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Trial record **1 of 1** for: CQAB149B2217

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Safety of Exercise and High-dose Salbutamol in Patients With Chronic Obstructive Pulmonary Disease (COPD) Receiving Therapeutic Doses of Indacaterol (QAB 149) and Salmeterol

This study has been completed.

Sponsor:
Novartis

Information provided by (Responsible Party):
Novartis

ClinicalTrials.gov Identifier:
NCT00531050

First received: September 17, 2007
Last updated: April 23, 2012
Last verified: April 2012
History of Changes

Results First Received: July 29, 2011

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Safety Study; Intervention Model: Crossover Assignment; Masking: Double Blind (Subject, Investigator); Primary Purpose: Treatment
Condition:	Chronic Obstructive Pulmonary Disease
Interventions:	Drug: Indacaterol Drug: Placebo Drug: 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
The study was double blind with regard to the administration of indacaterol and placebo and open label with regard to salmeterol. The study had 2 parts. Each Part of the study consisted of 3 treatment periods separated by a minimum of 7 days. The two parts of the study were separated by a minimum of 7 days.

Reporting Groups

	Description
Part 1: Sequence A, Part 2: Sequence A	Part 1: Sequence 'A' consisted of - Period 1, patient received a single inhaled dose of indacaterol 300µg capsule via the Concept1 inhaler device. Period 2, patient received single dose of salmeterol 50µg via Diskus dry powder inhaler (DPI). Period 3, patient received single dose of indacaterol matching placebo via the Concept1 inhaler device. Part 2: Sequence 'A' consisted of - Period 1, patients received a morning single inhalational dose of indacaterol 300µg and an evening single inhalation dose of indacaterol matching placebo via the Concept1 inhaler device. Period 2, patients received morning and evening single inhalational dose of salmeterol 50µg via Diskus DPI. Period 3, patients received single inhalation dose of indacaterol matching placebo in morning and evening via Concept1 device. In Part 2 of the study, at 20 minutes following each dose, patients received three doses of nebulized salbutamol 2.5 mg at 20 minute intervals.
Part 1 : Sequence B, Part 2: Sequence B	Part 1: Sequence 'B' consisted of - Period 1, patient received a single inhaled dose of indacaterol 300µg capsule administered via the Concept1 inhaler device. Period 2, patient received single dose of indacaterol matching placebo via the Concept1 inhaler device. Period 3, patient received single dose of salmeterol 50µg via Diskus DPI.

	Part 2: Sequence 'B' consisted of - Period 1, patients received a morning single inhalational dose of indacaterol 300µg and an evening single inhalation dose of indacaterol matching placebo via the Concept1 inhaler device. Period 2, patients received single inhalation dose of indacaterol matching placebo in morning and evening via Concept1 device. Period 3, patients received morning and evening single inhalational dose of salmeterol 50µg via Diskus DPI. In Part 2 of the study, at 20 minutes following each dose, patients received three doses of nebulized salbutamol 2.5 mg at 20 minute intervals.
Part 1: Sequence C, Part 2: Sequence C	Part 1: Sequence 'C' consisted of - Period 1, patient received single dose of indacaterol matching placebo via the Concept1 inhaler device. Period 2, patient received single dose of salmeterol 50µg via Diskus DPI. Period 3, patient received a single inhaled dose of indacaterol 300µg capsule administered via the Concept1 inhaler device. Part 2: Sequence 'C' consisted of - Period 1, patients received single inhalation dose of indacaterol matching placebo in morning and evening via Concept1 device. Period 2, patients received morning and evening single inhalational dose of salmeterol 50µg via Diskus DPI. Period 3, patients received a morning single inhalational dose of indacaterol 300µg and an evening single inhalation dose of indacaterol matching placebo via the Concept1 inhaler device . In Part 2 of the study, at 20 minutes following each dose, patients received three doses of nebulized salbutamol 2.5 mg at 20 minute intervals.
Part 1; Sequence D, Part 2: Sequence D	Part 1: Sequence 'D' consisted of - Period 1, patient received single dose of indacaterol matching placebo via the Concept1 inhaler device. Period 2, patient received a single inhaled dose of indacaterol 300µg capsule administered via the Concept1 inhaler device. Period 3, patient received single dose of salmeterol 50µg via Diskus DPI. Part 2: Sequence 'D' consisted of - Period 1, patients received single inhalation dose of indacaterol matching placebo in morning and evening via Concept1 device. Period 2, patients received a morning single inhalational dose of indacaterol 300µg and an evening single inhalation dose of indacaterol matching placebo via the Concept1 inhaler device. Period 3, patients received morning and evening single inhalational dose of salmeterol 50µg via Diskus DPI. In Part 2 of the study, at 20 minutes following each dose, patients received three doses of nebulized salbutamol 2.5 mg at 20 minute intervals.
Part 1: Sequence E, Part 2: Sequence E	Part 1: Sequence 'E' consisted of - Period 1, patient received single dose of salmeterol 50µg via Diskus DPI. Period 2, patient received a single inhaled dose of indacaterol 300µg capsule administered via the Concept1 inhaler device. Period 3, patient received single dose of indacaterol matching placebo via the Concept1 inhaler device.

	Part 2: Sequence 'E' consisted of - Period 1, patients received morning and evening single inhalational dose of salmeterol 50µg via Diskus DPI. Period 2, patients received a morning single inhalational dose of indacaterol 300µg and an evening single inhalation dose of indacaterol matching placebo via the Concept1 inhaler device. Period 3, patients received single inhalation dose of indacaterol matching placebo in morning and evening via Concept1 device. In Part 2 of the study, at 20 minutes following each dose, patients received three doses of nebulized salbutamol 2.5 mg at 20 minute intervals.
Part 1: Sequence F, Part 2: Sequence F	Part 1: Sequence 'F' consisted of - Period 1, patient received single dose of salmeterol 50µg via Diskus DPI. Period 2, patient received single dose of indacaterol matching placebo via the Concept1 inhaler device. Period 3, patient received a single inhaled dose of indacaterol 300µg capsule administered via the Concept1 inhaler device. Part 2: Sequence 'F' consisted of - Period 1, patients received morning and evening single inhalational dose of salmeterol 50µg via Diskus DPI. Period 2, patients received single inhalation dose of indacaterol matching placebo in morning and evening via Concept1 device. Period 3, patients received a morning single inhalational dose of indacaterol 300µg and an evening single inhalation dose of indacaterol matching placebo via the Concept1 inhaler device. In Part 2 of the study, at 20 minutes following each dose, patients received three doses of nebulized salbutamol 2.5 mg at 20 minute intervals.

Participant Flow for 6 periods

Period 1: Part 1: Period 1

	Part 1: Sequence A, Part 2: Sequence A	Part 1 : Sequence B, Part 2: Sequence B	Part 1: Sequence C, Part 2: Sequence C	Part 1; Sequence D, Part 2: Sequence D	Part 1: Sequence E, Part 2: Sequence E	Part 1: Sequence F, Part 2: Sequence F
STARTED	**4**	**5**	**4**	**5**	**4**	**5**
COMPLETED	**4**	**4**	**4**	**4**	**4**	**5**
NOT COMPLETED	**0**	**1**	**0**	**1**	**0**	**0**
Adverse						

Event	0	1	0	0	0	0
Protocol Deviation	0	0	0	1	0	0

Period 2: Part 1: Period 2

	Part 1: Sequence A, Part 2: Sequence A	Part 1 : Sequence B, Part 2: Sequence B	Part 1: Sequence C, Part 2: Sequence C	Part 1; Sequence D, Part 2: Sequence D	Part 1: Sequence E, Part 2: Sequence E	Part 1: Sequence F, Part 2: Sequence F
STARTED	4	4	4	4	4	5
COMPLETED	4	4	4	4	4	5
NOT COMPLETED	0	0	0	0	0	0

Period 3: Part 1: Period 3

	Part 1: Sequence A, Part 2: Sequence A	Part 1 : Sequence B, Part 2: Sequence B	Part 1: Sequence C, Part 2: Sequence C	Part 1; Sequence D, Part 2: Sequence D	Part 1: Sequence E, Part 2: Sequence E	Part 1: Sequence F, Part 2: Sequence F
STARTED	4	4	4	4	4	5
COMPLETED	3	4	4	4	4	5
NOT COMPLETED	1	0	0	0	0	0
Adverse Event	1	0	0	0	0	0

Period 4: Part 2: Period 1

	Part 1: Sequence A, Part 2: Sequence A	Part 1 : Sequence B, Part 2: Sequence B	Part 1: Sequence C, Part 2: Sequence C	Part 1; Sequence D, Part 2: Sequence D	Part 1: Sequence E, Part 2: Sequence E	Part 1: Sequence F, Part 2: Sequence F
STARTED	3	4	4	4	4	5
COMPLETED	3	4	4	4	4	4
NOT COMPLETED	0	0	0	0	0	1
Adverse Event	0	0	0	0	0	1

Period 5: Part 2: Period 2

	Part 1: Sequence A, Part 2: Sequence A	Part 1 : Sequence B, Part 2: Sequence B	Part 1: Sequence C, Part 2: Sequence C	Part 1; Sequence D, Part 2: Sequence D	Part 1: Sequence E, Part 2: Sequence E	Part 1: Sequence F, Part 2: Sequence F
STARTED	3	4	4	4	4	4
COMPLETED	3	4	4	4	4	4
NOT COMPLETED	0	0	0	0	0	0

Period 6: Part 2: Period 3

	Part 1: Sequence A, Part 2: Sequence A	Part 1 : Sequence B, Part 2: Sequence B	Part 1: Sequence C, Part 2: Sequence C	Part 1; Sequence D, Part 2: Sequence D	Part 1: Sequence E, Part 2: Sequence E	Part 1: Sequence F, Part 2: Sequence F
STARTED	3	4	4	4	4	4

COMPLETED	**2**	**4**	**4**	**4**	**4**	**3**
NOT COMPLETED	**1**	**0**	**0**	**0**	**0**	**1**
Abnormal test procedure	**1**	**0**	**0**	**0**	**0**	**1**

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
Part 1: Sequence A, Part 2: Sequence A	Part 1: Sequence 'A' consisted of - Period 1, patient received a single inhaled dose of indacaterol 300µg capsule via the Concept1 inhaler device. Period 2, patient received single dose of salmeterol 50µg via Diskus dry powder inhaler (DPI). Period 3, patient received single dose of indacaterol matching placebo via the Concept1 inhaler device. Part 2: Sequence 'A' consisted of - Period 1, patients received a morning single inhalational dose of indacaterol 300µg and an evening single inhalation dose of indacaterol matching placebo via the Concept1 inhaler device. Period 2, patients received morning and evening single inhalational dose of salmeterol 50µg via Diskus DPI. Period 3, patients received single inhalation dose of indacaterol matching placebo in morning and evening via Concept1 device. In Part 2 of the study, at 20 minutes following each dose, patients received three doses of nebulized salbutamol 2.5 mg at 20 minute intervals.

Part 1 : Sequence B, Part 2: Sequence B	Part 1: Sequence 'B' consisted of - Period 1, patient received a single inhaled dose of indacaterol 300µg capsule administered via the Concept1 inhaler device. Period 2, patient received single dose of indacaterol matching placebo via the Concept1 inhaler device. Period 3, patient received single dose of salmeterol 50µg via Diskus DPI. Part 2: Sequence 'B' consisted of - Period 1, patients received a morning single inhalational dose of indacaterol 300µg and an evening single inhalation dose of indacaterol matching placebo via the Concept1 inhaler device. Period 2, patients received single inhalation dose of indacaterol matching placebo in morning and evening via Concept1 device. Period 3, patients received morning and evening single inhalational dose of salmeterol 50µg via Diskus DPI. In Part 2 of the study, at 20 minutes following each dose, patients received three doses of nebulized salbutamol 2.5 mg at 20 minute intervals.
Part 1: Sequence C, Part 2: Sequence C	Part 1: Sequence 'C' consisted of - Period 1, patient received single dose of indacaterol matching placebo via the Concept1 inhaler device. Period 2, patient received single dose of salmeterol 50µg via Diskus DPI. Period 3, patient received a single inhaled dose of indacaterol 300µg capsule administered via the Concept1 inhaler device. Part 2: Sequence 'C' consisted of - Period 1, patients received single inhalation dose of indacaterol matching placebo in morning and evening via Concept1 device. Period 2, patients received morning and evening single inhalational dose of salmeterol 50µg via Diskus DPI. Period 3, patients received a morning single inhalational dose of indacaterol 300µg and an evening single inhalation dose of indacaterol matching placebo via the Concept1 inhaler device . In Part 2 of the study, at 20 minutes following each dose, patients received three doses of nebulized salbutamol 2.5 mg at 20 minute intervals.
Part 1; Sequence D, Part 2: Sequence D	Part 1: Sequence 'D' consisted of - Period 1, patient received single dose of indacaterol matching placebo via the Concept1 inhaler device. Period 2, patient received a single inhaled dose of indacaterol 300µg capsule administered via the Concept1 inhaler device. Period 3, patient received single dose of salmeterol 50µg via Diskus DPI. Part 2: Sequence 'D' consisted of - Period 1, patients received single inhalation dose of indacaterol matching placebo in morning and evening via Concept1 device. Period 2, patients received a morning single inhalational dose of indacaterol 300µg and an evening single inhalation dose of indacaterol matching placebo via the Concept1 inhaler device. Period 3, patients received morning and evening single inhalational dose of salmeterol 50µg via Diskus DPI. In Part 2 of the study, at 20 minutes following each dose, patients received three doses of nebulized salbutamol 2.5 mg at 20 minute intervals.

Part 1: Sequence E, Part 2: Sequence E	Part 1: Sequence 'E' consisted of - Period 1, patient received single dose of salmeterol 50µg via Diskus DPI. Period 2, patient received a single inhaled dose of indacaterol 300µg capsule administered via the Concept1 inhaler device. Period 3, patient received single dose of indacaterol matching placebo via the Concept1 inhaler device. Part 2: Sequence 'E' consisted of - Period 1, patients received morning and evening single inhalational dose of salmeterol 50µg via Diskus DPI. Period 2, patients received a morning single inhalational dose of indacaterol 300µg and an evening single inhalation dose of indacaterol matching placebo via the Concept1 inhaler device. Period 3, patients received single inhalation dose of indacaterol matching placebo in morning and evening via Concept1 device. In Part 2 of the study, at 20 minutes following each dose, patients received three doses of nebulized salbutamol 2.5 mg at 20 minute intervals.
Part 1: Sequence F, Part 2: Sequence F	Part 1: Sequence 'F' consisted of - Period 1, patient received single dose of salmeterol 50µg via Diskus DPI. Period 2, patient received single dose of indacaterol matching placebo via the Concept1 inhaler device. Period 3, patient received a single inhaled dose of indacaterol 300µg capsule administered via the Concept1 inhaler device. Part 2: Sequence 'F' consisted of - Period 1, patients received morning and evening single inhalational dose of salmeterol 50µg via Diskus DPI. Period 2, patients received single inhalation dose of indacaterol matching placebo in morning and evening via Concept1 device. Period 3, patients received a morning single inhalational dose of indacaterol 300µg and an evening single inhalation dose of indacaterol matching placebo via the Concept1 inhaler device. In Part 2 of the study, at 20 minutes following each dose, patients received three doses of nebulized salbutamol 2.5 mg at 20 minute intervals.
Total	Total of all reporting groups

Baseline Measures

	Part 1: Sequence A, Part 2: Sequence A	Part 1 : Sequence B, Part 2: Sequence B	Part 1: Sequence C, Part 2: Sequence C	Part 1; Sequence D, Part 2: Sequence D	Part 1: Sequence E, Part 2: Sequence E	Part 1: Sequence F, Part 2: Sequence F	Total
Number of Participants [units: participants]	**4**	**5**	**4**	**5**	**4**	**5**	**27**

Age [units: years] Mean (Standard Deviation)	**59.0 (9.20)**	**63.0 (7.58)**	**58.5 (5.07)**	**58.4 (5.18)**	**60.5 (5.80)**	**61.6 (5.86)**	**60.3 (6.17)**
Gender [units: participants]							
Female	**2**	**2**	**1**	**1**	**1**	**0**	**7**
Male	**2**	**3**	**3**	**4**	**3**	**5**	**20**

Outcome Measures

Hide All Outcome Measures

1. Primary: Percentage of Participants With Maximum Heart Rate Increase During Exercise in Part 1 of the Study [Time Frame: 24-hours post-dose on Day 1 (of each treatment)]

Measure Type	Primary
Measure Title	Percentage of Participants With Maximum Heart Rate Increase During Exercise in Part 1 of the Study
Measure Description	The percentage of patients with an increase of more than 10 beats per minute (bpm) in their heart rate following treatment with indacaterol and salmeterol compared to treatment with placebo was determined.
Time Frame	24-hours post-dose on Day 1 (of each treatment)
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 population consisted of all subjects who received at least one dose of study medication after randomization.

Reporting Groups

	Description
Part 1: Indacaterol 300µg	Patient received a single inhaled dose of indacaterol 300µg capsule via the Concept1 inhaler device. For each treatment period and for each patient, the doses were to be administered at approximately the same time in the morning (i.e. between 8 and 9am).
Part 1 : Salmeterol 50µg	Patient received single dose of salmeterol 50µg via Diskus DPI. For each treatment period and for each patient, the doses were to be administered at approximately the same time in the morning (i.e. between 8 and 9am).

Measured Values

	Part 1: Indacaterol 300µg	Part 1 : Salmeterol 50µg
Number of Participants Analyzed [units: participants]	**25**	**25**
Percentage of Participants With Maximum Heart Rate Increase During Exercise in Part 1 of the Study [units: Percentage of participants] Number (95% Confidence Interval)	**20.00 (6.83 to 40.70)**	**16.0 (4.54 to 36.0)**

No statistical analysis provided for Percentage of Participants With Maximum Heart Rate Increase During Exercise in Part 1 of the Study

2. Primary: Percentage of Participants With Maximum Heart Rate Increase During Salbutamol Administration in Part 2 of the Study [Time Frame: 24 hours post dose on Day 1]

Measure Type	Primary
Measure Title	Percentage of Participants With Maximum Heart Rate Increase During Salbutamol Administration in Part 2 of the Study
Measure Description	The percentage of patients with an increase of >= 10 beats per minute (bpm) in their heart rate (HR) following treatment with indacaterol and salmeterol compared to treatment with placebo over 24 hours in Part 2 was determined. • 0-12 hours: post first dose measurements up to second dose

	• 12-24 hours: post second dose measurement up to and including the 24 hour measurement • 0-24 hours: all post dose measurements up to and including the 24 hour measurement
Time Frame	24 hours post dose on Day 1
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.
Safety population. ECG monitoring was not performed successfully for three subjects in Part 2 during the afternoon monitoring. These subjects were therefore excluded from the analysis of heart rate. In a patient where data for the second 12 hour period is missing, 0-24 is not reported; hence the discrepancy of 4 and 3 subjects.

Reporting Groups

	Description
Part 2:Indacaterol 300µg Morning/Placebo Evening	Patients received a morning single inhalational dose of indacaterol 300µg and an evening single inhalation dose of indacaterol matching placebo via the Concept1 inhaler device. For each treatment period and for each patient, the doses were to be administered at approximately the same time in the morning (i.e. between 8 and 9am) and the evening dose between 8 and 9pm. 20 minutes following each dose, patients received three doses of nebulized salbutamol 2.5 mg at 20 minute intervals.
Part 2:Salmeterol 50µg Morning/Salmeterol 50µg Evening	Patients received morning and evening single inhalational dose of salmeterol 50µg via Diskus dry powder inhaler (DPI). For each treatment period and for each patient, the doses were to be administered at approximately the same time in the morning (i.e. between 8 and 9am) and the evening dose between 8 and 9pm. 20 minutes following each dose, patients received three doses of nebulized salbutamol 2.5 mg at 20 minute intervals.

Measured Values

	Part 2:Indacaterol 300µg Morning/Placebo Evening	**Part 2:Salmeterol 50µg Morning/Salmeterol 50µg Evening**

Number of Participants Analyzed [units: participants]	**23**	**23**
Percentage of Participants With Maximum Heart Rate Increase During Salbutamol Administration in Part 2 of the Study [units: Percentage of participants] Number (95% Confidence Interval)		
0 - 12 hours (N= 23,23)	**17.39 (4.95 to 38.78)**	**17.39 (4.95 to 38.78)**
12 - 24 hours (N= 20, 20)	**10.00 (1.23 to 31.70)**	**25.00 (8.66 to 49.10)**
0 - 24 hours (N= 23, 23)	**13.04 (2.78 to 33.59)**	**17.39 (4.95 to 38.78)**

No statistical analysis provided for Percentage of Participants With Maximum Heart Rate Increase During Salbutamol Administration in Part 2 of the Study

3. Primary: Maximum Heart Rate During Exercise in Part 1 [Time Frame: 2 hour post-dose on Day 1]

Measure Type	Primary
Measure Title	Maximum Heart Rate During Exercise in Part 1
Measure Description	Maximum heart rate was generally taken from the continuous ECG monitoring. Analysis based on mixed effects analysis using model with treatment and period as fixed effects and subject as random effect.
Time Frame	2 hour post-dose on Day 1
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 population consisted of all subjects who received at least one dose of study medication after randomization.

Reporting Groups

	Description
Part 1: Indacaterol 300µg	Patient received a single inhaled dose of indacaterol 300µg capsule via the Concept1 inhaler device. For each treatment period and for each patient, the doses were to be administered at approximately the same time in the morning (i.e. between 8 and 9am).
Part 1 : Salmeterol 50µg	Patient received single dose of salmeterol 50µg via Diskus DPI. For each treatment period and for each patient, the doses were to be administered at approximately the same time in the morning (i.e. between 8 and 9am).
Part 1: Placebo	Patient received single dose of indacaterol matching placebo via the Concept1 inhaler device. For each treatment period and for each patient, the doses were to be administered at approximately the same time in the morning (i.e. between 8 and 9am).

Measured Values

	Part 1: Indacaterol 300µg	**Part 1 : Salmeterol 50µg**	**Part 1: Placebo**
Number of Participants Analyzed [units: participants]	**26**	**25**	**26**
Maximum Heart Rate During Exercise in Part 1 [units: Beats per minute (bpm)] Least Squares Mean (95% Confidence Interval)	**133.13 (125.90 to 140.36)**	**131.18 (123.86 to 138.49)**	**129.96 (122.73 to 137.19)**

No statistical analysis provided for Maximum Heart Rate During Exercise in Part 1

4. Primary: Maximum Heart Rate (HR) During Salbutamol Administration in Part 2 [Time Frame: 24 hours post dose on Day 1]

Measure Type	Primary
Measure Title	Maximum Heart Rate (HR) During Salbutamol Administration in Part 2

Measure Description	Maximum HR (0-12 hours): maximum (max) of post dose measurement up to second administration. Maximum HR (12-24 hours): max of the post second administration of salbutamol measurements. Maximum HR (0-24 hours): max of all post dose measurements up to and including the 24 hour measurement. Mixed effects analysis model used period baseline HR as the covariate. The maximum HR for 0-24 hours (h) is the maximum of the maximum HR for the two 12h periods and thus the average (LS means) of the maximum HRs for 0-24h will be equal to or greater than the average of the maximum for the two periods.
Time Frame	24 hours post dose on Day 1
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 population consisted of all subjects who received at least one dose of study medication after randomization. ECG monitoring was not performed successfully for three subjects in Part 2 during the afternoon monitoring. These subjects were therefore excluded from the analysis of heart rate.

Reporting Groups

	Description
Part 2:Indacaterol 300µg Morning/Placebo Evening	Patients received a morning single inhalational dose of indacaterol 300µg and an evening single inhalation dose of indacaterol matching placebo via the Concept1 inhaler device. For each treatment period and for each patient, the doses were to be administered at approximately the same time in the morning (i.e. between 8 and 9am) and the evening dose between 8 and 9pm. 20 minutes following each dose, patients received three doses of nebulized salbutamol 2.5 mg at 20 minute intervals.
Part 2:Salmeterol 50µg Morning/Salmeterol 50µg Evening	Patients received morning and evening single inhalational dose of salmeterol 50µg via Diskus dry powder inhaler (DPI). For each treatment period and for each patient, the doses were to be administered at approximately the same time in the morning (i.e. between 8 and 9am) and the evening dose between 8 and 9pm. 20 minutes following each dose, patients received three doses of nebulized salbutamol 2.5 mg at 20 minute intervals.

Part 2:Placebo Morning/Placebo Evening	Patients received single inhalation dose of indacaterol matching placebo in morning and evening via Concept1 device. For each treatment period and for each patient, the doses were to be administered at approximately the same time in the morning (i.e. between 8 and 9am) and the evening dose between 8 and 9pm. 20 minutes following each dose, patients received three doses of nebulized salbutamol 2.5 mg at 20 minute intervals.

Measured Values

	Part 2:Indacaterol 300µg Morning/Placebo Evening	Part 2:Salmeterol 50µg Morning/Salmeterol 50µg Evening	Part 2:Placebo Morning/Placebo Evening
Number of Participants Analyzed [units: participants]	**23**	**24**	**23**
Maximum Heart Rate (HR) During Salbutamol Administration in Part 2 [units: Beats per minute (bpm)] Least Squares Mean (95% Confidence Interval)			
0 - 12 hours (N= 23, 24, 23)	**98.026 (90.407 to 105.645)**	**98.087 (90.575 to 105.598)**	**97.960 (90.317 to 105.603)**
12 - 24 hours (N= 20, 21, 20)	**97.179 (91.195 to 103.164)**	**99.954 (94.047 to 105.861)**	**97.786 (91.779 to 103.794)**
0 - 24 hours (N= 23, 24, 23)	**102.501 (95.504 to 109.498)**	**102.303 (95.394 to 109.212)**	**103.951 (96.931 to 110.971)**

No statistical analysis provided for Maximum Heart Rate (HR) During Salbutamol Administration in Part 2

5. Secondary: Change in Heart Rate During Exercise in Part 1 [Time Frame: 1.5 hour post dose to max heart rate during exercise]

Measure Type	Secondary

Measure Title	Change in Heart Rate During Exercise in Part 1
Measure Description	Change in heart rate is calculated from the 1.5 hour post dose to the maximum heart rate during exercise. Analysis of covariance included treatment and period as fixed effects, subject as random effect and 1.5 hour pre-exercise/post dose heart rate as a covariate.
Time Frame	1.5 hour post dose to max heart rate during exercise
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 population consisted of all subjects who received at least one dose of study medication after randomization.

Reporting Groups

	Description
Part 1: Indacaterol 300µg	Patient received a single inhaled dose of indacaterol 300µg capsule via the Concept1 inhaler device. For each treatment period and for each patient, the doses were to be administered at approximately the same time in the morning (i.e. between 8 and 9am).
Part 1 : Salmeterol 50µg	Patient received single dose of salmeterol 50µg via Diskus DPI. For each treatment period and for each patient, the doses were to be administered at approximately the same time in the morning (i.e. between 8 and 9am).
Part 1: Placebo	Patient received single dose of indacaterol matching placebo via the Concept1 inhaler device. For each treatment period and for each patient, the doses were to be administered at approximately the same time in the morning (i.e. between 8 and 9am).

Measured Values

	Part 1: Indacaterol 300µg	**Part 1 : Salmeterol 50µg**	**Part 1: Placebo**
Number of Participants Analyzed [units: participants]	**26**	**25**	**26**
Change in Heart Rate During Exercise in Part 1			

[units: Beats per minute (bpm)] Least Squares Mean (95% Confidence Interval)	**66.246 (58.941 to 73.551)**	**64.265 (56.868 to 71.663)**	**63.058 (55.761 to 70.355)**

No statistical analysis provided for Change in Heart Rate During Exercise in Part 1

6. Secondary: Trough Forced Expiratory Volume in 1 Second (FEV1) During Part 1 and Part 2 [Time Frame: 23 hours 30 minutes and 24 hours post-dose at Day 1]

Measure Type	Secondary
Measure Title	Trough Forced Expiratory Volume in 1 Second (FEV1) During Part 1 and Part 2
Measure Description	FEV1 was measured with spirometry conducted according to internationally accepted standards. Trough FEV1 was defined as the mean of the 23 hours 30 minutes and 24 hours post morning dose FEV1 measurements. Analysis of covariance included pre-dose FEV1 as covariate.
Time Frame	23 hours 30 minutes and 24 hours post-dose at Day 1
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 population consisted of all subjects who received at least one dose of study medication after randomization.

Reporting Groups

	Description
Part 1: Indacaterol 300µg	Patient received a single inhaled dose of indacaterol 300µg capsule via the Concept1 inhaler device. For each treatment period and for each patient, the doses were to be administered at approximately the same time in the morning (i.e. between 8 and 9am).
Part 1 : Salmeterol 50µg	Patient received single dose of salmeterol 50µg via Diskus DPI. For each

	treatment period and for each patient, the doses were to be administered at approximately the same time in the morning (i.e. between 8 and 9am).
Part 1: Placebo	Patient received single dose of indacaterol matching placebo via the Concept1 inhaler device. For each treatment period and for each patient, the doses were to be administered at approximately the same time in the morning (i.e. between 8 and 9am).
Part 2:Indacaterol 300µg Morning/Placebo Evening	Patients received a morning single inhalational dose of indacaterol 300µg and an evening single inhalation dose of indacaterol matching placebo via the Concept1 inhaler device. For each treatment period and for each patient, the doses were to be administered at approximately the same time in the morning (i.e. between 8 and 9am) and the evening dose between 8 and 9pm. 20 minutes following each dose, patients received three doses of nebulized salbutamol 2.5 mg at 20 minute intervals.
Part 2:Salmeterol 50µg Morning/Salmeterol 50µg Evening	Patients received morning and evening single inhalational dose of salmeterol 50µg via Diskus dry powder inhaler (DPI). For each treatment period and for each patient, the doses were to be administered at approximately the same time in the morning (i.e. between 8 and 9am) and the evening dose between 8 and 9pm. 20 minutes following each dose, patients received three doses of nebulized salbutamol 2.5 mg at 20 minute intervals.
Part 2:Placebo Morning/Placebo Evening	Patients received single inhalation dose of indacaterol matching placebo in morning and evening via Concept1 device. For each treatment period and for each patient, the doses were to be administered at approximately the same time in the morning (i.e. between 8 and 9am) and the evening dose between 8 and 9pm. 20 minutes following each dose, patients received three doses of nebulized salbutamol 2.5 mg at 20 minute intervals.

Measured Values

	Part 1: Indacaterol 300µg	**Part 1 : Salmeterol 50µg**	**Part 1: Placebo**	**Part 2:Indacaterol 300µg Morning/Placebo Evening**	**Part 2:Salmeterol 50µg Morning/Salmeterol 50µg Evening**	**Part 2:Placebo Morning/Placebo Evening**
Number of Participants						

Analyzed [units: participants]	**26**	**25**	**26**	**23**	**24**	**23**
Trough Forced Expiratory Volume in 1 Second (FEV1) During Part 1 and Part 2 [units: Liters] Least Squares Mean (95% Confidence Interval)	**1.72 (1.65 to 1.79)**	**1.59 (1.52 to 1.66)**	**1.56 (1.49 to 1.63)**	**1.75 (1.67 to 1.82)**	**1.68 (1.60 to 1.75)**	**1.54 (1.46 to 1.62)**

No statistical analysis provided for Trough Forced Expiratory Volume in 1 Second (FEV1) During Part 1 and Part 2

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	No text entered.
Additional Description	All patients who received at least one dose of treatment were included in the safety and tolerability evaluation.

Reporting Groups

	Description
Part 1:Indacaterol 300mcg	Patient received a single inhaled dose of indacaterol 300µg capsule via the Concept1 inhaler device. For each treatment period and for each patient, the doses were to be administered at approximately the same time in the morning (i.e. between 8 and 9am).
Part 1:Salmeterol 50mcg	Patient received single dose of salmeterol 50µg via Diskus DPI. For each treatment period and for each patient, the doses were to be administered at approximately the same time in the morning (i.e. between 8 and 9am).
Part 1:Placebo	Patient received single dose of indacaterol matching placebo via the Concept1 inhaler device. For each treatment period and for each patient, the doses were to be administered at approximately the same time in the morning (i.e. between 8 and 9am).

Part 2:Indacaterol 300µg Morning/Placebo Evening	Patients received a morning single inhalational dose of indacaterol 300µg and an evening single inhalation dose of indacaterol matching placebo via the Concept1 inhaler device. For each treatment period and for each patient, the doses were to be administered at approximately the same time in the morning (i.e. between 8 and 9am) and the evening dose between 8 and 9pm. 20 minutes following each dose, patients received three doses of nebulized salbutamol 2.5 mg at 20 minute intervals.
Part 2:Salmeterol AM 50mcg/Salmeterol PM 50mcg	Patients received morning and evening single inhalational dose of salmeterol 50µg via Diskus dry powder inhaler (DPI). For each treatment period and for each patient, the doses were to be administered at approximately the same time in the morning (i.e. between 8 and 9am) and the evening dose between 8 and 9pm. 20 minutes following each dose, patients received three doses of nebulized salbutamol 2.5 mg at 20 minute intervals.
Part 2:Placebo Morning/Placebo Evening	Patients received single inhalation dose of indacaterol matching placebo in morning and evening via Concept1 device. For each treatment period and for each patient, the doses were to be administered at approximately the same time in the morning (i.e. between 8 and 9am) and the evening dose between 8 and 9pm. 20 minutes following each dose, patients received three doses of nebulized salbutamol 2.5 mg at 20 minute intervals.

Serious Adverse Events

	Part 1:Indacaterol 300mcg	Part 1:Salmeterol 50mcg	Part 1:Placebo	Part 2:Indacaterol 300µg Morning/Placebo Evening	Part 2:Salmeterol AM 50mcg/Salmeterol PM 50mcg	Part 2:Placebo Morning/Placebo Evening
Total, serious adverse events						
# participants affected / at risk	**1/26 (3.85%)**	**0/25 (0.00%)**	**1/26 (3.85%)**	**0/23 (0.00%)**	**0/24 (0.00%)**	**0/23 (0.00%)**
Respiratory, thoracic and mediastinal disorders						
Chronic obstructive pulmonary disease						

† 1						
# participants affected / at risk	0/26 (0.00%)	0/25 (0.00%)	1/26 (3.85%)	0/23 (0.00%)	0/24 (0.00%)	0/23 (0.00%)
Surgical and medical procedures						
Tonsillectomy † 1						
# participants affected / at risk	1/26 (3.85%)	0/25 (0.00%)	0/26 (0.00%)	0/23 (0.00%)	0/24 (0.00%)	0/23 (0.00%)

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

Other Adverse Events

Hide Other Adverse Events

Time Frame	No text entered.
Additional Description	All patients who received at least one dose of treatment were included in the safety and tolerability evaluation.

Frequency Threshold

Threshold above which other adverse events are reported	3%

Reporting Groups

	Description
Part 1:Indacaterol 300mcg	Patient received a single inhaled dose of indacaterol 300µg capsule via the Concept1 inhaler device. For each treatment period and for each patient, the doses were to be administered at approximately the same time in the morning (i.e. between 8 and 9am).
Part 1:Salmeterol 50mcg	Patient received single dose of salmeterol 50µg via Diskus DPI. For each treatment

	period and for each patient, the doses were to be administered at approximately the same time in the morning (i.e. between 8 and 9am).
Part 1:Placebo	Patient received single dose of indacaterol matching placebo via the Concept1 inhaler device. For each treatment period and for each patient, the doses were to be administered at approximately the same time in the morning (i.e. between 8 and 9am).
Part 2:Indacaterol 300µg Morning/Placebo Evening	Patients received a morning single inhalational dose of indacaterol 300µg and an evening single inhalation dose of indacaterol matching placebo via the Concept1 inhaler device. For each treatment period and for each patient, the doses were to be administered at approximately the same time in the morning (i.e. between 8 and 9am) and the evening dose between 8 and 9pm. 20 minutes following each dose, patients received three doses of nebulized salbutamol 2.5 mg at 20 minute intervals.
Part 2:Salmeterol AM 50mcg/Salmeterol PM 50mcg	Patients received morning and evening single inhalational dose of salmeterol 50µg via Diskus dry powder inhaler (DPI). For each treatment period and for each patient, the doses were to be administered at approximately the same time in the morning (i.e. between 8 and 9am) and the evening dose between 8 and 9pm. 20 minutes following each dose, patients received three doses of nebulized salbutamol 2.5 mg at 20 minute intervals.
Part 2:Placebo Morning/Placebo Evening	Patients received single inhalation dose of indacaterol matching placebo in morning and evening via Concept1 device. For each treatment period and for each patient, the doses were to be administered at approximately the same time in the morning (i.e. between 8 and 9am) and the evening dose between 8 and 9pm. 20 minutes following each dose, patients received three doses of nebulized salbutamol 2.5 mg at 20 minute intervals.

Other Adverse Events

	Part 1:Indacaterol 300mcg	Part 1:Salmeterol 50mcg	Part 1:Placebo	Part 2:Indacaterol 300µg Morning/Placebo Evening	Part 2:Salmeterol AM 50mcg/Salmeterol PM 50mcg	Part 2:Placebo Morning/Placebo Evening
Total, other (not including serious) adverse events						
# participants affected / at risk	**9/26 (34.62%)**	**4/25 (16.00%)**	**4/26 (15.38%)**	**8/23 (34.78%)**	**8/24 (33.33%)**	**6/23 (26.09%)**

Cardiac disorders						
Atrial fibrillation † 1						
# participants affected / at risk	**0/26 (0.00%)**	**0/25 (0.00%)**	**0/26 (0.00%)**	**0/23 (0.00%)**	**1/24 (4.17%)**	**0/23 (0.00%)**
Palpitations † 1						
# participants affected / at risk	**0/26 (0.00%)**	**0/25 (0.00%)**	**0/26 (0.00%)**	**0/23 (0.00%)**	**1/24 (4.17%)**	**0/23 (0.00%)**
Gastrointestinal disorders						
Abdominal pain † 1						
# participants affected / at risk	**0/26 (0.00%)**	**0/25 (0.00%)**	**0/26 (0.00%)**	**1/23 (4.35%)**	**0/24 (0.00%)**	**0/23 (0.00%)**
Diarrhoea † 1						
# participants affected / at risk	**1/26 (3.85%)**	**0/25 (0.00%)**	**0/26 (0.00%)**	**1/23 (4.35%)**	**1/24 (4.17%)**	**0/23 (0.00%)**
Gingivitis † 1						
# participants affected / at risk	**0/26 (0.00%)**	**0/25 (0.00%)**	**0/26 (0.00%)**	**0/23 (0.00%)**	**1/24 (4.17%)**	**0/23 (0.00%)**
Toothache † 1						
# participants affected / at risk	**0/26 (0.00%)**	**0/25 (0.00%)**	**1/26 (3.85%)**	**0/23 (0.00%)**	**0/24 (0.00%)**	**0/23 (0.00%)**
General disorders						
Catheter thrombosis † 1						
# participants affected / at risk	**0/26 (0.00%)**	**1/25 (4.00%)**	**0/26 (0.00%)**	**0/23 (0.00%)**	**0/24 (0.00%)**	**0/23 (0.00%)**
Chills † 1						

# participants affected / at risk	0/26 (0.00%)	0/25 (0.00%)	0/26 (0.00%)	1/23 (4.35%)	0/24 (0.00%)	0/23 (0.00%)
Fatigue † [1]						
# participants affected / at risk	0/26 (0.00%)	0/25 (0.00%)	0/26 (0.00%)	0/23 (0.00%)	0/24 (0.00%)	1/23 (4.35%)
Feeling hot † [1]						
# participants affected / at risk	0/26 (0.00%)	0/25 (0.00%)	1/26 (3.85%)	0/23 (0.00%)	0/24 (0.00%)	0/23 (0.00%)
Pyrexia † [1]						
# participants affected / at risk	1/26 (3.85%)	0/25 (0.00%)	0/26 (0.00%)	0/23 (0.00%)	0/24 (0.00%)	0/23 (0.00%)
Infections and infestations						
Nasopharyngitis † [1]						
# participants affected / at risk	1/26 (3.85%)	0/25 (0.00%)	0/26 (0.00%)	1/23 (4.35%)	0/24 (0.00%)	1/23 (4.35%)
Tooth abscess † [1]						
# participants affected / at risk	0/26 (0.00%)	0/25 (0.00%)	1/26 (3.85%)	0/23 (0.00%)	0/24 (0.00%)	0/23 (0.00%)
Injury, poisoning and procedural complications						
Procedural dizziness † [1]						
# participants affected / at risk	0/26 (0.00%)	0/25 (0.00%)	1/26 (3.85%)	0/23 (0.00%)	0/24 (0.00%)	0/23 (0.00%)
Musculoskeletal and connective tissue disorders						
Musculoskeletal						

chest pain † 1						
# participants affected / at risk	1/26 (3.85%)	0/25 (0.00%)	0/26 (0.00%)	0/23 (0.00%)	0/24 (0.00%)	0/23 (0.00%)
Neck pain † 1						
# participants affected / at risk	0/26 (0.00%)	0/25 (0.00%)	0/26 (0.00%)	0/23 (0.00%)	0/24 (0.00%)	1/23 (4.35%)
Nervous system disorders						
Dizziness † 1						
# participants affected / at risk	1/26 (3.85%)	0/25 (0.00%)	0/26 (0.00%)	0/23 (0.00%)	1/24 (4.17%)	2/23 (8.70%)
Headache † 1						
# participants affected / at risk	0/26 (0.00%)	1/25 (4.00%)	1/26 (3.85%)	0/23 (0.00%)	2/24 (8.33%)	1/23 (4.35%)
Neuropathy peripheral † 1						
# participants affected / at risk	1/26 (3.85%)	0/25 (0.00%)	0/26 (0.00%)	0/23 (0.00%)	0/24 (0.00%)	0/23 (0.00%)
Tremor † 1						
# participants affected / at risk	0/26 (0.00%)	0/25 (0.00%)	0/26 (0.00%)	2/23 (8.70%)	3/24 (12.50%)	2/23 (8.70%)
Respiratory, thoracic and mediastinal disorders						
Cough † 1						
# participants affected / at risk	2/26 (7.69%)	0/25 (0.00%)	1/26 (3.85%)	1/23 (4.35%)	0/24 (0.00%)	0/23 (0.00%)
Dyspnoea † 1						
# participants	1/26 (3.85%)	1/25 (4.00%)	1/26 (3.85%)			

affected / at risk				0/23 (0.00%)	0/24 (0.00%)	0/23 (0.00%)
Pharyngolaryngeal pain † 1						
# participants affected / at risk	1/26 (3.85%)	0/25 (0.00%)	0/26 (0.00%)	0/23 (0.00%)	0/24 (0.00%)	0/23 (0.00%)
Productive cough † 1						
# participants affected / at risk	0/26 (0.00%)	1/25 (4.00%)	0/26 (0.00%)	0/23 (0.00%)	1/24 (4.17%)	0/23 (0.00%)
Skin and subcutaneous tissue disorders						
Erythema † 1						
# participants affected / at risk	1/26 (3.85%)	0/25 (0.00%)	0/26 (0.00%)	0/23 (0.00%)	0/24 (0.00%)	0/23 (0.00%)
Hyperhidrosis † 1						
# participants affected / at risk	0/26 (0.00%)	0/25 (0.00%)	1/26 (3.85%)	0/23 (0.00%)	0/24 (0.00%)	0/23 (0.00%)
Hypoaesthesia facial † 1						
# participants affected / at risk	0/26 (0.00%)	0/25 (0.00%)	0/26 (0.00%)	1/23 (4.35%)	1/24 (4.17%)	1/23 (4.35%)
Nail disorder † 1						
# participants affected / at risk	0/26 (0.00%)	0/25 (0.00%)	0/26 (0.00%)	0/23 (0.00%)	1/24 (4.17%)	0/23 (0.00%)
Pruritus generalised † 1						
# participants affected / at risk	0/26 (0.00%)	0/25 (0.00%)	0/26 (0.00%)	1/23 (4.35%)	0/24 (0.00%)	0/23 (0.00%)
Vascular disorders						
Diastolic						

hypertension † 1						
# participants affected / at risk	**0/26 (0.00%)**	**0/25 (0.00%)**	**0/26 (0.00%)**	**1/23 (4.35%)**	**0/24 (0.00%)**	**0/23 (0.00%)**

† 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:	Novartis
ClinicalTrials.gov Identifier:	NCT00531050 History of Changes
Other Study ID Numbers:	**CQAB149B2217**
Study First Received:	September 17, 2007
Results First Received:	July 29, 2011
Last Updated:	April 23, 2012
Health Authority:	Belgium: Federal Agency for Medicinal Products and Health Products