Clinical trial results:
Efficacy, safety and tolerability of Influcid tablets in patients (1 to 65 years old) suffering from upper respiratory tract infections with flu-like symptoms.
A randomized, international, multicenter, controlled clinical trial.

Summary

EudraCT number	2010-021422-35
Trial protocol	DE
Global end of trial date	02 August 2011

Results information

Result version number	v1 (current)
This version publication date	05 July 2016
First version publication date	02 August 2015

Trial information

Trial identification

Sponsor protocol code	09-NI-EP-001

Additional study identifiers

ISRCTN number	ISRCTN60440500
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Deutsche Homöopathie-Union, DHU-Arzneimittel GmbH & Co. KG
Sponsor organisation address	Ottostraße 24, Karlsruhe, Germany, D-76227
Public contact	Deutsche Homöopathie-Union, DHU-Arzneimittel GmbH & Co. KG, Ottostrasse 24, D-76227 Karlsruhe, + 49 (0)721 409301, info@dhu.com
Scientific contact	Deutsche Homöopathie-Union, DHU-Arzneimittel GmbH & Co. KG, Ottostrasse 24, D-76227 Karlsruhe , + 49 (0)721 409301, info@dhu.com

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	02 August 2011
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 August 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The actual study has been set up to evaluate systematically the efficacy and tolerability of Influcid. Patients received standard symptomatic medication, which was taken on demand (ST group) or Influcid for 7 days in addition to the same on demand symptomatic treatment (IFC group). Response at day 4, defined as absence of fever and absence or very mild degree of upper respiratory tract infection symptoms, was the primary outcome measure.

Protection of trial subjects:

All patients received standard symptomatic medication on demand. One half of the patients received additionally Influcid. Examinations performed consisted mainly of a physical examination including evaluation of upper respiratory tract infection complaints and the assessment of upper respiratory tract infection symptoms via a questionnaire. Apart from this questionnaire, physical examination did not differ significantly from routine physical examination, neither did it involve any particular risk for the patient.
At inclusion a throat swab (for a group A beta-hemolytic streptococci rapid test) and a nasopharyngeal swab (for an influenza test) were taken. Patients were informed about a possible slight discomfort caused by these tests via the patient informed consent form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 November 2010
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	Ukraine: 300
Country: Number of subjects enrolled	Germany: 223
Worldwide total number of subjects	523
EEA total number of subjects	223

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	24

months)	
Children (2-11 years)	240
Adolescents (12-17 years)	40
Adults (18-64 years)	219
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited during one cold season going from end of November 2010 until beginning of April 2011.
In Ukraine, patients were recruited at 4 general practitioner sites and 8 pediatric sites located mostly in polyclinics.
In Germany, patients were recruited at 4 general practitioners practices and 6 pediatric practices.

Pre-assignment

Screening details:

A total of 533 patients gave their informed consent to participate in the trial. 10 of these 533 patients were screening failures due to a postive rapid test for group A beta-hemolytic streptococci at enrolment.
A total of 523 patients were randomised.

Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	ST [SAF]

Arm description:

The control group "ST" was treated only with symptomatic medication on-demand.

Arm type	Active comparator
Investigational medicinal product name	Paracetamol
Investigational medicinal product code	IMP N° PR02
Other name	ben-u-ron®
Pharmaceutical forms	Syrup
Routes of administration	Oral use

Dosage and administration details:

ben-u-ron® syrup [IMP N° PR02] was offered to all patients of both arms.
5 ml syrup contained 200 mg paracetamol. The prescribed dosage of paracetamol was dependent on age and body weight. Generally 10-15 mg paracetamol per kg body weight as individual dose, up to 60 mg / kg body weight as total daily dose were recommended.
The respective dose interval was dependent on symptoms and maximum daily dose, and was not to fall below 6 hours.

Investigational medicinal product name	Oxymetazoline hydrochloride 0.05%
Investigational medicinal product code	IMP N° PR04
Other name	Nasivin®
Pharmaceutical forms	Nasal spray
Routes of administration	Nasal use

Dosage and administration details:

Nasivin® syrup [IMP N° PR04] was offered to patients aged 6 years or older of both arms.
1 spray squirt with 45 µl solution contained 22.5 µg of oxymetazoline hydrochloride. The solution was to be squirted 2-3 times per day into every nostril. The individual dose was not to be administered more than 3 times per day. The spray was not to be used for more than 7 days.

Investigational medicinal product name	Oxymetazoline hydrochloride 0.025%
Investigational medicinal product code	IMP N° PR05
Other name	Nasivin®
Pharmaceutical forms	Nasal spray
Routes of administration	Nasal use

Dosage and administration details:

Nasivin® syrup [IMP N° PR05] was offered to patients aged 1-5 years or older of both arms.
1 spray squirt with 45 µl solution contained 11.25 µg of oxymetazoline hydrochloride. The solution was to be squirted 2-3 times per day into every nostril. The individual dose was not to be administered more than 3 times per day. The spray was not to be used for more than 7 days.

Investigational medicinal product name	Ambroxol hydrochloride
Investigational medicinal product code	IMP N° PR03
Other name	Mucosolvan®
Pharmaceutical forms	Syrup
Routes of administration	Oral use

Dosage and administration details:

Mucosolvan® syrup [IMP N° PR03] was offered to all patients of both arms.
5 ml syrup contained 30 mg ambroxol hydrochloride. Children up to 2 years old were to take 1.25 ml of syrup twice a day. For this age group, the syrup was only to be given according to the direction of the investigator. Children from 2 to 5 years were to take 1.25 ml of syrup three times a day. Children from 6 to 12 years were to take 2.5 ml of syrup 2-3 times a day. Adults and adolescents of 12 years and old were to take 5 ml of syrup 3 times a day during the first 2-3 days, thereafter 5 ml solution twice a day. When dosing for adults - adolescents, an increase of efficacy could be achieved by giving 10 ml of syrup twice a day.

Arm title	IFC [SAF]

Arm description:

The test group "IFC" received 7 days of treatment with Influcid tablets (day 1 - day 7) additionally to on-demand symptomatic treatment

Arm type	Experimental
Investigational medicinal product name	Paracetamol
Investigational medicinal product code	IMP N° PR02
Other name	ben-u-ron®
Pharmaceutical forms	Syrup
Routes of administration	Oral use

Dosage and administration details:

ben-u-ron® syrup [IMP N° PR02] was offered to all patients of both arms.
5 ml syrup contained 200 mg paracetamol. The prescribed dosage of paracetamol was dependent on age and body weight. Generally 10-15 mg paracetamol per kg body weight as individual dose, up to 60 mg / kg body weight as total daily dose were recommended.
The respective dose interval was dependent on symptoms and maximum daily dose, and was not to fall below 6 hours.

Investigational medicinal product name	Ambroxol hydrochloride
Investigational medicinal product code	IMP N° PR03
Other name	Mucosolvan®
Pharmaceutical forms	Syrup
Routes of administration	Oral use

Dosage and administration details:

Mucosolvan® syrup [IMP N° PR03] was offered to all patients of both arms.
5 ml syrup contained 30 mg ambroxol hydrochloride. Children up to 2 years old were to take 1.25 ml of syrup twice a day. For this age group, the syrup was only to be given according to the direction of the investigator. Children from 2 to 5 years were to take 1.25 ml of syrup three times a day. Children from 6 to 12 years were to take 2.5 ml of syrup 2-3 times a day. Adults and adolescents of 12 years and old were to take 5 ml of syrup 3 times a day during the first 2-3 days, thereafter 5 ml solution twice a day. When dosing for adults - adolescents, an increase of efficacy could be achieved by giving 10 ml of syrup twice a day.

Investigational medicinal product name	Aconitum D3, Bryonia D2, Eupatorium perfoliatum D1, Gelsemium D3, Ipecacuanha D3 and Phosphorus D5
Investigational medicinal product code	IMP N° PR01
Other name	Influcid®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Test drug was provided to patients of IFC arm only . Separate blisters for children (<12 years) and

adolescents, adults (≥12 years) were provided. Acute dosage (first 72 hours) comprised intake of 1 tablet every 2 hours (8 tablets per day) for children and 1 tablet every hour (12 tablets per day) for adolescents, adults. Maintenance dosage (following 96 hours) comprised intake of 1 tablet 3 times a day (3 tablets per day) for children and 2 tablets 3 times a day (6 tablets per day) for adolescents, adults. [Note: Patients, who were randomised until noon at baseline, took the complete acute dosage on study days 1-3 and started with the maintenance dosage on study day 4.
Patients, who were randomised at baseline after noon, took half of the acute dosage on study day 1. These patients took the complete acute dosage on study days 2-4 and started with the maintenance dosage on study day 5.]

Investigational medicinal product name	Oxymetazoline hydrochloride 0.05%
Investigational medicinal product code	IMP N° PR04
Other name	Nasivin®
Pharmaceutical forms	Nasal spray
Routes of administration	Nasal use

Dosage and administration details:

Nasivin® syrup [IMP N° PR04] was offered to patients aged 6 years or older of both arms.
1 spray squirt with 45 µl solution contained 22.5 µg of oxymetazoline hydrochloride. The solution was to be squirted 2-3 times per day into every nostril. The individual dose was not to be administered more than 3 times per day. The spray was not to be used for more than 7 days.

Investigational medicinal product name	Oxymetazoline hydrochloride 0.025%
Investigational medicinal product code	IMP N° PR05
Other name	Nasivin®
Pharmaceutical forms	Nasal spray
Routes of administration	Nasal use

Dosage and administration details:

Nasivin® syrup [IMP N° PR05] was offered to patients aged 1-5 years or older of both arms.
1 spray squirt with 45 µl solution contained 11.25 µg of oxymetazoline hydrochloride. The solution was to be squirted 2-3 times per day into every nostril. The individual dose was not to be administered more than 3 times per day. The spray was not to be used for more than 7 days.

Number of subjects in period 1	ST [SAF]	IFC [SAF]
Started	258	265
1st FU visit completed (day 4±1)	258	264
Termination visit completed (day 15±2)	246	256
2nd FU visit completed (day 8±1)	256	262
Completed	246	256
Not completed	12	9
Non compliance/Parents incompliance	-	2
Lost to follow-up	1	1
Protocol deviation	11	5
Lack of efficacy	-	1

Baseline characteristics

Reporting groups	
Reporting group title	ST [SAF]
Reporting group description:	
The control group "ST" was treated only with symptomatic medication on-demand.	
Reporting group title	IFC [SAF]
Reporting group description:	
The test group "IFC" received 7 days of treatment with Influcid tablets (day 1 - day 7) additionally to on-demand symptomatic treatment	

Reporting group values	ST [SAF]	IFC [SAF]	Total
Number of subjects	258	265	523
Age categorical Units: Subjects			
< 12 years	133	131	264
≥ 12 years	125	134	259
Age continuous Units: years			
median	10	12	
inter-quartile range (Q1-Q3)	5 to 32	5 to 33	-
Gender categorical Units: Subjects			
Male	120	106	226
Female	138	159	297
Influenza A and B test results Units: Subjects			
Influenza A and B negative	219	229	448
Influenza A positive	33	21	54
Influenza B positive	6	12	18
Not recorded	0	3	3
Fever			
Assessment of axillary measurement of body temperature [°C] at physicians office.			
Units: Subjects			
no (≤37.2°C)	2	0	2
mild (>37.2°C but <37.5°C)	0	0	0
moderate (≥37.5°C but <38.5°C)	224	226	450
high (≥38.5°C)	32	39	71
Presence of hyperemia of mucosa Units: Subjects			
no	28	24	52
yes	230	241	471
Presence of nasal breathing impairment Units: Subjects			
no	27	38	65
yes	231	227	458
Ability to perform daily activities Units: Subjects			
no	211	198	409

yes	47	67	114
Presence of nasal symptoms [URTI symptom 1] Units: Subjects			
no	16	30	46
yes	242	235	477
Presence of Pharyngeal symptoms [URTI symptom 2] Units: Subjects			
no	24	21	45
yes	234	244	478
Presence of Cough [URTI symptom 3] Units: Subjects			
no	48	67	115
yes	210	198	408
Presence of Feeling tired [URTI symptom 4] Units: Subjects			
no	7	4	11
yes	251	261	512
Presence of Weakness [URTI symptom 5] Units: Subjects			
no	8	9	17
yes	250	256	506
Presence of Body aches [URTI symptom 6] Units: Subjects			
no	50	53	103
yes	208	212	420
Presence of Irritable/whiny [URTI symptom 7]			
This symptom has been assessed for chidren [patients <12 years] only.			
Units: Subjects			
no	17	16	33
yes	116	115	231
Not applicable [patients >12 years]	125	134	259
Presence of Less active [URTI symptom 8]			
This symptom has been assessed for chidren [patients <12 years] only.			
Units: Subjects			
no	5	5	10
yes	128	126	254
Not applicable [patients >12 years]	125	134	259
Body temperature			
Axillary measurement of body temperature [°C] at physicians office.			
Units: [°C]			
median	37.9	37.9	
inter-quartile range (Q1-Q3)	37.8 to 38.2	37.8 to 38.2	-
WURSS-21 total sum score			
The WURSS-21 total sum score is calculated as sum of items 2 to 20 of the Wisconsin Upper Respiratory Symptom Survey 21 (WURSS-21) which is a 21-item illness-specific health-related quality of life questionnaire. [Note: Available diary WURSS-21 questionnaire data at baseline was recorded for: N=230 (ST [SAF]);			

N=240 (IFC [SAF]); N=208 (ST arm [PP analysis set]); N=230 (ST arm [ITT analysis set]); N=238 (IFC arm [ITT analysis set]) and N=209 (IFC arm [PP analysis set]) patients.]			
Units: SCORE			
median	75	72	
inter-quartile range (Q1-Q3)	59 to 92	53 to 92.5	-

Subject analysis sets

Subject analysis set title	IFC arm [PP analysis set]
Subject analysis set type	Per protocol

Subject analysis set description:

This subject analysis set consists of all patients of IFC arm without major protocol violations.
N=41 out of N=265 IFC patients have been excluded from 'IFC arm [PP analysis set]' due to relevant protocol violations.

Subject analysis set title	ST arm [PP analysis set]
Subject analysis set type	Per protocol

Subject analysis set description:

This subject analysis set consists of all patients of ST arm without major protocol violations.
N=37 out of N=258 ST patients have been excluded from 'ST arm [PP analysis set]' due to relevant protocol violations.

Subject analysis set title	ST arm [ITT analysis set]
Subject analysis set type	Intention-to-treat

Subject analysis set description:

This subject analysis set consists of all patients of ST arm who contributed post-baseline efficacy data.
N=2 out of N=258 ST patients have been excluded from 'ST arm [ITT analysis set]' due to missing post-baseline efficacy data.

Subject analysis set title	IFC arm [ITT analysis set]
Subject analysis set type	Intention-to-treat

Subject analysis set description:

This subject analysis set consists of all patients of IFC arm who contributed post-baseline efficacy data.
N=4 out of N=265 IFC patients have been excluded from 'IFC arm [ITT analysis set]' due to missing post-baseline efficacy data.

Reporting group values	IFC arm [PP analysis set]	ST arm [PP analysis set]	ST arm [ITT analysis set]
Number of subjects	224	221	256
Age categorical			
Units: Subjects			
< 12 years	117	110	131
≥ 12 years	107	111	125
Age continuous			
Units: years			
median	10	12	10.5
inter-quartile range (Q1-Q3)	4 to 33	5 to 33	5 to 32.5
Gender categorical			
Units: Subjects			
Male	88	102	118
Female	136	119	138
Influenza A and B test results			
Units: Subjects			
Influenza A and B negative	198	196	219
Influenza A positive	12	20	31
Influenza B positive	11	5	6
Not recorded	3	0	0
Fever			

Assessment of axillary measurement of body temperature [°C] at physicians office.			
Units: Subjects			
no (≤37.2°C)	0	0	2
mild (>37.2°C but <37.5°C)	0	0	0
moderate (≥37.5°C but <38.5°C)	191	195	222
high (≥38.5°C)	33	26	32
Presence of hyperemia of mucosa Units: Subjects			
no	23	18	28
yes	201	203	228
Presence of nasal breathing impairment Units: Subjects			
no	36	24	27
yes	188	197	229
Ability to perform daily activities Units: Subjects			
no	172	182	209
yes	52	39	47
Presence of nasal symptoms [URTI symptom 1] Units: Subjects			
no	29	14	16
yes	195	207	240
Presence of Pharyngeal symptoms [URTI symptom 2] Units: Subjects			
no	19	17	24
yes	205	204	232
Presence of Cough [URTI symptom 3] Units: Subjects			
no	60	44	48
yes	164	177	208
Presence of Feeling tired [URTI symptom 4] Units: Subjects			
no	3	7	7
yes	221	214	249
Presence of Weakness [URTI symptom 5] Units: Subjects			
no	8	7	8
yes	216	214	248
Presence of Body aches [URTI symptom 6] Units: Subjects			
no	45	37	48
yes	179	184	208
Presence of Irritable/whiny [URTI symptom 7]			
This symptom has been assessed for chidren [patients <12 years] only.			
Units: Subjects			
no	14	11	17
yes	103	99	114

Not applicable [patients >12 years]	107	111	125
Presence of Less active [URTI symptom 8]			
This symptom has been assessed for chidren [patients <12 years] only.			
Units: Subjects			
no	5	3	5
yes	112	107	126
Not applicable [patients >12 years]	107	111	125
Body temperature			
Axillary measurement of body temperature [°C] at physicians office.			
Units: [°C]			
median	37.9	37.9	37.9
inter-quartile range (Q1-Q3)	37.8 to 38.2	37.8 to 38.2	37.8 to 38.2
WURSS-21 total sum score			
The WURSS-21 total sum score is calculated as sum of items 2 to 20 of the Wisconsin Upper Respiratory Symptom Survey 21 (WURSS-21) which is a 21-item illness-specific health-related quality of life questionnaire. [Note: Available diary WURSS-21 questionnaire data at baseline was recorded for: N=230 (ST [SAF]); N=240 (IFC [SAF]); N=208 (ST arm [PP analysis set]); N=230 (ST arm [ITT analysis set]); N=238 (IFC arm [ITT analysis set]) and N=209 (IFC arm [PP analysis set]) patients.]			
Units: SCORE			
median	70	77	75
inter-quartile range (Q1-Q3)	54 to 92	60 to 93.5	59 to 92

Reporting group values	IFC arm [ITT analysis set]		
Number of subjects	261		
Age categorical Units: Subjects			
< 12 years	130		
≥ 12 years	131		
Age continuous Units: years			
median	12		
inter-quartile range (Q1-Q3)	4 to 33		
Gender categorical Units: Subjects			
Male	104		
Female	157		
Influenza A and B test results Units: Subjects			
Influenza A and B negative	227		
Influenza A positive	19		
Influenza B positive	12		
Not recorded	3		
Fever			
Assessment of axillary measurement of body temperature [°C] at physicians office.			
Units: Subjects			
no (≤37.2°C)	0		
mild (>37.2°C but <37.5°C)	0		
moderate (≥37.5°C but <38.5°C)	222		
high (≥38.5°C)	39		
Presence of hyperemia of mucosa Units: Subjects			

no	24		
yes	237		
Presence of nasal breathing impairment Units: Subjects			
no	38		
yes	223		
Ability to perform daily activities Units: Subjects			
no	196		
yes	65		
Presence of nasal symptoms [URTI symptom 1] Units: Subjects			
no	30		
yes	231		
Presence of Pharyngeal symptoms [URTI symptom 2] Units: Subjects			
no	21		
yes	240		
Presence of Cough [URTI symptom 3] Units: Subjects			
no	67		
yes	194		
Presence of Feeling tired [URTI symptom 4] Units: Subjects			
no	4		
yes	257		
Presence of Weakness [URTI symptom 5] Units: Subjects			
no	9		
yes	252		
Presence of Body aches [URTI symptom 6] Units: Subjects			
no	53		
yes	208		
Presence of Irritable/whiny [URTI symptom 7]			
This symptom has been assessed for chidren [patients <12 years] only.			
Units: Subjects			
no	16		
yes	114		
Not applicable [patients >12 years]	131		
Presence of Less active [URTI symptom 8]			
This symptom has been assessed for chidren [patients <12 years] only.			
Units: Subjects			
no	5		
yes	125		
Not applicable [patients >12 years]	131		

Body temperature			
Axillary measurement of body temperature [°C] at physicians office.			
Units: [°C]			
median	37.9		
inter-quartile range (Q1-Q3)	37.8 to 38.2		
WURSS-21 total sum score			
The WURSS-21 total sum score is calculated as sum of items 2 to 20 of the Wisconsin Upper Respiratory Symptom Survey 21 (WURSS-21) which is a 21-item illness-specific health-related quality of life questionnaire. [Note: Available diary WURSS-21 questionnaire data at baseline was recorded for: N=230 (ST [SAF]); N=240 (IFC [SAF]); N=208 (ST arm [PP analysis set]); N=230 (ST arm [ITT analysis set]); N=238 (IFC arm [ITT analysis set]) and N=209 (IFC arm [PP analysis set]) patients.]			
Units: SCORE			
median	72		
inter-quartile range (Q1-Q3)	54 to 93		

End points

End points reporting groups

Reporting group title	ST [SAF]
Reporting group description:	
The control group "ST" was treated only with symptomatic medication on-demand.	
Reporting group title	IFC [SAF]
Reporting group description:	
The test group “IFC” received 7 days of treatment with Influcid tablets (day 1 - day 7) additionally to on-demand symptomatic treatment	
Subject analysis set title	IFC arm [PP analysis set]
Subject analysis set type	Per protocol
Subject analysis set description:	
This subject analysis set consists of all patients of IFC arm without major protocol violations. N=41 out of N=265 IFC patients have been excluded from 'IFC arm [PP analysis set]' due to relevant protocol violations.	
Subject analysis set title	ST arm [PP analysis set]
Subject analysis set type	Per protocol
Subject analysis set description:	
This subject analysis set consists of all patients of ST arm without major protocol violations. N=37 out of N=258 ST patients have been excluded from 'ST arm [PP analysis set]' due to relevant protocol violations.	
Subject analysis set title	ST arm [ITT analysis set]
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
This subject analysis set consists of all patients of ST arm who contributed post-baseline efficacy data. N=2 out of N=258 ST patients have been excluded from 'ST arm [ITT analysis set]' due to missing post-baseline efficacy data.	
Subject analysis set title	IFC arm [ITT analysis set]
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
This subject analysis set consists of all patients of IFC arm who contributed post-baseline efficacy data. N=4 out of N=265 IFC patients have been excluded from 'IFC arm [ITT analysis set]' due to missing post-baseline efficacy data.	

Primary: Fraction of patients with symptom alleviation at day 4 of the study

End point title	Fraction of patients with symptom alleviation at day 4 of the study
End point description:	
Symptoms alleviation is defined as: - Absence of fever (axillary temperature ≤ 37.2°C) and - Absence or very mild degree of the symptoms assessed by Wisconsin Upper Respiratory Symptom Survey 21 (WURSS-21) which is a 21-item illness-specific health-related quality of life questionnaire. Fever was measured 3-times daily by the patient (or in case of children by their parents) at home. Mean value covering last 24 hours was basis for this definition. Absence or very mild degree of symptoms is defined as answer to question “How sick do you feel today?” with “0” (not sick) or “1” (very mildly) for both assessments at day 4 (WURSS-21 was filled in twice daily by the patient or in case of children by their parents at home).	
End point type	Primary
End point timeframe:	
Study day 4	

End point values	IFC arm [PP analysis set]	ST arm [PP analysis set]	ST arm [ITT analysis set]	IFC arm [ITT analysis set]
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	224	221	252[1]	259[2]
Units: Patients				
No	191	209	235	219
Yes	33	12	17	40

Notes:

[1] - 4 out of 256 ST arm [ITT analysis set] patients were excluded from due to invalid diary data.

[2] - 2 out of 261 IFC arm [ITT analysis set] patients were excluded from due to invalid diary data.

Statistical analyses

Statistical analysis title	Test for equality of fractions between arms [PP]

Statistical analysis description:

Explorative analysis of upper respiratory tract infection [URTI] symptom alleviation at day 4. Categorization of symptom alleviation at day 4 ('Response' [Yes/No]) was tested for treatment related differences.

Presented values for risk difference are related to the difference in responsive patients between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [PP analysis set] v IFC arm [PP analysis set]
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0011 [3]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	9.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.33
upper limit	15.27

Notes:

[3] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly higher number of patients with URTI symptom alleviation (“Response”) at study day 4 in IFC compared to ST arm [PP analysis set].

Statistical analysis title	Test for equality of fractions between arms [ITT]

Statistical analysis description:

Explorative analysis of URTI symptom alleviation at day 4. Categorization of symptom alleviation at day 4 ('Response' [Yes/No]) was tested for treatment related differences.
Presented values for risk difference are related to the difference in responsive patients between treatments taking into account the direction 'IFC - ST'.

Comparison groups	IFC arm [ITT analysis set] v ST arm [ITT analysis set]
Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0018 [4]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	8.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	2.93
upper limit	14.47

Notes:

[4] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly higher number of patients with URTI symptom alleviation (“Response”) at study day 4 in IFC compared to ST arm [ITT analysis set].

Secondary: Time to symptom alleviation

End point title	Time to symptom alleviation

End point description:

The first day a patient had rated item 1 of WURSS-21 (“How sick do you feel today”) not higher than 1 (=”very mildly sick”) for both morning and evening assessments was used for evaluating the time to symptom alleviation.
Only patients with valid diary data and WURSS-21 item 1 assessed at baseline were considered. Symptom had to be present at baseline, i.e. assessment of WURSS-21 item 1 (if available) at baseline visit had to be scored with value ">1". Finally, only patients who who had a symptom alleviation until study day 14 could be taken into account for this analysis.

End point type	Secondary

End point timeframe:

Study day 2 to study day 14

End point values	ST arm [ITT analysis set]	IFC arm [ITT analysis set]		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	215[5]	236[6]		
Units: [days]				
median (inter-quartile range (Q1-Q3))	8 (7 to 10)	7 (5 to 8)		

Notes:

[5] - 41 out of 256 ST arm [ITT analysis set] patients were excluded due to missing data.

[6] - 25 out of 261 IFC arm [ITT analysis set] patients were excluded due to missing data.

Statistical analyses

Statistical analysis title	Time to symptom alleviation [ITT]

Statistical analysis description:

Explorative analysis of time to symptom alleviation. Time to symptom alleviation [days] was tested for treatment related differences.

Presented values for estimated location shift are related to the difference in time to symptom alleviation between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	451
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001 [7]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	-1

Notes:

[7] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly shorter time to symptom alleviation [days] in IFC compared to ST arm [ITT analysis set].

Secondary: Fraction of patients with symptom alleviation as defined for primary objective at study day 2, 3, 5, etc. until end of study

End point title	Fraction of patients with symptom alleviation as defined for primary objective at study day 2, 3, 5, etc. until end of study

End point description:

Presented counts refer to the number of patients per study day with observed symptom alleviation.

Symptoms alleviation is defined as:
- Absence of fever (axillary temperature ≤ 37.2°C) and
- Absence or very mild degree of the symptoms assessed by Wisconsin Upper Respiratory Symptom Survey 21 (WURSS-21).

Fever was measured 3-times daily by the patient (or in case of children by their parents) at home. Mean value covering last 24 hours was basis for this definition.
Absence or very mild degree of symptoms is defined as answer to question "How sick do you feel today?" with "0" (not sick) or "1" (very mildly) for both assessments at corresponding day (WURSS-21 was filled in twice daily by the patient or in case of children by their parents at home).

End point type	Secondary

End point timeframe:

study day 2 to study day 14

End point values	ST arm [ITT analysis set]	IFC arm [ITT analysis set]		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	252[8]	259[9]		
Units: patients				
Day 2	1	2		
Day 3	7	15		
Day 4	17	40		
Day 5	31	76		
Day 6	53	111		
Day 7	73	150		
Day 8	109	178		
Day 9	141	194		
Day 10	169	204		
Day 11	181	212		
Day 12	198	219		
Day 13	207	227		
Day 14	217	230		

Notes:

[8] - 4 out of 256 ST arm [ITT analysis set] patients were excluded from due to invalid diary data.

[9] - 2 out of 261 IFC arm [ITT analysis set] patients were excluded from due to invalid diary data.

Attachments (see zip file)	Difference between treatment arms per

Statistical analyses

Statistical analysis title	Day 2: Equality of fractions between arms [ITT]

Statistical analysis description:

Explorative analysis of URTI symptom alleviation as defined for primary endpoint. Categorization of symptom alleviation ('Response' [Yes/No]) was tested for treatment related differences.
Presented values for risk difference are related to the difference in responsive patients between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	other[10]
P-value	= 0.5787
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	2.1

Notes:

[10] - Contributing categories are "No" and "Yes". Missing data category, resulting from invalid diary data is not taken into account (invalid diary data was observed for 4 patients of ST and 2 patients of IFC arm, respectively).

Statistical analysis title	Day 3: Equality of fractions between arms [ITT]

Statistical analysis description:

Explorative analysis of URTI symptom alleviation as defined for primary endpoint. Categorization of symptom alleviation ('Response' [Yes/No]) was tested for treatment related differences.
Presented values for risk difference are related to the difference in responsive patients between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	other[11]
P-value	= 0.0933
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	6.9

Notes:

[11] - Contributing categories are "No" and "Yes". Missing data category, resulting from invalid diary data is not taken into account (invalid diary data was observed for 4 patients of ST and 2 patients of IFC arm, respectively).

Statistical analysis title	Day 4: Equality of fractions between arms [ITT]

Statistical analysis description:

Explorative analysis of URTI symptom alleviation as defined for primary endpoint. Categorization of symptom alleviation ('Response' [Yes/No]) was tested for treatment related differences.
Presented values for risk difference are related to the difference in responsive patients between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	other[12]
P-value	= 0.0018 [13]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	8.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.9
upper limit	14.5

Notes:

[12] - Contributing categories are "No" and "Yes". Missing data category, resulting from invalid diary data is not taken into account (invalid diary data was observed for 4 patients of ST and 2 patients of IFC arm, respectively).
[13] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly higher number of patients with URTI symptom alleviation (“Response”) at study day 4 in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	Day 5: Equality of fractions between arms [ITT]

Statistical analysis description:

Explorative analysis of URTI symptom alleviation as defined for primary endpoint. Categorization of symptom alleviation ('Response' [Yes/No]) was tested for treatment related differences.
Presented values for risk difference are related to the difference in responsive patients between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	other[14]
P-value	< 0.0001 [15]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	17
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.8
upper limit	24.3

Notes:

[14] - Contributing categories are "No" and "Yes". Missing data category, resulting from invalid diary data is not taken into account (invalid diary data was observed for 4 patients of ST and 2 patients of IFC arm, respectively).
[15] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly higher number of patients with URTI symptom alleviation (“Response”) at study day 5 in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	Day 6: Equality of fractions between arms [ITT]

Statistical analysis description:

Explorative analysis of URTI symptom alleviation as defined for primary endpoint. Categorization of symptom alleviation ('Response' [Yes/No]) was tested for treatment related differences.
Presented values for risk difference are related to the difference in responsive patients between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	other[16]
P-value	< 0.0001 [17]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	21.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.6
upper limit	30.1

Notes:

[16] - Contributing categories are "No" and "Yes". Missing data category, resulting from invalid diary data is not taken into account (invalid diary data was observed for 4 patients of ST and 2 patients of IFC arm, respectively).
[17] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly higher number of patients with URTI symptom alleviation (“Response”) at study day 6 in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	Day 7: Equality of fractions between arms [ITT]

Statistical analysis description:

Explorative analysis of URTI symptom alleviation as defined for primary endpoint. Categorization of symptom alleviation ('Response' [Yes/No]) was tested for treatment related differences.
Presented values for risk difference are related to the difference in responsive patients between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	other[18]
P-value	< 0.0001 [19]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	28.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	20.3
upper limit	37.6

Notes:

[18] - Contributing categories are "No" and "Yes". Missing data category, resulting from invalid diary data is not taken into account (invalid diary data was observed for 4 patients of ST and 2 patients of IFC arm, respectively).
[19] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly higher number of patients with URTI symptom alleviation (“Response”) at study day 7 in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	Day 8: Equality of fractions between arms [ITT]

Statistical analysis description:

Explorative analysis of URTI symptom alleviation as defined for primary endpoint. Categorization of symptom alleviation ('Response' [Yes/No]) was tested for treatment related differences.
Presented values for risk difference are related to the difference in responsive patients between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	other[20]
P-value	< 0.0001 [21]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	25.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	16.8
upper limit	34.2

Notes:

[20] - Contributing categories are "No" and "Yes". Missing data category, resulting from invalid diary data is not taken into account (invalid diary data was observed for 4 patients of ST and 2 patients of IFC arm, respectively).
[21] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly higher number of patients with URTI symptom alleviation (“Response”) at study day 8 in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	Day 9: Equality of fractions between arms [ITT]

Statistical analysis description:

Explorative analysis of URTI symptom alleviation as defined for primary endpoint. Categorization of symptom alleviation ('Response' [Yes/No]) was tested for treatment related differences.
Presented values for risk difference are related to the difference in responsive patients between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	other[22]
P-value	< 0.0001 [23]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	19
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.5
upper limit	27.4

Notes:

[22] - Contributing categories are "No" and "Yes". Missing data category, resulting from invalid diary data is not taken into account (invalid diary data was observed for 4 patients of ST and 2 patients of IFC arm, respectively).
[23] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly higher number of patients with URTI symptom alleviation (“Response”) at study day 9 in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	Day 10: Equality of fractions between arms [ITT]

Statistical analysis description:

Explorative analysis of URTI symptom alleviation as defined for primary endpoint. Categorization of symptom alleviation ('Response' [Yes/No]) was tested for treatment related differences.
Presented values for risk difference are related to the difference in responsive patients between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	other[24]
P-value	= 0.0029 [25]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	11.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.7
upper limit	19.7

Notes:

[24] - Contributing categories are "No" and "Yes". Missing data category, resulting from invalid diary data is not taken into account (invalid diary data was observed for 4 patients of ST and 2 patients of IFC arm, respectively).
[25] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly higher number of patients with URTI symptom alleviation (“Response”) at study day 10 in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	Day 11: Equality of fractions between arms [ITT]

Statistical analysis description:

Explorative analysis of URTI symptom alleviation as defined for primary endpoint. Categorization of symptom alleviation ('Response' [Yes/No]) was tested for treatment related differences.
Presented values for risk difference are related to the difference in responsive patients between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	other[26]
P-value	= 0.0072 [27]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	10
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.4
upper limit	17.7

Notes:

[26] - Contributing categories are "No" and "Yes". Missing data category, resulting from invalid diary data is not taken into account (invalid diary data was observed for 4 patients of ST and 2 patients of IFC arm, respectively).
[27] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly higher number of patients with URTI symptom alleviation (“Response”) at study day 11 in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	Day 12: Equality of fractions between arms [ITT]

Statistical analysis description:

Explorative analysis of URTI symptom alleviation as defined for primary endpoint. Categorization of symptom alleviation ('Response' [Yes/No]) was tested for treatment related differences.
Presented values for risk difference are related to the difference in responsive patients between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	other[28]
P-value	= 0.0809
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	13.1

Notes:

[28] - Contributing categories are "No" and "Yes". Missing data category, resulting from invalid diary data is not taken into account (invalid diary data was observed for 4 patients of ST and 2 patients of IFC arm, respectively).

Statistical analysis title	Day 13: Equality of fractions between arms [ITT]

Statistical analysis description:

Explorative analysis of URTI symptom alleviation as defined for primary endpoint. Categorization of symptom alleviation ('Response' [Yes/No]) was tested for treatment related differences.
Presented values for risk difference are related to the difference in responsive patients between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	other[29]
P-value	= 0.0822
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	5.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	12.1

Notes:

[29] - Contributing categories are "No" and "Yes". Missing data category, resulting from invalid diary data is not taken into account (invalid diary data was observed for 4 patients of ST and 2 patients of IFC arm, respectively).

Statistical analysis title	Day 14: Equality of fractions between arms [ITT]

Statistical analysis description:

Explorative analysis of URTI symptom alleviation as defined for primary endpoint. Categorization of symptom alleviation ('Response' [Yes/No]) was tested for treatment related differences.
Presented values for risk difference are related to the difference in responsive patients between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]

Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	other[30]
P-value	= 0.358
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	8.8

Notes:

[30] - Contributing categories are "No" and "Yes". Missing data category, resulting from invalid diary data is not taken into account (invalid diary data was observed for 4 patients of ST and 2 patients of IFC arm, respectively).

Secondary: Fraction of patients with maintenance of symptom alleviation as defined for primary objective until end of study

End point title	Fraction of patients with maintenance of symptom alleviation as defined for primary objective until end of study

End point description:

Subjects who showed URTI symptom alleviation as defined for primary endpoint within study period were evaluated for duration of (initial) response's duration.
Only patients with occurrence of symptom alleviation are shown.
Patients not showing URTI symptom alleviation throughout the whole study period are not considered.

End point type	Secondary

End point timeframe:

study day 2 to study day 14

End point values	ST arm [ITT analysis set]	IFC arm [ITT analysis set]		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	228[31]	242[32]		
Units: patients				
Maintenance until end of study	199	213		
Reoccurrence of symptom(s)	29	29		

Notes:

[31] - 24 patients had no symptom at all during the whole study.

[32] - 17 patients had no symptom at all during the whole study.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to return to normal daily activity [investigators' assessment]

End point title	Time to return to normal daily activity [investigators' assessment]

End point description:

Patients who were rated as having an impaired ability to perform their normal daily activities at baseline visit were evaluated for their individual time to return to normal daily activity, as assessed by the physician at FU calls and visits.
The table shows the cumulated number of patients resuming normal daily activity at respective call/visit

or earlier (Note: categories are ordered with respect to study schedule).

End point type	Secondary

End point timeframe:

1st FU call, 2nd FU call, 1st FU visit, 2nd FU visit and termination visit

End point values	ST arm [ITT analysis set]	IFC arm [ITT analysis set]		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	209[33]	196[34]		
Units: patients				
1st FU call (day 2)	11	11		
2nd FU call (day 3)	30	41		
1st FU visit (day 4±1)	58	94		
2nd FU visit (day 8±1)	136	171		
Termination visit (day 15 ±2)	196	186		

Notes:

[33] - 47 ST arm [ITT set] patients had no impairment at baseline and are therefore not considered.

[34] - 65 IFC arm [ITT set] patients had no impairment at baseline and are therefore not considered.

Statistical analyses

Statistical analysis title	FU call 1:Equality of fractions between arms [ITT]

Statistical analysis description:

Explorative analysis of patients patients resuming normal daily activity at FU call 1.
(Only patients with impairment of normal daily activities as assessed at baseline are considered in analysis.)
Presented values for risk difference are related to the difference between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	405
Analysis specification	Pre-specified
Analysis type	other[35]
P-value	= 0.8769
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.57
upper limit	5.26

Notes:

[35] - Binary categorization of "Resumption normal daily activity at FU call 1" [Yes/No] based on cumulated counts is basis for presented statistical test.

Statistical analysis title	FU call 2:Equality of fractions between arms [ITT]

Statistical analysis description:

Explorative analysis of patients patients resuming normal daily activity at or prior to FU call 2.
(Only patients with impairment of normal daily activities as assessed at baseline are considered in analysis.)
Presented values for risk difference are related to the difference between treatments taking into account

the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	405
Analysis specification	Pre-specified
Analysis type	other[36]
P-value	= 0.0825
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	6.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.35
upper limit	14.48

Notes:

[36] - Binary categorization of "Resumption normal daily activity at or prior to FU call 2" [Yes/No] based on cumulated counts is basis for presented statistical test.

Statistical analysis title	FU visit1:Equality of fractions between arms [ITT]

Statistical analysis description:

Explorative analysis of patients patients resuming normal daily activity at or prior to FU visit 1.
(Only patients with impairment of normal daily activities as assessed at baseline are considered in analysis.)
Presented values for risk difference are related to the difference between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	405
Analysis specification	Pre-specified
Analysis type	other[37]
P-value	< 0.0001 [38]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	20.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.46
upper limit	29.96

Notes:

[37] - Binary categorization of "Resumption normal daily activity at or prior to FU visit 1" [Yes/No] based on cumulated counts is basis for presented statistical test.
[38] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly higher number of patients with resumption normal daily activity at or prior to FU visit 1 in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	FU visit2:Equality of fractions between arms [ITT]

Statistical analysis description:

Explorative analysis of patients patients resuming normal daily activity at or prior to FU visit 2.
(Only patients with impairment of normal daily activities as assessed at baseline are considered in analysis.)
Presented values for risk difference are related to the difference between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]

Number of subjects included in analysis	405
Analysis specification	Pre-specified
Analysis type	other[39]
P-value	< 0.0001 [40]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	22.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.7
upper limit	30.64

Notes:

[39] - Binary categorization of "Resumption normal daily activity at or prior to FU visit 2" [Yes/No] based on cumulated counts is basis for presented statistical test.
[40] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly higher number of patients with resumption normal daily activity at or prior to FU visit 2 in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	T. visit :Equality of fractions between arms [ITT]

Statistical analysis description:

Explorative analysis of patients patients resuming normal daily activity at or prior to termination visit. (Only patients with impairment of normal daily activities as assessed at baseline are considered in analysis.)
Presented values for risk difference are related to the difference between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	405
Analysis specification	Pre-specified
Analysis type	other[41]
P-value	= 0.6271
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.87
upper limit	6.11

Notes:

[41] - Binary categorization of "Resumption normal daily activity at or prior to termination visit" [Yes/No] based on cumulated counts is basis for presented statistical test.

Secondary: Resolution of individual symptoms (analysed via WURSS-21)

End point title	Resolution of individual symptoms (analysed via WURSS-21)

End point description:

WURSS-21 items 2-20 assessed in patients diary are basis for individual symptom resolution evaluation. Between each distinct item, the number of subjects initially suffering a respective symptom (assessed by baseline WURSS-21 questionnaire item ratings '>1') may differ.
The table therefore presents (i) the number of patients initially suffering from symptom /item, (ii) the number of patients with symptom resolved within study period - by WURSS-21 item.
Note that the number of patients with symptom remaining unresolved at the end of study is the difference between (i) and (ii).
The endpoint has been evaluated for N=504 ITT analysis set patients, as for N=6 patients (ST=4; IFC=2) no diary WURSS-21 records were available and for additional N=7 patients (ST=2; IFC=5) no baseline WURSS-21 questionnaire rating was available.

End point type	Secondary
End point timeframe: study day 2 to study day 14	

End point values	ST arm [ITT analysis set]	IFC arm [ITT analysis set]		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	250[42]	254[43]		
Units: patients				
Item 2: Present impairment at baseline	184	173		
Item 2: Resolution within study period	169	165		
Item 3: Present impairment at baseline	194	199		
Item 3: Resolution within study period	177	190		
Item 4: Present impairment at baseline	176	165		
Item 4: Resolution within study period	168	162		
Item 5: Present impairment at baseline	182	186		
Item 5: Resolution within study period	171	184		
Item 6: Present impairment at baseline	182	194		
Item 6: Resolution within study period	172	188		
Item 7: Present impairment at baseline	194	184		
Item 7: Resolution within study period	173	166		
Item 8: Present impairment at baseline	141	150		
Item 8: Resolution within study period	132	146		
Item 9: Present impairment at baseline	208	204		
Item 9: Resolution within study period	199	200		
Item10: Present impairment at baseline	103	97		
Item 10: Resolution within study period	97	95		
Item11: Present impairment at baseline	238	244		
Item11: Resolution within study period	220	237		
Item12: Present impairment at baseline	183	171		
Item12: Resolution within study period	171	163		
Item13: Present impairment at baseline	220	229		
Item13: Resolution within study period	203	216		
Item14: Present impairment at baseline	217	216		
Item14: Resolution within study period	200	200		
Item15: Present impairment at baseline	211	210		
Item15: Resolution within study period	191	202		
Item16: Present impairment at baseline	208	215		
Item16: Resolution within study period	192	207		
Item17: Present impairment at baseline	207	213		
Item17: Resolution within study period	191	205		
Item18: Present impairment at baseline	208	215		
Item18: Resolution within study period	195	207		
Item19: Present impairment at baseline	202	211		
Item19: Resolution within study period	187	203		
Item20: Present impairment at baseline	200	213		
Item20: Resolution within study period	187	205		

Notes:

[42] - 6 ST arm [ITT set] patients had either missing baseline WURSS-21 questionnaire or no diary data.
[43] - 7 IFC arm [ITT set] patients had either missing baseline WURSS-21 questionnaire or no diary data.

Statistical analyses

Statistical analysis title	Item 2: Equality of fractions between arms [ITT]

Statistical analysis description:

Explorative analysis referring to observed resolution within study period [Yes/No] within those patients initially suffering from symptom (assessed by baseline WURSS-21 questionnaire item ratings '>1').

Presented values for risk difference are related to the difference in patients with resolution of symptom between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[44]
P-value	= 0.1748
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	3.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.08
upper limit	9.13

Notes:

[44] - The total number of patients contributing to this analysis is the number of patients with "item's impairment present at baseline" for each comparison group.

Statistical analysis title	Item 3: Equality of fractions between arms [ITT]

Statistical analysis description:

Explorative analysis referring to observed resolution within study period [Yes/No] within those patients initially suffering from symptom (assessed by baseline WURSS-21 questionnaire item ratings '>1').

Presented values for risk difference are related to the difference in patients with resolution of symptom between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[45]
P-value	= 0.0909
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	4.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.18
upper limit	9.67

Notes:

[45] - The total number of patients contributing to this analysis is the number of patients with "item's impairment present at baseline" for each comparison group.

Statistical analysis title	Item 4: Equality of fractions between arms [ITT]

Statistical analysis description:

Explorative analysis referring to observed resolution within study period [Yes/No] within those patients initially suffering from symptom (assessed by baseline WURSS-21 questionnaire item ratings '>1').

Presented values for risk difference are related to the difference in patients with resolution of symptom between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[46]
P-value	= 0.1543
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	2.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.55
upper limit	7.01

Notes:

[46] - The total number of patients contributing to this analysis is the number of patients with "item's impairment present at baseline" for each comparison group.

Statistical analysis title	Item 5: Equality of fractions between arms [ITT]

Statistical analysis description:

Explorative analysis referring to observed resolution within study period [Yes/No] within those patients initially suffering from symptom (assessed by baseline WURSS-21 questionnaire item ratings '>1').

Presented values for risk difference are related to the difference in patients with resolution of symptom between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[47]
P-value	= 0.0098 [48]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	4.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	9.28

Notes:

[47] - The total number of patients contributing to this analysis is the number of patients with "item's impairment present at baseline" for each comparison group.

[48] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly higher number of patients with item 5 resolution in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	Item 6: Equality of fractions between arms [ITT]

Statistical analysis description:

Explorative analysis referring to observed resolution within study period [Yes/No] within those patients initially suffering from symptom (assessed by baseline WURSS-21 questionnaire item ratings '>1').

Presented values for risk difference are related to the difference in patients with resolution of symptom between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[49]
P-value	= 0.2489
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.24
upper limit	7.04

Notes:

[49] - The total number of patients contributing to this analysis is the number of patients with "item's impairment present at baseline" for each comparison group.

Statistical analysis title	Item 7: Equality of fractions between arms [ITT]

Statistical analysis description:

Explorative analysis referring to observed resolution within study period [Yes/No] within those patients initially suffering from symptom (assessed by baseline WURSS-21 questionnaire item ratings '>1').

Presented values for risk difference are related to the difference in patients with resolution of symptom between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[50]
P-value	= 0.7392
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.61
upper limit	7.7

Notes:

[50] - The total number of patients contributing to this analysis is the number of patients with "item's impairment present at baseline" for each comparison group.

Statistical analysis title	Item 8: Equality of fractions between arms [ITT]

Statistical analysis description:

Explorative analysis referring to observed resolution within study period [Yes/No] within those patients initially suffering from symptom (assessed by baseline WURSS-21 questionnaire item ratings '>1').

Presented values for risk difference are related to the difference in patients with resolution of symptom

between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[51]
P-value	= 0.1251
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	3.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.76
upper limit	9.19

Notes:

[51] - The total number of patients contributing to this analysis is the number of patients with "item's impairment present at baseline" for each comparison group.

Statistical analysis title	Item 9: Equality of fractions between arms [ITT]

Statistical analysis description:

Explorative analysis referring to observed resolution within study period [Yes/No] within those patients initially suffering from symptom (assessed by baseline WURSS-21 questionnaire item ratings '>1').

Presented values for risk difference are related to the difference in patients with resolution of symptom between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[52]
P-value	= 0.1695
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	2.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.48
upper limit	6.21

Notes:

[52] - The total number of patients contributing to this analysis is the number of patients with "item's impairment present at baseline" for each comparison group.

Statistical analysis title	Item 10: Equality of fractions between arms [ITT]

Statistical analysis description:

Explorative analysis referring to observed resolution within study period [Yes/No] within those patients initially suffering from symptom (assessed by baseline WURSS-21 questionnaire item ratings '>1').

Presented values for risk difference are related to the difference in patients with resolution of symptom between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]

Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[53]
P-value	= 0.1747
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	3.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.57
upper limit	10.1

Notes:

[53] - The total number of patients contributing to this analysis is the number of patients with "item's impairment present at baseline" for each comparison group.

Statistical analysis title	Item11: Equality of fractions between arms [ITT]

Statistical analysis description:

Explorative analysis referring to observed resolution within study period [Yes/No] within those patients initially suffering from symptom (assessed by baseline WURSS-21 questionnaire item ratings '>1').

Presented values for risk difference are related to the difference in patients with resolution of symptom between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[54]
P-value	= 0.0202 [55]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	4.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.32
upper limit	9.07

Notes:

[54] - The total number of patients contributing to this analysis is the number of patients with "item's impairment present at baseline" for each comparison group.
[55] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly higher number of patients with item 11 resolution in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	Item12: Equality of fractions between arms [ITT]

Statistical analysis description:

Explorative analysis referring to observed resolution within study period [Yes/No] within those patients initially suffering from symptom (assessed by baseline WURSS-21 questionnaire item ratings '>1').

Presented values for risk difference are related to the difference in patients with resolution of symptom between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]

Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[56]
P-value	= 0.4442
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	1.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.47
upper limit	7.23

Notes:

[56] - The total number of patients contributing to this analysis is the number of patients with "item's impairment present at baseline" for each comparison group.

Statistical analysis title	Item13: Equality of fractions between arms [ITT]

Statistical analysis description:

Explorative analysis referring to observed resolution within study period [Yes/No] within those patients initially suffering from symptom (assessed by baseline WURSS-21 questionnaire item ratings '>1').

Presented values for risk difference are related to the difference in patients with resolution of symptom between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[57]
P-value	= 0.3844
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	2.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.02
upper limit	7.13

Notes:

[57] - The total number of patients contributing to this analysis is the number of patients with "item's impairment present at baseline" for each comparison group.

Statistical analysis title	Item14: Equality of fractions between arms [ITT]

Statistical analysis description:

Explorative analysis referring to observed resolution within study period [Yes/No] within those patients initially suffering from symptom (assessed by baseline WURSS-21 questionnaire item ratings '>1').

Presented values for risk difference are related to the difference in patients with resolution of symptom between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]

Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[58]
P-value	= 0.8671
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.03
upper limit	5.89

Notes:

[58] - The total number of patients contributing to this analysis is the number of patients with "item's impairment present at baseline" for each comparison group.

Statistical analysis title	Item15: Equality of fractions between arms [ITT]

Statistical analysis description:

Explorative analysis referring to observed resolution within study period [Yes/No] within those patients initially suffering from symptom (assessed by baseline WURSS-21 questionnaire item ratings '>1').

Presented values for risk difference are related to the difference in patients with resolution of symptom between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[59]
P-value	= 0.0196 [60]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	5.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.47
upper limit	10.87

Notes:

[59] - The total number of patients contributing to this analysis is the number of patients with "item's impairment present at baseline" for each comparison group.
[60] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly higher number of patients with item 15 resolution in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	Item16: Equality of fractions between arms [ITT]

Statistical analysis description:

Explorative analysis referring to observed resolution within study period [Yes/No] within those patients initially suffering from symptom (assessed by baseline WURSS-21 questionnaire item ratings '>1').

Presented values for risk difference are related to the difference in patients with resolution of symptom between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]

Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[61]
P-value	= 0.0775
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	3.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.92
upper limit	8.86

Notes:

[61] - The total number of patients contributing to this analysis is the number of patients with "item's impairment present at baseline" for each comparison group.

Statistical analysis title	Item17: Equality of fractions between arms [ITT]

Statistical analysis description:

Explorative analysis referring to observed resolution within study period [Yes/No] within those patients initially suffering from symptom (assessed by baseline WURSS-21 questionnaire item ratings '>1').

Presented values for risk difference are related to the difference in patients with resolution of symptom between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[62]
P-value	= 0.0794
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	3.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.95
upper limit	8.89

Notes:

[62] - The total number of patients contributing to this analysis is the number of patients with "item's impairment present at baseline" for each comparison group.

Statistical analysis title	Item18: Equality of fractions between arms [ITT]

Statistical analysis description:

Explorative analysis referring to observed resolution within study period [Yes/No] within those patients initially suffering from symptom (assessed by baseline WURSS-21 questionnaire item ratings '>1').

Presented values for risk difference are related to the difference in patients with resolution of symptom between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]

Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[63]
P-value	= 0.2312
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	2.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.09
upper limit	7.15

Notes:

[63] - The total number of patients contributing to this analysis is the number of patients with "item's impairment present at baseline" for each comparison group.

Statistical analysis title	Item19: Equality of fractions between arms [ITT]

Statistical analysis description:

Explorative analysis referring to observed resolution within study period [Yes/No] within those patients initially suffering from symptom (assessed by baseline WURSS-21 questionnaire item ratings '>1').

Presented values for risk difference are related to the difference in patients with resolution of symptom between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[64]
P-value	= 0.1074
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	3.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.29
upper limit	8.56

Notes:

[64] - The total number of patients contributing to this analysis is the number of patients with "item's impairment present at baseline" for each comparison group.

Statistical analysis title	Item20: Equality of fractions between arms [ITT]

Statistical analysis description:

Explorative analysis referring to observed resolution within study period [Yes/No] within those patients initially suffering from symptom (assessed by baseline WURSS-21 questionnaire item ratings '>1').

Presented values for risk difference are related to the difference in patients with resolution of symptom between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]

Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[65]
P-value	= 0.2046
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	2.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.01
upper limit	7.49

Notes:

[65] - The total number of patients contributing to this analysis is the number of patients with "item's impairment present at baseline" for each comparison group.

Secondary: Time to resolution of individual symptoms (analysed via diary WURSS-21)

End point title	Time to resolution of individual symptoms (analysed via diary WURSS-21)

End point description:

Analysis refers to the observed time point, when an item's resolution within study period was recorded in patients diary.
Only patients with corresponding "item's impairment present at baseline" who showed resolution within study period contribute to this analysis.

The endpoint has been evaluated for N=504 ITT analysis set patients, as for N=6 patients (ST=4; IFC=2) no diary WURSS-21 records were available and for additional N=7 patients (ST=2; IFC=5) no baseline WURSS-21 questionnaire rating was available. As stated above, the number of analysed patients differs between items, depending on the number of patients with observed resolution.
[Please also refer to endpoint 'Resolution of individual symptoms (analysed via WURSS-21)']

End point type	Secondary

End point timeframe:

study day 2 to study day 14

End point values	ST arm [ITT analysis set]	IFC arm [ITT analysis set]		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	250[66]	254[67]		
Units: [days]				
median (inter-quartile range (Q1-Q3))				
Item 2 (Runny nose)	8 (6 to 10)	6 (4 to 8)		
Item 3 (Plugged nose)	8 (5 to 9)	6 (4 to 8)		
Item 4 (Sneezing)	6 (4 to 8)	4 (3 to 6)		
Item 5 (Sore throat)	6 (5 to 8)	5 (4 to 7)		
Item 6 (Scratchy throat)	6 (4 to 8)	5 (4 to 7)		
Item 7 (Cough)	9 (7 to 11)	7 (4 to 9)		
Item 8 (Hoarseness)	6 (3 to 8)	4 (3 to 7)		
Item 9 (Head congestion)	6 (5 to 8)	4 (3 to 6)		
Item 10 (Chest congestion)	7 (4 to 10)	5 (3 to 8)		
Item 11 (Feeling tired)	8 (6 to 10)	6 (4 to 7)		
Item 12 (Think clearly)	7 (5 to 9)	5 (4 to 7)		

Item 13 (Sleep well)	7 (5 to 9)	5 (3 to 7)		
Item 14 (Breathe easily)	8 (5 to 9)	6 (4 to 7)		
Item 15 (Walk / climb stairs / exercise)	8 (6 to 10)	6 (4 to 7)		
Item 16 (Accomplish daily activities)	8 (6 to 9)	6 (4 to 7)		
Item 17 (Work outside the home)	8 (6 to 10)	6 (4 to 7)		
Item 18 (Work inside the home)	7 (5 to 9)	5 (4 to 7)		
Item 19 (Interact with others)	7 (5 to 9)	5 (4 to 7)		
Item 20 (Live your personal life)	7 (5 to 9)	5 (4 to 7)		

Notes:

[66] - 6 ST arm [ITT set] patients had either missing baseline WURSS-21 questionnaire or no diary data.
[67] - 7 IFC arm [ITT set] patients had either missing baseline WURSS-21 questionnaire or no diary data.

Statistical analyses

Statistical analysis title	Item 2: Time to symptom resolution [ITT]

Statistical analysis description:

Explorative analysis of individual item’s/ symptom’s time to resolution. Time to symptom resolution [days] was tested for treatment related differences.
Presented values for estimated location shift are related to the difference in time to symptom resolution between treatments taking into account the direction 'IFC - ST'. Negative values indicate a shorter duration until symptom alleviation for IFC patients compared to ST patients.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[68]
P-value	< 0.0001 [69]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	-1

Notes:

[68] - The total number of patients contributing to this test is the number of patients with item's “Resolution within study period” as presented in secondary end point “Resolution of individual symptoms (analysed via WURSS-21)”.
[69] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly shorter time to symptom resolution [days] in IFC compared to ST arm [ITT analysis set] for WURSS-21 item 2.

Statistical analysis title	Item 3: Time to symptom resolution [ITT]

Statistical analysis description:

Explorative analysis of individual item’s/ symptom’s time to resolution. Time to symptom resolution [days] was tested for treatment related differences.
Presented values for estimated location shift are related to the difference in time to symptom resolution between treatments taking into account the direction 'IFC - ST'. Negative values indicate a shorter duration until symptom alleviation for IFC patients compared to ST patients.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]

Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[70]
P-value	< 0.0001 [71]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	-1

Notes:

[70] - The total number of patients contributing to this test is the number of patients with item's "Resolution within study period" as presented in secondary end point "Resolution of individual symptoms (analysed via WURSS-21)".
[71] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly shorter time to symptom resolution [days] in IFC compared to ST arm [ITT analysis set] for WURSS-21 item 3.

Statistical analysis title	Item 4: Time to symptom resolution [ITT]

Statistical analysis description:

Explorative analysis of individual item's/ symptom's time to resolution. Time to symptom resolution [days] was tested for treatment related differences.
Presented values for estimated location shift are related to the difference in time to symptom resolution between treatments taking into account the direction 'IFC - ST'. Negative values indicate a shorter duration until symptom alleviation for IFC patients compared to ST patients.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[72]
P-value	< 0.0001 [73]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	-1

Notes:

[72] - The total number of patients contributing to this test is the number of patients with item's "Resolution within study period" as presented in secondary end point "Resolution of individual symptoms (analysed via WURSS-21)".
[73] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly shorter time to symptom resolution [days] in IFC compared to ST arm [ITT analysis set] for WURSS-21 item 4.

Statistical analysis title	Item 5: Time to symptom resolution [ITT]

Statistical analysis description:

Explorative analysis of individual item's/ symptom's time to resolution. Time to symptom resolution [days] was tested for treatment related differences.
Presented values for estimated location shift are related to the difference in time to symptom resolution between treatments taking into account the direction 'IFC - ST'. Negative values indicate a shorter duration until symptom alleviation for IFC patients compared to ST patients.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[74]
P-value	< 0.0001 [75]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	-1

Notes:

[74] - The total number of patients contributing to this test is the number of patients with item's "Resolution within study period" as presented in secondary end point "Resolution of individual symptoms (analysed via WURSS-21)".
[75] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly shorter time to symptom resolution [days] in IFC compared to ST arm [ITT analysis set] for WURSS-21 item 5.

Statistical analysis title	Item 6: Time to symptom resolution [ITT]

Statistical analysis description:

Explorative analysis of individual item's/ symptom's time to resolution. Time to symptom resolution [days] was tested for treatment related differences.
Presented values for estimated location shift are related to the difference in time to symptom resolution between treatments taking into account the direction 'IFC - ST'. Negative values indicate a shorter duration until symptom alleviation for IFC patients compared to ST patients.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[76]
P-value	= 0.0003 [77]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	0

Notes:

[76] - The total number of patients contributing to this test is the number of patients with item's "Resolution within study period" as presented in secondary end point "Resolution of individual symptoms (analysed via WURSS-21)".
[77] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly shorter time to symptom resolution [days] in IFC compared to ST arm [ITT analysis set] for WURSS-21 item 6.

Statistical analysis title	Item 7: Time to symptom resolution [ITT]

Statistical analysis description:

Explorative analysis of individual item's/ symptom's time to resolution. Time to symptom resolution [days] was tested for treatment related differences.
Presented values for estimated location shift are related to the difference in time to symptom resolution

between treatments taking into account the direction 'IFC - ST'. Negative values indicate a shorter duration until symptom alleviation for IFC patients compared to ST patients.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[78]
P-value	< 0.0001 [79]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	-1

Notes:

[78] - The total number of patients contributing to this test is the number of patients with item's "Resolution within study period" as presented in secondary end point "Resolution of individual symptoms (analysed via WURSS-21)".
[79] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly shorter time to symptom resolution [days] in IFC compared to ST arm [ITT analysis set] for WURSS-21 item 7.

Statistical analysis title	Item 8: Time to symptom resolution [ITT]

Statistical analysis description:

Explorative analysis of individual item's/ symptom's time to resolution. Time to symptom resolution [days] was tested for treatment related differences.
Presented values for estimated location shift are related to the difference in time to symptom resolution between treatments taking into account the direction 'IFC - ST'. Negative values indicate a shorter duration until symptom alleviation for IFC patients compared to ST patients.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[80]
P-value	= 0.0015 [81]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	0

Notes:

[80] - The total number of patients contributing to this test is the number of patients with item's "Resolution within study period" as presented in secondary end point "Resolution of individual symptoms (analysed via WURSS-21)".
[81] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly shorter time to symptom resolution [days] in IFC compared to ST arm [ITT analysis set] for WURSS-21 item 8.

Statistical analysis title	Item 9: Time to symptom resolution [ITT]

Statistical analysis description:

Explorative analysis of individual item’s/ symptom’s time to resolution. Time to symptom resolution [days] was tested for treatment related differences.
Presented values for estimated location shift are related to the difference in time to symptom resolution between treatments taking into account the direction 'IFC - ST'. Negative values indicate a shorter duration until symptom alleviation for IFC patients compared to ST patients.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[82]
P-value	< 0.0001 [83]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	-1

Notes:

[82] - The total number of patients contributing to this test is the number of patients with item's “Resolution within study period” as presented in secondary end point “Resolution of individual symptoms (analysed via WURSS-21)”.
[83] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly shorter time to symptom resolution [days] in IFC compared to ST arm [ITT analysis set] for WURSS-21 item 9.

Statistical analysis title	Item10: Time to symptom resolution [ITT]

Statistical analysis description:

Explorative analysis of individual item’s/ symptom’s time to resolution. Time to symptom resolution [days] was tested for treatment related differences.
Presented values for estimated location shift are related to the difference in time to symptom resolution between treatments taking into account the direction 'IFC - ST'. Negative values indicate a shorter duration until symptom alleviation for IFC patients compared to ST patients.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[84]
P-value	= 0.0012 [85]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	-1

Notes:

[84] - The total number of patients contributing to this test is the number of patients with item's “Resolution within study period” as presented in secondary end point “Resolution of individual symptoms (analysed via WURSS-21)”.
[85] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly shorter time to symptom resolution [days] in IFC compared to ST arm [ITT analysis set] for WURSS-21

item 10.

Statistical analysis title	Item11: Time to symptom resolution [ITT]

Statistical analysis description:

Explorative analysis of individual item’s/ symptom’s time to resolution. Time to symptom resolution [days] was tested for treatment related differences.
Presented values for estimated location shift are related to the difference in time to symptom resolution between treatments taking into account the direction 'IFC - ST'. Negative values indicate a shorter duration until symptom alleviation for IFC patients compared to ST patients.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[86]
P-value	< 0.0001 [87]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	-1

Notes:

[86] - The total number of patients contributing to this test is the number of patients with item's “Resolution within study period” as presented in secondary end point “Resolution of individual symptoms (analysed via WURSS-21)”.
[87] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly shorter time to symptom resolution [days] in IFC compared to ST arm [ITT analysis set] for WURSS-21 item 11.

Statistical analysis title	Item12: Time to symptom resolution [ITT]

Statistical analysis description:

Explorative analysis of individual item’s/ symptom’s time to resolution. Time to symptom resolution [days] was tested for treatment related differences.
Presented values for estimated location shift are related to the difference in time to symptom resolution between treatments taking into account the direction 'IFC - ST'. Negative values indicate a shorter duration until symptom alleviation for IFC patients compared to ST patients.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[88]
P-value	< 0.0001 [89]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	-1

Notes:

[88] - The total number of patients contributing to this test is the number of patients with item's "Resolution within study period" as presented in secondary end point "Resolution of individual symptoms (analysed via WURSS-21)".
[89] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly shorter time to symptom resolution [days] in IFC compared to ST arm [ITT analysis set] for WURSS-21 item 12.

Statistical analysis title	Item13: Time to symptom resolution [ITT]

Statistical analysis description:

Explorative analysis of individual item's/ symptom's time to resolution. Time to symptom resolution [days] was tested for treatment related differences.
Presented values for estimated location shift are related to the difference in time to symptom resolution between treatments taking into account the direction 'IFC - ST'. Negative values indicate a shorter duration until symptom alleviation for IFC patients compared to ST patients.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[90]
P-value	< 0.0001 [91]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	-1

Notes:

[90] - The total number of patients contributing to this test is the number of patients with item's "Resolution within study period" as presented in secondary end point "Resolution of individual symptoms (analysed via WURSS-21)".
[91] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly shorter time to symptom resolution [days] in IFC compared to ST arm [ITT analysis set] for WURSS-21 item 13.

Statistical analysis title	Item14: Time to symptom resolution [ITT]

Statistical analysis description:

Explorative analysis of individual item's/ symptom's time to resolution. Time to symptom resolution [days] was tested for treatment related differences.
Presented values for estimated location shift are related to the difference in time to symptom resolution between treatments taking into account the direction 'IFC - ST'. Negative values indicate a shorter duration until symptom alleviation for IFC patients compared to ST patients.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[92]
P-value	< 0.0001 [93]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	-1

Notes:

[92] - The total number of patients contributing to this test is the number of patients with item's "Resolution within study period" as presented in secondary end point "Resolution of individual symptoms (analysed via WURSS-21)".
[93] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly shorter time to symptom resolution [days] in IFC compared to ST arm [ITT analysis set] for WURSS-21 item 14.

Statistical analysis title	Item15: Time to symptom resolution [ITT]

Statistical analysis description:

Explorative analysis of individual item's/ symptom's time to resolution. Time to symptom resolution [days] was tested for treatment related differences.
Presented values for estimated location shift are related to the difference in time to symptom resolution between treatments taking into account the direction 'IFC - ST'. Negative values indicate a shorter duration until symptom alleviation for IFC patients compared to ST patients.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[94]
P-value	< 0.0001 [95]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	-1

Notes:

[94] - The total number of patients contributing to this test is the number of patients with item's "Resolution within study period" as presented in secondary end point "Resolution of individual symptoms (analysed via WURSS-21)".
[95] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly shorter time to symptom resolution [days] in IFC compared to ST arm [ITT analysis set] for WURSS-21 item 15.

Statistical analysis title	Item16: Time to symptom resolution [ITT]

Statistical analysis description:

Explorative analysis of individual item's/ symptom's time to resolution. Time to symptom resolution [days] was tested for treatment related differences.
Presented values for estimated location shift are related to the difference in time to symptom resolution between treatments taking into account the direction 'IFC - ST'. Negative values indicate a shorter duration until symptom alleviation for IFC patients compared to ST patients.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]

Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[96]
P-value	< 0.0001 [97]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	-1

Notes:

[96] - The total number of patients contributing to this test is the number of patients with item's "Resolution within study period" as presented in secondary end point "Resolution of individual symptoms (analysed via WURSS-21)".
[97] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly shorter time to symptom resolution [days] in IFC compared to ST arm [ITT analysis set] for WURSS-21 item 16.

Statistical analysis title	Item17: Time to symptom resolution [ITT]

Statistical analysis description:

Explorative analysis of individual item's/ symptom's time to resolution. Time to symptom resolution [days] was tested for treatment related differences.
Presented values for estimated location shift are related to the difference in time to symptom resolution between treatments taking into account the direction 'IFC - ST'. Negative values indicate a shorter duration until symptom alleviation for IFC patients compared to ST patients.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[98]
P-value	< 0.0001 [99]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	-1

Notes:

[98] - The total number of patients contributing to this test is the number of patients with item's "Resolution within study period" as presented in secondary end point "Resolution of individual symptoms (analysed via WURSS-21)".
[99] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly shorter time to symptom resolution [days] in IFC compared to ST arm [ITT analysis set] for WURSS-21 item 17.

Statistical analysis title	Item18: Time to symptom resolution [ITT]

Statistical analysis description:

Explorative analysis of individual item's/ symptom's time to resolution. Time to symptom resolution [days] was tested for treatment related differences.
Presented values for estimated location shift are related to the difference in time to symptom resolution between treatments taking into account the direction 'IFC - ST'. Negative values indicate a shorter duration until symptom alleviation for IFC patients compared to ST patients.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[100]
P-value	< 0.0001 [101]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	-1

Notes:

[100] - The total number of patients contributing to this test is the number of patients with item's "Resolution within study period" as presented in secondary end point "Resolution of individual symptoms (analysed via WURSS-21)".
[101] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly shorter time to symptom resolution [days] in IFC compared to ST arm [ITT analysis set] for WURSS-21 item 18.

Statistical analysis title	Item19: Time to symptom resolution [ITT]

Statistical analysis description:

Explorative analysis of individual item's/ symptom's time to resolution. Time to symptom resolution [days] was tested for treatment related differences.
Presented values for estimated location shift are related to the difference in time to symptom resolution between treatments taking into account the direction 'IFC - ST'. Negative values indicate a shorter duration until symptom alleviation for IFC patients compared to ST patients.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[102]
P-value	< 0.0001 [103]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	-1

Notes:

[102] - The total number of patients contributing to this test is the number of patients with item's "Resolution within study period" as presented in secondary end point "Resolution of individual symptoms (analysed via WURSS-21)".
[103] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly shorter time to symptom resolution [days] in IFC compared to ST arm [ITT analysis set] for WURSS-21 item 19.

Statistical analysis title	Item20: Time to symptom resolution [ITT]

Statistical analysis description:

Explorative analysis of individual item's/ symptom's time to resolution. Time to symptom resolution [days] was tested for treatment related differences.
Presented values for estimated location shift are related to the difference in time to symptom resolution

between treatments taking into account the direction 'IFC - ST'. Negative values indicate a shorter duration until symptom alleviation for IFC patients compared to ST patients.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[104]
P-value	< 0.0001 [105]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	-1

Notes:

[104] - The total number of patients contributing to this test is the number of patients with item's "Resolution within study period" as presented in secondary end point "Resolution of individual symptoms (analysed via WURSS-21)".
[105] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly shorter time to symptom resolution [days] in IFC compared to ST arm [ITT analysis set] for WURSS-21 item 20.

Secondary: Area under the curve (AUC) describing severity and course of the infection

End point title	Area under the curve (AUC) describing severity and course of the infection

End point description:

WURSS-21 questionnaire was answered by patients/parents twice a day. The cumulated (until study day 14) scorings for symptom (items2-11), quality of life (items12-20) and total (items 2-20) sum scores are shown here. In order to be able to compare between time-related randomization groups (i.e. patients randomized "till noon" or "after noon"), analysis was based on distance to baseline [DTB] (Evaluation "per day" would skew the calculation results as "till noon patients" would have answered one additional questionnaire compared to "after noon patients"). Presented AUC values refer to DTB=13.5. The endpoint has been evaluated for N=504 ITT analysis set patients, as for N=6 patients (ST=4; IFC=2) no diary WURSS-21 records were available and for additional N=7 patients (ST=2; IFC=5) no baseline WURSS-21 questionnaire rating was available. Please note that due to missing single items in baseline WURSS-21 questionnaire, AUC for sum scores could not be derived for all 504 analyzed patients.

End point type	Secondary

End point timeframe:

study day 2 to study day 14

End point values	ST arm [ITT analysis set]	IFC arm [ITT analysis set]		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	250[106]	254[107]		
Units: SCORE				
median (inter-quartile range (Q1-Q3))				
Symptom sum score (WURSS items 2-11)	425 (289.5 to 610.5)	304 (197 to 453)		
QoL sum score (WURSS items 12-20)	484 (285 to 710)	342 (192 to 524)		

Total sum score (WURSS items 2-20)	928 (597 to 1312)	643.5 (395 to 952)		

Notes:

[106] - Thereof subjects with evaluable data per sum score:
Symptom: N=240 | QoL: N= 234 | Total: N= 230
[107] - Thereof subjects with evaluable data per sum score:
Symptom: N=242 | QoL: N= 247 | Total: N= 238

Statistical analyses

Statistical analysis title	AUC: Symptom sum score [ITT]

Statistical analysis description:

Explorative analysis of symptom sum score as calculated from WURSS-21 questionnaire items 2 to 11. Sum score AUC values were tested for treatment related differences.
Presented values for estimated location shift are related to the difference in AUC between treatments taking into account the direction 'IFC - ST'. Negative values indicate lower scores (lower severity) for IFC group patients compared to ST group patients.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[108]
P-value	< 0.0001 [109]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-111
Confidence interval	
level	95 %
sides	2-sided
lower limit	-149
upper limit	-74

Notes:

[108] - The total number of patients contributing to this test is the number of patients with valid baseline assessment for contributing to score calculation WURSS-21 items (2-11).
[109] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly lower severity (WURSS-21 symptom sum score) within study period in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	AUC: QoL sum score [ITT]

Statistical analysis description:

Explorative analysis of QoL sum score as calculated from WURSS-21 questionnaire items 12 to 20. Sum score AUC values were tested for treatment related differences.

Presented values for estimated location shift are related to the difference in AUC between treatments taking into account the direction 'IFC - ST'. Negative values indicate lower scores (lower severity) for IFC group patients compared to ST group patients.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[110]
P-value	< 0.0001 [111]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-127

Confidence interval	
level	95 %
sides	2-sided
lower limit	-175
upper limit	-76

Notes:

[110] - The total number of patients contributing to this test is the number of patients with valid baseline assessment for contributing to score calculation WURSS-21 items (12-20).
[111] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly lower severity (WURSS-21 QoL sum score) within study period in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	AUC: Total sum score [ITT]

Statistical analysis description:

Explorative analysis of total sum score as calculated from WURSS-21 questionnaire items 2 to 20. Sum score AUC values were tested for treatment related differences.

Presented values for estimated location shift are related to the difference in AUC between treatments taking into account the direction 'IFC - ST'. Negative values indicate lower scores (lower severity) for IFC group patients compared to ST group patients.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	other[112]
P-value	< 0.0001 [113]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-246
Confidence interval	
level	95 %
sides	2-sided
lower limit	-331
upper limit	-162

Notes:

[112] - The total number of patients contributing to this test is the number of patients with valid baseline assessment for contributing to score calculation WURSS-21 items (2-20).
[113] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly lower severity (WURSS-21 total sum score) within study period in IFC compared to ST arm [ITT analysis set].

Secondary: Total amount and amount per day of paracetamol consumption

End point title	Total amount and amount per day of paracetamol consumption

End point description:

Paracetamol has been dispensed at discretion of the treating physician. Intake has been recorded in patient diary. The total amount [mg] of medication taken as well as the amount [mg] per day (average dosage) were calculated by considering (i) all patients with valid diary data [N=511; ITT both arms] and (ii) only those patients with valid diary data, to whom paracetamol has been actually dispensed.
[Note: Presented values refer to the amount of active substance.]

End point type	Secondary

End point timeframe:

study day 1 to study day 14

End point values	ST arm [ITT analysis set]	IFC arm [ITT analysis set]		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	252[114]	259[115]		
Units: mg				
median (inter-quartile range (Q1-Q3))				
Total amount [mg] (all patients)	1750 (400 to 5450)	600 (0 to 2200)		
Total amount [mg] (dispensed medication)	2200 (800 to 6000)	1000 (400 to 2600)		
Average dosage [mg] (all patients)	533.3 (200 to 1020.5)	300 (0 to 750)		
Average dosage [mg] (dispensed medication)	600 (400 to 1100)	466.7 (200 to 800)		

Notes:

[114] - 4 ST [ITT] patients had no valid diary data. Paracetamol dispense was recorded for N=228 patients.
[115] - 2 IFC [ITT] patients had no valid diary data. Paracetamol dispense was recorded for N=205 patients.

Statistical analyses

Statistical analysis title	Paracetamol: Total amount (all patients) [ITT]

Statistical analysis description:

Explorative analysis of the total (cumulated) amount of paracetamol taken. Analysis accounts for all patients with valid diary data. The total amount was tested for treatment related differences.
Presented values for estimated location shift are related to the difference in consumed paracetamol between treatments taking into account the direction 'IFC - ST'

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	other[116]
P-value	< 0.0001 [117]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-900
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1400
upper limit	-500

Notes:

[116] - Analysis is based on diary data entries from all patients with valid diary data.

[117] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly lower amount of paracetamol consumed in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	Paracetamol: Total amount (dispensed medication)

Statistical analysis description:

Explorative analysis of the total (cumulated) amount of paracetamol taken. Analysis accounts for all patients with valid diary data to whom paracetamol has been dispensed. The total amount was tested for treatment related differences.
Presented values for estimated location shift are related to the difference in consumed paracetamol between treatments taking into account the direction 'IFC - ST'

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]

Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	other[118]
P-value	< 0.0001 [119]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-1000
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1500
upper limit	-600

Notes:

[118] - Analysis is based on valid diary data entries from patients with recorded dispense of paracetamol (as prescribed by treating physician on his/her discretion).
[119] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly lower amount of paracetamol consumed in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	Paracetamol: Average dosage (all patients) [ITT]

Statistical analysis description:

Explorative analysis of the average amount of paracetamol taken by all patients with valid diary data is defined as the cumulated amount of paracetamol taken by these patients divided by the number of days of intake. The average dosage was tested for treatment related differences.
Presented values for estimated location shift are related to the difference in paracetamol dosis between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	other[120]
P-value	< 0.0001 [121]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-200
Confidence interval	
level	95 %
sides	2-sided
lower limit	-300
upper limit	-100

Notes:

[120] - Analysis is based on diary data entries from all patients with valid diary data.

[121] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly lower average amount of paracetamol consumed in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	Paracetamol: Average dosage (dispensed medication)

Statistical analysis description:

Explorative analysis of the average amount of paracetamol taken by all patients with valid diary data to whom paracetamol has been dispensed, which is defined as the cumulated amount of paracetamol taken by these patients divided by the number of days of intake. The average dosage was tested for treatment related differences.
Presented values for estimated location shift are related to the difference in paracetamol dosis between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]

Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	other[122]
P-value	= 0.0005 [123]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-175
Confidence interval	
level	95 %
sides	2-sided
lower limit	-250
upper limit	-65

Notes:

[122] - Analysis is based on valid diary data entries from patients with recorded dispense of paracetamol.
[123] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly lower average amount of paracetamol consumed in IFC compared to ST arm [ITT analysis set].

Secondary: Total amount and amount per day of ambroxol consumption

End point title	Total amount and amount per day of ambroxol consumption

End point description:

Ambroxol has been dispensed at discretion of the treating physician. Intake has been recorded in patient diary. The total amount [mg] of medication taken as well as the amount [mg] per day were calculated by considering (i) all patients with valid diary data [N=511; ITT both arms] and (ii) only those patients with valid diary data, to whom ambroxol has been actually dispensed.
[Note: Presented values refer to the amount of active substance.]

End point type	Secondary

End point timeframe:

study day 1 to study day 14

End point values	ST arm [ITT analysis set]	IFC arm [ITT analysis set]		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	252[124]	259[125]		
Units: [mg]				
median (inter-quartile range (Q1-Q3))				
Total amount [mg] (all patients)	315 (112.5 to 630)	112.5 (0 to 390)		
Total amount [mg] (dispensed medication)	375 (157.5 to 660)	240 (75 to 501)		
Average dosage [mg] (all patients)	38 (17.7 to 69.5)	22 (0 to 55.7)		
Average dosage [mg] (dispensed medication)	42.5 (22.5 to 72.9)	37.5 (20 to 70)		

Notes:

[124] - 4 ST [ITT] patients had no valid diary data. Ambroxol dispense was recorded for N=227 patients.
[125] - 2 IFC [ITT] patients had no valid diary data. Ambroxol dispense was recorded for N=187 patients.

Statistical analyses

Statistical analysis title	Ambroxol: Total amount (all patients) [ITT]

Statistical analysis description:

Explorative analysis of the total (cumulated) amount of ambroxol taken. Analysis accounts for all patients with valid diary data. The total amount was tested for treatment related differences.
Presented values for estimated location shift are related to the difference in consumed ambroxol between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	other[126]
P-value	< 0.0001 [127]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-135
Confidence interval	
level	95 %
sides	2-sided
lower limit	-180
upper limit	-90

Notes:

[126] - Analysis is based on diary data entries from all patients with valid diary data.

[127] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly lower amount of ambroxol consumed in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	Ambroxol: Total amount (dispensed medication)

Statistical analysis description:

Explorative analysis of the total (cumulated) amount of ambroxol taken. Analysis accounts for all patients with valid diary data to whom ambroxol has been dispensed. The total amount was tested for treatment related differences.
Presented values for estimated location shift are related to the difference in consumed ambroxol between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	other[128]
P-value	= 0.0004 [129]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-97.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-150
upper limit	-45

Notes:

[128] - Analysis is based on valid diary data entries from patients with recorded dispense of ambroxol.

[129] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly lower amount of ambroxol consumed in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	Ambroxol: Average dosage (all patients) [ITT]

Statistical analysis description:

Explorative analysis of the average amount of ambroxol taken by all patients with valid diary data is defined as the cumulated amount of ambroxol taken by these patients divided by the number of days of intake. The average dosage was tested for treatment related differences.

Presented values for estimated location shift are related to the difference in ambroxol dosis between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	other[130]
P-value	< 0.0001 [131]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-11.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.8
upper limit	-4

Notes:

[130] - Analysis is based on diary data entries from all patients with valid diary data.

[131] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly lower average amount of ambroxol consumed in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	Ambroxol: Average dosage (dispensed medication)

Statistical analysis description:

Explorative analysis of the average amount of ambroxol taken by all patients with valid diary data to whom ambroxol has been dispensed, which is defined as the cumulated amount of ambroxol taken by these patients divided by the number of days of intake. The average dosage was tested for treatment related differences.
Presented values for estimated location shift are related to the difference in ambroxol dosis between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	other[132]
P-value	= 0.1971
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-2.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9
upper limit	1.3

Notes:

[132] - Analysis is based on valid diary data entries from patients with recorded dispense of ambroxol.

Secondary: Total amount and amount per day of oxymetazoline consumption

End point title	Total amount and amount per day of oxymetazoline consumption

End point description:

Oxymetazoline has been dispensed at discretion of the treating physician. Intake has been recorded in patient diary. The total amount [µg] of medication taken as well as the amount [µg] per day were calculated by considering (i) all patients with valid diary data [N=511; ITT both arms] and (ii) only those patients with valid diary data, to whom oxymetazoline has been actually dispensed.
[Note: Presented values refer to the amount of active substance.]

End point type	Secondary

End point timeframe:

study day 1 to study day 14

End point values	ST arm [ITT analysis set]	IFC arm [ITT analysis set]		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	252[133]	259[134]		
Units: [µg]				
median (inter-quartile range (Q1-Q3))				
Total amount [µg] (all patients)	720 (253.1 to 1080)	292.5 (0 to 675)		
Total amount [µg] (dispensed medication)	810 (472.5 to 1147.5)	472.5 (202.5 to 810)		
Average dosage [µg] (all patients)	96.3 (48.9 to 135)	60.8 (0 to 112.5)		
Average dosage [µg] (dispensed medication)	108.4 (61.9 to 135)	80.3 (45 to 127)		

Notes:

[133] - 4 ST [ITT] patients had no valid diary data. Oxymetazoline dispense was listed for N=222 patients.
[134] - 2 IFC [ITT] patients had no valid diary data. Oxymetazoline dispense was listed for N=196 patients.

Statistical analyses

Statistical analysis title	Oxymetazoline: Total amount (all patients) [ITT]

Statistical analysis description:

Explorative analysis of the total (cumulated) amount of oxymetazoline taken. Analysis accounts for all patients with valid diary data. The total amount was tested for treatment related differences. Presented values for estimated location shift are related to the difference in consumed oxymetazoline between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	other[135]
P-value	< 0.0001 [136]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-315
Confidence interval	
level	95 %
sides	2-sided
lower limit	-405
upper limit	-202.5

Notes:

[135] - Analysis is based on diary data entries from all patients with valid diary data.

[136] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly lower amount of oxymetazoline consumed in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	Oxymetazoline: Total amount (dispensed medication)

Statistical analysis description:

Explorative analysis of the total (cumulated) amount of oxymetazoline taken. Analysis accounts for all patients with valid diary data to whom oxymetazoline has been dispensed. The total amount was tested

for treatment related differences.
Presented values for estimated location shift are related to the difference in consumed oxymetazoline between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	other[137]
P-value	< 0.0001 [138]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-270
Confidence interval	
level	95 %
sides	2-sided
lower limit	-360
upper limit	-157.5

Notes:

[137] - Analysis is based on valid diary data entries from patients with recorded dispense of oxymetazoline.
[138] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly lower amount of oxymetazoline consumed in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	Oxymetazoline: Average dosage (all patients) [ITT]

Statistical analysis description:

Explorative analysis of the average amount of oxymetazoline taken by all patients with valid diary data is defined as the cumulated amount of oxymetazoline taken by these patients divided by the number of days of intake. The average dosage was tested for treatment related differences.
Presented values for estimated location shift are related to the difference in oxymetazoline dosis between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	other[139]
P-value	< 0.0001 [140]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-28.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-43.4
upper limit	-13.5

Notes:

[139] - Analysis is based on diary data entries from all patients with valid diary data.

[140] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly lower average amount of oxymetazoline consumed in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	Oxymetazoline:Average dosage(dispensed medication)

Statistical analysis description:

Explorative analysis of the average amount of oxymetazoline taken by all patients with valid diary data to whom oxymetazoline has been dispensed, which is defined as the cumulated amount of oxymetazoline taken by these patients divided by the number of days of intake. The average dosage was tested for treatment related differences.
Presented values for estimated location shift are related to the difference in oxymetazoline dosis between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]

Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	other[141]
P-value	= 0.0026 [142]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-16.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-29.25
upper limit	-4.5

Notes:

[141] - Analysis is based on valid diary data entries from patients with recorded dispense of oxymetazoline.
[142] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly lower average amount of oxymetazoline consumed in IFC compared to ST arm [ITT analysis set].

Secondary: Duration of symptomatic medication consumption

End point title	Duration of symptomatic medication consumption

End point description:

Symptomatic medication (paracetamol, ambroxol, oxymetazoline 0.05% and 0.025%) have been dispensed at discretion of the treating physician. Intake has been recorded in patient diary. The number of days with recorded symptomatic medication intake is presented by considering (i) all patients with valid diary data [N=511; ITT both arms] and (ii) only those patients with valid diary data, to whom symptomatic medication has been actually dispensed.
Number of days with individual substances (paracetamol, ambroxol and oxymetazoline) as well as with "any symptomatic medication" is presented.
[Note: The number of patients with distinct symptomatic medication actually dispensed may be obtained from respective 'Total amount and amount per day' endpoint data presentations.]

End point type	Secondary

End point timeframe:

study day 1 to study day 14

End point values	ST arm [ITT analysis set]	IFC arm [ITT analysis set]		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	252[143]	259[144]		
Units: [days]				
median (inter-quartile range (Q1-Q3))				
Days with: Any sympt.med. (all patients)	9 (7 to 12)	6 (4 to 9)		
Days with: Any sympt.med. (dispensed medication)	9 (7 to 12)	7 (5 to 9)		
Days with: paracetamol (all patients)	3 (1 to 5)	2 (0 to 3)		
Days with: paracetamol (dispensed medication)	4 (2 to 5)	2 (1 to 3)		
Days with: ambroxol (all patients)	8 (5 to 11)	4 (0 to 8)		
Days with: ambroxol (dispensed medication)	8 (6 to 12)	6 (4 to 9)		
Days with: oxymetazoline (all patients)	7 (4 to 9)	4 (0 to 7)		
Days with: oxymetazoline (dispensed medication)	7 (6 to 10)	5 (3 to 8)		

Notes:

[143] - 4 ST [ITT] patients had no valid diary. Any sympt. med. dispense was recorded for N=252 patients.
[144] - 2 IFC [ITT] patients had no valid diary. Any sympt. med. dispense was lrecorded for N=234 patients.

Statistical analyses

Statistical analysis title	Duration: Any sympt.med. (all patients) [ITT]

Statistical analysis description:

Explorative analysis of any symptomatic medication intake duration for all patients with valid diary data is defined as the number of days with any symptomatic medication intake as recorded in patient diary. The duration [days] was tested for treatment related differences.
Presented values for estimated location shift are related to the difference in duration of any symptomatic medication intake between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	other[145]
P-value	< 0.0001 [146]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	-2

Notes:

[145] - Analysis is based on diary data entries from all patients with valid diary data.

[146] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly shorter duration of any symptomatic medication consumed in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	Duration: Any sympt.med. (dispensed medication)

Statistical analysis description:

Explorative analysis of any symptomatic medication intake duration for all patients with valid diary data to whom any symptomatic medication was dispensed is defined as the number of days of any symptomatic medication intake as recorded in patient diary for those patients. Duration was tested for treatment related differences.
Presented values for estimated location shift are related to the difference in duration of intake between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	other[147]
P-value	< 0.0001 [148]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	-1

Notes:

[147] - Analysis is based on valid diary data entries from patients with recorded dispense of either paracetamol, ambroxol or oxymetazoline.
[148] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly shorter duration of any symptomatic medication consumed in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	Duration: Paracetamol (all patients) [ITT]

Statistical analysis description:

Explorative analysis of paracetamol intake duration for all patients with valid diary data is defined as the number of days with paracetamol intake as recorded in patient diary. The duration [days] was tested for treatment related differences.
Presented values for estimated location shift are related to the difference in duration of paracetamol intake between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	other[149]
P-value	< 0.0001 [150]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	-1

Notes:

[149] - Analysis is based on diary data entries from all patients with valid diary data.

[150] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly shorter duration of paracetamol consumed in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	Duration: Ambroxol (all patients) [ITT]

Statistical analysis description:

Explorative analysis of ambroxol intake duration for all patients with valid diary data is defined as the number of days with ambroxol intake as recorded in patient diary.
The duration [days] was tested for treatment related differences.
Presented values for estimated location shift are related to the difference in duration of ambroxol intake between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	other[151]
P-value	< 0.0001 [152]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4
upper limit	-2

Notes:

[151] - Analysis is based on diary data entries from all patients with valid diary data.

[152] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly shorter duration of ambroxol consumed in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	Duration: Paracetamol (dispensed medication) [ITT]

Statistical analysis description:

Explorative analysis of paracetamol intake duration for all patients with valid diary data to whom paracetamol was dispensed is defined as the number of days of paracetamol intake as recorded in patient diary for those patients. The duration [days] was tested for treatment related differences.
Presented values for estimated location shift are related to the difference in duration of paracetamol intake between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	other[153]
P-value	< 0.0001 [154]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	-1

Notes:

[153] - Analysis is based on valid diary data entries from patients with recorded dispense of paracetamol.
[154] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly shorter duration of paracetamol consumed in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	Duration: Ambroxol (dispensed medication) [ITT]

Statistical analysis description:

Explorative analysis of ambroxol intake duration for all patients with valid diary data to whom ambroxol was dispensed is defined as the number of days of ambroxol intake as recorded in patient diary for those patients. The duration [days] was tested for treatment related differences.
Presented values for estimated location shift are related to the difference in duration of ambroxol intake between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	other[155]
P-value	< 0.0001 [156]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	-1

Notes:

[155] - Analysis is based on valid diary data entries from patients with recorded dispense of ambroxol.

[156] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly shorter duration of ambroxol consumed in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	Duration: Oxymetazoline (all patients) [ITT]

Statistical analysis description:

Explorative analysis of oxymetazoline intake duration for all patients with valid diary data is defined as the number of days with oxymetazoline intake as recorded in patient diary. The duration [days] was tested for treatment related differences.
Presented values for estimated location shift are related to the difference in duration of oxymetazoline intake between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	other[157]
P-value	< 0.0001 [158]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	-1

Notes:

[157] - Analysis is based on diary data entries from all patients with valid diary data.

[158] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly shorter duration of oxymetazoline consumed in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	Duration: Oxymetazoline(dispensed medication)[ITT]

Statistical analysis description:

Explorative analysis of oxymetazoline intake duration for all patients with valid diary data to whom oxymetazoline was dispensed is defined as the number of days of oxymetazoline intake as recorded in patient diary for those patients. The duration [days] was tested for treatment related differences.
Presented values for estimated location shift are related to the difference in duration of oxymetazoline intake between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	other[159]
P-value	< 0.0001 [160]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Hodges Lehman estimate of location shift
Point estimate	-2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	-1

Notes:

[159] - Analysis is based on valid diary data entries from patients with recorded dispense of oxymetazoline.
[160] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly shorter duration of oxymetazoline consumed in IFC compared to ST arm [ITT analysis set].

Secondary: Fraction of patients who must be withdrawn from the study due to prohibited medication

End point title	Fraction of patients who must be withdrawn from the study due to prohibited medication

End point description:

The analysis of withdrawals due to prohibited medication was based on the consumption of concomitant medication recorded in the diary and CRF.

End point type	Secondary

End point timeframe:

study day 2 to study day 14

End point values	ST arm [ITT analysis set]	IFC arm [ITT analysis set]		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	256	261		
Units: patients				
Withdrawal due to prohibited medication	9	5		
No withdrawal OR not due to prohibited medication	247	256		

Statistical analyses

Statistical analysis title	Test for equality of fractions between arms [ITT]

Statistical analysis description:

Explorative analysis of fraction of patients who must be withdrawn from the study due to prohibited medication.
Presented values for risk difference are related to the difference in prohibited medication related withdrawals between treatments taking into account the direction 'IFC - ST'

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	517
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2625
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	-1.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.8
upper limit	1.6

Secondary: Treatment outcome according to integrative medicine outcomes scale (IMOS)

End point title	Treatment outcome according to integrative medicine outcomes scale (IMOS)

End point description:

Treatment outcome was assessed by both the investigator and the patient at each study visit using IMOS (5-point rating scale).
Distinct values are presented for physicians and patients answers. The total number of patients assessments varies between presented visits as discontinuations occured between visits.

End point type	Secondary

End point timeframe:

1st FU visit, 2nd FU visit and termination visit

End point values	ST arm [ITT analysis set]	IFC arm [ITT analysis set]		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	256[161]	261[162]		
Units: patients				
1st FU V.: Complete recovery (physician)	5	13		
1st FU V.: Major improvement (physician)	62	143		
1st FU V.: Slight to moderate improvement (phys.)	121	82		
1st FU V.: No change (physician)	54	17		
1st FU V.: Deterioration (physician)	14	6		
2nd FU V.: Complete recovery (physician)	28	118		
2nd FU V.: Major improvement (physician)	164	121		
2nd FU V.: Slight to moderate improvement (phys.)	48	16		
2nd FU V.: No change (physician)	5	0		
2nd FU V.: Deterioration (physician)	6	4		
Term. V.: Complete recovery (physician)	186	225		
Term. V.: Major improvement (physician)	47	22		
Term. V.: Slight to moderate improvement (phys.)	10	2		
Term. V.: No change (physician)	0	3		
Term. V.: Deterioration (physician)	3	4		
1st FU V.: Complete recovery (patient)	7	18		
1st FU V.: Major improvement (patient)	58	129		

1st FU V.: Slight to moderate improvement (pat.)	121	89		
1st FU V.: No change (patient)	52	17		
1st FU V.: Deterioration (patient)	18	8		
2nd FU V.: Complete recovery (patient)	29	115		
2nd FU V.: Major improvement (patient)	164	126		
2nd FU V.: Slight to moderate improvement (pat.)	47	14		
2nd FU V.: No change (patient)	5	0		
2nd FU V.: Deterioration (patient)	6	4		
Term. V.: Complete recovery (patient)	191	225		
Term. V.: Major improvement (patient)	42	22		
Term. V.: Slight to moderate improvement (pat.)	9	2		
Term. V.: No change (patient)	1	3		
Term. V.: Deterioration (patient)	3	4		

Notes:

[161] - Total assessments per visit:
1st FU: N=256
2ndFU: N=252
Termination: N=246
[162] - Total assessments per visit:
1st FU: N=261
2ndFU: N=259
Termination: N=256

Statistical analyses

Statistical analysis title	IMOS 1st FU: At least 'major impr.' (patient)[ITT]

Statistical analysis description:

Explorative analysis of combined IMOS categories.
Binary categorization of IMOS is done by considering groups "complete recovery or major improvement" and "slight to moderate improvement or no change or deterioration" resulting from combination of IMOS assessment categories.

Presented values for risk difference are related to the difference between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	517
Analysis specification	Pre-specified
Analysis type	other[163]
P-value	< 0.001 [164]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	30.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	22.5
upper limit	39.36

Notes:

[163] - Analysis refers to patients' assessments.

[164] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly higher fraction of patients with IMOS assessed as 'complete recovery or major improvement' in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	IMOS 1st FU: At least 'major impr.' (physician)

Statistical analysis description:

Explorative analysis of combined IMOS categories.
Binary categorization of IMOS is done by considering groups "complete recovery or major improvement" and "slight to moderate improvement or no change or deterioration" resulting from combination of IMOS assessment categories.

Presented values for risk difference are related to the difference between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	517
Analysis specification	Pre-specified
Analysis type	other[165]
P-value	< 0.001 [166]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	33.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	25.19
upper limit	42.01

Notes:

[165] - Analysis refers to physicians' assessments.

[166] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly higher fraction of patients with IMOS assessed as 'complete recovery or major improvement' in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	IMOS 2nd FU: At least 'major impr.' (patient)

Statistical analysis description:

Explorative analysis of combined IMOS categories.
Binary categorization of IMOS is done by considering groups "complete recovery or major improvement" and "slight to moderate improvement or no change or deterioration" resulting from combination of IMOS assessment categories.

Presented values for risk difference are related to the difference between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	517
Analysis specification	Pre-specified
Analysis type	other[167]
P-value	< 0.001 [168]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	16.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.99
upper limit	22.93

Notes:

[167] - Analysis refers to patients' assessments. [Note: 1 missing assessment in ST arm.]

[168] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly higher fraction of patients with IMOS assessed as 'complete recovery or major improvement' in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	IMOS 2nd FU: At least 'major impr.' (physician)

Statistical analysis description:

Explorative analysis of combined IMOS categories.
Binary categorization of IMOS is done by considering groups "complete recovery or major improvement" and "slight to moderate improvement or no change or deterioration" resulting from combination of IMOS assessment categories.

Presented values for risk difference are related to the difference between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	517
Analysis specification	Pre-specified
Analysis type	other[169]
P-value	< 0.001 [170]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	16.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.51
upper limit	22.66

Notes:

[169] - Analysis refers to physicians' assessments. [Note: 1 missing assessment in ST arm.]

[170] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly higher fraction of patients with IMOS assessed as 'complete recovery or major improvement’ in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	IMOS Term. V.: At least 'major impr.' (patient)

Statistical analysis description:

Explorative analysis of combined IMOS categories.
Binary categorization of IMOS is done by considering groups "complete recovery or major improvement" and "slight to moderate improvement or no change or deterioration" resulting from combination of IMOS assessment categories.

Presented values for risk difference are related to the difference between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	517
Analysis specification	Pre-specified
Analysis type	other[171]
P-value	= 0.333
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	1.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.22
upper limit	5.76

Notes:

[171] - Analysis refers to patients' assessments.

Statistical analysis title	IMOS Term. V.: At least 'major impr.' (physician)

Statistical analysis description:

Explorative analysis of combined IMOS categories.

Binary categorization of IMOS is done by considering groups "complete recovery or major improvement" and "slight to moderate improvement or no change or deterioration" resulting from combination of IMOS assessment categories.

Presented values for risk difference are related to the difference between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	517
Analysis specification	Pre-specified
Analysis type	other[172]
P-value	= 0.333
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	1.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.22
upper limit	5.76

Notes:

[172] - Analysis refers to physicians' assessments.

Statistical analysis title	IMOS 1st FU: 'Complete recovery' (patient)

Statistical analysis description:

Explorative analysis of combined IMOS categories.
Binary categorization of IMOS is done by considering groups "complete recovery" and "major improvement or slight to moderate improvement or no change or deterioration" as resulting from combination of IMOS assessment categories. I.e. binary categorization in terms of complete recovery [Yes/No] is evaluated.

Presented values for risk difference are related to the difference between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	517
Analysis specification	Pre-specified
Analysis type	other[173]
P-value	= 0.027 [174]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	4.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.11
upper limit	8.22

Notes:

[173] - Analysis refers to patients' assessments.

[174] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly higher fraction of completely recovered patients (IMOS assessment) in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	IMOS 1st FU: 'Complete recovery' (physician)

Statistical analysis description:

Explorative analysis of combined IMOS categories.
Binary categorization of IMOS is done by considering groups "complete recovery" and "major improvement or slight to moderate improvement or no change or deterioration" as resulting from

combination of IMOS assessment categories. I.e. binary categorization in terms of complete recovery [Yes/No] is evaluated.

Presented values for risk difference are related to the difference between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	517
Analysis specification	Pre-specified
Analysis type	other[175]
P-value	= 0.06
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	3.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	6.55

Notes:

[175] - Analysis refers to physicians' assessments.

Statistical analysis title	IMOS 2nd FU: 'Complete recovery' (patient)

Statistical analysis description:

Explorative analysis of combined IMOS categories.
Binary categorization of IMOS is done by considering groups "complete recovery" and "major improvement or slight to moderate improvement or no change or deterioration" as resulting from combination of IMOS assessment categories. I.e. binary categorization in terms of complete recovery [Yes/No] is evaluated.

Presented values for risk difference are related to the difference between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	517
Analysis specification	Pre-specified
Analysis type	other[176]
P-value	< 0.001 [177]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	32.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	25.28
upper limit	40.51

Notes:

[176] - Analysis refers to patients' assessments. [Note: 1 missing assessment in ST arm.]

[177] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly higher fraction of completely recovered patients (IMOS assessment) in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	IMOS 2nd FU: 'Complete recovery' (physician)

Statistical analysis description:

Explorative analysis of combined IMOS categories.
Binary categorization of IMOS is done by considering groups "complete recovery" and "major improvement or slight to moderate improvement or no change or deterioration" as resulting from combination of IMOS assessment categories. I.e. binary categorization in terms of complete recovery

[Yes/No] is evaluated.

Presented values for risk difference are related to the difference between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	517
Analysis specification	Pre-specified
Analysis type	other[178]
P-value	< 0.001 [179]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	34.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	26.86
upper limit	42.04

Notes:

[178] - Analysis refers to physicians' assessments. [Note: 1 missing assessment in ST arm.]

[179] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly higher fraction of completely recovered patients (IMOS assessment) in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	IMOS Term. V.: 'Complete recovery' (patient)

Statistical analysis description:

Explorative analysis of combined IMOS categories.
Binary categorization of IMOS is done by considering groups "complete recovery" and "major improvement or slight to moderate improvement or no change or deterioration" as resulting from combination of IMOS assessment categories. I.e. binary categorization in terms of complete recovery [Yes/No] is evaluated.

Presented values for risk difference are related to the difference between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	517
Analysis specification	Pre-specified
Analysis type	other[180]
P-value	= 0.002 [181]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	10.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.29
upper limit	17.21

Notes:

[180] - Analysis refers to patients' assessments.

[181] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly higher fraction of completely recovered patients (IMOS assessment) in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	IMOS Term. V.: 'Complete recovery' (physician)

Statistical analysis description:

Explorative analysis of combined IMOS categories.
Binary categorization of IMOS is done by considering groups "complete recovery" and "major improvement or slight to moderate improvement or no change or deterioration" as resulting from

combination of IMOS assessment categories. I.e. binary categorization in terms of complete recovery [Yes/No] is evaluated.

Presented values for risk difference are related to the difference between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	517
Analysis specification	Pre-specified
Analysis type	other[182]
P-value	< 0.001 [183]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	12.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.19
upper limit	19.37

Notes:

[182] - Analysis refers to physicians' assessments.

[183] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly higher fraction of completely recovered patients (IMOS assessment) in IFC compared to ST arm [ITT analysis set].

Secondary: Satisfaction with treatment according to integrative medicine patient satisfaction scale [IMPSS]

End point title	Satisfaction with treatment according to integrative medicine patient satisfaction scale [IMPSS]

End point description:

IMPSS has been assessed by patients / parents at study termination visit.

End point type	Secondary

End point timeframe:

Study termination visit.

End point values	ST arm [ITT analysis set]	IFC arm [ITT analysis set]		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	246[184]	256[185]		
Units: patients				
not applicable	1	0		
Very satisfied	84	196		
Satisfied	120	53		
Neutral	37	4		
Dissatisfied	4	3		
Very dissatisfied	0	0		

Notes:

[184] - Total assessments:
Termination: N=246
[185] - Total assessments:
Termination: N=256

Statistical analyses

Statistical analysis title	IMPSS: Very satisfied patients [ITT]

Statistical analysis description:

Explorative analysis of combined IMPSS categories.
Binary categorization of IMPSS is done by considering the "very satisfied" group against all other categories.

Presented values for risk difference are related to the difference between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	502
Analysis specification	Pre-specified
Analysis type	other[186]
P-value	< 0.0001 [187]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	42.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	34.56
upper limit	51.08

Notes:

[186] - Analysis refers to patients' assessments at termination visit.

[187] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly higher fraction of patients beeing "very satisfied" (IMPSS) in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	IMPSS: Neutral and dissatisfied patients [ITT]

Statistical analysis description:

Explorative analysis of combined IMPSS categories.
Binary categorization of IMPSS is done by considering the combined "neutral or dissatisfied or very dissatisfied" group against combination of remaining categories.

Presented values for risk difference are related to the difference between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	502
Analysis specification	Pre-specified
Analysis type	other[188]
P-value	< 0.0001 [189]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	-14.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.29
upper limit	-9.2

Notes:

[188] - Analysis refers to patients' assessments at termination visit.

[189] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly lower fraction of patients beeing "neutral or dissatisfied or very dissatisfied" (IMPSS) in IFC compared to ST arm [ITT analysis set].

Secondary: Patients’ / parents’ assessment of tolerability of treatment

End point title	Patients' / parents' assessment of tolerability of treatment

End point description:

Tolerability of treatment has been assessed by patients / parents and investigators at each of FU calls and visits on a verbal rating scale.
Distinct values are presented for physicians and patients answers. The total number of patients assessments varies between presented calls and visits as (i) some calls were not done and (ii) discontinuations have occurred between visits.

End point type	Secondary

End point timeframe:

FU calls and visits

End point values	ST arm [ITT analysis set]	IFC arm [ITT analysis set]		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	256[190]	261[191]		
Units: patients				
1st FU call: Excellent (patient)	43	79		
1st FU call: Good (patient)	202	179		
1st FU call: Moderate (patient)	7	3		
1st FU call: Poor (patient)	3	0		
1st FU call: not assessed (patient)	1	0		
2nd FU call: Excellent (patient)	38	83		
2nd FU call: Good (patient)	184	161		
2nd FU call: Moderate (patient)	13	3		
2nd FU call: Poor (patient)	2	0		
2nd FU call: not assessed (patient)	1	0		
1st FU visit: Excellent (patient)	55	118		
1st FU visit: Good (patient)	183	140		
1st FU visit: Moderate (patient)	11	3		
1st FU visit: Poor (patient)	4	0		
1st FU visit: not assessed (patient)	3	0		
2nd FU visit: Excellent (patient)	63	145		
2nd FU visit: Good (patient)	174	112		
2nd FU visit: Moderate (patient)	9	2		
2nd FU visit: Poor (patient)	2	0		
2nd FU visit: not assessed (patient)	4	0		
Term. visit: Excellent (patient)	70	175		
Term. visit: Good (patient)	163	79		
Term. visit: Moderate (patient)	7	2		
Term. visit: Poor (patient)	2	0		
Term. visit: not assessed (patient)	4	0		
1st FU call: Excellent (physician)	45	80		
1st FU call: Good (physician)	203	178		
1st FU call: Moderate (physician)	5	3		
1st FU call: Poor (physician)	2	0		
1st FU call: not assessed (physician)	1	0		
2nd FU call: Excellent (physician)	39	81		
2nd FU call: Good (physician)	187	164		
2nd FU call: Moderate (physician)	9	2		
2nd FU call: Poor (physician)	2	0		

2nd FU call: not assessed (physician)	1	0		
1st FU visit: Excellent (physician)	55	118		
1st FU visit: Good (physician)	185	141		
1st FU visit: Moderate (physician)	11	2		
1st FU visit: Poor (physician)	2	0		
1st FU visit: not assessed (physician)	3	0		
2nd FU visit: Excellent (physician)	63	139		
2nd FU visit: Good (physician)	175	118		
2nd FU visit: Moderate (physician)	9	2		
2nd FU visit: Poor (physician)	1	0		
2nd FU visit: not assessed (physician)	4	0		
Term. visit: Excellent (physician)	71	172		
Term. visit: Good (physician)	165	82		
Term. visit: Moderate (physician)	5	2		
Term. visit: Poor (physician)	1	0		
Term. visit: not assessed (physician)	4	0		

Notes:

[190] - Totals:
1st call: N=256
2nd call: N=238
1st FU V.: N=256
2nd FU V.: N=252
Term. V.: N=246

[191] - Totals:
1st call: N=261
2nd call: N=247
1st FU V.: N=261
2nd FU V.: N=259
Term. V.: N=256

Statistical analyses

Statistical analysis title	1st FU call: 'Excellent' tolerability (patient)

Statistical analysis description:

Explorative analysis of combined tolerability assessment related categories.
Binary categorization of tolerability is done by considering the "excellent" category against all other categories.
[Note: Missing assessments are not considered.]

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	517
Analysis specification	Pre-specified
Analysis type	other[192]
P-value	= 0.0003 [193]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	13.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.8
upper limit	21

Notes:

[192] - Analysis refers to patients' assessments.

[193] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly

higher fraction of patients with 'excellent' tolerability of treatment in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	1st FU call: 'Excellent' tolerability (physician)

Statistical analysis description:

Explorative analysis of combined tolerability assessment related categories.
Binary categorization of tolerability is done by considering the "excellent" category against all other categories.
[Note: Missing assessments are not considered.]

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	517
Analysis specification	Pre-specified
Analysis type	other[194]
P-value	= 0.0006 [195]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	13
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.3
upper limit	20.7

Notes:

[194] - Analysis refers to physicians' assessments.

[195] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly higher fraction of patients with 'excellent' tolerability of treatment in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	2nd FU call: 'Excellent' tolerability (patient)

Statistical analysis description:

Explorative analysis of combined tolerability assessment related categories.
Binary categorization of tolerability is done by considering the "excellent" category against all other categories.
[Note: Missing assessments are not considered.]

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	517
Analysis specification	Pre-specified
Analysis type	other[196]
P-value	< 0.0001 [197]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	17.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.6
upper limit	25.5

Notes:

[196] - Analysis refers to patients' assessments.

[197] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly higher fraction of patients with 'excellent' tolerability of treatment in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	2nd FU call: 'Excellent' tolerability (physician)

Statistical analysis description:

Explorative analysis of combined tolerability assessment related categories.
Binary categorization of tolerability is done by considering the "excellent" category against all other categories.
[Note: Missing assessments are not considered.]

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	517
Analysis specification	Pre-specified
Analysis type	other[198]
P-value	< 0.0001 [199]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	16.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.4
upper limit	24.3

Notes:

[198] - Analysis refers to physicians' assessments.

[199] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly higher fraction of patients with 'excellent' tolerability of treatment in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	1st FU visit: 'Excellent' tolerability (patient)

Statistical analysis description:

Explorative analysis of combined tolerability assessment related categories.
Binary categorization of tolerability is done by considering the "excellent" category against all other categories.
[Note: Missing assessments are not considered.]

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	517
Analysis specification	Pre-specified
Analysis type	other[200]
P-value	< 0.0001 [201]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	23.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	15.2
upper limit	31.8

Notes:

[200] - Analysis refers to patients' assessments.

[201] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly higher fraction of patients with 'excellent' tolerability of treatment in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	1st FU visit: 'Excellent' tolerability (physician)

Statistical analysis description:

Explorative analysis of combined tolerability assessment related categories.
Binary categorization of tolerability is done by considering the "excellent" category against all other categories.
[Note: Missing assessments are not considered.]

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]

Number of subjects included in analysis	517
Analysis specification	Pre-specified
Analysis type	other[202]
P-value	< 0.0001 [203]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	23.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	15.2
upper limit	31.8

Notes:

[202] - Analysis refers to physicians' assessments.

[203] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly higher fraction of patients with 'excellent' tolerability of treatment in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	2nd FU visit: 'Excellent' tolerability (patient)

Statistical analysis description:

Explorative analysis of combined tolerability assessment related categories.
Binary categorization of tolerability is done by considering the "excellent" category against all other categories.
[Note: Missing assessments are not considered.]

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	517
Analysis specification	Pre-specified
Analysis type	other[204]
P-value	< 0.0001 [205]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	30.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	22.1
upper limit	39.1

Notes:

[204] - Analysis refers to patients' assessments.

[205] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly higher fraction of patients with 'excellent' tolerability of treatment in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	2nd FU visit: 'Excellent' tolerability (physician)

Statistical analysis description:

Explorative analysis of combined tolerability assessment related categories.
Binary categorization of tolerability is done by considering the "excellent" category against all other categories.
[Note: Missing assessments are not considered.]

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]

Number of subjects included in analysis	517
Analysis specification	Pre-specified
Analysis type	other[206]
P-value	< 0.0001 [207]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	28.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	19.7
upper limit	36.8

Notes:

[206] - Analysis refers to physicians' assessments.

[207] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly higher fraction of patients with 'excellent' tolerability of treatment in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	Term. visit: 'Excellent' tolerability (patient)

Statistical analysis description:

Explorative analysis of combined tolerability assessment related categories.
Binary categorization of tolerability is done by considering the "excellent" category against all other categories.
[Note: Missing assessments are not considered.]

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]
Number of subjects included in analysis	517
Analysis specification	Pre-specified
Analysis type	other[208]
P-value	< 0.0001 [209]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	39.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	31
upper limit	47.9

Notes:

[208] - Analysis refers to patients' assessments.

[209] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly higher fraction of patients with 'excellent' tolerability of treatment in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	Term. visit: 'Excellent' tolerability (physician)

Statistical analysis description:

Explorative analysis of combined tolerability assessment related categories.
Binary categorization of tolerability is done by considering the "excellent" category against all other categories.
[Note: Missing assessments are not considered.]

Comparison groups	ST arm [ITT analysis set] v IFC arm [ITT analysis set]

Number of subjects included in analysis	517
Analysis specification	Pre-specified
Analysis type	other[210]
P-value	< 0.0001 [211]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	37.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	29.3
upper limit	46.4

Notes:

[210] - Analysis refers to physicians' assessments.

[211] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly higher fraction of patients with 'excellent' tolerability of treatment in IFC compared to ST arm [ITT analysis set].

Other pre-specified: Present complaints of upper respiratory tract infection: Fever, mucosal hyperaemia, nasal breathing impairment

End point title	Present complaints of upper respiratory tract infection: Fever, mucosal hyperaemia, nasal breathing impairment

End point description:

Presence of individual URTI symptoms fever, mucosal hyperaemia [MucHyp] and nasal breathing impairment [NBImp] has been assessed by physician at each visit.

End point type	Other pre-specified

End point timeframe:

1st FU visit, 2nd FU visit and termination visit

End point values	IFC arm [PP analysis set]	ST arm [ITT analysis set]		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	261[212]	256[213]		
Units: patients				
1st FU V.: Presence of fever	46	80		
1st FU V.: Absence of fever	215	176		
1st FU V.: missing data: fever	0	0		
2nd FU V.: Presence of fever	8	16		
2nd FU V.: Absence of fever	251	235		
2nd FU V.: missing data: fever	0	1		
Term. V.: Presence of fever	5	8		
Term. V.: Absence of fever	251	238		
Term. V.: missing data: fever	0	0		
1st FU V.: Presence of MucHyp	188	208		
1st FU V.: Absence of MucHyp	73	48		
1st FU V.: missing data: MucHyp	0	0		
2nd FU V.: Presence of MucHyp	55	96		
2nd FU V.: Absence of MucHyp	204	155		
2nd FU V.: missing data: MucHyp	0	1		
Term. V.: Presence of MucHyp	12	16		
Term. V.: Absence of MucHyp	244	230		

Term. V.: missing data: MucHyp	0	0		
1st FU V.: Presence of NBImp	169	208		
1st FU V.: Absence of NBImp	92	48		
1st FU V.: missing data: NBImp	0	0		
2nd FU V.: Presence of NBImp	68	111		
2nd FU V.: Absence of NBImp	191	140		
2nd FU V.: missing data: NBImp	0	1		
Term. V.: Presence of NBImp	23	26		
Term. V.: Absence of NBImp	233	220		
Term. V.: missing data: NBImp	0	0		

Notes:

[212] - Total assessments per visit:
1st FU: N=261
2ndFU: N=259
Termination: N=256

[213] - Total assessments per visit:
1st FU: N=256
2ndFU: N=252
Termination: N=246

Statistical analyses

Statistical analysis title	1st FU: Presence of fever

Statistical analysis description:

Explorative analysis of URTI complaint's presence as assessed by physical examination at each visit [ITT analysis set]. Binary categorization "absence" vs. "presence" with respect to symptom is considered.

Presented values for risk difference are related to the difference in symptom's presence between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [PP analysis set]
Number of subjects included in analysis	517
Analysis specification	Pre-specified
Analysis type	other[214]
P-value	= 0.0003 [215]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	-13.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.3
upper limit	-5.9

Notes:

[214] - Analysis refers to physicians' physical examination assessments not taking missing values into account.

[215] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly lower fraction of patients with presence of fever (assessed by physical examination) in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	2nd FU: Presence of fever

Statistical analysis description:

Explorative analysis of URTI complaint's presence as assessed by physical examination at each visit [ITT analysis set]. Binary categorization "absence" vs. "presence" with respect to symptom is considered.

Presented values for risk difference are related to the difference in symptom's presence between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [PP analysis set]

Number of subjects included in analysis	517
Analysis specification	Pre-specified
Analysis type	other[216]
P-value	= 0.0798
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	-3.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.4
upper limit	0.8

Notes:

[216] - Analysis refers to physicians' physical examination assessments not taking missing values into account.

Statistical analysis title	Term.visit: Presence of fever

Statistical analysis description:

Explorative analysis of URTI complaint's presence as assessed by physical examination at each visit [ITT analysis set]. Binary categorization "absence" vs. "presence" with respect to symptom is considered.

Presented values for risk difference are related to the difference in symptom's presence between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [PP analysis set]
Number of subjects included in analysis	517
Analysis specification	Pre-specified
Analysis type	other[217]
P-value	= 0.3597
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.5
upper limit	1.9

Notes:

[217] - Analysis refers to physicians' physical examination assessments not taking missing values into account.

Statistical analysis title	1st FU: Presence of mucosal hyperaemia

Statistical analysis description:

Explorative analysis of URTI complaint's presence as assessed by physical examination at each visit [ITT analysis set]. Binary categorization "absence" vs. "presence" with respect to symptom is considered.

Presented values for risk difference are related to the difference in symptom's presence between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [PP analysis set]
Number of subjects included in analysis	517
Analysis specification	Pre-specified
Analysis type	other[218]
P-value	= 0.0133 [219]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	-9.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.9
upper limit	-1.6

Notes:

[218] - Analysis refers to physicians' physical examination assessments not taking missing values into account.
[219] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly lower fraction of patients with present mucosal hyperaemia (assessed by physical examination) in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	2nd FU: Presence of mucosal hyperaemia

Statistical analysis description:

Explorative analysis of URTI complaint's presence as assessed by physical examination at each visit [ITT analysis set]. Binary categorization "absence" vs. "presence" with respect to symptom is considered.

Presented values for risk difference are related to the difference in symptom's presence between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [PP analysis set]
Number of subjects included in analysis	517
Analysis specification	Pre-specified
Analysis type	other[220]
P-value	< 0.0001 [221]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	-17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-25.2
upper limit	-8.8

Notes:

[220] - Analysis refers to physicians' physical examination assessments not taking missing values into account.
[221] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly lower fraction of patients with present mucosal hyperaemia (assessed by physical examination) in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	Term.visit: Presence of mucosal hyperaemia

Statistical analysis description:

Explorative analysis of URTI complaint's presence as assessed by physical examination at each visit [ITT analysis set]. Binary categorization "absence" vs. "presence" with respect to symptom is considered.

Presented values for risk difference are related to the difference in symptom's presence between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [PP analysis set]
Number of subjects included in analysis	517
Analysis specification	Pre-specified
Analysis type	other[222]
P-value	= 0.3753
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	-1.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.2
upper limit	2.6

Notes:

[222] - Analysis refers to physicians' physical examination assessments not taking missing values into account.

Statistical analysis title	1st FU: Presence of nasal breathing impairment

Statistical analysis description:

Explorative analysis of URTI complaint's presence as assessed by physical examination at each visit [ITT analysis set]. Binary categorization "absence" vs. "presence" with respect to symptom is considered.

Presented values for risk difference are related to the difference in symptom's presence between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [PP analysis set]
Number of subjects included in analysis	517
Analysis specification	Pre-specified
Analysis type	other[223]
P-value	< 0.0001 [224]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	-16.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.4
upper limit	-8.6

Notes:

[223] - Analysis refers to physicians' physical examination assessments not taking missing values into account.
[224] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly lower fraction of patients with present nasal breathing impairment(assessed by physical examination) in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	2nd FU: Presence of nasal breathing impairment

Statistical analysis description:

Explorative analysis of URTI complaint's presence as assessed by physical examination at each visit [ITT analysis set]. Binary categorization "absence" vs. "presence" with respect to symptom is considered.

Presented values for risk difference are related to the difference in symptom's presence between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [PP analysis set]
Number of subjects included in analysis	517
Analysis specification	Pre-specified
Analysis type	other[225]
P-value	< 0.0001 [226]
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	-18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-26.5
upper limit	-9.4

Notes:

[225] - Analysis refers to physicians' physical examination assessments not taking missing values into account.
[226] - A statistically significant difference (at alpha level 0.05) is concluded, indicating a significantly lower fraction of patients with present nasal breathing impairment (assessed by physical examination) in IFC compared to ST arm [ITT analysis set].

Statistical analysis title	Term.visit: Presence of nasal breathing impairment

Statistical analysis description:

Explorative analysis of URTI complaint's presence as assessed by physical examination at each visit [ITT analysis set]. Binary categorization "absence" vs. "presence" with respect to symptom is considered.

Presented values for risk difference are related to the difference in symptom's presence between treatments taking into account the direction 'IFC - ST'.

Comparison groups	ST arm [ITT analysis set] v IFC arm [PP analysis set]
Number of subjects included in analysis	517
Analysis specification	Pre-specified
Analysis type	other[227]
P-value	= 0.5498
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.2
upper limit	4

Notes:

[227] - Analysis refers to physicians' physical examination assessments not taking missing values into account.

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Whole study period.	
Adverse event reporting additional description:	
Adverse event [AE] monitoring has been done at all post-baseline visits and during both FU calls. All AEs, irrespective of severity, seriousness and relationship to study drug, had to be monitored by the investigator until they had satisfactorily subsided or stabilised to such an extent that further marked improvement was not longer to be expected.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	12

Reporting groups	
Reporting group title	ST [SAF]
Reporting group description:	
The control group "ST" was treated only with symptomatic medication on-demand.	
Reporting group title	IFC [SAF]
Reporting group description:	
The test group “IFC” received 7 days of treatment with Influcid tablets (day 1 - day 7) additionally to on-demand symptomatic treatment	

Serious adverse events	ST [SAF]	IFC [SAF]	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 258 (0.00%)	0 / 265 (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: 1 %

Non-serious adverse events	ST [SAF]	IFC [SAF]	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 258 (5.81%)	13 / 265 (4.91%)	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	3 / 258 (1.16%)	4 / 265 (1.51%)	
occurrences (all)	3	5	
Vomiting			
subjects affected / exposed	0 / 258 (0.00%)	3 / 265 (1.13%)	
occurrences (all)	0	3	

Nausea subjects affected / exposed occurrences (all)	3 / 258 (1.16%) 3	1 / 265 (0.38%) 1	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	1 / 258 (0.39%) 1	3 / 265 (1.13%) 3	
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	1 / 258 (0.39%) 1	3 / 265 (1.13%) 3	
Infections and infestations Bronchitis subjects affected / exposed occurrences (all)	7 / 258 (2.71%) 7	1 / 265 (0.38%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 October 2010	Amendment 1 corresponds to the implementation of protocol final V2.0 from 14OCT2010 which included the changes to the original protocol (final V1.0 from 28JUN2010) required by the ethics committee of the Bavarian State Medical Association (Germany). In addition the patient informed consents for adults, legal representatives and children were updated and a patient informed consent for adolescents was implemented in Germany.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported