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Clinical Trial Results Website

Sponsor

Novartis Pharmaceuticals

Generic Drug Name

Indacaterol acetate/Mometasone furoate/QMF149

Trial Indication(s)

Asthma

Protocol Number

CQVM149B2303

Protocol Title

A multi-center, randomized, 12-week treatment, doubleblind study to assess the efficacy and safety of QMF149 (150/80 microgram) compared with MF Twisthaler® (200 microgram) in adult and adolescent patients with asthma

Clinical Trial Phase

Phase of Drug Development

III

Study Start/End Dates

Study Start Date: January 2017 (Actual)
Primary Completion Date: November 2018 (Actual)
Study Completion Date: November 2018 (Actual)

Reason for Termination (If applicable)

Study Design/Methodology

This study used a multi-center, randomized, double-blind, double-dummy, 12-week treatment, parallel-group design. The 12-week treatment period was followed by a 30-day Follow-up period. At the screening visit, informed consent was obtained, and current asthma and non-asthma medications were reviewed and adjusted. All patients were required to be on a stable dose of low ICS (with or without LABA) for at least 1 month prior to entering into Run-in period. During the Run-in period, all patients received an open-label fluticasone propionate 100 µg b.i.d. delivered via Accuhaler. Patients meeting the eligibility criteria at the end of Run-in period were randomized to one of the two treatment groups (QMF149 150/80 µg o.d. delivered via Concept1 or MF 200 µg o.d. delivered via Twisthaler) with an equal (1:1) randomization ratio

Centers

126 centers in 22 countries: Germany(14), Japan(5), Estonia(5), Hungary(7), Russia(6), Slovakia (Slovak Republic)(13), Korea, Republic of(8), Latvia(7), Sweden(3), Lithuania(2), Bulgaria(3), Malaysia(3), South Africa(6), Peru(5), Thailand(4), Poland(4), Italy(5), India(12), Vietnam(2), Philippines(3), Colombia(5), Chile(4)

Objectives:

Primary objective- was to demonstrate the superiority of QMF149 150/80 µg o.d. (in the evening) delivered via Concept1 compared with MF 200 µg o.d. (in the evening) delivered via Twisthaler in terms of trough FEV1 after 12 weeks of treatment in adults and adolescents.

Secondary objective
was to demonstrate the superiority of QMF149 150/80 µg to MF 200 µg o.d. in terms of Asthma Control Questionnaire (ACQ)-7 score after 12 weeks of treatment.
Lung function- evaluate the efficacy of QMF149 150/80 µg o.d. versus MF 200 µg o.d. in terms of:
□□Trough FEV1 at Day 2 of treatment period (defined as the mean of 23 hours 15 min and 23 hours 45 min FEV1 values post dose of Day 1)
□□Pre-dose FEV1 (defined as the mean of −45 min and −15 min FEV1 values pre-evening dose) at 4 weeks
□□Forced Vital Capacity (FVC) and Forced Expiratory Flow (FEF) between 25% and 75% of FVC (FEF25-75) over 12 weeks
□□Morning and Evening Peak Expiratory Flow Rate (PEF) over 4 and 12 weeks of treatment
Symptoms and asthma control

- Percent of patients achieving the minimal clinically important difference (MCID) in ACQ-7 (i.e., at least 0.5 improvement from baseline) at Week 12
- Percentage of asthma symptom free days, the percentage of nights without nighttime awakenings, and the percentage of mornings without symptoms on awakening as recorded by daily electronic Diary (eDiary) over 12 weeks of treatment
- Asthma control as assessed by ACQ-7 at Week 4
- Rescue salbutamol/albuterol usage (mean daily, nighttime and daytime use) from eDiary recordings over 12 weeks of treatment
- Percentage of rescue medication free days over 12 weeks of treatment
- Quality of life as assessed by Asthma Quality of Life Questionnaire (AQLQ) over 12 weeks of Treatment

Exacerbations (categorized as mild, moderate, and severe)

- Time to first asthma exacerbation by exacerbation category
- Annual rate of asthma exacerbations by exacerbation category

Test Product (s), Dose(s), and Mode(s) of Administration

The study drug QMF149 (indacaterol acetate/MF) was supplied to the investigators as powder in hard capsules at dose strength of 150/80 µg to be delivered via Concept1 inhaler once daily (in the evening). The comparative treatment MF was supplied as powder in the dose strength of 200 µg to be delivered via Twisthaler once daily (in the evening). In addition, the placebos (placebo delivered as powder via Twisthaler and placebo delivered as powder in capsules via Concept1) enabled the double-dummy design of the study. All test materials were supplied by Novartis.

Statistical Methods

The comparison of QMF149 150/80 µg versus MF 200 µg were evaluated by testing the following null hypothesis (H0) versus the alternative hypothesis (Ha):

H0: QMF149 treatment group is equal to MF treatment group in trough FEV1 at Week 12

Ha: QMF149 treatment group is not equal to MF treatment group in trough FEV1 at Week 12

The primary variable was analyzed using a Mixed Model for Repeated Measure (MMRM) on the FAS. The model contained treatment, age (12 to 17 or ≥ 18 years), region, visit (Days 2 and 85), and treatment-by-visit interaction as fixed effects with baseline FEV1 measurement, baseline-by-visit interaction, FEV1 prior to inhalation and FEV1 within 15 to 30 min post inhalation of salbutamol/albuterol (components of SABA reversibility) as covariates, and center nested within region as a random effect. The within-patient correlation was modeled using an unstructured covariance matrix in the mixed model. The key secondary endpoint was analyzed using the same MMRM (including all available visits) on the FAS as used for the primary analysis but included Baseline ACQ-7 score instead of Baseline FEV1. For multiplicity adjustment, a hierarchical testing procedure was applied to control the type-I error rate for the primary and the key secondary endpoints, i.e., the key secondary endpoint ACQ-7 was tested only

if the primary endpoint (trough FEV1) is significant at the 2-sided 0.05 level.
Other spirometry parameters, FEV1, FVC and FEF25-75 were also analyzed using MMRM. The proportion of patients who achieved an improvement of at least 0.5 in ACQ-7 (i.e. decrease of ACQ-7 score of at least 0.5 from baseline) at post-baseline visits were analyzed using a logistic regression model. The mean rescue medication use, mean asthma symptoms scores and mean morning/evening PEF as well as AQLQ at Week 12 were analyzed using an ANCOVA model. Asthma exacerbations were summarized over 12 weeks of treatment.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:

-Patients with a documented diagnosis of asthma for a period of at least 3 months prior to Screening Visit

- Patients who have used low dose ICS , with or without controller (ie, LABA, Leukotriene Receptor Antagonist) at stable dose for at least 1 month prior to Screening Visit

-Adult patients who are symptomatic at screening despite treatment with existing therapy. Patients with ACQ-7 score ≥ 1.5 at Visit 101 and at Visit 102 (inadequately controlled).

- Adolescent patients :
-If taking only ICS (without LABA) and are symptomatic at screening despite treatment with low doses of ICS. These patients must have ACQ-7 score ≥ 1.5 at Visit 101
and at Visit 102 .
-If taking ICS (low dose)/ LABA, and have ACQ-7 score ≥1 and <1.5 at Visit 101: they must have ACQ-7 score≥1.5 at Visit 102 (prior to randomization).

-Pre-bronchodilator FEV1≥ 60 % and < 90 % of the predicted normal value for the patient after withholding bronchodilators at both Visits 101 and 102

-Patients who demonstrate an increase in FEV1 of 12% and ≥ 200 mL within 30 minutes after administration of 400 microgram salbutamol/360 microgram albuterol (or equivalent dose) at Visit 101.

Exclusion Criteria:

-Patients who have smoked or inhaled tobacco products (including electronic cigarettes) within the 6 month period prior to Visit 1, or who have a smoking history of greater than or equal to 10 pack year.

-Patients who have had an asthma attack/exacerbation requiring systemic steroids or hospitalization (> 24 hours) or emergency room visit (≤ 24 hours) as follows:
-For adults: within 6 weeks of Screening Visit. If patients experience an asthma attack/exacerbation requiring systemic steroids or emergency room visit between Visit 1 and Visit 102 they may be re-screened 6 weeks after recovery from the exacerbation
-For adolescents: Severe asthma attack/exacerbation requiring systemic corticosteroids in the last 6 months, OR hospitalization (> 24 hours) due to severe asthma attack/exacerbation requiring systemic corticosteroids in the last 6 months, OR emergency room visit (≤ 24 hours) due to severe asthma attack/exacerbation requiring systemic corticosteroids within the last 6 months.
-Patients who ever required intubation for a severe asthma attack/exacerbation

- Patients with a clinical condition (eg. glaucoma, cataract and fragility fractures) which may be worsened by ICS administration (according to investigator's medical judgment)

-Patients who have had a respiratory tract infection or asthma worsening within 4 weeks prior to Screening Visit or between Visit 1and Visit 102. Patients may be re-screened 4 weeks after recovery from their respiratory tract infection or asthma worsening.

- Patients with any chronic conditions affecting the upper respiratory tract (eg. chronic sinusitis) which in the opinion of the investigator may interfere with the study.

- Patients with a history of chronic lung diseases other than asthma, including (but not limited to) COPD, sarcoidosis, interstitial lung disease, cystic fibrosis, clinically significant bronchiectasis and active tuberculosis.

-Patients with Type I diabetes or uncontrolled Type II diabetes.

-Patients with narcolepsy and/or insomnia.

-Patients on Maintenance Immunotherapy (desensitization) for allergies or less than 3 months prior to Visit 101 or patients on Maintenance Immunotherapy for more than 3 months prior to Visit 101 but expected to change throughout the course of the study.

-Patients with diagnosed rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption or with known intolerance to lactose or milk products.
--Patients who use a long acting muscarinic antagonist (LAMA) within 3 months prior to Visit 1.

Participant Flow Table

Overall Study

	QMF149 150/80 µg	MF 200 µg	Total
Arm/Group Description	QMF149 150/80 microgram o.d. delivered via Concept1	MF 200 microgram o.d. delivered via Twisthaler®	
Started	398	404	802
Full analysis set	395	399	794
Completed	394	383	777
Not Completed	4	21	25
Protocol deviation	3	4	7
Adverse Event	1	8	9
Lost to Follow-up	0	1	1
Non-compliance with study treatment	0	1	1

Physician Decision	0	2	2
Subject/guardian decision	0	4	4
Technical problems	0	1	1

Baseline Characteristics

	QMF149 150/80 µg	MF 200 µg	Total
Arm/Group Description	QMF149 150/80 microgram o.d. delivered via Concept1	MF 200 microgram o.d. delivered via Twisthaler®	
Number of Participants [units: participants]	398	404	802
Age Continuous (units: Years) Mean ± Standard Deviation			
	46.1±16.26	45.1±16.27	45.6±16.26
Sex: Female, Male (units:) Count of Participants (Not Applicable)			
Female	247	241	488
Male	151	163	314
Race (NIH/OMB) (units:) Count of Participants (Not Applicable)			

American Indian or Alaska Native	0	0	0
Asian	98	101	199
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	5	6
White	262	265	527
More than one race	0	0	0
Unknown or Not Reported	37	33	70

Summary of Efficacy

Primary Outcome Result(s)

trough FEV1
(Time Frame: week 12)

	QMF149 150/80 µg	MF 200 µg
Arm/Group Description	QMF149 150/80 microgram o.d. delivered via Concept1	MF 200 microgram o.d. delivered via Twisthaler®
Number of Participants Analyzed [units: participants]	395	399
trough FEV1 (units: Liters)		

Least Squares Mean ± Standard Error		
(n=377,375)	2.562 ± 0.0134	2.379 ± 0.0134

Statistical Analysis

Groups	QMF149 150/80 µg, MF 200 µg
P Value	<0.001
Method	Mixed Models Analysis
Mean Difference (Net)	0.182
95 % Confidence Interval 2-Sided	0.148 to 0.217

Secondary Outcome Result(s)

ACQ-7
(Time Frame: week 12)

	QMF149 150/80 µg	**MF 200 µg**
Arm/Group Description	QMF149 150/80 microgram o.d. delivered via Concept1	MF 200 microgram o.d. delivered via Twisthaler®
Number of Participants Analyzed [units: participants]	395	399
ACQ-7 (units: Units on a scale)		

Least Squares Mean ± Standard Error		
(n=375,369)	1.323 ± 0.0411	1.540 ± 0.0411

Statistical Analysis

Groups	QMF149 150/80 µg, MF 200 µg
P Value	<0.001
Method	Mixed Models Analysis
Mean Difference (Net)	-0.218
95 % Confidence Interval 2-Sided	-0.293 to -0.143

trough FEV1 at day 2

(Time Frame: Day 2)

	QMF149 150/80 µg	**MF 200 µg**
Arm/Group Description	QMF149 150/80 microgram o.d. delivered via Concept1	MF 200 microgram o.d. delivered via Twisthaler®
Number of Participants Analyzed [units: participants]	395	399
trough FEV1 at day 2 (units: Liters) Least Squares Mean ± Standard Error		

(n=389,393)	2.490 ± 0.0108	2.358 ± 0.0108

Statistical Analysis

Groups	QMF149 150/80 µg, MF 200 µg
P Value	<0.001
Method	Mixed Models Analysis
Mean Difference (Net)	0.132
95 % Confidence Interval 2-Sided	0.105 to 0.158

Pre-dose FEV1 at week 4

(Time Frame: week 4)

	QMF149 150/80 µg	**MF 200 µg**
Arm/Group Description	QMF149 150/80 microgram o.d. delivered via Concept1	MF 200 microgram o.d. delivered via Twisthaler®
Number of Participants Analyzed [units: participants]	395	399
Pre-dose FEV1 at week 4 (units: Liters) Least Squares Mean ± Standard Error		
(n=389,386)	2.545 ± 0.0132	2.369 ± 0.0131

Statistical Analysis

Groups	QMF149 150/80 µg, MF 200 µg
P Value	<0.001
Method	Mixed Models Analysis
Mean Difference (Net)	0.176
95 % Confidence Interval 2-Sided	0.145 to 0.207

FVC over 12 weeks

(Time Frame: week 12)

	QMF149 150/80 µg	MF 200 µg
Arm/Group Description	QMF149 150/80 microgram o.d. delivered via Concept1	MF 200 microgram o.d. delivered via Twisthaler®
Number of Participants Analyzed [units: participants]	395	399
FVC over 12 weeks (units: Liters) Least Squares Mean ± Standard Error		
Pre dose trough FVC (n=383,379)	3.453 ± 0.0169	3.353 ± 0.0169
Pre-dose trough FEF25-75% (n=383,379)	2.030 ± 0.0228	1.742 ± 0.0228

Statistical Analysis

Groups	QMF149 150/80 µg, MF 200 µg	Pre-dose trough FVC
P Value	<0.001	
Method	Mixed Models Analysis	
Mean Difference (Net)	0.100	
95 % Confidence Interval 2-Sided	0.061 to 0.139	

Statistical Analysis

Groups	QMF149 150/80 µg, MF 200 µg	Pre-dose trough FEF25-75%
P Value	<0.001	
Method	Mixed Models Analysis	
Mean Difference (Net)	0.288	
95 % Confidence Interval 2-Sided	0.231 to 0.345	

PEF over 4 and 12 weeks

(Time Frame: week 12)

	QMF149 150/80 µg	MF 200 µg
Arm/Group Description	QMF149 150/80 microgram o.d. delivered via Concept1	MF 200 microgram o.d. delivered via Twisthaler®

Number of Participants Analyzed [units: participants]	395	399
PEF over 4 and 12 weeks (units: L/min) Least Squares Mean ± Standard Error		
Mean Morning PEF (n=382,382)	31.0 ± 1.98	3.8 ± 1.97
Mean Evening PEF (n=386,386)	26.8 ± 1.84	0.7 ± 1.84

Statistical Analysis

Groups	QMF149 150/80 µg, MF 200 µg	Mean Morning PEF
P Value	<0.001	
Method	Mixed Models Analysis	
Mean Difference (Net)	27.2	
95 % Confidence Interval 2-Sided	22.1 to 32.4	

Statistical Analysis

Groups	QMF149 150/80 µg, MF 200 µg	Mean Evening PEF
P Value	<0.001	
Method	Mixed Models Analysis	
Mean Difference (Net)	26.1	

95 % Confidence Interval 2-Sided	21.0 to 31.2

Percentage of patients with ACQ-7 MID at week 12

(Time Frame: week 12)

	QMF149 150/80 µg	MF 200 µg
Arm/Group Description	QMF149 150/80 microgram o.d. delivered via Concept1	MF 200 microgram o.d. delivered via Twisthaler®
Number of Participants Analyzed [units: participants]	395	399
Percentage of patients with ACQ-7 MID at week 12 (units: Percentage)		
(n=375,370)	74.7	64.9

Daily e-diary over 12 weeks

(Time Frame: week 12)

	QMF149 150/80 µg	MF 200 µg
Arm/Group Description	QMF149 150/80 microgram o.d. delivered via Concept1	MF 200 microgram o.d. delivered via Twisthaler®
Number of Participants Analyzed [units: participants]	395	399

Daily e-diary over 12 weeks (units: Percentage) Least Squares Mean ± Standard Error		
% of nights with no night-time awakenings (n=384,384)	13.4 ± 1.37	8.7 ± 1.36
% of mornings with no symptoms on awakening (n=384,384)	14.7 ± 1.53	11.2 ± 1.53
% of asthma symptom-free days (n=373,380)	17.1 ± 1.68	14.4 ± 1.65

ACQ-7 at week 4

(Time Frame: week 4)

	QMF149 150/80 µg	**MF 200 µg**
Arm/Group Description	QMF149 150/80 microgram o.d. delivered via Concept1	MF 200 microgram o.d. delivered via Twisthaler®
Number of Participants Analyzed [units: participants]	395	399
ACQ-7 at week 4 (units: Units on a scale) Least Squares Mean ± Standard Error		
(n=372,378)	1.454 ± 0.0408	1.658 ± 0.0406

Statistical Analysis

Groups	QMF149 150/80 µg, MF 200 µg

P Value	<0.001
Method	Mixed Models Analysis
Mean Difference (Net)	-0.204
95 % Confidence Interval 2-Sided	-0.277 to -0.131

Rescue medication use over 12 weeks

(Time Frame: week 12)

	QMF149 150/80 µg	MF 200 µg
Arm/Group Description	QMF149 150/80 microgram o.d. delivered via Concept1	MF 200 microgram o.d. delivered via Twisthaler®
Number of Participants Analyzed [units: participants]	395	399
Rescue medication use over 12 weeks (units: Number of puffs of rescue medication) Least Squares Mean ± Standard Error		
Night-time number of puffs of rescue medication (n=384,384)	-0.26 ± 0.025	-0.16 ± 0.025
Daytime number of puffs of rescue medication (n=388,389)	-0.39 ± 0.033	-0.24 ± 0.032

Statistical Analysis

Groups	QMF149 150/80 µg, MF 200 µg	Night-time number of puffs of rescue medication

P Value	<0.001
Method	Mixed Models Analysis
Mean Difference (Net)	-0.11
95 % Confidence Interval 2-Sided	-0.16 to -0.05

Statistical Analysis

Groups	QMF149 150/80 µg, MF 200 µg	Daytime number of puffs of rescue medication
P Value	<0.001	
Method	Mixed Models Analysis	
Mean Difference (Net)	-0.15	
95 % Confidence Interval 2-Sided	-0.22 to -0.08	

Percentage of rescue medication free days over 12 weeks

(Time Frame: week 12)

	QMF149 150/80 µg	**MF 200 µg**
Arm/Group Description	QMF149 150/80 microgram o.d. delivered via Concept1	MF 200 microgram o.d. delivered via Twisthaler®
Number of Participants Analyzed [units: participants]	395	399

Percentage of rescue medication free days over 12 weeks (units: Percentage) Least Squares Mean ± Standard Error		
(n=384,385)	22.2 ± 1.81	14.1 ± 1.80

Statistical Analysis

Groups	QMF149 150/80 µg, MF 200 µg
P Value	<0.001
Method	Mixed Models Analysis
Mean Difference (Net)	8.1
95 % Confidence Interval 2-Sided	4.3 to 11.8

Quality of life assessed by AQLQ-S 12

(Time Frame: week 12)

	QMF149 150/80 µg	**MF 200 µg**
Arm/Group Description	QMF149 150/80 microgram o.d. delivered via Concept1	MF 200 microgram o.d. delivered via Twisthaler®
Number of Participants Analyzed [units: participants]	395	399
Quality of life assessed by AQLQ-S 12		

(units: Score) Least Squares Mean ± Standard Error		
(n=381,379)	5.779 ± 0.0475	5.630 ± 0.0473

Statistical Analysis

Groups	QMF149 150/80 µg, MF 200 µg
P Value	<0.001
Method	Mixed Models Analysis
Mean Difference (Net)	0.149
95 % Confidence Interval 2-Sided	0.064 to 0.234

Asthma exacerbation over 12 weeks

(Time Frame: Week 12)

	QMF149 150/80 µg	**MF 200 µg**
Arm/Group Description	QMF149 150/80 microgram o.d. delivered via Concept1	MF 200 microgram o.d. delivered via Twisthaler®
Number of Participants Analyzed [units: participants]	395	399
Asthma exacerbation over 12 weeks (units: Number of patients)		
Mild asthma exacerbation	11	29

Moderate asthma exacerbation	7	23
Severe asthma exacerbation	3	11
Moderate or severe asthma exacerbation	10	32

The Annual Rate of Asthma Exacerbations (Moderate or Severe) Over the 12 Week Treatment Period

(Time Frame: Week 12)

	QMF149 150/80 µg	**MF 200 µg**
Arm/Group Description	QMF149 150/80 microgram o.d. delivered via Concept1	MF 200 microgram o.d. delivered via Twisthaler®
Number of Participants Analyzed [units: participants]	395	399
The Annual Rate of Asthma Exacerbations (Moderate or Severe) Over the 12 Week Treatment Period (units: Number of exacerbation)		
Moderate or severe asthma exacerbation (n=394,397)	0.08	0.31
All (mild, moderate, severe) asthma exacerbation (n=394, 397)	0.20	0.67

Time to first Asthma Exacerbations (Moderate or Severe) Over the 12 Week Treatment Period

(Time Frame: Week 12)

	QMF149 150/80 µg	**MF 200 µg**

Arm/Group Description	QMF149 150/80 microgram o.d. delivered via Concept1	MF 200 microgram o.d. delivered via Twisthaler®
Number of Participants Analyzed [units: participants]	395	399
Time to first Asthma Exacerbations (Moderate or Severe) Over the 12 Week Treatment Period (units: Count of participants)		
(n=394,397)	10	32

Statistical Analysis

Groups	QMF149 150/80 µg, MF 200 µg
P Value	<0.001
Method	Regression, Cox
Hazard Ratio (HR)	0.29
95 % Confidence Interval 2-Sided	0.14 to 0.59

Summary of Safety

Safety Results

All-Cause Mortality

	QMF149 150/80 N = 396	MF 200 N = 399
Arm/Group Description	QMF149 150/80 microgram o.d. delivered via Concept1	MF 200 microgram o.d. delivered via Twisthaler®
Total participants affected	0 (0.00%)	0 (0.00%)

Serious Adverse Events by System Organ Class

Time Frame	12 weeks
Additional Description	AE additional description
Source Vocabulary for Table Default	MedDRA (21.1)
Assessment Type for Table Default	Systematic Assessment

	QMF149 150/80 N = 396	MF 200 N = 399

Arm/Group Description	QMF149 150/80 microgram o.d. delivered via Concept1	MF 200 microgram o.d. delivered via Twisthaler®
Total participants affected	5 (1.26%)	7 (1.75%)
Gastrointestinal disorders		
Appendix disorder	0 (0.00%)	1 (0.25%)
Dental cyst	1 (0.25%)	0 (0.00%)
Hepatobiliary disorders		
Autoimmune hepatitis	0 (0.00%)	1 (0.25%)
Infections and infestations		
Abscess oral	1 (0.25%)	0 (0.00%)
Bronchitis	0 (0.00%)	2 (0.50%)
Urinary tract infection	0 (0.00%)	1 (0.25%)
Viral upper respiratory tract infection	0 (0.00%)	1 (0.25%)
Injury, poisoning and procedural complications		
Ankle fracture	0 (0.00%)	1 (0.25%)
Fibula fracture	0 (0.00%)	1 (0.25%)
Incisional hernia	1 (0.25%)	0 (0.00%)
Tibia fracture	0 (0.00%)	1 (0.25%)
Musculoskeletal and connective tissue disorders		

Back pain	0 (0.00%)	1 (0.25%)
Osteoarthritis	1 (0.25%)	0 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Prostate cancer	1 (0.25%)	0 (0.00%)
Respiratory, thoracic and mediastinal disorders		
Asthma	1 (0.25%)	1 (0.25%)

Other Adverse Events by System Organ Class

Time Frame	12 weeks
Additional Description	AE additional description
Source Vocabulary for Table Default	MedDRA (21.1)
Assessment Type for Table Default	Systematic Assessment
Frequent Event Reporting Threshold	1%

	QMF149 150/80 N = 396	**MF 200 N = 399**
Arm/Group Description	QMF149 150/80 microgram o.d. delivered via Concept1	MF 200 microgram o.d. delivered via Twisthaler®
Total participants affected	69 (17.42%)	106 (26.57%)

Infections and infestations		
Bronchitis	1 (0.25%)	5 (1.25%)
Influenza	4 (1.01%)	4 (1.00%)
Nasopharyngitis	17 (4.29%)	19 (4.76%)
Pharyngitis	5 (1.26%)	2 (0.50%)
Sinusitis	5 (1.26%)	5 (1.25%)
Upper respiratory tract infection	4 (1.01%)	10 (2.51%)
Viral upper respiratory tract infection	1 (0.25%)	5 (1.25%)
Injury, poisoning and procedural complications		
Overdose	5 (1.26%)	10 (2.51%)
Nervous system disorders		
Headache	4 (1.01%)	9 (2.26%)
Respiratory, thoracic and mediastinal disorders		
Asthma	20 (5.05%)	60 (15.04%)
Cough	5 (1.26%)	4 (1.00%)
Dysphonia	5 (1.26%)	2 (0.50%)
Dyspnoea	0 (0.00%)	4 (1.00%)
Rhinitis allergic	4 (1.01%)	0 (0.00%)

Other Relevant Findings

None

Conclusion:

The study met the primary and key secondary endpoints, demonstrating statistically significant improvements in both lung function and symptoms in the QMF149 150/80ug treatment group vs. MF Twisthaler 200 µg treatment group. Improvements in rescue medication, PEF, exacerbation rates, ACQ-7 (% of patients achieving MID) and AQLQ parameters were also observed in QMF groups compared to MF and provide support for clinical meaningful benefit of QMF149 in terms of both lung function and asthma control.
QMF149 150/80 µg o.d. was generally safe and well tolerated, with no evidence of increased risk compared with MF Twisthaler 200 µg. Overall, this study provides evidence for the additional benefit of a LABA, indacaterol, in a once daily, low-dose LABA/ICS combination (QMF149 150/80 µg).

Date of Clinical Trial Report

05-Mar-2019