Clinical trial results:
Double-blind, randomised, placebo-controlled, multi-centre phase II study to evaluate the efficacy and safety of three different dosages of oral Trichuris suis ova (TSO) suspension in active Crohn's disease

Summary

EudraCT number	2006-000720-13
Trial protocol	DE AT DK CZ
Global end of trial date	18 February 2014

Results information

Result version number	v1 (current)
This version publication date	25 September 2016
First version publication date	25 September 2016
Summary attachment (see zip file)	Study Report Synopsis (TSU2_CSR_synopsis_Final_20150730 - EudraCT-DB.pdf)

Trial information

Trial identification

Sponsor protocol code	TSU-2/CDA

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01279577
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Dr Falk Pharma GmbH
Sponsor organisation address	Leinenweberstrasse 5, Freiburg, Germany, 79108
Public contact	Department of Medical Science, Dr Falk Pharma GmbH, ++49 761-1514-0,
Scientific contact	Department of Medical Science, Dr Falk Pharma GmbH, ++49 761-1514-0,

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 July 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 February 2014
Global end of trial reached?	Yes
Global end of trial date	18 February 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of three doses of oral TSO suspension vs. placebo for the induction of remission in Crohn’s disease.

Protection of trial subjects:

Prior to recruitment of patients, all relevant documents of the clinical study were submitted and approved by the Independent Ethics Committees (IECs) responsible for the participating investigators. Written consent documents embodied the elements of informed consent as described in the Declaration of Helsinki, the ICH Guidelines for Good Clinical Practice (GCP) and were in accordance with all applicable laws and regulations. The informed consent form and patient information sheet described the planned and permitted uses, transfers and disclosures of the patient’s personal data and personal health information for purposes of conducting the study. The informed consent form and the patient information sheet further explained the nature of the study, its objectives and potential risks and benefits as well as the date informed consent was given. Before being enrolled in the clinical trial, every patient was informed that participation in this trial was voluntary and that he/she could withdraw from the study at any time without giving a reason and without having to fear any loss in his/her medical care. The patient’s consent was obtained in writing before the start of the study. By signing the informed consent, the patient declared that he/she was participating voluntarily and intended to follow the study protocol instructions and the instructions of the investigator and to answer the questions asked during the course of the trial. For colonoscopy and biopsy sampling to be performed for confirmation of diagnosis of collagenous colitis by the central pathologist, the patients received the standard preparation for bowel cleansing and sedation during the colonoscopy as routinely performed at the study sites.

Background therapy:

No concomitant background therapy, except stable dosing with oral mesalazine, was allowed during the trial.

Evidence for comparator:

Using a placebo arm in this clinical trial as reference was ethically justified and in accordance with Article 29 of the Declaration of Helsinki (2008), as there were compelling and scientifically sound methodological reasons for the use of a placebo control in this trial, since this was a proof-of-concept study for induction of clinical remission with TSO in mild-moderately active Crohn's disease patients.

Actual start date of recruitment	16 November 2010
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	Austria: 8
Country: Number of subjects enrolled	Czech Republic: 11
Country: Number of subjects enrolled	Denmark: 10
Country: Number of subjects enrolled	Germany: 188

Country: Number of subjects enrolled	Switzerland: 35
Worldwide total number of subjects	252
EEA total number of subjects	217

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)	249
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This clinical trial was conducted in 53 sites in 5 countries: 1 center in Austria, 5 centers in the Czech Republic, 2 centers in Denmark, 43 centers in Germany, and 2 centers in Switzerland. First patient was screened (entered) at the 16 Nov 2010. Last patient completed his last visit at 18 Feb 2014

Pre-assignment

Screening details:

446 patients were screened to fullfill the In-/Exclusion criteria. Of them, 252 patients were randomized and treated with TSO or placebo.

Pre-assignment period milestones

Number of subjects started	446[1]
Number of subjects completed	252

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Protocol deviation: 194

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 446 patients were screened. During screening, the In/Exclusion criteria with regard to laboratory and clinical signs of disease activity were prospectively checked: 252 patients had a proof of active inflammatory Crohn's disease and were subsequently randomized and treated in the double-blind phase.

Period 1

Period 1 title	Double-blind 12-week treatment phase (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

The appearance and taste of the placebo solution was indistinguishable from the verum TSO suspension.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Placebo solution (15 ml/day) fortnightly (6-times)

Arm type	Placebo
Investigational medicinal product name	Placebo solution
Investigational medicinal product code	Placebo
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

15ml placebo solution/bottle to be administered fortnightly (i.e., every 2 weeks) 6-times during the treatment period

Arm title	TSO 250

Arm description:

Suspension of 250 embryonated, viable TSO/15 ml/day fortnightly (i.e., every 2 weeks), 6 times during treatment phase

Arm type	Experimental
Investigational medicinal product name	Suspension of 250 embryonated, viable TSO/15 ml
Investigational medicinal product code	TSO 250
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Suspension of 250 embryonated, viable TSO/15 ml/day fortnightly (i.e., every 2 weeks), 6 times during treatment phase

Arm title	TSO 2.500

Arm description:

Suspension of 2.500 embryonated, viable TSO/15 ml/day fortnightly (i.e., every 2 weeks), 6 times during treatment phase

Arm type	Experimental
Investigational medicinal product name	Suspension of 250 embryonated, viable TSO/15 ml/day
Investigational medicinal product code	TSO 2.500
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Suspension of 2.500 embryonated, viable TSO/15 ml/day fortnightly (i.e., every 2 weeks), 6 times during treatment phase

Arm title	TSO 7.500

Arm description:

Suspension of 7.500 embryonated, viable TSO/15 ml/day fortnightly (i.e., every 2 weeks), 6 times during treatment phase

Arm type	Experimental
Investigational medicinal product name	Suspension of 7.500 embryonated, viable TSO/15 ml/day fortnightly
Investigational medicinal product code	TSO 7.500
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Suspension of 7.500 embryonated, viable TSO/15 ml/day fortnightly (i.e., every 2 weeks), 6 times during treatment phase

Number of subjects in period 1	Placebo	TSO 250	TSO 2.500
Started	70	39	71
Completed	51	27	51
Not completed	19	12	20
Consent withdrawn by subject	1	2	3
Forbidden concomitant treatment with antibiotics	1	1	-
Adverse event, non-fatal	1	2	1
Pregnancy	-	-	-
Lack of efficacy	16	7	16

Number of subjects in period 1	TSO 7.500
Started	72
Completed	55
Not completed	17
Consent withdrawn by subject	4
Forbidden concomitant treatment with antibiotics	-
Adverse event, non-fatal	1
Pregnancy	2
Lack of efficacy	10

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Placebo solution (15 ml/day) fortnightly (6-times)	
Reporting group title	TSO 250
Reporting group description:	
Suspension of 250 embryonated, viable TSO/15 ml/day fortnightly (i.e., every 2 weeks), 6 times during treatment phase	
Reporting group title	TSO 2.500
Reporting group description:	
Suspension of 2.500 embryonated, viable TSO/15 ml/day fortnightly (i.e., every 2 weeks), 6 times during treatment phase	
Reporting group title	TSO 7.500
Reporting group description:	
Suspension of 7.500 embryonated, viable TSO/15 ml/day fortnightly (i.e., every 2 weeks), 6 times during treatment phase	

Reporting group values	Placebo	TSO 250	TSO 2.500
Number of subjects	70	39	71
Age categorical Units: Subjects			
Adults (18-64 years)	69	39	70
From 65-84 years	1	0	1
Age continuous Units: years			
arithmetic mean	37.7	37.8	37.8
standard deviation	± 12.8	± 9.5	± 11
Gender categorical Units: Subjects			
Female	44	20	42
Male	26	19	29
Ethnic Group Units: Subjects			
White	70	39	70
Hispanic	0	0	0
Arabic	0	0	1
Inuit	0	0	0
Smoking status Units: Subjects			
Current smoker	18	14	20
Former smoker	22	10	23
Non-smoker	30	15	28
Disease Localization Units: Subjects			
Ileocecal	37	18	34
Ileocolonic	14	12	16
Colonic	12	9	13
Missing	7	0	8

Concomitant mesalamine treatment Units: Subjects			
yes	12	9	16
no	58	30	55
Stool Calprotectin >5x ULN at Baseline Units: Subjects			
Yes	49	29	58
no	21	10	13
CRP > 2x ULN at Baseline Units: Subjects			
Yes	38	17	32
No	32	22	39
BMI Units: kg/squaremeter			
arithmetic mean	24.2	23.1	24.5
standard deviation	± 4.4	± 4.2	± 4.6
CDAI at Baseline Units: Points			
arithmetic mean	271	267	266
standard deviation	± 47	± 40	± 39
Stool calprotectin at Baseline Units: µg/g stool			
arithmetic mean	1146	1073	1614
standard deviation	± 1846	± 1473	± 2115
Disease duration Units: Years			
arithmetic mean	9.5	8	7.9
standard deviation	± 7.4	± 6.8	± 7.8
CRP Units: mg/ml			
median	10.8	6.9	8.8
full range (min-max)	0.1 to 150.8	0.1 to 99.9	0.1 to 135.5

Reporting group values	TSO 7.500	Total	
Number of subjects	72	252	
Age categorical Units: Subjects			
Adults (18-64 years)	71	249	
From 65-84 years	1	3	
Age continuous Units: years			
arithmetic mean	34.8		
standard deviation	± 11	-	
Gender categorical Units: Subjects			
Female	48	154	
Male	24	98	
Ethnic Group Units: Subjects			
White	70	249	
Hispanic	1	1	

Arabic	0	1	
Inuit	1	1	
Smoking status Units: Subjects			
Current smoker	21	73	
Former smoker	18	73	
Non-smoker	33	106	
Disease Localization Units: Subjects			
Ileocecal	38	127	
Ileocolonic	16	58	
Colonic	12	46	
Missing	6	21	
Concomitant mesalamine treatment Units: Subjects			
yes	17	54	
no	55	198	
Stool Calprotectin >5x ULN at Baseline Units: Subjects			
Yes	50	186	
no	22	66	
CRP > 2x ULN at Baseline Units: Subjects			
Yes	41	128	
No	31	124	
BMI Units: kg/squaremeter			
arithmetic mean	24.9		
standard deviation	± 5.9	-	
CDAI at Baseline Units: Points			
arithmetic mean	271		
standard deviation	± 47	-	
Stool calprotectin at Baseline Units: µg/g stool			
arithmetic mean	1452		
standard deviation	± 2226	-	
Disease duration Units: Years			
arithmetic mean	6.4		
standard deviation	± 6.4	-	
CRP Units: mg/ml			
median	12.8		
full range (min-max)	0.1 to 121.2	-	

End points

End points reporting groups	
Reporting group title	Placebo
Reporting group description:	
Placebo solution (15 ml/day) fortnightly (6-times)	
Reporting group title	TSO 250
Reporting group description:	
Suspension of 250 embryonated, viable TSO/15 ml/day fortnightly (i.e., every 2 weeks), 6 times during treatment phase	
Reporting group title	TSO 2.500
Reporting group description:	
Suspension of 2.500 embryonated, viable TSO/15 ml/day fortnightly (i.e., every 2 weeks), 6 times during treatment phase	
Reporting group title	TSO 7.500
Reporting group description:	
Suspension of 7.500 embryonated, viable TSO/15 ml/day fortnightly (i.e., every 2 weeks), 6 times during treatment phase	

Primary: Number (%) of patients with clinical remission (CDAI <150)	
End point title	Number (%) of patients with clinical remission (CDAI <150)
End point description:	
Number (%) of patients with clinical remission defined as a Clinical Disease Activity Index (according to Best) of <150 points at week 12 (last observation carried forward)	
End point type	Primary
End point timeframe:	
at Week 12 (LOCF)	

End point values	Placebo	TSO 250	TSO 2.500	TSO 7.500
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	70	39	71	72
Units: Number of patients	30	15	25	34

Statistical analyses

Statistical analysis title	Final Analysis (FAS): TSO 250 vs placebo
Comparison groups	Placebo v TSO 250
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.6725 [2]
Method	Normal approximation test
Parameter estimate	Risk difference (RD)
Point estimate	-0.044

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.236
upper limit	0.148

Notes:

[1] - Test for superiority of TSO 250 versus placebo. Normal approximation tests for rates were used to test the three null hypotheses on each step against their alternative hypotheses. In order to adjust for multiplicity, a closed testing procedure with the Simes intersection test was employed for hypothesis testing on each step. For confirmatory hypothesis testing the inverse normal method of combining the p-values of the normal approximation.
[2] - Testing of H0 (пPla > пTSO250) by means of the normal approximation test for rates (α = 0.025 one-sided). A closed testing procedure with the Simes intersection test was used toadjust for multiplicity testing of all TSO groups versus placebo

Statistical analysis title	Final Analysis (FAS): TSO 2.500 vs placebo
Comparison groups	Placebo v TSO 2.500
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.824 [4]
Method	Normal approximation test
Parameter estimate	Risk difference (RD)
Point estimate	-0.076
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.237
upper limit	0.084

Notes:

[3] - Test for superiority of TSO 2.500 versus placebo. Normal approximation tests for rates were used to test the three null hypotheses on each step against their alternative hypotheses. In order to adjust for multiplicity, a closed testing procedure with the Simes intersection test was employed for hypothesis testing on each step. For confirmatory hypothesis testing the inverse normal method of combining the p-values of the normal approximation.
[4] - Testing of H0 (пPla > пTSO2.500) by means of the normal approximation test for rates (α = 0.025 one-sided). A closed testing procedure with the Simes intersection test was used toadjust for multiplicity testing of all TSO groups versus placebo

Statistical analysis title	Final Analysis (FAS): TSO 7.500 vs placebo
Comparison groups	Placebo v TSO 7.500
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	= 0.3006 [6]
Method	Normal approximation test
Parameter estimate	Risk difference (RD)
Point estimate	0.044
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.12
upper limit	0.207

Notes:

[5] - Test for superiority of TSO 7.500 versus placebo. Normal approximation tests for rates were used to test the three null hypotheses on each step against their alternative hypotheses. In order to adjust for multiplicity, a closed testing procedure with the Simes intersection test was employed for hypothesis testing on each step. For confirmatory hypothesis testing the inverse normal method of combining the p-values of the normal approximation.

[6] - Testing of H0 (πPla > πTSO7.500) by means of the normal approximation test for rates (α = 0.025 one-sided). A closed testing procedure with the Simes intersection test was used toadjust for multiplicity testing of all TSO groups versus placebo

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 12 weeks	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	14.0
Reporting groups	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	TSO 250
Reporting group description: -	
Reporting group title	TSO 2.500
Reporting group description: -	
Reporting group title	TSO 7.500
Reporting group description: -	

Serious adverse events	Placebo	TSO 250	TSO 2.500
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 70 (17.14%)	2 / 39 (5.13%)	4 / 71 (5.63%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Surgical and medical procedures			
Intestinal resection			
subjects affected / exposed	0 / 70 (0.00%)	0 / 39 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillectomy			
subjects affected / exposed	1 / 70 (1.43%)	0 / 39 (0.00%)	0 / 71 (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
Pregnancy, puerperium and perinatal conditions			
Pregnancy			
subjects affected / exposed	0 / 70 (0.00%)	0 / 39 (0.00%)	0 / 71 (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
Abortion spontaneous			

subjects affected / exposed	0 / 70 (0.00%)	0 / 39 (0.00%)	0 / 71 (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
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 70 (1.43%)	0 / 39 (0.00%)	0 / 71 (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
Gastrointestinal disorders			
Crohn's disease deterioration			
subjects affected / exposed	3 / 70 (4.29%)	1 / 39 (2.56%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	2 / 70 (2.86%)	1 / 39 (2.56%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileal stenosis			
subjects affected / exposed	0 / 70 (0.00%)	0 / 39 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	0 / 70 (0.00%)	0 / 39 (0.00%)	0 / 71 (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
Small intestinal stenosis			
subjects affected / exposed	1 / 70 (1.43%)	0 / 39 (0.00%)	0 / 71 (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
Skin and subcutaneous tissue disorders			
Granuloma skin			
subjects affected / exposed	0 / 70 (0.00%)	0 / 39 (0.00%)	0 / 71 (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

Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 70 (0.00%)	0 / 39 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tubulointerstitial nephritis			
subjects affected / exposed	1 / 70 (1.43%)	0 / 39 (0.00%)	0 / 71 (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
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 70 (1.43%)	0 / 39 (0.00%)	0 / 71 (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
Musculoskeletal and connective tissue disorders			
Fistula			
subjects affected / exposed	0 / 70 (0.00%)	0 / 39 (0.00%)	0 / 71 (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
Intervertebral disc protrusion			
subjects affected / exposed	0 / 70 (0.00%)	0 / 39 (0.00%)	0 / 71 (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			
Pyelocystitis			
subjects affected / exposed	0 / 70 (0.00%)	0 / 39 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 70 (0.00%)	0 / 39 (0.00%)	0 / 71 (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
Anal abscess			

subjects affected / exposed	1 / 70 (1.43%)	0 / 39 (0.00%)	0 / 71 (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
Gastroenteritis norovirus			
subjects affected / exposed	1 / 70 (1.43%)	0 / 39 (0.00%)	0 / 71 (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	TSO 7.500		
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 72 (11.11%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Surgical and medical procedures			
Intestinal resection			
subjects affected / exposed	0 / 72 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tonsillectomy			
subjects affected / exposed	0 / 72 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Pregnancy			
subjects affected / exposed	2 / 72 (2.78%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Abortion spontaneous			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Hypersensitivity			

subjects affected / exposed	0 / 72 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Crohn's disease deterioration			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			
subjects affected / exposed	0 / 72 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ileal stenosis			
subjects affected / exposed	0 / 72 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rectal haemorrhage			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Small intestinal stenosis			
subjects affected / exposed	0 / 72 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Granuloma skin			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 72 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Tubulointerstitial nephritis			
subjects affected / exposed	0 / 72 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 72 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Fistula			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intervertebral disc protrusion			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pyelocystitis			
subjects affected / exposed	0 / 72 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sinusitis			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Anal abscess			
subjects affected / exposed	0 / 72 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis norovirus			

subjects affected / exposed	0 / 72 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo	TSO 250	TSO 2.500
Total subjects affected by non-serious adverse events			
subjects affected / exposed	53 / 70 (75.71%)	28 / 39 (71.79%)	56 / 71 (78.87%)
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 70 (11.43%)	10 / 39 (25.64%)	13 / 71 (18.31%)
occurrences (all)	8	11	13
Dizzine			
subjects affected / exposed	2 / 70 (2.86%)	2 / 39 (5.13%)	1 / 71 (1.41%)
occurrences (all)	2	2	1
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	0 / 70 (0.00%)	2 / 39 (5.13%)	1 / 71 (1.41%)
occurrences (all)	0	2	1
Gastrointestinal disorders			
Crohn's disease deterioration			
subjects affected / exposed	20 / 70 (28.57%)	12 / 39 (30.77%)	22 / 71 (30.99%)
occurrences (all)	20	12	22
Abdominal pain			
subjects affected / exposed	7 / 70 (10.00%)	1 / 39 (2.56%)	10 / 71 (14.08%)
occurrences (all)	7	1	12
Nausea			
subjects affected / exposed	3 / 70 (4.29%)	2 / 39 (5.13%)	4 / 71 (5.63%)
occurrences (all)	3	3	4
Flatulence			
subjects affected / exposed	3 / 70 (4.29%)	2 / 39 (5.13%)	3 / 71 (4.23%)
occurrences (all)	3	2	3
Abdominal pain upper			
subjects affected / exposed	1 / 70 (1.43%)	0 / 39 (0.00%)	2 / 71 (2.82%)
occurrences (all)	1	0	2

Haematochezia			
subjects affected / exposed	0 / 70 (0.00%)	2 / 39 (5.13%)	1 / 71 (1.41%)
occurrences (all)	0	2	1
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 70 (1.43%)	3 / 39 (7.69%)	1 / 71 (1.41%)
occurrences (all)	1	3	1
Oropharyngeal pain			
subjects affected / exposed	1 / 70 (1.43%)	2 / 39 (5.13%)	2 / 71 (2.82%)
occurrences (all)	1	2	2
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 70 (4.29%)	3 / 39 (7.69%)	4 / 71 (5.63%)
occurrences (all)	3	3	6
Back pain			
subjects affected / exposed	5 / 70 (7.14%)	3 / 39 (7.69%)	5 / 71 (7.04%)
occurrences (all)	5	3	5
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	9 / 70 (12.86%)	6 / 39 (15.38%)	9 / 71 (12.68%)
occurrences (all)	9	6	9
Urinary tract infection			
subjects affected / exposed	3 / 70 (4.29%)	1 / 39 (2.56%)	0 / 71 (0.00%)
occurrences (all)	3	1	0

Non-serious adverse events	TSO 7.500		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	54 / 72 (75.00%)		
Nervous system disorders			
Headache			
subjects affected / exposed	13 / 72 (18.06%)		
occurrences (all)	16		
Dizzine			
subjects affected / exposed	3 / 72 (4.17%)		
occurrences (all)	3		
General disorders and administration site conditions			

Influenza like illness subjects affected / exposed occurrences (all)	0 / 72 (0.00%) 0		
Gastrointestinal disorders Crohn's disease deterioration subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Flatulence subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Haematochezia subjects affected / exposed occurrences (all)	 14 / 72 (19.44%) 14 9 / 72 (12.50%) 10 6 / 72 (8.33%) 6 4 / 72 (5.56%) 4 7 / 72 (9.72%) 7 0 / 72 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all)	 0 / 72 (0.00%) 0 0 / 72 (0.00%) 0		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all)	 7 / 72 (9.72%) 7 4 / 72 (5.56%) 4		

Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	10 / 72 (13.89%)		
occurrences (all)	10		
Urinary tract infection			
subjects affected / exposed	2 / 72 (2.78%)		
occurrences (all)	2		

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