



Clinical trial results:

A 52-Week, Randomized, Double-Blind, Parallel-Group, Placebo-Controlled Study to Evaluate the Efficacy and Safety of a 200-mcg Dose of IPP-201101 Plus Standard of Care in Patients With Systemic Lupus Erythematosus

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2015-003341-25 |
| Trial protocol | HU DE FR GB IT |
| Global end of trial date | 24 January 2018 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 09 February 2019 |
| First version publication date | 09 February 2019 |

Trial information

Trial identification

| | |
|-----------------------|----------------|
| Sponsor protocol code | IPP-201101/005 |
|-----------------------|----------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02504645 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | ImmuPharma France SA |
| Sponsor organisation address | 5, rue du Rhône, 68100, France, |
| Public contact | Robert Zimmer, ImmuPharma SA, 00 33 (0)6 18 22 16 50, robert.zimmer@immupharma.com |
| Scientific contact | Robert Zimmer, ImmuPharma SA, 00 33 (0)6 18 22 16 50, robert.zimmer@immupharma.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 January 2019 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 24 January 2018 |
| Global end of trial reached? | Yes |
| Global end of trial date | 24 January 2018 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the efficacy of a 200-mcg dose every 4 weeks for 48 weeks of IPP-201101 compared with placebo in patients with active systemic lupus erythematosus (SLE) as assessed by the SLE responder index (SRI) at week 52.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 01 December 2015 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Poland: 32 |
| Country: Number of subjects enrolled | Czech Republic: 15 |
| Country: Number of subjects enrolled | France: 7 |
| Country: Number of subjects enrolled | Germany: 4 |
| Country: Number of subjects enrolled | Hungary: 24 |
| Country: Number of subjects enrolled | United States: 73 |
| Country: Number of subjects enrolled | Mauritius: 49 |
| Worldwide total number of subjects | 204 |
| EEA total number of subjects | 82 |

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) | 204 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Participants should fulfilled study eligibility criteria to be randomized.

Pre-assignment

Screening details:

303 participants were enrolled and 204 were randomized. 2 were randomized but not treated. The 99 who were not randomised did not meet study entry criteria.

Period 1

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

Arms

| | |
|------------------------------|--|
| Are arms mutually exclusive? | Yes |
| Arm title | Standard of care + 200 mcg SC IPP-201101 |

Arm description:

200 mcg SC IPP-201101 every 4 weeks

| | |
|--|-----------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | IPP-201101 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

200 mcg administered subcutaneoulsy every 4 weeks.

| | |
|------------------|-------------------------------|
| Arm title | Standard of care + Placebo SC |
|------------------|-------------------------------|

Arm description:

Placebo was administered subcutaneously every 4 weeks

| | |
|--|-----------------------------------|
| Arm type | Placebo |
| Investigational medicinal product name | placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Placebo was administered subcutaneously every 4 weeks

| Number of subjects in period 1 | Standard of care + 200 mcg SC IPP- 201101 | Standard of care + Placebo SC |
|--------------------------------|---|----------------------------------|
| | | |
| Started | 101 | 103 |
| Completed | 77 | 76 |
| Not completed | 24 | 27 |
| Consent withdrawn by subject | 6 | 6 |
| Adverse event, non-fatal | 6 | 3 |
| Other | 5 | 4 |
| Pregnancy | 1 | 2 |
| Lost to follow-up | 2 | 4 |
| Protocol deviation | 2 | 4 |
| Lack of efficacy | 2 | 4 |

Baseline characteristics

Reporting groups

| | |
|---|--|
| Reporting group title | Standard of care + 200 mcg SC IPP-201101 |
| Reporting group description: 200 mcg SC IPP-201101 every 4 weeks | |
| Reporting group title | Standard of care + Placebo SC |
| Reporting group description: Placebo was administered subcutaneously every 4 weeks | |

| Reporting group values | Standard of care + 200 mcg SC IPP- 201101 | Standard of care + Placebo SC | Total |
|--|---|----------------------------------|-------|
| Number of subjects | 101 | 103 | 204 |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 101 | 103 | 204 |
| Age continuous Units: years median standard deviation | 42.55 ± 11.86 | 43.69 ± 11.49 | - |
| Gender categorical Units: Subjects | | | |
| Female | 96 | 94 | 190 |
| Male | 5 | 9 | 14 |
| Race Units: Subjects | | | |
| White | 59 | 66 | 125 |
| Black or African American | 14 | 10 | 24 |
| Native Hawaiian or Other Pacific Islander | 0 | 2 | 2 |
| Asian | 4 | 1 | 5 |
| Other | 24 | 24 | 48 |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Ethnicity Units: Subjects | | | |
| Not Hispanic or Latino | 88 | 84 | 172 |
| Hispanic or Latino | 13 | 19 | 32 |

End points

End points reporting groups

| | |
|---|--|
| Reporting group title | Standard of care + 200 mcg SC IPP-201101 |
| Reporting group description: | |
| 200 mcg SC IPP-201101 every 4 weeks | |
| Reporting group title | Standard of care + Placebo SC |
| Reporting group description: | |
| Placebo was administered subcutaneously every 4 weeks | |

Primary: Proportion of patients responders using the SRI at week 52

| | |
|--|--|
| End point title | Proportion of patients responders using the SRI at week 52 |
| End point description: | |
| A SRI response was defined as a reduction from baseline in the SLEDAI-2K score of at least 4 points, no worsening in PhGA (with worsening defined as an increase in PhGA of more than 0.30 point from baseline), no new BILAG A body system score, and no more than 1 new BILAG B body system score from baseline. | |
| End point type | Primary |
| End point timeframe: | |
| At week 52 | |

| End point values | Standard of care + 200 mcg SC IPP-201101 | Standard of care + Placebo SC | | |
|-----------------------------|--|-------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 101 | 101 | | |
| Units: patients | | | | |
| responders | 53 | 45 | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Primary Analysis of SRI Response at Week 52 |
| Comparison groups | Standard of care + Placebo SC v Standard of care + 200 mcg SC IPP-201101 |
| Number of subjects included in analysis | 202 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.2631 |
| Method | Chi-squared |

Post-hoc: Proportion of responders of EU patients having anti-dsDNA at randomization

| | |
|------------------------|--|
| End point title | Proportion of responders of EU patients having anti-dsDNA at randomization |
| End point description: | |
| End point type | Post-hoc |
| End point timeframe: | |
| At week 52 | |

| End point values | Standard of care + 200 mcg SC IPP-201101 | Standard of care + Placebo SC | | |
|-----------------------------|--|-------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 52 | 55 | | |
| Units: patient | | | | |
| Responders | 32 | 26 | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Post Hoc analysis |
| Comparison groups | Standard of care + Placebo SC v Standard of care + 200 mcg SC IPP-201101 |
| Number of subjects included in analysis | 107 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0218 |
| Method | Chi-squared |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All adverse events (AEs) and serious adverse events (SAEs) are reported from informed consent signature and up to 30 days post last dose.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 19.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Standard of care + IPP-201101 SC 200 mcg |
|-----------------------|--|

| | |
|--------------------------------|--|
| Reporting group description: - | |
|--------------------------------|--|

| | |
|-----------------------|-------------------------------|
| Reporting group title | Standard of care + Placebo SC |
|-----------------------|-------------------------------|

| | |
|--------------------------------|--|
| Reporting group description: - | |
|--------------------------------|--|

| Serious adverse events | Standard of care + IPP-201101 SC 200 mcg | Standard of care + Placebo SC | |
|---|--|----------------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 13 / 101 (12.87%) | 16 / 101 (15.84%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Mesothelioma malignant | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 0 / 101 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Uterine leiomyoma | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 0 / 101 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 101 (0.99%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertension | | | |

| | | | |
|--|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 101 (0.00%) | 2 / 101 (1.98%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pregnancy, puerperium and perinatal conditions | | | |
| Pregnancy | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 3 / 101 (2.97%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Face Edema | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 0 / 101 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Pelvic fluid collection | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 0 / 101 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Uterine Hemorrhage | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 0 / 101 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pleural effusion | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 0 / 101 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 101 (0.99%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |

| | | | |
|---|-----------------|-----------------|--|
| Subdural Hematoma | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 101 (0.99%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 0 / 101 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocarditis | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 0 / 101 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Cerebrovascular Accident | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 0 / 101 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoesthesia | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 0 / 101 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Migraine | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 0 / 101 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Syncope | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 101 (0.99%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tension headache | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 101 (0.99%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Blood and lymphatic system disorders | | | |
| Anemia | | | |
| subjects affected / exposed | 2 / 101 (1.98%) | 1 / 101 (0.99%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 101 (0.99%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 101 (0.99%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colitis | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 101 (0.99%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nausea | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 101 (0.99%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Cholecystitis | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 0 / 101 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Butterfly rash | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 0 / 101 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cutaneous lupus erythematosus | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 101 (0.99%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 101 (0.99%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hematuria | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 101 (0.99%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Proteinuria | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 101 (0.99%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal failure | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 0 / 101 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 0 / 101 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteonecrosis | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 101 (0.99%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Systemic lupus erythematosus | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 2 / 101 (1.98%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|--|-----------------------------------|-----------------------------------|--|
| Infections and infestations Gastroenteritis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 101 (0.99%) 0 / 1 0 / 0 | 0 / 101 (0.00%) 0 / 0 0 / 0 | |
| Gastroenteritis salmonella subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 101 (0.00%) 0 / 0 0 / 0 | 1 / 101 (0.99%) 0 / 1 0 / 0 | |
| Kidney infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 101 (0.99%) 0 / 1 0 / 0 | 0 / 101 (0.00%) 0 / 0 0 / 0 | |
| Lower Respiratory Tract Infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 101 (0.99%) 0 / 1 0 / 0 | 0 / 101 (0.00%) 0 / 0 0 / 0 | |
| Pneumonia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 101 (0.00%) 0 / 0 0 / 0 | 1 / 101 (0.99%) 0 / 1 0 / 0 | |

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

| Non-serious adverse events | Standard of care + IPP-201101 SC 200 mcg | Standard of care + Placebo SC | |
|---|--|----------------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 94 / 101 (93.07%) | 96 / 101 (95.05%) | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 3 / 101 (2.97%) | 7 / 101 (6.93%) | |
| occurrences (all) | 4 | 9 | |
| Nervous system disorders | | | |
| Headache | | | |

| | | | |
|--|-------------------------|-------------------------|--|
| subjects affected / exposed occurrences (all) | 12 / 101 (11.88%) 18 | 17 / 101 (16.83%) 31 | |
| Migraine subjects affected / exposed occurrences (all) | 5 / 101 (4.95%) 5 | 1 / 101 (0.99%) 1 | |
| Blood and lymphatic system disorders Leukopenia subjects affected / exposed occurrences (all) | 8 / 101 (7.92%) 9 | 7 / 101 (6.93%) 11 | |
| General disorders and administration site conditions Injection site erythema subjects affected / exposed occurrences (all) | 5 / 101 (4.95%) 21 | 0 / 101 (0.00%) 0 | |
| Mucosal ulceration subjects affected / exposed occurrences (all) | 4 / 101 (3.96%) 9 | 8 / 101 (7.92%) 8 | |
| Pyrexia subjects affected / exposed occurrences (all) | 5 / 101 (4.95%) 8 | 5 / 101 (4.95%) 6 | |
| Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all) | 6 / 101 (5.94%) 8 | 7 / 101 (6.93%) 11 | |
| Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) | 6 / 101 (5.94%) 8 | 2 / 101 (1.98%) 2 | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 3 / 101 (2.97%) 3 | 6 / 101 (5.94%) 6 | |
| Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all) | 12 / 101 (11.88%) 17 | 13 / 101 (12.87%) 15 | |
| Rash | | | |

| | | | |
|---|-------------------------|-------------------------|--|
| subjects affected / exposed occurrences (all) | 12 / 101 (11.88%) 14 | 8 / 101 (7.92%) 13 | |
| Renal and urinary disorders Proteinuria subjects affected / exposed occurrences (all) | 3 / 101 (2.97%) 3 | 6 / 101 (5.94%) 6 | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 12 / 101 (11.88%) 13 | 13 / 101 (12.87%) 19 | |
| Arthritis subjects affected / exposed occurrences (all) | 15 / 101 (14.85%) 25 | 14 / 101 (13.86%) 27 | |
| Back pain subjects affected / exposed occurrences (all) | 9 / 101 (8.91%) 9 | 9 / 101 (8.91%) 10 | |
| Myalgia subjects affected / exposed occurrences (all) | 6 / 101 (5.94%) 7 | 1 / 101 (0.99%) 1 | |
| Systemic lupus erythematosus subjects affected / exposed occurrences (all) | 2 / 101 (1.98%) 2 | 10 / 101 (9.90%) 11 | |
| Infections and infestations Bronchitis subjects affected / exposed occurrences (all) | 7 / 101 (6.93%) 7 | 8 / 101 (7.92%) 8 | |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 8 / 101 (7.92%) 14 | 7 / 101 (6.93%) 8 | |
| Pharyngitis subjects affected / exposed occurrences (all) | 2 / 101 (1.98%) 2 | 5 / 101 (4.95%) 5 | |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 20 / 101 (19.80%) 25 | 28 / 101 (27.72%) 32 | |
| Urinary tract infection | | | |

| | | | |
|-----------------------------|-------------------|------------------|--|
| subjects affected / exposed | 23 / 101 (22.77%) | 10 / 101 (9.90%) | |
| occurrences (all) | 32 | 19 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|--------------|--|
| 01 June 2016 | Exclusion criteria "(e)" updated to clarify wash out period in case of use of B-cell depleting agent |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported