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An Exploratory Study, to Assess the Effect of Repeat-dose Inhaled Indacaterol Maleate (300 µg) on Dynamic and Static Lung Hyperinflation, Subjective Breathlessness and Health Status in Patients With Chronic Obstructive Pulmonary Disease(COPD)

This study has been completed.

Sponsor:
Novartis

Information provided by:
Novartis

ClinicalTrials.gov Identifier:
NCT00636961

First received: March 10, 2008
Last updated: July 29, 2011
Last verified: July 2011
History of Changes

Results First Received: July 29, 2011

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Safety/Efficacy Study; Intervention Model: Crossover Assignment; Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor); Primary Purpose: Supportive Care
Condition:	Chronic Obstructive Pulmonary Disease
	Drug: Indacaterol 300µg

Interventions:	Drug: Placebo

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
Sequence 1: Indacaterol 300µg Followed by Placebo	In period I, indacaterol 300µg was taken by inhalation once daily via the Concept 1 inhaler device for 2 weeks. In period II, matching placebo was taken by inhalation once daily via the Concept 1 inhaler device for 2 weeks. For each treatment period and for each patient, the doses were to be administered between 7am and 12am. A period of at least 4 days but no more than 21 days separated each treatment period. Rescue medication (short-acting beta-agonist (SABA)) was prescribed by the investigator for the duration of the study.
Sequence 2 : Placebo Followed by Indacaterol 300µg	In period I, matching placebo was taken by inhalation once daily via the Concept 1 inhaler device for 2 weeks. In period II, indacaterol 300µg was taken by inhalation once daily via the Concept 1 inhaler device for 2 weeks. For each treatment period and for each patient, the doses were to be administered between 7am and 12am. A period of at least 4 days but no more than 21 days separated each treatment period. Rescue medication (short-acting beta-agonist (SABA)) was prescribed by the investigator for the duration of the study.

Participant Flow for 2 periods

Period 1: Period 1

	Sequence 1: Indacaterol 300µg Followed by Placebo	Sequence 2 : Placebo Followed by Indacaterol 300µg
STARTED	14	13
COMPLETED	13	12
NOT COMPLETED	1	1
Administrative problems	1	1

Period 2: Period 2

	Sequence 1: Indacaterol 300µg Followed by Placebo	Sequence 2 : Placebo Followed by Indacaterol 300µg
STARTED	13	12
COMPLETED	12	12
NOT COMPLETED	1	0
Adverse Event	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.
No text entered.

Reporting Groups

	Description
Sequence 1: Indacaterol 300µg Followed by Placebo	In period I, indacaterol 300µg was taken by inhalation once daily via the Concept 1 inhaler device for 2 weeks. In period II, matching placebo was taken by inhalation once daily via the Concept 1 inhaler device for 2 weeks. For each treatment period and for each patient, the doses were to be administered between 7am and 12am. A period of at least 4 days but no more than 21 days separated each treatment period. Rescue medication (short-acting beta-agonist (SABA)) was prescribed by the investigator for the duration of the study.
Sequence 2 : Placebo Followed by Indacaterol 300µg	In period I, matching placebo was taken by inhalation once daily via the Concept 1 inhaler device for 2 weeks. In period II, indacaterol 300µg was taken by inhalation once daily via the Concept 1 inhaler device for 2 weeks. For each treatment period and for each patient, the doses were to be administered between 7am and 12am. A period of at least 4 days but no more than 21 days separated each treatment period. Rescue medication (short-acting beta-agonist (SABA)) was prescribed by the investigator for the duration of the study.
Total	Total of all reporting groups

Baseline Measures

	Sequence 1: Indacaterol 300µg Followed by Placebo	Sequence 2 : Placebo Followed by Indacaterol 300µg	Total
Number of Participants [units: participants]	**14**	**13**	**27**
Age [1] **[units: years] Mean (Standard Deviation)**	**62.6 (8.30)**	**59.8 (5.81)**	**61.3 (7.22)**
Gender [units: participants]			
Female	**4**	**5**	**9**
Male	**10**	**8**	**18**

[1] Baseline measurements are based on total randomized patients.

Outcome Measures

Hide All Outcome Measures

1. Primary: Inspiratory Capacity (IC) at Peak Time and at Isotime on Day 14 [Time Frame: Day 14]

Measure Type	Primary
Measure Title	Inspiratory Capacity (IC) at Peak Time and at Isotime on Day 14
Measure Description	Inspiratory capacity (IC) at peak time and at isotime were the primary pharmacodynamic (PD) variables of interest. IC was measured at two minute intervals during exercise. Isotime was defined as the time the subject was still exercising in the shortest of all sub-maximal exercise tests (3-minutes resting pedaling, 3-minutes unloaded pedaling and exercise with loaded pedaling). Peak time was defined as the last measurement taken in the exercise period. The primary analysis consisted of a linear mixed effects model with baseline IC measurement as covariate.
Time Frame	Day 14
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 safety analysis set consisted of all patients who received study medication and had at least one assessment.

Reporting Groups

	Description
Indacaterol 300ug	Patients received indacaterol 300µg via the Concept 1 inhaler device once daily (between 7 am and 12 am) for 2 weeks. Rescue medication (SABA) was prescribed by the investigator for the duration of the study.
Placebo	Patients received matching placebo via the Concept 1 inhaler device once daily in the morning (between 7 am to 12am)

	for 2 weeks. Rescue medication (SABA) was prescribed by the investigator for the duration of the study.

Measured Values

	Indacaterol 300ug	Placebo
Number of Participants Analyzed [units: participants]	**25**	**25**
Inspiratory Capacity (IC) at Peak Time and at Isotime on Day 14 [units: Liters] Least Squares Mean (90% Confidence Interval)		
IC at Peak	**2.36 (2.25 to 2.48)**	**2.05 (1.93 to 2.16)**
IC at Isotime	**2.37 (2.25 to 2.48)**	**2.10 (1.99 to 2.21)**

No statistical analysis provided for Inspiratory Capacity (IC) at Peak Time and at Isotime on Day 14

2. Secondary: Static Inspiratory Capacity (IC) at Day 14 [Time Frame: Day 14]

Measure Type	Secondary
Measure Title	Static Inspiratory Capacity (IC) at Day 14
Measure Description	Inspiratory Capacity (IC) at resting (static IC) was measured by using whole body plethysmography. The day 14 measurement was analyzed using an analysis of variance including baseline (day -2) as a covariate,
Time Frame	Day 14
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 safety analysis set consisted of all patients who received study medication and had at least one assessment.

Reporting Groups

	Description
Indacaterol 300ug	Patients received indacaterol 300µg via the Concept 1 inhaler device once daily (between 7 am and 12 am) for 2 weeks. Rescue medication (SABA) was prescribed by the investigator for the duration of the study.
Placebo	Patients received matching placebo via the Concept 1 inhaler device once daily in the morning (between 7 am to 12am) for 2 weeks. Rescue medication (SABA) was prescribed by the investigator for the duration of the study.

Measured Values

	Indacaterol 300ug	Placebo
Number of Participants Analyzed [units: participants]	**26**	**26**
Static Inspiratory Capacity (IC) at Day 14 [units: Liters] Least Squares Mean (90% Confidence Interval)	**2.55 (2.46 to 2.65)**	**2.37 (2.28 to 2.47)**

No statistical analysis provided for Static Inspiratory Capacity (IC) at Day 14

3. Secondary: Trough Forced Expiratory Volume in 1 Second (FEV1) Measured by Spirometry on Day 14 [Time Frame: Day 14]

Measure Type	Secondary
Measure Title	Trough Forced Expiratory Volume in 1 Second (FEV1) Measured by Spirometry on Day 14
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. The linear mixed model included the baseline FEV1 measurement as covariate.

Time Frame	Day 14
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 safety analysis set consisted of all patients who received study medication and had at least one assessment.

Reporting Groups

	Description
Indacaterol 300ug	Patients received indacaterol 300µg via the Concept 1 inhaler device once daily (between 7 am and 12 am) for 2 weeks. Rescue medication (SABA) was prescribed by the investigator for the duration of the study.
Placebo	Patients received matching placebo via the Concept 1 inhaler device once daily in the morning (between 7 am to 12am) for 2 weeks. Rescue medication (SABA) was prescribed by the investigator for the duration of the study.

Measured Values

	Indacaterol 300ug	**Placebo**
Number of Participants Analyzed [units: participants]	**25**	**25**
Trough Forced Expiratory Volume in 1 Second (FEV1) Measured by Spirometry on Day 14 [units: Liters] Least Squares Mean (90% Confidence Interval)	**1.68 (1.59 to 1.76)**	**1.53 (1.45 to 1.62)**

No statistical analysis provided for Trough Forced Expiratory Volume in 1 Second (FEV1) Measured by Spirometry on Day 14

4. Secondary: Chronic Activity Related Breathlessness Measured by Transition Dyspnoea Index (TDI) at Day 14 [Time Frame: Day 14]

Measure Type	Secondary

Measure Title	Chronic Activity Related Breathlessness Measured by Transition Dyspnoea Index (TDI) at Day 14
Measure Description	Dyspnoea was measured during the treatment period using the transition dyspnoea index (TDI), which captures changes from baseline. The TDI has three domains; functional impairment, magnitude of task and magnitude of effort. TDI domains are rated from -3 (major deterioration) to 3 (major improvement) and rates are summed for transition focal score ranging from -9 to 9; minus scores indicate deterioration. A TDI focal score of 1 was considered to be a clinically significant and meaningful improvement from baseline. Analysis of variance included period baseline dyspnoea index (BDI) as covariate.
Time Frame	Day 14
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 safety analysis set consisted of all patients who received study medication and had at least one assessment.

Reporting Groups

	Description
Indacaterol 300ug	Patients received indacaterol 300µg via the Concept 1 inhaler device once daily (between 7 am and 12 am) for 2 weeks. Rescue medication (SABA) was prescribed by the investigator for the duration of the study.
Placebo	Patients received matching placebo via the Concept 1 inhaler device once daily in the morning (between 7 am to 12am) for 2 weeks. Rescue medication (SABA) was prescribed by the investigator for the duration of the study.

Measured Values

	Indacaterol 300ug	**Placebo**
Number of Participants Analyzed [units: participants]	**20**	**22**
Chronic Activity Related Breathlessness Measured by Transition Dyspnoea Index (TDI) at Day 14 [units: Score on a scale] Least Squares Mean (90% Confidence Interval)	**1.0 (-0.3 to 2.4)**	**-2.3 (-3.6 to -1.0)**

No statistical analysis provided for Chronic Activity Related Breathlessness Measured by Transition Dyspnoea Index (TDI) at Day 14

5. Secondary: Dyspnoea Measured by Borg CR10 Scale at Day 1, Day 14 [Time Frame: Day 1, Day 14]

Measure Type	Secondary
Measure Title	Dyspnoea Measured by Borg CR10 Scale at Day 1, Day 14
Measure Description	The modified Borg CR10 Scale consists of 12-point score that the patients point to so as to indicate their level of dyspnoea (where 0 indicates no breathlessness at all to 12 indicates maximum breathlessness), before and during exercise testing. A reduction in this score indicates an improvement. Isotime was defined as the time the subject was still exercising in the shortest of all sub-maximal exercise tests. Peak time was defined as the last measurement taken in the exercise period. Analysis of variance included period, treatment and sequence as fixed effects and subject as random effect.
Time Frame	Day 1, Day 14
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 safety analysis set consisted of all patients who received study medication and had at least one assessment.

Reporting Groups

	Description
Indacaterol 300ug	Patients received indacaterol 300µg via the Concept 1 inhaler device once daily (between 7 am and 12 am) for 2 weeks. Rescue medication (SABA) was prescribed by the investigator for the duration of the study.
Placebo	Patients received matching placebo via the Concept 1 inhaler device once daily in the morning (between 7 am to 12am) for 2 weeks. Rescue medication (SABA) was prescribed by the investigator for the duration of the study.

Measured Values

	Indacaterol 300ug	Placebo
Number of Participants Analyzed [units: participants]	26	26
Dyspnoea Measured by Borg CR10 Scale at Day 1, Day 14 [units: Score on a scale] Least Squares Mean (90% Confidence Interval)		
Day 1 : score at Peak (n= 26, 26)	8.2 (7.4 to 8.9)	7.9 (7.2 to 8.7)
Day 14: score at Peak (n= 25, 25)	8.1 (7.5 to 8.8)	8.7 (8.1 to 9.4)
Day 1 : score at Isotime (n= 26, 26)	5.9 (5.0 to 6.7)	5.8 (4.9 to 6.6)
Day 14 : score at Isotime(n= 25, 25)	5.2 (4.4 to 6.0)	6.7 (5.9 to 7.5)

No statistical analysis provided for Dyspnoea Measured by Borg CR10 Scale at Day 1, Day 14

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	No text entered.
Additional Description	The safety analysis set that consisted of all patients who received study medication and had at least one assessment.

Reporting Groups

	Description

Indacaterol 300ug	Patients received indacaterol 300µg via the Concept 1 inhaler device once daily (between 7 am and 12 am) for 2 weeks. Rescue medication (SABA) was prescribed by the investigator for the duration of the study.
Placebo	Patients received matching placebo via the Concept 1 inhaler device once daily in the morning (between 7 am to 12am) for 2 weeks. Rescue medication (SABA) was prescribed by the investigator for the duration of the study.

Serious Adverse Events

	Indacaterol 300ug	Placebo
Total, serious adverse events		
# participants affected / at risk	**0/26 (0.00%)**	**0/26 (0.00%)**

Other Adverse Events

Hide Other Adverse Events

Time Frame	No text entered.
Additional Description	The safety analysis set that consisted of all patients who received study medication and had at least one assessment.

Frequency Threshold

Threshold above which other adverse events are reported	3%

Reporting Groups

	Description
Indacaterol 300ug	Patients received indacaterol 300µg via the Concept 1 inhaler device once daily (between 7 am and 12 am) for 2 weeks. Rescue medication (SABA) was prescribed by the investigator for the duration of the study.
Placebo	Patients received matching placebo via the Concept 1 inhaler device once daily in the morning (between 7 am to 12am) for 2 weeks. Rescue medication (SABA) was prescribed by the investigator for the duration of the study.

Other Adverse Events

	Indacaterol 300ug	Placebo
Total, other (not including serious) adverse events		
# participants affected / at risk	9/26 (34.62%)	9/26 (34.62%)
Ear and labyrinth disorders		
Vertigo † [1]		
# participants affected / at risk	1/26 (3.85%)	0/26 (0.00%)
Eye disorders		
Conjunctivitis allergic † [1]		
# participants affected / at risk	0/26 (0.00%)	1/26 (3.85%)
Gastrointestinal disorders		
Abdominal pain † [1]		
# participants affected / at risk	0/26 (0.00%)	1/26 (3.85%)
Constipation † [1]		
# participants affected / at risk	0/26 (0.00%)	1/26 (3.85%)
Diarrhoea † [1]		
# participants affected / at risk	1/26 (3.85%)	1/26 (3.85%)
Dry mouth † [1]		
# participants affected / at risk	0/26 (0.00%)	1/26 (3.85%)
Tongue coated † [1]		
# participants affected / at risk	0/26 (0.00%)	1/26 (3.85%)
Infections and infestations		
Nasopharyngitis † [1]		
# participants affected / at risk	2/26 (7.69%)	0/26 (0.00%)

Injury, poisoning and procedural complications		
Fall † 1		
# participants affected / at risk	0/26 (0.00%)	1/26 (3.85%)
Investigations		
Blood pressure increased † 1		
# participants affected / at risk	0/26 (0.00%)	1/26 (3.85%)
Electrocardiogram ST segment depression † 1		
# participants affected / at risk	0/26 (0.00%)	1/26 (3.85%)
Metabolism and nutrition disorders		
Gout † 1		
# participants affected / at risk	1/26 (3.85%)	0/26 (0.00%)
Musculoskeletal and connective tissue disorders		
Back pain † 1		
# participants affected / at risk	0/26 (0.00%)	2/26 (7.69%)
Osteitis † 1		
# participants affected / at risk	0/26 (0.00%)	1/26 (3.85%)
Pain in jaw † 1		
# participants affected / at risk	0/26 (0.00%)	1/26 (3.85%)
Nervous system disorders		
Headache † 1		
# participants affected / at risk	3/26 (11.54%)	1/26 (3.85%)
Psychiatric disorders		
Anxiety † 1		
# participants affected / at risk	1/26 (3.85%)	0/26 (0.00%)
Renal and urinary disorders		

Nephritis † 1		
# participants affected / at risk	**0/26 (0.00%)**	**1/26 (3.85%)**
Respiratory, thoracic and mediastinal disorders		
Cough † 1		
# participants affected / at risk	**2/26 (7.69%)**	**0/26 (0.00%)**
Surgical and medical procedures		
Tooth extraction † 1		
# participants affected / at risk	**0/26 (0.00%)**	**1/26 (3.85%)**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA 10.X

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 Pharmaceuticals
phone: 862-778-8300

No publications provided

Responsible Party:	External Affairs, Novartis
ClinicalTrials.gov Identifier:	NCT00636961 History of Changes
Other Study ID Numbers:	**CQAB149B2318**
Study First Received:	March 10, 2008
Results First Received:	July 29, 2011
Last Updated:	July 29, 2011
Health Authority:	Germany: Federal Institute for Drugs and Medical Devices