The Effect of QVA149 on Patient Reported Dyspnea in Moderate to Severe Chronic Obstructive Pulmonary Disease (COPD) (BLAZE)

This study has been completed.

Sponsor:
Novartis Pharmaceuticals

Information provided by (Responsible Party):
Novartis (Novartis Pharmaceuticals)

ClinicalTrials.gov Identifier:
NCT01490125

First received: November 15, 2011
Last updated: November 5, 2013
Last verified: November 2013
History of Changes

Results First Received: August 9, 2013

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Safety/Efficacy Study; Intervention Model: Crossover Assignment; Masking: Double Blind (Subject, Investigator); Primary Purpose: Treatment
Condition:	Chronic Obstructive Pulmonary Disease
Interventions:	Drug: QVA149 Drug: Tiotropium Drug: Placebo to QVA149 Drug: Placebo to tiotropium Drug: Salbutamol/albuterol

Participant Flow

Hide Participant Flow

Recruitment Details

Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations
247 patients were randomized. Of these 247, one patient was misrandomized, did not receive study treatment and was excluded from any analysis set. Of 246 patients, 191 completed the study. This is a crossover study; therefore, participants are counted more than once depending on their dosing sequences.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
Participants were randomized to 1 of 6 treatment sequences to receive 1 of 3 treatment combinations; then, crossed to the other 2 possible treatment combinations for a total of 3 treatment periods. Each treatment combination period was followed by a 14 day washout.

Reporting Groups

	Description
QVA149+ Placebo+ Tiotropium	Participants were randomized to sequence QVA149 + placebo + tiotropium.
QVA149+ Tiotropium+ Placebo	Participants were randomized to sequence QVA149 + tiotropium + placebo.

Placebo + QVA149 + Tiotropium	Participants were randomized to sequence placebo + QVA149 + tiotropium
Placebo+ Tiotropium + QVA149	Participants were randomized to sequence placebo + tiotropium + QVA149
Tiotropium + QVA149+ Placebo	Participants were randomized to sequence tiotropium + QVA149 + placebo
Tiotropium + Placebo +QVA149	Participants were randomized to sequence tiotropium + placebo + QVA149

Participant Flow for 3 periods

Period 1: Period I

	QVA149+ Placebo+ Tiotropium	QVA149+ Tiotropium+ Placebo	Placebo + QVA149 + Tiotropium	Placebo+ Tiotropium + QVA149	Tiotropium + QVA149+ Placebo	Tiotropium + Placebo +QVA149
STARTED	43	42	41	38	40	42
COMPLETED	37	37	37	33	36	37
NOT COMPLETED	6	5	4	5	4	5
Adverse Event	4	1	1	3	2	4
Protocol Violation	1	1	1	1	0	0
Withdrawal by Subject	1	3	2	1	2	1

Period 2: Period II

	QVA149+ Placebo+ Tiotropium	QVA149+ Tiotropium+ Placebo	Placebo + QVA149 + Tiotropium	Placebo+ Tiotropium + QVA149	Tiotropium + QVA149+ Placebo	Tiotropium + Placebo +QVA149
STARTED	37	37	37	33	36	37
COMPLETED	34	33	34	30	32	35
NOT COMPLETED	3	4	3	3	4	2
Adverse Event	2	3	2	2	4	2
Protocol Violation	0	0	1	1	0	0
Lost to Follow-up	0	1	0	0	0	0
Withdrawal by Subject	1	0	0	0	0	0

Period 3: Period III

	QVA149+ Placebo+ Tiotropium	QVA149+ Tiotropium+ Placebo	Placebo + QVA149 + Tiotropium	Placebo+ Tiotropium + QVA149	Tiotropium + QVA149+ Placebo	Tiotropium + Placebo +QVA149
STARTED	34	33	34	30	32	35
COMPLETED	31	32	34	28	31	35

NOT COMPLETED	**3**	**1**	**0**	**2**	**1**	**0**
Adverse Event	**3**	**1**	**0**	**1**	**0**	**0**
Death	**0**	**0**	**0**	**1**	**0**	**0**
Lack of Efficacy	**0**	**0**	**0**	**0**	**1**	**0**

Baseline Characteristics

Hide Baseline Characteristics

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
One misrandomized participant did not receive study treatment, was discontinued and not included in the full analysis set used for demographics.

Reporting Groups

	Description
All Participants	All participants who entered the study and were randomized to any of the 3 treatment combinations: QVA149 plus placebo to tiotropium; tiotropium plus placebo to QVA149 or placebo to QVA149 plus placebo to tiotropium.

Baseline Measures

	All Participants
Number of Participants [units: participants]	**246**
Age [units: years] Mean (Standard Deviation)	**62.8 (8.19)**
Gender [units: participants]	
Female	**73**
Male	**173**

Outcome Measures

Hide All Outcome Measures

1. Primary: Total Total Transient Dyspnea Index (TDI) Score After 6 Weeks of Treatment QVA149 Compared to Placebo [Time Frame: Baseline and 6 weeks]

Measure Type	Primary
Measure Title	Total Total Transient Dyspnea Index (TDI) Score After 6 Weeks of Treatment QVA149 Compared to Placebo
Measure Description	Total Transient Dyspnea Index (TDI) is part of the BDI/TDI questionnaire where participants indicated whether they improved or deteriorated since their Baseline Dyspnea Index (BDI). The BDI and TDI each had 3 domains: activities, tasks, and effort. BDI domains were rated from 0 (very severe) to 4 (none) and the rates summed for the total BDI score ranging from 0 to 12; the lower the score the worse the severity of dyspnea. TDI domains were rated from -6 (major deterioration) to 6 (major improvement) and the rates summed for the total TDI score ranging from -18 to 18. However, to ensure comparability with the TDI paper version, all TDI values were divided by 2 before the analysis. If data was missing or insufficient for any one of the domains a BDI/TDI was calculated. BDI = Baseline Dyspnea Index

	taken 75 min prior to the first dose in each treatment period. TDI = Transition Dyspnea Index taken after 6 weeks of treatment 75 min prior to the last dose in each treatment period.
Time Frame	Baseline and 6 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The analysis set includes all randomized patients who received at least one dose of study drug and for whom data are available. Data was analyzed according to the treatment they were randomized. In this cross-over design the number of patients on each treatment does not add up to the total number of patients.

Reporting Groups

	Description
QVA149 + Placebo to Tiotropium	Participants received QVA149 plus placebo to tiotropium during 1 of 3 treatment periods, once a day for 6 weeks. Participants were provided with a salbutamol/albuterol inhaler to use as rescue medication.
Tiotropium + Placebo to QVA149	Participants received tiotropium 18 µg plus placebo to QVA149 during 1 of 3 treatment periods once a day for 6 weeks. Participants were provided with a salbutamol/albuterol inhaler to use as rescue medication.
Placebo	Participants received placebo to QVA149 plus placebo to tiotropium during 1 of 3 treatment periods once a day for 6 weeks. Participants were provided with a salbutamol/albuterol inhaler to use as rescue medication.

Measured Values

	QVA149 + Placebo to Tiotropium	**Tiotropium + Placebo to QVA149**	**Placebo**
Number of Participants Analyzed [units: participants]	**220**	**0**	**218**
Total Total Transient Dyspnea Index (TDI) Score After 6 Weeks of Treatment QVA149 Compared to Placebo [units: Units on a scale] Mean (Standard Deviation)			
BDI	**7.34 (2.033)**		**7.33 (2.206)**
TDI	**0.98 (2.666)**		**-0.38 (2.308)**

No statistical analysis provided for Total Total Transient Dyspnea Index (TDI) Score After 6 Weeks of Treatment QVA149 Compared to Placebo

2. Secondary: Total Total Transient Dyspnea Index (TDI) Score After 6 Weeks of Treatment QVA149 Compared to Tiotropium [Time Frame: Baseline and 6 weeks]

Measure Type	Secondary
Measure Title	Total Total Transient Dyspnea Index (TDI) Score After 6 Weeks of Treatment QVA149 Compared to Tiotropium
Measure Description	Total Transient Dyspnea Index (TDI) is part of the BDI/TDI questionnaire where participants indicated whether they improved or deteriorated since their Baseline Dyspnea Index (BDI). The BDI and TDI each had 3 domains: activities, tasks, and effort. BDI domains were rated from 0 (very severe) to 4 (none) and the rates summed for the total BDI score ranging from 0 to 12; the lower the score the worse the severity of dyspnea. TDI domains were rated from -6 (major deterioration) to 6 (major improvement) and the rates summed for the total TDI score ranging from -18 to 18. However, to ensure comparability with the TDI paper version, all TDI values were divided by 2 before the analysis. If data was missing or insufficient for any one of the domains a BDI/TDI was calculated. BDI = Baseline Dyspnea Index taken 75 min prior to the first dose in each treatment period. TDI = Transition Dyspnea Index taken after 6 weeks of treatment 75 min prior to the last dose in each treatment period.

Time Frame	Baseline and 6 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The analysis set includes all randomized patients who received at least one dose of study drug and for whom data are available. Data was analyzed according to the treatment they were randomized. In this cross-over design the number of patients on each treatment does not add up to the total number of patients.

Reporting Groups

	Description
QVA149 + Placebo to Tiotropium	Participants received QVA149 plus placebo to tiotropium during 1 of 3 treatment periods, once a day for 6 weeks. Participants were provided with a salbutamol/albuterol inhaler to use as rescue medication.
Tiotropium + Placebo to QVA149	Participants received tiotropium 18 µg plus placebo to QVA149 during 1 of 3 treatment periods once a day for 6 weeks. Participants were provided with a salbutamol/albuterol inhaler to use as rescue medication.
Placebo	Participants received placebo to QVA149 plus placebo to tiotropium during 1 of 3 treatment periods once a day for 6 weeks. Participants were provided with a salbutamol/albuterol inhaler to use as rescue medication.

Measured Values

	QVA149 + Placebo to Tiotropium	**Tiotropium + Placebo to QVA149**	**Placebo**
Number of Participants Analyzed [units: participants]	**220**	**217**	**0**
Total Total Transient Dyspnea Index (TDI) Score After 6 Weeks of Treatment QVA149 Compared to Tiotropium [units: Units on a scale] Mean (Standard Deviation)			
BDI	**7.34 (2.033)**	**7.31 (2.199)**	
TDI	**0.98 (2.666)**	**0.47 (2.184)**	

No statistical analysis provided for Total Total Transient Dyspnea Index (TDI) Score After 6 Weeks of Treatment QVA149 Compared to Tiotropium

3. Secondary: Standardized Forced Expiratory Volume in 1 Second (FEV1) Area Under the Curve (AUC) 5min-4h After First Dose and 6 Weeks of Treatment With QVA149 Compared to Placebo and Tiotropium [Time Frame: 5min-4hr at day 1 and week 6 post-dose]

Measure Type	Secondary
Measure Title	Standardized Forced Expiratory Volume in 1 Second (FEV1) Area Under the Curve (AUC) 5min-4h After First Dose and 6 Weeks of Treatment With QVA149 Compared to Placebo and Tiotropium
Measure Description	Forced Expiratory Volume in 1 second (FEV1) was measured with spirometry conducted according to internationally accepted standards. Measurements were taken at 5 min- 4hr post-dose of day 1 and week 6. The standardized FEV1 Area under the curve (AUC) was calculated as the sum of trapezoids divided by the length of time.
Time Frame	5min-4hr at day 1 and week 6 post-dose
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.

The analysis set includes all randomized patients who received at least one dose of study drug and for whom data are available. Data was analyzed according to the treatment they were randomized. In this cross-over design the number of patients on each treatment does not add up to the total number of patients.

Reporting Groups

	Description
QVA149 + Placebo to Tiotropium	Participants received QVA149 plus placebo to tiotropium during 1 of 3 treatment periods, once a day for 6 weeks. Participants were provided with a salbutamol/albuterol inhaler to use as rescue medication.
Tiotropium + Placebo to QVA149	Participants received tiotropium 18 µg plus placebo to QVA149 during 1 of 3 treatment periods once a day for 6 weeks. Participants were provided with a salbutamol/albuterol inhaler to use as rescue medication.
Placebo	Participants received placebo to QVA149 plus placebo to tiotropium during 1 of 3 treatment periods once a day for 6 weeks. Participants were provided with a salbutamol/albuterol inhaler to use as rescue medication.

Measured Values

	QVA149 + Placebo to Tiotropium	Tiotropium + Placebo to QVA149	Placebo
Number of Participants Analyzed [units: participants]	**223**	**220**	**218**
Standardized Forced Expiratory Volume in 1 Second (FEV1) Area Under the Curve (AUC) 5min-4h After First Dose and 6 Weeks of Treatment With QVA149 Compared to Placebo and Tiotropium [units: Liters] Least Squares Mean (Standard Error)			
Day 1 (n=220,219,2117)	**1.564 (0.0082)**	**1.496 (0.0082)**	**1.352 (0.0082)**
Week 6 (n=205,209,206)	**1.636 (0.0122)**	**1.529 (0.0122)**	**1.302 (0.0122)**

No statistical analysis provided for Standardized Forced Expiratory Volume in 1 Second (FEV1) Area Under the Curve (AUC) 5min-4h After First Dose and 6 Weeks of Treatment With QVA149 Compared to Placebo and Tiotropium

4. Secondary: Standardized Forced Vital Capacity (FVC) Area Under the Curve (AUC) 5min-4 Hrs After First Dose and 6 Weeks of Treatment With QVA149 Compared to Placebo and Tiotropium [Time Frame: 5min-4hr at day 1 and week 6 post-dose]

Measure Type	Secondary
Measure Title	Standardized Forced Vital Capacity (FVC) Area Under the Curve (AUC) 5min-4 Hrs After First Dose and 6 Weeks of Treatment With QVA149 Compared to Placebo and Tiotropium
Measure Description	Forced Vital Capacity (FVC) is the total amount of air that can be exhaled by the patient after a full inhalation. The FVC was measured via spirometry conducted according to internationally accepted standards at 5 min-4 hr post dose of day 1 and week 6.
Time Frame	5min-4hr at day 1 and week 6 post-dose
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The analysis set includes all randomized patients who received at least one dose of study drug and for whom data are available. Data was analyzed according to the treatment they were randomized. In this cross-over design the number of patients on each treatment does not add up to the total number of patients.

Reporting Groups

	Description
QVA149 + Placebo to Tiotropium	Participants received QVA149 plus placebo to tiotropium during 1 of 3 treatment periods, once a day for 6 weeks. Participants were provided with a salbutamol/albuterol inhaler to use as rescue medication.
Tiotropium + Placebo to QVA149	Participants received tiotropium 18 µg plus placebo to QVA149 during 1 of 3 treatment periods once a day for 6 weeks. Participants were provided with a salbutamol/albuterol inhaler to use as rescue medication.
Placebo	Participants received placebo to QVA149 plus placebo to tiotropium during 1 of 3 treatment periods once a day for 6 weeks. Participants were provided with a salbutamol/albuterol inhaler to use as rescue medication.

Measured Values

	QVA149 + Placebo to Tiotropium	Tiotropium + Placebo to QVA149	Placebo
Number of Participants Analyzed [units: participants]	**223**	**220**	**218**
Standardized Forced Vital Capacity (FVC) Area Under the Curve (AUC) 5min-4 Hrs After First Dose and 6 Weeks of Treatment With QVA149 Compared to Placebo and Tiotropium [units: Liters] Least Squares Mean (Standard Error)			
Day 1 (n=210,219,217)	**3.340 (0.0190)**	**3.249 (0.0191)**	**3.020 (0.0191)**
Week 6 (n= 205,209,206)	**3.393 (0.0254)**	**3.269 (0.0253)**	**2.957 (0.0253)**

No statistical analysis provided for Standardized Forced Vital Capacity (FVC) Area Under the Curve (AUC) 5min-4 Hrs After First Dose and 6 Weeks of Treatment With QVA149 Compared to Placebo and Tiotropium

5. Secondary: Change From Baseline in The Capacity of Daily Living During the Morning (CDLM) Score Averaged Over 6 Weeks of Treatment [Time Frame: Baseline and 6 weeks]

Measure Type	Secondary
Measure Title	Change From Baseline in The Capacity of Daily Living During the Morning (CDLM) Score Averaged Over 6 Weeks of Treatment
Measure Description	The Capacity of Daily Living during the Morning (CDLM) is a self-administered daily assessment. The CDLM asks COPD patients to (i) report their ability to carry out 6 morning activities and (ii) rate the difficulty in performing those activities on a five point Likert-type scale ranging from “not at all difficult” to “extremely difficult”. For each of the six morning activities a score ranging from 0 (=so difficult that they could not carry out the activity by themselves) to 5 (not at all difficult to carry out the activity by themselves) is calculated by using the responses from the two questions for each activity. Daily CDLM is calculated using the scores average from the 6 morning activities. CDLM is calculated as the average daily CDLM score over 6 weeks of treatment. The change from baseline in CDLM score over 6 weeks is analyzed using a MIXED model with baseline CDLM score as a covariate. A CDLM score of 0.20 is considered to be a minimal clinically important difference.
Time Frame	Baseline and 6 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The analysis set includes all randomized patients who received at least one dose of study drug and for whom data are available. Data was

analyzed according to the treatment they were randomized. In this cross-over design the number of patients on each treatment does not add up to the total number of patients.

Reporting Groups

	Description
QVA149 + Placebo to Tiotropium	Participants received QVA149 plus placebo to tiotropium during 1 of 3 treatment periods, once a day for 6 weeks. Participants were provided with a salbutamol/albuterol inhaler to use as rescue medication.
Tiotropium + Placebo to QVA149	Participants received tiotropium 18 µg plus placebo to QVA149 during 1 of 3 treatment periods once a day for 6 weeks. Participants were provided with a salbutamol/albuterol inhaler to use as rescue medication.
Placebo	Participants received placebo to QVA149 plus placebo to tiotropium during 1 of 3 treatment periods once a day for 6 weeks. Participants were provided with a salbutamol/albuterol inhaler to use as rescue medication.

Measured Values

	QVA149 + Placebo to Tiotropium	Tiotropium + Placebo to QVA149	Placebo
Number of Participants Analyzed [units: participants]	**167**	**173**	**164**
Change From Baseline in The Capacity of Daily Living During the Morning (CDLM) Score Averaged Over 6 Weeks of Treatment [units: Units on a scale] Least Squares Mean (Standard Error)	**0.09 (0.020)**	**0.08 (0.020)**	**-0.01 (0.020)**

No statistical analysis provided for Change From Baseline in The Capacity of Daily Living During the Morning (CDLM) Score Averaged Over 6 Weeks of Treatment

6. Secondary: Change From Baseline in the Mean Daily Number of Puffs of Rescue Medication Used Over the 6 Weeks of Treatment [Time Frame: Baseline and 6 weeks]

Measure Type	Secondary
Measure Title	Change From Baseline in the Mean Daily Number of Puffs of Rescue Medication Used Over the 6 Weeks of Treatment
Measure Description	The number of puffs of rescue medication taken by participants, were collected each day during the study via entries in e-diaries
Time Frame	Baseline and 6 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The analysis set includes all randomized patients who received at least one dose of study drug and for whom data are available. Data was analyzed according to the treatment they were randomized. In this cross-over design the number of patients on each treatment does not add up to the total number of patients.

Reporting Groups

	Description
QVA149 + Placebo to Tiotropium	Participants received QVA149 plus placebo to tiotropium during 1 of 3 treatment periods, once a day for 6 weeks. Participants were provided with a salbutamol/albuterol inhaler to use as rescue medication.
Tiotropium + Placebo to QVA149	Participants received tiotropium 18 µg plus placebo to QVA149 during 1 of 3 treatment periods once a day for 6 weeks. Participants were provided with a salbutamol/albuterol inhaler to use as rescue medication.
Placebo	Participants received placebo to QVA149 plus placebo to tiotropium during 1 of 3 treatment periods once a

	day for 6 weeks. Participants were provided with a salbutamol/albuterol inhaler to use as rescue medication.

Measured Values

	QVA149 + Placebo to Tiotropium	Tiotropium + Placebo to QVA149	Placebo
Number of Participants Analyzed [units: participants]	**212**	**215**	**206**
Change From Baseline in the Mean Daily Number of Puffs of Rescue Medication Used Over the 6 Weeks of Treatment [units: puffs] Least Squares Mean (Standard Deviation)	**-1.02 (0.202)**	**-0.57 (0.202)**	**0.41 (0.203)**

No statistical analysis provided for Change From Baseline in the Mean Daily Number of Puffs of Rescue Medication Used Over the 6 Weeks of Treatment

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	No text entered.
Additional Description	No text entered.

Reporting Groups

	Description
QVA149 + Placebo to Tiotropium	Participants received QVA149 plus placebo to tiotropium during 1 of 3 treatment periods, once a day for 6 weeks. Participants were provided with a salbutamol/albuterol inhaler to use as rescue medication.
Tiotropium + Placebo to QVA149	Participants received tiotropium 18 µg plus placebo to QVA149 during 1 of 3 treatment periods once a day for 6 weeks. Participants were provided with a salbutamol/albuterol inhaler to use as rescue medication.
Placebo	Participants received placebo to QVA149 plus placebo to tiotropium during 1 of 3 treatment periods once a day for 6 weeks. Participants were provided with a salbutamol/albuterol inhaler to use as rescue medication.

Serious Adverse Events

	QVA149 + Placebo to Tiotropium	Tiotropium + Placebo to QVA149	Placebo
Total, serious adverse events			
# participants affected / at risk	**6/223 (2.69%)**	**6/220 (2.73%)**	**5/218 (2.29%)**
Cardiac disorders			
Atrial fibrillation † 1			
# participants affected / at risk	**0/223 (0.00%)**	**1/220 (0.45%)**	**0/218 (0.00%)**
Cardiac arrest † 1			
# participants affected / at risk	**1/223 (0.45%)**	**0/220 (0.00%)**	**0/218 (0.00%)**
Left ventricular failure † 1			
# participants affected / at risk	**1/223 (0.45%)**	**0/220 (0.00%)**	**0/218 (0.00%)**

Gastrointestinal disorders			
Abdominal pain upper † 1			
# participants affected / at risk	**0/223 (0.00%)**	**0/220 (0.00%)**	**1/218 (0.46%)**
General disorders			
Influenza like illness † 1			
# participants affected / at risk	**1/223 (0.45%)**	**0/220 (0.00%)**	**0/218 (0.00%)**
Infections and infestations			
Bronchopneumonia † 1			
# participants affected / at risk	**0/223 (0.00%)**	**0/220 (0.00%)**	**1/218 (0.46%)**
Lower respiratory tract infection † 1			
# participants affected / at risk	**0/223 (0.00%)**	**1/220 (0.45%)**	**0/218 (0.00%)**
Pleural infection bacterial † 1			
# participants affected / at risk	**1/223 (0.45%)**	**0/220 (0.00%)**	**0/218 (0.00%)**
Pneumonia † 1			
# participants affected / at risk	**0/223 (0.00%)**	**1/220 (0.45%)**	**1/218 (0.46%)**
Musculoskeletal and connective tissue disorders			
Synovial cyst † 1			
# participants affected / at risk	**1/223 (0.45%)**	**0/220 (0.00%)**	**0/218 (0.00%)**
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Gastric cancer † 1			
# participants affected / at risk	**0/223 (0.00%)**	**1/220 (0.45%)**	**0/218 (0.00%)**
Metastases to bone † 1			
# participants affected / at risk	**0/223 (0.00%)**	**1/220 (0.45%)**	**0/218 (0.00%)**
Salivary gland neoplasm † 1			
# participants affected / at risk	**1/223 (0.45%)**	**0/220 (0.00%)**	**0/218 (0.00%)**
Nervous system disorders			
Cerebral artery occlusion † 1			
# participants affected / at risk	**0/223 (0.00%)**	**0/220 (0.00%)**	**1/218 (0.46%)**
Ischaemic stroke † 1			
# participants affected / at risk	**0/223 (0.00%)**	**0/220 (0.00%)**	**1/218 (0.46%)**
Psychiatric disorders			
Alcohol abuse † 1			
# participants affected / at risk	**0/223 (0.00%)**	**0/220 (0.00%)**	**1/218 (0.46%)**
Depression † 1			
			0/218 (0.00%)

# participants affected / at risk	0/223 (0.00%)	1/220 (0.45%)	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease † 1			
# participants affected / at risk	3/223 (1.35%)	2/220 (0.91%)	1/218 (0.46%)

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA

Other Adverse Events

Hide Other Adverse Events

Time Frame	No text entered.
Additional Description	No text entered.

Frequency Threshold

Threshold above which other adverse events are reported	0.5

Reporting Groups

	Description
QVA149 + Placebo to Tiotropium	Participants received QVA149 plus placebo to tiotropium during 1 of 3 treatment periods, once a day for 6 weeks. Participants were provided with a salbutamol/albuterol inhaler to use as rescue medication.
Tiotropium + Placebo to QVA149	Participants received tiotropium 18 µg plus placebo to QVA149 during 1 of 3 treatment periods once a day for 6 weeks. Participants were provided with a salbutamol/albuterol inhaler to use as rescue medication.
Placebo	Participants received placebo to QVA149 plus placebo to tiotropium during 1 of 3 treatment periods once a day for 6 weeks. Participants were provided with a salbutamol/albuterol inhaler to use as rescue medication.

Other Adverse Events

	QVA149 + Placebo to Tiotropium	Tiotropium + Placebo to QVA149	Placebo
Total, other (not including serious) adverse events			
# participants affected / at risk	51/223 (22.87%)	58/220 (26.36%)	70/218 (32.11%)
Blood and lymphatic system disorders			
Anaemia † 1			
# participants affected / at risk	0/223 (0.00%)	2/220 (0.91%)	0/218 (0.00%)
Gastrointestinal disorders			
Constipation † 1			
# participants affected / at risk	2/223 (0.90%)	0/220 (0.00%)	0/218 (0.00%)
Diarrhoea † 1			
# participants affected / at risk	2/223 (0.90%)	1/220 (0.45%)	1/218 (0.46%)
Dry mouth † 1			
# participants affected / at risk	1/223 (0.45%)	2/220 (0.91%)	0/218 (0.00%)
Vomiting † 1			
# participants affected / at risk	2/223 (0.90%)	1/220 (0.45%)	0/218 (0.00%)

General disorders			
Fatigue † 1			
# participants affected / at risk	**0/223 (0.00%)**	**4/220 (1.82%)**	**3/218 (1.38%)**
Influenza like illness † 1			
# participants affected / at risk	**2/223 (0.90%)**	**0/220 (0.00%)**	**1/218 (0.46%)**
Infections and infestations			
Bronchitis † 1			
# participants affected / at risk	**0/223 (0.00%)**	**0/220 (0.00%)**	**2/218 (0.92%)**
Gastroenteritis † 1			
# participants affected / at risk	**0/223 (0.00%)**	**0/220 (0.00%)**	**2/218 (0.92%)**
Influenza † 1			
# participants affected / at risk	**0/223 (0.00%)**	**1/220 (0.45%)**	**4/218 (1.83%)**
Lower respiratory tract infection † 1			
# participants affected / at risk	**2/223 (0.90%)**	**1/220 (0.45%)**	**1/218 (0.46%)**
Nasopharyngitis † 1			
# participants affected / at risk	**14/223 (6.28%)**	**8/220 (3.64%)**	**13/218 (5.96%)**
Respiratory tract infection † 1			
# participants affected / at risk	**0/223 (0.00%)**	**0/220 (0.00%)**	**2/218 (0.92%)**
Sinusitis † 1			
# participants affected / at risk	**1/223 (0.45%)**	**0/220 (0.00%)**	**2/218 (0.92%)**
Upper respiratory tract infection † 1			
# participants affected / at risk	**1/223 (0.45%)**	**2/220 (0.91%)**	**4/218 (1.83%)**
Upper respiratory tract infection bacterial † 1			
# participants affected / at risk	**2/223 (0.90%)**	**0/220 (0.00%)**	**1/218 (0.46%)**
Urinary tract infection † 1			
# participants affected / at risk	**2/223 (0.90%)**	**2/220 (0.91%)**	**2/218 (0.92%)**
Metabolism and nutrition disorders			
Hypercholesterolaemia † 1			
# participants affected / at risk	**0/223 (0.00%)**	**4/220 (1.82%)**	**0/218 (0.00%)**
Hyperlipidaemia † 1			
# participants affected / at risk	**0/223 (0.00%)**	**2/220 (0.91%)**	**1/218 (0.46%)**
Musculoskeletal and connective tissue disorders			
Arthralgia † 1			
# participants affected / at risk	**2/223 (0.90%)**	**0/220 (0.00%)**	**1/218 (0.46%)**
Back pain † 1			
# participants affected / at risk	**1/223 (0.45%)**	**2/220 (0.91%)**	**1/218 (0.46%)**
Nervous system disorders			
Headache † 1			
# participants affected / at risk	**2/223 (0.90%)**	**6/220 (2.73%)**	**3/218 (1.38%)**
Sciatica † 1			
# participants affected / at risk	**0/223 (0.00%)**	**0/220 (0.00%)**	**2/218 (0.92%)**
Somnolence † 1			
# participants affected / at risk	**0/223 (0.00%)**	**0/220 (0.00%)**	**2/218 (0.92%)**

Psychiatric disorders			
Insomnia † 1			
# participants affected / at risk	**0/223 (0.00%)**	**1/220 (0.45%)**	**2/218 (0.92%)**
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease † 1			
# participants affected / at risk	**15/223 (6.73%)**	**19/220 (8.64%)**	**19/218 (8.72%)**
Cough † 1			
# participants affected / at risk	**7/223 (3.14%)**	**8/220 (3.64%)**	**5/218 (2.29%)**
Dyspnoea † 1			
# participants affected / at risk	**0/223 (0.00%)**	**6/220 (2.73%)**	**9/218 (4.13%)**
Oropharyngeal pain † 1			
# participants affected / at risk	**2/223 (0.90%)**	**1/220 (0.45%)**	**2/218 (0.92%)**
Rhinorrhoea † 1			
# participants affected / at risk	**0/223 (0.00%)**	**0/220 (0.00%)**	**2/218 (0.92%)**
Sputum increased † 1			
# participants affected / at risk	**0/223 (0.00%)**	**2/220 (0.91%)**	**0/218 (0.00%)**
Throat irritation † 1			
# participants affected / at risk	**3/223 (1.35%)**	**1/220 (0.45%)**	**2/218 (0.92%)**
Vascular disorders			
Hypertension † 1			
# participants affected / at risk	**3/223 (1.35%)**	**3/220 (1.36%)**	**4/218 (1.83%)**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA

Limitations and Caveats

Hide Limitations and Caveats

Limitations of the study, such as early termination leading to small numbers of participants analyzed and technical problems with measurement leading to unreliable or uninterpretable data
No text entered.

More Information

Hide More Information

Certain Agreements:

Principal Investigators are **NOT** employed by the organization sponsoring the study.
There **IS** an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.
The agreement is: ☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **less than or equal to 60 days**. The sponsor cannot require changes to the communication and cannot extend the embargo. ☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **more than 60 days but less than or equal to 180 days**. The sponsor cannot require changes to the communication and cannot extend the embargo. Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed.

Restriction Description: The terms and conditions of Novartis' agreements with its investigators may vary. However, Novartis does not prohibit any investigator from publishing. Any publications from a single-site are postponed until the publication of the pooled data (i.e., data from all sites) in the clinical trial.

Results Point of Contact:

Name/Title: Study director
Organization: Novartis
phone: 41 61 324 1111

Publications automatically indexed to this study by ClinicalTrials.gov Identifier (NCT Number):

Mahler DA, Decramer M, D'Urzo A, Worth H, White T, Alagappan VK, Chen H, Gallagher N, Kulich K, Banerji D. Dual bronchodilation with QVA149 reduces patient-reported dyspnoea in COPD: the BLAZE study. Eur Respir J. 2014 Jun;43(6):1599-609. doi: 10.1183/09031936.00124013. Epub 2013 Oct 31.

Responsible Party:	Novartis (Novartis Pharmaceuticals)
ClinicalTrials.gov Identifier:	NCT01490125 History of Changes
Other Study ID Numbers:	**CQVA149A2322** 2011-000229-63 (EudraCT Number)
Study First Received:	November 15, 2011
Results First Received:	August 9, 2013
Last Updated:	November 5, 2013
Health Authority:	Belgium: Federal Agency for Medicinal Products and Health Products Canada: Ethics Review Committee Canada: Health Canada Germany: Ethics Commission Germany: Federal Institute for Drugs and Medical Devices Spain: Ministry of Health and Consumption Spain: Comité Ético de Investigación Clínica Spain: Ethics Committee United Kingdom: Medicines and Healthcare Products Regulatory Agency United Kingdom: Research Ethics Committee