Clinical trial results:
Mucosal immune regulation by high dose vitamin D treatment in Crohn's disease

Summary

EudraCT number	2013-000971-34
Trial protocol	DK
Global end of trial date	22 November 2018

Results information

Result version number	v1 (current)
This version publication date	24 June 2020
First version publication date	24 June 2020
Summary attachment (see zip file)	summary (Summary.pdf)

Trial information

Trial identification

Sponsor protocol code	01052013

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Aarhus University Hospital
Sponsor organisation address	Palle Juul Jensens boulevard 99, Aarhus N, Denmark, 8200
Public contact	Jørgen Agnholt, Hepatology and Gastroenterology department, Aarhus University Hospital, joeragnh@rm.dk
Scientific contact	Jørgen Agnholt, Hepatology and Gastroenterology department, Aarhus University Hospital, joeragnh@rm.dk

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	30 May 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 November 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

We hypotheses that treatment with high dose vitamin D alone or combined with infliximab to Crohn's disease patients with disease activity increases the anti-inflammatory response in the intestinal mucosa. This would result in changed VDR expression in mucosa together with changed expression of IL17A, Il17F, IL22 and IL4 in mucosa compared to placebo.
Secondary vitamin D treatment decreases the disease activity measured by inflammatory markers and endoscopic score. Other pro- and anti-inflammatory mucosal cytokines will also be affected by vitamin D treatment.
The intervention was 7 weeks. Afterwards all patients were admitted to open infliximab treatment as standard treatment and was followed 52 weeks or until their infliximab treatment was stopped.
10 healthy were included to test if high dose vitamin D also had impact on healthy intestinal mucosa. The results from the healthy is already published (N. F: Bak 2018, Eur J Nutr)

Protection of trial subjects:

Laboratory analyses for adverse reactions related to the Infliximab and Cholecalciferol treatment will be carried out at baseline, week 2 and 6. Safety markers are collected at screening. Chest X-ray is performed at screening if this has not been done within the last year – or if participants have been exposed to TB-endemic areas after prior TB screening.

Blood samples were done the day of the control visit to minimise the number of hospitalvisits.

Colonoscopy/sigmideoscopy
When the endoscope is moved forward it can cause a slight to moderate discomfort like a feeling like too much air in the intestines. To reduce this, patients were offered treatment with midazolam and fentanyl during the examination. There are no pain sensing nerves in the intestinal mucosa and therefore, the biopsy procedure is usually not associated with pain. There is a minor risk of bleeding and perforation of the intestine during colonoscopy. The risk is approximately 1:1000 in elderly with intestinal disease (inflammation, ischemia or tumour). The risk is estimated to be less than 1:1000 in healthy individuals. The risks will be minimised since experienced physicians will perform all colonoscopies.

Background therapy: -
Evidence for comparator: -

Actual start date of recruitment	01 July 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 40
Worldwide total number of subjects	40
EEA total number of subjects	40

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	40
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Patients with colon or/and ilieoceacal Crohn's disease with active disease assessed by HBI score recruited. Patients were screened with blood samples, urine examinations, x-ray and finally colonoscopy according to in- and exclusion criteria.

Period 1

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

Blinding implementation details:

patients are blinded until week 7 . afterwards all patients in follow up are treated with open infliximab

Arms

Are arms mutually exclusive?	Yes
Arm title	Infliximab+vitamin D

Arm description: -

Arm type	Experimental
Investigational medicinal product name	infliximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate and solution for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

5 mg/kg infused over 3 hours

Investigational medicinal product name	dekristol
Investigational medicinal product code	
Other name	Vitamin D3
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

5 mg as a bolus and afterwards 0.5 mg daily in 7 weeks

Arm title	Infliximab+placebo vitamin D

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	infliximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate and solution for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

5 mg/kg infused over 3 hours

Investigational medicinal product name	placebo dekristol
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:
placebo capsules, same amount as the active drug

Arm title	Placebo infliximab+Vitamin D

Arm description: -

Arm type	Experimental
Investigational medicinal product name	dekristol
Investigational medicinal product code	
Other name	Vitamin D3
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:
5 mg as a bolus and afterwards 0.5 mg daily in 7 weeks

Investigational medicinal product name	natriumchloride
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:
placebo infliximab same amount was given as the active drug

Arm title	PLacebo infliximab+placebo vitamin D

Arm description: -

Arm type	Placebo
Investigational medicinal product name	placebo dekristol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:
placebo capsules, same amount as the active drug

Investigational medicinal product name	natriumchloride
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:
placebo infliximab same amount was given as the active drug

Number of subjects in period 1	Infliximab+vitamin D	Infliximab+placebo vitamin D	Placebo infliximab+Vitamin D
Started	8	8	16
Completed	7	8	16
Not completed	1	0	0
Adverse event, non-fatal	1	-	-

Number of subjects in period 1	PLacebo infliximab+placebo vitamin D
Started	8
Completed	8
Not completed	0
Adverse event, non-fatal	-

Baseline characteristics

Reporting groups	
Reporting group title	Infliximab+vitamin D
Reporting group description: -	
Reporting group title	Infliximab+placebo vitamin D
Reporting group description: -	
Reporting group title	Placebo infliximab+Vitamin D
Reporting group description: -	
Reporting group title	PLacebo infliximab+placebo vitamin D
Reporting group description: -	

Reporting group values	Infliximab+vitamin D	Infliximab+placebo vitamin D	Placebo infliximab+Vitamin D
Number of subjects	8	8	16
Age categorical Units: Subjects			
Adults (18-64 years)	8	8	16
Age continuous Units: years			
median	28	26	35
full range (min-max)	21 to 49	20 to 53	20 to 59
Gender categorical Units: Subjects			
Female	4	4	8
male	4	4	8
Family history of CD or UC Units: Subjects			
Family history of CD or UC	1	2	3
no family history	7	6	13
smoking Units: Subjects			
smoking	3	1	1
non smoking	5	7	15
Former or present stenosis Units: Subjects			
Former or present stenosis	3	3	1
no stenosis	5	5	15
Former abdominal surgery Units: Subjects			
Former abdominal surgery	1	0	3
no surgery	7	8	13
Former or present fistula Units: Subjects			
former or present fistula	0	1	1
no fistula	8	7	15
Former or present abcess Units: Subjects			

Former or present abcess	0	2	2
no abcess	8	6	14
Former or present fissure Units: Subjects			
dormer or present fissure	0	0	1
no fissure	8	8	15
Other autoimmune diseases Units: Subjects			
other autoimmune diseases	0	2	2
no autoimmune diseases	8	6	14
Extra intestinal manifestations Units: Subjects			
EIM	2	2	5
no EIM	6	6	11
Fatigue Units: Subjects			
Fatigue	4	5	13
no fatigue	4	3	3
Former infliximab treatment Units: Subjects			
former infliximab treatment	2	3	4
no former infliximab	6	5	12
Former Adalimumab treatment Units: Subjects			
former adalimumab treatment	0	0	2
no former adalimumab	8	8	14
Former treatment with other biologicals Units: Subjects			
former treatment with other biologicals	0	0	1
no former other biologicals	8	8	15
budesonide users (3 mg/day) Units: Subjects			
budesonide users	0	1	0
no budesonide	8	7	16
azathioprine users Units: Subjects			
azathioprine users	3	6	3
no azathioprine	5	2	13
BMI Units: kg/m2			
median	25	22.8	24.8
full range (min-max)	21.5 to 29.9	20.5 to 44.3	18.7 to 32.9
Harvey-Bradshaw index Units: score			
median	7	6.5	7
full range (min-max)	5 to 14	5 to 16	5 to 11
Calprotectin Units: mg/kg			
median	884	718	895
full range (min-max)	114 to 2174	163 to 3366	113 to 2094

25-hydroxyviatmin D			
Units: nmol/l			
median	45	73	66.5
full range (min-max)	11 to 83	33 to 88	32 to 94
CRP			
Units: mg/l			
median	5.3	16.5	8.8
full range (min-max)	0.6 to 25.6	0.6 to 38.5	0.3 to 25
Leucocytes			
Units: 10^9/l			
median	7.67	7.1	7.6
full range (min-max)	5 to 11.6	5.6 to 9.4	5 to 11.5
Haemoglobin			
Units: mmol/l			
median	8.7	8.6	8.5
full range (min-max)	7.5 to 10.2	6.4 to 9.5	6.9 to 9.7
Short health score			
Units: score			
median	21	20	14.5
full range (min-max)	11 to 32	3 to 33	4 to 36
Endoscopic CDEIS score			
Units: score			
median	13	18	14
full range (min-max)	11 to 32	7 to 33	6 to 29
years since diagnosis			
Units: years			
median	2.3	3.3	1.2
full range (min-max)	0 to 4.7	0 to 16.2	0 to 23.9

Reporting group values	PLacebo infliximab+placebo vitamin D	Total	
Number of subjects	8	40	
Age categorical			
Units: Subjects			
Adults (18-64 years)	8	40	
Age continuous			
Units: years			
median	30		
full range (min-max)	22 to 48	-	
Gender categorical			
Units: Subjects			
Female	5	21	
male	3	19	
Family history of CD or UC			
Units: Subjects			
Family history of CD or UC	1	7	
no family history	7	33	
smoking			
Units: Subjects			
smoking	3	8	
non smoking	5	32	

Former or present stenosis Units: Subjects			
Former or present stenosis	3	10	
no stenosis	5	30	
Former abdominal surgery Units: Subjects			
Former abdominal surgery	1	5	
no surgery	7	35	
Former or present fistula Units: Subjects			
former or present fistula	0	2	
no fistula	8	38	
Former or present abcess Units: Subjects			
Former or present abcess	1	5	
no abcess	7	35	
Former or present fissure Units: Subjects			
dormer or present fissure	0	1	
no fissure	8	39	
Other autoimmune diseases Units: Subjects			
other autoimmune diseases	1	5	
no autoimmune diseases	7	35	
Extra intestinal manifestations Units: Subjects			
EIM	0	9	
no EIM	8	31	
Fatigue Units: Subjects			
Fatigue	4	26	
no fatigue	4	14	
Former infliximab treatment Units: Subjects			
former infliximab treatment	1	10	
no former infliximab	7	30	
Former Adalimumab treatment Units: Subjects			
former adalimumab treatment	1	3	
no former adalimumab	7	37	
Former treatment with other biologicals Units: Subjects			
former treatment with other biologicals	0	1	
no former other biologicals	8	39	
budesonide users (3 mg/day) Units: Subjects			
budesonide users	0	1	
no budesonide	8	39	
azathioprine users Units: Subjects			

azathioprine users	1	13	
no azathioprine	7	27	

BMI			
Units: kg/m2			
median	28.8		
full range (min-max)	23.1 to 34.2	-	
Harvey-Bradshaw index			
Units: score			
median	5		
full range (min-max)	5 to 10	-	
Calprotectin			
Units: mg/kg			
median	714		
full range (min-max)	256 to 6000	-	
25-hydroxyviatmin D			
Units: nmol/l			
median	72.5		
full range (min-max)	21 to 90	-	
CRP			
Units: mg/l			
median	6.3		
full range (min-max)	0.8 to 45.9	-	
Leucocytes			
Units: 10^9/l			
median	8.2		
full range (min-max)	3.7 to 15.8	-	
Haemoglobin			
Units: mmol/l			
median	8.5		
full range (min-max)	6.6 to 10	-	
Short health score			
Units: score			
median	21		
full range (min-max)	5 to 33	-	
Endoscopic CDEIS score			
Units: score			
median	19		
full range (min-max)	6 to 49	-	
years since diagnosis			
Units: years			
median	1.9		
full range (min-max)	0.1 to 7.8	-	

End points

End points reporting groups

Reporting group title	Infliximab+vitamin D
Reporting group description: -	
Reporting group title	Infliximab+placebo vitamin D
Reporting group description: -	
Reporting group title	Placebo infliximab+Vitamin D
Reporting group description: -	
Reporting group title	PLacebo infliximab+placebo vitamin D
Reporting group description: -	

Primary: VDR expression

End point title	VDR expression

End point description:

End point type	Primary

End point timeframe:

VDR mRNA expression given week 0 and 7.

End point values	Infliximab+vitamin D	Infliximab+placebo vitamin D	Placebo infliximab+Vitamin D	PLacebo infliximab+placebo vitamin D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7[1]	8[2]	14[3]	8[4]
Units: relative quantification				
median (confidence interval 95%)				
week 0	0.079 (0.015 to 0.14)	0.25 (0.054 to 0.43)	0.11 (0.048 to 0.17)	0.13 (0.029 to 0.23)
week 7	0.055 (0.004 to 0.11)	0.2 (0.013 to 0.39)	0.15 (0.055 to 0.25)	0.092 (0 to 0.19)

Notes:

[1] - 7 week 0 and 7 week 7

[2] - 8 week 0 and 7 week 7

[3] - 14 week 0 and 16 week 7

[4] - 8 w 0 and 5 week 7

Statistical analyses

Statistical analysis title	mixed model

Statistical analysis description:

All mRNA expression were tested with mixed model and data was logarithm transformed. Within every group changes from week 7 to week 0 was tested and median ratios are used to describe changes within the groups. afterwards these changes were compared the following way: infliximab+vitamin D versus infliximab+placebovitamin D and placebo infliximab+ vitamin D versus placebo infliximab+ placebo vitamin D. This description fits all mRNA measurements.

Comparison groups	Infliximab+placebo vitamin D v Placebo infliximab+Vitamin D v Infliximab+vitamin D v PLacebo infliximab+placebo vitamin D

Number of subjects included in analysis	37
Analysis specification	Post-hoc
Analysis type	other
P-value	< 0.05
Method	Mixed models analysis

Primary: IL22 expression

End point title	IL22 expression

End point description:

End point type	Primary

End point timeframe:

mRNA IL22 expression week 0 and 7.

End point values	Infliximab+vitamin D	Infliximab+placebo vitamin D	Placebo infliximab+Vitamin D	PLacebo infliximab+placebo vitamin D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6[5]	8[6]	14[7]	8[8]
Units: relative quantification				
median (confidence interval 95%)				
week 0	0.0011 (0 to 0.0029)	0.00067 (0 to 0.0016)	0.00065 (0 to 0.0013)	0.00038 (0 to 0.0009)
week 7	0.00003 (0 to 0.00006)	0.00007 (0 to 0.00018)	0.00031 (0.00004 to 0.00057)	0.00022 (0 to 0.00053)

Notes:

[5] - w7=7

[6] - w7=7

[7] - w7=15

[8] - w7=5

Statistical analyses

Statistical analysis title	mixed model
Comparison groups	Infliximab+vitamin D v Infliximab+placebo vitamin D v Placebo infliximab+Vitamin D v PLacebo infliximab+placebo vitamin D
Number of subjects included in analysis	36
Analysis specification	Post-hoc
Analysis type	other
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	median ratio
Confidence interval	
level	95 %
sides	2-sided

Primary: IL17F expression

End point title	IL17F expression

End point description:

End point type	Primary

End point timeframe:

mRNA IL17F expression week 0 and 7

End point values	Infliximab+vitamin D	Infliximab+placebo vitamin D	Placebo infliximab+Vitamin D	PLacebo infliximab+placebo vitamin D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7[9]	8[10]	14	8[11]
Units: relative quantification				
median (confidence interval 95%)				
week 0	0.00034 (0 to 0.00071)	0.00017 (0 to 0.00035)	0.00019 (0.00004 to 0.00033)	0.00022 (0 to 0.00045)
week 7	0.00008 (0 to 0.00017)	0.00006 (0 to 0.00012)	0.00017 (0.00005 to 0.00029)	0.00021 (0 to 0.00044)

Notes:

[9] - w7= 7

[10] - w7= 7

[11] - w7 = 5

Statistical analyses

Statistical analysis title	mixed model
Comparison groups	Infliximab+placebo vitamin D v Infliximab+vitamin D v Placebo infliximab+Vitamin D v PLacebo infliximab+placebo vitamin D
Number of subjects included in analysis	37
Analysis specification	Post-hoc
Analysis type	other
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	median ratio
Confidence interval	
level	95 %
sides	2-sided

Primary: IL17A expression

End point title	IL17A expression

End point description:

End point type	Primary

End point timeframe:

mRNA IL17A mucosa expression week 0 and 7.

End point values	Infliximab+vitamin D	Infliximab+placebo vitamin D	Placebo infliximab+Vitamin D	PLacebo infliximab+placebo vitamin D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	8[12]	14[13]	8[14]
Units: relative quantification				
median (confidence interval 95%)				
week 0	0.00088 (-0.00005 to 0.0018)	0.0007 (-0.0000007 to 0.0014)	0.0014 (0.00035 to 0.0024)	0.00052 (-0.000005 to 0.001)
week 7	0.00017 (-0.000008 to 0.00034)	0.00027 (-0.00001 to 0.00056)	0.00063 (0.00018 to 0.0011)	0.00032 (-0.00006 to 0.00069)

Notes:

[12] - w7=7

[13] - w7=15

[14] - w7=5

Statistical analyses

Statistical analysis title	mixed model
Comparison groups	Infliximab+vitamin D v Infliximab+placebo vitamin D v Placebo infliximab+Vitamin D v PLacebo infliximab+placebo vitamin D
Number of subjects included in analysis	37
Analysis specification	Post-hoc
Analysis type	other
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	median ratio
Confidence interval	
level	95 %
sides	2-sided

Secondary: TGFbeta expression

End point title	TGFbeta expression

End point description:

End point type	Secondary

End point timeframe:

mRNA expression week 0 an 7

End point values	Infliximab+vitamin D	Infliximab+placebo vitamin D	Placebo infliximab+Vitamin D	PLacebo infliximab+placebo vitamin D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	8[15]	14[16]	8[17]
Units: relative quantification				
median (confidence interval 95%)				
week 0	0.015 (0.0043 to 0.026)	0.011 (0.0033 to 0.0186)	0.017 (0.0084 to 0.026)	0.017 (0.0052 to 0.03)
week 6	0.013 (0.0025 to 0.023)	0.008 (0.0016 to 0.014)	0.012 (0.0054 to 0.019)	0.02 (0.0024 to 0.038)

Notes:

[15] - w7=7

[16] - w7=16

[17] - w7=5

Statistical analyses

Statistical analysis title	mixed model
Comparison groups	Infliximab+vitamin D v Infliximab+placebo vitamin D v Placebo infliximab+Vitamin D v PLacebo infliximab+placebo vitamin D
Number of subjects included in analysis	37
Analysis specification	Post-hoc
Analysis type	other
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	median ratio
Confidence interval	
level	95 %
sides	2-sided

Secondary: IL10 expression

End point title	IL10 expression

End point description:

End point type	Secondary

End point timeframe:

IL10 mRNA expression week 0 and 7.

End point values	Infliximab+vitamin D	Infliximab+placebo vitamin D	Placebo infliximab+Vitamin D	PLacebo infliximab+placebo vitamin D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	8[18]	14[19]	8[20]
Units: relative quantification				
median (confidence interval 95%)				
week 0	0.00049 (0.00015 to 0.00083)	0.00048 (0.00016 to 0.00079)	0.00056 (0.00028 to 0.00083)	0.00032 (0.00011 to 0.00054)

week 7	0.00024 (0.00005 to 0.00042)	0.00036 (0.00008 to 0.00063)	0.00035 (0.00017 to 0.00054)	0.0003 (0.00004 to 0.00054)

Notes:

[18] - w7=7

[19] - w7=16

[20] - w7=5

Statistical analyses

No statistical analyses for this end point

Secondary: IFNgamma

End point title	IFNgamma

End point description:

End point type	Secondary

End point timeframe:

mRNA IFNgamma expression week 0 an 7. logarithmic transformed data.

End point values	Infliximab+vitamin D	Infliximab+placebo vitamin D	Placebo infliximab+Vitamin D	PLacebo infliximab+placebo vitamin D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	8[21]	14[22]	8[23]
Units: relative quantification				
median (confidence interval 95%)				
week 0	0.00049 (0 to 0.001)	0.0011 (0 to 0.0022)	0.00076 (0.00019 to 0.0013)	0.00052 (0 to 0.0011)
week 7	0.0001 (0 to 0.00021)	0.0004 (0 to 0.00085)	0.00036 (0.00009 to 0.00063)	0.0005 (0 to 0.0011)

Notes:

[21] - w7=7

[22] - w7=16

[23] - w7=5

Statistical analyses

No statistical analyses for this end point

Secondary: TNFalpha expression

End point title	TNFalpha expression

End point description:

End point type	Secondary

End point timeframe:

mRNA expression week 0 and 7

End point values	Infliximab+vitamin D	Infliximab+placebo vitamin D	Placebo infliximab+Vitamin D	PLacebo infliximab+placebo vitamin D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	8[24]	14[25]	8[26]
Units: relative quantification				
median (confidence interval 95%)				
week 0	0.0027 (0.0014 to 0.004)	0.0023 (0.0013 to 0.0034)	0.0024 (0.0016 to 0.0032)	0.0019 (0.001 to 0.0028)
week 7	0.0016 (0.00045 to 0.0028)	0.0011 (0.0003 to 0.0019)	0.0016 (0.00083 to 0.0024)	0.0023 (0.00041 to 0.0042)

Notes:

[24] - w7=7

[25] - w7=16

[26] - w7=5

Statistical analyses

No statistical analyses for this end point

Secondary: CAMP expression

End point title	CAMP expression

End point description:

End point type	Secondary

End point timeframe:

mRNA expression of CAMP week 0 and 7

End point values	Infliximab+vitamin D	Infliximab+placebo vitamin D	Placebo infliximab+Vitamin D	PLacebo infliximab+placebo vitamin D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	8[27]	14[28]	8[29]
Units: relative quantification				
median (confidence interval 95%)				
week 0	0.00059 (0.000086 to 0.0011)	0.00053 (0.000095 to 0.00097)	0.0007 (0.00028 to 0.0011)	0.00059 (0.00011 to 0.0011)
week 7	0.00023 (-0.00001 to 0.00047)	0.00026 (-0.000013 to 0.00053)	0.00073 (0.00021 to 0.0013)	0.00075 (-0.00013 to 0.0016)

Notes:

[27] - w7=7

[28] - w7=16

[29] - w7=5

Statistical analyses

No statistical analyses for this end point

Secondary: CDEIS score

End point title	CDEIS score

End point description:

End point type	Secondary

End point timeframe:

CDEIS score are given week 0 and week 7

End point values	Infliximab+vitamin D	Infliximab+placebo vitamin D	Placebo infliximab+Vitamin D	PLacebo infliximab+placebo vitamin D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8[30]	8	16	8
Units: score				
median (confidence interval 95%)				
week 0	17.49 (11.4 to 23.58)	18.30 (11.92 to 24.68)	14 (10.55 to 17.45)	17.39 (11.33 to 23.44)
week 7	2.37 (0.57 to 4.17)	4.31 (1.18 to 7.45)	10.49 (5.1 to 15.89)	12.11 (3.3 to 20.92)

Notes:

[30] - w7=7

Statistical analyses

No statistical analyses for this end point

Secondary: Calprotectin

End point title	Calprotectin

End point description:

End point type	Secondary

End point timeframe:

calprotectin measurements during intervention (week 0 to 7) and during follow up.

End point values	Infliximab+vitamin D	Infliximab+placebo vitamin D	Placebo infliximab+Vitamin D	PLacebo infliximab+placebo vitamin D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	8	16	8
Units: mg/kg				
median (confidence interval 95%)				
week 0	644 (180 to 1109)	712 (199 to 1226)	639 (305 to 972)	782 (218 to 1346)

week 2	116 (22 to 210)	254 (70 to 437)	575 (274 to 877)	1150 (288 to 2011)
week 6	61 (11 to 110)	151 (41 to 260)	395 (187 to 602)	678 (187 to 1169)
follow up week 15	32 (0 to 69)	205 (0 to 431)	87 (22 to 152)	328 (0 to 747)
follow up week 23	81 (0 to 198)	321 (0 to 731)	64 (10 to 118)	166 (0 to 429)
follow up week 31	74 (0 to 178)	132 (0 to 302)	62 (0 to 129)	132 (0 to 302)
follow up week 52	62 (0 to 129)	67 (0 to 149)	65 (22 to 107)	113 (0 to 253)

Statistical analyses

No statistical analyses for this end point

Secondary: HBI score

End point title	HBI score

End point description:

End point type	Secondary

End point timeframe:

HBI score week 0, 2 and 6 during intervention and in follow up week 15, 23, 31 and 52. The given medians are from log transformed data which are back-transformed to reflect the mixed model data.

End point values	Infliximab+vitamin D	Infliximab+placebo vitamin D	Placebo infliximab+Vitamin D	PLacebo infliximab+placebo vitamin D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	8	16	8
Units: score				
median (confidence interval 95%)				
week 0	8 (6.3 to 9.7)	7.5 (5.8 to 9.2)	6.9 (5.6 to 8.1)	6.8 (5 to 8.5)
week 2	4.1 (1.7 to 6.6)	4.5 (2.1 to 6.9)	5.1 (3.4 to 6.9)	5.8 (3.3 to 8.2)
week 6	3.5 (1 to 6)	3.8 (1.2 to 6.2)	6 (4.2 to 7.8)	5.9 (3.4 to 8.4)
follow up week 15	2.1 (1 to 3.3)	4.8 (2.3 to 7.4)	3.7 (2.3 to 5)	2.7 (1.3 to 4.2)
follow up week 23	3.9 (1.1 to 6.7)	3.7 (1 to 6.4)	3.3 (1.8 to 4.8)	2.3 (1 to 3.9)
follow up week 31	2.9 (1 to 4.7)	4.2 (1 to 7.3)	3.2 (2 to 4.5)	3.1 (1.2 to 4.9)
follow up week 52	4.3 (1.6 to 7.1)	3.7 (1.6 to 5.9)	3.2 (1.9 to 4.4)	1.9 (1 to 3.3)

Statistical analyses

No statistical analyses for this end point

Secondary: CRP

End point title	CRP

End point description:

End point type	Secondary

End point timeframe:

CRP week 0, 2 and 6 and 15, 23, 31 and 52.The given medians are from log transformed data which are back-transformed to reflect the mixed model data.

End point values	Infliximab+vitamin D	Infliximab+placebo vitamin D	Placebo infliximab+Vitamin D	PLacebo infliximab+placebo vitamin D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	8	16	8
Units: mg/l				
median (confidence interval 95%)				
week 0	3.9 (0.2 to 7.7)	10.7 (0.5 to 20.9)	5.1 (1.7 to 8.5)	7.5 (0.4 to 14.6)
week 2	1.7 (0.2 to 3.3)	3.1 (0.3 to 5.8)	4.2 (1.5 to 6.9)	8.1 (0.8 to 15.5)
week 6	1.4 (0.2 to 2.5)	3.3 (0.5 to 6)	5.1 (2 to 8.1)	6.4 (1.1 to 11.7)
follow up week 15	1 (0.2 to 1.9)	3.3 (0.7 to 5.8)	1.6 (0.8 to 2.4)	2.4 (0.4 to 4.5)
follow up week 23	1.3 (0 to 2.6)	3.3 (0.2 to 6.3)	1.2 (0.5 to 2)	2.5 (0 to 5.1)
follow up week 31	1.2 (0.1 to 2.3)	2.9 (0.4 to 5.5)	1.1 (0.5 to 1.8)	2.8 (0.3 to 5.3)
follow up week 52	1 (0 to 2)	4.1 (0.4 to 7.8)	1.6 (0.7 to 2.6)	2.1 (0.1 to 4.2)

Statistical analyses

No statistical analyses for this end point

Secondary: Short health score

End point title	Short health score

End point description:

End point type	Secondary

End point timeframe:

Short health during intervention

End point values	Infliximab+vitamin D	Infliximab+placebo vitamin D	Placebo infliximab+Vitamin D	PLacebo infliximab+placebo vitamin D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	8	16	8
Units: score				
median (confidence interval 95%)				
week 0	19.3 (10.9 to 27.6)	16.1 (9.1 to 23.1)	14.2 (9.9 to 18.6)	16.2 (9.2 to 23.2)
week 2	16.3 (6.5 to 26.1)	9.4 (3.8 to 15)	12.6 (7.3 to 17.9)	10.7 (4.4 to 17.1)

week 6	11.4 (3.7 to 19.2)	9.6 (3.4 to 15.8)	10.9 (5.9 to 15.9)	10.9 (3.9 to 17.9)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: 25-hydroxyvitamin D

End point title	25-hydroxyvitamin D

End point description:

End point type	Other pre-specified

End point timeframe:

25 hydroxyvitamin D measurement for safety

End point values	Infliximab+vitamin D	Infliximab+placebo vitamin D	Placebo infliximab+Vitamin D	PLacebo infliximab+placebo vitamin D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	8	16	8
Units: nmol/l				
median (confidence interval 95%)				
week 0	42 (29 to 55)	61 (42 to 80)	64 (50 to 78)	62 (43 to 81)
week 2	167 (134 to 201)	49 (39 to 58)	172 (148 to 196)	57 (46 to 69)
week 6	192 (152 to 233)	47 (38 to 57)	219 (187 to 251)	57 (45 to 68)
follow up week 15	109 (81 to 138)	41 (30 to 51)	148 (122 to 173)	59 (45 to 68)
follow up week 23	84 (57 to 111)	55 (40 to 71)	115 (92 to 139)	65 (45 to 84)
follow up week 31	87 (66 to 107)	71 (55 to 86)	98 (84 to 112)	64 (50 to 79)
follow up week 52	64 (50 to 79)	64 (48 to 81)	83 (70 to 96)	57 (43 to 71)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: calcium ion

End point title	calcium ion

End point description:

End point type	Other pre-specified

End point timeframe:

calcium ion measured for safety during intervention and follow up

End point values	Infliximab+vitamin D	Infliximab+placebo vitamin D	Placebo infliximab+Vitamin D	PLacebo infliximab+placebo vitamin D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	8	16	8
Units: mmol/l				
median (confidence interval 95%)				
week 0	1.27 (1.25 to 1.3)	1.25 (1.23 to 1.27)	1.25 (1.24 to 1.27)	1.26 (1.24 to 1.28)
week 2	1.27 (1.25 to 1.29)	1.25 (1.23 to 1.27)	1.28 (1.26 to 1.29)	1.24 (1.22 to 1.26)
week 6	1.27 (1.24 to 1.29)	1.25 (1.23 to 1.27)	1.27 (1.25 to 1.28)	1.25 (1.23 to 1.27)
follow up week 15	1.27 (1.25 to 1.29)	1.24 (1.23 to 1.26)	1.27 (1.26 to 1.28)	1.25 (1.23 to 1.26)
follow up week 23	1.25 (1.23 to 1.27)	1.24 (1.22 to 1.26)	1.26 (1.25 to 1.27)	1.23 (1.22 to 1.25)
follow up week 31	1.26 (1.23 to 1.28)	1.25 (1.23 to 1.27)	1.26 (1.24 to 1.28)	1.25 (1.22 to 1.27)
follow up week 52	1.25 (1.22 to 1.27)	1.25 (1.22 to 1.27)	1.27 (1.25 to 1.29)	1.25 (1.22 to 1.28)

Statistical analyses

No statistical analyses for this end point

Post-hoc: CYP27B1 expression

End point title	CYP27B1 expression
End point description:	
End point type	Post-hoc
End point timeframe:	
mRNA expression in CYP27B1 week 0 and 7	

End point values	Infliximab+vitamin D	Infliximab+placebo vitamin D	Placebo infliximab+Vitamin D	PLacebo infliximab+placebo vitamin D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7[31]	8[32]	14[33]	8[34]
Units: relative quantification				
median (confidence interval 95%)				
week 0	0.0019 (0 to 0.0053)	0.0024 (0 to 0.0064)	0.0022 (0 to 0.0049)	0.0009 (0 to 0.0024)
week 7	0.00005 (0 to 0.00014)	0.00012 (0 to 0.00031)	0.0012 (0 to 0.0024)	0.001 (0 to 0.0028)

Notes:
[31] - w7=4
[32] - w7=6
[33] - w7=15
[34] - w7=5

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

adverse event are reported separately during week 0 to 7 the intervention and separately from follow up week 8 to 52.

Adverse event reporting additional description:

patients were questioned if they have had adverse events every time they went for control visits

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10

Reporting groups

Reporting group title	Infliximab+vitamin D - intervention

Reporting group description:

from week 0 to 7

Reporting group title	Infliximab+placebo vitamin D - intervention

Reporting group description:

week 0 to 7

Reporting group title	Placebo infliximab+Vitamin D - intervention

Reporting group description:

week 0 to 7

Reporting group title	Placebo infliximab+placebo vitamin D - intervention

Reporting group description:

week 0 to 7

Reporting group title	Infliximab+vitamin D - follow up

Reporting group description: -

Reporting group title	Infliximab+placebo vitamin D - follow up

Reporting group description:

week 8 to 52

Reporting group title	Placebo infliximab+Vitamin D - follow up

Reporting group description:

week 8 to 52

Reporting group title	PLacebo infliximab+placebo vitamin D - follow up

Reporting group description: -

Serious adverse events	Infliximab+vitamin D - intervention	Infliximab+placebo vitamin D - intervention	Placebo infliximab+Vitamin D - intervention
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 8 (25.00%)	1 / 8 (12.50%)	0 / 16 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Abdominal pain	Additional description: sever abdominal pain after colonoscopy, patient was in hospitalised and examined and observed for perforation. no perforation was found.		

subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 16 (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			
Stenosis	Additional description: fibrostenosis		
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 16 (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
Product issues			
Allergic respiratory symptom	Additional description: infusion reaction with second infusion treatment, this was infliximab (patient were unblinded after the reaction)		
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Throat irritation	Additional description: patient experienced throat irritation and other unspecified symptoms. she was in hospitalised to observation for drug induced reaction. this was not the case. The unspecified symptoms were unrelated to the study drug		
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo infliximab+placebo vitamin D - intervention	Infliximab+vitamin D - follow up	Infliximab+placebo vitamin D - follow up
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 7 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Abdominal pain	Additional description: sever abdominal pain after colonoscopy, patient was in hospitalised and examined and observed for perforation. no perforation was found.		
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Stenosis	Additional description: fibrostenosis		

subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 7 (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
Product issues			
Allergic respiratory symptom	Additional description: infusion reaction with second infusion treatment, this was infliximab (patient were unblinded after the reaction)		
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 7 (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			
Throat irritation	Additional description: patient experienced throat irritation and other unspecified symptoms. she was in hospitalised to observation for drug induced reaction. this was not the case. The unspecified symptoms were unrelated to the study drug		
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 7 (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	Placebo infliximab+Vitamin D - follow up	PLacebo infliximab+placebo vitamin D - follow up	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 16 (0.00%)	0 / 6 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
Abdominal pain	Additional description: sever abdominal pain after colonoscoscopy, patient was in hospitalised and examined and observed for perforation. no perforation was found.		
subjects affected / exposed	0 / 16 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Stenosis	Additional description: fibrostenosis		
subjects affected / exposed	0 / 16 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Allergic respiratory symptom	Additional description: infusion reaction with second infusion treatment, this was infliximab (patient were unblinded after the reaction)		

subjects affected / exposed	0 / 16 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Throat irritation	Additional description: patient experienced throat irritation and other unspecified symptoms. she was in hospitalised to observation for drug induced reaction. this was not the case. The unspecified symptoms were unrelated to the study drug		
subjects affected / exposed	0 / 16 (0.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Infliximab+vitamin D - intervention	Infliximab+placebo vitamin D - intervention	Placebo infliximab+Vitamin D - intervention
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 8 (50.00%)	5 / 8 (62.50%)	7 / 16 (43.75%)
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Insomnia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Iron deficiency			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Hypophosphataemia			

subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Conjunctivitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Gastroenteritis			
subjects affected / exposed	0 / 8 (0.00%)	2 / 8 (25.00%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Abdominal pain			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	3 / 16 (18.75%)
occurrences (all)	0	1	3
Overgrowth bacterial	Additional description: In the small bowel		
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Parasitic test positive	Additional description: threadworm seen at endoscopy		
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Flatulence			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Dyspepsia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Gastric hypomotility			

subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Fistula			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Stenosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Transaminases increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Dermatitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Hidradenitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Acne			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Dermatitis allergic			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			

Weight increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Pharyngitis			
subjects affected / exposed	0 / 8 (0.00%)	3 / 8 (37.50%)	1 / 16 (6.25%)
occurrences (all)	0	3	1
Candida infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Cystitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Placebo infliximab+placebo vitamin D - intervention	Infliximab+vitamin D - follow up	Infliximab+placebo vitamin D - follow up
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 8 (50.00%)	4 / 6 (66.67%)	7 / 7 (100.00%)
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Insomnia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Iron deficiency			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Conjunctivitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	2 / 7 (28.57%)
occurrences (all)	0	1	2
Abdominal pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Overgrowth bacterial	Additional description: In the small bowel		
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Parasitic test positive	Additional description: threadworm seen at endoscopy		
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Vomiting			

subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Gastric hypomotility			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Fistula			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Stenosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Transaminases increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Dermatitis			
subjects affected / exposed	0 / 8 (0.00%)	3 / 6 (50.00%)	0 / 7 (0.00%)
occurrences (all)	0	3	0
Hidradenitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Acne			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Dermatitis allergic			

subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Weight increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Pharyngitis			
subjects affected / exposed	0 / 8 (0.00%)	2 / 6 (33.33%)	3 / 7 (42.86%)
occurrences (all)	0	2	4
Candida infection			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Influenza			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Placebo infliximab+Vitamin D - follow up	PLacebo infliximab+placebo vitamin D - follow up	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 16 (62.50%)	5 / 6 (83.33%)	
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 16 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			

Dizziness			
subjects affected / exposed	0 / 16 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 16 (6.25%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Insomnia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
Iron deficiency			
subjects affected / exposed	2 / 16 (12.50%)	1 / 6 (16.67%)	
occurrences (all)	2	1	
Hypophosphataemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Eye disorders			
Conjunctivitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 16 (0.00%)	2 / 6 (33.33%)	
occurrences (all)	0	2	
Gastroenteritis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Abdominal pain			
subjects affected / exposed	3 / 16 (18.75%)	2 / 6 (33.33%)	
occurrences (all)	3	2	
Overgrowth bacterial	Additional description: In the small bowel		
subjects affected / exposed	2 / 16 (12.50%)	0 / 6 (0.00%)	
occurrences (all)	2	0	
Constipation			

subjects affected / exposed	1 / 16 (6.25%)	1 / 6 (16.67%)	
occurrences (all)	1	1	
Parasitic test positive	Additional description: threadworm seen at endoscopy		
subjects affected / exposed	0 / 16 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Flatulence			
subjects affected / exposed	0 / 16 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Vomiting			
subjects affected / exposed	0 / 16 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Dyspepsia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Gastric hypomotility			
subjects affected / exposed	0 / 16 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Fistula			
subjects affected / exposed	0 / 16 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Stenosis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Hepatobiliary disorders			
Transaminases increased			
subjects affected / exposed	1 / 16 (6.25%)	1 / 6 (16.67%)	
occurrences (all)	1	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 16 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 16 (6.25%)	1 / 6 (16.67%)	
occurrences (all)	1	1	
Dermatitis			

subjects affected / exposed	1 / 16 (6.25%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Hidradenitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Acne			
subjects affected / exposed	0 / 16 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Dermatitis allergic			
subjects affected / exposed	1 / 16 (6.25%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Urticaria			
subjects affected / exposed	0 / 16 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Endocrine disorders			
Weight increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 6 (16.67%)	
occurrences (all)	1	1	
Infections and infestations			
Pharyngitis			
subjects affected / exposed	2 / 16 (12.50%)	2 / 6 (33.33%)	
occurrences (all)	2	2	
Candida infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Influenza			
subjects affected / exposed	0 / 16 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Cystitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported