Improvement in health status of chronic obstructive pulmonary disease (COPD) patients with indacaterol/glycopyrronium therapy: Real-world evidence from an observational study in Ireland

Brian O'Doherty[1]; Jane Dorman[2]; Karen McGrath[3]; Kevin Kelly[4]; David Molony[5]; Seán Lacey[6]; Sarah Whelan[7]; Simon Schmid[8]; Shane Sullivan[7]

[1]Gorey Medical Centre, Conal House, St. Michaels Road, Gorey, Co. Wexford, Ireland; [2]6 The Mall, Rathquarter, Sligo, Ireland; [3]SantryGP.ie Clinic, Unit 1 Northwood House, Northwood Business Park, Santry, Dublin, Ireland; [4]Western House Medical Centre, Western Rd, Clonmel, Co. Tipperary, Ireland; [5]The Red House Family Practice, Mallow, Co. Cork, Ireland; [6]Department of Mathematics, Cork Institute of Technology, Rossa Avenue, Bishopstown, Cork, T12 P928, Ireland; [7]Novartis Ireland Limited, Vista Building, Elm Park, Merrion Road, Dublin 4, Ireland; [8]Sandoz AG, Square 3, Novartis Campus, Fabrikstrasse 2, 4056 Basel, Switzerland

Introduction

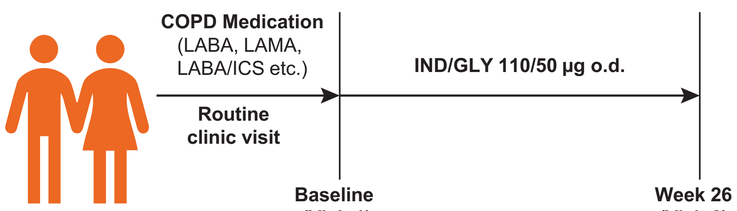
- In Ireland, approximately 500,000 people aged ≥40 years have chronic obstructive pulmonary disease (COPD), of whom over 200,000 have moderate or severe disease[1]
- Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2019 recommends COPD management based on symptoms or health status and lung function assessments. It recommends the use of validated questionnaires including clinical COPD questionnaire (CCQ) for assessment of health status in routine clinical practice[2]
- CCQ is a short (10-item), self-administered health-related quality of life (HRQoL) questionnaire consisting of symptoms, functional and mental state domains[3]
  - A reduction of 0.4 points in the CCQ total score indicates a minimal clinically important difference (MCID)[4]
- Indacaterol/glycopyrronium (IND/GLY) 110/50 µg once-daily (o.d.) is a fixed-dose combination of long-acting β_2-agonist/long-acting muscarinic antagonist (LABA/LAMA) approved in over 90 countries, including Ireland, for the management of COPD[5]
- To date, there is no evidence on the effectiveness of IND/GLY 110/50 µg o.d. on Irish COPD patients in a real-world setting
  - The ANÁIL study aimed to evaluate the health status of Irish COPD patients initiated on IND/GLY 110/50 µg o.d. using the CCQ tool in a real-world primary care setting in Ireland

Methods

Study design

- This was a prospective, open-label, multicentre, non-randomised, real-world study in Irish COPD patients (**Figure 1**)
  - Patients were initiated on or switched to IND/GLY 110/50 µg o.d. irrespective of prior therapy and followed for 26 weeks

Figure 1. Study design



ICS, inhaled corticosteroid; IND/GLY, indacaterol/glycopyrronium; LABA, long-acting β_2-agonist; LAMA, long-acting muscarinic antagonist; o.d., once daily

Patients

Key inclusion criteria

- Men and women aged >40 years
- Smoking history of >10 pack-years
- Post-bronchodilator forced expiratory volume in 1 sec (FEV_1)/forced vital capacity (FVC) <0.70
- Patients initiated on IND/GLY 110/50 µg o.d. regardless of prior therapy for COPD

Key exclusion criteria

- Patients with previous or current diagnosis of asthma
- Patients with cardiac or respiratory diseases unrelated to COPD
- Patients with known sensitivity to the active ingredients or any excipients in IND/GLY 110/50 µg dosage form

Outcomes

- Change from baseline in the CCQ total score and the proportion of patients achieving MCID of ≥0.4 unit reduction from baseline after 26 weeks of treatment with IND/GLY 110/50 µg o.d.
- Change from baseline in CCQ symptoms, functional and mental state domain scores after 26 weeks of treatment with IND/GLY 110/50 µg o.d.
- Change in CCQ total score and responders on switch to IND/GLY 110/50 µg o.d. from previous COPD treatments
- Safety in terms of adverse events (AEs), serious adverse events (SAEs), and discontinuation of IND/GLY 110/50 µg o.d. within 6 months of initiation

Statistical analysis

- All analyses were done descriptively. Categorical variables were summarised as absolute numbers and percentages; numerical data were summarised using standard statistical terms
- CCQ responders were defined as patients who achieved the MCID of ≥0.4 units difference from baseline in CCQ total score
- The correlation between CCQ total score and CCQ domain scores was assessed by Spearmen's correlation coefficient method
- Overall cohort consisted of patients who completed CCQ assessment at baseline, and CCQ cohort included patients who completed CCQ assessment at both baseline and Week 26

Results

Baseline demographics and clinical characteristics

- Of the 204 patients screened, 200 met the inclusion criteria and were included in the study
  - A total of 198 patients completed the CCQ assessment at baseline, and 156 patients completed the CCQ assessment at Week 26 and were included in CCQ cohort
- Baseline demographics and clinical characteristics are described in **Table 1**

Table 1. Baseline demographics and clinical characteristics (overall cohort)

Characteristic	Patients
Age, years	66.3 ± 9.54
Gender, n (%); n = 198	
Men	102 (51.5)
Women	96 (48.5)
BMI (kg/m²)	27.4 ± 5.63
Smokers, n (%)†; n = 195	96 (49.2)
Number of pack-years	45.4
Lung function assessments (n = 187)	
FEV_1, L	1.64 ± 0.65
FVC, L	2.73 ± 0.95
FEV_1/FVC, L	0.60 ± 0.11
Number of exacerbations in previous 12 months	1.99 ± 1.33
Severity of COPD, n (%)†; n = 195	
Group A	53 (27.2)
Group B	94 (48.2)
Group C	39 (20.0)
Group D	9 (4.6)

Data presented as mean ± SD, unless otherwise specified.

COPD severity is based on GOLD 2014 criteria

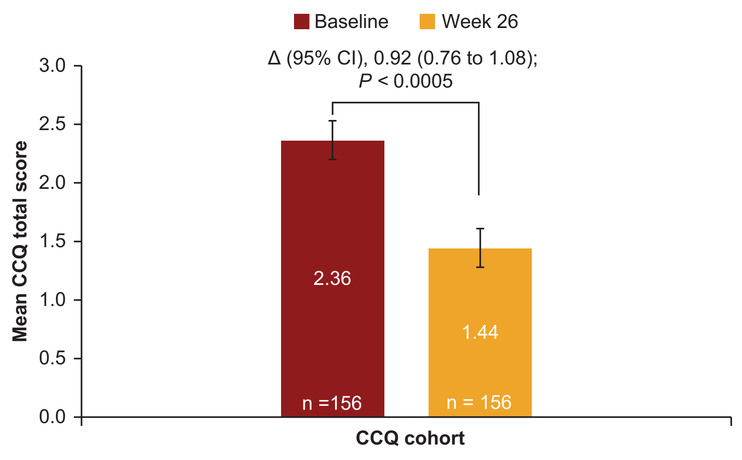
†Valid percent

BMI, body mass index; FEV_1, forced expiratory volume in one second; FVC, forced vital capacity; GOLD, Global Initiative for Chronic Obstructive Lung Disease

Change in CCQ total score from baseline and responder analysis

- At Week 26, IND/GLY 110/50 µg o.d. significantly reduced the CCQ total score from baseline by 0.98 in the overall cohort (2.42 vs 1.44; $P < 0.0005$)
- In the CCQ cohort, the mean CCQ total score decreased by 0.92 between baseline and Week 26 following treatment with IND/GLY 110/50 µg o.d. (2.36 vs 1.44; $P < 0.0005$; **Figure 2**)
- Decrease in the CCQ scores upon initiating IND/GLY 110/50 µg o.d. was independent of the baseline lung function and exacerbation history (data not shown)

Figure 2. Change in the mean CCQ total scores between baseline and Week 26 (CCQ cohort)



Data presented as mean (95% CI). Δ, difference in CCQ total score between baseline and Week 26

CCQ, clinical COPD questionnaire

- At Week 26, 72.4% (113/156) of patients achieved MCID of ≥0.4 unit reduction in the mean CCQ total score from baseline with IND/GLY 110/50 µg o.d.

Change in CCQ domain scores from baseline

- The mean CCQ domain scores (symptoms, functional and mental scores) decreased from baseline to Week 26 (**Figure 3**), and positively correlated with the decrease in the mean CCQ total score (Spearman's correlation coefficient (r_s) of 0.811, 0.845 and 0.72 for symptoms, functional and mental score, respectively)

Figure 3. CCQ domain scores at baseline and Week 26 (CCQ cohort)

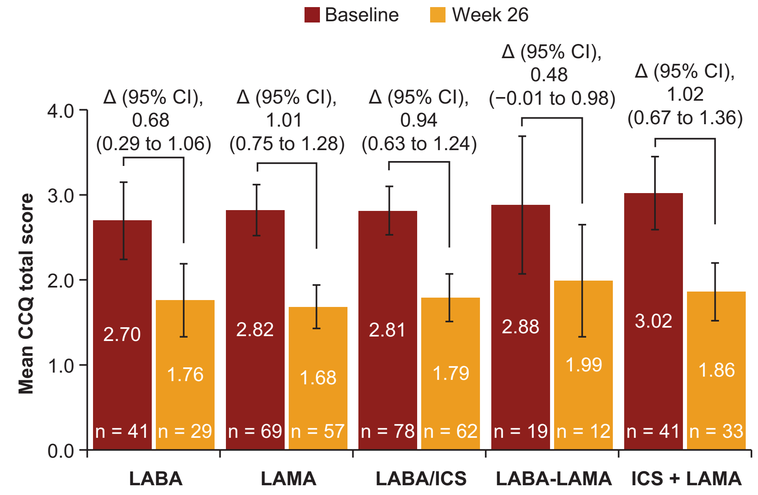
Δ, difference between the baseline and Week 26

CCQ, clinical COPD questionnaire; CI, confidence interval

Change in CCQ total scores in subgroups based on prior COPD treatment

- Decrease in the mean CCQ total score was observed in patients who switched to IND/GLY 110/50 µg o.d. from previous COPD treatments including LABA, LABA/ICS, LAMA, LABA-LAMA and ICS-containing triple therapy (**Figure 4**)

Figure 4. CCQ total score after switching to IND/GLY 110/50 µg from prior COPD treatments



Data presented as mean (95% CI). Δ, difference in CCQ total score between baseline and Week 26

CCQ, clinical COPD questionnaire; ICS, inhaled corticosteroid; LABA, long-acting β_2-agonist; LAMA, long-acting muscarinic antagonist

- The odds of having a particular treatment in CCQ responders versus CCQ non-responders is presented in **Table 2**

Table 2. CCQ responder analysis for COPD treatments at baseline

Treatment	OR (95% CI)
LABA	0.29 (0.12 to 0.71)
LABA/ICS	0.90 (0.40 to 2.05)
LAMA	1.42 (0.89 to 1.73)
SABA	1.19 (0.50 to 2.85)
SABA/SAMA*	NA
SAMA	4.31 (0.53 to 35.10)
Theophylline*	NA

OR calculated as odds of CCQ responders treated with particular COPD treatment/odds of CCQ non-responders treated with particular COPD treatment

*The OR could not be calculated as there were no patients who had the drug and who were CCQ non-responders

CCQ, clinical COPD questionnaire; ICS, inhaled corticosteroid; LABA, long-acting β_2-agonist; LAMA, long-acting muscarinic antagonist; NA, not available; OR, odds ratio; SABA, short-acting β_2-agonist; SAMA, short-acting muscarinic antagonist

Safety

- Twenty percent of patients reported at least one AE, with exacerbation/infected COPD being the most common (n = 14), reported by 11 patients. IND/GLY 110/50 µg was discontinued by 57 patients during the study
- In total, seven SAEs were reported in six patients. Three deaths due to myocardial infarction, unrelated cause, and pulmonary embolism occurred during the study period
- No AEs were definitely caused by the study drug

Conclusions

- In the real-world Irish setting, indacaterol/glycopyrronium 110/50 µg o.d. demonstrated a statistically significant and clinically meaningful improvement in health status
- Majority of COPD patients initiated on indacaterol/glycopyrronium 110/50 µg o.d. were classified as CCQ responders
- Majority (75%) of patients who completed the study continued treatment with indacaterol/glycopyrronium 110/50 µg o.d.
- Indacaterol/glycopyrronium 110/50 µg o.d. was well tolerated with safety profile similar to randomised clinical trials

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