



Clinical trial results:

A Phase 2 Multicenter, Randomized, Double-blind, Placebo-Controlled Trial to Evaluate Toreforant (JNJ-38518168) for the Treatment of Subjects with Moderate to Severe Plaque type Psoriasis

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2015-000277-12 |
| Trial protocol | PL |
| Global end of trial date | 11 March 2016 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 18 February 2017 |
| First version publication date | 18 February 2017 |

Trial information

Trial identification

| | |
|-----------------------|-----------------|
| Sponsor protocol code | 38518168PSO2001 |
|-----------------------|-----------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02295865 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Janssen-Cilag International N.V. |
| Sponsor organisation address | Antwerpseweg 15-17, Beerse, Belgium, B-2340 |
| Public contact | Clinical Registry group, Janssen-Cilag International N.V., ClinicalTrialsEU@its.jnj.com |
| Scientific contact | Clinical Registry group, Janssen-Cilag International N.V., ClinicalTrialsEU@its.jnj.com |

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|---------------|
| Analysis stage | Final |
| Date of interim/final analysis | 11 March 2016 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 11 March 2016 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The main objective was to evaluate the efficacy of JNJ-38518168 in subjects with moderate to severe plaque-type psoriasis and to assess the safety and tolerability of JNJ-38518168 in subjects with moderate to severe plaque-type psoriasis.

Protection of trial subjects:

The safety assessments included vital signs, general physical examination, adverse events (AEs), concomitant medication review, electrocardiograms (ECGs), pregnancy testing, laboratory testing, urine testing.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 14 December 2014 |
| 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 | Poland: 41 |
| Country: Number of subjects enrolled | United States: 20 |
| Worldwide total number of subjects | 61 |
| EEA total number of subjects | 41 |

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) | 55 |
| From 65 to 84 years | 6 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The study was conducted at Poland (5 sites) and United States (9 sites) from 14 December 2014 to 11 March 2016.

Pre-assignment

Screening details:

A total of 80 subjects were screened, of which 62 subjects were randomized at Week 0. A total of 61 subjects were treated and enrolled in the study.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes |
| Arm title | Placebo |

Arm description:

Subjects received 3*30 milligram(mg) placebo tablets and 1*3 mg placebo tablet orally at the same time each day upto week 12.

| | |
|--|----------|
| 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 oral dose of 3*30 mg tablet of placebo along with 1*3 mg tablet of placebo at the same time each day upto week 12.

| | |
|------------------|--------------------------------|
| Arm title | JNJ-38518168 30 milligram (mg) |
|------------------|--------------------------------|

Arm description:

Subjects in the JNJ-38518168 30 milligram (mg) group received 1*30 mg JNJ-38518168 tablet together with 2*30 mg placebo tablets and 1*3 mg placebo tablet at the same time each day upto week 12.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | JNJ-38518168 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received oral dose of JNJ-38518168 1*30 mg tablet each day upto week 12.

| | |
|--|----------|
| 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 oral dose of 2*30 mg placebo and 1*3 mg placebo tablet each day upto week 12.

| | |
|---|--------------------------------|
| Arm title | JNJ-38518168 60 milligram (mg) |
| Arm description: | |
| Subjects in the JNJ-38518168 60 mg group received 2*30 mg JNJ-38518168 tablets, 1*30 mg placebo tablet and 1*3 mg placebo tablet orally at the same time each day upto week 12. | |
| Arm type | Experimental |
| Investigational medicinal product name | JNJ-38518168 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| Subjects received oral dose of JNJ-38518168, 2*30 mg tablet each day upto week 12. | |
| 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 oral dose of 1*30 mg placebo and 1*3 mg placebo tablet each day upto week 12. | |

| Number of subjects in period 1 | Placebo | JNJ-38518168 30 milligram (mg) | JNJ-38518168 60 milligram (mg) |
|---------------------------------------|---------|--------------------------------|--------------------------------|
| Started | 6 | 29 | 26 |
| Completed | 6 | 25 | 20 |
| Not completed | 0 | 4 | 6 |
| Adverse event, non-fatal | - | 3 | - |
| Other | - | - | 1 |
| Pregnancy | - | - | 1 |
| Adverse event, serious non-fatal | - | - | 1 |
| Lost to follow-up | - | - | 1 |
| Lack of efficacy | - | 1 | 2 |

Baseline characteristics

Reporting groups

| | |
|---|--------------------------------|
| Reporting group title | Placebo |
| Reporting group description: | |
| Subjects received 3*30 milligram(mg) placebo tablets and 1*3 mg placebo tablet orally at the same time each day upto week 12. | |
| Reporting group title | JNJ-38518168 30 milligram (mg) |
| Reporting group description: | |
| Subjects in the JNJ-38518168 30 milligram (mg) group received 1*30 mg JNJ-38518168 tablet together with 2*30 mg placebo tablets and 1*3 mg placebo tablet at the same time each day upto week 12. | |
| Reporting group title | JNJ-38518168 60 milligram (mg) |
| Reporting group description: | |
| Subjects in the JNJ-38518168 60 mg group received 2*30 mg JNJ-38518168 tablets, 1*30 mg placebo tablet and 1*3 mg placebo tablet orally at the same time each day upto week 12. | |

| Reporting group values | Placebo | JNJ-38518168 30 milligram (mg) | JNJ-38518168 60 milligram (mg) |
|---|---------|--------------------------------|--------------------------------|
| Number of subjects | 6 | 29 | 26 |
| Title for AgeCategorical Units: subjects | | | |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 5 | 27 | 23 |
| From 65 to 84 years | 1 | 2 | 3 |
| 85 years and over | 0 | 0 | 0 |
| Title for AgeContinuous Units: years | | | |
| arithmetic mean | 46.8 | 42.2 | 41.4 |
| standard deviation | ± 18.95 | ± 14.06 | ± 18.25 |
| Title for Gender Units: subjects | | | |
| Female | 0 | 11 | 5 |
| Male | 6 | 18 | 21 |

| Reporting group values | Total | | |
|---|-------|--|--|
| Number of subjects | 61 | | |
| Title for AgeCategorical Units: subjects | | | |
| Children (2-11 years) | 0 | | |
| Adolescents (12-17 years) | 0 | | |
| Adults (18-64 years) | 55 | | |
| From 65 to 84 years | 6 | | |
| 85 years and over | 0 | | |
| Title for AgeContinuous Units: years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |

| | | | |
|------------------|----|--|--|
| Title for Gender | | | |
| Units: subjects | | | |
| Female | 16 | | |
| Male | 45 | | |

End points

End points reporting groups

| | |
|---|--------------------------------|
| Reporting group title | Placebo |
| Reporting group description: Subjects received 3*30 milligram(mg) placebo tablets and 1*3 mg placebo tablet orally at the same time each day upto week 12. | |
| Reporting group title | JNJ-38518168 30 milligram (mg) |
| Reporting group description: Subjects in the JNJ-38518168 30 milligram (mg) group received 1*30 mg JNJ-38518168 tablet together with 2*30 mg placebo tablets and 1*3 mg placebo tablet at the same time each day upto week 12. | |
| Reporting group title | JNJ-38518168 60 milligram (mg) |
| Reporting group description: Subjects in the JNJ-38518168 60 mg group received 2*30 mg JNJ-38518168 tablets, 1*30 mg placebo tablet and 1*3 mg placebo tablet orally at the same time each day upto week 12. | |

Primary: Percentage of Subjects who Achieved Psoriasis Area and Severity Index (PASI) 75 Response at Week 12

| | |
|--|---|
| End point title | Percentage of Subjects who Achieved Psoriasis Area and Severity Index (PASI) 75 Response at Week 12 |
| End point description: The PASI score is a combined assessment of lesion severity and area affected into a single score. Body is divided into 4 regions:head, arms, trunk, and legs. For each region, percent (%) area of skin involved is estimated:0=0%, 1=less than (<) 10%, 2=10 to <30%, 3=30 to <50%, 4=50 to <70%, 5=70 to <90%, 6=90 to 100%. Severity is estimated by clinical symptoms: erythema, induration, scaling; scale:0= none to 4=maximum. Final PASI=sum of severity parameters for each region*area score*weight of region (head:0.1,arms:0.2,body:0.3,legs:0.4);total possible score range: 0=no disease to 72= maximal disease. A PASI 75 response is defined as greater than or equal to (>=) 75 % improvement in PASI score from baseline.The efficacy analyses included all randomized and treated | |
| End point type | Primary |
| End point timeframe: Week 12 | |

| End point values | Placebo | JNJ-38518168 30 milligram (mg) | JNJ-38518168 60 milligram (mg) | |
|---------------------------------|-----------------|--------------------------------|--------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 6 | 29 | 26 | |
| Units: percentage of responders | | | | |
| number (not applicable) | 16.7 | 20.7 | 19.2 | |

Statistical analyses

| | |
|--|--|
| Statistical analysis title | Statistical analysis 1 |
| Statistical analysis description: Bayesian analyses with credible interval were reported. | |
| Comparison groups | JNJ-38518168 30 milligram (mg) v Placebo |

| | |
|---|---------------|
| Number of subjects included in analysis | 35 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Difference |
| Point estimate | 14.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.1 |
| upper limit | 30.9 |

| | |
|--|--|
| Statistical analysis title | Statistical analysis 2 |
| Statistical analysis description: Bayesian analyses with credible interval were reported. | |
| Comparison groups | Placebo v JNJ-38518168 60 milligram (mg) |
| Number of subjects included in analysis | 32 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Difference |
| Point estimate | 8.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5 |
| upper limit | 24.3 |

Secondary: Percentage of Subjects Who Achieved a Score of 0 or 1 on the Investigator's Global Assessment (IGA) at Week 12

| | |
|---|--|
| End point title | Percentage of Subjects Who Achieved a Score of 0 or 1 on the Investigator's Global Assessment (IGA) at Week 12 |
| End point description: The IGA documents the investigator's assessment of the participants psoriasis at a given time point. Overall lesions are graded for induration, erythema, and scaling on a scale of 0 to 4 (higher score = more severe). The participant's psoriasis is assessed as 5-point scale as follows: 0=cleared, 1=minimal, 2=mild, 3=moderate, 4=severe. The efficacy analyses included all randomized and treated subjects. | |
| End point type | Secondary |
| End point timeframe: Week 12 | |

| End point values | Placebo | JNJ-38518168 30 milligram (mg) | JNJ-38518168 60 milligram (mg) | |
|---------------------------------|-----------------|--------------------------------------|--------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 6 | 29 | 26 | |
| Units: percentage of responders | | | | |
| number (not applicable) | 16.7 | 20.7 | 19.2 | |

Statistical analyses

| Statistical analysis title | Statistical analysis 1 |
|--|--|
| Statistical analysis description: Bayesian analyses with credible interval were reported. | |
| Comparison groups | Placebo v JNJ-38518168 30 milligram (mg) |
| Number of subjects included in analysis | 35 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Difference |
| Point estimate | 14.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.6 |
| upper limit | 33.2 |

| Statistical analysis title | Statistical analysis 2 |
|--|--|
| Statistical analysis description: Bayesian analyses with credible interval were reported. | |
| Comparison groups | Placebo v JNJ-38518168 60 milligram (mg) |
| Number of subjects included in analysis | 32 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Difference |
| Point estimate | 13.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.6 |
| upper limit | 32.1 |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Upto Week 16

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 18.1 |
|--------------------|------|

Reporting groups

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

Reporting group description:

Subjects received 3*30 milligram(mg) placebo tablets and 1*3 mg placebo tablet orally at the same time each day upto week 12.

| | |
|-----------------------|--------------------|
| Reporting group title | JNJ-38518168 30 mg |
|-----------------------|--------------------|

Reporting group description:

Subjects in the JNJ-38518168 30 milligram (mg) group received 1*30 mg JNJ-38518168 tablet together with 2*30 mg placebo tablets and 1*3 mg placebo tablet at the same time each day upto week 12.

| | |
|-----------------------|--------------------|
| Reporting group title | JNJ-38518168 60 mg |
|-----------------------|--------------------|

Reporting group description:

Subjects in the JNJ-38518168 60 mg group received 2*30 mg JNJ-38518168 tablets, 1 x 30 mg placebo tablet and 1*3 mg placebo tablet orally at the same time each day upto week 12.

| Serious adverse events | Placebo | JNJ-38518168 30 mg | JNJ-38518168 60 mg |
|---|---------------|--------------------|--------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 30 (0.00%) | 1 / 26 (3.85%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Blood and lymphatic system disorders | | | |
| Leukopenia | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 30 (0.00%) | 1 / 26 (3.85%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| 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 | Placebo | JNJ-38518168 30 mg | JNJ-38518168 60 mg |
|---|----------------|--------------------|--------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 2 / 5 (40.00%) | 15 / 30 (50.00%) | 14 / 26 (53.85%) |
| Vascular disorders | | | |

| | | | |
|--|--|---|---|
| Hypertension subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 0 / 30 (0.00%) 0 | 1 / 26 (3.85%) 1 |
| Pregnancy, puerperium and perinatal conditions Pregnancy subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 0 / 30 (0.00%) 0 | 1 / 26 (3.85%) 1 |
| General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) Pain subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 0 / 5 (0.00%) 0 0 / 5 (0.00%) 0 | 1 / 30 (3.33%) 1 1 / 30 (3.33%) 1 0 / 30 (0.00%) 0 | 1 / 26 (3.85%) 1 0 / 26 (0.00%) 0 1 / 26 (3.85%) 1 |
| Reproductive system and breast disorders Dysmenorrhoea subjects affected / exposed occurrences (all) Genital Tract Inflammation subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 0 / 5 (0.00%) 0 | 1 / 30 (3.33%) 1 1 / 30 (3.33%) 1 | 0 / 26 (0.00%) 0 0 / 26 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Oropharyngeal Pain subjects affected / exposed occurrences (all) Productive Cough subjects affected / exposed occurrences (all) Respiratory Tract Congestion | 0 / 5 (0.00%) 0 0 / 5 (0.00%) 0 0 / 5 (0.00%) 0 | 2 / 30 (6.67%) 2 1 / 30 (3.33%) 1 1 / 30 (3.33%) 1 | 1 / 26 (3.85%) 1 0 / 26 (0.00%) 0 0 / 26 (0.00%) 0 |

| | | | |
|--|--------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 1 / 30 (3.33%) 1 | 0 / 26 (0.00%) 0 |
| Rhinorrhoea subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 2 / 30 (6.67%) 2 | 0 / 26 (0.00%) 0 |
| Sinus Congestion subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 1 / 30 (3.33%) 2 | 0 / 26 (0.00%) 0 |
| Investigations | | | |
| Alanine Aminotransferase Increased subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 2 / 30 (6.67%) 2 | 0 / 26 (0.00%) 0 |
| Aspartate Aminotransferase Increased subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 1 / 30 (3.33%) 1 | 0 / 26 (0.00%) 0 |
| Blood Creatine Phosphokinase Increased subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 1 / 30 (3.33%) 1 | 0 / 26 (0.00%) 0 |
| Blood Creatinine Increased subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 1 / 30 (3.33%) 1 | 0 / 26 (0.00%) 0 |
| Serum Ferritin Increased subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 0 / 30 (0.00%) 0 | 1 / 26 (3.85%) 1 |
| Injury, poisoning and procedural complications | | | |
| Meniscus Injury subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 0 / 30 (0.00%) 0 | 1 / 26 (3.85%) 1 |
| Skin Abrasion subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 0 / 30 (0.00%) 0 | 1 / 26 (3.85%) 1 |
| Cardiac disorders | | | |
| Atrial Fibrillation subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 1 / 30 (3.33%) 1 | 0 / 26 (0.00%) 0 |

| | | | |
|---|----------------|----------------|----------------|
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 2 / 30 (6.67%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Somnolence | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 1 / 30 (3.33%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Syncope | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 1 / 30 (3.33%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 30 (0.00%) | 1 / 26 (3.85%) |
| occurrences (all) | 1 | 0 | 1 |
| Toothache | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 30 (0.00%) | 1 / 26 (3.85%) |
| occurrences (all) | 0 | 0 | 1 |
| Skin and subcutaneous tissue disorders | | | |
| Psoriasis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 1 / 30 (3.33%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rash | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 1 / 30 (3.33%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Skin Lesion | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 30 (0.00%) | 1 / 26 (3.85%) |
| occurrences (all) | 0 | 0 | 1 |
| Renal and urinary disorders | | | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 30 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Back Pain | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 30 (0.00%) | 0 / 26 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Infections and infestations | | | |

| | | | |
|------------------------------------|----------------|----------------|-----------------|
| Bronchitis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 30 (0.00%) | 1 / 26 (3.85%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 30 (0.00%) | 1 / 26 (3.85%) |
| occurrences (all) | 0 | 0 | 1 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 1 / 30 (3.33%) | 3 / 26 (11.54%) |
| occurrences (all) | 1 | 1 | 4 |
| Oral Herpes | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 1 / 30 (3.33%) | 0 / 26 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pulpitis Dental | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 30 (0.00%) | 1 / 26 (3.85%) |
| occurrences (all) | 0 | 0 | 1 |
| Rotavirus Infection | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 30 (0.00%) | 1 / 26 (3.85%) |
| occurrences (all) | 0 | 0 | 1 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 30 (0.00%) | 1 / 26 (3.85%) |
| occurrences (all) | 0 | 0 | 1 |
| Metabolism and nutrition disorders | | | |
| Decreased Appetite | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 30 (0.00%) | 1 / 26 (3.85%) |
| occurrences (all) | 0 | 0 | 1 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|--|
| 19 September 2014 | The highest dose of study agent to be tested was reduced from 90 mg once daily to 60 mg once daily based upon feedback from the FDA; Text on safety margins and adjusted values based upon the change in dose was clarified as appropriate; Screening period expanded to no more than 42 days prior to the first administration of study agent to allow more flexibility for subject screening; To ensure patient safety, a new discontinuation of treatment criterion was added. This criterion stated that all subjects whose postbaseline serum creatinine increase met toxicity Grade 3 and higher based on the Common Terminology Criteria for Adverse Events(CTCAE), version 4.0, were to be discontinued from further study treatment; To establish a baseline triglyceride value, a baseline fasting lipid panel test was added to further assess the risk of increase in triglyceride levels from baseline if needed; Corrections were made to the safety analysis section in statistical methods to summarize number and percentage of subjects by maximum CTCAE grade for each treatment group for each laboratory parameter. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported