Clinical trial results:
A Multicenter, Open label, Non-comparative Study to Evaluate the Safety of Entocort EC for the Treatment of Crohn's Disease in Paediatric Subjects Aged 5 to 17 Years, Inclusive

Summary

EudraCT number	2011-003743-22
Trial protocol	DE IT
Global end of trial date	10 September 2014

Results information

Result version number	v1 (current)
This version publication date	01 February 2017
First version publication date	13 May 2015

Trial information

Trial identification

Sponsor protocol code	D9422C00001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01444092
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca R&D Molndal
Sponsor organisation address	Pepparedsleden 1, Mölndal, Sweden, SE-431 83
Public contact	Tore Persson, AstraZeneca R&D Molndal, +46 31 7766069, tore.teb.persson@astrazeneca.com
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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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	26 December 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 September 2014
Global end of trial reached?	Yes
Global end of trial date	10 September 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to investigate the safety of Entocort EC in a pediatric population treated for mild-to-moderate Crohn’s disease

Protection of trial subjects:

None

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 November 2011
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	Poland: 40
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	United States: 47
Country: Number of subjects enrolled	Italy: 15
Country: Number of subjects enrolled	Canada: 19
Worldwide total number of subjects	123
EEA total number of subjects	57

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)	23
Adolescents (12-17 years)	100
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was to enroll approximately 110 subjects at study centers in the United States and at multiple centers throughout Europe and Canada.

Pre-assignment

Screening details:

Eligibility for study enrollment will be assessed at the screening and enrollment visit (Visit 1). If appropriate, subjects will be enrolled into the study and begin to receive study medication at this visit. 123 subjects were screened and 108 were enrolled.

Period 1

Period 1 title	Enrollment/screening/start of treatment
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Entocort

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Entocort EC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

9 or 6 mg once daily in the morning

Number of subjects in period 1[1]	Entocort
Started	108
Completed	108

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Out of 123 enrolled patients under Trial information only 108 were treated. 15 patients were enrolled but not treated (did not meet the criteria for entering).

Period 2

Period 2 title	Overall study
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Entocort
Arm description: Entocort EC 9 or 6 mg/day	
Arm type	Experimental
Investigational medicinal product name	Entocort EC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

9 or 6 mg once daily in the morning

Number of subjects in period 2	Entocort
Started	108
Completed	91
Not completed	17
Consent withdrawn by subject	1
Study-specific criterion	1
Adverse event, non-fatal	8
Lack of efficacy	6
Protocol deviation	1

Baseline characteristics

Reporting groups	
Reporting group title	Entocort

Reporting group description: -

Reporting group values	Entocort	Total	
Number of subjects	108	108	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	18	18	
Adolescents (12-17 years)	90	90	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous Units: Years			
arithmetic mean	13.7		
standard deviation	± 2.4	-	
Gender, Male/Female Units: Participants			
Female	51	51	
Male	57	57	
Age, Customized Units: Subjects			
=<8 Yrs	5	5	
>8 Yrs	103	103	
Race, Customized Units: Subjects			
Asian	1	1	
Black Or African American	4	4	
Other	3	3	
White	100	100	

End points

End points reporting groups

Reporting group title	Entocort
Reporting group description: -	
Reporting group title	Entocort
Reporting group description:	
Entocort EC 9 or 6 mg/day	

Primary: Any adverse event

End point title	Any adverse event[1]
End point description:	
End point type	Primary
End point timeframe:	
12 weeks	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Detailed information about the adverse events is to be found in the Adverse events section.

End point values	Entocort			
Subject group type	Reporting group			
Number of subjects analysed	108			
Units: Patients	79			

Statistical analyses

No statistical analyses for this end point

Secondary: PCDAI

End point title	PCDAI
End point description:	
Paediatric Crohn’s Disease Activity Index	
End point type	Secondary
End point timeframe:	
8 weeks	

End point values	Entocort			
Subject group type	Reporting group			
Number of subjects analysed	105[2]			
Units: Score				
arithmetic mean (standard deviation)				
Baseline (Day1)	19.1 (± 10.1)			
Change after 8 weeks	-10 (± 10.1)			

Notes:

[2] - Full analysis set (all patients with a PCDAI after 8 weeks)

Statistical analyses

No statistical analyses for this end point

Secondary: IMPACT 3

End point title	IMPACT 3

End point description:

End point type	Secondary

End point timeframe:

8 weeks

End point values	Entocort			
Subject group type	Reporting group			
Number of subjects analysed	107			
Units: Score				
arithmetic mean (standard deviation)				
Baseline (Day 1)	132.1 (± 18.8)			
Change after 8 weeks	7.9 (± 13.3)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 12 weeks	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.0
Reporting groups	
Reporting group title	Entocort
Reporting group description: Entocort™ EC 9/6/3 mg	

Serious adverse events	Entocort		
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 108 (7.41%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Gastrointestinal disorders			
Crohn's disease			
subjects affected / exposed	4 / 108 (3.70%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Diarrhoea haemorrhagic			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Small intestinal obstruction			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Erythema nodosum			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Entocort		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	78 / 108 (72.22%)		
Vascular disorders			
Pallor			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Influenza like illness			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Malaise			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	3 / 108 (2.78%)		
occurrences (all)	3		
Tenderness			

subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Menstrual disorder			
subjects affected / exposed	2 / 108 (1.85%)		
occurrences (all)	2		
Dysmenorrhoea			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Metrorrhagia			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 108 (2.78%)		
occurrences (all)	3		
Respiratory tract congestion			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Psychiatric disorders			
Affect lability			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Agitation			
subjects affected / exposed	2 / 108 (1.85%)		
occurrences (all)	2		
Anxiety			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Depression			
subjects affected / exposed	2 / 108 (1.85%)		
occurrences (all)	2		
Insomnia			
subjects affected / exposed	6 / 108 (5.56%)		
occurrences (all)	6		
Irritability			

subjects affected / exposed	14 / 108 (12.96%)		
occurrences (all)	14		
Sleep disorder			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Mood swings			
subjects affected / exposed	3 / 108 (2.78%)		
occurrences (all)	3		
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Blood albumin decreased			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Blood cortisol decreased			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Blood cortisol increased			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Haemoglobin decreased			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
C-reactive protein increased			
subjects affected / exposed	2 / 108 (1.85%)		
occurrences (all)	2		
Mean cell volume decreased			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Occult blood positive			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Protein urine present			

subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Red blood cell sedimentation rate increased			
subjects affected / exposed	3 / 108 (2.78%)		
occurrences (all)	3		
Urine output decreased			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Incision site complication			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Contusion			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Procedural pain			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Cardiac disorders			
Tachycardia			
subjects affected / exposed	2 / 108 (1.85%)		
occurrences (all)	2		
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	3 / 108 (2.78%)		
occurrences (all)	3		
Dizziness			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	9 / 108 (8.33%)		
occurrences (all)	9		
Lethargy			

subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Memory impairment			
subjects affected / exposed	4 / 108 (3.70%)		
occurrences (all)	4		
Migraine			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Psychomotor hyperactivity			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Syncope			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 108 (4.63%)		
occurrences (all)	5		
Increased tendency to bruise			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Lymphadenopathy			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Eye disorders			
Iritis			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Scleritis			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Abdominal pain			

subjects affected / exposed	16 / 108 (14.81%)			
occurrences (all)	16			
Abdominal mass				
subjects affected / exposed	1 / 108 (0.93%)			
occurrences (all)	1			
Abdominal pain lower				
subjects affected / exposed	1 / 108 (0.93%)			
occurrences (all)	1			
Abdominal tenderness				
subjects affected / exposed	1 / 108 (0.93%)			
occurrences (all)	1			
Anal fissure				
subjects affected / exposed	2 / 108 (1.85%)			
occurrences (all)	2			
Anal haemorrhage				
subjects affected / exposed	1 / 108 (0.93%)			
occurrences (all)	1			
Anal skin tags				
subjects affected / exposed	1 / 108 (0.93%)			
occurrences (all)	1			
Breath odour				
subjects affected / exposed	1 / 108 (0.93%)			
occurrences (all)	1			
Cheilosis				
subjects affected / exposed	1 / 108 (0.93%)			
occurrences (all)	1			
Constipation				
subjects affected / exposed	2 / 108 (1.85%)			
occurrences (all)	2			
Crohn's disease				
subjects affected / exposed	7 / 108 (6.48%)			
occurrences (all)	7			
Diarrhoea				
subjects affected / exposed	2 / 108 (1.85%)			
occurrences (all)	2			
Dyspepsia				

subjects affected / exposed	3 / 108 (2.78%)		
occurrences (all)	3		
Enterocolitis			
subjects affected / exposed	2 / 108 (1.85%)		
occurrences (all)	2		
Haematochezia			
subjects affected / exposed	3 / 108 (2.78%)		
occurrences (all)	3		
Proctalgia			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	6 / 108 (5.56%)		
occurrences (all)	6		
Rectal haemorrhage			
subjects affected / exposed	2 / 108 (1.85%)		
occurrences (all)	2		
Vomiting			
subjects affected / exposed	5 / 108 (4.63%)		
occurrences (all)	5		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	2 / 108 (1.85%)		
occurrences (all)	2		
Acne			
subjects affected / exposed	15 / 108 (13.89%)		
occurrences (all)	15		
Dry skin			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Erythema nodosum			
subjects affected / exposed	2 / 108 (1.85%)		
occurrences (all)	2		
Hair growth abnormal			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		

Hirsutism subjects affected / exposed occurrences (all)	5 / 108 (4.63%) 5		
Lipohypertrophy subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
Pruritus subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
Rash subjects affected / exposed occurrences (all)	2 / 108 (1.85%) 2		
Skin striae subjects affected / exposed occurrences (all)	2 / 108 (1.85%) 2		
Renal and urinary disorders Haematuria subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
Endocrine disorders Cushingoid subjects affected / exposed occurrences (all)	13 / 108 (12.04%) 13		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
Back pain subjects affected / exposed occurrences (all)	2 / 108 (1.85%) 2		
Fistula subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
Musculoskeletal discomfort subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		

Musculoskeletal pain subjects affected / exposed occurrences (all)	2 / 108 (1.85%) 2			
Myalgia subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1			
Osteoporosis subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1			
Pain in extremity subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1			
Infections and infestations Acarodermatitis subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1			
Conjunctivitis subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1			
Enteritis infectious subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1			
Gastroenteritis subjects affected / exposed occurrences (all)	2 / 108 (1.85%) 2			
Otitis externa subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1			
Nasopharyngitis subjects affected / exposed occurrences (all)	4 / 108 (3.70%) 4			
Pharyngitis subjects affected / exposed occurrences (all)	4 / 108 (3.70%) 4			
Rhinitis				

subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Rectal abscess			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Tooth abscess			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	3 / 108 (2.78%)		
occurrences (all)	3		
Urinary tract infection			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Viral infection			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Viral pharyngitis			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	6 / 108 (5.56%)		
occurrences (all)	6		
Dehydration			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Hyperamylasaemia			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Hyperphagia			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Increased appetite			
subjects affected / exposed	17 / 108 (15.74%)		
occurrences (all)	17		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 May 2013	The body weight cutoff for 9 mg or 6 mg/day was changed from 30 kg to 25 kg

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported