Clinical trial results:
A Multicenter, Open-Label, Non-Comparative Study to Evaluate the Safety of Entocort™ EC as a Maintenance Treatment for Crohn's Disease in Pediatric Subjects Aged 5 to 17 Years, Inclusive

Summary

EudraCT number	2011-003742-40
Trial protocol	DE
Global end of trial date	13 February 2014

Results information

Result version number	v1 (current)
This version publication date	01 February 2017
First version publication date	09 August 2015

Trial information

Trial identification

Sponsor protocol code	D9422C00002

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	AstraZeneca R&D
Sponsor organisation address	Pepparedsleden 1, Mölndal, Sweden, 431 83
Public contact	Tore Persson, AstraZeneca R&D, +46 31 7766069, tore.teb.persson@astrazeneca.com
Scientific contact	Stefan Eklund, MD, AstraZeneca R&D, Mölndal, +46 31 7762557, Stefan.Eklund@astrazeneca.co

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	27 January 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 February 2014
Global end of trial reached?	Yes
Global end of trial date	13 February 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 mild-to-moderate Crohn's disease population for the maintenance of clinical remission.

Protection of trial subjects:

Subjects could discontinue IP and assessments at any time at the discretion of the investigator. Subjects were also free to withdraw from the study at any time, without prejudice to further treatment. Specific reasons for withdrawal of a subject from this study and the procedures to be followed when a subject was withdrawn are listed in the CSP. For subjects who were discontinued, the subjects and parents/guardians of the subject were asked about the reasons for their discontinuation and about the presence of any Adverse events (AEs). If possible, they were seen and underwent final assessment by the investigator. Adverse events were followed, and any IPs and study materials were returned by the subject/parents/guardians.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 December 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	United States: 19
Country: Number of subjects enrolled	Canada: 9
Country: Number of subjects enrolled	European Union: 27
Worldwide total number of subjects	55
EEA total number of subjects	0

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)	7
Adolescents (12-17 years)	48
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects could enter this study from
the pediatric Entocort induction protocol (D9442C00001) but this was not mandatory. If subjects fulfilled the eligibility criteria as stated and were in Crohn's disease clinical remission, they could enter this study.

Pre-assignment

Screening details:

Subjects could enter this study from
the pediatric Entocort induction protocol (D9442C00001) but this was not mandatory. If subjects fulfilled the eligibility criteria as stated and were in Crohn's disease clinical remission, they could enter this study.

Period 1

Period 1 title	Full study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Not blinded

Arms

Arm title	Entocort

Arm description:

Entocort EC 6 mg/day for 8 weeks, then 3 mg/day for 2 weeks, then no drug for 2 weeks

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:

6 mg/day

Number of subjects in period 1	Entocort
Started	50
Completed	41
Not completed	9
Adverse event, non-fatal	3
1 study specific, 1 not specified	2
Protocol deviation	1
Lack of efficacy	3

Baseline characteristics

Reporting groups[1]	
Reporting group title	Full study
Reporting group description: -	

Notes:

[1] - The number of subjects reported to be in the baseline period is not equal to the worldwide number of subjects enrolled in the trial. It is expected that these numbers will be the same.
Justification: 55 patients were screened/enrolled, but only 50 of them met the inclusion/exclusion criteria; all analyses are based on these 50.

Reporting group values	Full study	Total	
Number of subjects	50	50	
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)	7	7	
Adolescents (12-17 years)	43	43	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous			
Age in years			
Units: years			
median	15		
full range (min-max)	8 to 17	-	
Gender Categorical Units: Subjects			
Female	20	20	
Male	30	30	

Subject analysis sets	
Subject analysis set title	Safety analysis set
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety analysis set consisted of all subjects who took at least 1 dose of Entocort™ EC.

Subject analysis set title	Full analysis set (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

The FAS consisted of all subjects included in the safety analysis set who had a complete post baseline (Visit 4) data for PCDAI assessment.

Reporting group values	Safety analysis set	Full analysis set (FAS)	
Number of subjects	50	49	

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)	7	6	
Adolescents (12-17 years)	43	43	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous			
Age in years			
Units: years			
median	15	15	
full range (min-max)	8 to 17	8 to 17	
Gender Categorical Units: Subjects			
Female	20	20	
Male	30	29	

End points

End points reporting groups

Reporting group title	Entocort
Reporting group description:	
Entocort EC 6 mg/day for 8 weeks, then 3 mg/day for 2 weeks, then no drug for 2 weeks	
Subject analysis set title	Safety analysis set
Subject analysis set type	Safety analysis
Subject analysis set description:	
The safety analysis set consisted of all subjects who took at least 1 dose of Entocort™ EC.	
Subject analysis set title	Full analysis set (FAS)
Subject analysis set type	Full analysis
Subject analysis set description:	
The FAS consisted of all subjects included in the safety analysis set who had a complete post baseline (Visit 4) data for PCDAI assessment.	

Primary: Patients with adverse events

End point title	Patients with adverse events[1]
End point description:	
Did the patient have an adverse event?	
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: Since this study only had one arm, only descriptive statistics has been used. No comparisons, no statistical tests and no confidence intervals.

End point values	Safety analysis set			
Subject group type	Subject analysis set			
Number of subjects analysed	50			
Units: Patient	37			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in PCDAI

End point title	Change in PCDAI
End point description:	
Pediatric Crohn’s disease activity index	
End point type	Secondary
End point timeframe:	
12 weeks	

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	49			
Units: Units on a scale				
arithmetic mean (standard deviation)	2 (± 7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in IMPACT III

End point title	Change in IMPACT III

End point description:

End point type	Secondary

End point timeframe:

12 weeks

End point values	Safety analysis set			
Subject group type	Subject analysis set			
Number of subjects analysed	49			
Units: Units on a scale				
arithmetic mean (standard deviation)	1.2 (± 8.6)			

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	16.1.1

Reporting groups	
Reporting group title	Safety population

Reporting group description: -

Serious adverse events	Safety population		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 50 (8.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Gastrointestinal disorders			
Crohn's disease			
subjects affected / exposed	3 / 50 (6.00%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Ileal obstruction			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal ulceration and perforation			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 4 %

Non-serious adverse events	Safety population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	36 / 50 (72.00%)		
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences (all)	2		
General disorders and administration site conditions			
Irritability			
subjects affected / exposed	4 / 50 (8.00%)		
occurrences (all)	4		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	8 / 50 (16.00%)		
occurrences (all)	11		
Crohn's disease			
subjects affected / exposed	4 / 50 (8.00%)		
occurrences (all)	4		
Diarrhoea			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences (all)	2		
Dyspepsia			
subjects affected / exposed	3 / 50 (6.00%)		
occurrences (all)	3		
Haematochizia			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences (all)	2		
Vomiting			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	6 / 50 (12.00%)		
occurrences (all)	6		
Hirsutism			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences (all)	2		

Psychiatric disorders Mood swings subjects affected / exposed occurrences (all)	 4 / 50 (8.00%) 4		
Endocrine disorders Cushingoid subjects affected / exposed occurrences (all)	 4 / 50 (8.00%) 4		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all)	 3 / 50 (6.00%) 3 2 / 50 (4.00%) 2		
Infections and infestations Gastroenteritis subjects affected / exposed occurrences (all) Gastroenteritis viral subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all)	 2 / 50 (4.00%) 2 2 / 50 (4.00%) 2 3 / 50 (6.00%) 3 3 / 50 (6.00%) 3		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) Increased appetite subjects affected / exposed occurrences (all)	 3 / 50 (6.00%) 3 4 / 50 (8.00%) 4		

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