



## Clinical trial results:

### A randomised, double-blind, placebo-controlled, parallel-group trial to assess clinical efficacy and safety of NNC0114-0006 in subjects with active Crohn's disease

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

## Summary

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2012-002432-93    |
| Trial protocol           | CZ HU ES PL BG SK |
| Global end of trial date | 19 December 2014  |

## Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 27 July 2016 |
| First version publication date | 27 July 2016 |

## Trial information

### Trial identification

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | NN8828-4004 |
|-----------------------|-------------|

### Additional study identifiers

|                                    |                 |
|------------------------------------|-----------------|
| ISRCTN number                      | -               |
| ClinicalTrials.gov id (NCT number) | NCT01751152     |
| WHO universal trial number (UTN)   | U1111-1130-8441 |

Notes:

## Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Novo Nordisk A/S  |
| Sponsor organisation address | Novo Allé, Bagsvaerd, Denmark, 2880   |
| Public contact               | Global Clinical Registry (GCR,1452), Novo Nordisk A/S, clinicaltrials@novonordisk.com |
| Scientific contact           | Global Clinical Registry (GCR,1452), Novo Nordisk A/S, clinicaltrials@novonordisk.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                       | 26 June 2015     |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 19 December 2014 |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 19 December 2014 |
| Was the trial ended prematurely?                     | Yes              |

Notes:

## General information about the trial

Main objective of the trial:

To compare the effect on disease activity of a single intravenous (i.v.) dose of NNC0114-0006 with placebo in subjects with moderately to severely active Crohn's disease.

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki, ICH Good Clinical Practice and FDA 21 CFR 312.50 and 56.

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 14 February 2013 |
| 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 | Slovakia: 2            |
| Country: Number of subjects enrolled | Bulgaria: 3            |
| Country: Number of subjects enrolled | Czech Republic: 13     |
| Country: Number of subjects enrolled | Russian Federation: 12 |
| Country: Number of subjects enrolled | Serbia: 10             |
| Country: Number of subjects enrolled | United States: 4       |
| Country: Number of subjects enrolled | Poland: 9              |
| Worldwide total number of subjects   | 53                     |
| EEA total number of subjects         | 27                     |

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          | 0 |

|                           |    |
|---------------------------|----|
| months)                   |    |
| Children (2-11 years)     | 0  |
| Adolescents (12-17 years) | 0  |
| Adults (18-64 years)      | 52 |
| From 65 to 84 years       | 1  |
| 85 years and over         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

Of the 32 sites in 8 countries that screened subjects, 24 sites in 7 countries randomised subjects to treatment as follows:

Bulgaria: 2 sites; Czech Republic: 4 sites; Poland: 5 sites; Serbia: 4 sites; Russia: 4 sites; Slovakia: 2 sites; United States: 3 sites.

### Pre-assignment

Screening details:

Not applicable

### Period 1

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

Blinding implementation details:

A qualified unblinded person, not involved in the conduct of the trial, was appointed to take care of all steps in trial drug handling from receipt to destruction, and only administration of the infusion was performed by blinded site staff otherwise involved in the trial.

### Arms

|                              |                       |
|------------------------------|-----------------------|
| Are arms mutually exclusive? | Yes                   |
| <b>Arm title</b>             | Double-Blind: Placebo |

Arm description:

Subjects received a single dose of placebo (for NNC0114-0006) and followed up for 24 weeks. If considered relevant and safe by the investigator at week 12 and the subject accepted, an open-label dose of NNC0114-0006 (25 mg/kg) was administered. If subjects received an open-label administration of the NNC0114-0006 at week 12, these subjects were additionally followed at weeks 13 and 36.

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

Dosage and administration details:

Placebo was administered as an i.v. infusion over a period of 30 minutes. The total dose was calculated based on the body weight.

|                  |                                     |
|------------------|-------------------------------------|
| <b>Arm title</b> | Double-Blind: NNC0114-0006 25 mg/kg |
|------------------|-------------------------------------|

Arm description:

Subjects received a single dose of NNC0114-0006 and followed up for 24 weeks. If considered relevant and safe by the investigator at week 12 and the subject accepted, one additional open-label dose of NNC0114-0006 was administered at the same dose level. If subjects received an open-label administration of the NNC0114-0006 at week 12, these subjects were additionally followed at weeks 13 and 36.

|  |                                  |
|--|----------------------------------|
| Arm type                               | Experimental                     |
| Investigational medicinal product name | NNC0114-0006                     |
| Investigational medicinal product code |                                  |
| Other name                             |                                  |
| Pharmaceutical forms                   | Powder for solution for infusion |
| Routes of administration               | Intravenous use                  |

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**Dosage and administration details:**

NNC0114-0006 was administered as an i.v. infusion over a period of 30 minutes. The total dose was calculated based on the body weight.

| Number of subjects in period 1 | Double-Blind:<br>Placebo | Double-Blind:<br>NNC0114-0006 25<br>mg/kg |
|--------------------------------|--------------------------|---|
|                                |                          |   |
| Started                        | 17                       | 36  |
| Completed Week 12              | 15                       | 31  |
| Completed                      | 14                       | 29  |
| Not completed                  | 3                        | 7   |
| Adverse event, non-fatal       | 1                        | 1   |
| Sponsor closure of trial       | 1                        | 5   |
| Unclassified                   | 1                        | 1   |

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**Period 2**

|                              |                   |
|------------------------------|-------------------|
| Period 2 title               | Open-Label Period |
| Is this the baseline period? | No                |
| Allocation method            | Not applicable    |
| Blinding used                | Not blinded       |

Blinding implementation details:

Not applicable

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**Arms**

|                              |   |
|------------------------------|---|
| Are arms mutually exclusive? | Yes                                       |
| <b>Arm title</b>             | Open-Label: Placebo-NNC0114-0006 25 mg/kg |

Arm description:

Subjects, who received a single dose of placebo (for NNC0114-0006) in double-blind period and accepted an open-label dose of NNC0114-0006, were administered a single dose of NNC0114-0006 at Week 12. Subjects were additionally followed at weeks 13 and 36.

|  |                                  |
|--|----------------------------------|
| Arm type                               | Experimental                     |
| Investigational medicinal product name | NNC0114-0006                     |
| Investigational medicinal product code |                                  |
| Other name                             |                                  |
| Pharmaceutical forms                   | Powder for solution for infusion |
| Routes of administration               | Intravenous use                  |

Dosage and administration details:

NNC0114-0006 was administered as an i.v. infusion over a period of 30 minutes. The total dose was calculated based on the body weight.

|                  |   |
|------------------|---|
| <b>Arm title</b> | Open-Label: NNC0114-0006 25 mg/kg-NNC0114-0006 25 mg/kg |
|------------------|---|

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**Arm description:**

Subjects, who received a single dose of NNC0114-0006 in double-blind period and accepted for an additional open-label dose of NNC0114-0006, were administered a single dose of NNC0114-0006 at Week 12. Subjects were additionally followed at weeks 13 and 36.

|  |                                  |
|--|----------------------------------|
| Arm type                               | Experimental                     |
| Investigational medicinal product name | NNC0114-0006                     |
| Investigational medicinal product code |                                  |
| Other name                             |                                  |
| Pharmaceutical forms                   | Powder for solution for infusion |
| Routes of administration               | Intravenous use                  |

**Dosage and administration details:**

NNC0114-0006 was administered as an i.v. infusion over a period of 30 minutes. The total dose was calculated based on the body weight.

| Number of subjects in period 2 | Open-Label:<br>Placebo-NNC0114-<br>0006 25 mg/kg | Open-Label:<br>NNC0114-0006 25<br>mg/kg-NNC0114-<br>0006 25 mg/kg |
|--------------------------------|--|---|
|                                |  |   |
| Started                        | 15   | 28  |
| Completed                      | 11   | 22  |
| Not completed                  | 4  | 6   |
| Adverse event, non-fatal       | -  | 1   |
| Sponsor closure of trial       | 3  | 4   |
| Protocol deviation             | 1  | 1   |

## Baseline characteristics

### Reporting groups

|                       |                       |
|-----------------------|-----------------------|
| Reporting group title | Double-Blind: Placebo |
|-----------------------|-----------------------|

Reporting group description:

Subjects received a single dose of placebo (for NNC0114-0006) and followed up for 24 weeks. If considered relevant and safe by the investigator at week 12 and the subject accepted, an open-label dose of NNC0114-0006 (25 mg/kg) was administered. If subjects received an open-label administration of the NNC0114-0006 at week 12, these subjects were additionally followed at weeks 13 and 36.

|                       |                                     |
|-----------------------|-------------------------------------|
| Reporting group title | Double-Blind: NNC0114-0006 25 mg/kg |
|-----------------------|-------------------------------------|

Reporting group description:

Subjects received a single dose of NNC0114-0006 and followed up for 24 weeks. If considered relevant and safe by the investigator at week 12 and the subject accepted, one additional open-label dose of NNC0114-0006 was administered at the same dose level. If subjects received an open-label administration of the NNC0114-0006 at week 12, these subjects were additionally followed at weeks 13 and 36.

| Reporting group values             | Double-Blind:<br>Placebo | Double-Blind:<br>NNC0114-0006 25<br>mg/kg | Total |
|------------------------------------|--------------------------|---|-------|
| Number of subjects                 | 17                       | 36  | 53    |
| Age categorical<br>Units: Subjects |                          |   |       |

|   |                 |                 |    |
|---|-----------------|-----------------|----|
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation   | 36.4<br>± 10.9  | 32<br>± 13.2    | -  |
| Gender categorical<br>Units: Subjects   |                 |                 |    |
| Female  | 5               | 17              | 22 |
| Male  | 12              | 19              | 31 |
| Crohn's Disease Activity Index  |                 |                 |    |
| Number of subjects analysed in NNC0114-0006 25 mg/kg group = 35.  |                 |                 |    |
| Units: score on a scale<br>arithmetic mean<br>standard deviation  | 316.4<br>± 45.8 | 309.5<br>± 58.1 | -  |
| Inflammatory bowel disease<br>questionnaire (IBDQ) score<br>Units: score on a scale<br>arithmetic mean<br>standard deviation        | 123.8<br>± 29.3 | 124.9<br>± 31.9 | -  |
| Short Form Health Survey (SF-36v2)<br>physical component scores<br>Units: score on a scale<br>arithmetic mean<br>standard deviation | 38.7<br>± 4.7   | 38.2<br>± 7.3   | -  |
| SF-36v2 mental component scores<br>Units: score on a scale<br>arithmetic mean<br>standard deviation                                 | 35.6<br>± 11.1  | 36.1<br>± 10.4  | -  |





## End points

### End points reporting groups

|                       |                       |
|-----------------------|-----------------------|
| Reporting group title | Double-Blind: Placebo |
|-----------------------|-----------------------|

#### Reporting group description:

Subjects received a single dose of placebo (for NNC0114-0006) and followed up for 24 weeks. If considered relevant and safe by the investigator at week 12 and the subject accepted, an open-label dose of NNC0114-0006 (25 mg/kg) was administered. If subjects received an open-label administration of the NNC0114-0006 at week 12, these subjects were additionally followed at weeks 13 and 36.

|                       |                                     |
|-----------------------|-------------------------------------|
| Reporting group title | Double-Blind: NNC0114-0006 25 mg/kg |
|-----------------------|-------------------------------------|

#### Reporting group description:

Subjects received a single dose of NNC0114-0006 and followed up for 24 weeks. If considered relevant and safe by the investigator at week 12 and the subject accepted, one additional open-label dose of NNC0114-0006 was administered at the same dose level. If subjects received an open-label administration of the NNC0114-0006 at week 12, these subjects were additionally followed at weeks 13 and 36.

|                       |   |
|-----------------------|---|
| Reporting group title | Open-Label: Placebo-NNC0114-0006 25 mg/kg |
|-----------------------|---|

#### Reporting group description:

Subjects, who received a single dose of placebo (for NNC0114-0006) in double-blind period and accepted an open-label dose of NNC0114-0006, were administered a single dose of NNC0114-0006 at Week 12. Subjects were additionally followed at weeks 13 and 36.

|                       |   |
|-----------------------|---|
| Reporting group title | Open-Label: NNC0114-0006 25 mg/kg-NNC0114-0006 25 mg/kg |
|-----------------------|---|

#### Reporting group description:

Subjects, who received a single dose of NNC0114-0006 in double-blind period and accepted for an additional open-label dose of NNC0114-0006, were administered a single dose of NNC0114-0006 at Week 12. Subjects were additionally followed at weeks 13 and 36.

|                            |                     |
|----------------------------|---------------------|
| Subject analysis set title | Open-label: Placebo |
|----------------------------|---------------------|

|                           |                 |
|---------------------------|-----------------|
| Subject analysis set type | Safety analysis |
|---------------------------|-----------------|

#### Subject analysis set description:

Subjects received a single dose of placebo in double-blind period and did not accept an additional dose of NNC0114-0006. Subjects were followed up for 24 weeks.

|                            |                                   |
|----------------------------|-----------------------------------|
| Subject analysis set title | Open-label: NNC0114-0006 25 mg/kg |
|----------------------------|-----------------------------------|

|                           |                 |
|---------------------------|-----------------|
| Subject analysis set type | Safety analysis |
|---------------------------|-----------------|

#### Subject analysis set description:

Subjects received a single dose of NNC0114-0006 in double-blind period and did not accept an additional dose of NNC0114-0006. Subjects were followed up for 24 weeks.

### Primary: Change in Crohn's Disease Activity Index (CDAI)

|                 |   |
|-----------------|---|
| End point title | Change in Crohn's Disease Activity Index (CDAI) |
|-----------------|---|

#### End point description:

Change from baseline in CDAI at week 4. The CDAI is a composite disease specific score consisting of 8 factors: number of liquid or very soft stool, abdominal pain, general wellbeing, complications of Crohn's disease, use of antidiarrheals, abdominal mass, hematocrit and body weight. CDAI scores below 150 represent remission and scores over 450 represent very severe Crohn's disease.

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

#### End point timeframe:

From baseline to Week 4

|                                      |                       |                                     |  |  |
|--------------------------------------|-----------------------|-------------------------------------|--|--|
| <b>End point values</b>              | Double-Blind: Placebo | Double-Blind: NNC0114-0006 25 mg/kg |  |  |
| Subject group type                   | Reporting group       | Reporting group                     |  |  |
| Number of subjects analysed          | 15 <sup>[1]</sup>     | 33 <sup>[2]</sup>                   |  |  |
| Units: score on a scale              |                       |                                     |  |  |
| arithmetic mean (standard deviation) | -112 (± 83)           | -125 (± 70)                         |  |  |

Notes:

[1] - Subjects with available data for CDAI at Week 0 and Week 4.

[2] - Subjects with available data for CDAI at Week 0 and Week 4.

## Statistical analyses

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | NNC0114-0006 25 mg/kg vs Placebo |
|-----------------------------------|----------------------------------|

Statistical analysis description:

Analysis was performed using an analysis of variance (ANOVA) model on the last value before rescue/week 4. The model included treatment, prior failure to biological therapy (Yes/No), CDAI (below 330, 330 or more) and the interaction between the two strata as fixed factors and baseline CDAI as continuous covariate. Number of subjects in this analysis was 52 (35 subjects in NNC0114-0006 25 mg/kg group and 17 in placebo group). Due to EUDRACT error, on adding the 2 groups, N is shown 48.

|   |   |
|---|---|
| Comparison groups                       | Double-Blind: Placebo v Double-Blind: NNC0114-0006 25 mg/kg |
| Number of subjects included in analysis | 48  |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | superiority   |
| P-value                                 | = 0.3812  |
| Method                                  | ANOVA   |
| Parameter estimate                      | Mean difference (final values)                              |
| Point estimate                          | -20   |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -67   |
| upper limit                             | 26  |

## Secondary: Change in CDAI

|                 |                |
|-----------------|----------------|
| End point title | Change in CDAI |
|-----------------|----------------|

End point description:

Change from baseline in CDAI at week 12. The CDAI is a composite disease specific score consisting of 8 factors: number of liquid or very soft stool, abdominal pain, general wellbeing, complications of Crohn's disease, use of antidiarrheals, abdominal mass, hematocrit and body weight. CDAI scores below 150 represent remission and scores over 450 represent very severe Crohn's disease.

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

End point timeframe:

From baseline to Week 12

| End point values                     | Double-Blind:<br>Placebo | Double-Blind:<br>NNC0114-0006<br>25 mg/kg |  |  |
|--------------------------------------|--------------------------|---|--|--|
| Subject group type                   | Reporting group          | Reporting group                           |  |  |
| Number of subjects analysed          | 14 <sup>[3]</sup>        | 27 <sup>[4]</sup>                         |  |  |
| Units: score on a scale              |                          |   |  |  |
| arithmetic mean (standard deviation) | -111 (± 104)             | -156 (± 83)                               |  |  |

Notes:

[3] - Subjects with available data for CDAI at Week 0 and Week 12.

[4] - Subjects with available data for CDAI at Week 0 and Week 12.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Clinical Remission, Defined as CDAI of Less Than 150

|  |  |
|--|--|
| End point title  | Clinical Remission, Defined as CDAI of Less Than 150 |
| End point description:   |  |
| The CDAI is a composite disease specific score consisting of 8 factors: number of liquid or very soft stool, abdominal pain, general wellbeing, complications of Crohn's disease, use of antidiarrheals, abdominal mass, hematocrit and body weight. CDAI scores below 150 represent remission and scores over 450 represent very severe Crohn's disease. Percentage of subjects with clinical remission at week 8 are reported. |  |
| End point type   | Secondary  |
| End point timeframe:   |  |
| At week 8  |  |

| End point values              | Double-Blind:<br>Placebo | Double-Blind:<br>NNC0114-0006<br>25 mg/kg |  |  |
|-------------------------------|--------------------------|---|--|--|
| Subject group type            | Reporting group          | Reporting group                           |  |  |
| Number of subjects analysed   | 14 <sup>[5]</sup>        | 32 <sup>[6]</sup>                         |  |  |
| Units: percentage of subjects |                          |   |  |  |
| number (not applicable)       | 28.6                     | 37.5                                      |  |  |

Notes:

[5] - Subjects with available data for CDAI at week 0 and week 8.

[6] - Subjects with available data for CDAI at week 0 and week 8.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change in the Inflammatory Bowel Disease Questionnaire (IBDQ) Score

|  |   |
|--|---|
| End point title  | Change in the Inflammatory Bowel Disease Questionnaire (IBDQ) Score |
| End point description:   |   |
| The IBDQ is a health related quality of life questionnaire specific to IBDs. IBDQ include 32 items covering four domains with a recall period of two weeks. The four domains covered are bowel symptoms, systemic systems, social function, and emotional health. Each item is scored from 1 to 7 and the overall score for the IBDQ is the sum of responses to each of the items. The overall score range from 32 to 224 with higher scores indicating better health related quality of life. |   |
| End point type   | Secondary   |

End point timeframe:  
From baseline to Week 4

| End point values                     | Double-Blind:<br>Placebo | Double-Blind:<br>NNC0114-0006<br>25 mg/kg |  |  |
|--------------------------------------|--------------------------|---|--|--|
| Subject group type                   | Reporting group          | Reporting group                           |  |  |
| Number of subjects analysed          | 16 <sup>[7]</sup>        | 35 <sup>[8]</sup>                         |  |  |
| Units: score on scale                |                          |   |  |  |
| arithmetic mean (standard deviation) | 22.5 (± 19.3)            | 33.7 (± 26.3)                             |  |  |

Notes:

[7] - Subjects with available data for IBDQ at week 0 and week 4.

[8] - Subjects with available data for IBDQ at week 0 and week 4.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Changes in the Short Form Health Survey (SF-36v2) Physical and Mental Component Scores

|                 |  |
|-----------------|--|
| End point title | Changes in the Short Form Health Survey (SF-36v2) Physical and Mental Component Scores |
|-----------------|--|

End point description:

Change from baseline in SF-36v2 physical and mental component scores at week 4. The SF-36v2 is a health survey which assesses the functional status and well-being of the patient utilising 36 questions designed to measure 8 domains: physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional and mental health. Physical and mental health scores represent overall physical and mental health. Each domain is scored on 100-point scale with higher scores indicating a better health state.

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

End point timeframe:

From baseline to Week 4

| End point values                     | Double-Blind:<br>Placebo | Double-Blind:<br>NNC0114-0006<br>25 mg/kg |  |  |
|--------------------------------------|--------------------------|---|--|--|
| Subject group type                   | Reporting group          | Reporting group                           |  |  |
| Number of subjects analysed          | 16 <sup>[9]</sup>        | 35 <sup>[10]</sup>                        |  |  |
| Units: scores on a scale             |                          |   |  |  |
| arithmetic mean (standard deviation) |                          |   |  |  |
| Change in Physical Component Score   | 3.2 (± 5.5)              | 6 (± 5.5)                                 |  |  |
| Change in Mental Component Score     | 5.5 (± 10.1)             | 7 (± 8.4)                                 |  |  |

Notes:

[9] - Subjects with available data for SF-36v2 at week 0 and week 4.

[10] - Subjects with available data for SF-36v2 at week 0 and week 4.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Incidence of Adverse Events (AEs)

|  |                                   |
|--|-----------------------------------|
| End point title  | Incidence of Adverse Events (AEs) |
| End point description:<br>An AE is any undesirable medical event occurring to a subject in a clinical trial, whether or not related to the trial product(s). A serious AE (SAE) is an experience that at any dose is fatal, life-threatening, disabling or which results in the patient being hospitalised or, if already in hospital, that hospitalisation is prolonged, or occurrence of congenital anomaly. |                                   |
| End point type   | Secondary                         |
| End point timeframe:<br>Up to weeks 24 or 36   |                                   |

| End point values            | Double-Blind:<br>Placebo | Double-Blind:<br>NNC0114-0006<br>25 mg/kg | Open-Label:<br>Placebo-<br>NNC0114-0006<br>25 mg/kg | Open-Label:<br>NNC0114-0006<br>25 mg/kg-<br>NNC0114-0006<br>25 mg/kg |
|-----------------------------|--------------------------|---|---|--|
| Subject group type          | Reporting group          | Reporting group                           | Reporting group                                     | Reporting group  |
| Number of subjects analysed | 17 <sup>[11]</sup>       | 36 <sup>[12]</sup>                        | 15 <sup>[13]</sup>                                  | 28 <sup>[14]</sup>   |
| Units: events               |                          |   |   |  |
| All AEs                     | 15                       | 45  | 5   | 37   |
| SAEs                        | 0                        | 1   | 1   | 7  |

Notes:

[11] - Safety analysis set: All randomized and exposed subjects.

[12] - Safety analysis set: All randomized and exposed subjects.

[13] - Safety analysis set: All randomized and exposed subjects.

[14] - Safety analysis set: All randomized and exposed subjects.

| End point values            | Open-label:<br>Placebo | Open-label:<br>NNC0114-0006<br>25 mg/kg |  |  |
|-----------------------------|------------------------|---|--|--|
| Subject group type          | Subject analysis set   | Subject analysis set                    |  |  |
| Number of subjects analysed | 2 <sup>[15]</sup>      | 8 <sup>[16]</sup>                       |  |  |
| Units: events               |                        |   |  |  |
| All AEs                     | 0                      | 1                                       |  |  |
| SAEs                        | 0                      | 0                                       |  |  |

Notes:

[15] - Safety analysis set: All randomized and exposed subjects.

[16] - Safety analysis set: All randomized and exposed subjects.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Incidence of Anti-NNC0114-0006 Antibodies

|   |   |
|---|---|
| End point title   | Incidence of Anti-NNC0114-0006 Antibodies |
| End point description:<br>Percentage of subjects with antibodies against NNC01140006. |   |
| End point type  | Secondary                                 |
| End point timeframe:<br>Up to weeks 24 or 36  |   |

| <b>End point values</b>       | Double-Blind:<br>Placebo | Double-Blind:<br>NNC0114-0006<br>25 mg/kg |  |  |
|-------------------------------|--------------------------|---|--|--|
| Subject group type            | Reporting group          | Reporting group                           |  |  |
| Number of subjects analysed   | 17 <sup>[17]</sup>       | 36 <sup>[18]</sup>                        |  |  |
| Units: percentage of patients |                          |   |  |  |
| number (not applicable)       | 0                        | 0   |  |  |

Notes:

[17] - Safety analysis set: All randomized and exposed subjects.

[18] - Safety analysis set: All randomized and exposed subjects.

### Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to 24 or 36 weeks

Adverse event reporting additional description:

Analysis was performed on the safety analysis set.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 17.1 |
|--------------------|------|

### Reporting groups

|                       |                       |
|-----------------------|-----------------------|
| Reporting group title | Double-blind: Placebo |
|-----------------------|-----------------------|

Reporting group description:

Subjects received a single dose of placebo (for NNC0114-0006) and followed up for 24 weeks. If considered relevant and safe by the investigator at week 12 and the subject accepted, an open-label dose of NNC0114-0006 was administered. If subjects received an open-label administration of the NNC0114-0006 at week 12, these subjects were additionally followed at weeks 13 and 36.

|                       |                                     |
|-----------------------|-------------------------------------|
| Reporting group title | Double-blind: NNC0114-0006 25 mg/kg |
|-----------------------|-------------------------------------|

Reporting group description:

Subjects received a single dose of NNC0114-0006 and followed up for 24 weeks. If considered relevant and safe by the investigator at week 12 and the subject accepted, one additional open-label dose of NNC0114-0006 was administered at the same dose level. If subjects received an open-label administration of the NNC0114-0006 at week 12, these subjects were additionally followed at weeks 13 and 36.

|                       |                     |
|-----------------------|---------------------|
| Reporting group title | Open-label: Placebo |
|-----------------------|---------------------|

Reporting group description:

Subjects received a single dose of placebo in double-blind period and did not accept an additional dose of NNC0114-0006. Subjects were followed up for 24 weeks.

|                       |   |
|-----------------------|---|
| Reporting group title | Open-label: Placebo-NNC0114-0006 25 mg/kg |
|-----------------------|---|

Reporting group description:

Subjects, who received a single dose of placebo (for NNC0114-0006) in double-blind period and accepted an open-label dose of NNC0114-0006, were administered a single dose of NNC0114-0006 at week 12. Subjects were additionally followed at weeks 13 and 36.

|                       |                                   |
|-----------------------|-----------------------------------|
| Reporting group title | Open-label: NNC0114-0006 25 mg/kg |
|-----------------------|-----------------------------------|

Reporting group description:

Subjects received a single dose of NNC0114-0006 in double-blind period and did not accept an additional dose of NNC0114-0006. Subjects were followed up for 24 weeks.

|                       |   |
|-----------------------|---|
| Reporting group title | Open-label: NNC0114-0006 25 mg/kg-NNC0114-0006 25 mg/kg |
|-----------------------|---|

Reporting group description:

Subjects, who received a single dose of NNC0114-0006 in double-blind period and accepted for an additional open-label dose of NNC0114-0006, were administered a single dose of NNC0114-0006 at week 12. Subjects were additionally followed at weeks 13 and 36.

| Serious adverse events                            | Double-blind: Placebo | Double-blind: NNC0114-0006 25 mg/kg | Open-label: Placebo |
|---|-----------------------|-------------------------------------|---------------------|
| Total subjects affected by serious adverse events |                       |                                     |                     |
| subjects affected / exposed                       | 0 / 17 (0.00%)        | 1 / 36 (2.78%)                      | 0 / 2 (0.00%)       |
| number of deaths (all causes)                     | 0                     | 0                                   | 0                   |
| number of deaths resulting from                   | 0                     | 0                                   | 0                   |

|   |  |   |   |
|---|--|---|---|
| adverse events  |  |   |   |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |  |   |   |
| Renal neoplasm  |  |   |   |
| subjects affected / exposed   | 0 / 17 (0.00%)                                   | 0 / 36 (0.00%)                          | 0 / 2 (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   |
| Blood and lymphatic system disorders                                |  |   |   |
| Anaemia   |  |   |   |
| subjects affected / exposed   | 0 / 17 (0.00%)                                   | 1 / 36 (2.78%)                          | 0 / 2 (0.00%)   |
| occurrences causally related to treatment / all                     | 0 / 0  | 0 / 1                                   | 0 / 0   |
| deaths causally related to treatment / all                          | 0 / 0  | 0 / 0                                   | 0 / 0   |
| Gastrointestinal disorders  |  |   |   |
| Crohn's disease   |  |   |   |
| subjects affected / exposed   | 0 / 17 (0.00%)                                   | 0 / 36 (0.00%)                          | 0 / 2 (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   |
| Ileus   |  |   |   |
| subjects affected / exposed   | 0 / 17 (0.00%)                                   | 0 / 36 (0.00%)                          | 0 / 2 (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   |
| Reproductive system and breast disorders                            |  |   |   |
| Uterine inflammation  |  |   |   |
| subjects affected / exposed   | 0 / 17 (0.00%)                                   | 0 / 36 (0.00%)                          | 0 / 2 (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   |
| Infections and infestations   |  |   |   |
| Clostridium difficile infection                                     |  |   |   |
| subjects affected / exposed   | 0 / 17 (0.00%)                                   | 0 / 36 (0.00%)                          | 0 / 2 (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   |
| <b>Serious adverse events</b>                                       | Open-label: Placebo-<br>NNC0114-0006 25<br>mg/kg | Open-label:<br>NNC0114-0006 25<br>mg/kg | Open-label:<br>NNC0114-0006 25<br>mg/kg-NNC0114-<br>0006 25 mg/kg |
| Total subjects affected by serious adverse events                   |  |   |   |
| subjects affected / exposed   | 1 / 15 (6.67%)                                   | 0 / 8 (0.00%)                           | 4 / 28 (14.29%)   |



|   |                |               |                 |
|---|----------------|---------------|-----------------|
| 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) |                |               |                 |
| Renal neoplasm  |                |               |                 |
| subjects affected / exposed   | 0 / 15 (0.00%) | 0 / 8 (0.00%) | 1 / 28 (3.57%)  |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0         | 0 / 0           |
| Blood and lymphatic system disorders                                |                |               |                 |
| Anaemia   |                |               |                 |
| subjects affected / exposed   | 0 / 15 (0.00%) | 0 / 8 (0.00%) | 0 / 28 (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           |
| Gastrointestinal disorders  |                |               |                 |
| Crohn's disease   |                |               |                 |
| subjects affected / exposed   | 1 / 15 (6.67%) | 0 / 8 (0.00%) | 3 / 28 (10.71%) |
| occurrences causally related to treatment / all                     | 0 / 1          | 0 / 0         | 0 / 3           |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0         | 0 / 0           |
| Ileus   |                |               |                 |
| subjects affected / exposed   | 0 / 15 (0.00%) | 0 / 8 (0.00%) | 1 / 28 (3.57%)  |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0         | 0 / 0           |
| Reproductive system and breast disorders                            |                |               |                 |
| Uterine inflammation  |                |               |                 |
| subjects affected / exposed   | 0 / 15 (0.00%) | 0 / 8 (0.00%) | 1 / 28 (3.57%)  |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0         | 0 / 0           |
| Infections and infestations   |                |               |                 |
| Clostridium difficile infection                                     |                |               |                 |
| subjects affected / exposed   | 0 / 15 (0.00%) | 0 / 8 (0.00%) | 1 / 28 (3.57%)  |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0         | 0 / 0           |

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

| <b>Non-serious adverse events</b>   | Double-blind:<br>Placebo | Double-blind:<br>NNC0114-0006 25<br>mg/kg | Open-label: Placebo |
|---|--------------------------|---|---------------------|
| Total subjects affected by non-serious<br>adverse events<br>subjects affected / exposed | 6 / 17 (35.29%)          | 10 / 36 (27.78%)                          | 0 / 2 (0.00%)       |
| Investigations  |                          |   |                     |
| Alanine aminotransferase abnormal<br>subjects affected / exposed                        | 1 / 17 (5.88%)           | 0 / 36 (0.00%)                            | 0 / 2 (0.00%)       |
| occurrences (all)   | 1                        | 0   | 0                   |
| Aspartate aminotransferase<br>abnormal<br>subjects affected / exposed                   | 1 / 17 (5.88%)           | 0 / 36 (0.00%)                            | 0 / 2 (0.00%)       |
| occurrences (all)   | 1                        | 0   | 0                   |
| Blood lactate dehydrogenase<br>abnormal<br>subjects affected / exposed                  | 1 / 17 (5.88%)           | 0 / 36 (0.00%)                            | 0 / 2 (0.00%)       |
| occurrences (all)   | 1                        | 0   | 0                   |
| Blood uric acid abnormal<br>subjects affected / exposed                                 | 1 / 17 (5.88%)           | 0 / 36 (0.00%)                            | 0 / 2 (0.00%)       |
| occurrences (all)   | 1                        | 0   | 0                   |
| Gamma-glutamyltransferase<br>abnormal<br>subjects affected / exposed                    | 1 / 17 (5.88%)           | 0 / 36 (0.00%)                            | 0 / 2 (0.00%)       |
| occurrences (all)   | 1                        | 0   | 0                   |
| Lipase abnormal<br>subjects affected / exposed  | 1 / 17 (5.88%)           | 0 / 36 (0.00%)                            | 0 / 2 (0.00%)       |
| occurrences (all)   | 1                        | 0   | 0                   |
| Injury, poisoning and procedural<br>complications                                       |                          |   |                     |
| Road traffic accident<br>subjects affected / exposed                                    | 1 / 17 (5.88%)           | 1 / 36 (2.78%)                            | 0 / 2 (0.00%)       |
| occurrences (all)   | 1                        | 1   | 0                   |
| Nervous system disorders  |                          |   |                     |
| Dysgeusia<br>subjects affected / exposed  | 1 / 17 (5.88%)           | 0 / 36 (0.00%)                            | 0 / 2 (0.00%)       |
| occurrences (all)   | 1                        | 0   | 0                   |
| Headache<br>subjects affected / exposed   | 0 / 17 (0.00%)           | 2 / 36 (5.56%)                            | 0 / 2 (0.00%)       |
| occurrences (all)   | 0                        | 5   | 0                   |
| General disorders and administration<br>site conditions                                 |                          |   |                     |

|  |                     |                     |                    |
|--|---------------------|---------------------|--------------------|
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)              | 1 / 17 (5.88%)<br>1 | 2 / 36 (5.56%)<br>2 | 0 / 2 (0.00%)<br>0 |
| Gastrointestinal disorders   |                     |                     |                    |
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)       | 0 / 17 (0.00%)<br>0 | 3 / 36 (8.33%)<br>4 | 0 / 2 (0.00%)<br>0 |
| Anal fistula<br>subjects affected / exposed<br>occurrences (all)         | 0 / 17 (0.00%)<br>0 | 0 / 36 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 |
| Crohn's disease<br>subjects affected / exposed<br>occurrences (all)      | 0 / 17 (0.00%)<br>0 | 0 / 36 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)            | 0 / 17 (0.00%)<br>0 | 2 / 36 (5.56%)<br>2 | 0 / 2 (0.00%)<br>0 |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)             | 1 / 17 (5.88%)<br>1 | 1 / 36 (2.78%)<br>1 | 0 / 2 (0.00%)<br>0 |
| Respiratory, thoracic and mediastinal disorders                          |                     |                     |                    |
| Respiratory disorder<br>subjects affected / exposed<br>occurrences (all) | 1 / 17 (5.88%)<br>1 | 0 / 36 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 |
| Skin and subcutaneous tissue disorders                                   |                     |                     |                    |
| Acne<br>subjects affected / exposed<br>occurrences (all)                 | 1 / 17 (5.88%)<br>1 | 0 / 36 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 |
| Seborrhoea<br>subjects affected / exposed<br>occurrences (all)           | 1 / 17 (5.88%)<br>1 | 0 / 36 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 |
| Musculoskeletal and connective tissue disorders                          |                     |                     |                    |
| Arthralgia<br>subjects affected / exposed<br>occurrences (all)           | 1 / 17 (5.88%)<br>1 | 1 / 36 (2.78%)<br>1 | 0 / 2 (0.00%)<br>0 |
| Fistula discharge  |                     |                     |                    |

|  |                     |                     |                    |
|--|---------------------|---------------------|--------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 17 (0.00%)<br>0 | 0 / 36 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 |
| Infections and infestations                      |                     |                     |                    |
| Nasopharyngitis                                  |                     |                     |                    |
| subjects affected / exposed                      | 0 / 17 (0.00%)      | 3 / 36 (8.33%)      | 0 / 2 (0.00%)      |
| occurrences (all)                                | 0                   | 3                   | 0                  |
| Respiratory tract infection                      |                     |                     |                    |
| subjects affected / exposed                      | 1 / 17 (5.88%)      | 1 / 36 (2.78%)      | 0 / 2 (0.00%)      |
| occurrences (all)                                | 1                   | 1                   | 0                  |

| <b>Non-serious adverse events</b>                        | Open-label: Placebo-<br>NNC0114-0006 25<br>mg/kg | Open-label:<br>NNC0114-0006 25<br>mg/kg | Open-label:<br>NNC0114-0006 25<br>mg/kg-NNC0114-<br>0006 25 mg/kg |
|--|--|---|---|
| Total subjects affected by non-serious<br>adverse events |  |   |   |
| subjects affected / exposed                              | 4 / 15 (26.67%)                                  | 1 / 8 (12.50%)                          | 9 / 28 (32.14%)   |
| Investigations   |  |   |   |
| Alanine aminotransferase abnormal                        |  |   |   |
| subjects affected / exposed                              | 0 / 15 (0.00%)                                   | 0 / 8 (0.00%)                           | 0 / 28 (0.00%)  |
| occurrences (all)  | 0  | 0                                       | 0   |
| Aspartate aminotransferase<br>abnormal                   |  |   |   |
| subjects affected / exposed                              | 0 / 15 (0.00%)                                   | 0 / 8 (0.00%)                           | 0 / 28 (0.00%)  |
| occurrences (all)  | 0  | 0                                       | 0   |
| Blood lactate dehydrogenase<br>abnormal                  |  |   |   |
| subjects affected / exposed                              | 0 / 15 (0.00%)                                   | 0 / 8 (0.00%)                           | 0 / 28 (0.00%)  |
| occurrences (all)  | 0  | 0                                       | 0   |
| Blood uric acid abnormal                                 |  |   |   |
| subjects affected / exposed                              | 0 / 15 (0.00%)                                   | 0 / 8 (0.00%)                           | 0 / 28 (0.00%)  |
| occurrences (all)  | 0  | 0                                       | 0   |
| Gamma-glutamyltransferase<br>abnormal                    |  |   |   |
| subjects affected / exposed                              | 0 / 15 (0.00%)                                   | 0 / 8 (0.00%)                           | 0 / 28 (0.00%)  |
| occurrences (all)  | 0  | 0                                       | 0   |
| Lipase abnormal  |  |   |   |
| subjects affected / exposed                              | 0 / 15 (0.00%)                                   | 0 / 8 (0.00%)                           | 0 / 28 (0.00%)  |
| occurrences (all)  | 0  | 0                                       | 0   |
| Injury, poisoning and procedural<br>complications        |  |   |   |

|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| Road traffic accident<br>subjects affected / exposed<br>occurrences (all)  | 0 / 15 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  | 0 / 28 (0.00%)<br>0 |
| Nervous system disorders<br>Dysgeusia<br>subjects affected / exposed<br>occurrences (all)                                      | 0 / 15 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  | 0 / 28 (0.00%)<br>0 |
| Headache<br>subjects affected / exposed<br>occurrences (all)   | 1 / 15 (6.67%)<br>1 | 0 / 8 (0.00%)<br>0  | 1 / 28 (3.57%)<br>1 |
| General disorders and administration<br>site conditions<br>Pyrexia<br>subjects affected / exposed<br>occurrences (all)         | 0 / 15 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  | 2 / 28 (7.14%)<br>3 |
| Gastrointestinal disorders<br>Abdominal pain<br>subjects affected / exposed<br>occurrences (all)                               | 0 / 15 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  | 2 / 28 (7.14%)<br>3 |
| Anal fistula<br>subjects affected / exposed<br>occurrences (all)   | 1 / 15 (6.67%)<br>1 | 0 / 8 (0.00%)<br>0  | 0 / 28 (0.00%)<br>0 |
| Crohn's disease<br>subjects affected / exposed<br>occurrences (all)  | 0 / 15 (0.00%)<br>0 | 1 / 8 (12.50%)<br>1 | 1 / 28 (3.57%)<br>1 |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)  | 0 / 15 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  | 2 / 28 (7.14%)<br>2 |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)   | 0 / 15 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  | 2 / 28 (7.14%)<br>3 |
| Respiratory, thoracic and mediastinal<br>disorders<br>Respiratory disorder<br>subjects affected / exposed<br>occurrences (all) | 0 / 15 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  | 0 / 28 (0.00%)<br>0 |
| Skin and subcutaneous tissue disorders   |                     |                     |                     |

|   |                |               |                |
|---|----------------|---------------|----------------|
| Acne  |                |               |                |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 8 (0.00%) | 1 / 28 (3.57%) |
| occurrences (all)                               | 0              | 0             | 1              |
| Seborrhoea                                      |                |               |                |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 8 (0.00%) | 0 / 28 (0.00%) |
| occurrences (all)                               | 0              | 0             | 0              |
| Musculoskeletal and connective tissue disorders |                |               |                |
| Arthralgia                                      |                |               |                |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 8 (0.00%) | 1 / 28 (3.57%) |
| occurrences (all)                               | 0              | 0             | 1              |
| Fistula discharge                               |                |               |                |
| subjects affected / exposed                     | 1 / 15 (6.67%) | 0 / 8 (0.00%) | 1 / 28 (3.57%) |
| occurrences (all)                               | 1              | 0             | 1              |
| Infections and infestations                     |                |               |                |
| Nasopharyngitis                                 |                |               |                |
| subjects affected / exposed                     | 1 / 15 (6.67%) | 0 / 8 (0.00%) | 0 / 28 (0.00%) |
| occurrences (all)                               | 1              | 0             | 0              |
| Respiratory tract infection                     |                |               |                |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 0 / 8 (0.00%) | 0 / 28 (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  |
|-------------------|--|
| 30 September 2013 | 1) Exclusion criterion amended as recombinant immunoblot assay agent no longer available for the anti-HCV antibody confirmatory test.<br>2) Text regarding re-screening was modified to include repeat of endoscopy within 8 weeks of the initial screening. |
| 10 October 2014   | 1) Extension of timelines.<br>2) Change of two inclusion criteria.   |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Because of the small trial population, the planned statistical analyses did not have the intended power and the results should be interpreted with caution.

Notes: