Sponsor

Novartis Pharmaceuticals

Generic Drug Name

Indacaterol acetate/glycopyrronium bromide/mometasone furoate

Trial Indication(s)

Asthma

Protocol Number

CQVM149B2302

Protocol Title

A multicenter, randomized, 52-week, double-blind, parallelgroup, active controlled study to compare the efficacy and safety of QVM149 with QMF149 in patients with asthma

Clinical Trial Phase

Phase 3

Phase of Drug Development

Phase 3

Study Start/End Dates

Study Start Date: December 2015 (Actual)
Primary Completion Date: June 2019 (Actual)
Study Completion Date: June 2019 (Actual)

Study Design/Methodology

This study used a 52-week treatment, randomized, double-blind, double-dummy, parallel-group design.

A total of 3092 patients with asthma were randomized into the 5 treatment groups with a randomization ratio of 1:1:1:1:1 (approximately 617 patients per treatment group):

- QVM149 150/50/80 µg once daily (o.d.) delivered via Concept1 device
- QVM149 150/50/160 µg o.d. delivered via Concept1 device
- QMF149 150/160 µg o.d delivered via Concept1 device
- QMF149 150/320 µg o.d. delivered via the Concept1 device
- Salmeterol/fluticasone 50/500 µg twice daily (b.i.d.) delivered via Accuhaler®.

The study consisted of 4 Epochs: Screening Epoch of 2 weeks, Run-In Epoch of 2 weeks, Double-blind Treatment Epoch of 52 weeks (from randomization to Week 52) and Follow-up Epoch of 30 days.

Centers

415 centers in 41 countries: Argentina (32), Austria (4), Belgium (12), Bulgaria (5), Canada (12), Chile (5), China (13), Colombia (4), Croatia (5), Denmark (2), Estonia (4), Finland (1), France (1), Germany (34), Greece (9), Hungary (17), India (35), Ireland (2), Israel (8), Italy (10), Japan (23), Jordan (2), Latvia (10), Lebanon (4), Lithuania (11), Mexico (9), Netherlands (9), Peru (5), Philippines (5), Poland (13), Portugal (4), Romania (17), Russian Federation (44), Slovakia (11), South Africa (5), Spain (12), Sweden (2), Switzerland (1), Thailand (7), United Kingdom (3), and Vietnam (3)

Objectives:

The primary objective was to demonstrate superiority of either QVM149 150/50/80 µg o.d. to QMF149 150/160 µg o.d. or QVM149 150/50/160 µg o.d. to QMF149 150/320 µg o.d., all delivered via Concept1 in terms of trough Forced Expiratory Volume in 1 second (FEV1) after 26 weeks of treatment in patients with asthma.

The key secondary objective was to demonstrate superiority of either QVM149 150/50/80 µg o.d. to QMF149 150/160 µg o.d. or QVM149 150/50/160 µg o.d. to QMF149 150/320 µg o.d., all delivered via Concept1 in terms of asthma control, as assessed by the Asthma Control Questionnaire (ACQ-7), after 26 weeks of treatment in patients with asthma.

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

QVM149 (indacaterol acetate/glycopyrronium bromide/mometasone furoate) was supplied as powder in hard capsules at dose strength of 150/50/80 µg and 150/50/160 µg to be delivered via Concept1 inhaler. QVM149 was inhaled once daily for 52 weeks.

QMF149 (indacaterol acetate/mometasone furoate) was supplied as powder in hard capsules at dose strength of 150/160 µg and 150/320 µg to be delivered via Concept1 inhaler. QMF149 was inhaled once daily for 52 weeks.

Salmeterol/fluticasone 50/500 µg was supplied as powder to be delivered via Accuhaler inhaler. It was inhaled twice daily for 52 weeks.

Statistical Methods

The comparisons of QVM149 150/50/80 µg o.d. vs. QMF149 150/160 µg o.d. and QVM149 150/50/160 µg o.d. vs. QMF149 150/320 µg o.d., all delivered via Concept1, was evaluated by testing the following null hypothesis (H0) versus the alternative hypothesis (Ha):

H_0: QVM149 treatment group was equal to QMF149 treatment group in trough FEV1 at Week 26

H_a: QVM149 treatment group was not equal to QMF149 treatment group in trough FEV1 at Week 26

The primary variable was analyzed using a mixed model for repeated measure (MMRM) on the full analysis set (FAS). The model contained treatment, region, visit (Days 2, 184 and 365), 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 short acting β2-adrenergic agonist (SABA) reversibility) as covariates, and center nested within region as a random effect. The estimated adjusted treatment difference (QVM149 − QMF149) was displayed along with the associated standard error, 2-sided 95% confidence interval (CI), and p-value (2-sided).

The key secondary endpoints was analyzed using the similar MMRM model (including all available visits) on the FAS as used for the primary analysis but included baseline ACQ-7 score instead of baseline FEV1.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:
- Patients with a diagnosis of asthma, (GINA 2015) for a period of at least 1 year prior to Visit 1 (Screening).
- Patients who have used medium or high dose of ICS/LABA combinations for asthma for at least 3 months and at stable medium or high doses of ICS/LABA for at least 1 month prior to Visit 1.
- Patients must be symptomatic at screening despite treatment with mid or high stable doses of ICS/LABA. Patients with ACQ-7 score ≥ 1.5 at Visit 101 and at Visit 102 (before randomization).
- Patients with documented history of at least one asthma exacerbation which required medical care from a physician, ER visit (or local equivalent structure) or hospitalization in the 12 months prior to Visit 1, and required systemic corticosteroid treatment.
- Pre-bronchodilator FEV1 of < 80 % of the predicted normal value for the patient according to ATS/ERS guidelines after withholding bronchodilators at both visits 101 and 102.
-Withholding period of bronchodilators prior to spirometry: SABA for ≥ 6 hrs, Twice daily LABA (or FDC of ICS/LABA) for ≥ 12 hrs, Once daily LABA (or FDC of ICS/LABA) for ≥ 24 hrs, SAMA for ≥ 8 hrs, Short acting xanthines for 12 hrs, Long acting xanthines for 24 hrs, .
- Washout period of each drug should be kept as close as possible as above and should not be longer. If longer washout period is needed due to scheduling issues, please contact Novartis Medical monitor.
- A one-time repeat of percentage predicated FEV1 (Pre-bronchodilator) at Visit 101 and/or Visit 102 is allowed in an ad-hoc visit. Repeat of Visit 101 spirometry should be done in an ad-hoc visit to be scheduled on a date that would provide sufficient time to

receive confirmation from the spirometry data central reviewer of the validity of the assessment before randomization. Run-in medication should be dispensed once spirometry assessment met inclusion criteria (ATS/ERS quality criteria, FEV1 % predicted normal value, and reversibility) as per equipment
- A one-time rescreen is allowed in case the patient fails to meet the criteria at the repeat, provided the patient returned to the required treatment as per inclusion criteria 4
- Patients who demonstrate an increase in FEV1 of 12% and 200 mL within 30 minutes after administration of 400 µg salbutamol/360 µg albuterol (or equivalent dose) at Visit 101.All patients must perform a reversibility test at Visit 101. If reversibility is not demonstrated at Visit 101 then one of the following criteria need to be met.
-Reversibility should be repeated once.
-Patients may be permitted to enter the study with historical evidence of reversibility that was performed according to ATS/ERS guidelines within 2 years prior to Visit 1.
- Alternatively, patients may be permitted to enter the study with a historical positive bronchoprovocation test that was performed within 2 years prior to Visit 1. If reversibility is not demonstrated at Visit 101 (or after repeated assessment in an ad-hoc visit) and historical evidence of reversibility/bronchoprovocation is not available (or was not performed according to the ATS/ERS guidelines patients must be screen failed
- Spacer devices are permitted during reversibility testing only. The Investigator or delegate may decide whether or not to use a spacer for the reversibility testing

Exclusion Criteria:
- Patients who have had an asthma attack/exacerbation requiring systemic steroids or hospitalization or emergency room visit within 6 weeks of Visit 1 (Screening). If patients experience an asthma attack/exacerbation requiring systemic steroids or hospitalization or emergency room visit between Visit 1 and Visit 102 they may be re-screened 6 weeks after recovery from the exacerbation.
- Patients who have ever required intubation for a severe asthma attack/exacerbation.
- Patients who have a clinical condition which is likely to be worsened by ICS administration (e.g. glaucoma, cataract and fragility fractures) who are according to investigator’s medical judgment at risk participating in the study.
- Patients treated with a LAMA for asthma within 3 months prior Visit 1 (Screening).
- Patients with narrow-angle glaucoma, symptomatic benign prostatic hyperplasia (BPH) or bladder-neck obstruction or severe renal impairment or urinary retention. BPH patients who are stable on treatment can be considered).
- Patients who have had a respiratory tract infection or asthma worsening as determined by investigator within 4 weeks prior to Visit 1 (Screening) or between Visit 1 and Visit 102. Patients may be re-screened 4 weeks after recovery from their respiratory tract infection or asthma worsening.
- Patients with evidence upon visual inspection (laboratory culture is not required) of clinically significant (in the opinion of investigator) oropharyngeal candidiasis at Visit 102 or earlier, with or without treatment. Patients may be re-screened once their candidiasis has been treated and has resolved.
- Patients with any chronic conditions affecting the upper respiratory tract (e.g. chronic sinusitis) which in the opinion of the

investigator may interfere with the study evaluation or optimal participation in the study.
- Patients with a history of chronic lung diseases other than asthma, including (but not limited to) chronic obstructive pulmonary disease, sarcoidosis, interstitial lung disease, cystic fibrosis, clinically significant bronchiectasis and active tuberculosis.
- Patients with Type I diabetes or uncontrolled Type II diabetes.
- Patients who, either in the judgment of the investigator or the responsible Novartis personnel, have a clinically significant condition such as (but not limited to) unstable ischemic heart disease, New York Heart Association (NYHA) Class III/IV left ventricular failure arrhythmia, uncontrolled hypertension, cerebrovascular disease, psychiatric disease, neurodegenerative diseases, or other neurological disease, uncontrolled hypo- and hyperthyroidism and other autoimmune diseases, hypokalemia, hyperadrenergic state, or ophthalmologic disorder or patients with a medical condition that might compromise patient safety or compliance, interfere with evaluation, or preclude completion of the study.
- Patients with paroxysmal (e.g., intermittent) atrial fibrillation are excluded. Patients with persistent atrial fibrillation as defined by continuous atrial fibrillation for at least 6 months and controlled with a rate control strategy (i.e., selective beta blockers, calcium channel blocker, pacemaker placement, digoxin or ablation therapy) for at least 6 months may be considered for inclusion. In such patients, atrial fibrillation must be present at the run-in visit (Visit 101) with a resting ventricular rate < 100/min. At Visit 101 the atrial fibrillation must be confirmed by central reading.
- Patients with a history of myocardial infarction (this should be confirmed clinically by the investigator) within the previous 12 months.
- Concomitant use of agents known to prolong the QT interval unless it can be permanently discontinued for the duration of study
- Patients with a history of long QT syndrome or whose QTc measured at Visit 101 (Fridericia method) is prolonged (> 450 msec for males and > 460 msec for females) and confirmed by a central assessor (these patients should not be rescreened).
- Patients with a history of hypersensitivity to lactose, any of the study drugs or to similar drugs within the class including untoward reactions to sympathomimetic amines or inhaled medication or any component thereof.
- Patients who have not achieved an acceptable spirometry result at Visit 101 in accordance with ATS/ERS criteria for acceptability and repeatability. A one-time repeat spirometry is allowed in an ad-hoc visit scheduled as close as possible from the first attempt (but not on the same day) if the spirometry did not qualify due to ATS/ERS criteria at Visit 101 and/or Visit 102. If the patient fails the repeat assessment, the patient may be rescreened once, provided the patient returns to the required treatment as per inclusion criteria 4.
- Patients unable to use the Concept1 dry powder inhaler, Accuhaler or a metered dose inhaler. Spacer devices are not permitted.
- History of alcohol or other substance abuse.
- Patients with a known history of non-compliance to medication or who were unable or unwilling to complete a patient diary or who are unable or unwilling to use Electronic Peak Flow with e-diary device.
- Patients who do not maintain regular day/night, waking/sleeping cycles (e.g., night shift workers).

Participant Flow Table

Overall Study

	QVM149 150/50/160 µg o.d.	QVM149 150/50/80 µg o.d.	QMF149 150/320 µg o.d.	QMF149 150/160 µg o.d.	Salmeterol/fluticasone 50/500 µg b.i.d.	Total
Arm/Group Description	QVM149 150/50/160 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QVM149 150/50/80 µg (indacaterol acetate/glycopyrronium/mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/320 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/160 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	Salmeterol xinafoate /fluticasone propionate 50/500 µg twice daily (b.i.d.) delivered via Accuhaler®	
Started	619	620	618	617	618	3092
Full Analysis Set (FAS)	615	616	611	607	612	3061
Safety Set (SAF)	616	617	613	608	618	3072
Completed	580	582	577	580	582	2901
Not Completed	39	38	41	37	36	191
Subject/guardian decision	34	26	26	25	27	138
Protocol Deviation	2	3	4	8	4	21
Death	1	1	4	0	0	6
Lost to Follow-up	1	1	2	0	1	5
Physician Decision	1	7	5	2	4	19
Pregnancy	0	0	0	2	0	2

Baseline Characteristics

	QVM149 150/50/160 µg o.d.	QVM149 150/50/80 µg o.d.	QMF149 150/320 µg o.d.	QMF149 150/160 µg o.d.	Salmeterol/fluticasone 50/500 µg b.i.d.	Total
Arm/Group Description	QVM149 150/50/160 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QVM149 150/50/80 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/320 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/160 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	Salmeterol xinafoate /fluticasone propionate 50/500 µg twice daily (b.i.d.) delivered via Accuhaler®	
Number of Participants [units: participants]	619	620	618	617	618	3092
Age Continuous (units: years) Mean ± Standard Deviation						
	52.1±12.91	52.4±12.71	52.0±12.81	51.8±12.86	52.9±12.23	52.2±12.70
Sex: Female, Male (units: Participants) Count of Participants (Not Applicable)						
Female	381	362	380	378	417	1918
Male	238	258	238	239	201	1174
Race/Ethnicity, Customized (units: Participants) Count of Participants (Not Applicable)						
Caucasian	456	458	453	452	468	2287
Black	4	5	3	4	1	17
Asian	139	133	133	135	131	671

Native American	7	8	8	4	5	32
Unknown	0	0	0	1	0	1
Other	13	16	21	21	13	84

Primary Outcome Result(s)

Trough Forced Expiratory Volume in 1 Second (Trough FEV1) of QVM149 versus QMF149 at week 26

(Time Frame: 26 weeks)

	QVM149 150/50/160 µg o.d.	QVM149 150/50/80 µg o.d.	QMF149 150/320 µg o.d.	QMF149 150/160 µg o.d.	Salmeterol/fluticasone 50/500 µg b.i.d.
Arm/Group Description	QVM149 150/50/160 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QVM149 150/50/80 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/320 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/160 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	Salmeterol xinafoate /fluticasone propionate 50/500 µg twice daily (b.i.d.) delivered via Accuhaler®
Number of Participants Analyzed [units: participants]	614	614	606	602	607
Trough Forced Expiratory Volume in 1 Second (Trough FEV1) of QVM149 versus QMF149 at week 26 (units: litre (L)) Least Squares Mean ± Standard Error					
	2.050 ± 0.0128	2.029 ± 0.0129	1.984 ± 0.0129	1.953 ± 0.0130	1.930 ± 0.0131

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., QMF149 150/320 µg o.d.
P Value	<0.001
Method	Other Mixed Model for Repeated Measures (MMRM)
Other LS Mean	0.065
Standard Error of the mean	0.0176
95 % Confidence Interval 2-Sided	0.031 to 0.099

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., QMF149 150/160 µg o.d.
P Value	<0.001
Method	Other MMRM
Other LS Mean	0.076
Standard Error of the mean	0.0176
95 % Confidence Interval 2-Sided	0.041 to 0.111

Secondary Outcome Result(s)

Asthma Control Questionnaire (ACQ-7) at Week 26 and Week 52

(Time Frame: 26 weeks, 52 weeks)

	QVM149 150/50/160 µg o.d.	QVM149 150/50/80 µg o.d.	QMF149 150/320 µg o.d.	QMF149 150/160 µg o.d.	Salmeterol/fluticasone 50/500 µg b.i.d.
Arm/Group Description	QVM149 150/50/160 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QVM149 150/50/80 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/320 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/160 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	Salmeterol xinafoate /fluticasone propionate 50/500 µg twice daily (b.i.d.) delivered via Accuhaler®
Number of Participants Analyzed [units: participants]	607	595	596	598	599
Asthma Control Questionnaire (ACQ-7) at Week 26 and Week 52 (units: Score on a scale) Least Squares Mean ± Standard Error					
Week 26	1.542 ± 0.0329	1.543 ± 0.0330	1.528 ± 0.0329	1.614 ± 0.0331	1.628 ± 0.0329
Week 52	1.406 ± 0.0334	1.535 ± 0.0337	1.465 ± 0.0335	1.545 ± 0.0338	1.527 ± 0.0335

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., QMF149 150/320 µg o.d.	Week 26
P Value	0.729	
Method	Other MMRM	
Other LS Mean	0.014	
Standard Error of the mean	0.0406	

95 % Confidence Interval 2-Sided	-0.066 to 0.094

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Week 26
P Value	0.034	
Method	Other MMRM	
Other LS Mean	-0.086	
Standard Error of the mean	0.0404	
95 % Confidence Interval 2-Sided	-0.165 to -0.006	

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., QMF149 150/160 µg o.d.	Week 26
P Value	0.085	
Method	Other MMRM	
Other LS Mean	-0.071	
Standard Error of the mean	0.0409	
95 % Confidence Interval 2-Sided	-0.151 to 0.010	

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Week 26
P Value	0.038	
Method	Other MMRM	
Other LS Mean	-0.084	
Standard Error of the mean	0.0406	
95 % Confidence Interval 2-Sided	-0.164 to -0.005	

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., QMF149 150/320 µg o.d.	Week 52
P Value	0.157	
Method	Other MMRM	
Other LS Mean	-0.059	
Standard Error of the mean	0.0415	
95 % Confidence Interval 2-Sided	-0.140 to 0.023	

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Week 52
P Value	0.003	
Method	Other MMRM	
Other LS Mean	-0.121	
Standard Error of the mean	0.0414	
95 % Confidence Interval 2-Sided	-0.202 to -0.040	

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., QMF149 150/160 µg o.d.	Week 52
P Value	0.814	
Method	Other MMRM	
Other LS Mean	-0.010	
Standard Error of the mean	0.0420	
95 % Confidence Interval 2-Sided	-0.092 to 0.072	

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Week 52
P Value	0.845	
Method	Other MMRM	
Other LS Mean	0.008	
Standard Error of the mean	0.0416	
95 % Confidence Interval 2-Sided	-0.073 to 0.090	

Trough Forced Expiratory Volume in 1 Second (Trough FEV1) of QVM149 versus salmeterol/fluticasone at week 26

(Time Frame: 26 weeks)

	QVM149 150/50/160 µg o.d.	QVM149 150/50/80 µg o.d.	QMF149 150/320 µg o.d.	QMF149 150/160 µg o.d.	Salmeterol/fluticasone 50/500 µg b.i.d.
Arm/Group Description	QVM149 150/50/160 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QVM149 150/50/80 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/320 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/160 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	Salmeterol xinafoate /fluticasone propionate 50/500 µg twice daily (b.i.d.) delivered via Accuhaler®
Number of Participants Analyzed [units: participants]	614	614	606	602	607

Trough Forced Expiratory Volume in 1 Second (Trough FEV1) of QVM149 versus salmeterol/fluticasone at week 26
(units: litre (L))
Least Squares Mean ± Standard Error

2.050 ± 0.0128	2.029 ± 0.0129	1.984 ± 0.0129	1.953 ± 0.0130	1.930 ± 0.0131

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.
P Value	<0.001
Method	Other MMRM
Other LS Mean	0.119
Standard Error of the mean	0.0177
95 % Confidence Interval 2-Sided	0.085 to 0.154

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.
P Value	<0.001
Method	Other MMRM
Other LS Mean	0.099
Standard Error of the mean	0.0177
95 % Confidence Interval 2-Sided	0.064 to 0.133

Trough FEV1 at week 52

(Time Frame: 52 weeks)

	QVM149 150/50/160 µg o.d.	QVM149 150/50/80 µg o.d.	QMF149 150/320 µg o.d.	QMF149 150/160 µg o.d.	Salmeterol/fluticasone 50/500 µg b.i.d.
Arm/Group Description	QVM149 150/50/160 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QVM149 150/50/80 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/320 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/160 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	Salmeterol xinafoate /fluticasone propionate 50/500 µg twice daily (b.i.d.) delivered via Accuhaler®
Number of Participants Analyzed [units: participants]	614	614	606	602	607
Trough FEV1 at week 52 (units: litre (L)) Least Squares Mean ± Standard Error					
	2.050 ± 0.0129	1.992 ± 0.0130	1.965 ± 0.0130	1.930 ± 0.0130	1.905 ± 0.0132

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., QMF149 150/320 µg o.d.
P Value	<0.001
Method	Other MMRM
Other LS Mean	0.086
Standard Error of the mean	0.0176

95 % Confidence Interval 2-Sided	0.051 to 0.120

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.
P Value	<0.001
Method	Other MMRM
Other LS Mean	0.145
Standard Error of the mean	0.0178
95 % Confidence Interval 2-Sided	0.111 to 0.180

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., QMF149 150/160 µg o.d.
P Value	<0.001
Method	Other MMRM
Other LS Mean	0.062
Standard Error of the mean	0.0178
95 % Confidence Interval 2-Sided	0.027 to 0.096

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.
P Value	<0.001
Method	Other MMRM
Other LS Mean	0.087
Standard Error of the mean	0.0179
95 % Confidence Interval 2-Sided	0.052 to 0.122

Pre-dose Forced Vital Capacity (FVC) at week 4 and week 12

(Time Frame: 4 weeks, 12 weeks)

	QVM149 150/50/160 µg o.d.	QVM149 150/50/80 µg o.d.	QMF149 150/320 µg o.d.	QMF149 150/160 µg o.d.	Salmeterol/fluticasone 50/500 µg b.i.d.
Arm/Group Description	QVM149 150/50/160 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QVM149 150/50/80 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/320 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/160 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	Salmeterol xinafoate /fluticasone propionate 50/500 µg twice daily (b.i.d.) delivered via Accuhaler®
Number of Participants Analyzed [units: participants]	606	594	592	596	598

Pre-dose Forced Vital Capacity (FVC) at week 4 and week 12
(units: litre (L))
Least Squares Mean ± Standard Error

Week 4	3.091 ± 0.0161	3.059 ± 0.0163	3.018 ± 0.0163	3.020 ± 0.0163	2.952 ± 0.0163
Week 12	3.067 ± 0.0162	3.065 ± 0.0164	3.011 ± 0.0163	3.014 ± 0.0164	2.965 ± 0.0163

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., QMF149 150/320 µg o.d.	Week 4
P Value	<0.001	
Method	Other MMRM	
Other LS Mean	0.073	
Standard Error of the mean	0.0218	
95 % Confidence Interval 2-Sided	0.030 to 0.116	

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Week 4
P Value	<0.001	
Method	Other MMRM	
Other LS Mean	0.139	
Standard Error of the mean	0.0217	

95 % Confidence Interval 2-Sided	0.096 to 0.181

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., QMF149 150/160 µg o.d.	Week 4
P Value	0.074	
Method	Other MMRM	
Other LS Mean	0.039	
Standard Error of the mean	0.0220	
95 % Confidence Interval 2-Sided	-0.004 to 0.082	

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Week 4
P Value	<0.001	
Method	Other MMRM	
Other LS Mean	0.108	
Standard Error of the mean	0.0219	
95 % Confidence Interval 2-Sided	0.065 to 0.150	

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., QMF149 150/320 µg o.d.	Week 12
P Value	0.010	
Method	Other MMRM	
Other LS Mean	0.056	
Standard Error of the mean	0.0219	
95 % Confidence Interval 2-Sided	0.014 to 0.099	

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Week 12
P Value	<0.001	
Method	Other MMRM	
Other LS Mean	0.102	
Standard Error of the mean	0.0218	
95 % Confidence Interval 2-Sided	0.059 to 0.145	

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., QMF149 150/160 µg o.d.	Week 12
P Value	0.022	
Method	Other MMRM	
Other LS Mean	0.050	
Standard Error of the mean	0.0221	
95 % Confidence Interval 2-Sided	0.007 to 0.094	

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Week 12
P Value	<0.001	
Method	Other MMRM	
Other LS Mean	0.099	
Standard Error of the mean	0.0220	
95 % Confidence Interval 2-Sided	0.056 to 0.142	

Trough Forced Expiratory Flow (FEF) between 25% and 75% of FVC (FEF25-75) at 52 weeks

(Time Frame: Up to Week 52)

	QVM149 150/50/160 µg o.d.	QVM149 150/50/80 µg o.d.	QMF149 150/320 µg o.d.	QMF149 150/160 µg o.d.	Salmeterol/fluticasone 50/500 µg b.i.d.
Arm/Group Description	QVM149 150/50/160 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QVM149 150/50/80 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/320 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/160 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	Salmeterol xinafoate /fluticasone propionate 50/500 µg twice daily (b.i.d.) delivered via Accuhaler®
Number of Participants Analyzed [units: participants]	614	614	606	602	607
Trough Forced Expiratory Flow (FEF) between 25% and 75% of FVC (FEF25-75) at 52 weeks (units: L/s) Least Squares Mean ± Standard Error					
	1.354 ± 0.0190	1.263 ± 0.0192	1.260 ± 0.0191	1.214 ± 0.0192	1.207 ± 0.0194

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., QMF149 150/320 µg o.d.
P Value	<0.001
Method	Other MMRM
Other LS Mean	0.095
Standard Error of the mean	0.0254
95 % Confidence Interval 2-Sided	0.045 to 0.145

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.
P Value	<0.001
Method	Other MMRM
Other LS Mean	0.147
Standard Error of the mean	0.0256
95 % Confidence Interval 2-Sided	0.097 to 0.198

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., QMF149 150/160 µg o.d.
P Value	0.057
Method	Other MMRM
Other LS Mean	0.049
Standard Error of the mean	0.0256
95 % Confidence Interval 2-Sided	-0.001 to 0.099

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.

P Value	0.029
Method	Other MMRM
Other LS Mean	0.056
Standard Error of the mean	0.0258
95 % Confidence Interval 2-Sided	0.006 to 0.107

Change from baseline in morning and evening Peak Expiratory Flow Rate (PEF) over 26 and 52 weeks of treatment

(Time Frame: Baseline, 26 weeks, 52 weeks)

	QVM149 150/50/160 µg o.d.	QVM149 150/50/80 µg o.d.	QMF149 150/320 µg o.d.	QMF149 150/160 µg o.d.	Salmeterol/fluticasone 50/500 µg b.i.d.
Arm/Group Description	QVM149 150/50/160 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QVM149 150/50/80 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/320 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/160 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	Salmeterol xinafoate /fluticasone propionate 50/500 µg twice daily (b.i.d.) delivered via Accuhaler®
Number of Participants Analyzed [units: participants]	596	584	581	584	586
Change from baseline in morning and evening Peak Expiratory Flow Rate (PEF) over 26 and 52 weeks of treatment (units: L/min) Least Squares Mean ± Standard Error					
Week 26 - Mean morning PEF	47.7 ± 1.93	40.5 ± 1.95	29.5 ± 1.95	25.6 ± 1.95	12.5 ± 1.95

Week 26 - Mean evening PEF	39.6 ± 1.87	34.7 ± 1.88	22.8 ± 1.88	20.6 ± 1.89	10.4 ± 1.89
Week 52 - Mean morning PEF	47.5 ± 2.03	41.2 ± 2.05	28.8 ± 2.05	25.6 ± 2.06	12.7 ± 2.05
Week 52 - Mean evening PEF	38.7 ± 1.97	35.0 ± 1.99	21.2 ± 1.99	20.1 ± 2.00	9.2 ± 1.99

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., QMF149 150/320 µg o.d.	Week 26 - Mean morning PEF
P Value	<0.001	
Method	Other Linear Mixed Model (LMM)	
Other LS Mean	18.2	
Standard Error of the mean	2.59	
95 % Confidence Interval 2-Sided	13.2 to 23.3	

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Week 26 - Mean morning PEF
P Value	<0.001	

Method	Other LMM
Other LS Mean	35.3
Standard Error of the mean	2.58
95 % Confidence Interval 2-Sided	30.2 to 40.3

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., QMF149 150/160 µg o.d.	Week 26 - Mean morning PEF
P Value	<0.001	
Method	Other LMM	
Other LS Mean	14.9	
Standard Error of the mean	2.61	
95 % Confidence Interval 2-Sided	9.8 to 20.0	

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Week 26 - Mean morning PEF
P Value	<0.001	
Method	Other LMM	

Other LS Mean	28.0
Standard Error of the mean	2.60
95 % Confidence Interval 2-Sided	22.9 to 33.1

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., QMF149 150/320 µg o.d.	Week 26 - Mean evening PEF
P Value	<0.001	
Method	Other LMM	
Other LS Mean	16.8	
Standard Error of the mean	2.53	
95 % Confidence Interval 2-Sided	11.8 to 21.7	

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Week 26 - Mean evening PEF
P Value	<0.001	
Method	Other LMM	

Other LS Mean	29.1
Standard Error of the mean	2.53
95 % Confidence Interval 2-Sided	24.2 to 34.1

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., QMF149 150/160 µg o.d.	Week 26 - Mean evening PEF
P Value	<0.001	
Method	Other LMM	
Other LS Mean	14.1	
Standard Error of the mean	2.55	
95 % Confidence Interval 2-Sided	9.1 to 19.1	

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Week 26 - Mean evening PEF
P Value	<0.001	
Method	Other LMM	

Other LS Mean	24.3
Standard Error of the mean	2.54
95 % Confidence Interval 2-Sided	19.3 to 29.3

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., QMF149 150/320 µg o.d.	Week 52 - Mean morning PEF
P Value	<0.001	
Method	Other LMM	
Other LS Mean	18.7	
Standard Error of the mean	2.72	
95 % Confidence Interval 2-Sided	13.4 to 24.1	

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Week 52 - Mean morning PEF
P Value	<0.001	
Method	Other LMM	

Other LS Mean	34.8
Standard Error of the mean	2.70
95 % Confidence Interval 2-Sided	29.5 to 40.1

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., QMF149 150/160 µg o.d.	Week 52 - Mean morning PEF
P Value	<0.001	
Method	Other LMM	
Other LS Mean	15.6	
Standard Error of the mean	2.74	
95 % Confidence Interval 2-Sided	10.2 to 20.9	

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Week 52 - Mean morning PEF
P Value	<0.001	
Method	Other LMM	

Other LS Mean	28.5
Standard Error of the mean	2.72
95 % Confidence Interval 2-Sided	23.2 to 33.8

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., QMF149 150/320 µg o.d.	Week 52 - Mean evening PEF
P Value	<0.001	
Method	Other LMM	
Other LS Mean	17.5	
Standard Error of the mean	2.66	
95 % Confidence Interval 2-Sided	12.3 to 22.8	

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Week 52 - Mean evening PEF
P Value	<0.001	
Method	Other LMM	

Other LS Mean	29.5
Standard Error of the mean	2.66
95 % Confidence Interval 2-Sided	24.2 to 34.7

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., QMF149 150/160 µg o.d.	Week 52 - Mean evening PEF
P Value	<0.001	
Method	Other LMM	
Other LS Mean	15.0	
Standard Error of the mean	2.69	
95 % Confidence Interval 2-Sided	9.7 to 20.2	

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Week 52 - Mean evening PEF
P Value	<0.001	
Method	Other LMM	

Other LS Mean	25.8
Standard Error of the mean	2.68
95 % Confidence Interval 2-Sided	20.5 to 31.0

Change from baseline in percentage of asthma symptom-free days over 52 weeks

(Time Frame: Baseline, 52 weeks)

	QVM149 150/50/160 µg o.d.	QVM149 150/50/80 µg o.d.	QMF149 150/320 µg o.d.	QMF149 150/160 µg o.d.	Salmeterol/fluticasone 50/500 µg b.i.d.
Arm/Group Description	QVM149 150/50/160 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QVM149 150/50/80 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/320 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/160 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	Salmeterol xinafoate /fluticasone propionate 50/500 µg twice daily (b.i.d.) delivered via Accuhaler®
Number of Participants Analyzed [units: participants]	566	552	559	554	558
Change from baseline in percentage of asthma symptom-free days over 52 weeks (units: Percentage of days) Least Squares Mean ± Standard Error					
	22.4 ± 1.35	18.0 ± 1.36	22.2 ± 1.36	18.0 ± 1.37	18.9 ± 1.36

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., QMF149 150/320 µg o.d.
P Value	0.907

Method	Other LMM
Other LS Mean	0.2
Standard Error of the mean	1.81
95 % Confidence Interval 2-Sided	-3.3 to 3.8

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.
P Value	0.055
Method	Other LMM
Other LS Mean	3.5
Standard Error of the mean	1.81
95 % Confidence Interval 2-Sided	-0.1 to 7.0

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., QMF149 150/160 µg o.d.
P Value	0.997
Method	Other LMM

Other LS Mean	0.0
Standard Error of the mean	1.83
95 % Confidence Interval 2-Sided	-3.6 to 3.6

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.
P Value	0.606
Method	Other LMM
Other LS Mean	-0.9
Standard Error of the mean	1.82
95 % Confidence Interval 2-Sided	-4.5 to 2.6

Change from baseline in percentage of days with no daytime symptoms over 52 weeks

(Time Frame: Baseline, 52 weeks)

	QVM149 150/50/160 µg o.d.	QVM149 150/50/80 µg o.d.	QMF149 150/320 µg o.d.	QMF149 150/160 µg o.d.	Salmeterol/fluticasone 50/500 µg b.i.d.
Arm/Group Description	QVM149 150/50/160 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.)	QVM149 150/50/80 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.)	QMF149 150/320 µg (indacaterol acetate/mometasone furoate) once daily	QMF149 150/160 µg (indacaterol acetate/mometasone furoate) once daily	Salmeterol xinafoate /fluticasone propionate 50/500 µg twice daily (b.i.d.) delivered via Accuhaler®

	delivered via Concept1 device	delivered via Concept1 device	(o.d.) delivered via Concept1 device	(o.d.) delivered via Concept1 device	
Number of Participants Analyzed [units: participants]	594	577	579	579	578
Change from baseline in percentage of days with no daytime symptoms over 52 weeks (units: Percentage of days) Least Squares Mean ± Standard Error					
	22.5 ± 1.32	17.9 ± 1.34	21.8 ± 1.33	18.0 ± 1.34	18.8 ± 1.34

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., QMF149 150/320 µg o.d.
P Value	0.712
Method	Other LMM
Other LS Mean	0.7
Standard Error of the mean	1.78
95 % Confidence Interval 2-Sided	-2.8 to 4.2

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.
P Value	0.038

Method	Other LMM
Other LS Mean	3.7
Standard Error of the mean	1.78
95 % Confidence Interval 2-Sided	0.2 to 7.2

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., QMF149 150/160 µg o.d.
P Value	0.943
Method	Other LMM
Other LS Mean	-0.1
Standard Error of the mean	1.80
95 % Confidence Interval 2-Sided	-3.7 to 3.4

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.
P Value	0.612

Method	Other LMM
Other LS Mean	-0.9
Standard Error of the mean	1.79
95 % Confidence Interval 2-Sided	-4.4 to 2.6

Change from baseline in percentage of nights with no night-time awakenings over 52 weeks

(Time Frame: Baseline, 52 weeks)

	QVM149 150/50/160 µg o.d.	QVM149 150/50/80 µg o.d.	QMF149 150/320 µg o.d.	QMF149 150/160 µg o.d.	Salmeterol/fluticasone 50/500 µg b.i.d.
Arm/Group Description	QVM149 150/50/160 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QVM149 150/50/80 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/320 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/160 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	Salmeterol xinafoate /fluticasone propionate 50/500 µg twice daily (b.i.d.) delivered via Accuhaler®
Number of Participants Analyzed [units: participants]	599	584	582	584	586
Change from baseline in percentage of nights with no night-time awakenings over 52 weeks (units: Percentage of days) Least Squares Mean ± Standard Error					
	18.0 ± 1.11	17.6 ± 1.12	18.4 ± 1.13	16.1 ± 1.13	16.9 ± 1.12

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., QMF149 150/320 µg o.d.
P Value	0.809
Method	Other LMM
Other LS Mean	-0.4
Standard Error of the mean	1.51
95 % Confidence Interval 2-Sided	-3.3 to 2.6

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.
P Value	0.467
Method	Other LMM
Other LS Mean	1.1
Standard Error of the mean	1.50
95 % Confidence Interval 2-Sided	-1.9 to 4.0

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., QMF149 150/160 µg o.d.

P Value	0.318
Method	Other LMM
Other LS Mean	1.5
Standard Error of the mean	1.52
95 % Confidence Interval 2-Sided	-1.5 to 4.5

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.
P Value	0.640
Method	Other LMM
Other LS Mean	0.7
Standard Error of the mean	1.51
95 % Confidence Interval 2-Sided	-2.3 to 3.7

Change from baseline in percentage of mornings with no symptoms on rising over 52 weeks

(Time Frame: Baseline, 52 weeks)

	QVM149 150/50/160 µg o.d.	**QVM149 150/50/80 µg o.d.**	**QMF149 150/320 µg o.d.**	**QMF149 150/160 µg o.d.**	**Salmeterol/fluticasone 50/500 µg b.i.d.**
Arm/Group Description	QVM149 150/50/160 µg (indacaterol	QVM149 150/50/80 µg (indacaterol	QMF149 150/320 µg (indacaterol	QMF149 150/160 µg (indacaterol	Salmeterol xinafoate /fluticasone propionate

	acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	50/500 µg twice daily (b.i.d.) delivered via Accuhaler®
Number of Participants Analyzed [units: participants]	599	584	582	584	586
Change from baseline in percentage of mornings with no symptoms on rising over 52 weeks (units: Percentage of days) Least Squares Mean ± Standard Error					
	19.5 ± 1.33	18.5 ± 1.35	19.9 ± 1.35	15.5 ± 1.35	15.6 ± 1.34

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., QMF149 150/320 µg o.d.
P Value	0.814
Method	Other LMM
Other LS Mean	-0.4
Standard Error of the mean	1.83
95 % Confidence Interval 2-Sided	-4.0 to 3.2

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.

P Value	0.036
Method	Other LMM
Other LS Mean	3.8
Standard Error of the mean	1.83
95 % Confidence Interval 2-Sided	0.2 to 7.4

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., QMF149 150/160 µg o.d.
P Value	0.098
Method	Other LMM
Other LS Mean	3.1
Standard Error of the mean	1.84
95 % Confidence Interval 2-Sided	-0.6 to 6.7

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.
P Value	0.118

Method	Other LMM
Other LS Mean	2.9
Standard Error of the mean	1.84
95 % Confidence Interval 2-Sided	-0.7 to 6.5

Change from baseline in percentage of days without rescue medication use over 26 and 52 weeks

(Time Frame: Baseline, 26 weeks, 52 weeks)

	QVM149 150/50/160 µg o.d.	QVM149 150/50/80 µg o.d.	QMF149 150/320 µg o.d.	QMF149 150/160 µg o.d.	Salmeterol/fluticasone 50/500 µg b.i.d.
Arm/Group Description	QVM149 150/50/160 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QVM149 150/50/80 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/320 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/160 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	Salmeterol xinafoate /fluticasone propionate 50/500 µg twice daily (b.i.d.) delivered via Accuhaler®
Number of Participants Analyzed [units: participants]	590	577	578	580	579
Change from baseline in percentage of days without rescue medication use over 26 and 52 weeks (units: Percentage of days) Least Squares Mean ± Standard Error					
Week 26	22.5 ± 1.32	19.5 ± 1.33	23.3 ± 1.33	18.2 ± 1.33	19.6 ± 1.33
Week 52	25.0 ± 1.36	21.9 ± 1.36	24.9 ± 1.36	20.8 ± 1.37	21.8 ± 1.36

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., QMF149 150/320 µg o.d.	Week 26
P Value	0.645	
Method	Other LMM	
Other LS Mean	-0.8	
Standard Error of the mean	1.74	
95 % Confidence Interval 2-Sided	-4.2 to 2.6	

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Week 26
P Value	0.095	
Method	Other LMM	
Other LS Mean	2.9	
Standard Error of the mean	1.73	
95 % Confidence Interval 2-Sided	-0.5 to 6.3	

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., QMF149 150/160 µg o.d.	Week 26

P Value	0.460
Method	Other LMM
Other LS Mean	1.3
Standard Error of the mean	1.75
95 % Confidence Interval 2-Sided	-2.1 to 4.7

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Week 26
P Value	0.971	
Method	Other LMM	
Other LS Mean	-0.1	
Standard Error of the mean	1.75	
95 % Confidence Interval 2-Sided	-3.5 to 3.4	

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., QMF149 150/320 µg o.d.	Week 52
P Value	0.963	

Method	Other LMM
Other LS Mean	0.1
Standard Error of the mean	1.78
95 % Confidence Interval 2-Sided	-3.4 to 3.6

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Week 52
P Value	0.075	
Method	Other LMM	
Other LS Mean	3.2	
Standard Error of the mean	1.77	
95 % Confidence Interval 2-Sided	-0.3 to 6.6	

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., QMF149 150/160 µg o.d.	Week 52
P Value	0.517	

Method	Other LMM
Other LS Mean	1.2
Standard Error of the mean	1.79
95 % Confidence Interval 2-Sided	-2.3 to 4.7

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Week 52
P Value	0.956	
Method	Other LMM	
Other LS Mean	0.1	
Standard Error of the mean	1.78	
95 % Confidence Interval 2-Sided	-3.4 to 3.6	

Percentage of patients achieving the minimal clinically important difference (MCID) ACQ ≥ 0.5 at Week 26 and Week 52

(Time Frame: 26 weeks, 52 weeks)

	QVM149 150/50/160 µg o.d.	**QVM149 150/50/80 µg o.d.**	**QMF149 150/320 µg o.d.**	**QMF149 150/160 µg o.d.**	**Salmeterol/fluticasone 50/500 µg b.i.d.**
Arm/Group Description	QVM149 150/50/160 µg (indacaterol	QVM149 150/50/80 µg (indacaterol	QMF149 150/320 µg (indacaterol	QMF149 150/160 µg (indacaterol	Salmeterol xinafoate /fluticasone propionate

	acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	50/500 µg twice daily (b.i.d.) delivered via Accuhaler®
Number of Participants Analyzed [units: participants]	615	616	611	607	612
Percentage of patients achieving the minimal clinically important difference (MCID) ACQ ≥ 0.5 at Week 26 and Week 52 (units: Percentage of participants)					
Week 26	71.2	71.7	74.2	70.7	67.4
Week 52	78.8	72.8	77.9	73.1	72.8

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., QMF149 150/320 µg o.d.	Week 26
P Value	0.535	
Method	Other Logistic regression model	
Odds Ratio (OR)	0.92	
95 % Confidence Interval 2-Sided	0.70 to 1.20	

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Week 26
P Value	0.151	

Method	Other Logistic regression model
Odds Ratio (OR)	1.21
95 % Confidence Interval 2-Sided	0.93 to 1.57

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., QMF149 150/160 µg o.d.	Week 26
P Value	0.380	
Method	Other Logistic regression model	
Odds Ratio (OR)	1.13	
95 % Confidence Interval 2-Sided	0.86 to 1.48	

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Week 26
P Value	0.172	
Method	Other Logistic regression model	
Odds Ratio (OR)	1.20	

95 % Confidence Interval 2-Sided	0.92 to 1.57

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., QMF149 150/320 µg o.d.	Week 52
P Value	0.510	
Method	Other Logistic regression model	
Odds Ratio (OR)	1.10	
95 % Confidence Interval 2-Sided	0.83 to 1.47	

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Week 52
P Value	0.017	
Method	Other Logistic regression model	
Odds Ratio (OR)	1.41	
95 % Confidence Interval 2-Sided	1.06 to 1.86	

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., QMF149 150/160 µg o.d.	Week 52
P Value	0.744	
Method	Other Logistic regression model	
Odds Ratio (OR)	1.05	
95 % Confidence Interval 2-Sided	0.79 to 1.38	

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Week 52
P Value	0.922	
Method	Other Logistic regression model	
Odds Ratio (OR)	0.99	
95 % Confidence Interval 2-Sided	0.75 to 1.29	

Time to first hospitalization for asthma exacerbation

(Time Frame: 52 weeks on average, up to 416 days)

	QVM149 150/50/160 µg o.d.	QVM149 150/50/80 µg o.d.	QMF149 150/320 µg o.d.	QMF149 150/160 µg o.d.	Salmeterol/fluticasone 50/500 µg b.i.d.
Arm/Group Description	QVM149 150/50/160 µg (indacaterol acetate/glycopyrronium/	QVM149 150/50/80 µg (indacaterol acetate/glycopyrronium/	QMF149 150/320 µg (indacaterol acetate/mometasone	QMF149 150/160 µg (indacaterol acetate/mometasone	Salmeterol xinafoate /fluticasone propionate 50/500 µg twice daily

	mometasone furoate) once daily (o.d.) delivered via Concept1 device	mometasone furoate) once daily (o.d.) delivered via Concept1 device	furoate) once daily (o.d.) delivered via Concept1 device	furoate) once daily (o.d.) delivered via Concept1 device	(b.i.d.) delivered via Accuhaler®
Number of Participants Analyzed [units: participants]	615	616	611	607	612
Time to first hospitalization for asthma exacerbation (units: days) Median (Full Range)					
	367.0 (2 to 416)	367.0 (2 to 396)	367.0 (1 to 411)	367.0 (1 to 408)	367.0 (1 to 416)

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., QMF149 150/320 µg o.d.
P Value	0.371
Method	Regression, Cox
Hazard Ratio (HR)	0.66
95 % Confidence Interval 2-Sided	0.27 to 1.63

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.
P Value	0.996

Method	Regression, Cox
Hazard Ratio (HR)	1.00
95 % Confidence Interval 2-Sided	0.37 to 2.66

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., QMF149 150/160 µg o.d.
P Value	0.145
Method	Regression, Cox
Hazard Ratio (HR)	1.89
95 % Confidence Interval 2-Sided	0.80 to 4.47

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.
P Value	0.150
Method	Regression, Cox
Hazard Ratio (HR)	1.88

95
% Confidence Interval 0.80 to 4.43
2-Sided

Time to first asthma exacerbation by exacerbation category

(Time Frame: 52 weeks on average, up to 416 days)

	QVM149 150/50/160 µg o.d.	QVM149 150/50/80 µg o.d.	QMF149 150/320 µg o.d.	QMF149 150/160 µg o.d.	Salmeterol/fluticasone 50/500 µg b.i.d.
Arm/Group Description	QVM149 150/50/160 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QVM149 150/50/80 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/320 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/160 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	Salmeterol xinafoate /fluticasone propionate 50/500 µg twice daily (b.i.d.) delivered via Accuhaler®
Number of Participants Analyzed [units: participants]	615	616	611	607	612
Time to first asthma exacerbation by exacerbation category (units: days) Median (Full Range)					
Moderate or severe asthma exacerbation	366.0 (2 to 416)	366.0 (2 to 396)	366.0 (1 to 411)	365.0 (1 to 387)	365.0 (1 to 416)
Severe asthma exacerbation	366.0 (2 to 416)	366.0 (2 to 396)	366.0 (1 to 411)	366.0 (1 to 389)	366.0 (1 to 416)
All (mild, moderate or severe) asthma	363.0 (2 to 416)	364.0 (2 to 396)	361.0 (1 to 411)	360.0 (1 to 384)	278.0 (1 to 416)

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Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., QMF149 150/320 µg o.d.	Moderate or severe asthma exacerbation
P Value	0.523	
Method	Regression, Cox	
Hazard Ratio (HR)	0.94	
95 % Confidence Interval 2-Sided	0.77 to 1.15	

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Moderate or severe asthma exacerbation
P Value	<0.001	
Method	Regression, Cox	
Hazard Ratio (HR)	0.70	
95 % Confidence Interval 2-Sided	0.58 to 0.84	

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., QMF149 150/160 µg o.d.	Moderate or severe asthma exacerbation
P Value	0.164	
Method	Regression, Cox	
Hazard Ratio (HR)	0.87	
95 % Confidence Interval 2-Sided	0.72 to 1.06	

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Moderate or severe asthma exacerbation
P Value	0.005	
Method	Regression, Cox	
Hazard Ratio (HR)	0.76	
95 % Confidence Interval 2-Sided	0.63 to 0.92	

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., QMF149 150/320 µg o.d.	Severe asthma exacerbation
P Value	0.476	

Method	Regression, Cox
Hazard Ratio (HR)	0.92
95 % Confidence Interval 2-Sided	0.72 to 1.16

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Severe asthma exacerbation
P Value	<0.001	
Method	Regression, Cox	
Hazard Ratio (HR)	0.68	
95 % Confidence Interval 2-Sided	0.54 to 0.85	

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., QMF149 150/160 µg o.d.	Severe asthma exacerbation
P Value	0.243	
Method	Regression, Cox	
Hazard Ratio (HR)	0.88	

95 % Confidence Interval 2-Sided	0.70 to 1.09

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Severe asthma exacerbation
P Value	0.027	
Method	Regression, Cox	
Hazard Ratio (HR)	0.78	
95 % Confidence Interval 2-Sided	0.63 to 0.97	

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., QMF149 150/320 µg o.d.	All (mild, moderate, severe) asthma exacerbation
P Value	0.497	
Method	Regression, Cox	
Hazard Ratio (HR)	0.94	
95 % Confidence Interval 2-Sided	0.79 to 1.12	

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	All (mild, moderate, severe) asthma exacerbation
P Value	<0.001	
Method	Regression, Cox	
Hazard Ratio (HR)	0.71	
95 % Confidence Interval 2-Sided	0.60 to 0.84	

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., QMF149 150/160 µg o.d.	All (mild, moderate, severe) asthma exacerbation
P Value	0.126	
Method	Regression, Cox	
Hazard Ratio (HR)	0.87	
95 % Confidence Interval 2-Sided	0.73 to 1.04	

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	All (mild, moderate, severe) asthma exacerbation
P Value	<0.001	

Method	Regression, Cox
Hazard Ratio (HR)	0.72
95 % Confidence Interval 2-Sided	0.61 to 0.85

Annual rate of asthma exacerbations by exacerbation category

(Time Frame: 52 weeks)

	QVM149 150/50/160 µg o.d.	QVM149 150/50/80 µg o.d.	QMF149 150/320 µg o.d.	QMF149 150/160 µg o.d.	Salmeterol/fluticasone 50/500 µg b.i.d.
Arm/Group Description	QVM149 150/50/160 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QVM149 150/50/80 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/320 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/160 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	Salmeterol xinafoate /fluticasone propionate 50/500 µg twice daily (b.i.d.) delivered via Accuhaler®
Number of Participants Analyzed [units: participants]	615	616	611	607	612
Annual rate of asthma exacerbations by exacerbation category (units: Exacerbations per year) Mean (95% Confidence Interval)					
Moderate or severe asthma exacerbation	0.46 (0.39 to 0.54)	0.58 (0.50 to 0.67)	0.54 (0.47 to 0.63)	0.67 (0.58 to 0.77)	0.72 (0.63 to 0.82)
Severe asthma	0.26 (0.22 to 0.31)	0.38 (0.32 to 0.45)	0.33 (0.28 to 0.39)	0.41 (0.35 to 0.48)	0.45 (0.39 to 0.53)

exacerbation					
All (mild, moderate, severe) asthma exacerbation	0.74 (0.64 to 0.85)	0.86 (0.75 to 0.98)	0.93 (0.82 to 1.06)	0.98 (0.86 to 1.11)	1.23 (1.08 to 1.39)

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., QMF149 150/320 µg o.d.	Moderate or severe asthma exacerbation
P Value	0.120	
Method	Other Generalized linear model	
Other Rate ratio	0.85	
95 % Confidence Interval 2-Sided	0.68 to 1.04	

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Moderate or severe asthma exacerbation
P Value	<0.001	
Method	Other Generalized linear model	
Other Rate ratio	0.64	

95 % Confidence Interval 2-Sided	0.52 to 0.78

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., QMF149 150/160 µg o.d.	Moderate or severe asthma exacerbation
P Value	0.170	
Method	Other Generalized linear modeñ	
Other Rate ratio	0.87	
95 % Confidence Interval 2-Sided	0.71 to 1.06	

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Moderate or severe asthma exacerbation
P Value	0.041	
Method	Other Generalized linear model	
Other Rate ratio	0.81	
95 % Confidence Interval 2-Sided	0.66 to 0.99	

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., QMF149 150/320 µg o.d.	Severe asthma exacerbation
P Value	0.050	
Method	Other Generalized linear model	
Other Rate ratio	0.78	
95 % Confidence Interval 2-Sided	0.61 to 1.00	

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Severe asthma exacerbation
P Value	<0.001	
Method	Other Generalized linear model	
Other Rate ratio	0.58	
95 % Confidence Interval 2-Sided	0.45 to 0.73	

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., QMF149 150/160 µg o.d.	Severe asthma exacerbation
P Value	0.531	
Method	Other Generalized linear model	
Other Rate ratio	0.93	

95 % Confidence Interval 2-Sided	0.74 to 1.17

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Severe asthma exacerbation
P Value	0.117	
Method	Other Linear generalized model	
Other Rate ratio	0.84	
95 % Confidence Interval 2-Sided	0.67 to 1.05	

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., QMF149 150/320 µg o.d.	All (mild, moderate, severe) asthma exacerbation
P Value	0.016	
Method	Other Generalized linear model	
Other Rate ratio	0.79	
95 % Confidence Interval 2-Sided	0.66 to 0.96	

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	All (mild, moderate, severe) asthma exacerbation
P Value	<0.001	
Method	Other Generalized linear model	
Other Rate ratio	0.60	
95 % Confidence Interval 2-Sided	0.50 to 0.72	

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., QMF149 150/160 µg o.d.	All (mild, moderate, severe) asthma exacerbation
P Value	0.161	
Method	Other Generalized linear model	
Other Rate ratio	0.87	
95 % Confidence Interval 2-Sided	0.72 to 1.06	

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	All (mild, moderate, severe) asthma exacerbation
P Value	<0.001	

Method	Other Generalized linear model
Other Rate ratio	0.70
95 % Confidence Interval 2-Sided	0.58 to 0.84

Duration in days of asthma exacerbations by exacerbation category

(Time Frame: Up to Week 52)

	QVM149 150/50/160 µg o.d.	QVM149 150/50/80 µg o.d.	QMF149 150/320 µg o.d.	QMF149 150/160 µg o.d.	Salmeterol/fluticasone 50/500 µg b.i.d.
Arm/Group Description	QVM149 150/50/160 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QVM149 150/50/80 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/320 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/160 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	Salmeterol xinafoate /fluticasone propionate 50/500 µg twice daily (b.i.d.) delivered via Accuhaler®
Number of Participants Analyzed [units: participants]	615	616	611	607	612
Duration in days of asthma exacerbations by exacerbation category (units: days) Mean ± Standard Deviation					
Moderate or severe asthma exacerbation	4.5 ± 10.73	5.6 ± 12.87	6.7 ± 20.52	7.1 ± 17.17	8.1 ± 20.63
Severe asthma exacerbation	2.8 ± 7.31	4.1 ± 11.18	4.9 ± 19.07	4.5 ± 10.54	5.8 ± 18.24

All (mild, moderate, severe) asthma exacerbation	7.0 ± 16.02	8.1 ± 20.51	10.7 ± 28.70	9.6 ± 21.76	12.8 ± 29.21

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., QMF149 150/320 µg o.d.	Moderate or severe asthma exacerbation
P Value	0.183	
Method	Other van Elteren test	

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Moderate or severe asthma exacerbation
P Value	<0.001	
Method	Other van Elteren test	

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., QMF149 150/160 µg o.d.	Moderate or severe asthma exacerbation
P Value	0.155	
Method	Other van Elteren test	

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Moderate or severe asthma exacerbation

P Value	0.007
Method	Other van Elteren test

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., QMF149 150/320 µg o.d.	Severe asthma exacerbation
P Value	0.172	
Method	Other van Elteren test	

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Severe asthma exacerbation
P Value	<0.001	
Method	Other van Elteren test	

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., QMF149 150/160 µg o.d.	Severe asthma exacerbation
P Value	0.241	
Method	Other van Elteren test	

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Severe asthma exacerbation
P Value	0.033	
Method	Other van Elteren test	

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., QMF149 150/320 µg o.d.	All (mild, moderate, severe) asthma exacerbation
P Value	0.095	
Method	Other van Elteren test	

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	All (mild, moderate, severe) asthma exacerbation
P Value	<0.001	
Method	Other van Elteren test	

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., QMF149 150/160 µg o.d.	All (mild, moderate, severe) asthma exacerbation
P Value	0.090	
Method	Other van Elteren test	

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	All (mild, moderate, severe) asthma exacerbation
P Value	<0.001	
Method	Other van Elteren test	

Percentage of participants with at least one asthma exacerbation by exacerbation category

(Time Frame: Up to Week 52)

	QVM149 150/50/160 µg o.d.	QVM149 150/50/80 µg o.d.	QMF149 150/320 µg o.d.	QMF149 150/160 µg o.d.	Salmeterol/fluticasone 50/500 µg b.i.d.
Arm/Group Description	QVM149 150/50/160 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QVM149 150/50/80 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/320 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/160 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	Salmeterol xinafoate /fluticasone propionate 50/500 µg twice daily (b.i.d.) delivered via Accuhaler®
Number of Participants Analyzed [units: participants]	615	616	611	607	612
Percentage of participants with at least one asthma exacerbation by exacerbation category (units: percentage of participants)					
Moderate or severe asthma exacerbation	30.2	32.5	31.8	35.9	39.7
Severe asthma exacerbation	21.8	24.6	23.2	27.3	29.7
All (mild, moderate, severe) asthma exacerbation	40.2	40.2	41.9	44.0	50.5

Time in days to permanent discontinuation of study medication due to asthma exacerbation

(Time Frame: 52 weeks on average, up to 416 days)

	QVM149 150/50/160 µg o.d.	QVM149 150/50/80 µg o.d.	QMF149 150/320 µg o.d.	QMF149 150/160 µg o.d.	Salmeterol/fluticasone 50/500 µg b.i.d.
Arm/Group Description	QVM149 150/50/160 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QVM149 150/50/80 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/320 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/160 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	Salmeterol xinafoate /fluticasone propionate 50/500 µg twice daily (b.i.d.) delivered via Accuhaler®
Number of Participants Analyzed [units: participants]	615	616	611	607	612
Time in days to permanent discontinuation of study medication due to asthma exacerbation (units: days) Median (Full Range)					
	367.0 (11 to 416)	367.0 (2 to 399)	367.0 (3 to 411)	367.0 (2 to 408)	367.0 (2 to 416)

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., QMF149 150/320 µg o.d.
P Value	0.314
Method	Regression, Cox
Hazard Ratio (HR)	0.49
95 % Confidence Interval 2-Sided	0.12 to 1.96

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.
P Value	0.055
Method	Regression, Cox
Hazard Ratio (HR)	0.28
95 % Confidence Interval 2-Sided	0.08 to 1.03

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., QMF149 150/160 µg o.d.
P Value	0.306
Method	Regression, Cox
Hazard Ratio (HR)	0.62
95 % Confidence Interval 2-Sided	0.25 to 1.54

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.
P Value	0.566
Method	Regression, Cox

Hazard Ratio (HR)	0.76
95 % Confidence Interval 2-Sided	0.30 to 1.94

Total amount of oral corticosteroid used (in prednisone-equivalent mg doses) to treat asthma exacerbations

(Time Frame: Up to Week 52)

	QVM149 150/50/160 µg o.d.	QVM149 150/50/80 µg o.d.	QMF149 150/320 µg o.d.	QMF149 150/160 µg o.d.	Salmeterol/fluticasone 50/500 µg b.i.d.
Arm/Group Description	QVM149 150/50/160 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QVM149 150/50/80 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/320 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/160 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	Salmeterol xinafoate /fluticasone propionate 50/500 µg twice daily (b.i.d.) delivered via Accuhaler®
Number of Participants Analyzed [units: participants]	615	616	611	607	612
Total amount of oral corticosteroid used (in prednisone-equivalent mg doses) to treat asthma exacerbations (units: prednisone-equivalent milligram) Mean ± Standard Deviation					
	53.4 ± 169.76	72.0 ± 211.41	73.2 ± 235.90	82.5 ± 208.36	86.0 ± 199.79

Change from baseline in percentage of rescue medication free days over 26 and 52 weeks

(Time Frame: Baseline, 26 weeks, 52 weeks)

	QVM149 150/50/160 µg o.d.	QVM149 150/50/80 µg o.d.	QMF149 150/320 µg o.d.	QMF149 150/160 µg o.d.	Salmeterol/fluticasone 50/500 µg b.i.d.
Arm/Group Description	QVM149 150/50/160 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QVM149 150/50/80 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/320 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/160 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	Salmeterol xinafoate /fluticasone propionate 50/500 µg twice daily (b.i.d.) delivered via Accuhaler®
Number of Participants Analyzed [units: participants]	590	577	578	580	579
Change from baseline in percentage of rescue medication free days over 26 and 52 weeks (units: Percentage of days) Least Squares Mean ± Standard Error					
Week 26	22.5 ± 1.32	19.5 ± 1.33	23.3 ± 1.33	18.2 ± 1.33	19.6 ± 1.33
Week 52	25.0 ± 1.36	21.9 ± 1.36	24.9 ± 1.36	20.8 ± 1.37	21.8 ± 1.36

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., QMF149 150/320 µg o.d.	Week 26
P Value	0.645	
Method	Other LMM	
Other LS Mean	-0.8	
Standard Error of the mean	1.74	

95 % Confidence Interval 2-Sided	-4.2 to 2.6

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Week 26
P Value	0.095	
Method	Other LMM	
Other LS Mean	2.9	
Standard Error of the mean	1.73	
95 % Confidence Interval 2-Sided	-0.5 to 6.3	

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., QMF149 150/160 µg o.d.	Week 26
P Value	0.460	
Method	Other LMM	
Other LMM	1.3	
Standard Error of the mean	1.75	
95 % Confidence Interval 2-Sided	-2.1 to 4.7	

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Week 26
P Value	0.971	
Method	Other LMM	
Other LS Mean	-0.1	
Standard Error of the mean	1.75	
95 % Confidence Interval 2-Sided	-3.5 to 3.4	

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., QMF149 150/320 µg o.d.	Week 52
P Value	0.963	
Method	Other LMM	
Other LMM	0.1	
Standard Error of the mean	1.78	
95 % Confidence Interval 2-Sided	-3.4 to 3.6	

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Week 52
P Value	0.075	
Method	Other LMM	
Other LS Mean	3.2	
Standard Error of the mean	1.77	
95 % Confidence Interval 2-Sided	-0.3 to 6.6	

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., QMF149 150/160 µg o.d.	Week 52
P Value	0.517	
Method	Other LMM	
Other LS Mean	1.2	
Standard Error of the mean	1.79	
95 % Confidence Interval 2-Sided	-2.3 to 4.7	

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Week 52
P Value	0.956	
Method	Other LMM	
Other LS Mean	0.1	
Standard Error of the mean	1.78	
95 % Confidence Interval 2-Sided	-3.4 to 3.6	

Asthma Quality of Life Questionnaire (AQLQ) at Week 52

(Time Frame: 52 weeks)

	QVM149 150/50/160 µg o.d.	QVM149 150/50/80 µg o.d.	QMF149 150/320 µg o.d.	QMF149 150/160 µg o.d.	Salmeterol/fluticasone 50/500 µg b.i.d.
Arm/Group Description	QVM149 150/50/160 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QVM149 150/50/80 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/320 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/160 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	Salmeterol xinafoate /fluticasone propionate 50/500 µg twice daily (b.i.d.) delivered via Accuhaler®
Number of Participants Analyzed [units: participants]	606	593	595	599	594

Asthma Quality of Life Questionnaire (AQLQ) at Week 52
(units: Score on a scale)
Least Squares Mean ± Standard Error

5.555 ± 0.0354	5.445 ± 0.0358	5.535 ± 0.0356	5.499 ± 0.0358	5.495 ± 0.0357

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., QMF149 150/320 µg o.d.
P Value	0.690
Method	Other MMRM
Other LS Mean	0.020
Standard Error of the mean	0.0502
95 % Confidence Interval 2-Sided	-0.078 to 0.118

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.
P Value	0.232
Method	Other MMRM
Other LS Mean	0.060
Standard Error of the mean	0.0502
95 % Confidence Interval 2-Sided	-0.038 to 0.159

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., QMF149 150/160 µg o.d.
P Value	0.285
Method	Other MMRM
Other LS Mean	-0.054
Standard Error of the mean	0.0506
95 % Confidence Interval 2-Sided	-0.153 to 0.045

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.
P Value	0.319
Method	Other MMRM
Other LS Mean	-0.050
Standard Error of the mean	0.0505
95 % Confidence Interval 2-Sided	-0.150 to 0.049

Pre-dose FEV1 at weeks 4 and 12

(Time Frame: 4 weeks, 12 weeks)

	QVM149 150/50/160 µg o.d.	QVM149 150/50/80 µg o.d.	QMF149 150/320 µg o.d.	QMF149 150/160 µg o.d.	Salmeterol/fluticasone 50/500 µg b.i.d.
Arm/Group Description	QVM149 150/50/160 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QVM149 150/50/80 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/320 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/160 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	Salmeterol xinafoate /fluticasone propionate 50/500 µg twice daily (b.i.d.) delivered via Accuhaler®
Number of Participants Analyzed [units: participants]	606	594	592	596	598
Pre-dose FEV1 at weeks 4 and 12 (units: litres) Least Squares Mean ± Standard Deviation					
Week 4	2.032 ± 0.0122	1.983 ± 0.0123	1.963 ± 0.0124	1.950 ± 0.0123	1.887 ± 0.0123
Week 12	2.024 ± 0.0134	1.994 ± 0.0135	1.966 ± 0.0135	1.944 ± 0.0136	1.907 ± 0.0135

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., QMF149 150/320 µg o.d.	Week 4
P Value	<0.001	
Method	Other MMRM	
Other LS Mean	0.068	
Standard Error of the mean	0.0166	

95 % Confidence Interval 2-Sided	0.036 to 0.101

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Week 4
P Value	<0.001	
Method	Other MMRM	
Other LS Mean	0.145	
Standard Error of the mean	0.0165	
95 % Confidence Interval 2-Sided	0.113 to 0.177	

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., QMF149 150/160 µg o.d.	Week 4
P Value	0.049	
Method	Other MMRM	
Other LS Mean	0.033	
Standard Error of the mean	0.0167	
95 % Confidence Interval 2-Sided	0.000 to 0.066	

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Week 4
P Value	<0.001	
Method	Other MMRM	
Other LS Mean	0.096	
Standard Error of the mean	0.0166	
95 % Confidence Interval 2-Sided	0.064 to 0.129	

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., QMF149 150/320 µg o.d.	Week 12
P Value	0.002	
Method	Other MMRM	
Other LS Mean	0.058	
Standard Error of the mean	0.0184	
95 % Confidence Interval 2-Sided	0.022 to 0.094	

Statistical Analysis

Groups	QVM149 150/50/160 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Week 12
P Value	<0.001	
Method	Other MMRM	
Other LS Mean	0.117	
Standard Error of the mean	0.0183	
95 % Confidence Interval 2-Sided	0.081 to 0.153	

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., QMF149 150/160 µg o.d.	Week 12
P Value	0.007	
Method	Other MMRM	
Other LS Mean	0.050	
Standard Error of the mean	0.0185	
95 % Confidence Interval 2-Sided	0.013 to 0.086	

Statistical Analysis

Groups	QVM149 150/50/80 µg o.d., Salmeterol/fluticasone 50/500 µg b.i.d.	Week 12
P Value	<0.001	
Method	Other MMRM	
Other MMRM	0.087	
Standard Error of the mean	0.0184	
95 % Confidence Interval 2-Sided	0.051 to 0.123	

Percentage of participants with composite endpoint of serious asthma outcomes

(Time Frame: Up to Week 52)

	QVM149 150/50/160 µg o.d.	QVM149 150/50/80 µg o.d.	QMF149 150/320 µg o.d.	QMF149 150/160 µg o.d.	Salmeterol/fluticasone 50/500 µg b.i.d.
Arm/Group Description	QVM149 150/50/160 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QVM149 150/50/80 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/320 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/160 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	Salmeterol xinafoate /fluticasone propionate 50/500 µg twice daily (b.i.d.) delivered via Accuhaler®
Number of Participants Analyzed [units: participants]	616	617	613	608	618

Percentage of participants with composite endpoint of serious asthma outcomes
(units: Percentage of participants)

	1.4	2.5	1.9	1.6	1.2

Safety Results

All-Cause Mortality

	QVM149 150/50/160 µg o.d. N = 616	QVM149 150/50/80 µg o.d. N = 617	QMF149 150/320 µg o.d. N = 613	QMF149 150/160 µg o.d. N = 608	Salmeterol/fluticasone 50/500 µg b.i.d. N = 618
Arm/Group Description	QVM149 150/50/160 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QVM149 150/50/80 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/320 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/160 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	Salmeterol xinafoate /fluticasone propionate 50/500 µg twice daily (b.i.d.) delivered via Accuhaler®
Total participants affected	2 (0.32%)	1 (0.16%)	4 (0.65%)	0 (0.00%)	0 (0.00%)

Serious Adverse Events by System Organ Class

Time Frame	Adverse events were collected from first dose of study treatment until end of study treatment plus 30 days (52 weeks on average, up to 416 days).
Additional Description	Any signs or symptoms that occurs during study treatment plus the 30 days post treatment.
Source Vocabulary for Table Default	MedDRA (22.0)
Assessment Type for Table Default	Systematic Assessment

	QVM149 150/50/160 µg o.d. N = 616	**QVM149 150/50/80 µg o.d. N = 617**	**QMF149 150/320 µg o.d. N = 613**	**QMF149 150/160 µg o.d. N = 608**	**Salmeterol/fluticasone 50/500 µg b.i.d. N = 618**
Arm/Group Description	QVM149 150/50/160 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QVM149 150/50/80 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/320 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/160 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	Salmeterol xinafoate /fluticasone propionate 50/500 µg twice daily (b.i.d.) delivered via Accuhaler®
Total participants affected	46 (7.47%)	49 (7.94%)	52 (8.48%)	38 (6.25%)	39 (6.31%)
Blood and lymphatic system disorders					
Anaemia	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Immune thrombocytopenic purpura	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cardiac disorders					

Acute cardiac event	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)
Acute coronary syndrome	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Acute myocardial infarction	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)	1 (0.16%)
Arrhythmia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)
Atrial fibrillation	0 (0.00%)	1 (0.16%)	1 (0.16%)	1 (0.16%)	1 (0.16%)
Atrioventricular block complete	1 (0.16%)	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)
Cardiac failure	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)
Cardiac failure congestive	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)
Cardiac tamponade	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Extrasystoles	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)
Myocardial infarction	1 (0.16%)	0 (0.00%)	1 (0.16%)	2 (0.33%)	0 (0.00%)
Myocardial ischaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)
Palpitations	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Supraventricular tachycardia	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)
Ventricular extrasystoles	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)
Ear and labyrinth disorders					
Middle ear effusion	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)

Otorrhoea	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)
Eye disorders					
Cataract	0 (0.00%)	0 (0.00%)	2 (0.33%)	0 (0.00%)	0 (0.00%)
Optic ischaemic neuropathy	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)
Gastrointestinal disorders					
Abdominal hernia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)
Ascites	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Enteritis	0 (0.00%)	0 (0.00%)	2 (0.33%)	0 (0.00%)	0 (0.00%)
Gastrointestinal angiodysplasia	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gastrointestinal haemorrhage	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Intra-abdominal fluid collection	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Large intestine perforation	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)
Pancreatitis acute	1 (0.16%)	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Peritoneal adhesions	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Proctitis	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Rectal haemorrhage	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Rectal polyp	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Umbilical hernia	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (0.33%)	0 (0.00%)

General disorders and administration site conditions					
Fatigue	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Non-cardiac chest pain	2 (0.32%)	1 (0.16%)	0 (0.00%)	1 (0.16%)	0 (0.00%)
Pyrexia	0 (0.00%)	1 (0.16%)	1 (0.16%)	0 (0.00%)	0 (0.00%)
Sudden cardiac death	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)
Hepatobiliary disorders					
Bile duct stone	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)
Cholecystitis acute	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cholelithiasis	3 (0.49%)	0 (0.00%)	0 (0.00%)	1 (0.16%)	1 (0.16%)
Hepatic cirrhosis	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Liver injury	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)
Primary biliary cholangitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)
Steatohepatitis	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Immune system disorders					
Drug hypersensitivity	1 (0.16%)	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)
Sarcoidosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)
Infections and infestations					
Appendicitis	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (0.32%)

Bursitis infective	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cellulitis	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)	2 (0.32%)
Cholecystitis infective	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Chronic sinusitis	1 (0.16%)	0 (0.00%)	0 (0.00%)	2 (0.33%)	1 (0.16%)
Dengue fever	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Erysipelas	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gastroenteritis	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)
Hepatitis C	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Herpes zoster	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)
HIV infection	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Infectious pleural effusion	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)
Influenza	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)
Lower respiratory tract infection	1 (0.16%)	1 (0.16%)	3 (0.49%)	1 (0.16%)	2 (0.32%)
Mastoiditis	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nasopharyngitis	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Otitis media chronic	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Peritonitis	0 (0.00%)	1 (0.16%)	1 (0.16%)	0 (0.00%)	0 (0.00%)
Pneumonia	3 (0.49%)	2 (0.32%)	1 (0.16%)	3 (0.49%)	5 (0.81%)
Postoperative wound infection	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pulmonary tuberculosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)

Pyelonephritis acute	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)
Respiratory tract infection	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Rhinitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)
Salpingitis	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Sinusitis	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Upper respiratory tract infection bacterial	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)
Urinary tract infection	2 (0.32%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)
Urosepsis	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Viral upper respiratory tract infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)
Injury, poisoning and procedural complications					
Concussion	0 (0.00%)	2 (0.32%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Facial bones fracture	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Fall	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)
Foot fracture	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)
Fracture	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)
Hand fracture	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (0.33%)	0 (0.00%)
Head injury	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hip fracture	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)
Humerus fracture	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Injury	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)
Limb injury	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)
Lower limb fracture	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Lumbar vertebral fracture	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)	1 (0.16%)
Meniscus injury	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)
Multiple fractures	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Post procedural discomfort	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)
Rib fracture	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)
Skin abrasion	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Skin laceration	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)
Upper limb fracture	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)
Investigations					
Hepatic enzyme increased	0 (0.00%)	0 (0.00%)	2 (0.33%)	0 (0.00%)	0 (0.00%)
Transaminases increased	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Metabolism and nutrition disorders					
Type 2 diabetes mellitus	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)

Musculoskeletal and connective tissue disorders					
Back pain	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Intervertebral disc protrusion	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)
Jaw disorder	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Myalgia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)
Osteoarthritis	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (0.33%)	0 (0.00%)
Pathological fracture	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Rotator cuff syndrome	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)
Spinal deformity	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)					
Acute leukaemia	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Adenocarcinoma of colon	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Basal cell carcinoma	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)
Breast cancer	0 (0.00%)	1 (0.16%)	1 (0.16%)	0 (0.00%)	0 (0.00%)
Central nervous system lymphoma	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)

Chronic lymphocytic leukaemia	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)
Colon cancer	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Endometrial cancer	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)
Liposarcoma	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)
Lung neoplasm malignant	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)
Ovarian adenoma	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)
Prostate cancer	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)
Salivary gland adenoma	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)
Soft tissue sarcoma	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Squamous cell carcinoma	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Uterine cancer	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)
Uterine leiomyoma	0 (0.00%)	1 (0.16%)	0 (0.00%)	1 (0.16%)	0 (0.00%)
Nervous system disorders					
Alcoholic seizure	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)
Carpal tunnel syndrome	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)
Cerebral infarction	0 (0.00%)	0 (0.00%)	1 (0.16%)	1 (0.16%)	0 (0.00%)
Cerebrovascular accident	0 (0.00%)	1 (0.16%)	0 (0.00%)	1 (0.16%)	0 (0.00%)

Cerebrovascular disorder	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)
Cervicobrachial syndrome	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dizziness	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)
Hypertensive encephalopathy	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)
Ischaemic neuropathy	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)
Ischaemic stroke	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)
Loss of consciousness	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)
Lumbar radiculopathy	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)
Seizure	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Syncope	0 (0.00%)	0 (0.00%)	1 (0.16%)	1 (0.16%)	0 (0.00%)
Transient global amnesia	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Transient ischaemic attack	2 (0.32%)	1 (0.16%)	1 (0.16%)	0 (0.00%)	0 (0.00%)
Pregnancy, puerperium and perinatal conditions					
Abortion spontaneous	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)
Psychiatric disorders					
Depression	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)
Suicide attempt	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Renal and urinary disorders					
Calculus urethral	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)
Nephritis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)
Nephrolithiasis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)
Renal colic	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)
Urinary retention	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)
Reproductive system and breast disorders					
Cystocele	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Endometriosis	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Ovarian cyst	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Postmenopausal haemorrhage	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Uterine polyp	1 (0.16%)	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Respiratory, thoracic and mediastinal disorders					
Asthma	9 (1.46%)	15 (2.43%)	12 (1.96%)	8 (1.32%)	9 (1.46%)
Bronchitis chronic	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)
Cough	0 (0.00%)	2 (0.32%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dyspnoea	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Haemothorax	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)
Nasal polyps	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)	1 (0.16%)

Nasal septum deviation	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pleural effusion	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)	1 (0.16%)
Pulmonary embolism	1 (0.16%)	0 (0.00%)	3 (0.49%)	0 (0.00%)	0 (0.00%)
Sinus polyp	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Sleep apnoea syndrome	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)
Skin and subcutaneous tissue disorders					
Angioedema	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)
Urticaria	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (0.32%)
Vascular disorders					
Angiopathy	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)
Aortic dissection	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Aortic dissection rupture	0 (0.00%)	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Deep vein thrombosis	2 (0.32%)	0 (0.00%)	0 (0.00%)	1 (0.16%)	0 (0.00%)
Haemorrhagic vasculitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.16%)
Hypertension	0 (0.00%)	2 (0.32%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypertensive crisis	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Thrombophlebitis	1 (0.16%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Varicose vein	2 (0.32%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Other Adverse Events by System Organ Class

Time Frame	Adverse events were collected from first dose of study treatment until end of study treatment plus 30 days (52 weeks on average, up to 416 days).
Additional Description	Any signs or symptoms that occurs during study treatment plus the 30 days post treatment.
Source Vocabulary for Table Default	MedDRA (22.0)
Assessment Type for Table Default	Systematic Assessment
Frequent Event Reporting Threshold	2%

	QVM149 150/50/160 µg o.d. N = 616	**QVM149 150/50/80 µg o.d. N = 617**	**QMF149 150/320 µg o.d. N = 613**	**QMF149 150/160 µg o.d. N = 608**	**Salmeterol/fluticasone 50/500 µg b.i.d. N = 618**
Arm/Group Description	QVM149 150/50/160 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QVM149 150/50/80 µg (indacaterol acetate/glycopyrronium/ mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/320 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	QMF149 150/160 µg (indacaterol acetate/mometasone furoate) once daily (o.d.) delivered via Concept1 device	Salmeterol xinafoate /fluticasone propionate 50/500 µg twice daily (b.i.d.) delivered via Accuhaler®
Total participants affected	367 (59.58%)	387 (62.72%)	377 (61.50%)	392 (64.47%)	419 (67.80%)
General disorders and administration site conditions					
Pyrexia	17 (2.76%)	11 (1.78%)	10 (1.63%)	10 (1.64%)	15 (2.43%)
Infections and infestations					
Bronchitis	49 (7.95%)	48 (7.78%)	46 (7.50%)	44 (7.24%)	55 (8.90%)

Influenza	19 (3.08%)	21 (3.40%)	23 (3.75%)	26 (4.28%)	25 (4.05%)
Lower respiratory tract infection	13 (2.11%)	12 (1.94%)	12 (1.96%)	17 (2.80%)	22 (3.56%)
Nasopharyngitis	64 (10.39%)	76 (12.32%)	73 (11.91%)	64 (10.53%)	83 (13.43%)
Pharyngitis	22 (3.57%)	21 (3.40%)	20 (3.26%)	19 (3.13%)	20 (3.24%)
Respiratory tract infection viral	18 (2.92%)	17 (2.76%)	11 (1.79%)	29 (4.77%)	22 (3.56%)
Rhinitis	12 (1.95%)	20 (3.24%)	17 (2.77%)	20 (3.29%)	11 (1.78%)
Sinusitis	14 (2.27%)	18 (2.92%)	9 (1.47%)	17 (2.80%)	14 (2.27%)
Upper respiratory tract infection	33 (5.36%)	45 (7.29%)	52 (8.48%)	48 (7.89%)	52 (8.41%)
Upper respiratory tract infection bacterial	17 (2.76%)	22 (3.57%)	27 (4.40%)	28 (4.61%)	29 (4.69%)
Urinary tract infection	8 (1.30%)	5 (0.81%)	10 (1.63%)	9 (1.48%)	13 (2.10%)
Viral upper respiratory tract infection	21 (3.41%)	31 (5.02%)	38 (6.20%)	26 (4.28%)	47 (7.61%)
Musculoskeletal and connective tissue disorders					
Arthralgia	2 (0.32%)	14 (2.27%)	5 (0.82%)	12 (1.97%)	10 (1.62%)
Back pain	12 (1.95%)	18 (2.92%)	18 (2.94%)	16 (2.63%)	14 (2.27%)

Nervous system disorders					
Headache	23 (3.73%)	30 (4.86%)	24 (3.92%)	34 (5.59%)	25 (4.05%)
Respiratory, thoracic and mediastinal disorders					
Asthma	243 (39.45%)	242 (39.22%)	249 (40.62%)	265 (43.59%)	306 (49.51%)
Cough	24 (3.90%)	18 (2.92%)	11 (1.79%)	14 (2.30%)	15 (2.43%)
Dysphonia	24 (3.90%)	13 (2.11%)	10 (1.63%)	9 (1.48%)	12 (1.94%)
Rhinitis allergic	19 (3.08%)	17 (2.76%)	9 (1.47%)	15 (2.47%)	20 (3.24%)
Vascular disorders					
Hypertension	16 (2.60%)	19 (3.08%)	14 (2.28%)	17 (2.80%)	23 (3.72%)

Conclusion:

Considering the totality of the study results, high and medium doses of QVM149 demonstrated clinically meaningful benefits in patients with poorly controlled asthma. Both doses of QVM149 showed meaningful improvements over the corresponding QMF149 doses for trough FEV1 at 26 weeks and for multiple other lung function endpoints. Both doses of QVM149 also demonstrated reductions in exacerbations compared to high dose salmeterol/fluticasone 50/500 µg b.i.d. (standard of care treatment with established benefits in asthma patients). Clinically relevant improvements were demonstrated in ACQ-7 of ≥ 0.5 units (minimal clinically important difference, MCID) in all treatment groups at 26 and 52 weeks, however no significant treatment differences were observed among groups. The least squares mean change from baseline in ACQ-7 score was approximately −1 (or better for high dose QVM149 and QMF149), which is 2-fold the MCID.

Overall safety was comparable across treatment groups (i.e. adverse events, laboratory values, deaths, major adverse cardiovascular events (MACE) and vital signs). The overall incidence of MACE and deaths were comparable and any differences among treatment groups were not considered clinically meaningful. The safety findings support the following:

- There is no evidence of an additional safety risk when a long acting muscarinic antagonist (LAMA) is added to a long acting β2-adrenergic agonist/inhaled corticosteroids (LABA/ICS) combination (QMF149).
- QVM149 has a comparable safety profile to salmeterol/fluticasone 50/500 µg b.i.d., which is a commercially available standard of care, with a well-established safety profile.
- There were no clinically meaningful differences in ICS-related events between any of the treatment groups.
- The cardiovascular safety profile is comparable among all treatment groups.

Date of Clinical Trial Report

16-Sep-2019