



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
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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
Arm title	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.

Arm title	Double-Blind: NNC0114-0006 25 mg/kg
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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

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: Placebo	Double-Blind: NNC0114-0006 25 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

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

Arms

Are arms mutually exclusive?	Yes
Arm title	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.

Arm title	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: Placebo-NNC0114- 0006 25 mg/kg	Open-Label: NNC0114-0006 25 mg/kg-NNC0114- 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
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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
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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: Placebo	Double-Blind: NNC0114-0006 25 mg/kg	Total
Number of subjects	17	36	53
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	36.4 ± 10.9	32 ± 13.2	-
Gender categorical 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 arithmetic mean standard deviation	316.4 ± 45.8	309.5 ± 58.1	-
Inflammatory bowel disease questionnaire (IBDQ) score Units: score on a scale arithmetic mean standard deviation	123.8 ± 29.3	124.9 ± 31.9	-
Short Form Health Survey (SF-36v2) physical component scores Units: score on a scale arithmetic mean standard deviation	38.7 ± 4.7	38.2 ± 7.3	-
SF-36v2 mental component scores Units: score on a scale arithmetic mean standard deviation	35.6 ± 11.1	36.1 ± 10.4	-

End points

End points reporting groups

Reporting group title	Double-Blind: Placebo
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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
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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
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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
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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
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Subject analysis set type	Safety analysis
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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
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Subject analysis set type	Safety analysis
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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)
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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
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End point timeframe:

From baseline to Week 4

End point values	Double-Blind: Placebo	Double-Blind: NNC0114-0006 25 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15 ^[1]	33 ^[2]		
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

Statistical analysis title	NNC0114-0006 25 mg/kg vs Placebo
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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
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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
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End point timeframe:

From baseline to Week 12

End point values	Double-Blind: Placebo	Double-Blind: NNC0114-0006 25 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14 ^[3]	27 ^[4]		
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: Placebo	Double-Blind: NNC0114-0006 25 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14 ^[5]	32 ^[6]		
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: Placebo	Double-Blind: NNC0114-0006 25 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16 ^[7]	35 ^[8]		
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
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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
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End point timeframe:

From baseline to Week 4

End point values	Double-Blind: Placebo	Double-Blind: NNC0114-0006 25 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16 ^[9]	35 ^[10]		
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)
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End point description:

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
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End point timeframe:

Up to weeks 24 or 36

End point values	Double-Blind: Placebo	Double-Blind: NNC0114-0006 25 mg/kg	Open-Label: Placebo- NNC0114-0006 25 mg/kg	Open-Label: NNC0114-0006 25 mg/kg- NNC0114-0006 25 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17 ^[11]	36 ^[12]	15 ^[13]	28 ^[14]
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: Placebo	Open-label: NNC0114-0006 25 mg/kg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2 ^[15]	8 ^[16]		
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
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End point description:

Percentage of subjects with antibodies against NNC01140006.

End point type	Secondary
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End point timeframe:

Up to weeks 24 or 36

End point values	Double-Blind: Placebo	Double-Blind: NNC0114-0006 25 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17 ^[17]	36 ^[18]		
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

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
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.1
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Reporting groups

Reporting group title	Double-blind: Placebo
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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
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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
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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
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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
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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
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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
Serious adverse events	Open-label: Placebo- NNC0114-0006 25 mg/kg	Open-label: NNC0114-0006 25 mg/kg	Open-label: NNC0114-0006 25 mg/kg-NNC0114- 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 %

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

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

subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 36 (0.00%) 0	0 / 2 (0.00%) 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

Non-serious adverse events	Open-label: Placebo- NNC0114-0006 25 mg/kg	Open-label: NNC0114-0006 25 mg/kg	Open-label: NNC0114-0006 25 mg/kg-NNC0114- 0006 25 mg/kg
Total subjects affected by non-serious 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 abnormal			
subjects affected / exposed	0 / 15 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase 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 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 complications			

Road traffic accident subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	0 / 28 (0.00%) 0
Nervous system disorders Dysgeusia subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	0 / 28 (0.00%) 0
Headache subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 8 (0.00%) 0	1 / 28 (3.57%) 1
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	2 / 28 (7.14%) 3
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	2 / 28 (7.14%) 3
Anal fistula subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 8 (0.00%) 0	0 / 28 (0.00%) 0
Crohn's disease subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 8 (12.50%) 1	1 / 28 (3.57%) 1
Diarrhoea subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	2 / 28 (7.14%) 2
Vomiting subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	2 / 28 (7.14%) 3
Respiratory, thoracic and mediastinal disorders Respiratory disorder subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	0 / 8 (0.00%) 0	0 / 28 (0.00%) 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. 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. 2) Change of two inclusion criteria.

Notes:

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: