Clinical trial results:
Open-label, multi-centre, proof of concept phase IIa clinical trial on the efficacy and tolerability of an 8 week oral treatment with once daily 9 mg budesonide in patients with active ulcerative colitis

Summary

EudraCT number	2014-005635-14
Trial protocol	DE LV HU LT
Global end of trial date	20 February 2017

Results information

Result version number	v1 (current)
This version publication date	11 October 2018
First version publication date	11 October 2018

Trial information

Trial identification

Sponsor protocol code	BUX-3/UCA

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02550418
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Dr. Falk Pharma GmbH
Sponsor organisation address	Leinenweberstrasse 5, Freiburg, Germany, 79288
Public contact	Clinical Research and Development, Dr. Falk Pharma GmbH, 0049 7611514-0, zentrale@drfalkpharma.de
Scientific contact	Clinical Research and Development, Dr. Falk Pharma GmbH, 0049 7611514-0, zentrale@drfalkpharma.de

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	22 February 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 January 2017
Global end of trial reached?	Yes
Global end of trial date	20 February 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to evaluate the efficacy of a 8-week treatment with once-daily 9 mg budesonide in patients with active ulcerative colitis.

Protection of trial subjects:

Close supervision of subjects by implementing interim visits every 14 days to guarantee their safety and wellbeing. Prior to recruitment of patients, all relevant documents of the clinical study were submitted to and proved 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.

Background therapy:

None

Evidence for comparator:

Not applicable

Actual start date of recruitment	13 October 2015
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	Germany: 4
Country: Number of subjects enrolled	Hungary: 7
Country: Number of subjects enrolled	Latvia: 37
Country: Number of subjects enrolled	Lithuania: 13
Worldwide total number of subjects	61
EEA total number of subjects	61

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)	56
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

In total 61 patients from Germany, Hungary, Lithuania and Latvia were enrolled and treated.

Pre-assignment

Screening details:

Patients signing the informed consent form were screened for 7 to 10 days to evaluate eligibility for the study. A total of 66 patients was screened for enrolment into the study. Five patients could not be included into the treatment phase. The most frequent reason for screening failure was violation of eligibility criteria.

Period 1

Period 1 title	8-week open-label treatment phase (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Not applicable

Arms

Arm title	Open-label treatment with budesonide

Arm description:

8-week treatment with one budesonide 9 mg capsule, hard (BUX-PV) once-daily.

Analysis set: Full Analysis Set, which was defined according to the intention-to-treat principle and included all patients who received at least one dose of the investigational medicinal product.

Arm type	Experimental
Investigational medicinal product name	Budesonide 9 mg capsule, hard (BUX-PV)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

One budesonide 9 mg capsule, hard (BUX-PV) once-daily in the morning.

Number of subjects in period 1	Open-label treatment with budesonide
Started	61
Completed	49
Not completed	12
Adverse event, non-fatal	2
Lack of patient's co-operation	1
Lack of efficacy	9

Baseline characteristics

Reporting groups	
Reporting group title	Open-label treatment with budesonide

Reporting group description:

8-week treatment with one budesonide 9 mg capsule, hard (BUX-PV) once-daily.

Analysis set: Full Analysis Set, which was defined according to the intention-to-treat principle and included all patients who received at least one dose of the investigational medicinal product.

Reporting group values	Open-label treatment with budesonide	Total	
Number of subjects	61	61	
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)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	56	56	
From 65-84 years	5	5	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	42.2		
standard deviation	± 14.5	-	
Gender categorical Units: Subjects			
Female	29	29	
Male	32	32	

End points

End points reporting groups

Reporting group title	Open-label treatment with budesonide

Reporting group description:

8-week treatment with one budesonide 9 mg capsule, hard (BUX-PV) once-daily.

Analysis set: Full Analysis Set, which was defined according to the intention-to-treat principle and included all patients who received at least one dose of the investigational medicinal product.

Primary: Clinical remission at week 8 / EOT

End point title	Clinical remission at week 8 / EOT[1]

End point description:

Percentage of patients being in clinical remission at week 8 / EOT. Clinical remission was defined as Clinical Activity Index (CAI) total score ≤ 4, with subscores 1 and 2 of 0 at week 8 / EOT.

End point type	Primary

End point timeframe:

After 8-week treatment: week 8 / EOT

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: No formal statistical hypothesis testing was planned for this study. Results were summarized in tables as descriptive statistics only.

End point values	Open-label treatment with budesonide			
Subject group type	Reporting group			
Number of subjects analysed	61			
Units: subjects	29			

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical and endoscopic remission at week 8 / EOT

End point title	Clinical and endoscopic remission at week 8 / EOT

End point description:

The proportion of patients being in combined clinical and endoscopic remission at week 8 / EOT. Combined clinical and endoscopic remission was defined as modified Disease Activity Index (mDAI) stool frequency subscore = 0, rectal bleeding subscore = 0, mucosal appearance subscore = 0 or 1 and physician's rating of disease activity subscore = 0 or 1 at week 8 / EOT.

End point type	Secondary

End point timeframe:

After 8-week treatment: week 8 / EOT

End point values	Open-label treatment with budesonide			
Subject group type	Reporting group			
Number of subjects analysed	61			
Units: Subjects	10			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From baseline to week 8 / EOT

Adverse event reporting additional description:

All adverse events which occurred from the first drug administration to week 8 / EOT.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	Open-label treatment with budesonide

Reporting group description:

8-week treatment with one budesonide 9 mg capsule, hard (BUX-PV) once-daily.

Analysis set: The Safety Analysis Set included all patients who received at least one dose of the investigational medicinal product and had at least one follow-up value for the safety variables to be analysed. If the administration of any investigational medicinal product was not certain, the patient was included in the Safety Analysis Set.

Serious adverse events	Open-label treatment with budesonide		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 61 (1.64%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Open-label treatment with budesonide		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 61 (37.70%)		
Investigations			

C-reactive protein increased			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
Eosinophil count increased			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
Lipase increased			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
Lymphocyte count decreased			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
Post-traumatic pain			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 61 (6.56%)		
occurrences (all)	4		
Migraine			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	2		
Syncope			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
Eosinophilia			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		

Neutropenia subjects affected / exposed occurrences (all)	1 / 61 (1.64%) 1		
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all)	1 / 61 (1.64%) 1		
Gastrointestinal disorders Colitis ulcerative subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Gastrointestinal inflammation subjects affected / exposed occurrences (all) Large intestine polyp subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Oral mucosal erythema subjects affected / exposed occurrences (all) Rectal tenesmus subjects affected / exposed occurrences (all)	7 / 61 (11.48%) 7 1 / 61 (1.64%) 1 1 / 61 (1.64%) 1 2 / 61 (3.28%) 2 1 / 61 (1.64%) 1 1 / 61 (1.64%) 1 1 / 61 (1.64%) 1		
Reproductive system and breast disorders Dysmenorrhoea subjects affected / exposed occurrences (all)	1 / 61 (1.64%) 1		
Skin and subcutaneous tissue disorders Erythema nodosum			

subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
Infections and infestations			
Herpes simplex			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
Influenza			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
Respiratory tract infection			
subjects affected / exposed	2 / 61 (3.28%)		
occurrences (all)	2		
Sinusitis			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		

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