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Trial record **1 of 1** for: CQAB149B2334

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Efficacy, Safety, and Tolerability of Once Daily Indacaterol in Chronic Obstructive Pulmonary Disease (COPD) Using Formoterol Twice Daily as Active Control

This study has been completed.

Sponsor:
Novartis

Information provided by:
Novartis

ClinicalTrials.gov Identifier:
NCT00393458

First received: October 25, 2006
Last updated: July 22, 2011
Last verified: July 2011
History of Changes

Full Text View | **Tabular View** | **Study Results** | Disclaimer | How to Read a Study Record

Results First Received: July 22, 2011

Study Type:	Interventional
Study Design:	Allocation: Randomized; Intervention Model: Parallel Assignment; Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor); Primary Purpose: Treatment
Condition:	Chronic Obstructive Pulmonary Disease
Interventions:	Drug: Indacaterol Drug: Formoterol Drug: Placebo to indacaterol

	Drug: Placebo to formoterol

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
No text entered.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
No text entered.

Reporting Groups

	Description
Indacaterol 300 µg Plus Placebo to Formoterol	Patients inhaled indacaterol 300 µg once daily via a single-dose dry-powder inhaler (SDDPI), placebo to indacaterol once daily via a SDDPI, and placebo to formoterol twice daily via the manufacturer's proprietary inhalation device (Aerolizer®). Indacaterol, placebo to indacaterol, and placebo to formoterol were taken in the morning between 8:00 and 10:00 AM; placebo to formoterol was taken again 12 hours later in the evening between 8:00 and 10:00 PM. Daily inhaled corticosteroid treatment (if applicable) was to remain stable throughout the study. The short-acting β2-agonist salbutamol/albuterol was available for rescue use throughout the study.
Indacaterol 600 µg Plus Placebo to Formoterol	Patients inhaled indacaterol 600 µg (two 300 µg capsules) once daily via single-dose dry-powder inhalers (SDDPI) plus placebo to formoterol twice daily via the manufacturer's proprietary inhalation device (Aerolizer®). Indacaterol and placebo to formoterol were taken in the morning between 8:00 and 10:00 AM; placebo to formoterol was taken again 12 hours later in the evening between 8:00 and 10:00 PM. Daily inhaled corticosteroid treatment (if applicable) was to remain stable throughout the study. The short-acting β2-agonist salbutamol/albuterol was available for rescue use throughout the study.

Formoterol 12 µg Plus Placebo to Indacaterol	Patients inhaled formoterol 12 µg twice daily via the manufacturer's proprietary inhalation device (Aerolizer®) plus placebo to indacaterol once daily via a single-dose dry-powder inhaler (SDDPI). Formoterol and placebo to indacaterol were taken in the morning between 8:00 and 10:00 AM; formoterol was taken again 12 hours later in the evening between 8:00 and 10:00 PM. Daily inhaled corticosteroid treatment (if applicable) was to remain stable throughout the study. The short-acting β2-agonist salbutamol/albuterol was available for rescue use throughout the study.
Placebo to Indacaterol Plus Placebo to Formoterol	Patients inhaled placebo to indacaterol once daily via a single-dose dry-powder inhaler (SDDPI) plus placebo to formoterol twice daily via the manufacturer's proprietary inhalation device (Aerolizer®). Placebo to indacaterol and placebo to formoterol were taken in the morning between 8:00 and 10:00 AM; placebo to formoterol was taken again 12 hours later in the evening between 8:00 and 10:00 PM. Daily inhaled corticosteroid treatment (if applicable) was to remain stable throughout the study. The short-acting β2-agonist salbutamol/albuterol was available for rescue use throughout the study.

Participant Flow: Overall Study

	Indacaterol 300 µg Plus Placebo to Formoterol	Indacaterol 600 µg Plus Placebo to Formoterol	Formoterol 12 µg Plus Placebo to Indacaterol	Placebo to Indacaterol Plus Placebo to Formoterol
STARTED	437	428	435	432
Exposed to Study Medication or Placebo	437	425	434	432
COMPLETED	338	326	323	295
NOT COMPLETED	99	102	112	137
Adverse Event	35	24	40	35
Subject withdrew consent	27	40	33	50
Unsatisfactory therapeutic effect	12	9	12	30
Protocol deviation	11	11	11	10

Administrative problems	**7**	**8**	**5**	**2**
Lost to Follow-up	**5**	**6**	**5**	**3**
Abnormal laboratory value(s)	**1**	**1**	**0**	**0**
Death	**1**	**1**	**5**	**5**
Abnormal test procedure result(s)	**0**	**1**	**1**	**2**
Subject no longer requires study drug	**0**	**1**	**0**	**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.
No text entered.

Reporting Groups

	Description
Indacaterol 300 µg Plus Placebo to Formoterol	Patients inhaled indacaterol 300 µg once daily via a single-dose dry-powder inhaler (SDDPI), placebo to indacaterol once daily via a SDDPI, and placebo to formoterol twice daily via the manufacturer's proprietary inhalation device (Aerolizer®). Indacaterol, placebo to indacaterol, and placebo to formoterol were taken in the morning between 8:00 and 10:00 AM; placebo to formoterol was taken again 12 hours later in the evening

	between 8:00 and 10:00 PM. Daily inhaled corticosteroid treatment (if applicable) was to remain stable throughout the study. The short-acting β2-agonist salbutamol/albuterol was available for rescue use throughout the study.
Indacaterol 600 µg Plus Placebo to Formoterol	Patients inhaled indacaterol 600 µg (two 300 µg capsules) once daily via single-dose dry-powder inhalers (SDDPI) plus placebo to formoterol twice daily via the manufacturer's proprietary inhalation device (Aerolizer®). Indacaterol and placebo to formoterol were taken in the morning between 8:00 and 10:00 AM; placebo to formoterol was taken again 12 hours later in the evening between 8:00 and 10:00 PM. Daily inhaled corticosteroid treatment (if applicable) was to remain stable throughout the study. The short-acting β2-agonist salbutamol/albuterol was available for rescue use throughout the study.
Formoterol 12 µg Plus Placebo to Indacaterol	Patients inhaled formoterol 12 µg twice daily via the manufacturer's proprietary inhalation device (Aerolizer®) plus placebo to indacaterol once daily via a single-dose dry-powder inhaler (SDDPI). Formoterol and placebo to indacaterol were taken in the morning between 8:00 and 10:00 AM; formoterol was taken again 12 hours later in the evening between 8:00 and 10:00 PM. Daily inhaled corticosteroid treatment (if applicable) was to remain stable throughout the study. The short-acting β2-agonist salbutamol/albuterol was available for rescue use throughout the study.
Placebo to Indacaterol Plus Placebo to Formoterol	Patients inhaled placebo to indacaterol once daily via a single-dose dry-powder inhaler (SDDPI) plus placebo to formoterol twice daily via the manufacturer's proprietary inhalation device (Aerolizer®). Placebo to indacaterol and placebo to formoterol were taken in the morning between 8:00 and 10:00 AM; placebo to formoterol was taken again 12 hours later in the evening between 8:00 and 10:00 PM. Daily inhaled corticosteroid treatment (if applicable) was to remain stable throughout the study. The short-acting β2-agonist salbutamol/albuterol was available for rescue use throughout the study.
Total	Total of all reporting groups

Baseline Measures

	Indacaterol 300 µg Plus Placebo to Formoterol	Indacaterol 600 µg Plus Placebo to Formoterol	Formoterol 12 µg Plus Placebo to Indacaterol	Placebo to Indacaterol Plus Placebo to Formoterol	Total
Number of					**1728**

Participants [units: participants]	**437**	**425**	**434**	**432**	
Age [1] [units: years] Mean (Standard Deviation)	**63.9 (8.57)**	**62.9 (8.74)**	**63.6 (8.49)**	**63.2 (8.28)**	**63.4 (8.52)**
Gender [units: participants]					
Female	**86**	**98**	**86**	**80**	**350**
Male	**351**	**327**	**348**	**352**	**1378**

[1] Demographic data are based on all subjects in the safety population, which includes all patients who received at least 1 dose of study drug. Three patients in the indacaterol 600 µg plus placebo to formoterol and one patient in the formoterol 12 µg plus placebo to indacaterol group were not exposed to any study treatment.

Outcome Measures

Hide All Outcome Measures

1. Primary: Trough Forced Expiratory Volume in 1 Second (FEV1) at Week 12 + 1 Day, Day 85 [Time Frame: Week 12 + 1 day, Day 85]

Measure Type	Primary
Measure Title	Trough Forced Expiratory Volume in 1 Second (FEV1) at Week 12 + 1 Day, Day 85
Measure Description	FEV1 was measured with spirometry conducted according to internationally accepted standards. Trough FEV1 was defined as the average of measurements made 23 hours 10 minutes and 23 hours 45 minutes post-dose at the end of treatment. The analysis included baseline FEV1, FEV1 pre-dose and 30 minutes post-dose of salbutamol/albuterol during screening, and FEV1 pre-dose and 1 hour post-dose of ipratropium during screening as covariates.
Time Frame	Week 12 + 1 day, Day 85
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.
Modified intent-to-treat (ITT) population: All randomized patients who received at least 1 dose of study drug, excluding patients from a number of centers.

Reporting Groups

	Description
Indacaterol 300 µg Plus Placebo to Formoterol	Patients inhaled indacaterol 300 µg once daily via a single-dose dry-powder inhaler (SDDPI), placebo to indacaterol once daily via a SDDPI, and placebo to formoterol twice daily via the manufacturer's proprietary inhalation device (Aerolizer®). Indacaterol, placebo to indacaterol, and placebo to formoterol were taken in the morning between 8:00 and 10:00 AM; placebo to formoterol was taken again 12 hours later in the evening between 8:00 and 10:00 PM. Daily inhaled corticosteroid treatment (if applicable) was to remain stable throughout the study. The short-acting β2-agonist salbutamol/albuterol was available for rescue use throughout the study.
Indacaterol 600 µg Plus Placebo to Formoterol	Patients inhaled indacaterol 600 µg (two 300 µg capsules) once daily via single-dose dry-powder inhalers (SDDPI) plus placebo to formoterol twice daily via the manufacturer's proprietary inhalation device (Aerolizer®). Indacaterol and placebo to formoterol were taken in the morning between 8:00 and 10:00 AM; placebo to formoterol was taken again 12 hours later in the evening between 8:00 and 10:00 PM. Daily inhaled corticosteroid treatment (if applicable) was to remain stable throughout the study. The short-acting β2-agonist salbutamol/albuterol was available for rescue use throughout the study.
Formoterol 12 µg Plus Placebo to Indacaterol	Patients inhaled formoterol 12 µg twice daily via the manufacturer's proprietary inhalation device (Aerolizer®) plus placebo to indacaterol once daily via a single-dose dry-powder inhaler (SDDPI). Formoterol and placebo to indacaterol were taken in the morning between 8:00 and 10:00 AM; formoterol was taken again 12 hours later in the evening between 8:00 and 10:00 PM. Daily inhaled corticosteroid treatment (if applicable) was to remain stable throughout the study. The short-acting β2-agonist salbutamol/albuterol was available for rescue use throughout the study.
Placebo to Indacaterol Plus Placebo to Formoterol	Patients inhaled placebo to indacaterol once daily via a single-dose dry-powder inhaler

	(SDDPI) plus placebo to formoterol twice daily via the manufacturer's proprietary inhalation device (Aerolizer®). Placebo to indacaterol and placebo to formoterol were taken in the morning between 8:00 and 10:00 AM; placebo to formoterol was taken again 12 hours later in the evening between 8:00 and 10:00 PM. Daily inhaled corticosteroid treatment (if applicable) was to remain stable throughout the study. The short-acting β2-agonist salbutamol/albuterol was available for rescue use throughout the study.

Measured Values

	Indacaterol 300 µg Plus Placebo to Formoterol	Indacaterol 600 µg Plus Placebo to Formoterol	Formoterol 12 µg Plus Placebo to Indacaterol	Placebo to Indacaterol Plus Placebo to Formoterol
Number of Participants Analyzed [units: participants]	**389**	**374**	**379**	**371**
Trough Forced Expiratory Volume in 1 Second (FEV1) at Week 12 + 1 Day, Day 85 [units: Liters] Least Squares Mean (Standard Error)	**1.48 (0.012)**	**1.48 (0.013)**	**1.38 (0.013)**	**1.31 (0.013)**

No statistical analysis provided for Trough Forced Expiratory Volume in 1 Second (FEV1) at Week 12 + 1 Day, Day 85

2. Secondary: Percentage of Days of Poor Control During 52 Weeks of Treatment [Time Frame: Baseline to end of study (Week 52)]

Measure Type	Secondary
Measure Title	Percentage of Days of Poor Control During 52 Weeks of Treatment
Measure Description	Percentage of days of poor control was defined as the number of days in the patient diary with a score ≥ 2 (scale of 0-3, a higher number means more severe symptoms) for at least 2 of 5 symptoms (cough, wheeze, production of sputum, color of sputum, breathlessness) over 52 weeks divided by the number of evaluable days (days with ≥ 2 symptoms with scores). The analysis included baseline percentage of days of poor control, FEV1 pre-dose and 30

	minutes post-dose of salbutamol/albuterol during screening, and FEV1 pre-dose and 1 hour post-dose of ipratropium during screening as covariates.
Time Frame	Baseline to end of study (Week 52)
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.
Modified intent-to-treat (ITT) population: All randomized patients who received at least 1 dose of study drug, excluding patients from a number of centers.

Reporting Groups

	Description
Indacaterol 300 µg Plus Placebo to Formoterol	Patients inhaled indacaterol 300 µg once daily via a single-dose dry-powder inhaler (SDDPI), placebo to indacaterol once daily via a SDDPI, and placebo to formoterol twice daily via the manufacturer's proprietary inhalation device (Aerolizer®). Indacaterol, placebo to indacaterol, and placebo to formoterol were taken in the morning between 8:00 and 10:00 AM; placebo to formoterol was taken again 12 hours later in the evening between 8:00 and 10:00 PM. Daily inhaled corticosteroid treatment (if applicable) was to remain stable throughout the study. The short-acting β2-agonist salbutamol/albuterol was available for rescue use throughout the study.
Indacaterol 600 µg Plus Placebo to Formoterol	Patients inhaled indacaterol 600 µg (two 300 µg capsules) once daily via single-dose dry-powder inhalers (SDDPI) plus placebo to formoterol twice daily via the manufacturer's proprietary inhalation device (Aerolizer®). Indacaterol and placebo to formoterol were taken in the morning between 8:00 and 10:00 AM; placebo to formoterol was taken again 12 hours later in the evening between 8:00 and 10:00 PM. Daily inhaled corticosteroid treatment (if applicable) was to remain stable throughout the study. The short-acting β2-agonist salbutamol/albuterol was available for rescue use throughout the study.
Formoterol 12 µg Plus Placebo to Indacaterol	Patients inhaled formoterol 12 µg twice daily via the manufacturer's proprietary inhalation device (Aerolizer®) plus placebo to indacaterol once daily via a single-dose dry-powder inhaler (SDDPI). Formoterol and placebo to indacaterol were taken in the morning

	between 8:00 and 10:00 AM; formoterol was taken again 12 hours later in the evening between 8:00 and 10:00 PM. Daily inhaled corticosteroid treatment (if applicable) was to remain stable throughout the study. The short-acting β2-agonist salbutamol/albuterol was available for rescue use throughout the study.
Placebo to Indacaterol Plus Placebo to Formoterol	Patients inhaled placebo to indacaterol once daily via a single-dose dry-powder inhaler (SDDPI) plus placebo to formoterol twice daily via the manufacturer's proprietary inhalation device (Aerolizer®). Placebo to indacaterol and placebo to formoterol were taken in the morning between 8:00 and 10:00 AM; placebo to formoterol was taken again 12 hours later in the evening between 8:00 and 10:00 PM. Daily inhaled corticosteroid treatment (if applicable) was to remain stable throughout the study. The short-acting β2-agonist salbutamol/albuterol was available for rescue use throughout the study.

Measured Values

	Indacaterol 300 µg Plus Placebo to Formoterol	Indacaterol 600 µg Plus Placebo to Formoterol	Formoterol 12 µg Plus Placebo to Indacaterol	Placebo to Indacaterol Plus Placebo to Formoterol
Number of Participants Analyzed [units: participants]	**386**	**370**	**377**	**366**
Percentage of Days of Poor Control During 52 Weeks of Treatment [units: Percentage of days] Least Squares Mean (Standard Error)	**33.6 (1.43)**	**30.0 (1.46)**	**33.5 (1.45)**	**38.3 (1.47)**

No statistical analysis provided for Percentage of Days of Poor Control During 52 Weeks of Treatment

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	Safety population: All patients who received at least 1 dose of study drug.
Additional Description	Baseline to the end of the study (Week 52)

Reporting Groups

	Description
Indacaterol 300 µg Plus Placebo to Formoterol	Patients inhaled indacaterol 300 µg once daily via a single-dose dry-powder inhaler (SDDPI), placebo to indacaterol once daily via a SDDPI, and placebo to formoterol twice daily via the manufacturer's proprietary inhalation device (Aerolizer®). Indacaterol, placebo to indacaterol, and placebo to formoterol were taken in the morning between 8:00 and 10:00 AM; placebo to formoterol was taken again 12 hours later in the evening between 8:00 and 10:00 PM. Daily inhaled corticosteroid treatment (if applicable) was to remain stable throughout the study. The short-acting β2-agonist salbutamol/albuterol was available for rescue use throughout the study.
Indacaterol 600 µg Plus Placebo to Formoterol	Patients inhaled indacaterol 600 µg (two 300 µg capsules) once daily via single-dose dry-powder inhalers (SDDPI) plus placebo to formoterol twice daily via the manufacturer's proprietary inhalation device (Aerolizer®). Indacaterol and placebo to formoterol were taken in the morning between 8:00 and 10:00 AM; placebo to formoterol was taken again 12 hours later in the evening between 8:00 and 10:00 PM. Daily inhaled corticosteroid treatment (if applicable) was to remain stable throughout the study. The short-acting β2-agonist salbutamol/albuterol was available for rescue use throughout the study.
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Placebo to Indacaterol Plus Placebo to Formoterol	Patients inhaled placebo to indacaterol once daily via a single-dose dry-powder inhaler (SDDPI) plus placebo to formoterol twice daily via the manufacturer's proprietary inhalation device (Aerolizer®). Placebo to indacaterol and placebo to formoterol were taken in the morning between 8:00 and 10:00 AM; placebo to formoterol was taken

	again 12 hours later in the evening between 8:00 and 10:00 PM. Daily inhaled corticosteroid treatment (if applicable) was to remain stable throughout the study. The short-acting β2-agonist salbutamol/albuterol was available for rescue use throughout the study.

Serious Adverse Events

	Indacaterol 300 µg Plus Placebo to Formoterol	Indacaterol 600 µg Plus Placebo to Formoterol	Formoterol 12 µg Plus Placebo to Indacaterol	Placebo to Indacaterol Plus Placebo to Formoterol
Total, serious adverse events				
# participants affected / at risk	**63/437 (14.42%)**	**51/425 (12.00%)**	**69/434 (15.90%)**	**48/432 (11.11%)**
Blood and lymphatic system disorders				
Anaemia † [1]				
# participants affected / at risk	**0/437 (0.00%)**	**1/425 (0.24%)**	**0/434 (0.00%)**	**0/432 (0.00%)**
Cardiac disorders				
Acute myocardial infarction † [1]				
# participants affected / at risk	**1/437 (0.23%)**	**0/425 (0.00%)**	**0/434 (0.00%)**	**0/432 (0.00%)**
Angina pectoris † [1]				
# participants affected / at risk	**1/437 (0.23%)**	**1/425 (0.24%)**	**0/434 (0.00%)**	**1/432 (0.23%)**
Angina unstable † [1]				
# participants affected / at risk	**0/437 (0.00%)**	**1/425 (0.24%)**	**0/434 (0.00%)**	**0/432 (0.00%)**
Atrial fibrillation † [1]				
# participants affected / at risk	**3/437 (0.69%)**	**0/425 (0.00%)**	**1/434 (0.23%)**	**1/432 (0.23%)**

Atrial flutter † 1				
# participants affected / at risk	**0/437 (0.00%)**	**1/425 (0.24%)**	**0/434 (0.00%)**	**1/432 (0.23%)**
Atrial tachycardia † 1				
# participants affected / at risk	**0/437 (0.00%)**	**1/425 (0.24%)**	**0/434 (0.00%)**	**0/432 (0.00%)**
Atrioventricular block † 1				
# participants affected / at risk	**0/437 (0.00%)**	**0/425 (0.00%)**	**1/434 (0.23%)**	**0/432 (0.00%)**
Cardiac arrest † 1				
# participants affected / at risk	**0/437 (0.00%)**	**0/425 (0.00%)**	**0/434 (0.00%)**	**2/432 (0.46%)**
Cardiac failure † 1				
# participants affected / at risk	**1/437 (0.23%)**	**1/425 (0.24%)**	**1/434 (0.23%)**	**0/432 (0.00%)**
Cardiac failure congestive † 1				
# participants affected / at risk	**2/437 (0.46%)**	**0/425 (0.00%)**	**0/434 (0.00%)**	**1/432 (0.23%)**
Cardiomyopathy † 1				
# participants affected / at risk	**0/437 (0.00%)**	**1/425 (0.24%)**	**0/434 (0.00%)**	**0/432 (0.00%)**
Coronary artery disease † 1				
# participants affected / at risk	**0/437 (0.00%)**	**3/425 (0.71%)**	**0/434 (0.00%)**	**0/432 (0.00%)**
Ischaemic cardiomyopathy † 1				
# participants affected / at risk	**1/437 (0.23%)**	**0/425 (0.00%)**	**0/434 (0.00%)**	**0/432 (0.00%)**
Microvascular angina † 1				
# participants affected / at	**0/437 (0.00%)**	**1/425 (0.24%)**	**0/434 (0.00%)**	**0/432 (0.00%)**

risk				
Myocardial infarction † [1]				
# participants affected / at risk	1/437 (0.23%)	2/425 (0.47%)	1/434 (0.23%)	1/432 (0.23%)
Myocardial ischaemia † [1]				
# participants affected / at risk	2/437 (0.46%)	0/425 (0.00%)	0/434 (0.00%)	0/432 (0.00%)
Palpitations † [1]				
# participants affected / at risk	1/437 (0.23%)	0/425 (0.00%)	0/434 (0.00%)	0/432 (0.00%)
Pericarditis † [1]				
# participants affected / at risk	0/437 (0.00%)	0/425 (0.00%)	1/434 (0.23%)	0/432 (0.00%)
Sinus arrhythmia † [1]				
# participants affected / at risk	1/437 (0.23%)	0/425 (0.00%)	0/434 (0.00%)	0/432 (0.00%)
Sinus bradycardia † [1]				
# participants affected / at risk	0/437 (0.00%)	0/425 (0.00%)	1/434 (0.23%)	0/432 (0.00%)
Stress cardiomyopathy † [1]				
# participants affected / at risk	1/437 (0.23%)	0/425 (0.00%)	0/434 (0.00%)	0/432 (0.00%)
Ear and labyrinth disorders				
Vertigo † [1]				
# participants affected / at risk	0/437 (0.00%)	0/425 (0.00%)	0/434 (0.00%)	1/432 (0.23%)
Eye disorders				
Anterior capsule contraction † [1]				

# participants affected / at risk	0/437 (0.00%)	0/425 (0.00%)	1/434 (0.23%)	0/432 (0.00%)
Cataract † 1				
# participants affected / at risk	2/437 (0.46%)	0/425 (0.00%)	2/434 (0.46%)	1/432 (0.23%)
Macular degeneration † 1				
# participants affected / at risk	0/437 (0.00%)	0/425 (0.00%)	1/434 (0.23%)	0/432 (0.00%)
Retinal artery occlusion † 1				
# participants affected / at risk	0/437 (0.00%)	0/425 (0.00%)	1/434 (0.23%)	0/432 (0.00%)
Gastrointestinal disorders				
Abdominal pain upper † 1				
# participants affected / at risk	0/437 (0.00%)	0/425 (0.00%)	1/434 (0.23%)	0/432 (0.00%)
Appendicitis perforated † 1				
# participants affected / at risk	0/437 (0.00%)	0/425 (0.00%)	1/434 (0.23%)	0/432 (0.00%)
Colonic polyp † 1				
# participants affected / at risk	0/437 (0.00%)	0/425 (0.00%)	0/434 (0.00%)	1/432 (0.23%)
Duodenal ulcer † 1				
# participants affected / at risk	0/437 (0.00%)	1/425 (0.24%)	0/434 (0.00%)	0/432 (0.00%)
Femoral hernia † 1				
# participants affected / at risk	1/437 (0.23%)	1/425 (0.24%)	0/434 (0.00%)	0/432 (0.00%)
Gastric haemorrhage † 1				
# participants affected / at	0/437 (0.00%)	0/425 (0.00%)	0/434 (0.00%)	1/432 (0.23%)

risk				
Gastric ulcer † [1]				
# participants affected / at risk	**0/437 (0.00%)**	**1/425 (0.24%)**	**1/434 (0.23%)**	**0/432 (0.00%)**
Gastric ulcer haemorrhage † [1]				
# participants affected / at risk	**0/437 (0.00%)**	**1/425 (0.24%)**	**0/434 (0.00%)**	**0/432 (0.00%)**
Gastrointestinal haemorrhage † [1]				
# participants affected / at risk	**0/437 (0.00%)**	**1/425 (0.24%)**	**0/434 (0.00%)**	**1/432 (0.23%)**
Gastrointestinal necrosis † [1]				
# participants affected / at risk	**0/437 (0.00%)**	**0/425 (0.00%)**	**1/434 (0.23%)**	**0/432 (0.00%)**
Inguinal hernia † [1]				
# participants affected / at risk	**0/437 (0.00%)**	**1/425 (0.24%)**	**0/434 (0.00%)**	**2/432 (0.46%)**
Mallory-Weiss syndrome † [1]				
# participants affected / at risk	**0/437 (0.00%)**	**1/425 (0.24%)**	**0/434 (0.00%)**	**0/432 (0.00%)**
Pancreatitis † [1]				
# participants affected / at risk	**0/437 (0.00%)**	**0/425 (0.00%)**	**0/434 (0.00%)**	**1/432 (0.23%)**
Pancreatitis acute † [1]				
# participants affected / at risk	**1/437 (0.23%)**	**0/425 (0.00%)**	**0/434 (0.00%)**	**0/432 (0.00%)**
Swollen tongue † [1]				
# participants affected / at risk	**0/437 (0.00%)**	**0/425 (0.00%)**	**0/434 (0.00%)**	**1/432 (0.23%)**

General disorders				
Chest pain † [1]				
# participants affected / at risk	**1/437 (0.23%)**	**0/425 (0.00%)**	**1/434 (0.23%)**	**0/432 (0.00%)**
Hyperthermia † [1]				
# participants affected / at risk	**0/437 (0.00%)**	**0/425 (0.00%)**	**0/434 (0.00%)**	**1/432 (0.23%)**
Non-cardiac chest pain † [1]				
# participants affected / at risk	**0/437 (0.00%)**	**1/425 (0.24%)**	**0/434 (0.00%)**	**0/432 (0.00%)**
Sudden death † [1]				
# participants affected / at risk	**1/437 (0.23%)**	**0/425 (0.00%)**	**0/434 (0.00%)**	**3/432 (0.69%)**
Hepatobiliary disorders				
Cholecystitis acute † [1]				
# participants affected / at risk	**1/437 (0.23%)**	**0/425 (0.00%)**	**0/434 (0.00%)**	**1/432 (0.23%)**
Cholelithiasis † [1]				
# participants affected / at risk	**1/437 (0.23%)**	**0/425 (0.00%)**	**1/434 (0.23%)**	**2/432 (0.46%)**
Hepatitis alcoholic † [1]				
# participants affected / at risk	**1/437 (0.23%)**	**0/425 (0.00%)**	**0/434 (0.00%)**	**0/432 (0.00%)**
Immune system disorders				
Contrast media allergy † [1]				
# participants affected / at risk	**0/437 (0.00%)**	**0/425 (0.00%)**	**1/434 (0.23%)**	**0/432 (0.00%)**
Infections and infestations				

Appendicitis † 1				
# participants affected / at risk	**1/437 (0.23%)**	**0/425 (0.00%)**	**0/434 (0.00%)**	**0/432 (0.00%)**
Bronchitis † 1				
# participants affected / at risk	**0/437 (0.00%)**	**0/425 (0.00%)**	**0/434 (0.00%)**	**1/432 (0.23%)**
Erysipelas † 1				
# participants affected / at risk	**1/437 (0.23%)**	**0/425 (0.00%)**	**0/434 (0.00%)**	**0/432 (0.00%)**
Gastroenteritis † 1				
# participants affected / at risk	**0/437 (0.00%)**	**0/425 (0.00%)**	**0/434 (0.00%)**	**1/432 (0.23%)**
Lower respiratory tract infection † 1				
# participants affected / at risk	**2/437 (0.46%)**	**2/425 (0.47%)**	**5/434 (1.15%)**	**3/432 (0.69%)**
Lower respiratory tract infection bacterial † 1				
# participants affected / at risk	**1/437 (0.23%)**	**0/425 (0.00%)**	**2/434 (0.46%)**	**0/432 (0.00%)**
Nasopharyngitis † 1				
# participants affected / at risk	**0/437 (0.00%)**	**0/425 (0.00%)**	**0/434 (0.00%)**	**1/432 (0.23%)**
Otitis media chronic † 1				
# participants affected / at risk	**0/437 (0.00%)**	**1/425 (0.24%)**	**0/434 (0.00%)**	**0/432 (0.00%)**
Perianal abscess † 1				
# participants affected / at risk	**0/437 (0.00%)**	**1/425 (0.24%)**	**0/434 (0.00%)**	**0/432 (0.00%)**
Pneumonia † 1				

# participants affected / at risk	3/437 (0.69%)	2/425 (0.47%)	5/434 (1.15%)	2/432 (0.46%)
Postoperative wound infection † [1]				
# participants affected / at risk	0/437 (0.00%)	1/425 (0.24%)	0/434 (0.00%)	0/432 (0.00%)
Pulmonary tuberculosis † [1]				
# participants affected / at risk	1/437 (0.23%)	0/425 (0.00%)	0/434 (0.00%)	0/432 (0.00%)
Pyothorax † [1]				
# participants affected / at risk	0/437 (0.00%)	0/425 (0.00%)	1/434 (0.23%)	0/432 (0.00%)
Respiratory tract infection † [1]				
# participants affected / at risk	0/437 (0.00%)	1/425 (0.24%)	2/434 (0.46%)	0/432 (0.00%)
Septic shock † [1]				
# participants affected / at risk	0/437 (0.00%)	0/425 (0.00%)	1/434 (0.23%)	0/432 (0.00%)
Upper respiratory tract infection † [1]				
# participants affected / at risk	0/437 (0.00%)	0/425 (0.00%)	3/434 (0.69%)	0/432 (0.00%)
Upper respiratory tract infection bacterial † [1]				
# participants affected / at risk	4/437 (0.92%)	0/425 (0.00%)	5/434 (1.15%)	4/432 (0.93%)
Viral infection † [1]				
# participants affected / at risk	0/437 (0.00%)	0/425 (0.00%)	1/434 (0.23%)	0/432 (0.00%)

Viral upper respiratory tract infection † [1]				
# participants affected / at risk	**1/437 (0.23%)**	**0/425 (0.00%)**	**1/434 (0.23%)**	**0/432 (0.00%)**
Injury, poisoning and procedural complications				
Cardiac procedure complication † [1]				
# participants affected / at risk	**0/437 (0.00%)**	**0/425 (0.00%)**	**1/434 (0.23%)**	**0/432 (0.00%)**
Clavicle fracture † [1]				
# participants affected / at risk	**0/437 (0.00%)**	**1/425 (0.24%)**	**0/434 (0.00%)**	**0/432 (0.00%)**
Femoral neck fracture † [1]				
# participants affected / at risk	**0/437 (0.00%)**	**0/425 (0.00%)**	**1/434 (0.23%)**	**0/432 (0.00%)**
Foot fracture † [1]				
# participants affected / at risk	**0/437 (0.00%)**	**2/425 (0.47%)**	**0/434 (0.00%)**	**1/432 (0.23%)**
Hip fracture † [1]				
# participants affected / at risk	**0/437 (0.00%)**	**1/425 (0.24%)**	**0/434 (0.00%)**	**0/432 (0.00%)**
Humerus fracture † [1]				
# participants affected / at risk	**0/437 (0.00%)**	**0/425 (0.00%)**	**0/434 (0.00%)**	**1/432 (0.23%)**
Lower limb fracture † [1]				
# participants affected / at risk	**1/437 (0.23%)**	**0/425 (0.00%)**	**0/434 (0.00%)**	**0/432 (0.00%)**
Multiple fractures † [1]				

# participants affected / at risk	0/437 (0.00%)	1/425 (0.24%)	0/434 (0.00%)	0/432 (0.00%)
Pneumothorax traumatic † 1				
# participants affected / at risk	0/437 (0.00%)	0/425 (0.00%)	1/434 (0.23%)	0/432 (0.00%)
Rib fracture † 1				
# participants affected / at risk	2/437 (0.46%)	1/425 (0.24%)	1/434 (0.23%)	0/432 (0.00%)
Road traffic accident † 1				
# participants affected / at risk	1/437 (0.23%)	0/425 (0.00%)	0/434 (0.00%)	0/432 (0.00%)
Tendon rupture † 1				
# participants affected / at risk	1/437 (0.23%)	0/425 (0.00%)	0/434 (0.00%)	0/432 (0.00%)
Upper limb fracture † 1				
# participants affected / at risk	0/437 (0.00%)	1/425 (0.24%)	0/434 (0.00%)	0/432 (0.00%)
Wrist fracture † 1				
# participants affected / at risk	0/437 (0.00%)	0/425 (0.00%)	1/434 (0.23%)	0/432 (0.00%)
Investigations				
Blood creatine increased † 1				
# participants affected / at risk	1/437 (0.23%)	0/425 (0.00%)	0/434 (0.00%)	0/432 (0.00%)
Blood urea increased † 1				
# participants affected / at risk	1/437 (0.23%)	0/425 (0.00%)	0/434 (0.00%)	0/432 (0.00%)
Colonoscopy † 1				
# participants affected / at				

risk	0/437 (0.00%)	1/425 (0.24%)	0/434 (0.00%)	0/432 (0.00%)
Electrocardiogram QT prolonged † 1				
# participants affected / at risk	0/437 (0.00%)	0/425 (0.00%)	1/434 (0.23%)	0/432 (0.00%)
Laboratory test abnormal † 1				
# participants affected / at risk	0/437 (0.00%)	1/425 (0.24%)	0/434 (0.00%)	0/432 (0.00%)
Metabolism and nutrition disorders				
Hyperglycaemia † 1				
# participants affected / at risk	0/437 (0.00%)	1/425 (0.24%)	0/434 (0.00%)	0/432 (0.00%)
Hypokalaemia † 1				
# participants affected / at risk	0/437 (0.00%)	0/425 (0.00%)	1/434 (0.23%)	0/432 (0.00%)
Musculoskeletal and connective tissue disorders				
Back pain † 1				
# participants affected / at risk	0/437 (0.00%)	0/425 (0.00%)	0/434 (0.00%)	1/432 (0.23%)
Intervertebral disc protrusion † 1				
# participants affected / at risk	0/437 (0.00%)	1/425 (0.24%)	0/434 (0.00%)	0/432 (0.00%)
Osteoarthritis † 1				
# participants affected / at risk	1/437 (0.23%)	0/425 (0.00%)	1/434 (0.23%)	1/432 (0.23%)
Osteochondrosis † 1				

# participants affected / at risk	1/437 (0.23%)	0/425 (0.00%)	0/434 (0.00%)	1/432 (0.23%)
Rheumatoid arthritis † [1]				
# participants affected / at risk	0/437 (0.00%)	0/425 (0.00%)	0/434 (0.00%)	1/432 (0.23%)
Rotator cuff syndrome † [1]				
# participants affected / at risk	0/437 (0.00%)	0/425 (0.00%)	1/434 (0.23%)	0/432 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
Basal cell carcinoma † [1]				
# participants affected / at risk	0/437 (0.00%)	0/425 (0.00%)	1/434 (0.23%)	0/432 (0.00%)
Benign neoplasm of bladder † [1]				
# participants affected / at risk	1/437 (0.23%)	0/425 (0.00%)	0/434 (0.00%)	0/432 (0.00%)
Benign soft tissue neoplasm † [1]				
# participants affected / at risk	1/437 (0.23%)	0/425 (0.00%)	0/434 (0.00%)	0/432 (0.00%)
Bladder papilloma † [1]				
# participants affected / at risk	0/437 (0.00%)	0/425 (0.00%)	0/434 (0.00%)	1/432 (0.23%)
Breast cancer † [1]				
# participants affected / at risk	0/437 (0.00%)	1/425 (0.24%)	1/434 (0.23%)	0/432 (0.00%)
Bronchial carcinoma † [1]				
# participants affected / at risk	1/437 (0.23%)	0/425 (0.00%)	0/434 (0.00%)	0/432 (0.00%)
Carcinoid tumour of the small				

bowel † 1				
# participants affected / at risk	**0/437 (0.00%)**	**1/425 (0.24%)**	**0/434 (0.00%)**	**0/432 (0.00%)**
Cervix carcinoma stage 0 † 1				
# participants affected / at risk	**0/437 (0.00%)**	**1/425 (0.24%)**	**0/434 (0.00%)**	**0/432 (0.00%)**
Colon cancer † 1				
# participants affected / at risk	**0/437 (0.00%)**	**0/425 (0.00%)**	**1/434 (0.23%)**	**0/432 (0.00%)**
Gastric cancer † 1				
# participants affected / at risk	**0/437 (0.00%)**	**0/425 (0.00%)**	**0/434 (0.00%)**	**2/432 (0.46%)**
Laryngeal cancer † 1				
# participants affected / at risk	**0/437 (0.00%)**	**0/425 (0.00%)**	**0/434 (0.00%)**	**1/432 (0.23%)**
Laryngeal neoplasm † 1				
# participants affected / at risk	**0/437 (0.00%)**	**0/425 (0.00%)**	**1/434 (0.23%)**	**0/432 (0.00%)**
Lung neoplasm malignant † 1				
# participants affected / at risk	**0/437 (0.00%)**	**1/425 (0.24%)**	**1/434 (0.23%)**	**1/432 (0.23%)**
Metastases to bone † 1				
# participants affected / at risk	**0/437 (0.00%)**	**1/425 (0.24%)**	**0/434 (0.00%)**	**0/432 (0.00%)**
Non-small cell lung cancer stage I † 1				
# participants affected / at risk	**0/437 (0.00%)**	**1/425 (0.24%)**	**0/434 (0.00%)**	**0/432 (0.00%)**
Oesophageal carcinoma † 1				

# participants affected / at risk	1/437 (0.23%)	0/425 (0.00%)	0/434 (0.00%)	0/432 (0.00%)
Pancreatic carcinoma † 1				
# participants affected / at risk	0/437 (0.00%)	0/425 (0.00%)	1/434 (0.23%)	0/432 (0.00%)
Papilloma † 1				
# participants affected / at risk	0/437 (0.00%)	1/425 (0.24%)	0/434 (0.00%)	0/432 (0.00%)
Prostate cancer † 1				
# participants affected / at risk	2/437 (0.46%)	1/425 (0.24%)	1/434 (0.23%)	0/432 (0.00%)
Rectal cancer † 1				
# participants affected / at risk	1/437 (0.23%)	0/425 (0.00%)	0/434 (0.00%)	0/432 (0.00%)
Skin cancer † 1				
# participants affected / at risk	0/437 (0.00%)	0/425 (0.00%)	0/434 (0.00%)	1/432 (0.23%)
Tracheal cancer † 1				
# participants affected / at risk	1/437 (0.23%)	0/425 (0.00%)	0/434 (0.00%)	0/432 (0.00%)
Nervous system disorders				
Brain injury † 1				
# participants affected / at risk	0/437 (0.00%)	0/425 (0.00%)	0/434 (0.00%)	1/432 (0.23%)
Carotid artery stenosis † 1				
# participants affected / at risk	0/437 (0.00%)	1/425 (0.24%)	0/434 (0.00%)	0/432 (0.00%)
Cerebral infarction † 1				
# participants affected / at				

risk	1/437 (0.23%)	0/425 (0.00%)	0/434 (0.00%)	0/432 (0.00%)
Cerebral ischaemia † 1				
# participants affected / at risk	0/437 (0.00%)	1/425 (0.24%)	0/434 (0.00%)	0/432 (0.00%)
Cerebrovascular accident † 1				
# participants affected / at risk	0/437 (0.00%)	1/425 (0.24%)	1/434 (0.23%)	0/432 (0.00%)
Convulsion † 1				
# participants affected / at risk	0/437 (0.00%)	0/425 (0.00%)	2/434 (0.46%)	0/432 (0.00%)
Facial palsy † 1				
# participants affected / at risk	1/437 (0.23%)	0/425 (0.00%)	0/434 (0.00%)	0/432 (0.00%)
Grand mal convulsion † 1				
# participants affected / at risk	0/437 (0.00%)	0/425 (0.00%)	0/434 (0.00%)	1/432 (0.23%)
Loss of consciousness † 1				
# participants affected / at risk	0/437 (0.00%)	0/425 (0.00%)	0/434 (0.00%)	1/432 (0.23%)
Presyncope † 1				
# participants affected / at risk	1/437 (0.23%)	0/425 (0.00%)	0/434 (0.00%)	0/432 (0.00%)
Syncope † 1				
# participants affected / at risk	1/437 (0.23%)	0/425 (0.00%)	0/434 (0.00%)	0/432 (0.00%)
Vertebrobasilar insufficiency † 1				
# participants affected / at risk	1/437 (0.23%)	0/425 (0.00%)	0/434 (0.00%)	0/432 (0.00%)

Psychiatric disorders				
Alcohol withdrawal syndrome † [1]				
# participants affected / at risk	**1/437 (0.23%)**	**0/425 (0.00%)**	**0/434 (0.00%)**	**0/432 (0.00%)**
Anxiety † [1]				
# participants affected / at risk	**0/437 (0.00%)**	**1/425 (0.24%)**	**0/434 (0.00%)**	**0/432 (0.00%)**
Depression † [1]				
# participants affected / at risk	**1/437 (0.23%)**	**0/425 (0.00%)**	**0/434 (0.00%)**	**0/432 (0.00%)**
Renal and urinary disorders				
Nephrolithiasis † [1]				
# participants affected / at risk	**0/437 (0.00%)**	**0/425 (0.00%)**	**1/434 (0.23%)**	**0/432 (0.00%)**
Proteinuria † [1]				
# participants affected / at risk	**0/437 (0.00%)**	**0/425 (0.00%)**	**0/434 (0.00%)**	**1/432 (0.23%)**
Renal colic † [1]				
# participants affected / at risk	**0/437 (0.00%)**	**0/425 (0.00%)**	**1/434 (0.23%)**	**0/432 (0.00%)**
Renal failure acute † [1]				
# participants affected / at risk	**1/437 (0.23%)**	**0/425 (0.00%)**	**1/434 (0.23%)**	**0/432 (0.00%)**
Urinary incontinence † [1]				
# participants affected / at risk	**1/437 (0.23%)**	**0/425 (0.00%)**	**0/434 (0.00%)**	**0/432 (0.00%)**
Reproductive system and breast disorders				

Benign prostatic hyperplasia † 1				
# participants affected / at risk	**0/437 (0.00%)**	**1/425 (0.24%)**	**0/434 (0.00%)**	**2/432 (0.46%)**
Respiratory, thoracic and mediastinal disorders				
Acute pulmonary oedema † 1				
# participants affected / at risk	**1/437 (0.23%)**	**0/425 (0.00%)**	**0/434 (0.00%)**	**0/432 (0.00%)**
Apnoea † 1				
# participants affected / at risk	**0/437 (0.00%)**	**0/425 (0.00%)**	**0/434 (0.00%)**	**1/432 (0.23%)**
Bronchospasm † 1				
# participants affected / at risk	**0/437 (0.00%)**	**0/425 (0.00%)**	**1/434 (0.23%)**	**0/432 (0.00%)**
Chronic obstructive pulmonary disease † 1				
# participants affected / at risk	**18/437 (4.12%)**	**12/425 (2.82%)**	**32/434 (7.37%)**	**20/432 (4.63%)**
Dyspnoea † 1				
# participants affected / at risk	**3/437 (0.69%)**	**0/425 (0.00%)**	**1/434 (0.23%)**	**0/432 (0.00%)**
Emphysema † 1				
# participants affected / at risk	**0/437 (0.00%)**	**0/425 (0.00%)**	**1/434 (0.23%)**	**0/432 (0.00%)**
Epistaxis † 1				
# participants affected / at risk	**1/437 (0.23%)**	**0/425 (0.00%)**	**0/434 (0.00%)**	**0/432 (0.00%)**
Hypercapnia † 1				

# participants affected / at risk	0/437 (0.00%)	0/425 (0.00%)	0/434 (0.00%)	1/432 (0.23%)
Lung infiltration † 1				
# participants affected / at risk	0/437 (0.00%)	1/425 (0.24%)	0/434 (0.00%)	0/432 (0.00%)
Obliterative bronchiolitis † 1				
# participants affected / at risk	0/437 (0.00%)	0/425 (0.00%)	1/434 (0.23%)	0/432 (0.00%)
Pneumothorax † 1				
# participants affected / at risk	1/437 (0.23%)	0/425 (0.00%)	1/434 (0.23%)	0/432 (0.00%)
Productive cough † 1				
# participants affected / at risk	1/437 (0.23%)	0/425 (0.00%)	0/434 (0.00%)	0/432 (0.00%)
Pulmonary embolism † 1				
# participants affected / at risk	1/437 (0.23%)	0/425 (0.00%)	0/434 (0.00%)	1/432 (0.23%)
Respiratory arrest † 1				
# participants affected / at risk	0/437 (0.00%)	0/425 (0.00%)	0/434 (0.00%)	2/432 (0.46%)
Respiratory failure † 1				
# participants affected / at risk	3/437 (0.69%)	0/425 (0.00%)	5/434 (1.15%)	1/432 (0.23%)
Surgical and medical procedures				
Haemorrhoid operation † 1				
# participants affected / at risk	0/437 (0.00%)	0/425 (0.00%)	0/434 (0.00%)	1/432 (0.23%)
Vascular disorders				
Aortic aneurysm † 1				

# participants affected / at risk	2/437 (0.46%)	0/425 (0.00%)	0/434 (0.00%)	1/432 (0.23%)
Aortic aneurysm rupture † [1]				
# participants affected / at risk	0/437 (0.00%)	0/425 (0.00%)	0/434 (0.00%)	1/432 (0.23%)
Arterial occlusive disease † [1]				
# participants affected / at risk	0/437 (0.00%)	1/425 (0.24%)	0/434 (0.00%)	0/432 (0.00%)
Arteriosclerosis obliterans † [1]				
# participants affected / at risk	0/437 (0.00%)	1/425 (0.24%)	0/434 (0.00%)	0/432 (0.00%)
Femoral artery occlusion † [1]				
# participants affected / at risk	0/437 (0.00%)	1/425 (0.24%)	0/434 (0.00%)	0/432 (0.00%)
Hypertension † [1]				
# participants affected / at risk	0/437 (0.00%)	1/425 (0.24%)	0/434 (0.00%)	0/432 (0.00%)
Hypertensive crisis † [1]				
# participants affected / at risk	0/437 (0.00%)	0/425 (0.00%)	2/434 (0.46%)	0/432 (0.00%)
Iliac artery occlusion † [1]				
# participants affected / at risk	0/437 (0.00%)	1/425 (0.24%)	0/434 (0.00%)	0/432 (0.00%)
Peripheral ischaemia † [1]				
# participants affected / at risk	0/437 (0.00%)	1/425 (0.24%)	0/434 (0.00%)	0/432 (0.00%)
Shock † [1]				
# participants affected / at risk	0/437 (0.00%)	0/425 (0.00%)	1/434 (0.23%)	0/432 (0.00%)

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

Other Adverse Events

Hide Other Adverse Events

Time Frame	Safety population: All patients who received at least 1 dose of study drug.
Additional Description	Baseline to the end of the study (Week 52)

Frequency Threshold

Threshold above which other adverse events are reported	5%

Reporting Groups

	Description
Indacaterol 300 µg Plus Placebo to Formoterol	Patients inhaled indacaterol 300 µg once daily via a single-dose dry-powder inhaler (SDDPI), placebo to indacaterol once daily via a SDDPI, and placebo to formoterol twice daily via the manufacturer's proprietary inhalation device (Aerolizer®). Indacaterol, placebo to indacaterol, and placebo to formoterol were taken in the morning between 8:00 and 10:00 AM; placebo to formoterol was taken again 12 hours later in the evening between 8:00 and 10:00 PM. Daily inhaled corticosteroid treatment (if applicable) was to remain stable throughout the study. The short-acting β2-agonist salbutamol/albuterol was available for rescue use throughout the study.
Indacaterol 600 µg Plus Placebo to Formoterol	Patients inhaled indacaterol 600 µg (two 300 µg capsules) once daily via single-dose dry-powder inhalers (SDDPI) plus placebo to formoterol twice daily via the manufacturer's proprietary inhalation device (Aerolizer®). Indacaterol and placebo to formoterol were taken in the morning between 8:00 and 10:00 AM; placebo to formoterol was taken again 12 hours later in the evening between 8:00 and 10:00 PM. Daily inhaled corticosteroid treatment (if applicable) was to remain stable throughout the study. The short-acting β2-agonist salbutamol/albuterol was available for rescue use throughout the study.

Formoterol 12 µg Plus Placebo to Indacaterol	Patients inhaled formoterol 12 µg twice daily via the manufacturer's proprietary inhalation device (Aerolizer®) plus placebo to indacaterol once daily via a single-dose dry-powder inhaler (SDDPI). Formoterol and placebo to indacaterol were taken in the morning between 8:00 and 10:00 AM; formoterol was taken again 12 hours later in the evening between 8:00 and 10:00 PM. Daily inhaled corticosteroid treatment (if applicable) was to remain stable throughout the study. The short-acting β2-agonist salbutamol/albuterol was available for rescue use throughout the study.
Placebo to Indacaterol Plus Placebo to Formoterol	Patients inhaled placebo to indacaterol once daily via a single-dose dry-powder inhaler (SDDPI) plus placebo to formoterol twice daily via the manufacturer's proprietary inhalation device (Aerolizer®). Placebo to indacaterol and placebo to formoterol were taken in the morning between 8:00 and 10:00 AM; placebo to formoterol was taken again 12 hours later in the evening between 8:00 and 10:00 PM. Daily inhaled corticosteroid treatment (if applicable) was to remain stable throughout the study. The short-acting β2-agonist salbutamol/albuterol was available for rescue use throughout the study.

Other Adverse Events

	Indacaterol 300 µg Plus Placebo to Formoterol	Indacaterol 600 µg Plus Placebo to Formoterol	Formoterol 12 µg Plus Placebo to Indacaterol	Placebo to Indacaterol Plus Placebo to Formoterol
Total, other (not including serious) adverse events				
# participants affected / at risk	**199/437 (45.54%)**	**183/425 (43.06%)**	**164/434 (37.79%)**	**176/432 (40.74%)**
Infections and infestations				
Lower respiratory tract infection † [1]				
# participants affected / at risk	**25/437 (5.72%)**	**21/425 (4.94%)**	**17/434 (3.92%)**	**20/432 (4.63%)**
Nasopharyngitis † [1]				

# participants affected / at risk	73/437 (16.70%)	80/425 (18.82%)	62/434 (14.29%)	56/432 (12.96%)
Upper respiratory tract infection bacterial † 1				
# participants affected / at risk	26/437 (5.95%)	25/425 (5.88%)	20/434 (4.61%)	33/432 (7.64%)
Musculoskeletal and connective tissue disorders				
Muscle spasms † 1				
# participants affected / at risk	23/437 (5.26%)	25/425 (5.88%)	12/434 (2.76%)	6/432 (1.39%)
Respiratory, thoracic and mediastinal disorders				
Chronic obstructive pulmonary disease † 1				
# participants affected / at risk	128/437 (29.29%)	108/425 (25.41%)	112/434 (25.81%)	138/432 (31.94%)
Cough † 1				
# participants affected / at risk	32/437 (7.32%)	27/425 (6.35%)	17/434 (3.92%)	19/432 (4.40%)

† 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 (ie, data from all sites) in the clinical trial.

Results Point of Contact:

Name/Title: Study Director
Organization: Novartis Pharmaceuticals
phone: 862 778-8300

No publications provided by Novartis

Publications automatically indexed to this study:

Jones PW, Donohue JF, Nedelman J, Pascoe S, Pinault G, Lassen C. Correlating changes in lung function with patient outcomes in chronic obstructive pulmonary disease: a pooled analysis. Respir Res. 2011 Dec 29;12:161. doi: 10.1186/1465-9921-12-161.

Bleecker ER, Siler T, Owen R, Kramer B. Bronchodilator efficacy and safety of indacaterol 150 µg once daily in patients with COPD: an analysis of pooled data. Int J Chron Obstruct Pulmon Dis. 2011;6:431-8. doi: 10.2147/COPD.S21073. Epub 2011 Aug 18.

Jones PW, Mahler DA, Gale R, Owen R, Kramer B. Profiling the effects of indacaterol on dyspnoea and health status in patients with COPD. Respir Med. 2011 Jun;105(6):892-9. doi: 10.1016/j.rmed.2011.02.013. Epub 2011 Mar 11.

Worth H, Chung KF, Felser JM, Hu H, Rueegg P. Cardio- and cerebrovascular safety of indacaterol vs formoterol, salmeterol, tiotropium and placebo in COPD. Respir Med. 2011 Apr;105(4):571-9. doi: 10.1016/j.rmed.2010.11.027. Epub 2011 Jan 11.

Responsible Party:	External Affairs, Novartis
ClinicalTrials.gov Identifier:	NCT00393458 History of Changes
Other Study ID Numbers:	**CQAB149B2334**
Study First Received:	October 25, 2006
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Last Updated:	July 22, 2011
Health Authority:	Argentina: Administracion Nacional de Medicamentos, Alimentos y Tecnologia Medica Belgium: Federal Agency for Medicinal Products and Health Products Switzerland: Federal Office of Public Health Chile: Instituto de Salud Pública de Chile Colombia: INVIMA Instituto Nacional de Vigilancia de Medicamentos y Alimentos Czech Republic: State Institute for Drug Control Germany: Federal Institute for Drugs and Medical Devices Denmark: Danish Medicines Agency Ecuador: Public Health Ministry Egypt: Ministry of Health and Population Spain: Spanish Agency of Medicines Estonia: The State Agency of Medicine France: Afssaps - Agence française de sécurité sanitaire des produits de santé (Saint-Denis) United Kingdom: Medicines and Healthcare Products Regulatory Agency Hungary: National Institute of Pharmacy Israel: Ministry of Health Italy: National Monitoring Centre for Clinical Trials - Ministry of Health Korea: Food and Drug Administration Lithuania: State Medicine Control Agency - Ministry of Health

Latvia: State Agency of Medicines
Netherlands: Medicines Evaluation Board (MEB)
Peru: Ministry of Health
Romania: Ministry of Public Health
Russia: Ministry of Health of the Russian Federation
Slovakia: State Institute for Drug Control
Sweden: Medical Products Agency
Turkey: Ministry of Health