Clinical trial results:
Double-blind, randomized, placebo-controlled, phase III trial on the efficacy and tolerability of a 6-week treatment with budesonide effervescent tablets vs. placebo for induction of clinico-pathological remission in adult patients with active eosinophilic esophagitis

Summary

EudraCT number	2014-001484-12
Trial protocol	DE BE ES NL
Global end of trial date	04 October 2016

Results information

Result version number	v2 (current)
This version publication date	07 August 2019
First version publication date	26 August 2017
Version creation reason	• Changes to summary attachments Full paper
Summary attachment (see zip file)	Full paper (Lucendo-Miehlke_Gastroenterology_2019.pdf)

Trial information

Trial identification

Sponsor protocol code	BUL-1/EEA

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02434029
WHO universal trial number (UTN)	-
Other trial identifiers	EOS-1: Acronym

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	22 February 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	04 October 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of budesonide effervescent tablets for orodispersible use vs. placebo for the induction of clinico-pathological remission in adult patients with active eosinophilic esophagitis (EoE).

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 endoscopy and biopsy sampling to be performed for confirmation of diagnosis of eosinophilic esophagitis by the central pathologist, the patients received the standard preparation for sedation during the endoscopy as routinely performed at the study sites.

Background therapy:

No concomitant background therapy, except stable diets and/or stable treatment with protonpump-inhibitors was allowed during the trial.

Evidence for comparator:

Using a placebo arm in this clinical trial was ethically justified as there were compelling and scientifically sound methodological reasons for the use of a placebo control in this trial, since there were no comparator products with a marketing authorization for the treatment of EoE available. Moreover, the use of a placebo group was also justified, as it allowed to control for all other potential influences on the actual or apparent course of the disease other than those arising from the pharmacological action of budesonide (including but not limited to influences such as, spontaneous change in the disease, subject and investigator expectations, the effect of participating in this trial, or subjective elements of diagnosis or assessments), as stated in the "ICH Topic E10: Note for guidance on choice of control group in clinical trials" (CPMP/ICH/364/96).

Actual start date of recruitment	11 November 2015
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	Netherlands: 3
Country: Number of subjects enrolled	Spain: 34
Country: Number of subjects enrolled	Germany: 43
Country: Number of subjects enrolled	Switzerland: 8
Worldwide total number of subjects	88
EEA total number of subjects	80

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)	86
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

In total, 19 centers randomized patients: 10 centers in Germany (DE), 6 centers in Spain (ES), 2 centers in Switzerland (CH), and 1 center in The Netherlands (NL). First patient was screened (entered) at the 11Nov2015. Last patient completed his last visit at 04Oct2016

Pre-assignment

Screening details:

126 patients were screened to fullfill the In-/Exclusion criteria. Of them, 88 patients were randomized and treated with budesonide or placebo.

Pre-assignment period milestones

Number of subjects started	126[1]
Number of subjects completed	88

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Protocol deviation: 38

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: Of the 126 patients screened within the pre-assignment period, 38 patients did not fulfill the in-/exclusion criteria and therefore, were not randomized and did not enter the double-blind treatment period.

Period 1

Period 1 title	Double-blind 6-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 effervescent tablet for orodispersible use was indistinguishable from the verum effervescent tablet for orodispersible use.

Arms

Are arms mutually exclusive?	Yes
Arm title	Budesonide 1mg BID

Arm description:

Twice daily 1mg budesonide

Arm type	Experimental
Investigational medicinal product name	1mg budesonide effervescent tablet for orodispersible use
Investigational medicinal product code	BUET 1mg
Other name	Budesonide 1mg orodispersible tablet
Pharmaceutical forms	Effervescent tablet
Routes of administration	Oral use

Dosage and administration details:

Take one effervescent tablet each in the morning and in the evening after the meal. The effervescent tablet has to be placed on the tongue which allows rapid disintegration. The effervescent tablet dissolves rapidly and will be swallowed with saliva little by little.
Do not drink or eat during 30 minutes after study drug administration.

Arm title	Placebo BID

Arm description:

Twice daily Placebo

Arm type	Placebo
Investigational medicinal product name	Placebo effervescent tablet for orodispersible use
Investigational medicinal product code	Placebo
Other name	Placebo orodispersible tablet
Pharmaceutical forms	Effervescent tablet
Routes of administration	Oral use

Dosage and administration details:

Take one effervescent tablet each in the morning and in the evening after the meal. The effervescent tablet has to be placed on the tongue which allows rapid disintegration. The effervescent tablet dissolves rapidly and will be swallowed with saliva little by little.
Do not drink or eat during 30 minutes after study drug administration.

Number of subjects in period 1	Budesonide 1mg BID	Placebo BID
Started	59	29
Completed	56	25
Not completed	3	4
Lack of efficacy	3	4

Baseline characteristics

Reporting groups	
Reporting group title	Budesonide 1mg BID
Reporting group description: Twice daily 1mg budesonide	
Reporting group title	Placebo BID
Reporting group description: Twice daily Placebo	

Reporting group values	Budesonide 1mg BID	Placebo BID	Total
Number of subjects	59	29	88
Age categorical Units: Subjects			
Adults (18-64 years)	57	29	86
From 65-84 years	2	0	2
Age continuous Units: years			
arithmetic mean	37	36.9	
standard deviation	± 11.5	± 9.2	-
Gender categorical Units: Subjects			
Female	11	4	15
Male	48	25	73
Ethnic Group Units: Subjects			
White	59	29	88
Previous esophageal dilation Units: Subjects			
yes	9	5	14
no	50	24	74
Previous PPI trial conducted Units: Subjects			
yes	59	29	88
History of allergic disease Units: Subjects			
yes	47	23	70
no	12	6	18
Endoscopic disease activity Units: Subjects			
none	1	0	1
mild	9	3	12
moderate	30	17	47
severe	19	9	28
Duration since first symptoms Units: months			
arithmetic mean	134	139	
standard deviation	± 104.6	± 98.8	-

Duration since diagnosis Units: months arithmetic mean standard deviation	 48.8 ± 44.3	 57.6 ± 49.3	 -
Overall peak eos/mm2 hpf Units: eos/mm2 hpf arithmetic mean standard deviation	 242 ± 140.7	 239 ± 125	 -
Total Modified EEsAI Endoscopic Score (range: 0-9)			
Worst case assessment from all parts of the esophagus			
Units: points arithmetic mean standard deviation	 3.8 ± 1.46	 4.6 ± 1.32	 -
'Inflammatory signs' subscore - Modified EEsAI Endoscopic Score (range: 0-4)			
Worst case assessment from all parts of the esophagus			
Units: points arithmetic mean standard deviation	 2.7 ± 0.96	 3 ± 0.98	 -
'Fibrotic signs' subscore - Modified EEsAI Endoscopic Score (range: 0-4)			
Worst case assessment from all parts of the esophagus			
Units: points arithmetic mean standard deviation	 1 ± 1	 1.4 ± 0.91	 -
Dysphagia Numerical Rating Scale [NRS] (0-10)			
0 = no troubles to swallow 10 = most severe troubles to swallow			
Units: points arithmetic mean standard deviation	 5.8 ± 2.02	 5.9 ± 1.69	 -
Pain during swallowing NRS (0-10)			
0 = no pain during swallowing 10 = most severe pain during swallowing			
Units: points arithmetic mean standard deviation	 3.5 ± 2.78	 3.4 ± 3.17	 -
Patient’s Global Assessment of EoE activity (NRS 0-10)			
0 = no symptoms 10 = most severe symptoms			
Units: points arithmetic mean standard deviation	 5.9 ± 1.5	 6 ± 1.5	 -
Physician’s Global Assessment of EoE activity (NRS 0-10)			
considered all findings concerning the severity of the patient’s EoE (clinical, endoscopic, histologic) 0 = inactive EoE 10 = most active EoE			
Units: points arithmetic mean standard deviation	 6.1 ± 1.3	 6.2 ± 1.3	 -
Total weekly EEsAI-PRO (0-100)			

Eosinophilic Esophagitis Activity Index Patient Reported Outcome (EEsAI-PRO) score: The relevant items for the EEsAI-PRO Score were: - Frequency of trouble swallowing (with 4 increments ranging from never to daily) - Duration of dysphagia episodes (≤ 5 / > 5 minutes) - Presence / absence of pain during swallowing - Visual Dysphagia Questions (VDQ) on 8 foods of 8 different consistencies (hypothetical test meal; grades 0 to 3) resulting in a VDQ score - Behavioural change strategies on specific foods with 8 different consistencies: Range: 0 (no EoE activity) to 100 (most severe EoE)			
Units: points			
arithmetic mean	54.1	55.3	
standard deviation	± 15.5	± 15.8	-

End points

End points reporting groups

Reporting group title	Budesonide 1mg BID
Reporting group description: Twice daily 1mg budesonide	
Reporting group title	Placebo BID
Reporting group description: Twice daily Placebo	

Primary: Number (%) of patients with clinico-pathological remission at week 6 (LOCF) of double-blind phase

End point title	Number (%) of patients with clinico-pathological remission at week 6 (LOCF) of double-blind phase

End point description:

Rate of patients with clinico-pathological remission at week 6 (LOCF) DB defined as fulfilling both criteria:
- Histological remission, i.e., peak of <16 eos/mm2 hpf at week 6 (LOCF), AND
- Resolution of symptoms (i.e., no or only minimal problems) defined as a severity of ≤2 points on 0 to 10-point (0-10) NRS for dysphagia AND a severity of ≤2 points on 0-10 NRS for pain during swallowing on each day in the week prior to week 6 (LOCF).

Patients experiencing a food impaction at any time during the DB-treatment phase which needed endoscopic intervention or who needed an endoscopic dilation during the DB-treatment phase were assessed as treatment failures, and thus did not fulfill by definition the clinico-pathological remission criterion.

In case the primary endpoint proved to show superiority of budesonide over placebo, further key secondary endpoints could confirmatorily be tested in an a priori ordered manner until th efirst of them did not proved a superiority of budeson

End point type	Primary

End point timeframe:

at week 6 (LOCF) double-blind phase

End point values	Budesonide 1mg BID	Placebo BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	29		
Units: patients				
yes	34	0		
no	25	29		

Attachments (see zip file)	Primary endpoint (FAS-DB)/BUL1_Clin-histol_rem_source 2-

Statistical analyses

Statistical analysis title	Final Analysis (FAS): Budesonide 1mg vs placebo
Comparison groups	Budesonide 1mg BID v Placebo BID
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1E-8 [1]
Method	Fisher exact
Parameter estimate	Risk difference (RD)
Point estimate	57.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	38.22
upper limit	71.97

Notes:

[1] - The RD was 57.63% with two-sided 95% RCI [38.22%; 71.97%]. The one-sided p-value resulting from the Fisher's exact
test was 0.00000001. The inverse normal was 5.5935 and exceeded the critical value of 2.452, thus superiority was confirmatorily shown

Secondary: Number (%) of patients with histological remission at week 6 (LOCF) double-blind phase

End point title	Number (%) of patients with histological remission at week 6 (LOCF) double-blind phase

End point description:

First of the a priori ordered key secondary endpoints to be confirmatorily tested for superiority when the primary endpoint showed superiority of budesonide 1mg vs placebo.

End point type	Secondary

End point timeframe:

at week 6 (LOCF) double-blind phase.

End point values	Budesonide 1mg BID	Placebo BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	29		
Units: patients				
yes	55	0		
no	4	29		

Statistical analyses

Statistical analysis title	First a priori ordered key secondary endpoint

Statistical analysis description:

Efficacy significance testing continued in hierarchical fashion in support of labeling claims for the key secondary endpoints until the first of these comparisons of
BUET 1mg BID versus Placebo showed a one-sided p-value >0.025 (FAS-DB).

Comparison groups	Budesonide 1mg BID v Placebo BID

Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [2]
Method	Fisher exact
Parameter estimate	Risk difference (RD)
Point estimate	93.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	86.8
upper limit	99.6

Notes:

[2] - one-sided p-value

Secondary: Change in the peak eos/mm2 hpf from baseline to week 6 (LOCF) double-blind phase

End point title	Change in the peak eos/mm2 hpf from baseline to week 6 (LOCF) double-blind phase

End point description:

Second of the a priori ordered key secondary endpoints to be confirmatorily tested for superiority when the primary endpoint showed superiority of budesonide 1mg vs placebo.

End point type	Secondary

End point timeframe:

at week 6 (LOCF) double-blind phase

End point values	Budesonide 1mg BID	Placebo BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	29		
Units: eos/mm2 hpf				
arithmetic mean (standard deviation)	-225.5 (± 150.37)	-4.3 (± 135.64)		

Statistical analyses

Statistical analysis title	Second a priori ordered key secondary endpoint

Statistical analysis description:

Efficacy significance testing continued in hierarchical fashion in support of labeling claims for the key secondary endpoints until the first of these comparisons of
BUET 1mg BID versus Placebo showed a one-sided p-value >0.025 (FAS-DB).

Comparison groups	Budesonide 1mg BID v Placebo BID

Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [3]
Method	linear least squares model
Parameter estimate	Mean difference (final values)
Point estimate	-221.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-285
upper limit	-157.5

Notes:

[3] - One-sided p-value for effect between treatment groups from linear least squares model with treatment group and baseline value as covariate.

Secondary: Number (%) of patients with resolution of symptoms on each day in the week prior to week 6 (LOCF) double-blind phase

End point title	Number (%) of patients with resolution of symptoms on each day in the week prior to week 6 (LOCF) double-blind phase

End point description:

Third of the a priori ordered key secondary endpoints to be confirmatorily tested for superiority when the primary endpoint showed superiority of budesonide 1mg vs placebo.

End point type	Secondary

End point timeframe:

at week 6 (LOCF) double-blind phase

End point values	Budesonide 1mg BID	Placebo BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	29		
Units: patients				
yes	35	4		
no	24	25		

Statistical analyses

Statistical analysis title	Third a priori ordered key secondary endpoint

Statistical analysis description:

Efficacy significance testing continued in hierarchical fashion in support of labeling claims for the key secondary endpoints until the first of these comparisons of
BUET 1mg BID versus Placebo showed a one-sided p-value >0.025 (FAS-DB).

Comparison groups	Budesonide 1mg BID v Placebo BID

Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [4]
Method	Fisher exact
Parameter estimate	Risk difference (RD)
Point estimate	45.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	27.79
upper limit	63.27

Notes:

[4] - one-sided p-value

Secondary: Number (%) of patients with a total weekly EEsAI-PRO score of ≤ 20 at week 6 (LOCF) double-blind phase

End point title	Number (%) of patients with a total weekly EEsAI-PRO score of ≤ 20 at week 6 (LOCF) double-blind phase

End point description:

Fourth of the a priori ordered key secondary endpoints to be confirmatorily tested for superiority when the primary endpoint showed superiority of budesonide 1mg vs placebo.

End point type	Secondary

End point timeframe:

at week 6 (LOCF) double-blind phase

End point values	Budesonide 1mg BID	Placebo BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	29		
Units: patients				
yes	30	2		
no	29	27		

Statistical analyses

Statistical analysis title	Fourth a priori ordered secondary endpoint

Statistical analysis description:

Efficacy significance testing continued in hierarchical fashion in support of labeling claims for the key secondary endpoints until the first of these comparisons of
BUET 1mg BID versus Placebo showed a one-sided p-value >0.025 (FAS-DB).

Comparison groups	Placebo BID v Budesonide 1mg BID

Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [5]
Method	Fisher exact
Parameter estimate	Risk difference (RD)
Point estimate	43.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	28.21
upper limit	59.69

Notes:

[5] - one-sided p-value

Secondary: Number (%) of patients with an improvement from baseline to week 6 (LOCF) double-blind phase in the weekly Visual Dysphagia Questionnaire (VDQ) score

End point title	Number (%) of patients with an improvement from baseline to week 6 (LOCF) double-blind phase in the weekly Visual Dysphagia Questionnaire (VDQ) score

End point description:

Fifth of the a priori ordered key secondary endpoints to be confirmatorily tested for superiority when the primary endpoint showed superiority of budesonide 1mg vs placebo.

End point type	Secondary

End point timeframe:

at week 6 (LOCF) double-blind phase

End point values	Budesonide 1mg BID	Placebo BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	29		
Units: patients				
yes	30	11		
no	29	18		

Statistical analyses

Statistical analysis title	Fifth a priori ordered key secondary endpoint

Statistical analysis description:

Efficacy significance testing continued in hierarchical fashion in support of labeling claims for the key secondary endpoints until the first of these comparisons of
BUET 1mg BID versus Placebo showed a one-sided p-value >0.025 (FAS-DB).

Comparison groups	Placebo BID v Budesonide 1mg BID

Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1804 [6]
Method	Fisher exact
Parameter estimate	Risk difference (RD)
Point estimate	12.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.87
upper limit	34.7

Notes:

[6] - one-sided p-value.
As the one-sided p-value was above 0.025, statistical superiority in this endpoint, despite numerical higher values under budesonide, could not be proven and thus confirmatory testing had to be stopped at this point.

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 6 week double-blind phase	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.1
Reporting groups	
Reporting group title	Placebo BID
Reporting group description: Twice daily Placebo	
Reporting group title	Budesonide 1mg BID
Reporting group description: Twice daily 1mg budesonide	

Serious adverse events	Placebo BID	Budesonide 1mg BID	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 29 (0.00%)	0 / 59 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 0.03 %

Non-serious adverse events	Placebo BID	Budesonide 1mg BID	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 29 (41.38%)	37 / 59 (62.71%)	
Investigations			
Blood cortisol decreased			
subjects affected / exposed	0 / 29 (0.00%)	3 / 59 (5.08%)	
occurrences (all)	0	3	
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	1 / 29 (3.45%)	0 / 59 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			

Hypertension			
subjects affected / exposed	0 / 29 (0.00%)	2 / 59 (3.39%)	
occurrences (all)	0	2	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 29 (3.45%)	4 / 59 (6.78%)	
occurrences (all)	1	4	
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	1 / 29 (3.45%)	0 / 59 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 29 (3.45%)	0 / 59 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 29 (3.45%)	0 / 59 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 29 (3.45%)	1 / 59 (1.69%)	
occurrences (all)	1	1	
Dyspepsia			
subjects affected / exposed	1 / 29 (3.45%)	1 / 59 (1.69%)	
occurrences (all)	1	1	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 29 (0.00%)	3 / 59 (5.08%)	
occurrences (all)	0	3	
Nausea			
subjects affected / exposed	0 / 29 (0.00%)	2 / 59 (3.39%)	
occurrences (all)	0	2	
Oesophageal food impaction			
subjects affected / exposed	1 / 29 (3.45%)	0 / 59 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			

Asthma			
subjects affected / exposed	2 / 29 (6.90%)	0 / 59 (0.00%)	
occurrences (all)	2	0	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 29 (3.45%)	0 / 59 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Laryngitis			
subjects affected / exposed	1 / 29 (3.45%)	1 / 59 (1.69%)	
occurrences (all)	1	1	
Nasopharyngitis			
subjects affected / exposed	1 / 29 (3.45%)	2 / 59 (3.39%)	
occurrences (all)	1	2	
Local fungal infection	Additional description: In 14 patients under budesonide a local fungal infection (oral , oropharyngeal, and/or esophageal candidiasis) was suspected. Thereof, only 3 patients (5.1%) showed clinically mild symptoms with no impact on their daily life.		
subjects affected / exposed	0 / 29 (0.00%)	14 / 59 (23.73%)	
occurrences (all)	0	14	
Pharyngitis			
subjects affected / exposed	2 / 29 (6.90%)	1 / 59 (1.69%)	
occurrences (all)	2	1	
Sinusitis			
subjects affected / exposed	1 / 29 (3.45%)	0 / 59 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 29 (3.45%)	0 / 59 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection			
subjects affected / exposed	1 / 29 (3.45%)	0 / 59 (0.00%)	
occurrences (all)	1	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