



Clinical trial results:

A Randomized, Double-Blind, Parallel Group, Multicenter Study of Fluticasone Furoate/Vilanterol 200/25 mcg Inhalation Powder, Fluticasone Furoate/Vilanterol 100/25 mcg Inhalation Powder, and Fluticasone Furoate 100 mcg Inhalation Powder in the Treatment of Persistent Asthma in Adults and Adolescents

Summary

EudraCT number	2012-002797-32
Trial protocol	DE SE NL PL
Global end of trial date	15 October 2013

Results information

Result version number	v1 (current)
This version publication date	27 April 2016
First version publication date	19 February 2015

Trial information

Trial identification

Sponsor protocol code	HZA116863
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom,
Public contact	GSK Response Center, GlaxoSmithKline, +1 8664357343,
Scientific contact	GSK Response Center, GlaxoSmithKline, +1 8664357343,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	03 December 2013
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	15 October 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the efficacy and safety of once daily (evening) administration of FF/VI 100/25 with FF 100 in adult and adolescent subjects ≥ 12 years of age with moderate to severe, persistent bronchial asthma over 12 weeks.

Protection of trial subjects:

Upon initial entry into the trial, participants were assessed for their fitness for the study by a physical examination, chemistry/hematology laboratory tests, serum pregnancy (females of child-bearing potential), and electrocardiogram (ECG) results. Medical, asthma, and previous asthma treatment histories were obtained along with pulmonary function testing. Reversibility was also established. Stability limits of 80% of the participant's pre-albuterol FEV1 and peak expiratory flow rate were determined at the randomization visit to assist the investigators in monitoring participant's asthma status throughout the study. Twice each day (morning and evening), participants rated their asthma symptoms and measured their PEF. Participants were instructed to contact the investigator if the PEF fell below the established limit. Albuterol inhalation was provided for rescue use, and use was monitored each morning and evening when the other assessments were performed. Pulmonary function was assessed at each visit via spirometry. Vital signs were also taken at each visit, and the participants were questioned in regard to their health and non-serious adverse events/serious adverse events that may have occurred since their last visit. Two medics supported the study and were available for consultation with the investigators as needed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 September 2012
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	Netherlands: 62
Country: Number of subjects enrolled	Poland: 84
Country: Number of subjects enrolled	Sweden: 50
Country: Number of subjects enrolled	Germany: 129
Country: Number of subjects enrolled	Argentina: 241
Country: Number of subjects enrolled	Chile: 146
Country: Number of subjects enrolled	Mexico: 51
Country: Number of subjects enrolled	Romania: 192
Country: Number of subjects enrolled	Russian Federation: 295
Country: Number of subjects enrolled	Ukraine: 165
Country: Number of subjects enrolled	United States: 604

Worldwide total number of subjects	2019
EEA total number of subjects	517

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	120
Adults (18-64 years)	1646
From 65 to 84 years	252
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Participants meeting eligibility criteria at the Screening visit entered a 4-week Run-in Period for Baseline safety evaluations and measures of asthma status. Participants were then randomized to a 12-week Treatment Period. A total of 2019 participants were screened; 1039 were randomized and received ≥ 1 dose of study treatment.

Pre-assignment

Screening details:

One participant was determined to have been randomized at each of two United States sites. Upon discovery of the duplicate enrollment, the participant was withdrawn. To account for only one randomization by this participant, a total randomized population of 1039 was used as the basis for the study analysis.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Arms

Are arms mutually exclusive?	Yes
Arm title	FF 100 µg OD

Arm description:

Participants received Fluticasone Furoate (FF) 100 microgram (µg) inhalation powder once daily (OD) in the evening from a dry powder inhaler (DPI) for 12 weeks. Participants were provided albuterol/salbutamol inhalation aerosol to be used as rescue medication during the Treatment Period.

Arm type	Experimental
Investigational medicinal product name	Fluticasone furoate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Respiratory use

Dosage and administration details:

100 µg once daily

Arm title	FF/VI 100/25 µg OD
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Arm description:

Participants received FF/Vilanterol (VI) 100/25 µg inhalation powder OD in the evening from a DPI for 12 weeks. Participants were provided albuterol/salbutamol inhalation aerosol to be used as rescue medication during the Treatment Period.

Arm type	Experimental
Investigational medicinal product name	Fluticasone furoate/vilanterol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Respiratory use

Dosage and administration details:

100 µg/25 µg once daily

Arm title	FF/VI 200/25 µg OD
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Arm description:

Participants received FF/VI 200/25 µg inhalation powder OD in the evening from a DPI for 12 weeks.

Participants were provided albuterol/salbutamol inhalation aerosol to be used as rescue medication during the Treatment Period.

Arm type	Experimental
Investigational medicinal product name	Fluticasone furoate/vilanterol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Respiratory use

Dosage and administration details:

200 micrograms (µg)/25 µg once daily

Number of subjects in period 1^[1]	FF 100 µg OD	FF/VI 100/25 µg OD	FF/VI 200/25 µg OD
Started	347	346	346
Completed	296	314	321
Not completed	51	32	25
Consent withdrawn by subject	8	8	5
Physician decision	3	4	4
Adverse event, non-fatal	4	3	3
Protocol-defined Stopping Criteria	1	-	1
Lost to follow-up	-	1	1
Lack of efficacy	33	13	11
Protocol deviation	2	3	-

Notes:

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

Justification: Only 1039 of the 2019 enrolled/screened participants were randomized to treatment and received at least one dose of study medication during the treatment period (these participants comprised the Inten-to-Treat [ITT] Population). Disposition data are reported for these members of the ITT Population.

Baseline characteristics

Reporting groups

Reporting group title	FF 100 µg OD
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Reporting group description:

Participants received Fluticasone Furoate (FF) 100 microgram (µg) inhalation powder once daily (OD) in the evening from a dry powder inhaler (DPI) for 12 weeks. Participants were provided albuterol/salbutamol inhalation aerosol to be used as rescue medication during the Treatment Period.

Reporting group title	FF/VI 100/25 µg OD
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Reporting group description:

Participants received FF/Vilanterol (VI) 100/25 µg inhalation powder OD in the evening from a DPI for 12 weeks. Participants were provided albuterol/salbutamol inhalation aerosol to be used as rescue medication during the Treatment Period.

Reporting group title	FF/VI 200/25 µg OD
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Reporting group description:

Participants received FF/VI 200/25 µg inhalation powder OD in the evening from a DPI for 12 weeks. Participants were provided albuterol/salbutamol inhalation aerosol to be used as rescue medication during the Treatment Period.

Reporting group values	FF 100 µg OD	FF/VI 100/25 µg OD	FF/VI 200/25 µg OD
Number of subjects	347	346	346
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	44.7	45.9	46.6
standard deviation	± 15.89	± 16.14	± 14.72
Gender categorical			
Units: Subjects			
Female	199	205	224
Male	148	141	122
Race, customized			
Units: Subjects			
African American/African Heritage	26	20	28
American Indian or Alaska Native	0	0	2
Asian - East Asian Heritage	0	1	0
Asian - Japanese Heritage	1	0	0
Asian - South East Asian Heritage	3	1	2
Native Hawaiian or other Pacific Islander	0	1	0
White - White/Caucasian/European Heritage	305	307	300
Mixed Race	12	16	13
Missing	0	0	1

Reporting group values	Total		
Number of subjects	1039		
Age categorical			
Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	-		
Gender categorical Units: Subjects			
Female	628		
Male	411		
Race, customized Units: Subjects			
African American/African Heritage	74		
American Indian or Alaska Native	2		
Asian - East Asian Heritage	1		
Asian - Japanese Heritage	1		
Asian - South East Asian Heritage	6		
Native Hawaiian or other Pacific Islander	1		
White - White/Caucasian/European Heritage	912		
Mixed Race	41		
Missing	1		

End points

End points reporting groups

Reporting group title	FF 100 µg OD
Reporting group description: Participants received Fluticasone Furoate (FF) 100 microgram (µg) inhalation powder once daily (OD) in the evening from a dry powder inhaler (DPI) for 12 weeks. Participants were provided albuterol/salbutamol inhalation aerosol to be used as rescue medication during the Treatment Period.	
Reporting group title	FF/VI 100/25 µg OD
Reporting group description: Participants received FF/Vilanterol (VI) 100/25 µg inhalation powder OD in the evening from a DPI for 12 weeks. Participants were provided albuterol/salbutamol inhalation aerosol to be used as rescue medication during the Treatment Period.	
Reporting group title	FF/VI 200/25 µg OD
Reporting group description: Participants received FF/VI 200/25 µg inhalation powder OD in the evening from a DPI for 12 weeks. Participants were provided albuterol/salbutamol inhalation aerosol to be used as rescue medication during the Treatment Period.	

Primary: Change from Baseline in weighted mean forced expiratory volume in one second (FEV1) over 0 to 24 hours post-dose at the end of the 12-week treatment period

End point title	Change from Baseline in weighted mean forced expiratory volume in one second (FEV1) over 0 to 24 hours post-dose at the end of the 12-week treatment period
End point description: Pulmonary function was measured by FEV1, defined as the maximal amount of air that can be forcefully exhaled in one second. The weighted mean was calculated from the pre-dose FEV1 (within 30 minutes prior to dosing) and post-dose FEV1 measurements at 5, 15, and 30 minutes and at 1, 2, 3, 4, 5, 12, 16, 20, 23, and 24 hours on Day 84/Week 12. At each time point, the highest of three technically acceptable measurements was recorded. Change from Baseline was calculated as the weighted mean of the 24-hour serial FEV1 measures on Day 84/Week 12 minus the Baseline value. Baseline was the pre-dose FEV1 measurement value obtained at Visit 3. The analysis was performed using an Analysis of Covariance (ANCOVA) model with covariates of Baseline FEV1, region, sex, age, and treatment. Intent-to-Treat (ITT) Population: all participants randomized to treatment, who received at least one dose of the study medication	
End point type	Primary
End point timeframe: Baseline and Week 12	

End point values	FF 100 µg OD	FF/VI 100/25 µg OD	FF/VI 200/25 µg OD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	288 ^[1]	312 ^[2]	312 ^[3]	
Units: Liters				
least squares mean (standard error)	0.366 (± 0.0231)	0.474 (± 0.0221)	0.499 (± 0.0222)	

Notes:

[1] - ITT Population. Participants with non-missing covariates/Week 12 weighted mean data were analyzed.

[2] - ITT Population. Participants with non-missing covariates/Week 12 weighted mean data were

analyzed.

[3] - ITT Population. Participants with non-missing covariates/Week 12 weighted mean data were analyzed.

Statistical analyses

Statistical analysis title	FF 100 µg OD:FF/VI 100/25 µg OD
Comparison groups	FF 100 µg OD v FF/VI 100/25 µg OD
Number of subjects included in analysis	600
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.108
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.045
upper limit	0.171

Statistical analysis title	FF/VI 100/25 µg OD:FF/VI 200/25 µg OD
Comparison groups	FF/VI 100/25 µg OD v FF/VI 200/25 µg OD
Number of subjects included in analysis	624
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	0.024
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.037
upper limit	0.086

Secondary: Change from Baseline in clinic visit trough FEV1 at the end of the 12-week treatment period

End point title	Change from Baseline in clinic visit trough FEV1 at the end of the 12-week treatment period
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End point description:

Pulmonary function was measured by FEV1, defined as the maximal amount of air that can be forcefully exhaled in one second. Trough FEV1 is defined as a pre-dose FEV1 measurement taken at a clinic visit while still on-treatment. Change from Baseline in trough FEV1 at the end of the 12-week treatment period was defined using the 24-hour post-dose serial FEV1 measurement taken at the Week 12 clinic visit. Change from Baseline was calculated as the Week 12 trough FEV1 value minus the Baseline value. The analysis was performed using an ANCOVA model with covariates of Baseline trough FEV1, region, sex, age, and treatment. The last observation carried forward (LOCF) method was used to impute

missing data, in which the last non-missing post-Baseline on-treatment measurement at scheduled clinic visits was used to impute the missing measurements.

End point type	Secondary
End point timeframe:	
Baseline and Week 12	

End point values	FF 100 µg OD	FF/VI 100/25 µg OD	FF/VI 200/25 µg OD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	336 ^[4]	334 ^[5]	337 ^[6]	
Units: Liters				
least squares mean (standard error)	0.365 (± 0.022)	0.441 (± 0.0221)	0.457 (± 0.022)	

Notes:

[4] - ITT Population. Participants with non-missing covariates and post-Baseline FEV1 data were analyzed.

[5] - ITT Population. Participants with non-missing covariates and post-Baseline FEV1 data were analyzed.

[6] - ITT Population. Participants with non-missing covariates and post-Baseline FEV1 data were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the percentage of rescue-free 24-hour (hr) periods during the 12-week treatment period

End point title	Change from Baseline in the percentage of rescue-free 24-hour (hr) periods during the 12-week treatment period
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End point description:

The number of inhalations of rescue albuterol/salbutamol inhalation aerosol used during the day and night was recorded by the participants in a daily electronic diary (eDiary). A 24-hour (hr) period in which a participant's responses to both the morning and evening assessments indicated no use of rescue medication was considered to be rescue free. The Baseline value was derived from the last 7 days of the daily eDiary prior to the randomization of the participant. Change from Baseline was calculated as the averaged value during the 12-week treatment period minus the Baseline value. The analysis was performed using an ANCOVA model with covariates of Baseline, region, sex, age, and treatment.

End point type	Secondary
End point timeframe:	
Baseline and Weeks 1-12	

End point values	FF 100 µg OD	FF/VI 100/25 µg OD	FF/VI 200/25 µg OD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	346 ^[7]	345 ^[8]	346 ^[9]	
Units: Percentage of rescue-free 24-hr periods				
least squares mean (standard error)	22.6 (± 1.84)	34.8 (± 1.85)	35.8 (± 1.85)	

Notes:

[7] - ITT Population. Only those participants available at the specified time points were analyzed.

[8] - ITT Population. Only those participants available at the specified time points were analyzed.

[9] - ITT Population. Only those participants available at the specified time points were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the percentage of symptom-free 24-hour (hr) periods during the 12-week treatment period

End point title	Change from Baseline in the percentage of symptom-free 24-hour (hr) periods during the 12-week treatment period
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End point description:

Asthma symptoms were recorded in a daily eDairy by the participants every day in the morning and evening before taking any rescue or study medication and before the peak expiratory flow measurement. A 24-hour (hr) period in which a participant's responses to both the morning and evening assessments indicated no symptoms was considered to be symptom free. The Baseline value was derived from the last 7 days of the daily eDiary prior to the randomization of the participant. Change from Baseline was calculated as the averaged value during the 12-week treatment period minus the Baseline value. The analysis was performed using an ANCOVA model with covariates of Baseline, region, sex, age, and treatment.

End point type	Secondary
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End point timeframe:

Baseline and Weeks 1-12

End point values	FF 100 µg OD	FF/VI 100/25 µg OD	FF/VI 200/25 µg OD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	346 ^[10]	345 ^[11]	346 ^[12]	
Units: Percentage of symptom-free 24-hr periods				
least squares mean (standard error)	19.4 (± 1.74)	27.2 (± 1.74)	29 (± 1.74)	

Notes:

[10] - ITT Population. Only those participants available at the specified time points were analyzed.

[11] - ITT Population. Only those participants available at the specified time points were analyzed.

[12] - ITT Population. Only those participants available at the specified time points were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in daily morning (AM) peak expiratory flow (PEF) averaged over the 12-week treatment period

End point title	Change from Baseline in daily morning (AM) peak expiratory flow (PEF) averaged over the 12-week treatment period
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End point description:

Peak Expiratory Flow (PEF) is defined as the maximum airflow during a forced expiration beginning with the lungs fully inflated. PEF was measured by the participants using a hand-held electronic peak flow meter each evening prior to the dose of study medication and any rescue albuterol/salbutamol inhalation aerosol use and each morning. The best of three measurements was recorded. Change from Baseline (defined as the last 7 days prior to randomization of the participants) was calculated as the

value of the averaged daily AM PEF over the 12-week treatment period minus the Baseline value. The analysis was performed using an ANCOVA model with covariates of Baseline, region, sex, age, and treatment.

End point type	Secondary
End point timeframe:	
Baseline and Weeks 1-12	

End point values	FF 100 µg OD	FF/VI 100/25 µg OD	FF/VI 200/25 µg OD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	346 ^[13]	345 ^[14]	345 ^[15]	
Units: Liters per minute				
least squares mean (standard error)	19.1 (± 2.25)	44.3 (± 2.25)	47.7 (± 2.25)	

Notes:

[13] - ITT Population. Only those participants available at the specified time points were analyzed.

[14] - ITT Population. Only those participants available at the specified time points were analyzed.

[15] - ITT Population. Only those participants available at the specified time points were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in daily evening (PM) PEF averaged over the 12-week treatment period

End point title	Change from Baseline in daily evening (PM) PEF averaged over the 12-week treatment period
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End point description:

PEF is defined as the maximum airflow during a forced expiration beginning with the lungs fully inflated. PEF was measured by the participants using a hand-held electronic peak flow meter each evening prior to the dose of study medication and any rescue albuterol/salbutamol inhalation aerosol use and each morning. The best of three measurements was recorded. Change from Baseline (defined as the last 7 days prior to randomization of the participants) was calculated as the value of the averaged daily PM PEF over the 12-week treatment period minus the Baseline value. The analysis was performed using an ANCOVA model with covariates of Baseline, region, sex, age, and treatment.

End point type	Secondary
End point timeframe:	
Baseline and Weeks 1-12	

End point values	FF 100 µg OD	FF/VI 100/25 µg OD	FF/VI 200/25 µg OD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	346 ^[16]	345 ^[17]	346 ^[18]	
Units: Liters per minute				
least squares mean (standard error)	15.5 (± 2.24)	39.7 (± 2.24)	41.7 (± 2.24)	

Notes:

[16] - ITT Population. Only those participants available at the specified time points were analyzed.

[17] - ITT Population. Only those participants available at the specified time points were analyzed.

[18] - ITT Population. Only those participants available at the specified time points were analyzed.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious Adverse Events (SAEs) and non-serious AEs were collected from the first dose of study medication up to Week 12/Early Withdrawal.

Adverse event reporting additional description:

SAEs and AEs were collected in members of Intent-to-Treat (ITT) Population, comprised of all participants randomized to treatment who received at least one dose of the study medication.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.1
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Reporting groups

Reporting group title	FF 100 µg OD
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Reporting group description:

Participants received Fluticasone Furoate (FF) 100 microgram (µg) inhalation powder once daily (OD) in the evening from a dry powder inhaler (DPI) for 12 weeks. Participants were provided albuterol/salbutamol inhalation aerosol to be used as rescue medication during the Treatment Period.

Reporting group title	FF/VI 100/25 µg OD
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Reporting group description:

Participants received FF/Vilanterol (VI) 100/25 µg inhalation powder OD in the evening from a DPI for 12 weeks. Participants were provided albuterol/salbutamol inhalation aerosol to be used as rescue medication during the Treatment Period.

Reporting group title	FF/VI 200/25 µg OD
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Reporting group description:

Participants received FF/VI 200/25 µg inhalation powder OD in the evening from a DPI for 12 weeks. Participants were provided albuterol/salbutamol inhalation aerosol to be used as rescue medication during the Treatment Period.

Serious adverse events	FF 100 µg OD	FF/VI 100/25 µg OD	FF/VI 200/25 µg OD
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 347 (0.86%)	4 / 346 (1.16%)	1 / 346 (0.29%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Borderline mucinous tumour of ovary			
subjects affected / exposed	1 / 347 (0.29%)	0 / 346 (0.00%)	0 / 346 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Thermal burn			

subjects affected / exposed	0 / 347 (0.00%)	1 / 346 (0.29%)	0 / 346 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Occipital neuralgia			
subjects affected / exposed	0 / 347 (0.00%)	1 / 346 (0.29%)	0 / 346 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion threatened			
subjects affected / exposed	0 / 347 (0.00%)	0 / 346 (0.00%)	1 / 346 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Pancreatitis acute			
subjects affected / exposed	0 / 347 (0.00%)	1 / 346 (0.29%)	0 / 346 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	0 / 347 (0.00%)	1 / 346 (0.29%)	0 / 346 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	2 / 347 (0.58%)	0 / 346 (0.00%)	0 / 346 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	FF 100 µg OD	FF/VI 100/25 µg OD	FF/VI 200/25 µg OD
Total subjects affected by non-serious adverse events			
subjects affected / exposed	67 / 347 (19.31%)	54 / 346 (15.61%)	52 / 346 (15.03%)

Nervous system disorders			
Headache			
subjects affected / exposed	32 / 347 (9.22%)	29 / 346 (8.38%)	29 / 346 (8.38%)
occurrences (all)	38	35	41
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	12 / 347 (3.46%)	8 / 346 (2.31%)	7 / 346 (2.02%)
occurrences (all)	14	8	8
Nasopharyngitis			
subjects affected / exposed	26 / 347 (7.49%)	22 / 346 (6.36%)	25 / 346 (7.23%)
occurrences (all)	30	26	28

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported