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Trial record **1 of 1** for: CQAB149B2349

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Safety and Efficacy of Indacaterol Once Daily Versus Salmeterol Twice Daily in Chronic Obstructive Pulmonary Disease (COPD) (INSIST)

This study has been completed.

Sponsor:
Novartis Pharmaceuticals

Information provided by:
Novartis

ClinicalTrials.gov Identifier:
NCT00821093

First received: January 9, 2009
Last updated: July 22, 2011
Last verified: July 2011
History of Changes

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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 (COPD)
Interventions:	Drug: Indacaterol 150 µg Drug: Salmeterol 50 µg Drug: Placebo to indacaterol

	Drug: Placebo to salmeterol

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
Out of total 1123 randomized patients, two patients withdrew from study prior to exposure to study drug.

Reporting Groups

	Description
Indacaterol 150 µg	Patients inhaled indacaterol 150 µg once daily in the morning between 8:00 and 11:00 AM via a single-dose dry-powder inhaler (SDDPI) for 12 weeks. Patients also inhaled placebo to salmeterol twice daily, once in the morning between 8:00 and 11:00 AM and once in the evening between 8:00 and 11:00 PM via the manufacturer's proprietary multi-dose dry-powder inhaler (MDDPI, [DISKUS]) for 12 weeks. 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.
Salmeterol 50 µg	Patients inhaled salmeterol 50 µg twice daily, once in the morning between 8:00 and 11:00 AM and once in the evening between 8:00 and 11:00 PM via the manufacturer's proprietary multi-dose dry-powder inhaler (MDDPI, [DISKUS]) for 12 weeks. Patients also inhaled placebo to indacaterol once daily in the morning between 8:00 and 11:00 AM via a single-dose dry-powder inhaler (SDDPI) for 12 weeks. 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 150 µg	Salmeterol 50 µg

STARTED	**560**	**563**
Exposed to Drug	**559**	**562**
COMPLETED	**511**	**523**
NOT COMPLETED	**49**	**40**
Adverse Event	**20**	**12**
Withdrawal by Subject	**9**	**13**
Lost to Follow-up	**9**	**3**
Protocol deviation	**3**	**6**
Abnormal laboratory value(s)	**2**	**0**
Lack of Efficacy	**2**	**2**
Death	**2**	**1**
Abnormal test procedure result(s)	**1**	**1**
Administrative problems	**1**	**2**

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 150 µg	Patients inhaled indacaterol 150 µg once daily in the morning between 8:00 and 11:00 AM via a single-dose dry-powder inhaler (SDDPI) for 12 weeks. Patients also inhaled placebo to salmeterol twice daily, once in the morning between 8:00 and 11:00 AM and once in the evening between 8:00 and 11:00 PM via the manufacturer's proprietary multi-dose dry-powder inhaler (MDDPI, [DISKUS]) for 12 weeks. 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.
Salmeterol 50 µg	Patients inhaled salmeterol 50 µg twice daily, once in the morning between 8:00 and 11:00 AM and once in the evening between 8:00 and 11:00 PM via the manufacturer's proprietary multi-dose dry-powder inhaler (MDDPI, [DISKUS]) for 12 weeks. Patients also inhaled placebo to indacaterol once daily in the morning between 8:00 and 11:00 AM via a single-dose dry-powder inhaler (SDDPI) for 12 weeks. 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 150 µg	Salmeterol 50 µg	Total
Number of Participants [units: participants]	**559**	**562**	**1121**
Age [1] [units: years] Mean (Standard Deviation)	**62.4 (8.86)**	**63.2 (8.69)**	**62.8 (8.78)**
Gender [units: participants]			
Female	**189**	**147**	**336**
Male	**370**	**415**	**785**

[1] Demographic data are based on the safety set of patients.

Outcome Measures

Hide All Outcome Measures

1. Primary: Forced Expiratory Volume in 1 Second (FEV1) Standardized (With Respect to Time) Area Under the Curve (AUC) From 5 Minutes to 11 Hours 45 Minutes Post-dose at the End of the Study (Week 12, Day 84) [Time Frame: From 5 minutes to 11 hours 45 minutes post-dose at the end of the study (Week 12, Day 84)]

Measure Type	Primary
Measure Title	Forced Expiratory Volume in 1 Second (FEV1) Standardized (With Respect to Time) Area Under the Curve (AUC) From 5 Minutes to 11 Hours 45 Minutes Post-dose at the End of the Study (Week 12, Day 84)
Measure Description	FEV1 was measured with spirometry conducted according to internationally accepted standards. Measurements were made at 5 and 30 minutes; 1, 2, 3, 4, and 8 hours; 11 hours 10 minutes and 11 hours 45 minutes post-dose at the end of the study (Week 12, Day 84). Standardized FEV1 AUC was calculated by the trapezoidal rule. The analysis included baseline FEV1 and FEV1 pre-dose and 10-15 minutes post-dose of salbutamol/albuterol during screening as covariates.
Time Frame	From 5 minutes to 11 hours 45 minutes post-dose at the end of the study (Week 12, Day 84)
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.
Full analysis set: All randomized patients who received at least 1 dose of study drug, last observation carried forward (LOCF).

Reporting Groups

	Description
Indacaterol 150 µg	Patients inhaled indacaterol 150 µg once daily in the morning between 8:00 and 11:00 AM via a single-dose dry-powder inhaler (SDDPI) for 12 weeks. Patients also inhaled placebo to salmeterol twice daily, once in the morning between 8:00 and 11:00 AM and once in the evening between 8:00 and 11:00 PM via the manufacturer's proprietary multi-dose dry-powder inhaler (MDDPI, [DISKUS]) for 12 weeks. 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.
Salmeterol 50 µg	Patients inhaled salmeterol 50 µg twice daily, once in the morning between 8:00 and 11:00 AM and once in the evening

	between 8:00 and 11:00 PM via the manufacturer's proprietary multi-dose dry-powder inhaler (MDDPI, [DISKUS]) for 12 weeks. Patients also inhaled placebo to indacaterol once daily in the morning between 8:00 and 11:00 AM via a single-dose dry-powder inhaler (SDDPI) for 12 weeks. 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 150 µg	Salmeterol 50 µg
Number of Participants Analyzed [units: participants]	**504**	**488**
Forced Expiratory Volume in 1 Second (FEV1) Standardized (With Respect to Time) Area Under the Curve (AUC) From 5 Minutes to 11 Hours 45 Minutes Post-dose at the End of the Study (Week 12, Day 84) [units: Liters] Least Squares Mean (Standard Error)	**1.47 (0.009)**	**1.41 (0.010)**

No statistical analysis provided for Forced Expiratory Volume in 1 Second (FEV1) Standardized (With Respect to Time) Area Under the Curve (AUC) From 5 Minutes to 11 Hours 45 Minutes Post-dose at the End of the Study (Week 12, Day 84)

2. Secondary: Trough Forced Expiratory Volume in 1 Second (FEV1) 24 Hours Post-dose at the End of the Study (Week 12 + 1 Day, Day 85) [Time Frame: 24 hours post-dose at the end of the study (Week 12 + 1 day, Day 85)]

Measure Type	Secondary
Measure Title	Trough Forced Expiratory Volume in 1 Second (FEV1) 24 Hours Post-dose at the End of the Study (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 and FEV1 pre-dose and 10-15 minutes post-dose of salbutamol/albuterol during screening as covariates.

Time Frame	24 hours post-dose at the end of the study (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.
Full analysis set: All randomized patients who received at least 1 dose of study drug, last observation carried forward (LOCF).

Reporting Groups

	Description
Indacaterol 150 µg	Patients inhaled indacaterol 150 µg once daily in the morning between 8:00 and 11:00 AM via a single-dose dry-powder inhaler (SDDPI) for 12 weeks. Patients also inhaled placebo to salmeterol twice daily, once in the morning between 8:00 and 11:00 AM and once in the evening between 8:00 and 11:00 PM via the manufacturer's proprietary multi-dose dry-powder inhaler (MDDPI, [DISKUS]) for 12 weeks. 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.
Salmeterol 50 µg	Patients inhaled salmeterol 50 µg twice daily, once in the morning between 8:00 and 11:00 AM and once in the evening between 8:00 and 11:00 PM via the manufacturer's proprietary multi-dose dry-powder inhaler (MDDPI, [DISKUS]) for 12 weeks. Patients also inhaled placebo to indacaterol once daily in the morning between 8:00 and 11:00 AM via a single-dose dry-powder inhaler (SDDPI) for 12 weeks. 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 150 µg	**Salmeterol 50 µg**
Number of Participants Analyzed [units: participants]	**522**	**512**
Trough Forced Expiratory Volume in 1 Second (FEV1) 24 Hours Post-dose at the End of the Study (Week 12 + 1 Day, Day 85) [units: Liters]	**1.41 (0.009)**	**1.35 (0.010)**

Least Squares Mean (Standard Error)		

No statistical analysis provided for Trough Forced Expiratory Volume in 1 Second (FEV1) 24 Hours Post-dose at the End of the Study (Week 12 + 1 Day, Day 85)

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	12 weeks
Additional Description	The Safety set included all patients who received at least one dose of study drug.

Reporting Groups

	Description
Indacaterol 150 µg	Patients inhaled indacaterol 150 µg once daily in the morning between 8:00 and 11:00 AM via a single-dose dry-powder inhaler (SDDPI) for 12 weeks. Patients also inhaled placebo to salmeterol twice daily, once in the morning between 8:00 and 11:00 AM and once in the evening between 8:00 and 11:00 PM via the manufacturer's proprietary multi-dose dry-powder inhaler (MDDPI, [DISKUS]) for 12 weeks. 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.
Salmeterol 50 µg	Patients inhaled salmeterol 50 µg twice daily, once in the morning between 8:00 and 11:00 AM and once in the evening between 8:00 and 11:00 PM via the manufacturer's proprietary multi-dose dry-powder inhaler (MDDPI, [DISKUS]) for 12 weeks. Patients also inhaled placebo to indacaterol once daily in the morning between 8:00 and 11:00 AM via a single-dose dry-powder inhaler (SDDPI) for 12 weeks. 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 150 µg	Salmeterol 50 µg
Total, serious adverse events		

# participants affected / at risk	20/559 (3.58%)	16/562 (2.85%)
Cardiac disorders		
Acute coronary syndrome † 1		
# participants affected / at risk	0/559 (0.00%)	1/562 (0.18%)
Acute myocardial infarction † 1		
# participants affected / at risk	1/559 (0.18%)	0/562 (0.00%)
Angina pectoris † 1		
# participants affected / at risk	2/559 (0.36%)	0/562 (0.00%)
Atrial fibrillation † 1		
# participants affected / at risk	1/559 (0.18%)	0/562 (0.00%)
Atrial flutter † 1		
# participants affected / at risk	1/559 (0.18%)	0/562 (0.00%)
Cardiac failure congestive † 1		
# participants affected / at risk	1/559 (0.18%)	0/562 (0.00%)
Cardiopulmonary failure † 1		
# participants affected / at risk	1/559 (0.18%)	0/562 (0.00%)
Coronary artery disease † 1		
# participants affected / at risk	0/559 (0.00%)	1/562 (0.18%)
Myocardial infarction † 1		
# participants affected / at risk	1/559 (0.18%)	0/562 (0.00%)
Gastrointestinal disorders		
Abdominal pain upper † 1		
# participants affected / at risk	0/559 (0.00%)	1/562 (0.18%)
General disorders		
Asthenia † 1		

# participants affected / at risk	0/559 (0.00%)	1/562 (0.18%)
Pyrexia † [1]		
# participants affected / at risk	1/559 (0.18%)	0/562 (0.00%)
Immune system disorders		
Contrast media allergy † [1]		
# participants affected / at risk	0/559 (0.00%)	1/562 (0.18%)
Infections and infestations		
Bronchitis † [1]		
# participants affected / at risk	0/559 (0.00%)	1/562 (0.18%)
Cellulitis † [1]		
# participants affected / at risk	1/559 (0.18%)	0/562 (0.00%)
Pneumonia † [1]		
# participants affected / at risk	1/559 (0.18%)	0/562 (0.00%)
Upper respiratory tract infection bacterial † [1]		
# participants affected / at risk	2/559 (0.36%)	0/562 (0.00%)
Injury, poisoning and procedural complications		
Fall † [1]		
# participants affected / at risk	1/559 (0.18%)	0/562 (0.00%)
Lower limb fracture † [1]		
# participants affected / at risk	1/559 (0.18%)	0/562 (0.00%)
Skin laceration † [1]		
# participants affected / at risk	1/559 (0.18%)	0/562 (0.00%)
Investigations		
Weight decreased † [1]		

# participants affected / at risk	1/559 (0.18%)	1/562 (0.18%)
Metabolism and nutrition disorders		
Hyponatraemia † 1		
# participants affected / at risk	0/559 (0.00%)	1/562 (0.18%)
Musculoskeletal and connective tissue disorders		
Musculoskeletal pain † 1		
# participants affected / at risk	0/559 (0.00%)	1/562 (0.18%)
Pathological fracture † 1		
# participants affected / at risk	1/559 (0.18%)	0/562 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Gastric cancer † 1		
# participants affected / at risk	1/559 (0.18%)	0/562 (0.00%)
Lung adenocarcinoma † 1		
# participants affected / at risk	1/559 (0.18%)	0/562 (0.00%)
Lung neoplasm † 1		
# participants affected / at risk	0/559 (0.00%)	1/562 (0.18%)
Metastases to spine † 1		
# participants affected / at risk	1/559 (0.18%)	0/562 (0.00%)
Non-Hodgkin's lymphoma † 1		
# participants affected / at risk	1/559 (0.18%)	0/562 (0.00%)
Nervous system disorders		
Cerebral infarction † 1		
# participants affected / at risk	1/559 (0.18%)	0/562 (0.00%)
Cerebrovascular accident † 1		
# participants affected / at risk	1/559 (0.18%)	0/562 (0.00%)

Hemiparesis † 1		
# participants affected / at risk	**1/559 (0.18%)**	**1/562 (0.18%)**
Ischaemic stroke † 1		
# participants affected / at risk	**0/559 (0.00%)**	**1/562 (0.18%)**
Paraesthesia † 1		
# participants affected / at risk	**1/559 (0.18%)**	**0/562 (0.00%)**
Radicular syndrome † 1		
# participants affected / at risk	**0/559 (0.00%)**	**1/562 (0.18%)**
Spinal cord compression † 1		
# participants affected / at risk	**1/559 (0.18%)**	**0/562 (0.00%)**
Syncope † 1		
# participants affected / at risk	**0/559 (0.00%)**	**1/562 (0.18%)**
Transient ischaemic attack † 1		
# participants affected / at risk	**1/559 (0.18%)**	**0/562 (0.00%)**
Respiratory, thoracic and mediastinal disorders		
Chronic obstructive pulmonary disease † 1		
# participants affected / at risk	**4/559 (0.72%)**	**7/562 (1.25%)**
Respiratory failure † 1		
# participants affected / at risk	**0/559 (0.00%)**	**2/562 (0.36%)**
Vascular disorders		
Peripheral arterial occlusive disease † 1		
# participants affected / at risk	**1/559 (0.18%)**	**0/562 (0.00%)**

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

Other Adverse Events

Hide Other Adverse Events

Time Frame	12 weeks
Additional Description	The Safety set included all patients who received at least one dose of study drug.

Frequency Threshold

Threshold above which other adverse events are reported	5%

Reporting Groups

	Description
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Salmeterol 50 µg	Patients inhaled salmeterol 50 µg twice daily, once in the morning between 8:00 and 11:00 AM and once in the evening between 8:00 and 11:00 PM via the manufacturer's proprietary multi-dose dry-powder inhaler (MDDPI, [DISKUS]) for 12 weeks. Patients also inhaled placebo to indacaterol once daily in the morning between 8:00 and 11:00 AM via a single-dose dry-powder inhaler (SDDPI) for 12 weeks. 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 150 µg	Salmeterol 50 µg
Total, other (not including serious) adverse events		
# participants affected / at risk	**0/559 (0.00%)**	**0/562 (0.00%)**

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:

Korn S, Kerwin E, Atis S, Amos C, Owen R, Lassen C; INSIST study group. Indacaterol once-daily provides superior efficacy to salmeterol twice-daily in COPD: a 12-week study. Respir Med. 2011 May;105(5):719-26. doi: 10.1016/j.rmed.2011.02.008. Epub 2011 Mar 1.

Responsible Party:	External Affairs, Novartis Pharmaceuticals
ClinicalTrials.gov Identifier:	NCT00821093 History of Changes
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Study First Received:	January 9, 2009
Results First Received:	July 22, 2011
Last Updated:	July 22, 2011
Health Authority:	United States: Food and Drug Administration Turkey: Ministry of Health India: Drugs Controller General of India Germany: Ethics Commission Spain: Spanish Agency of Medicines Slovakia: State Institute for Drug Control Hungary: National Institute of Pharmacy Czech Republic: State Institute for Drug Control Germany: Federal Institute for Drugs and Medical Devices