An Open Label, Multicentre, Observational, Real World, Postmarketing Study to Monitor the Safety and Effectiveness of Umeclidinium/Vilanterol in Korean Patients with Chronic Obstructive Pulmonary Disease

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Eun-Yeong Cho[1], Jung-Eun Cho[1], Eun-Bin Lee[1], Seung Soo Yoo[2], Jung Hyun Chang[3]

[1]GlaxoSmithKline Korea, Seoul, Korea; [2]Kyungpook National University, Daegu, Korea; [3]Ewha Womans University Mokdong Hospital, Seoul, Korea

Introduction

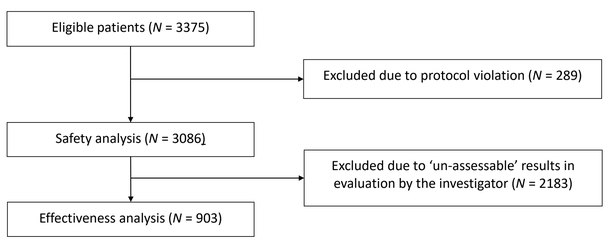
- Umeclidinium/vilanterol (UMEC/VI; ANORO ELLIPTA) is a commonly used dual bronchodilator. However, safety and efficacy data for UMEC/VI in Asian patients is currently lacking.
- This study evaluated the safety and effectiveness of UMEC/VI in Korean patients with chronic obstructive pulmonary disease (COPD) over a 6-year period.

Methods

- An open-label, multicentre, observational, postmarketing surveillance study (GSK sponsored study 204511).
- A total of 3375 patients were enrolled consecutively in 52 hospitals, by 53 physicians, between July 2014 and July 2020.
- 289 patients were excluded due to protocol violation. Thus, 3086 patients were included in the safety analysis. Among those, 903 patients were included in the effectiveness analysis set (**Figure 1**).
- Incidence and severity of adverse events (AEs) reported after administrating at least one dose of UMEC/VI were monitored, including unexpected adverse events (UAEs) and adverse drug reactions (ADRs).
- Effectiveness of UMEC/VI after 24 weeks of administration was also assessed using physician's evaluation (effective, ineffective/no change, worsening, indeterminable) and lung function improvement.

Key inclusion criteria	Key exclusion criteria
• Patients who were administered UMEC/VI (fixed-dose 62.5 µg/25 µg) at least once and were monitored for safety and effectiveness	• Patients with asthma • Acutely deteriorating COPD • Hypersensitivity to UMEC/VI or its components • A severe milk protein allergy, galactose intolerance, Lapp lactase deficiency, or glucose-galactose malabsorption

Figure 1. Study flow diagram



Results

Table 1. Characteristics of the patient population (N=3086)

Men, n (%)	2652 (85.9)
Age, years mean±SD	69.8±8.8
≥ 65 years	2255(73.07%)
Smoking history, n (%)	
Current smoker	814 (26.4)
Ex-smoker	1623 (52.6)
Never smoker	649 (21.0)
COPD exacerbation history (moderate/severe) ≤12 months, n (%)	
0	2807 (91.0)
1	220 (7.1)
2	44 (1.4)
≥3	15 (0.5)
COPD treatment prior to UMEC/VI treatment, n (%)	3086 (100.0)
Yes	1258 (40.8)
Classification of prior medication related to COPD†	1258 (100.0)
LABD* with or without ICS	1199 (95.3)
ICS/LABA	450 (35.8)
LABA	200 (15.9)
LAMA	776 (61.7)
Other LAMA/LABA (except UMEC/VI)	154 (12.2)

†The number of subjects (%) for the classification of prior medication related to COPD are calculated based on the subjects whose prior medication related to COPD is 'Yes'.
*LABD: Long-acting bronchodilator

Table 2. Summary of AE, ADR and SAE (N=3086)

	No. of patients with AEs, n (%)	No. of events
Total AEs	890 (28.8)	1463
Most frequent AEs*		
Dyspnoea	102 (3.3)	106
Cough	90 (2.9)	90
COPD	77 (2.5)	87
Upper respiratory tract infection	89 (2.9)	98
ADRs	67 (2.2)	74
SAEs	181 (5.9)	212
Serious ADRs	3 (0.1)	3
UAEs	665 (21.6)	1036
Unexpected ADRs	25 (0.8)	27
Unexpected SAEs	161 (5.2)	192
Unexpected serious ADRs	2 (0.06)	2

Abbreviations: ADR, adverse drug reaction; AE, adverse event; SAE, serious adverse event; UAE, unexpected adverse event.

- Of 3086 patients, 85.9% were male and 73.1% were aged ≥65 years. Mean age was 69.8 years and mean duration of disease was 2.5 years. Ex-smokers comprised 52.6% of the population, current smokers 26.4%, and never smokers 21.0%. Overall, 9.0% of patients (n=279) experienced moderate or severe COPD exacerbation at least once within ≤12 months and 40.8% patients used COPD treatment prior to enrolment (**Table 1**).
- Overall incidence of AEs was 28.8% (n=890), of which 2.2% (n=67) were ADRs. Serious AEs and UAEs were reported in 181 (5.9%) and 665 (21.6%) patients, respectively. Dyspnoea, cough, COPD and upper respiratory tract infection were the most reported AEs (11.6%). The most reported SAEs were COPD, pneumonia, and dyspnoea. Serious ADRs were reported by 3 patients (0.1%; one COPD, one pneumonia, one glaucoma). UAEs were seen in 21.6% of patients and unexpected ADRs in 0.8% of patients with nausea being the most reported (0.2%, n=6). Unexpected SAEs were reported by 5.2% patients and two unexpected serious ADRs (0.01%) were reported (one COPD, one pneumonia) (**Table 2**).

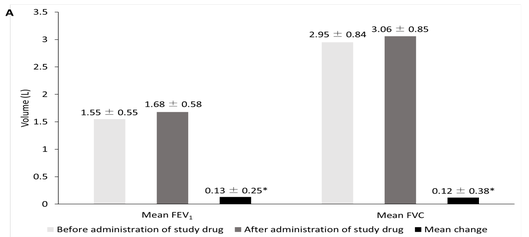
Table 3. Logistic regression for AEs: safety analysis set

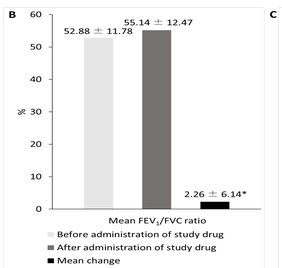
Variable	Parameter estimate	SE	Wald Chi-Square	p-value	OR	95% CI
Intercept	-1.98	0.37	29.02	< 0.0001		
Age (years)	0.00	0.00	0.04	0.8474	1.00	(0.99, 1.01)
Disease duration (years)	0.00	0.01	0.06	0.8010	1.00	(0.98, 1.03)
COPD exacerbation history (at least moderate severity) within ≤12 months						
Yes vs. no	0.32	0.14	5.30	0.0213*	1.37	(1.05, 1.80)
Smoking history						
Current smoker vs. non-smoker	-0.08	0.11	0.59	0.4406	0.92	(0.75, 1.14)
Ex-smoker vs. non-smoker	-0.30	0.12	5.61	0.0178*	0.74	(0.58, 0.95)
Medical history*						
Yes vs. no	-0.01	0.12	0.00	0.9581	0.99	(0.78, 1.27)
Total treatment administration duration within investigation period (days)	0.00	0.00	4.04	0.0445*	1.00	(1.00, 1.00)
Prior medication related to COPD						
Yes vs. no	0.21	0.09	5.11	0.0238*	1.23	(1.03, 1.47)
Concomitant medication related to COPD						
Yes vs. no	0.22	0.09	5.74	0.0166*	1.25	(1.04, 1.49)
Concomitant medication not related to COPD						
Yes vs. no	1.03	0.11	82.23	< 0.0001*	2.81	(2.25, 3.51)

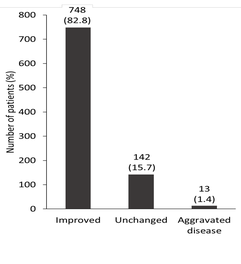
Dependent variable: reference category 'No'. Independent variable: factors with the p-value < 0.05 in the special populations and demographical and baseline data. In the analysis, age was used for elderly population and continuous data were used for disease duration and total treatment administration duration. *Includes previous diagnosis of CVD, osteoporosis, diabetes, and lung cancer.

- The factors significantly affecting AE occurrence were COPD exacerbation of at least moderate severity within ≤12-month(p=0.0213), smoking status (p=0.0178), total treatment administration period(p=0.0445), COPD-related prior medication (p=0.0238), COPD-related concomitant medication(p=0.0166), and concomitant medication not related to COPD (p=,0.0001) (**Table 3**).
- FEV1 values were collected before and after study drug administration in 898/903 patients in the effectiveness analysis. Mean FEV1±SD was 1.55±0.55 L before administration and 1.68±0.58 L after administration; mean change in FEV1 was 0.13±0.25 L (p<0.0001) **(Figure 2A).** Mean FVC was 2.95±0.84 L before administration and 3.06±0.85 L after administration; mean change in FVC was 0.12±0.38 L (p<0.0001) **(Figure 2A).** Mean change in FEV1/FVC ratio was 2.26±6.14% (p<0.0001) **(Figure 2B).**

Figure 2. (A) FEV1 and FVC measurements of patients before/after administration of study drug and mean change in FEV1; (B) Mean FEV1/FVC ratio measurements of patients before/after administration of study drug and mean change in FEV1/FVC ratio; (C) Investigator-assessed effectiveness







- Investigator-assessed effectiveness revealed most of patients(82.8%,n=748), showed overall disease improvement after UMEC/VI treatment (**Figure 2C**).

Summary

- In this study, UMEC/VI(62.5 µg/25 µg) was well tolerated in Korean patients with COPD. Adverse effects considered a 'class effect' of LAMA/LABA treatment were either not or rarely observed. The majority (82.8%) of patients analysed for effectiveness showed overall disease improvement after UMEC/VI treatment.

Conclusions

UMEC/VI administered to Korean patients according to the prescribing information, was well tolerated and can be considered an effective option for COPD treatment.

Abbreviations

COPD, chronic obstructive pulmonary disease; ICS, inhaled corticosteroid; LABA, long-acting beta-2-agonist; LABD, long-acting bronchodilator; LAMA, long-acting muscarinic antagonist; SD, standard deviation; UMEC/VI, umeclidinium trifenatate/vilanterol bromide

Disclosures

- This study was funded by GlaxoSmithKline (GSK study 204511).
- ANORO and ELLIPTA are owned by or licensed to the GSK group of companies.
- Audio recording of this poster was prepared by Eun-Yeong Cho, who is GSK employee and 1st author in this study.
- Eun-Yeong Cho, Jung-Eun Cho and Eun-Bin Lee are GlaxoSmithKline employees.
- Pf. Seung Soo Yoo and Pf. Jung Hyun Chang disclosed no conflict of interests.

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