |
| Week 44 Mild to Very Severe | 0 | 0 | 0 | 0 |
| Week 44 Moderate to None | 2 | 1 | 3 | 4 |
| Week 44 Moderate to Mild | 2 | 6 | 1 | 2 |
| Week 44 Moderate to Moderate | 0 | 0 | 1 | 1 |
| Week 44 Moderate to Severe | 0 | 1 | 0 | 0 |
| Week 44 Moderate to Very Severe | 0 | 0 | 0 | 0 |

| | | | | |
|---|---|---|---|---|
| Week 44 Severe to None | 0 | 3 | 2 | 2 |
| Week 44 Severe to Mild | 0 | 3 | 1 | 2 |
| Week 44 Severe to Moderate | 0 | 0 | 0 | 1 |
| Week 44 Severe to Severe | 0 | 0 | 0 | 0 |
| Week 44 Severe to Very Severe | 0 | 0 | 1 | 0 |
| Week 44 Very Severe to None | 0 | 0 | 0 | 0 |
| Week 44 Very Severe to Mild | 1 | 0 | 0 | 0 |
| Week 44 Very Severe to Moderate | 0 | 0 | 0 | 0 |
| Week 44 Very Severe to Severe | 0 | 0 | 0 | 0 |
| Week 44 Very Severe to Very Severe | 0 | 0 | 0 | 0 |
| Week 52 Mild to None (n=4, n=14, n=10, n=14, n=0) | 0 | 0 | 1 | 2 |
| Week 52 Mild to Mild | 0 | 0 | 0 | 0 |
| Week 52 Mild to Moderate | 0 | 1 | 0 | 0 |
| Week 52 Mild to Severe | 0 | 0 | 0 | 0 |
| Week 52 Mild to Very Severe | 0 | 0 | 0 | 0 |
| Week 52 Moderate to None | 2 | 2 | 5 | 6 |
| Week 52 Moderate to Mild | 2 | 4 | 1 | 0 |
| Week 52 Moderate to Moderate | 0 | 3 | 0 | 1 |
| Week 52 Moderate to Severe | 0 | 0 | 0 | 0 |
| Week 52 Moderate to Very Severe | 0 | 0 | 0 | 0 |
| Week 52 Severe to None | 0 | 3 | 1 | 3 |
| Week 52 Severe to Mild | 0 | 1 | 1 | 1 |
| Week 52 Severe to Moderate | 0 | 0 | 0 | 1 |
| Week 52 Severe to Severe | 0 | 0 | 0 | 0 |
| Week 52 Severe to Very Severe | 0 | 0 | 1 | 0 |
| Week 52 Very Severe to None | 0 | 0 | 0 | 0 |
| Week 52 Very Severe to Mild | 0 | 0 | 0 | 0 |
| Week 52 Very Severe to Moderate | 0 | 0 | 0 | 0 |
| Week 52 Very Severe to Severe | 0 | 0 | 0 | 0 |
| Week 52 Very Severe to Very Severe | 0 | 0 | 0 | 0 |

| **End point values** | Placebo | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 19 | | | |
| Units: Percentage of particpants | | | | |
| Week 4 Mild to None (n=20, n=19, n=20, n=19, n=15) | 1 | | | |
| Week 4 Mild to Mild | 1 | | | |
| Week 4 Mild to Moderate | 0 | | | |
| Week 4 Mild to Severe | 0 | | | |
| Week 4 Mild to Very Severe | 0 | | | |
| Week 4 Moderate to None | 0 | | | |
| Week 4 Moderate to Mild | 5 | | | |
| Week 4 Moderate to Moderate | 4 | | | |
| Week 4 Moderate to Severe | 0 | | | |
| Week 4 Moderate to Very Severe | 0 | | | |
| Week 4 Severe to None | 0 | | | |
| Week 4 Severe to Mild | 0 | | | |

| | | | | |
|---|---|---|---|---|
| Week 4 Severe to Moderate | 1 | | | |
| Week 4 Severe to Severe | 3 | | | |
| Week 4 Severe to Very Severe | 0 | | | |
| Week 4 Very Severe to None | 0 | | | |
| Week 4 Very Severe to Mild | 0 | | | |
| Week 4 Very Severe to Moderate | 0 | | | |
| Week 4 Very Severe to Severe | 0 | | | |
| Week 4 Very Severe to Very Severe | 0 | | | |
| Week 8 Mild to None (n=17, n=21, n=19, n=19, n=16) | 1 | | | |
| Week 8 Mild to Mild | 2 | | | |
| Week 8 Mild to Moderate | 0 | | | |
| Week 8 Mild to Severe | 0 | | | |
| Week 8 Mild to Very Severe | 0 | | | |
| Week 8 Moderate to None | 0 | | | |
| Week 8 Moderate to Mild | 6 | | | |
| Week 8 Moderate to Moderate | 3 | | | |
| Week 8 Moderate to Severe | 0 | | | |
| Week 8 Moderate to Very Severe | 0 | | | |
| Week 8 Severe to None | 0 | | | |
| Week 8 Severe to Mild | 1 | | | |
| Week 8 Severe to Moderate | 3 | | | |
| Week 8 Severe to Severe | 0 | | | |
| Week 8 Severe to Very Severe | 0 | | | |
| Week 8 Very Severe to None | 0 | | | |
| Week 8 Very Severe to Mild | 0 | | | |
| Week 8 Very Severe to Moderate | 0 | | | |
| Week 8 Very Severe to Severe | 0 | | | |
| Week 8 Very Severe to Very Severe | 0 | | | |
| Week 12 Mild to None (n=18, n=20, n=20, n=18, n=17 | 2 | | | |
| Week 12 Mild to Mild | 1 | | | |
| Week 12 Mild to Moderate | 0 | | | |
| Week 12 Mild to Severe | 0 | | | |
| Week 12 Mild to Very Severe | 0 | | | |
| Week 12 Moderate to None | 0 | | | |
| Week 12 Moderate to Mild | 6 | | | |
| Week 12 Moderate to Moderate | 4 | | | |
| Week 12 Moderate to Severe | 0 | | | |
| Week 12 Moderate to Very Severe | 0 | | | |
| Week 12 Severe to None | 0 | | | |
| Week 12 Severe to Mild | 1 | | | |
| Week 12 Severe to Moderate | 2 | | | |
| Week 12 Severe to Severe | 1 | | | |
| Week 12 Severe to Very Severe | 0 | | | |
| Week 12 Very Severe to None | 0 | | | |
| Week 12 Very Severe to Mild | 0 | | | |
| Week 12 Very Severe to Moderate | 0 | | | |
| Week 12 Very Severe to Severe | 0 | | | |
| Week 12 Very Severe to Very Severe | 0 | | | |
| Week 14 Mild to None (n=10, n=18, n=13, n=15, n=0) | 0 | | | |
| Week 14 Mild to Mild | 0 | | | |

| | | | | |
|---|---|---|---|---|
| Week 14 Mild to Moderate | 0 | | | |
| Week 14 Mild to Severe | 0 | | | |
| Week 14 Mild to Very Severe | 0 | | | |
| Week 14 Moderate to None | 0 | | | |
| Week 14 Moderate to Mild | 0 | | | |
| Week 14 Moderate to Moderate | 0 | | | |
| Week 14 Moderate to Severe | 0 | | | |
| Week 14 Moderate to Very Severe | 0 | | | |
| Week 14 Severe to None | 0 | | | |
| Week 14 Severe to Mild | 0 | | | |
| Week 14 Severe to Moderate | 0 | | | |
| Week 14 Severe to Severe | 0 | | | |
| Week 14 Severe to Very Severe | 0 | | | |
| Week 14 Very Severe to None | 0 | | | |
| Week 14 Very Severe to Mild | 0 | | | |
| Week 14 Very Severe to Moderate | 0 | | | |
| Week 14 Very Severe to Severe | 0 | | | |
| Week 14 Very Severe to Very Severe | 0 | | | |
| Week 18 Mild to None (n=9, n=18, n=14, n=14, n=0) | 0 | | | |
| Week 18 Mild to Mild | 0 | | | |
| Week 18 Mild to Moderate | 0 | | | |
| Week 18 Mild to Severe | 0 | | | |
| Week 18 Mild to Very Severe | 0 | | | |
| Week 18 Moderate to None | 0 | | | |
| Week 18 Moderate to Mild | 0 | | | |
| Week 18 Moderate to Moderate | 0 | | | |
| Week 18 Moderate to Severe | 0 | | | |
| Week 18 Moderate to Very Severe | 0 | | | |
| Week 18 Severe to None | 0 | | | |
| Week 18 Severe to Mild | 0 | | | |
| Week 18 Severe to Moderate | 0 | | | |
| Week 18 Severe to Severe | 0 | | | |
| Week 18 Severe to Very Severe | 0 | | | |
| Week 18 Very Severe to None | 0 | | | |
| Week 18 Very Severe to Mild | 0 | | | |
| Week 18 Very Severe to Moderate | 0 | | | |
| Week 18 Very Severe to Severe | 0 | | | |
| Week 18 Very Severe to Very Severe | 0 | | | |
| Week 22 Mild to None (n=8, n=18, n=13, n=16, n=0) | 0 | | | |
| Week 22 Mild to Mild | 0 | | | |
| Week 22 Mild to Moderate | 0 | | | |
| Week 22 Mild to Severe | 0 | | | |
| Week 22 Mild to Very Severe | 0 | | | |
| Week 22 Moderate to None | 0 | | | |
| Week 22 Moderate to Mild | 0 | | | |
| Week 22 Moderate to Moderate | 0 | | | |
| Week 22 Moderate to Severe | 0 | | | |
| Week 22 Moderate to Very Severe | 0 | | | |
| Week 22 Severe to None | 0 | | | |
| Week 22 Severe to Mild | 0 | | | |

| | | | | |
|---|---|---|---|---|
| Week 22 Severe to Moderate | 0 | | | |
| Week 22 Severe to Severe | 0 | | | |
| Week 22 Severe to Very Severe | 0 | | | |
| Week 22 Very Severe to None | 0 | | | |
| Week 22 Very Severe to Mild | 0 | | | |
| Week 22 Very Severe to Moderate | 0 | | | |
| Week 22 Very Severe to Severe | 0 | | | |
| Week 22 Very Severe to Very Severe | 0 | | | |
| Week 26 Mild to None (n=8, n=17, n=13, n=16, n=0) | 0 | | | |
| Week 26 Mild to Mild | 0 | | | |
| Week 26 Mild to Moderate | 0 | | | |
| Week 26 Mild to Severe | 0 | | | |
| Week 26 Mild to Very Severe | 0 | | | |
| Week 26 Moderate to None | 0 | | | |
| Week 26 Moderate to Mild | 0 | | | |
| Week 26 Moderate to Moderate | 0 | | | |
| Week 26 Moderate to Severe | 0 | | | |
| Week 26 Moderate to Very Severe | 0 | | | |
| Week 26 Severe to None | 0 | | | |
| Week 26 Severe to Mild | 0 | | | |
| Week 26 Severe to Moderate | 0 | | | |
| Week 26 Severe to Severe | 0 | | | |
| Week 26 Severe to Very Severe | 0 | | | |
| Week 26 Very Severe to None | 0 | | | |
| Week 26 Very Severe to Mild | 0 | | | |
| Week 26 Very Severe to Moderate | 0 | | | |
| Week 26 Very Severe to Severe | 0 | | | |
| Week 26 Very Severe to Very Severe | 0 | | | |
| Week 28 Mild to None (n=7, n=16, n=10, n=14, n=0) | 0 | | | |
| Week 28 Mild to Mild | 0 | | | |
| Week 28 Mild to Moderate | 0 | | | |
| Week 28 Mild to Severe | 0 | | | |
| Week 28 Mild to Very Severe | 0 | | | |
| Week 28 Moderate to None | 0 | | | |
| Week 28 Moderate to Mild | 0 | | | |
| Week 28 Moderate to Moderate | 0 | | | |
| Week 28 Moderate to Severe | 0 | | | |
| Week 28 Moderate to Very Severe | 0 | | | |
| Week 28 Severe to None | 0 | | | |
| Week 28 Severe to Mild | 0 | | | |
| Week 28 Severe to Moderate | 0 | | | |
| Week 28 Severe to Severe | 0 | | | |
| Week 28 Severe to Very Severe | 0 | | | |
| Week 28 Very Severe to None | 0 | | | |
| Week 28 Very Severe to Mild | 0 | | | |
| Week 28 Very Severe to Moderate | 0 | | | |
| Week 28 Very Severe to Severe | 0 | | | |
| Week 28 Very Severe to Very Severe | 0 | | | |
| Week 36 Mild to None (n=6, n=15, n=11, n=14, n=0) | 0 | | | |
| Week 36 Mild to Mild | 0 | | | |

| | | | | |
|---|---|---|---|---|
| Week 36 Mild to Moderate | 0 | | | |
| Week 36 Mild to Severe | 0 | | | |
| Week 36 Mild to Very Severe | 0 | | | |
| Week 36 Moderate to None | 0 | | | |
| Week 36 Moderate to Mild | 0 | | | |
| Week 36 Moderate to Moderate | 0 | | | |
| Week 36 Moderate to Severe | 0 | | | |
| Week 36 Moderate to Very Severe | 0 | | | |
| Week 36 Severe to None | 0 | | | |
| Week 36 Severe to Mild | 0 | | | |
| Week 36 Severe to Moderate | 0 | | | |
| Week 36 Severe to Severe | 0 | | | |
| Week 36 Severe to Very Severe | 0 | | | |
| Week 36 Very Severe to None | 0 | | | |
| Week 36 Very Severe to Mild | 0 | | | |
| Week 36 Very Severe to Moderate | 0 | | | |
| Week 36 Very Severe to Severe | 0 | | | |
| Week 36 Very Severe to Very Severe | 0 | | | |
| Week 44 Mild to None (n=5, n=15, n=10, n=14, n=0) | 0 | | | |
| Week 44 Mild to Mild | 0 | | | |
| Week 44 Mild to Moderate | 0 | | | |
| Week 44 Mild to Severe | 0 | | | |
| Week 44 Mild to Very Severe | 0 | | | |
| Week 44 Moderate to None | 0 | | | |
| Week 44 Moderate to Mild | 0 | | | |
| Week 44 Moderate to Moderate | 0 | | | |
| Week 44 Moderate to Severe | 0 | | | |
| Week 44 Moderate to Very Severe | 0 | | | |
| Week 44 Severe to None | 0 | | | |
| Week 44 Severe to Mild | 0 | | | |
| Week 44 Severe to Moderate | 0 | | | |
| Week 44 Severe to Severe | 0 | | | |
| Week 44 Severe to Very Severe | 0 | | | |
| Week 44 Very Severe to None | 0 | | | |
| Week 44 Very Severe to Mild | 0 | | | |
| Week 44 Very Severe to Moderate | 0 | | | |
| Week 44 Very Severe to Severe | 0 | | | |
| Week 44 Very Severe to Very Severe | 0 | | | |
| Week 52 Mild to None (n=4, n=14, n=10, n=14, n=0) | 0 | | | |
| Week 52 Mild to Mild | 0 | | | |
| Week 52 Mild to Moderate | 0 | | | |
| Week 52 Mild to Severe | 0 | | | |
| Week 52 Mild to Very Severe | 0 | | | |
| Week 52 Moderate to None | 0 | | | |
| Week 52 Moderate to Mild | 0 | | | |
| Week 52 Moderate to Moderate | 0 | | | |
| Week 52 Moderate to Severe | 0 | | | |
| Week 52 Moderate to Very Severe | 0 | | | |
| Week 52 Severe to None | 0 | | | |
| Week 52 Severe to Mild | 0 | | | |

| | | | | |
|---|---|---|---|---|
| Week 52 Severe to Moderate | 0 | | | |
| Week 52 Severe to Severe | 0 | | | |
| Week 52 Severe to Very Severe | 0 | | | |
| Week 52 Very Severe to None | 0 | | | |
| Week 52 Very Severe to Mild | 0 | | | |
| Week 52 Very Severe to Moderate | 0 | | | |
| Week 52 Very Severe to Severe | 0 | | | |
| Week 52 Very Severe to Very Severe | 0 | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline Patient Global Impression of Change (PGIC) for EoE Symptoms as Assessed Prior to Randomization Post-Baseline Visit

| | |
|---|---|
| End point title | Change From Baseline Patient Global Impression of Change (PGIC) for EoE Symptoms as Assessed Prior to Randomization Post-Baseline Visit |

End point description:

Change From Baseline PGIC for EoE Symptoms as Assessed Prior to Randomization at Weeks 4, 8, 12, 14, 18, 22, 26, 28, 36, 44, and 52
Note: Following Week 14, all patients in the placebo group were given APT-1011 3mg BID and results reflect change from baseline PGIC for EoE symptoms following 4, 8, 12, 14, 22, 30 or 38 weeks of treatment.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Weeks 4, 8, 12, 14, 18, 22, 26, 36, 44, and 52

| End point values | APT-1011 1.5 mg HS | APT-1011 1.5 mg BID | APT-1011 3 mg HS | APT-1011 3 mg BID |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 21 | 22 | 21 | 20 |
| Units: Percentage of particpants | | | | |
| Week 4 Much Worse (n=21, n=20, n=20, n=20, n=16) | 0 | 0 | 0 | 0 |
| Week 4 Moderately Worse | 0 | 0 | 0 | 0 |
| Week 4 A Little Worse | 1 | 0 | 1 | 2 |
| Week 4 Stayed the Same | 4 | 4 | 4 | 3 |
| Week 4 A Little Improved | 9 | 9 | 4 | 10 |
| Week 4 Moderately Improved | 4 | 3 | 6 | 2 |
| Week 4 Much Improved | 3 | 4 | 5 | 3 |
| Week 8 Much Worse (n=17, n=22, n=19, n=20, n=16) | 0 | 0 | 0 | 0 |
| Week 8 Moderately Worse | 0 | 0 | 0 | 0 |
| Week 8 A Little Worse | 1 | 0 | 1 | 0 |
| Week 8 Stayed the Same | 2 | 3 | 3 | 3 |
| Week 8 A Little Improved | 4 | 9 | 5 | 7 |
| Week 8 Moderately Improved | 7 | 4 | 4 | 6 |
| Week 8 Much Improved | 3 | 6 | 6 | 4 |

| | | | | |
|---|---|---|---|---|
| Week 12 Much Worse (n=18, n=22, n=20, n=19, n=17) | 0 | 0 | 0 | 0 |
| Week 12 Moderately Worse | 0 | 0 | 0 | 1 |
| Week 12 A Little Worse | 0 | 0 | 1 | 1 |
| Week 12 Stayed the Same | 1 | 4 | 4 | 3 |
| Week 12 A Little Improved | 6 | 5 | 2 | 6 |
| Week 12 Moderately Improved | 5 | 5 | 4 | 3 |
| Week 12 Much Improved | 6 | 8 | 9 | 5 |
| Week 14 Much Worse (n=10, n=18, n=13, n=15, n=0) | 0 | 0 | 0 | 0 |
| Week 14 Moderately Worse | 0 | 0 | 0 | 0 |
| Week 14 A Little Worse | 0 | 0 | 1 | 1 |
| Week 14 Stayed the Same | 0 | 3 | 1 | 1 |
| Week 14 A Little Improved | 3 | 4 | 1 | 5 |
| Week 14 Moderately Improved | 5 | 3 | 3 | 3 |
| Week 14 Much Improved | 2 | 8 | 7 | 5 |
| Week 18 Much Worse (n=9, n=18, n=14, n=14, n=0) | 0 | 0 | 0 | 0 |
| Week 18 Moderately Worse | 0 | 0 | 1 | 0 |
| Week 18 A Little Worse | 0 | 1 | 1 | 0 |
| Week 18 Stayed the Same | 0 | 3 | 0 | 1 |
| Week 18 A Little Improved | 2 | 1 | 1 | 4 |
| Week 18 Moderately Improved | 6 | 2 | 1 | 3 |
| Week 18 Much Improved | 1 | 11 | 10 | 6 |
| Week 22 Much Worse (n=8, n=18, n=14, n=16, n=0) | 0 | 0 | 1 | 0 |
| Week 22 Moderately Worse | 0 | 0 | 1 | 0 |
| Week 22 A Little Worse | 0 | 0 | 0 | 1 |
| Week 22 Stayed the Same | 0 | 3 | 0 | 1 |
| Week 22 A Little Improved | 2 | 1 | 2 | 5 |
| Week 22 Moderately Improved | 2 | 3 | 3 | 1 |
| Week 22 Much Improved | 4 | 11 | 7 | 8 |
| Week 26 Much Worse (n=8, n=18, n=13, n=16, n=0) | 0 | 0 | 0 | 0 |
| Week 26 Moderately Worse | 0 | 0 | 2 | 1 |
| Week 26 A Little Worse | 0 | 0 | 0 | 0 |
| Week 26 Stayed the Same | 0 | 2 | 0 | 1 |
| Week 26 A Little Improved | 3 | 1 | 0 | 4 |
| Week 26 Moderately Improved | 1 | 2 | 2 | 0 |
| Week 26 Much Improved | 4 | 13 | 9 | 10 |
| Week 28 Much Worse (n=7, n=17, n=10, n=14, n=0) | 0 | 0 | 0 | 0 |
| Week 28 Moderately Worse | 0 | 0 | 1 | 0 |
| Week 28 A Little Worse | 0 | 0 | 0 | 0 |
| Week 28 Stayed the Same | 0 | 3 | 0 | 0 |
| Week 28 A Little Improved | 1 | 0 | 1 | 2 |
| Week 28 Moderately Improved | 2 | 3 | 0 | 2 |
| Week 28 Much Improved | 4 | 11 | 8 | 10 |
| Week 36 Much Worse (n=6, n=16, n=11, n=14, n=0) | 0 | 0 | 0 | 0 |
| Week 36 Moderately Worse | 0 | 0 | 0 | 0 |
| Week 36 A Little Worse | 0 | 0 | 0 | 0 |
| Week 36 Stayed the Same | 1 | 0 | 1 | 0 |
| Week 36 A Little Improved | 1 | 1 | 0 | 3 |

| | | | | |
|---|---|---|---|---|
| Week 36 Moderately Improved | 1 | 1 | 0 | 2 |
| Week 36 Much Improved | 3 | 14 | 10 | 9 |
| Week 44 Much Worse (n=5, n=15, n=11, n=14, n=0) | 0 | 0 | 1 | 0 |
| Week 44 Moderately Worse | 0 | 0 | 0 | 0 |
| Week 44 A Little Worse | 0 | 0 | 0 | 0 |
| Week 44 Stayed the Same | 0 | 0 | 0 | 0 |
| Week 44 A Little Improved | 1 | 2 | 0 | 2 |
| Week 44 Moderately Improved | 1 | 1 | 2 | 2 |
| Week 44 Much Improved | 3 | 12 | 8 | 10 |
| Week 52 Much Worse (n=4, n=14, n=10, n=14, n=0) | 0 | 0 | 0 | 0 |
| Week 52 Moderately Worse | 0 | 0 | 0 | 0 |
| Week 52 A Little Worse | 0 | 0 | 1 | 0 |
| Week 52 Stayed the Same | 0 | 1 | 0 | 0 |
| Week 52 A Little Improved | 1 | 0 | 0 | 2 |
| Week 52 Moderately Improved | 2 | 3 | 1 | 1 |
| Week 52 Much Improved | 1 | 10 | 8 | 11 |

| **End point values** | Placebo | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 19 | | | |
| Units: Percentage of particpants | | | | |
| Week 4 Much Worse (n=21, n=20, n=20, n=20, n=16) | 0 | | | |
| Week 4 Moderately Worse | 1 | | | |
| Week 4 A Little Worse | 0 | | | |
| Week 4 Stayed the Same | 6 | | | |
| Week 4 A Little Improved | 4 | | | |
| Week 4 Moderately Improved | 4 | | | |
| Week 4 Much Improved | 1 | | | |
| Week 8 Much Worse (n=17, n=22, n=19, n=20, n=16) | 0 | | | |
| Week 8 Moderately Worse | 0 | | | |
| Week 8 A Little Worse | 0 | | | |
| Week 8 Stayed the Same | 3 | | | |
| Week 8 A Little Improved | 6 | | | |
| Week 8 Moderately Improved | 5 | | | |
| Week 8 Much Improved | 2 | | | |
| Week 12 Much Worse (n=18, n=22, n=20, n=19, n=17) | 0 | | | |
| Week 12 Moderately Worse | 0 | | | |
| Week 12 A Little Worse | 1 | | | |
| Week 12 Stayed the Same | 4 | | | |
| Week 12 A Little Improved | 2 | | | |
| Week 12 Moderately Improved | 8 | | | |
| Week 12 Much Improved | 2 | | | |
| Week 14 Much Worse (n=10, n=18, n=13, n=15, n=0) | 0 | | | |
| Week 14 Moderately Worse | 0 | | | |
| Week 14 A Little Worse | 0 | | | |

| | | | | |
|---|---|---|---|---|
| Week 14 Stayed the Same | 0 | | | |
| Week 14 A Little Improved | 0 | | | |
| Week 14 Moderately Improved | 0 | | | |
| Week 14 Much Improved | 0 | | | |
| Week 18 Much Worse (n=9, n=18, n=14, n=14, n=0) | 0 | | | |
| Week 18 Moderately Worse | 0 | | | |
| Week 18 A Little Worse | 0 | | | |
| Week 18 Stayed the Same | 0 | | | |
| Week 18 A Little Improved | 0 | | | |
| Week 18 Moderately Improved | 0 | | | |
| Week 18 Much Improved | 0 | | | |
| Week 22 Much Worse (n=8, n=18, n=14, n=16, n=0) | 0 | | | |
| Week 22 Moderately Worse | 0 | | | |
| Week 22 A Little Worse | 0 | | | |
| Week 22 Stayed the Same | 0 | | | |
| Week 22 A Little Improved | 0 | | | |
| Week 22 Moderately Improved | 0 | | | |
| Week 22 Much Improved | 0 | | | |
| Week 26 Much Worse (n=8, n=18, n=13, n=16, n=0) | 0 | | | |
| Week 26 Moderately Worse | 0 | | | |
| Week 26 A Little Worse | 0 | | | |
| Week 26 Stayed the Same | 0 | | | |
| Week 26 A Little Improved | 0 | | | |
| Week 26 Moderately Improved | 0 | | | |
| Week 26 Much Improved | 0 | | | |
| Week 28 Much Worse (n=7, n=17, n=10, n=14, n=0) | 0 | | | |
| Week 28 Moderately Worse | 0 | | | |
| Week 28 A Little Worse | 0 | | | |
| Week 28 Stayed the Same | 0 | | | |
| Week 28 A Little Improved | 0 | | | |
| Week 28 Moderately Improved | 0 | | | |
| Week 28 Much Improved | 0 | | | |
| Week 36 Much Worse (n=6, n=16, n=11, n=14, n=0) | 0 | | | |
| Week 36 Moderately Worse | 0 | | | |
| Week 36 A Little Worse | 0 | | | |
| Week 36 Stayed the Same | 0 | | | |
| Week 36 A Little Improved | 0 | | | |
| Week 36 Moderately Improved | 0 | | | |
| Week 36 Much Improved | 0 | | | |
| Week 44 Much Worse (n=5, n=15, n=11, n=14, n=0) | 0 | | | |
| Week 44 Moderately Worse | 0 | | | |
| Week 44 A Little Worse | 0 | | | |
| Week 44 Stayed the Same | 0 | | | |
| Week 44 A Little Improved | 0 | | | |
| Week 44 Moderately Improved | 0 | | | |
| Week 44 Much Improved | 0 | | | |
| Week 52 Much Worse (n=4, n=14, n=10, n=14, n=0) | 0 | | | |

| | | | | |
|---|---|---|---|---|
| Week 52 Moderately Worse | 0 | | | |
| Week 52 A Little Worse | 0 | | | |
| Week 52 Stayed the Same | 0 | | | |
| Week 52 A Little Improved | 0 | | | |
| Week 52 Moderately Improved | 0 | | | |
| Week 52 Much Improved | 0 | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline PGIC of Difficulty with Food or Pills as Assessed Prior to Randomization Post-Baseline Visit

| End point title | Change From Baseline PGIC of Difficulty with Food or Pills as Assessed Prior to Randomization Post-Baseline Visit |
|---|---|

End point description:

Change From Baseline PGIC of Difficulty with Food or Pills as Assessed Prior to Randomization at Weeks 4, 8, 12, 14, 18, 22, 26, 28, 36, 44, and 52
Note: Following Week 14, all patients in the placebo group were given APT-1011 3mg BID and results reflect change from baseline PGIC of difficulty with food or pills following 4, 8, 12, 14, 22, 30 or 38 weeks of treatment.

| End point type | Secondary |
|---|---|

End point timeframe:

Weeks 4, 8, 12, 14, 18, 22, 26, 36, 44, and 52

| End point values | APT-1011 1.5 mg HS | APT-1011 1.5 mg BID | APT-1011 3 mg HS | APT-1011 3 mg BID |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 21 | 22 | 21 | 20 |
| Units: Percentage of particpants | | | | |
| Week 4 Much Worse (n=21, n=20, n=20, n=20, n=16) | 0 | 0 | 0 | 0 |
| Week 4 Moderately Worse | 0 | 0 | 0 | 0 |
| Week 4 A Little Worse | 1 | 0 | 2 | 1 |
| Week 4 Stayed the Same | 4 | 3 | 4 | 5 |
| Week 4 A Little Improved | 8 | 10 | 4 | 9 |
| Week 4 Moderately Improved | 6 | 5 | 4 | 2 |
| Week 4 Much Improved | 2 | 2 | 6 | 3 |
| Week 8 Much Worse (n=17, n=22, n=19, n=20, n=16) | 0 | 0 | 1 | 0 |
| Week 8 Moderately Worse | 0 | 0 | 0 | 0 |
| Week 8 A Little Worse | 2 | 0 | 1 | 0 |
| Week 8 Stayed the Same | 2 | 5 | 1 | 4 |
| Week 8 A Little Improved | 3 | 5 | 5 | 5 |
| Week 8 Moderately Improved | 6 | 4 | 3 | 7 |
| Week 8 Much Improved | 4 | 8 | 8 | 4 |
| Week 12 Much Worse (n=18, n=22, n=20, n=19, n=17) | 0 | 0 | 0 | 0 |
| Week 12 Moderately Worse | 0 | 0 | 0 | 1 |

| | | | | |
|---|---|---|---|---|
| Week 12 A Little Worse | 0 | 0 | 2 | 1 |
| Week 12 Stayed the Same | 1 | 4 | 2 | 3 |
| Week 12 A Little Improved | 5 | 5 | 5 | 5 |
| Week 12 Moderately Improved | 6 | 4 | 2 | 3 |
| Week 12 Much Improved | 6 | 9 | 9 | 6 |
| Week 14 Much Worse (n=10, n=18, n=13, n=15, n=0) | 0 | 0 | 0 | 0 |
| Week 14 Moderately Worse | 0 | 0 | 0 | 0 |
| Week 14 A Little Worse | 0 | 0 | 2 | 0 |
| Week 14 Stayed the Same | 0 | 4 | 0 | 3 |
| Week 14 A Little Improved | 3 | 3 | 1 | 4 |
| Week 14 Moderately Improved | 4 | 3 | 2 | 3 |
| Week 14 Much Improved | 3 | 8 | 8 | 5 |
| Week 18 Much Worse (n=9, n=18, n=14, n=14, n=0) | 0 | 0 | 0 | 0 |
| Week 18 Moderately Worse | 0 | 0 | 1 | 0 |
| Week 18 A Little Worse | 0 | 1 | 1 | 1 |
| Week 18 Stayed the Same | 0 | 3 | 0 | 0 |
| Week 18 A Little Improved | 1 | 1 | 1 | 2 |
| Week 18 Moderately Improved | 6 | 4 | 2 | 4 |
| Week 18 Much Improved | 2 | 9 | 9 | 7 |
| Week 22 Much Worse (n=8, n=18, n=14, n=16, n=0) | 0 | 0 | 1 | 0 |
| Week 22 Moderately Worse | 0 | 0 | 1 | 0 |
| Week 22 A Little Worse | 0 | 0 | 0 | 1 |
| Week 22 Stayed the Same | 0 | 2 | 0 | 1 |
| Week 22 A Little Improved | 2 | 2 | 2 | 5 |
| Week 22 Moderately Improved | 2 | 5 | 3 | 0 |
| Week 22 Much Improved | 4 | 9 | 7 | 9 |
| Week 26 Much Worse (n=8, n=18, n=13, n=16, n=0) | 0 | 0 | 0 | 0 |
| Week 26 Moderately Worse | 0 | 0 | 2 | 1 |
| Week 26 A Little Worse | 0 | 1 | 0 | 0 |
| Week 26 Stayed the Same | 0 | 2 | 0 | 1 |
| Week 26 A Little Improved | 2 | 0 | 0 | 3 |
| Week 26 Moderately Improved | 4 | 3 | 2 | 1 |
| Week 26 Much Improved | 2 | 12 | 9 | 10 |
| Week 28 Much Worse (n=7, n=17, n=10, n=14, n=0) | 0 | 0 | 0 | 0 |
| Week 28 Moderately Worse | 0 | 0 | 1 | 0 |
| Week 28 A Little Worse | 0 | 0 | 0 | 0 |
| Week 28 Stayed the Same | 0 | 2 | 0 | 0 |
| Week 28 A Little Improved | 1 | 1 | 1 | 1 |
| Week 28 Moderately Improved | 2 | 3 | 0 | 4 |
| Week 28 Much Improved | 4 | 11 | 8 | 9 |
| Week 36 Much Worse (n=6, n=16, n=11, n=14, n=0) | 0 | 0 | 0 | 0 |
| Week 36 Moderately Worse | 0 | 0 | 0 | 0 |
| Week 36 A Little Worse | 0 | 0 | 0 | 0 |
| Week 36 Stayed the Same | 0 | 1 | 1 | 0 |
| Week 36 A Little Improved | 1 | 0 | 0 | 2 |
| Week 36 Moderately Improved | 3 | 3 | 0 | 3 |
| Week 36 Much Improved | 2 | 12 | 10 | 9 |

| | | | | |
|---|---|---|---|---|
| Week 44 Much Worse (n=5, n=15, n=11, n=14, n=0) | 0 | 0 | 1 | 0 |
| Week 44 Moderately Worse | 0 | 0 | 0 | 0 |
| Week 44 A Little Worse | 0 | 0 | 0 | 0 |
| Week 44 Stayed the Same | 0 | 1 | 0 | 0 |
| Week 44 A Little Improved | 1 | 0 | 0 | 2 |
| Week 44 Moderately Improved | 1 | 1 | 2 | 2 |
| Week 44 Much Improved | 3 | 13 | 8 | 10 |
| Week 52 Much Worse (n=4, n=14, n=10, n=14, n=0) | 0 | 0 | 0 | 0 |
| Week 52 Moderately Worse | 0 | 0 | 0 | 0 |
| Week 52 A Little Worse | 0 | 1 | 1 | 0 |
| Week 52 Stayed the Same | 1 | 0 | 0 | 0 |
| Week 52 A Little Improved | 0 | 0 | 0 | 2 |
| Week 52 Moderately Improved | 1 | 5 | 1 | 3 |
| Week 52 Much Improved | 2 | 8 | 8 | 9 |

| **End point values** | Placebo | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 19 | | | |
| Units: Percentage of particpants | | | | |
| Week 4 Much Worse (n=21, n=20, n=20, n=20, n=16) | 0 | | | |
| Week 4 Moderately Worse | 0 | | | |
| Week 4 A Little Worse | 1 | | | |
| Week 4 Stayed the Same | 5 | | | |
| Week 4 A Little Improved | 7 | | | |
| Week 4 Moderately Improved | 2 | | | |
| Week 4 Much Improved | 1 | | | |
| Week 8 Much Worse (n=17, n=22, n=19, n=20, n=16) | 0 | | | |
| Week 8 Moderately Worse | 0 | | | |
| Week 8 A Little Worse | 1 | | | |
| Week 8 Stayed the Same | 4 | | | |
| Week 8 A Little Improved | 5 | | | |
| Week 8 Moderately Improved | 5 | | | |
| Week 8 Much Improved | 1 | | | |
| Week 12 Much Worse (n=18, n=22, n=20, n=19, n=17) | 0 | | | |
| Week 12 Moderately Worse | 0 | | | |
| Week 12 A Little Worse | 0 | | | |
| Week 12 Stayed the Same | 3 | | | |
| Week 12 A Little Improved | 6 | | | |
| Week 12 Moderately Improved | 6 | | | |
| Week 12 Much Improved | 2 | | | |
| Week 14 Much Worse (n=10, n=18, n=13, n=15, n=0) | 0 | | | |
| Week 14 Moderately Worse | 0 | | | |
| Week 14 A Little Worse | 0 | | | |
| Week 14 Stayed the Same | 0 | | | |
| Week 14 A Little Improved | 0 | | | |

| | | | | |
|---|---|---|---|---|
| Week 14 Moderately Improved | 0 | | | |
| Week 14 Much Improved | 0 | | | |
| Week 18 Much Worse (n=9, n=18, n=14, n=14, n=0) | 0 | | | |
| Week 18 Moderately Worse | 0 | | | |
| Week 18 A Little Worse | 0 | | | |
| Week 18 Stayed the Same | 0 | | | |
| Week 18 A Little Improved | 0 | | | |
| Week 18 Moderately Improved | 0 | | | |
| Week 18 Much Improved | 0 | | | |
| Week 22 Much Worse (n=8, n=18, n=14, n=16, n=0) | 0 | | | |
| Week 22 Moderately Worse | 0 | | | |
| Week 22 A Little Worse | 0 | | | |
| Week 22 Stayed the Same | 0 | | | |
| Week 22 A Little Improved | 0 | | | |
| Week 22 Moderately Improved | 0 | | | |
| Week 22 Much Improved | 0 | | | |
| Week 26 Much Worse (n=8, n=18, n=13, n=16, n=0) | 0 | | | |
| Week 26 Moderately Worse | 0 | | | |
| Week 26 A Little Worse | 0 | | | |
| Week 26 Stayed the Same | 0 | | | |
| Week 26 A Little Improved | 0 | | | |
| Week 26 Moderately Improved | 0 | | | |
| Week 26 Much Improved | 0 | | | |
| Week 28 Much Worse (n=7, n=17, n=10, n=14, n=0) | 0 | | | |
| Week 28 Moderately Worse | 0 | | | |
| Week 28 A Little Worse | 0 | | | |
| Week 28 Stayed the Same | 0 | | | |
| Week 28 A Little Improved | 0 | | | |
| Week 28 Moderately Improved | 0 | | | |
| Week 28 Much Improved | 0 | | | |
| Week 36 Much Worse (n=6, n=16, n=11, n=14, n=0) | 0 | | | |
| Week 36 Moderately Worse | 0 | | | |
| Week 36 A Little Worse | 0 | | | |
| Week 36 Stayed the Same | 0 | | | |
| Week 36 A Little Improved | 0 | | | |
| Week 36 Moderately Improved | 0 | | | |
| Week 36 Much Improved | 0 | | | |
| Week 44 Much Worse (n=5, n=15, n=11, n=14, n=0) | 0 | | | |
| Week 44 Moderately Worse | 0 | | | |
| Week 44 A Little Worse | 0 | | | |
| Week 44 Stayed the Same | 0 | | | |
| Week 44 A Little Improved | 0 | | | |
| Week 44 Moderately Improved | 0 | | | |
| Week 44 Much Improved | 0 | | | |
| Week 52 Much Worse (n=4, n=14, n=10, n=14, n=0) | 0 | | | |
| Week 52 Moderately Worse | 0 | | | |
| Week 52 A Little Worse | 0 | | | |

| | | | | |
|---|---|---|---|---|
| Week 52 Stayed the Same | 0 | | | |
| Week 52 A Little Improved | 0 | | | |
| Week 52 Moderately Improved | 0 | | | |
| Week 52 Much Improved | 0 | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of subjects requiring emergency endoscopic food dis-impaction

| End point title | Percentage of subjects requiring emergency endoscopic food dis-impaction |
|---|---|

End point description:

Percentage of subjects requiring emergency endoscopic food dis-impaction by dose before Week 14, between Week 14 and Week 28, and between Week 28 and Week 52
Note: There were no patients in the placebo group after Week 14.

| End point type | Secondary |
|---|---|

End point timeframe:

before Week 14, between Week 14 and Week 28, between Week 28 and Week 52

| End point values | APT-1011 1.5 mg HS | APT-1011 1.5 mg BID | APT-1011 3 mg HS | APT-1011 3 mg BID |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 21 | 22 | 21 | 20 |
| Units: Percentage of particpants | | | | |
| Before Week 14 | 0 | 0 | 0 | 0 |
| Between Week 14 and Week 28 | 0 | 0 | 0 | 0 |
| Between Week 28 and Week 52 | 0 | 0 | 0 | 0 |

| End point values | Placebo | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 19 | | | |
| Units: Percentage of particpants | | | | |
| Before Week 14 | 0 | | | |
| Between Week 14 and Week 28 | 0 | | | |
| Between Week 28 and Week 52 | 0 | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of subjects requiring esophageal dilation

| End point title | Percentage of subjects requiring esophageal dilation |
|---|---|

End point description:

Percentage of subjects requiring esophageal dilation by dosing group and part of the study
Note: There were no patients in the placebo group after Week 14.

| End point type | Secondary |
|---|---|

End point timeframe:

baseline to Week 52

| End point values | APT-1011 1.5 mg HS | APT-1011 1.5 mg BID | APT-1011 3 mg HS | APT-1011 3 mg BID |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 21 | 22 | 21 | 20 |
| Units: Percentage of particpants | 0 | 0 | 0 | 0 |

| End point values | Placebo | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 19 | | | |
| Units: Percentage of particpants | 0 | | | |

### Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Number of Subjects Discontinuing Due to HPA Axis Suppression

| End point title | Number of Subjects Discontinuing Due to HPA Axis Suppression |
|---|---|

End point description:

Number of subjects discontinuing due to HPA axis suppression in the Safety Analysis Population
Note: There were no patients in the placebo group after Week 14.

| End point type | Other pre-specified |
|---|---|

End point timeframe:

baseline to Week 52

| End point values | APT-1011 1.5 mg HS | APT-1011 1.5 mg BID | APT-1011 3 mg HS | APT-1011 3 mg BID |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 21 | 22 | 21 | 20 |
| Units: Count of Participants | 0 | 0 | 0 | 0 |

| End point values | Placebo | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 19 | | | |
| Units: Count of Participants | 0 | | | |

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Frequency of Oral and Esophageal Candidiasis

| End point title | Frequency of Oral and Esophageal Candidiasis |
|---|---|

End point description:

Frequency of oral and esophageal candidiasis in the Safety Analysis Population
Note: There were no patients in the placebo group after Week 14.

| End point type | Other pre-specified |
|---|---|

End point timeframe:

baseline to Week 52

| End point values | APT-1011 1.5 mg HS | APT-1011 1.5 mg BID | APT-1011 3 mg HS | APT-1011 3 mg BID |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 21 | 22 | 21 | 20 |
| Units: Count of Participants | | | | |
| Oesophageal candidiasis | 0 | 2 | 0 | 8 |
| Oral candidiasis | 0 | 3 | 1 | 3 |

| End point values | Placebo | Single-Blind APT-1011 3 mg BID | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 19 | 34 | | |
| Units: Count of Participants | | | | |
| Oesophageal candidiasis | 0 | 1 | | |
| Oral candidiasis | 0 | 1 | | |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from the time of enrollment until the completion of the Follow-Up Visit which took place 2 weeks after the subject took the final dose of the study drug, if applicable.

| | |
|---|---|
| Assessment type | Systematic |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 22.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | APT-1011 1.5 mg HS |

Reporting group description:

Subjects received placebo 30 minutes after breakfast and 1.5 mg APT-1011 HS (at bedtime) daily

| | |
|---|---|
| Reporting group title | APT-1011 1.5 mg BID |

Reporting group description:

Subjects received 1.5 mg APT-1011 30 minutes after breakfast and at bedtime daily for a total daily dose of 3.0 mg

| | |
|---|---|
| Reporting group title | APT-1011 3 mg HS |

Reporting group description:

Subjects received placebo 30 minutes after breakfast and 3.0 mg APT-1011 at bedtime daily

| | |
|---|---|
| Reporting group title | APT-1011 3 mg BID |

Reporting group description:

Subjects received 3 mg APT-1011 30 minutes after breakfast and at bedtime daily for a total daily dose of 6.0 mg

| | |
|---|---|
| Reporting group title | Placebo |

Reporting group description:

Subjects received placebo 30 minutes after breakfast and HS (at bedtime) daily

| | |
|---|---|
| Reporting group title | Single-Blind APT-1011 3 mg BID |

Reporting group description: -

| Serious adverse events | APT-1011 1.5 mg HS | APT-1011 1.5 mg BID | APT-1011 3 mg HS |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 23 (0.00%) | 2 / 21 (9.52%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Hodgkin's disease | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Status epilepticus | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 1 / 21 (4.76%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Ureterolithiasis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 1 / 21 (4.76%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| **Serious adverse events** | APT-1011 3 mg BID | Placebo | Single-Blind APT-1011 3 mg BID |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Hodgkin's disease | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Status epilepticus | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Ureterolithiasis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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

| **Non-serious adverse events** | APT-1011 1.5 mg HS | APT-1011 1.5 mg BID | APT-1011 3 mg HS |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 10 / 21 (47.62%) | 20 / 23 (86.96%) | 16 / 21 (76.19%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Cartilage neoplasm | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 2 / 23 (8.70%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 4 | 1 |
| General disorders and administration site conditions | | | |
| Chills | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Early satiety | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Face oedema | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Fatigue | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gait disturbance | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Generalised oedema | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Oedema peripheral | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pain | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Peripheral swelling | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Temperature regulation disorder | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Immune system disorders | | | |
| Seasonal allergy | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Reproductive system and breast disorders | | | |
| Benign prostatic hyperplasia | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Epididymal cyst | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Erectile dysfunction | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Genital rash | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gynaecomastia | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Menstruation irregular | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Pelvic discomfort | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Peyronie's disease | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Prostatitis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 1 / 23 (4.35%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Aspiration | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Asthma | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cough | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperventilation | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Laryngeal inflammation | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasal congestion | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | 1 / 23 (4.35%) | 0 / 21 (0.00%) |
| occurrences (all) | 3 | 1 | 0 |
| Oropharyngeal pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 21 (9.52%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Oropharyngeal spasm | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulmonary congestion | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Sinus congestion | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Tonsillolith | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Depressed mood | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Depression | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Insomnia | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Libido decreased | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Post-traumatic stress disorder | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Stress | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Investigations | | | |
| ACTH stimulation test abnormal | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 23 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 1 | 0 | 1 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 23 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 1 | 0 | 1 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood glucose increased | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood pressure increased | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cortisol decreased | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 2 / 23 (8.70%) | 1 / 21 (4.76%) |
| occurrences (all) | 1 | 2 | 1 |
| Electrocardiogram QRS complex prolonged | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Heart rate increased | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lymphocyte count increased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neutrophil percentage decreased | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Protein urine present | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 1 / 23 (4.35%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Weight increased | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Arthropod bite | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Back injury | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Concussion | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Contusion | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 1 / 23 (4.35%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Corneal abrasion | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye injury | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hand fracture | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Limb injury | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle rupture | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Muscle strain | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Road traffic accident | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin laceration | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 2 / 21 (9.52%) |
| occurrences (all) | 0 | 0 | 2 |
| Tooth fracture | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Wound | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Congenital, familial and genetic disorders | | | |
| Gilbert's syndrome | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Cardiac disorders | | | |
| Atrioventricular block first degree | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bundle branch block right | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Palpitations | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Nervous system disorders | | | |
| Carpal tunnel syndrome | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Cervical radiculopathy | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 1 / 23 (4.35%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Headache | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 2 / 23 (8.70%) | 2 / 21 (9.52%) |
| occurrences (all) | 7 | 2 | 2 |
| Migraine | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 1 / 23 (4.35%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Somnolence | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Syncope | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Taste disorder | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 1 / 23 (4.35%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Blood and lymphatic system disorders | | | |
| Leukopenia | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear and labyrinth disorders | | | |

| | | | |
|---|---|---|---|
| Deafness bilateral | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 1 / 23 (4.35%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Ear pain | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Middle ear effusion | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 1 / 23 (4.35%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Abdominal distension | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Abdominal pain lower | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Angular cheilitis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Constipation | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 23 (0.00%) | 2 / 21 (9.52%) |
| occurrences (all) | 1 | 0 | 2 |
| Diarrhoea haemorrhagic | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dyspepsia | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 2 / 23 (8.70%) | 2 / 21 (9.52%) |
| occurrences (all) | 1 | 2 | 2 |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 1 / 23 (4.35%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Erosive oesophagitis | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 1 / 23 (4.35%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Faeces pale | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Faeces soft | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Flatulence | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 2 / 23 (8.70%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Gastric mucosa erythema | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastric polyps | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastritis erosive | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastritis haemorrhagic | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 1 / 23 (4.35%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Glossodynia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | 1 / 23 (4.35%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Haemorrhoids thrombosed | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hiatus hernia | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 2 / 23 (8.70%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 2 | 1 |
| Odynophagia | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 1 / 23 (4.35%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 1 | 1 |
| Oesophageal food impaction | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 1 / 23 (4.35%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Oesophageal ulcer | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oesophagitis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 2 / 21 (9.52%) |
| occurrences (all) | 0 | 0 | 2 |
| Oral pain | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Paraesthesia oral | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 1 / 23 (4.35%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Stomatitis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Toothache | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 1 / 23 (4.35%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Vomiting | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 21 (4.76%) | 1 / 23 (4.35%) | 1 / 21 (4.76%) |
| occurrences (all) | 1 | 1 | 1 |
| Hepatobiliary disorders | | | |
| Hepatic steatosis | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Acne | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Cutaneous calcification | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dermatitis contact | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ingrowing nail | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Pityriasis rosea | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 1 / 23 (4.35%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pruritus allergic | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash vesicular | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rosacea | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Renal and urinary disorders | | | |

| | | | |
|---|---|---|---|
| Hypertonic bladder | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Proteinuria | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Endocrine disorders | | | |
| Adrenal suppression | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypothyroidism | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 1 / 23 (4.35%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Arthritis | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Back pain | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | 2 / 23 (8.70%) | 0 / 21 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Flank pain | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Joint effusion | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Joint swelling | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 1 / 23 (4.35%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Muscle spasms | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Myalgia | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 1 / 23 (4.35%) | 0 / 21 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Neck pain | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 1 / 23 (4.35%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rotator cuff syndrome | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 1 / 23 (4.35%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Tendonitis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Tenosynovitis stenosans | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Infections and infestations | | | |
| Acute sinusitis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Bacterial vaginosis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 1 / 23 (4.35%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Conjunctivitis viral | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear infection | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Epididymitis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fungal infection | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 2 / 23 (8.70%) | 1 / 21 (4.76%) |
| occurrences (all) | 1 | 2 | 1 |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Genital infection fungal | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Helicobacter infection | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Impetigo | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infectious mononucleosis | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 2 / 23 (8.70%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 2 | 1 |
| Kidney infection | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|---|---|---|---|
| Nasopharyngitis | | | |
| subjects affected / exposed | 3 / 21 (14.29%) | 4 / 23 (17.39%) | 1 / 21 (4.76%) |
| occurrences (all) | 7 | 4 | 1 |
| Oral candidiasis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 3 / 23 (13.04%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 3 | 1 |
| Oral infection | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 1 / 23 (4.35%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Oropharyngeal candidiasis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Oesophageal candidiasis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 2 / 23 (8.70%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 4 | 0 |
| Otitis media | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 1 / 23 (4.35%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 1 / 23 (4.35%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 23 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 1 | 0 | 1 |
| Tinea infection | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 2 / 23 (8.70%) | 3 / 21 (14.29%) |
| occurrences (all) | 0 | 3 | 3 |

| | | | |
|---|---|---|---|
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 2 / 23 (8.70%) | 1 / 21 (4.76%) |
| occurrences (all) | 1 | 2 | 1 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 23 (0.00%) | 2 / 21 (9.52%) |
| occurrences (all) | 1 | 0 | 2 |
| Vulvovaginal mycotic infection | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastrointestinal viral infection | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Appetite disorder | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dehydration | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Glucose tolerance impaired | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypercholesterolaemia | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypovitaminosis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 23 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Type 2 diabetes mellitus | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 23 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| **Non-serious adverse events** | APT-1011 3 mg BID | Placebo | Single-Blind APT-1011 3 mg BID |
|---|---|---|---|

| | | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 19 / 20 (95.00%) | 6 / 19 (31.58%) | 21 / 34 (61.76%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Cartilage neoplasm | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Chills | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Early satiety | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |
| Face oedema | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fatigue | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 3 / 19 (15.79%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Gait disturbance | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Generalised oedema | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 19 (5.26%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Oedema peripheral | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pain | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Peripheral swelling | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Temperature regulation disorder | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Immune system disorders | | | |
| Seasonal allergy | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 1 | 0 | 1 |
| Reproductive system and breast disorders | | | |
| Benign prostatic hyperplasia | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Epididymal cyst | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 19 (5.26%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Erectile dysfunction | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 19 (5.26%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Genital rash | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gynaecomastia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Menstruation irregular | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pelvic discomfort | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |
| Peyronie's disease | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |
| Prostatitis | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Aspiration | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Asthma | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Cough | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 19 (5.26%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hyperventilation | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |
| Laryngeal inflammation | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 19 (5.26%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nasal congestion | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oropharyngeal pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 20 (10.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Oropharyngeal spasm | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 19 (5.26%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pulmonary congestion | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinus congestion | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tonsillolith | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 19 (5.26%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 2 / 20 (10.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Depressed mood | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Depression | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 1 | 0 | 1 |
| Libido decreased | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Post-traumatic stress disorder | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Stress | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|---|---|---|---|
| Investigations | | | |
| ACTH stimulation test abnormal | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 19 (5.26%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood glucose increased | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood pressure increased | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Cortisol decreased | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 2 / 34 (5.88%) |
| occurrences (all) | 1 | 0 | 2 |
| Electrocardiogram QRS complex prolonged | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Heart rate increased | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 19 (5.26%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Lymphocyte count increased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |
| Neutrophil percentage decreased | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Protein urine present | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |
| Weight increased | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Arthropod bite | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Back injury | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |
| Concussion | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Contusion | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Corneal abrasion | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |
| Eye injury | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |
| Hand fracture | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Limb injury | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |
| Muscle rupture | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle strain | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Road traffic accident | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin laceration | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Tooth fracture | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wound | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Congenital, familial and genetic disorders | | | |
| Gilbert's syndrome | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |
| Atrioventricular block first degree | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Bundle branch block right | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Palpitations | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nervous system disorders | | | |
| Carpal tunnel syndrome | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cervical radiculopathy | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dizziness | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Headache | | | |
| subjects affected / exposed | 3 / 20 (15.00%) | 2 / 19 (10.53%) | 2 / 34 (5.88%) |
| occurrences (all) | 4 | 2 | 3 |
| Migraine | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Somnolence | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Syncope | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Taste disorder | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| Leukopenia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |
| Ear and labyrinth disorders | | | |

| | | | |
|---|---|---|---|
| Deafness bilateral | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear pain | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |
| Middle ear effusion | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 1 | 0 | 1 |
| Abdominal pain lower | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 1 | 0 | 1 |
| Angular cheilitis | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Constipation | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |
| Diarrhoea | | | |
| subjects affected / exposed | 2 / 20 (10.00%) | 1 / 19 (5.26%) | 0 / 34 (0.00%) |
| occurrences (all) | 3 | 1 | 0 |
| Diarrhoea haemorrhagic | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dyspepsia | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 1 / 19 (5.26%) | 2 / 34 (5.88%) |
| occurrences (all) | 1 | 1 | 2 |
| Dysphagia | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Erosive oesophagitis | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 1 | 0 | 1 |
| Faeces pale | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Faeces soft | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Flatulence | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 1 | 0 | 1 |
| Gastric mucosa erythema | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastric polyps | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastritis erosive | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 1 | 0 | 1 |
| Gastritis haemorrhagic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |
| Glossodynia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haemorrhoids thrombosed | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |
| Hiatus hernia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 19 (5.26%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 1 | 1 |
| Nausea | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 1 / 19 (5.26%) | 1 / 34 (2.94%) |
| occurrences (all) | 1 | 1 | 1 |
| Odynophagia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oesophageal food impaction | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oesophageal ulcer | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |
| Oesophagitis | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Oral pain | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Paraesthesia oral | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Stomatitis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |
| Toothache | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 2 / 34 (5.88%) |
| occurrences (all) | 0 | 0 | 2 |
| Vomiting | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hepatobiliary disorders | | | |
| Hepatic steatosis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Acne | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cutaneous calcification | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 19 (5.26%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Dermatitis contact | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |
| Ingrowing nail | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pityriasis rosea | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pruritus allergic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 19 (5.26%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rash | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 1 | 0 | 1 |
| Rash vesicular | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |
| Rosacea | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal and urinary disorders | | | |

| | | | |
|---|---|---|---|
| Hypertonic bladder | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |
| Proteinuria | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 19 (5.26%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Endocrine disorders | | | |
| Adrenal suppression | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hypothyroidism | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Arthritis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Back pain | | | |
| subjects affected / exposed | 3 / 20 (15.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 3 | 0 | 1 |
| Flank pain | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Joint effusion | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Joint swelling | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle spasms | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 1 | 0 | 1 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neck pain | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 2 / 20 (10.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Rotator cuff syndrome | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tendonitis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tenosynovitis stenosans | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Acute sinusitis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bacterial vaginosis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cellulitis | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|---|---|---|---|
| Conjunctivitis viral | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 19 (5.26%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Ear infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Epididymitis | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Fungal infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |
| Genital infection fungal | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Helicobacter infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Impetigo | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |
| Infectious mononucleosis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Kidney infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Nasopharyngitis | | | |
| subjects affected / exposed | 5 / 20 (25.00%) | 1 / 19 (5.26%) | 4 / 34 (11.76%) |
| occurrences (all) | 5 | 1 | 4 |
| Oral candidiasis | | | |
| subjects affected / exposed | 3 / 20 (15.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 3 | 0 | 1 |
| Oral infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oropharyngeal candidiasis | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Oesophageal candidiasis | | | |
| subjects affected / exposed | 8 / 20 (40.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 8 | 0 | 1 |
| Otitis media | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pharyngitis | | | |
| subjects affected / exposed | 2 / 20 (10.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Tinea infection | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Tooth abscess | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 2 / 20 (10.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |

| | | | |
|---|---|---|---|
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 19 (5.26%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 19 (5.26%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 1 | 1 |
| Vulvovaginal mycotic infection | | | |
| subjects affected / exposed | 2 / 20 (10.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Gastrointestinal viral infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 1 / 34 (2.94%) |
| occurrences (all) | 0 | 0 | 1 |
| Metabolism and nutrition disorders | | | |
| Appetite disorder | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 19 (5.26%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Dehydration | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Glucose tolerance impaired | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hypercholesterolaemia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypovitaminosis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Type 2 diabetes mellitus | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 19 (0.00%) | 0 / 34 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 05 May 2017 | • To update secondary endpoints and statistical analyses after United States (US) Food and Drug Administration (FDA)'s review of the protocol;<br>• To clarify further the history of strictures and prior steroid responses;<br>• To clarify that EoE Symptom Score was to remain >3 at all visits before randomization;<br>• To confirm that diet was to remain stable after signing the Informed Consent Form (ICF);<br>• To move the change in number of dysphagia episodes at baseline from exploratory to a secondary endpoint;<br>• To clarify the schedule of visits at which adrenocorticotropic hormone (ACTH) is assessed;<br>• To add oral and esophageal candidiasis to safety endpoints;<br>• To update statistical methodology to include the Cochran-Mantel-Hanzel common odds ratio test and update analysis of secondary and exploratory efficacy;<br>• To include additional variables to the population pharmacokinetics (PopPK) model;<br>• To clarify time points in the study for assignment to single-blind treatment;<br>• To update the address of the central electrocardiogram (ECG) facility;<br>• Address inconsistencies between synopsis, protocol and schedules of assessment; |
| 06 September 2017 | • To address items raised by regulatory authorities in Canada, Belgium and Germany to provide additional clarity to the protocol.<br>• To update an exclusion criterion with the correct level of serum cortisol and clarify that cosyntropin will be administered intramuscularly as well as the timing of the first ACTH stimulation test;<br>• To clarify the timing of the analysis of the primary endpoint and safety analyses;<br>• To update the definition of high-dose proton pump inhibitors (PPI);<br>• To clarify location of text for signs and symptoms of adrenal suppression and hypercorticism;<br>• To clarify the definition of dysphagia;<br>• To amend exclusion criteria to exclude subjects with uncontrolled diabetes or hypertension;<br>• To clarify that subjects with morning serum cortisol levels (≤5 µg/dL [138 nmol/L]) not responsive to ACTH stimulation are to be excluded;<br>• To add leukotrienes and cromolyn sodium to exclusion criteria;<br>• To clarify testing required for infections with hepatitis B, hepatitis C, or human immunodeficiency virus (HIV) as part of exclusion criteria;<br>• To exclude subjects with documented active peptic ulcer;<br>• To exclude subjects with chronic infections such as tuberculosis (TB), active chicken pox or measles or absence of measles, mumps and rubella vaccine (MMR), other malignancies and severe bleeding disorders;<br>• To provide guidance of allowed amount of alcohol use;<br>• To clarify previous participation in clinical trials;<br>• To clarify that the ACTH stimulation test does not have to be following receipt of the morning serum cortisol level;<br>• To include Switzerland to the list of countries;<br>• To include optional HbA1C testing;<br>• To update Schedules of Events as applicable;<br>• To move the change in number of dysphagia episodes at baseline from exploratory to a secondary endpoint in the study schematic;<br>• To clarify acceptable contraception for female and male subjects; |

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|---|---|
| 16 July 2019 | o To clarify the timing of the “after-breakfast” dose related to the serum cortisol and sparse pharmacokinetic (PK) sampling draw.<br>o To correct an error regarding Safety Analyses.<br>o To clarify rescreening and informed consent form (ICF) procedures.<br>o To revise Exclusion #14 to include “or allergic rhinitis”<br>o To add “inhibitors” after all references to “Leukotriene"<br>o To include information regarding Interim analysis data for Part 1<br>o To clarify that the primary endpoint assessment will be performed at completion of Week 12 rather than Week 14.<br>o To update Schedules of Events as applicable<br>o To update references, correct minor inconsistencies and typographical errors |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported