



Clinical trial results:

A Randomized, Placebo-Controlled, Double Blind, Multicenter Phase 2 Study to Explore Tolerability, Safety, Pharmacokinetics, Pharmacodynamics and Efficacy of Intravenous Multiple Infusions of NI-0101, an anti-Toll Like Receptor 4 Monoclonal Antibody in Patients with Rheumatoid Arthritis

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2016-005017-45 |
| Trial protocol | HU BG PL GB |
| Global end of trial date | 17 May 2018 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 28 April 2019 |
| First version publication date | 28 April 2019 |

Trial information

Trial identification

| | |
|-----------------------|------------|
| Sponsor protocol code | NI-0101-04 |
|-----------------------|------------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | NovImmune S.A. |
| Sponsor organisation address | 14 Chemin des Aulx, 1228 Plan-les-Ouates, Switzerland, |
| Public contact | Emmanuel Monnet, NovImmune S.A., +41 22593 82 33, emonnet@novimmune.com |
| Scientific contact | Emmanuel Monnet, NovImmune S.A., +41 22593 82 33, emonnet@novimmune.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 | 07 December 2018 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 17 May 2018 |
| Global end of trial reached? | Yes |
| Global end of trial date | 17 May 2018 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

- To determine the preliminary tolerability and safety profile of multiple intravenous (i.v.) administrations of NI-0101
- To describe the Pharmacokinetic/Pharmacodynamic (PK/PD) profiles of NI-0101
- To determine NI-0101 preliminary efficacy
- To explore specific biomarkers as predictors of treatment response
- To explore the impact of the FcγRIIa genotype on the response to treatment
- To assess the immunogenicity of NI-0101

Protection of trial subjects:

The study protocol, patient information sheet, Informed Consent Form (ICF) and all other relevant study documentation and amendments were reviewed by Independent Ethics Committees in the United Kingdom (UK), Bulgaria, Hungary, Serbia, Bosnia, Poland, Moldova and Georgia. The study did not commence until formal approval had been granted.

Background therapy:

Methotrexate

Evidence for comparator:

No active comparator - placebo controlled

| | |
|---|-------------|
| Actual start date of recruitment | 01 May 2017 |
| 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: 2 |
| Country: Number of subjects enrolled | Bulgaria: 15 |
| Country: Number of subjects enrolled | Hungary: 13 |
| Country: Number of subjects enrolled | Serbia: 12 |
| Country: Number of subjects enrolled | Georgia: 36 |
| Country: Number of subjects enrolled | Moldova, Republic of: 11 |
| Country: Number of subjects enrolled | Bosnia and Herzegovina: 1 |
| Worldwide total number of subjects | 90 |
| EEA total number of subjects | 30 |

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) | 65 |
| From 65 to 84 years | 25 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Of the 250 patients with RA screened for eligibility, 90 were randomized into the treatment phase of the study. A total of 86 patients completed the study.

Pre-assignment

Screening details:

Subjects attended a screening visit within 4 weeks prior to the first treatment.

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, Monitor, Carer, Investigator, Assessor |

Arms

| | |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

| | |
|------------------|---------|
| Arm title | NI-0101 |
|------------------|---------|

Arm description:

Subjects treated with NI-0101

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | NI-0101 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

NI-0101 was administered by intravenous infusion, over a period of one hour, at a dose of 5 mg/kg. Infusions were performed every two weeks

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

Arm description:

Subject received a placebo

| | |
|--|-----------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Placebo was administered by intravenous infusion, over a period of one hour, at a dose of 5 mg/kg. Infusions were performed every two weeks

| Number of subjects in period 1 | NI-0101 | Placebo |
|---------------------------------------|---------|---------|
| Started | 61 | 29 |
| Completed | 57 | 29 |
| Not completed | 4 | 0 |
| Consent withdrawn by subject | 2 | - |
| Adverse event, non-fatal | 2 | - |

Baseline characteristics

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | NI-0101 |
|-----------------------|---------|

Reporting group description:

Subjects treated with NI-0101

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

Reporting group description:

Subject received a placebo

| Reporting group values | NI-0101 | Placebo | Total |
|--|---------|---------|-------|
| Number of subjects | 61 | 29 | 90 |
| 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) | 48 | 17 | 65 |
| From 65-84 years | 13 | 12 | 25 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 54.6 | 57.1 | - |
| standard deviation | ± 11.10 | ± 13.07 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 50 | 23 | 73 |
| Male | 11 | 6 | 17 |
| Steroids dose category (mg) | | | |
| Units: Subjects | | | |
| No steroid given | 20 | 9 | 29 |
| 1mg - 5mg | 6 | 8 | 14 |
| 5mg - 10mg | 35 | 12 | 47 |
| MTX dose category (mg/week) | | | |
| Units: Subjects | | | |
| 3.5mg - 10mg | 2 | 2 | 4 |
| 10mg - 20mg | 55 | 25 | 80 |
| 2mg - 25mg | 4 | 2 | 6 |
| Duration of RA | | | |
| Length of time since RA diagnosis | | | |
| Units: Years | | | |
| arithmetic mean | 8.5 | 5.4 | - |
| standard deviation | ± 7.86 | ± 4.82 | - |
| Age at RA diagnosis | | | |

| Age of participant when they were diagnosed with RA | | | |
|---|---------|---------|---|
| Units: Years | | | |
| arithmetic mean | 45.7 | 51.2 | |
| standard deviation | ± 11.56 | ± 13.62 | - |
| CRP | | | |
| Units: (mg/L) | | | |
| arithmetic mean | 18.3 | 13.4 | |
| standard deviation | ± 26.63 | ± 14.03 | - |
| ESR | | | |
| Units: (mm/hr) | | | |
| arithmetic mean | 45.3 | 43.1 | |
| standard deviation | ± 24.26 | ± 16.51 | - |

End points

End points reporting groups

| | |
|-------------------------------|---------|
| Reporting group title | NI-0101 |
| Reporting group description: | |
| Subjects treated with NI-0101 | |
| Reporting group title | Placebo |
| Reporting group description: | |
| Subject received a placebo | |

Primary: Change in DAS28-CRP Score from Baseline Visit to W12

| | |
|------------------------|--|
| End point title | Change in DAS28-CRP Score from Baseline Visit to W12 |
| End point description: | |
| | |
| End point type | Primary |
| End point timeframe: | |
| Baseline to week 12 | |

| End point values | NI-0101 | Placebo | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 56 | 29 | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline | 5.9 (± 0.90) | 5.8 (± 0.82) | | |
| SD14 (W2) | -0.3 (± 0.63) | -0.4 (± 0.52) | | |
| SD28 (W4) | -0.7 (± 0.86) | -0.6 (± 0.73) | | |
| SD42 (W6) | -1.1 (± 0.95) | -0.8 (± 0.89) | | |
| SD56 (W8) | -1.3 (± 1.02) | -1.1 (± 1.03) | | |
| SD70 (W10) | -1.4 (± 1.18) | -1.3 (± 1.07) | | |
| SD84 (W12) | -1.5 (± 1.35) | -1.3 (± 1.07) | | |

Statistical analyses

| | |
|---|------------------------------------|
| Statistical analysis title | Treatment effect NI-0101 - Placebo |
| Comparison groups | NI-0101 v Placebo |
| Number of subjects included in analysis | 85 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.4666 |
| Method | Least Square Means (SE) |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.2 |

| | |
|----------------------|----------------------------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.8 |
| upper limit | 0.4 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.28 |

Secondary: Change in DAS28-ESR Score from Baseline Visit to W12

| | |
|------------------------|--|
| End point title | Change in DAS28-ESR Score from Baseline Visit to W12 |
| End point description: | |
| | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline to week 12 | |

| End point values | NI-0101 | Placebo | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 56 | 29 | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline | 6.6 (± 0.89) | 6.6 (± 0.88) | | |
| SD14 (W2) | -0.4 (± 0.65) | -0.4 (± 0.52) | | |
| SD28 (W4) | -0.9 (± 0.88) | -0.7 (± 0.67) | | |
| SD42 (W6) | -1.2 (± 0.94) | -1.0 (± 0.87) | | |
| SD56 (W8) | -1.4 (± 1.05) | -1.3 (± 1.02) | | |
| SD70 (W10) | -1.6 (± 1.33) | -1.5 (± 1.11) | | |
| SD84 (W12) | -1.7 (± 1.41) | -1.4 (± 1.09) | | |

Statistical analyses

| | |
|---|------------------------------------|
| Statistical analysis title | Treatment effect NI-0101 – Placebo |
| Comparison groups | NI-0101 v Placebo |
| Number of subjects included in analysis | 85 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3395 |
| Method | Least Square Means (SE) |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.3 |

| | |
|----------------------|----------------------------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.9 |
| upper limit | 0.3 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.3 |

Secondary: Proportions of Patients with EULAR Response Criteria

| | |
|------------------------|--|
| End point title | Proportions of Patients with EULAR Response Criteria |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline to week 12 | |

| End point values | NI-0101 | Placebo | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 56 | 29 | | |
| Units: Participants | | | | |
| Response | 45 | 24 | | |
| No response | 11 | 5 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Tender or Swollen 28-Joint Counts Change from Baseline to W12

| | |
|------------------------|---|
| End point title | Tender or Swollen 28-Joint Counts Change from Baseline to W12 |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline to week 12 | |

| End point values | NI-0101 | Placebo | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 56 | 29 | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Tender 28-Joint Counts SD84 (W12) | -8.1 (± 7.67) | -6.3 (± 6.65) | | |
| Swollen 28-Joint Counts SD84 (W12) | -7.1 (± 6.87) | -6.1 (± 5.11) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of patients achieving ACR20 response

| | |
|------------------------|---|
| End point title | Proportion of patients achieving ACR20 response |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline to week 12 | |

| End point values | NI-0101 | Placebo | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 56 | 29 | | |
| Units: Patients | | | | |
| SD14 (W2) | 5 | 1 | | |
| SD28 (W4) | 15 | 5 | | |
| SD42 (W6) | 22 | 10 | | |
| SD56 (W8) | 24 | 14 | | |
| SD70 (W10) | 25 | 14 | | |
| SD84 (W12) | 33 | 16 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of patients achieving ACR50 response

| | |
|------------------------|---|
| End point title | Proportion of patients achieving ACR50 response |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline to week 12 | |

| End point values | NI-0101 | Placebo | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 56 | 29 | | |
| Units: Patients | | | | |
| SD14 (W2) | 0 | 0 | | |
| SD28 (W4) | 1 | 1 | | |
| SD42 (W6) | 6 | 2 | | |
| SD56 (W8) | 8 | 5 | | |
| SD70 (W10) | 9 | 5 | | |
| SD84 (W12) | 8 | 6 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of patients achieving ACR70 response

| | |
|------------------------|---|
| End point title | Proportion of patients achieving ACR70 response |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline to week 12 | |

| End point values | NI-0101 | Placebo | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 56 | 29 | | |
| Units: Patients | | | | |
| SD14 (W2) | 0 | 0 | | |
| SD28 (W4) | 0 | 0 | | |
| SD42 (W6) | 0 | 1 | | |
| SD56 (W8) | 1 | 1 | | |
| SD70 (W10) | 3 | 2 | | |
| SD84 (W12) | 6 | 3 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Any adverse event within the date of the start of treatment until the end-of-study visit has been reported.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 20.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | NI-0101 |
|-----------------------|---------|

Reporting group description: -

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

Reporting group description: -

| Serious adverse events | NI-0101 | Placebo | |
|---|----------------|----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 61 (4.92%) | 1 / 29 (3.45%) | |
| 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) | | | |
| Adenocarcinoma of colon | | | |
| subjects affected / exposed | 1 / 61 (1.64%) | 0 / 29 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ovarian cancer | | | |
| subjects affected / exposed | 1 / 61 (1.64%) | 0 / 29 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Infusion related reaction | | | |
| subjects affected / exposed | 1 / 61 (1.64%) | 0 / 29 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Appendicitis | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 61 (0.00%) | 1 / 29 (3.45%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peritoneal abscess | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | 1 / 29 (3.45%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 1 %

| Non-serious adverse events | NI-0101 | Placebo | |
|---|------------------|------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 31 / 61 (50.82%) | 15 / 29 (51.72%) | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Angiomyolipoma | | | |
| subjects affected / exposed | 1 / 61 (1.64%) | 0 / 29 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 2 / 61 (3.28%) | 0 / 29 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Surgical and medical procedures | | | |
| Baker's cyst excision | | | |
| subjects affected / exposed | 1 / 61 (1.64%) | 0 / 29 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| General disorders and administration site conditions | | | |
| Condition aggravated | | | |
| subjects affected / exposed | 5 / 61 (8.20%) | 0 / 29 (0.00%) | |
| occurrences (all) | 5 | 0 | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 61 (1.64%) | 1 / 29 (3.45%) | |
| occurrences (all) | 1 | 1 | |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | 1 / 29 (3.45%) | |
| occurrences (all) | 0 | 1 | |

| | | | |
|--------------------------------------|----------------|----------------|--|
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 3 / 61 (4.92%) | 0 / 29 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 1 / 61 (1.64%) | 0 / 29 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Blood glucose increased | | | |
| subjects affected / exposed | 1 / 61 (1.64%) | 0 / 29 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Blood pressure increased | | | |
| subjects affected / exposed | 1 / 61 (1.64%) | 0 / 29 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Fibrin D dimer increased | | | |
| subjects affected / exposed | 1 / 61 (1.64%) | 0 / 29 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | 1 / 29 (3.45%) | |
| occurrences (all) | 0 | 1 | |
| Heart rate increased | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | 1 / 29 (3.45%) | |
| occurrences (all) | 0 | 1 | |
| Platelet count decreased | | | |
| subjects affected / exposed | 1 / 61 (1.64%) | 0 / 29 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Cardiac disorders | | | |
| Angina pectoris | | | |
| subjects affected / exposed | 1 / 61 (1.64%) | 0 / 29 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Aortic valve stenosis | | | |
| subjects affected / exposed | 1 / 61 (1.64%) | 0 / 29 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Atrioventricular block first degree | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | 1 / 29 (3.45%) | |
| occurrences (all) | 0 | 1 | |
| Palpitations | | | |

| | | | |
|--|---------------------|---------------------|--|
| subjects affected / exposed occurrences (all) | 0 / 61 (0.00%) 0 | 1 / 29 (3.45%) 1 | |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 0 / 61 (0.00%) 0 | 2 / 29 (6.90%) 2 | |
| Blood and lymphatic system disorders Iron deficiency anemia subjects affected / exposed occurrences (all) | 2 / 61 (3.28%) 2 | 0 / 29 (0.00%) 0 | |
| Eye disorders Eye hemorrhage subjects affected / exposed occurrences (all) | 1 / 61 (1.64%) 1 | 0 / 29 (0.00%) 0 | |
| Gastrointestinal disorders Diarrhea subjects affected / exposed occurrences (all) | 2 / 61 (3.28%) 2 | 0 / 29 (0.00%) 0 | |
| Abdominal pain upper subjects affected / exposed occurrences (all) | 1 / 61 (1.64%) 1 | 0 / 29 (0.00%) 0 | |
| Chronic gastritis subjects affected / exposed occurrences (all) | 1 / 61 (1.64%) 1 | 0 / 29 (0.00%) 0 | |
| Duodenitis subjects affected / exposed occurrences (all) | 1 / 61 (1.64%) 1 | 0 / 29 (0.00%) 0 | |
| Food poisoning subjects affected / exposed occurrences (all) | 1 / 61 (1.64%) 1 | 0 / 29 (0.00%) 0 | |
| Gastritis subjects affected / exposed occurrences (all) | 0 / 61 (0.00%) 0 | 1 / 29 (3.45%) 1 | |
| Hiatus hernia subjects affected / exposed occurrences (all) | 1 / 61 (1.64%) 1 | 0 / 29 (0.00%) 0 | |
| Nausea | | | |

| | | | |
|---|---------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 0 / 61 (0.00%) 0 | 1 / 29 (3.45%) 1 | |
| Vomiting subjects affected / exposed occurrences (all) | 1 / 61 (1.64%) 1 | 0 / 29 (0.00%) 0 | |
| Skin and subcutaneous tissue disorders Dermatitis subjects affected / exposed occurrences (all) | 1 / 61 (1.64%) 1 | 0 / 29 (0.00%) 0 | |
| Skin ulcer subjects affected / exposed occurrences (all) | 1 / 61 (1.64%) 1 | 0 / 29 (0.00%) 0 | |
| Urticaria subjects affected / exposed occurrences (all) | 1 / 61 (1.64%) 1 | 0 / 29 (0.00%) 0 | |
| Renal and urinary disorders Renal cyst subjects affected / exposed occurrences (all) | 1 / 61 (1.64%) 1 | 0 / 29 (0.00%) 0 | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 0 / 61 (0.00%) 0 | 1 / 29 (3.45%) 1 | |
| Arthritis subjects affected / exposed occurrences (all) | 1 / 61 (1.64%) 1 | 0 / 29 (0.00%) 0 | |
| Neck pain subjects affected / exposed occurrences (all) | 0 / 61 (0.00%) 0 | 1 / 29 (3.45%) 1 | |
| Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) | 3 / 61 (4.92%) 3 | 3 / 29 (10.34%) 3 | |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 4 / 61 (6.56%) 4 | 1 / 29 (3.45%) 1 | |

| | | |
|-----------------------------|----------------|----------------|
| Asymptomatic bacteriuria | | |
| subjects affected / exposed | 3 / 61 (4.92%) | 0 / 29 (0.00%) |
| occurrences (all) | 3 | 0 |
| Bronchitis | | |
| subjects affected / exposed | 1 / 61 (1.64%) | 1 / 29 (3.45%) |
| occurrences (all) | 1 | 1 |
| Urinary tract infection | | |
| subjects affected / exposed | 2 / 61 (3.28%) | 0 / 29 (0.00%) |
| occurrences (all) | 2 | 0 |
| Bacteriuria | | |
| subjects affected / exposed | 0 / 61 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 1 |
| Cystitis | | |
| subjects affected / exposed | 0 / 61 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 1 |
| Enterococcal infection | | |
| subjects affected / exposed | 0 / 61 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 1 |
| Furuncle | | |
| subjects affected / exposed | 1 / 61 (1.64%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 |
| Gastroenteritis | | |
| subjects affected / exposed | 1 / 61 (1.64%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 |
| Influenza | | |
| subjects affected / exposed | 1 / 61 (1.64%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 |
| Pharyngitis | | |
| subjects affected / exposed | 1 / 61 (1.64%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 |
| Pneumonia | | |
| subjects affected / exposed | 1 / 61 (1.64%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 |
| Sinusitis | | |
| subjects affected / exposed | 0 / 61 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 1 |

| | | | |
|------------------------------------|----------------|----------------|--|
| Tracheitis | | | |
| subjects affected / exposed | 1 / 61 (1.64%) | 0 / 29 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Tracheobronchitis | | | |
| subjects affected / exposed | 1 / 61 (1.64%) | 0 / 29 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Metabolism and nutrition disorders | | | |
| Hyperglycemia | | | |
| subjects affected / exposed | 2 / 61 (3.28%) | 1 / 29 (3.45%) | |
| occurrences (all) | 2 | 1 | |
| Hyperlipidemia | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | 1 / 29 (3.45%) | |
| occurrences (all) | 0 | 1 | |
| Hyperuricemia | | | |
| subjects affected / exposed | 0 / 61 (0.00%) | 1 / 29 (3.45%) | |
| occurrences (all) | 0 | 1 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 06 February 2017 | The following amendments were made to protocol V1.0: <ul style="list-style-type: none">- Typographical corrections- ECG to be carried out at the end of treatment visit (SD84) only if either physical examination or vital signs or cardiac monitoring showed abnormalities- Clarification of frequency of vital signs assessments |
| 06 October 2017 | The following amendments were made to protocol V1.1 dated 6 February 2017: <ul style="list-style-type: none">- Addition of anti-RANKL as a prohibited concomitant medication within three months prior to screening; added to exclusion criteria and list of prohibited concomitant medications, as anti-RANKL therapy in the NI-0101-04 study could potentially confound the evaluation of potential effects of NI-0101.- Clarification of vital signs assessments to align the main body text with the schedule of assessment table and further describe vital signs assessments across visits.- Removal of the requirement to stratify patients across both arms of the study for FcRIIa genotype in a 2:1 ratio for RR/RH:HH. The FcRIIa genotype stratification was retained, but without a defined ratio to be achieved for the RR/RH and HH groups, to better match the frequency of the genotype in the population while maintaining stratification of the groups across treatment arms.- Clarification regarding class 2 analgesics (authorized for use to treat mild to moderate pain) as authorized concomitant therapies- Clarification that CRP is measured in a central laboratory and ESR is measured locally- Clarification that the pre-enrolment visit could occur within four weeks after the screening visit (rather than between three and four weeks after the screening visit)- Clarification of SAE reporting email address |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported