

# INFLOW study: a prospective observational study for assessment of indacaterol and other bronchodilators in symptomatic chronic obstructive pulmonary disease patients from Egypt

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**Background** The INdacaterol eFFectiveness and utiLizatiOn in COPD: real-World evaluation (INFLOW) study demonstrated significant improvements in health status with decreasing Clinical COPD Questionnaire (CCQ) scores in routine clinical practice with indacaterol (IND) and other bronchodilators from 12 countries in Asia, the Middle East and South Africa. Here, we report the data on real-life effectiveness of IND and other bronchodilators from Egypt.

**Methods** In this 6-month, noninterventional, open-label study, patients were prescribed IND (150 or 300 µg) or other long-acting β<sub>2</sub>-agonists (LABAs) or tiotropium (TIO) (monotherapy or in combination with IND or LABAs) as a part of routine medical care. Health status (CCQ scores), patient and physician satisfaction and safety were assessed.

**Results** Data were analysed from 152 patients (IND, *n*=88; IND+TIO, *n*=27; other-LABAs, *n*=6; TIO, *n*=10; and other-LABAs+TIO, *n*=21). At the end of the study, reduction from baseline CCQ total score was significant (*P*<0.0001) with IND and other treatments. Approximately 80% of patients were satisfied and physicians rated the current prescribed treatments as 'good' or 'very good' for over 70% of the patients. More than 80% of patients rated the indacaterol inhaler (Breezhaler) device as 'easy' and 'very easy to use',

## Introduction

Chronic obstructive pulmonary disease (COPD) is associated with progressively irreversible airflow limitation, which leads to decline in lung function and quality of life in elderly population [1].

The WHO estimates that 65 million people worldwide had moderate-to-severe COPD in 2004 and three million people died from COPD in 2005, which corresponds to 5% of all deaths globally, which would be the third leading cause by 2030 [2].

COPD is a significant public health challenge and the leading cause of morbidity and mortality, which contributes significantly to healthcare costs [3].

COPD prevalence varies in different geographic regions. A large epidemiological study that included data of greater than 60 000 interviewees from 11 countries of the Middle East, North Africa and Pakistan (BREATHE study) reported an overall prevalence of 3.6%, whereas the Asia-Pacific regional working group reported 6.3% prevalence across 12 Asian countries [4–6]. Despite the high COPD prevalence in the Middle East and North Africa [4], the BREATHE study reported that in these

and physicians rated over 70% of patients as 'clearly understood the use of the device'. No adverse events related to premature discontinuation were reported.

**Conclusion** In real-world settings, IND as monotherapy or in combination with TIO was effective in improving the health status in COPD patients and is well tolerated. The majority of patients reported that the Breezhaler device was easy to use. *Egypt J Bronchol* 2017 11:16–22

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**Keywords:** chronic obstructive pulmonary disease, Egypt, indacaterol, long-acting bronchodilator, real-life study

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countries COPD is underdiagnosed and inadequately treated [4]. The prevalence of COPD in Egypt is unknown as many times it remains undiagnosed [7].

Inhaled long-acting bronchodilators [long-acting β<sub>2</sub>-adrenergic agonists (LABAs) and long-acting muscarinic antagonists (LAMAs)] are central to the management of COPD. Global initiative for chronic obstructive lung disease (GOLD) recommends long-acting bronchodilators either alone or in combination for the maintenance treatment for COPD [1].

Long-acting bronchodilators with once-daily administration may be more convenient for patients and have the potential to improve compliance compared with more frequently administered agents. Once-daily agents may also affect the stability of airway tone, with the extended duration of bronchodilation provided by once-daily treatment increasing [8].

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Indacaterol (IND) maleate (Onbrez Breezhaler; Novartis, Basel, Switzerland) is a LABA, delivered through a low-resistance dry-powder inhaler, indicated for the maintenance treatment of airflow obstruction in adult COPD patients, which is approved in more than 100 countries as once-daily 150 and 300 µg doses; however, in the US it is approved as twice-daily 75 µg dose (Arcapta Neohaler; Novartis Pharma Stein AG Stein, Switzerland; Distributed by: Novartis Pharmaceuticals Corporation East Hanover, New Jersey 07936 © Novartis) [8].

In phase III studies, IND provided sustained 24-h bronchodilation and significantly better efficacy in terms of lung function, symptom control and health status compared with placebo, and comparable or superior efficacy compared with twice-daily LABAs and/or tiotropium (TIO) and was well tolerated [9,10].

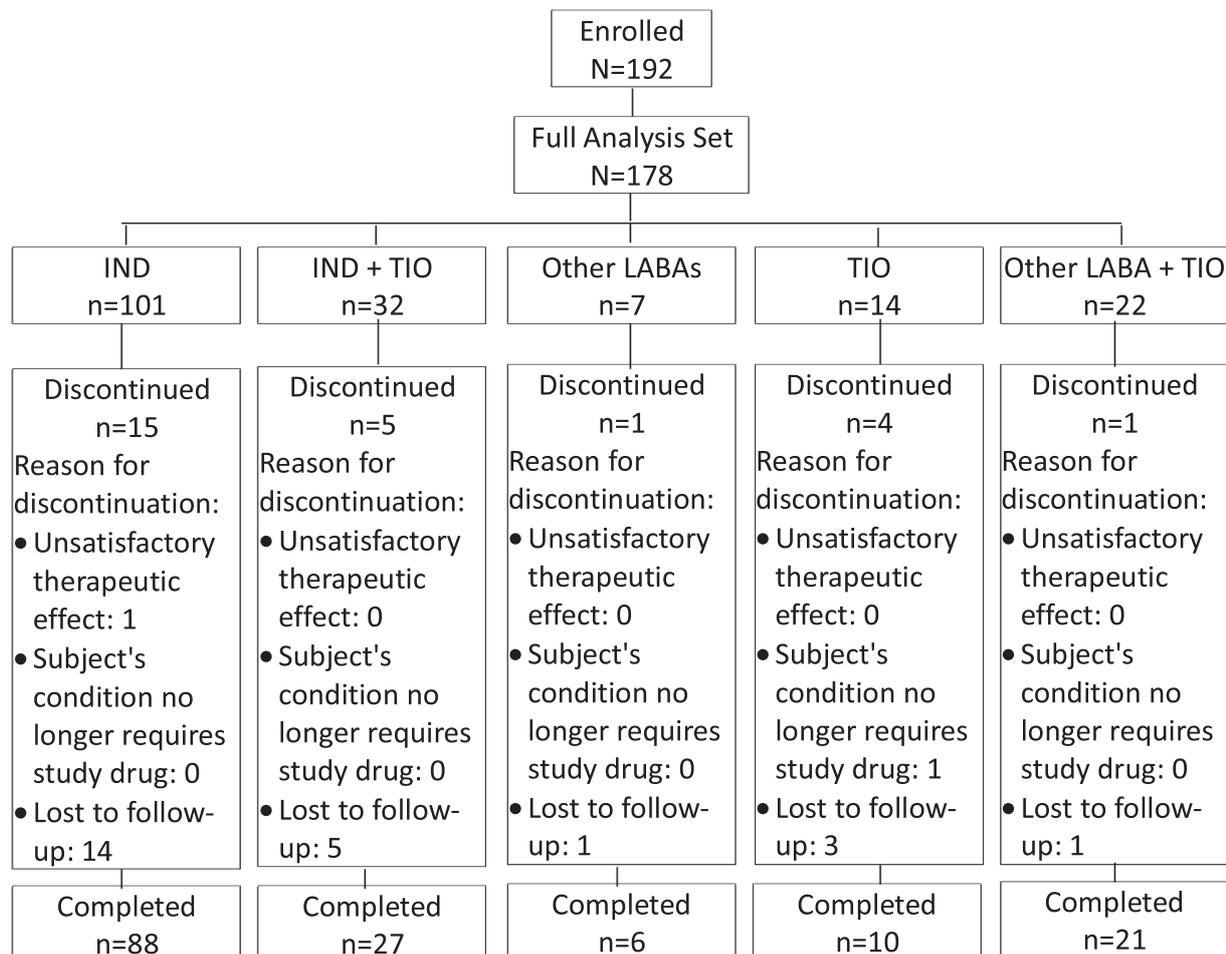
IND demonstrated better efficacy in terms of lung function and patient reported outcomes compared with TIO in a post-hoc analysis of pooled data from two prospective, controlled clinical trials including 1422

patients belonging to GOLD A and B groups without any history of exacerbations in the previous year [11].

Although the efficacy and safety data from controlled clinical trials are important, they may not accurately reflect outcomes observed in routine clinical practice owing to their study designs and stringent inclusion/exclusion criteria. Noninterventional studies provide useful complementary information on real-world effectiveness and safety of treatments when prescribed in routine clinical practice and in particular circumstances – for example, in different geographical regions and in ethnically diverse patient populations [12].

INFLOW (INdacaterol eFFectiveness and utiLizatiOn in COPD: real-World evaluation) programme comprised prospective, noninterventional studies conducted in the AMAC region (Asia, Middle East, and African countries) for assessing the effectiveness and safety of indacaterol (IND) and other bronchodilators in patients with symptomatic COPD.

Figure 1



Patient disposition. IND, indacaterol; TIO, tiotropium; n, number of patients in each group; N, total number of patients.

Overall pooled data and data at the individual country level were analysed to provide a comprehensive overview of the IND therapy. This manuscript presents the data on real-life effectiveness, safety and tolerability of IND treatment in patients with COPD from Egypt.

## Methods

### Study design

The INFLOW Egypt was a noninterventional, prospective, multicentre study conducted during the

period from 19 February 2013 to 16 January 2014 to assess the effectiveness and safety of IND, TIO and other inhaled LABAs in Egypt.

All treatments were prescribed according to the physician's judgement and clinical indication based on local prescribing information. The decision of prescribing treatments was independent of the decision to include the patient in the study.

**Table 1 Patients' demographics and baseline characteristics**

Parameters	IND	IND+TIO	Other LABAs	TIO	Other LABA+TIO	Total
	<i>n</i> =103	<i>n</i> =32	<i>n</i> =7	<i>n</i> =14	<i>n</i> =22	<i>N</i> =178
Age	58.26 (9.97)	60.19 (8.10)	62.29 (12.38)	57.57 (7.39)	60.50 (9.15)	58.99 (9.45)
Male [ <i>n</i> (%)]	99 (96.1)	32 (100.0)	7 (100.0)	12 (85.7)	22 (100.0)	172 (96.6)
Current smokers [ <i>n</i> (%)]	59 (57.3)	23 (71.9)	6 (85.7)	7 (50.0)	14 (63.6)	109 (61.2)
Packs/year	37.84 (31.25)	33.22 (22.89)	34.29 (26.99)	31.07 (16.89)	44.32 (29.80)	37.14 (28.61)
Prebronchodilator FEV <sub>1</sub> (l)	<i>n</i> =81 1.49 (0.66)	<i>n</i> =27 1.57 (0.78)	<i>n</i> =7 1.41 (0.56)	<i>n</i> =10 1.47 (0.71)	<i>n</i> =21 1.71 (0.56)	<i>n</i> =146 1.53 (0.66)
Postbronchodilator FEV <sub>1</sub> (l)	<i>n</i> =99 1.55 (0.76)	<i>n</i> =32 1.60 (0.74)	<i>n</i> =7 1.50 (0.55)	<i>n</i> =14 1.69 (0.70)	<i>n</i> =22 1.75 (0.62)	<i>n</i> =178 1.60 (0.72)
Prebronchodilator FEV <sub>1</sub> % predicted	<i>n</i> =82 49.12 (19.58)	<i>n</i> =27 47.96 (20.49)	<i>n</i> =7 49.37 (14.20)	<i>n</i> =11 55.55 (17.83)	<i>n</i> =21 52.72 (12.78)	<i>n</i> =148 49.91 (18.50)
Postbronchodilator FEV <sub>1</sub> % predicted	<i>n</i> =100 51.18 (19.27)	<i>n</i> =30 48.09 (21.63)	<i>n</i> =7 51.94 (15.55)	<i>n</i> =14 56.96 (18.51)	<i>n</i> =22 54.67 (15.47)	<i>n</i> =173 51.59 (19.02)
GOLD stage at study entry [ <i>n</i> (%)]						
GOLD I	4 (3.9)	2 (6.3)	0	1 (7.1)	0	7 (3.9)
GOLD II	46 (44.7)	9 (28.1)	2 (28.6)	5 (35.7)	16 (72.7)	78 (43.8)
GOLD III	40 (38.8)	17 (53.1)	5 (71.4)	7 (50.0)	5 (22.7)	74 (41.6)
GOLD IV	13 (12.6)	4 (12.5)	0	1 (7.1)	1 (4.5)	19 (10.7)
Number of COPD exacerbations in past 12 months ( <i>n</i> )	353	95	10	26	42	526
Number of hospitalizations due to COPD exacerbations in past 12 months ( <i>n</i> )	123	27	1	9	7	167
Prior COPD medication [ <i>n</i> (%)]						
Maintenance medication	93 (90.3)	29 (90.6)	6 (85.7)	11 (78.6)	22 (100.0)	161 (90.4)
Rescue medication	10 (9.7)	3 (9.4)	1 (14.3)	3 (21.4)	0	17 (9.6)
Baseline CCQ total scores	<i>n</i> =101 3.57 (0.90)	<i>n</i> =30 3.31 (0.81)	<i>n</i> =7 3.83 (1.24)	<i>n</i> =13 3.37 (0.70)	<i>n</i> =22 3.60 (0.96)	<i>n</i> =173 3.53 (0.89)

Data presented here are mean (SD) unless otherwise specified. CCQ, Clinical COPD Questionnaire; COPD, chronic obstructive pulmonary disease; FEV<sub>1</sub>, forced expiratory volume in 1 s; FVC, forced vital capacity; GOLD, global initiative for chronic obstructive lung disease; IND, indacaterol; LABA, long-acting  $\beta_2$ -agonist; TIO, tiotropium.

**Table 2 Patient satisfaction with previous treatment and current treatment**

	IND ( <i>n</i> =103)	IND+TIO ( <i>n</i> =32)	Other LABAs ( <i>n</i> =7)	TIO ( <i>n</i> =14)	Other LABA+TIO ( <i>n</i> =22)	Total ( <i>N</i> =178)
Patient satisfaction on previous treatment [ <i>n</i> (%)]						
Very satisfied	0	0	0	1 (7.1)	0	1 (0.6)
Satisfied	9 (8.7)	2 (6.3)	0	1 (7.1)	1 (4.5)	13 (7.3)
Average	37 (35.9)	8 (25.0)	0	1 (7.1)	4 (18.2)	50 (28.1)
Not satisfied	44 (42.7)	15 (46.9)	3 (42.9)	9 (64.3)	16 (72.7)	87 (48.9)
Patient satisfaction on current treatment [ <i>n</i> (%)]						
Very satisfied	42 (40.8)	9 (28.1)	2 (28.6)	0	2 (9.1)	55 (30.9)
Satisfied	37 (35.9)	17 (53.1)	4 (57.1)	9 (64.3)	18 (81.8)	85 (47.8)
Average	7 (6.8)	1 (3.1)	0	0	1 (4.5)	9 (5.1)
Not satisfied	0	0	0	0	0	0

For patients who switch cohort during the study, only data collected until the time of switch is included in the analysis. IND, indacaterol; LABA, long-acting  $\beta_2$ -agonist; TIO, tiotropium.

Patients were included in the IND, IND+TIO, other LABAs, TIO, and LABA+TIO groups and observed over 6 months ( $\pm 4$  weeks) and data originating from routine clinical practice were collected at baseline (study entry), month 1, month 3 and month 6. Study-specific visits, tests or monitoring were not compulsory for the observed patients. The study protocol was approved by the local ethics committees at participating centres.

**Patients**

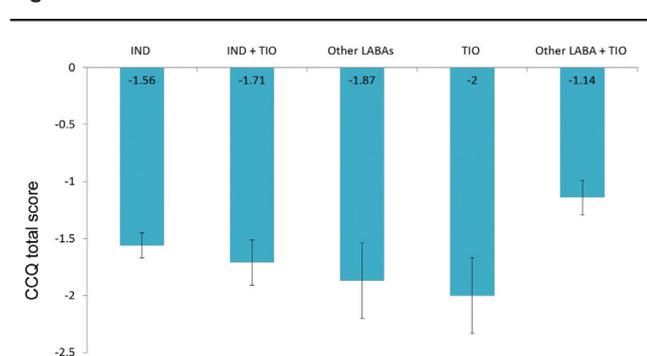
Key inclusion criteria were as follows: symptomatic mild-to-severe COPD [forced expiratory volume in 1 s ( $FEV_1$ )/forced vital capacity (FVC) $\leq 70\%$ ] according to the GOLD 2009 guidelines with a smoking history of at least 10 pack/year and aged 40 years and above [13]. Eligible patients were either on newly prescribed LABA or TIO as monotherapy or in combination, or switched from IND to other LABAs or TIO vice versa.

Key exclusion criteria included the following: prescribed drug contraindications, a previous diagnosis of asthma, acute exacerbations (requiring antibiotics or hospitalizations) at study entry, unwillingness or inability to comply with the study requirements, treatment with inhaled corticosteroids (ICS) at study entry or within 3 months before study entry, or treatment with two different LABAs, or in combination with ICS and triple therapy (LABA/LAMA/ICS).

**Assessments**

The effectiveness and patient acceptance, with the use of the Clinical COPD Questionnaire (CCQ), of IND monotherapy in relation to other LABA or TIO monotherapy, and IND+TIO combination therapy or other LABA+TIO combination were assessed. However, the CCQ total scores were not recorded at time of medication change and similarly by domains.

**Figure 2**



Changes from baseline in CCQ overall score in per-protocol set (last observation carried forward). Data are mean $\pm$ SE; all  $P < 0.0001$  for change in CCQ overall score from baseline to the end of the study. CCQ, Clinical COPD Questionnaire; LABA, long-acting  $\beta_2$ -agonist; TIO, tiotropium; IND, indacaterol.

Patient characteristics for COPD patients treated with IND and those treated with other LABA and TIO in a real-world scenario were described.

Evaluation of patients' persistence to previous and current treatments was carried out.

Evaluation of patients' and physicians' satisfaction with treatment was carried out.

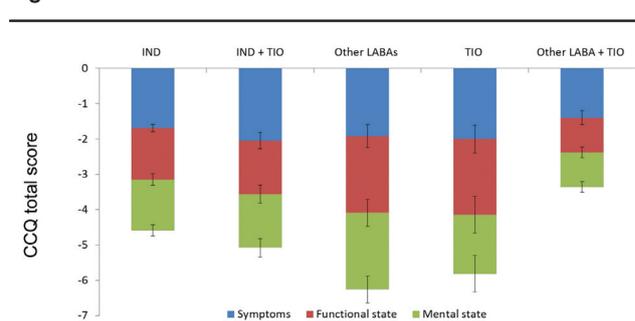
User-friendliness of Breezhaler device compared with other devices by patient and physician assessment was described.

Assessment of the safety and tolerability of IND, TIO, or other LABAs either as monotherapy or in combination was carried out.

**Statistical analyses**

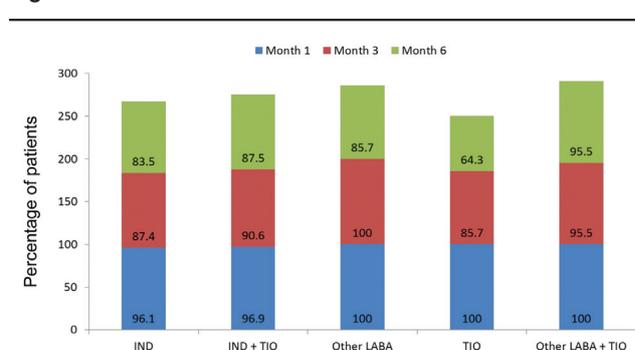
The full analysis set (FAS) comprised all patients who started treatment. The per-protocol population comprised the FAS but excluded patients who deviated from the

**Figure 3**



Changes from baseline in CCQ scores by domain (symptom, functional state and mental state) in per-protocol set (last observation carried forward). Data are mean $\pm$ SE; all  $P < 0.0001$  for change in CCQ scores by domain from baseline to the end of the study. CCQ, Clinical COPD Questionnaire; LABA, long-acting  $\beta_2$ -agonist; TIO, tiotropium; IND, indacaterol.

**Figure 4**



Persistence with treatment at month 1, 3 and at the end of the study. Full analysis set. Persistence is defined as a patient who is still taking the original COPD medication recorded, at baseline, at each subsequent time point. COPD, chronic obstructive pulmonary disease; LABA, long-acting  $\beta_2$ -agonist; TIO, tiotropium; IND, indacaterol.

protocol-specified criteria of age 40 years and above or baseline FEV<sub>1</sub>/FVC 70% or less.

The sample size was based on the feasible numbers of patients treated with the respective drugs, rather than on statistical considerations; a ratio of 2 : 1 (IND : other long-acting bronchodilators) was planned.

All effectiveness and safety evaluations were performed on the FAS except the CCQ-related analyses.

The CCQ analyses were performed on the per-protocol population. Changes from baseline in the CCQ total and domain scores were analysed using a two-sided *t*-test; a *P*-value less than 0.05 indicates a significant difference from baseline. If no CCQ value was available at the end of the study, then the last postbaseline observation was carried forward. Differences between treatments were not analysed.

## Results

Out of the 192 enrolled patients, 178 were included in the FAS, and 152 (85.4%) completed the trial (IND, 88; IND+TIO, 27; other LABAs, 6; TIO, 10 and LABA+TIO, 21). In total, 26 patients discontinued from the study, and the primary reason for discontinuation was loss to follow-up in 24 patients (13.5%) (Fig. 1).

Patient demographics and baseline characteristics are presented in Table 2. The mean age of the patients was 59±9.45 years, and the majority of them were male (*n*=172; 96.6%). All patients included in the study were Caucasians, with about 85% of patients having mild-to-moderate COPD (GOLD stage II and III) and about 11% of patients belonged to severe stage of COPD (GOLD IV). Baseline respiratory parameters were comparable between treatment groups. The mean baseline CCQ total score was 3.53 in all

**Table 3 Physician satisfaction with previous treatment and current treatment**

	IND ( <i>n</i> =103)	IND+TIO ( <i>n</i> =32)	Other LABAs ( <i>n</i> =7)	TIO ( <i>n</i> =14)	Other LABA+TIO ( <i>n</i> =22)	Total ( <i>N</i> =178)
<b>Effectiveness</b>						
Physician satisfaction on previous treatment [ <i>n</i> (%)]						
Below average	46 (44.7)	13 (40.6)	3 (42.9)	9 (64.3)	14 (63.6)	85 (47.8)
Average	35 (34.0)	11 (34.4)	0	2 (14.3)	6 (27.3)	54 (30.3)
Good	9 (8.7)	1 (3.1)	0	1 (7.1)	1 (4.5)	12 (6.7)
Very good	0	0	0	0	0	0
Physician satisfaction on current treatment [ <i>n</i> (%)]						
Below average	2 (1.9)	0	0	0	0	2 (1.1)
Average	26 (25.2)	5 (15.6)	2 (28.6)	1 (7.1)	2 (9.1)	36 (20.2)
Good	24 (23.3)	12 (37.5)	2 (28.6)	7 (50.0)	17 (77.3)	62 (34.8)
Very good	34 (33.0)	10 (31.3)	2 (28.6)	1 (7.1)	2 (9.1)	49 (27.5)
<b>Tolerability</b>						
Physician satisfaction on previous treatment [ <i>n</i> (%)]						
Below average	22 (21.4)	6 (18.8)	3 (42.9)	3 (21.4)	1 (4.5)	35 (19.7)
Average	45 (43.7)	15 (46.9)	0	6 (42.9)	13 (59.1)	79 (44.4)
Good	22 (21.4)	4 (12.5)	0	3 (21.4)	7 (31.8)	36 (20.2)
Very good	1 (1.0)	0	0	0	0	1 (0.6)
Physician satisfaction on current treatment [ <i>n</i> (%)]						
Below average	1 (1.0)	0	0	0	0	1 (0.6)
Average	10 (9.7)	0	1 (14.3)	1 (7.1)	0	12 (6.7)
Good	25 (24.3)	18 (56.3)	3 (42.9)	5 (35.7)	15 (68.2)	66 (37.1)
Very good	50 (48.5)	9 (28.1)	2 (28.6)	3 (21.4)	6 (27.3)	70 (39.3)
<b>Patient compliance</b>						
Physician satisfaction on previous treatment [ <i>n</i> (%)]						
Below average	33 (32.0)	9 (28.1)	3 (42.9)	5 (35.7)	5 (22.7)	55 (30.9)
Average	32 (31.1)	12 (37.5)	0	4 (28.6)	10 (45.5)	58 (32.6)
Good	21 (20.4)	3 (9.4)	0	3 (21.4)	6 (27.3)	33 (18.5)
Very good	4 (3.9)	1 (3.1)	0	0	0	5 (2.8)
Physician satisfaction on current treatment [ <i>n</i> (%)]						
Below average	1 (1.0)	1 (14.3)	1 (7.1)	0	0	1 (0.6)
Average	9 (8.7)	1 (14.3)	1 (7.1)	0	0	11 (6.2)
Good	28 (27.2)	15 (46.9)	3 (42.9)	5 (35.7)	10 (45.5)	61 (34.3)
Very good	48 (46.6)	12 (37.5)	2 (28.6)	3 (21.4)	11 (50.0)	76 (42.7)

For patients who switch cohort during the study, only data collected until the time of switch is included in the analysis. IND, indacaterol; LABA, long-acting  $\beta_2$ -agonist; TIO, tiotropium.

groups (Table 1). A total of 161 (90.4%) patients received maintenance medication for COPD and 17 (9.6%) patients received rescue medication.

In the per-protocol set, CCQ total scores significantly decreased from baseline to month 6/EOS in completers ( $-1.57 \pm 0.96$ ;  $P < 0.0001$ ) (Fig. 2). CCQ total scores also showed a significant decrease from baseline at month 6 in patients. Similarly, a significant decrease ( $P < 0.0001$ ) in all domains (symptoms, functional state and mental state) was observed (Fig. 3).

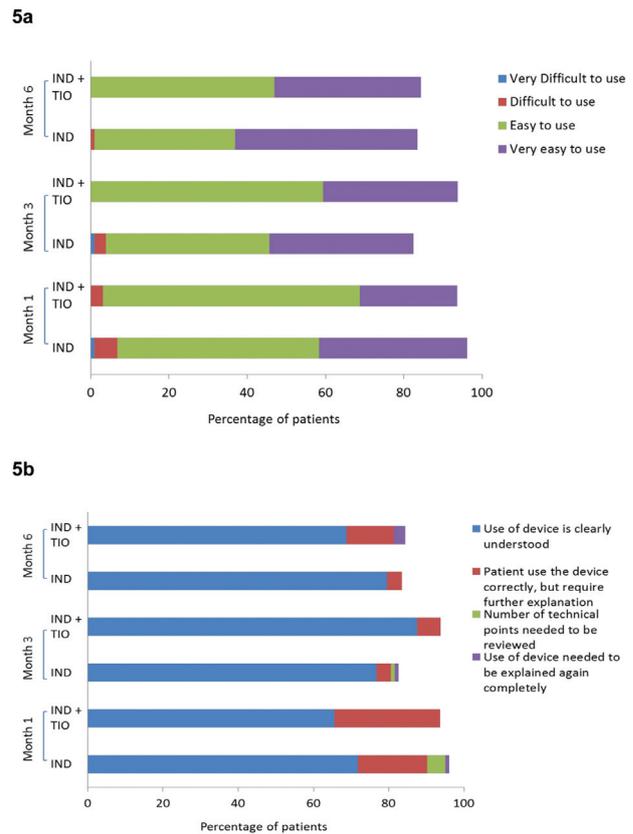
At month 1, 97.2% of patients were persistent with treatment, whereas 89.3% patients were persistent at month 3 and 84.3% patients were persistent at month 6 (Fig. 4).

Physician and patient satisfaction was analysed for the FAS. Patient's satisfaction for previous treatment was satisfied for 13 patients (7.3%), whereas 50 patients (28.1%) rated as average, and 87 patients (48.9%) rated as not satisfied (Table 2). The physician assessment was carried out on three domains - namely, effectiveness, tolerability and patient compliance. For previous treatment, physicians rated the effectiveness as below average for 85 (47.8%) patients and as average for 54 (30.3%) patients. Physicians rated the tolerability for 79 (44.4%) patients as average and for 35 (19.7%) patients as below average. The patient compliance was rated for 55 (30.9%) patients as below average and for 58 (32.6%) patients as average (Table 3). With current treatment, 140 (78.7%) patients were satisfied and very satisfied and physician's satisfaction was rated as good and very good in terms of effectiveness, tolerability and compliance for 111 (62.3%), 136 (76.4%) and 137 (77.0%) patients, respectively, with an overall missing data for 25 (14.0%) patients for current treatment (Tables 2 and 3).

At 1-month visit, 89.6% of patients rated the Breezhaler as easy and very easy to use, and the physician rated them as 'use of device clearly understood' for 70.4% patients. At 3-month visit, 82.2% of patients rated the Breezhaler as easy and very easy to use; the physician rated as 'use of device clearly understood' for 79.3% patients. At 6-month visit, 82.9% of patients rated the Breezhaler as easy and very easy to use; the physician rated for 77.0% patients as 'use of device clearly understood' (Fig. 5a and b).

The mean duration of exposure was as follows:  $22.97 \pm 8.01$  weeks for indacaterol;  $23.42 \pm 6.84$  weeks for indacaterol + tiotropium;  $23.84 \pm 5.41$  weeks for

Figure 5



(a, b) Patient and physician's assessment of inhaler device user-friendliness over the study. Full analysis set. For patients who switch cohort during the study, only data collected until the time of switch is included in the analysis. LABA, long-acting  $\beta_2$ -agonist; TIO, tiotropium; IND, indacaterol.

other LABA;  $21.30 \pm 8.32$  weeks for tiotropium; and  $25.43 \pm 4.94$  weeks for other LABA+tiotropium. The majority of patients in all groups were exposed to treatment for 24 weeks and more.

Most commonly reported adverse events (AEs) by system organ class are from respiratory thoracic and mediastinal disorders reported in 29 patients (16.3%). Incidences of AEs in at least 10% patients include COPD. None of the patients discontinued the study prematurely due to AEs. Moreover, no death was reported during the study (Table 4).

**Discussion**

The aim of the study was to assess the effectiveness and patients' and physicians acceptability of IND monotherapy in relation to other LABA, TIO or IND+TIO combination for the management of COPD through CCQ and other questionnaires along with their opinion towards the Breezhaler device in terms of ease of use.

**Table 4** Number (%) of patients with adverse events and serious adverse events

	IND (n=103)	IND+TIO (n=32)	Other LABAs (n=7)	TIO (n=14)	Other LABA+TIO (n=22)	Total (N=178)
Total AEs [n (%)]	29 (28.2)	4 (12.5)	3 (42.9)	2 (14.3)	9 (40.9)	47 (26.4)
n (%) of patients with most frequent AEs (occurring $\geq 2$ in any group)						
COPD	11 (10.7)	0	2 (28.6)	1 (7.1)	4 (18.2)	18 (10.1)
Cough	4 (3.9)	1 (3.1)	0	0	0	5 (2.8)
Lower respiratory tract infection	1 (1.0)	2 (6.3)	0	1 (7.1)	1 (4.5)	5 (2.8)
Infection	3 (2.9)	0	0	0	1 (4.5)	4 (2.2)
Dyspepsia	1 (1.0)	0	0	0	2 (9.1)	3 (1.7)
Tonsillitis	1 (1.0)	0	0	0	2 (9.1)	3 (1.7)
Oropharyngeal pain	2 (1.9)	0	1 (14.3)	0	0	3 (1.7)
Choking	2 (1.9)	0	0	0	0	2 (1.1)

AE, adverse event; COPD, chronic obstructive pulmonary disease; IND, indacaterol; LABA, long-acting  $\beta_2$ -agonist; TIO, tiotropium.

The results showed that indacaterol alone, or in combination with tiotropium or other LABA alone, or tiotropium alone significantly reduced CCQ scores ( $P < 0.0001$ ).

Persistence with COPD medication was 97.2% at month 1 and decreased to 84.3% at month 6. Persistence was 96.1% for IND at month 1 and decreased to 83.5% at month 6; the case was similar with IND+TIO (96.9% at month 1 and 87.5% at month 6), whereas for the TIO group persistence was 100% at month 1 and decreased to 64.3% at month 6.

With exception of COPD, incidence of AEs was at least 2% and no new AEs were reported in this study. IND showed good safety profile similar to other first-line drugs for the treatment of COPD.

In the real-world setting, indacaterol as monotherapy or in combination with tiotropium is effective in improving health status of COPD patients, is safe and well tolerated, and the majority of patients find the Breezhaler device easy to use.

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#### Conflicts of interest

There are no conflicts of interest.

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