UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, DC 20549

FORM 8-K

Current Report Pursuant
to Section 13 or 15(d) of the
Securities Exchange Act of 1934

Date of Report (Date of earliest event Reported): **May 21, 2013**

THERAVANCE, INC.

(Exact Name of Registrant as Specified in its Charter)

Delaware	**000-30319**	**94-3265960**
(State or Other Jurisdiction of Incorporation)	(Commission File Number)	(I.R.S. Employer Identification Number)

901 Gateway Boulevard
South San Francisco, California 94080
(650) 808-6000
(Addresses, including zip code, and telephone numbers, including area code, of principal executive offices)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

o Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

o Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

o Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

o Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Item 8.01 Other Events.

On May 21, 2013 at the American Thoracic Society International Conference in Philadelphia, Pennsylvania, GlaxoSmithKline plc (GSK) presented posters containing information from Phase 3 studies of the combination treatment fluticasone furoate/vilanterol (FF/VI), Phase 3 studies of the combination treatment umeclidinium bromide (UMEC)/VI. FF/VI, known in the United States as BREO™ ELLIPTA™ (100/25mcg), recently gained U.S. Food and Drug Administration approval as an inhaled long-term, once-daily maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema. It is also indicated to reduce exacerbations of COPD in patients with a history of exacerbations. It is not indicated for the relief of acute bronchospasm or the treatment of asthma. FF/VI remains in development elsewhere in the world for the maintenance treatment of asthma and COPD, with pending marketing authorization applications in a number of countries. It is not currently approved or licensed in the European Union or anywhere outside of the U.S. UMEC, a long-acting muscarinic antagonist, combined with VI, a LABA, is a once-daily investigational medicine for the maintenance treatment of patients with COPD. FF/VI and UMEC/VI are in development under the LABA collaboration agreement between GSK and Theravance, Inc. The posters are filed as Exhibits 99.1 to 99.4 to this report and are incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit	**Description**
Exhibit 99.1	Effect of fluticasone furoate (FF)/vilanterol (VI) compared with VI on COPD exacerbations: a pre-specified subgroup analysis

Exhibit 99.2 Efficacy of fluticasone furoate (FF)/vilanterol (VI) on lung function in COPD: a pre-specified subgroup analysis

Exhibit 99.3 The efficacy and safety of umeclidinium/vilanterol compared with tiotropium in COPD

Exhibit 99.4 Efficacy and safety of once-daily umeclidinium/vilanterol 62.5/25mcg in patients with COPD

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

THERAVANCE, INC.

Date: May 21, 2013

By: /s/ **Michael W. Aguiar**
Michael W. Aguiar
Chief Financial Officer

EXHIBIT INDEX

Exhibit No.	Description
Exhibit 99.1	Effect of fluticasone furoate (FF)/vilanterol (VI) compared with VI on COPD exacerbations: a pre-specified subgroup analysis
Exhibit 99.2	Efficacy of fluticasone furoate (FF)/vilanterol (VI) on lung function in COPD: a pre-specified subgroup analysis
Exhibit 99.3	The efficacy and safety of umeclidinium/vilanterol compared with tiotropium in COPD
Exhibit 99.4	Efficacy and safety of once-daily umeclidinium/vilanterol 62.5/25mcg in patients with COPD

POSTER NO. G16

Effect of fluticasone furoate (FF)/vilanterol (VI) compared with VI on COPD exacerbations: a pre-specified subgroup analysis

Dransfield MT(1), Calverley PMA(2), Bourbeau J(3), Jones P(4), Hanania NA(5), Mahler DA(6), Vestbo J(7), Wachtel A(8), Martinez F(9), Barnhart F(10), Midwinter DA(11), Lettis S(11), Crim C(10)

(1)University of Alabama at Birmingham, Birmingham, AL, USA; (2)University of Liverpool, Liverpool, UK; (3)McGill University, Montreal, Canada; (4)St George's University of London, London, UK; (5)Baylor College of Medicine, Houston, TX, USA; (6)Dartmouth Medical School, Hanover, NH, USA; (7)Manchester Academic Health Sciences Centre, Manchester, UK; (8)UCLA School of Medicine, Los Angeles, CA, USA; (9)University of Michigan, Ann Arbor, MI, USA; (10)Respiratory Medicine Development Center, GlaxoSmithKline, RTP, NC, USA; (11)Quantitative Sciences Division, GlaxoSmithKline, Uxbridge, UK

INTRODUCTION

- FF/VI is a novel, once-daily ICS/LABA combination therapy for treatment of patients with COPD, which significantly reduces the annual rate of moderate/severe COPD exacerbations compared with VI alone in COPD patients.(1)

OBJECTIVE

- This analysis compares the effect of FF/VI vs. VI on the annual rate of moderate/severe exacerbations of COPD in seven pre-specified subgroups.

METHODS

- Data from two phase III, multi-center, randomized, double-blind, parallel-group studies identical in design, conduct and analysis, were pooled.
- Patients: post-bronchodilator FEV_1 $\leq$70%; FEV_1/FVC ratio $\leq$70%; smoking history $\geq$10 pack-years; $\geq$1 documented COPD exacerbation (requiring corticosteroids, antibiotics, or hospitalization) in the year prior to screening.
- Patients were randomized to receive one of the following once-daily treatments via ELLIPTA™ dry powder inhaler for 52 weeks: FF/VI 50/25mcg, FF/VI 100/25mcg, FF/VI 200/25mcg or VI 25mcg.
- The primary endpoint was the annual rate of moderate/severe COPD exacerbations for FF/VI vs. VI
  - moderate exacerbation: worsening symptoms of COPD requiring treatment with oral corticosteroids and/or antibiotics
  - severe exacerbation: worsening symptoms of COPD requiring treatment with inpatient hospitalization.
- Pooled study data for FF/VI vs. VI were evaluated for the following subgroups:
  - gender
  - age
  - reversibility ($\geq$12% and 200mL FEV_1 post-albuterol/salbutamol)
  - smoking status
  - cardiovascular (CV) history/risk (current or past medical history of $\geq$1 of arrhythmia, cerebrovascular accident, congestive heart failure, coronary artery disease, diabetes mellitus, hypercholesterolemia, hypertension, myocardial infarction)
  - geographic region
  - race.

Table 1. Pooled patient demographics and screening characteristics (ITT population)

	FF/VI 50/25mcg (N=820)	FF/VI 100/25mcg (N=806)	FF/VI 200/25mcg (N=811)	VI 25mcg (N=818)
Age, years	63.6 (9.31)	63.8 (9.17)	63.6 (9.07)	63.6 (9.36)
Female sex, n (%)	344 (42)	353 (44)	344 (42)	344 (42)
Current smoker, n (%)	364 (44)	359 (45)	352 (43)	364 (44)
Smoking history, pack-years	46.2 (26.7)	46.6 (27.5)	46.3 (29.5)	45.7 (27.2)
Post-bronchodilator FEV_1, L	1.29 (0.48)	1.30 (0.48)	1.27 (0.45)	1.28 (0.46)
% predicted post-bronchodilator FEV_1	45.4 (13.6)	46.0 (13.4)	45.2 (13.4)	45.2 (13.0)
$\geq$1 exacerbation requiring oral/systemic corticosteroids and/or antibiotics, not requiring hospitalization, n (%)	764 (93.2)	744 (92.3)	742 (91.5)	755 (92.3)
$\geq$1 exacerbation requiring hospitalization, n (%)	173 (21.1)	169 (21.0)	174 (21.5)	146 (17.8)

Values are mean (SD) unless otherwise stated

RESULTS

Study population and demographics

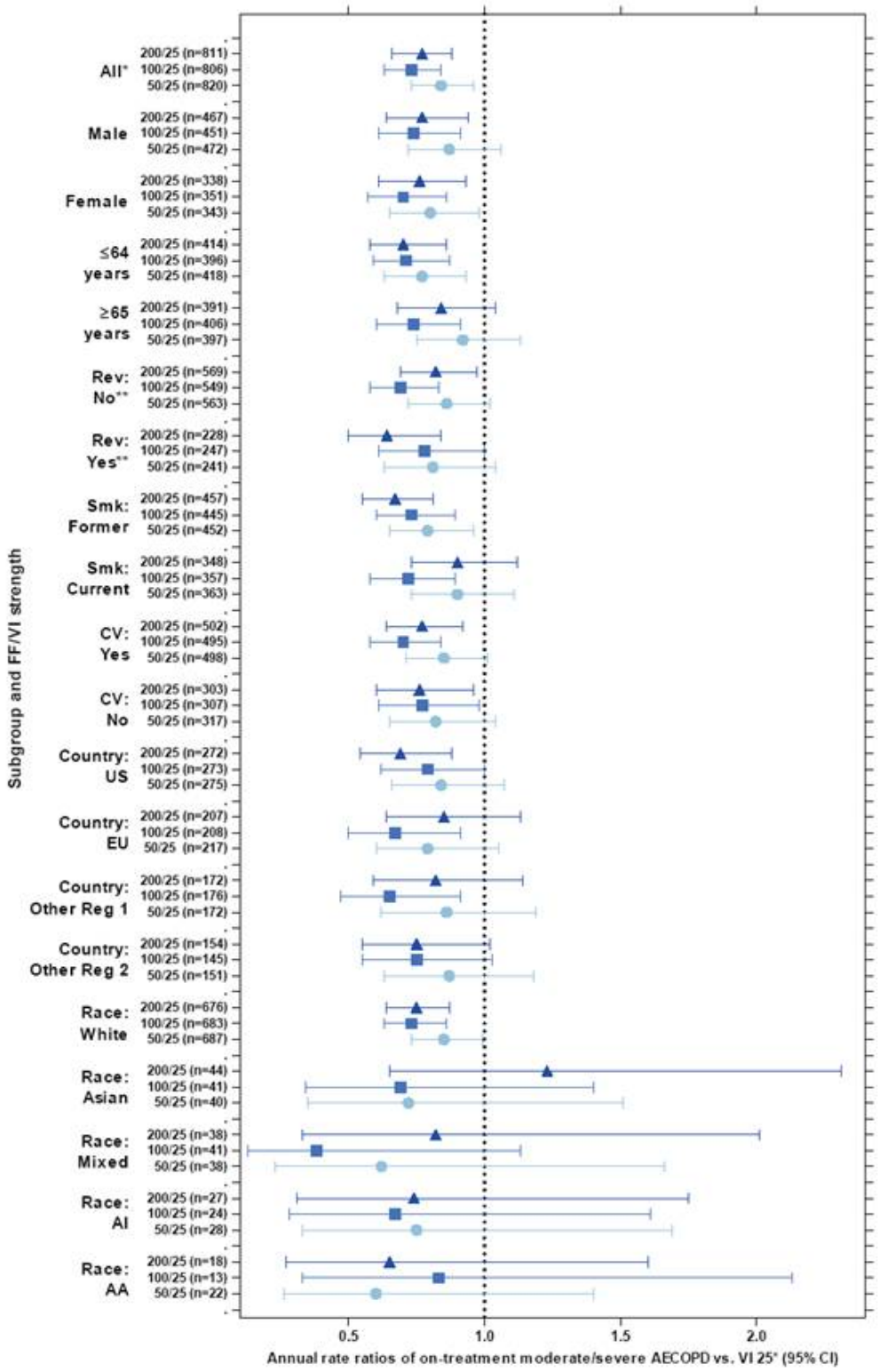
- 3255 patients were randomized and received at least one dose of study medication (ITT population); 2406 patients completed the studies.

- Demographics and screening characteristics were well matched between the different treatment arms (Table 1).

Efficacy: subgroup analysis (Figure 1)

- All three strengths of FF/VI reduced moderate/severe acute exacerbation of COPD (AECOPD) rates vs. VI in all subgroups, with the exception of Asians receiving 200/25mcg (n=44)
    - because of the small sample in the non-White race subgroups, the confidence intervals for these treatment comparisons were very wide.
- In several clinically relevant subgroups (gender, smoking status, reversibility and CV history/risk), 100/25 and 200/25 strengths of FF/VI provided significant reduction in moderate/severe AECOPD vs. VI alone, except for current smokers (200/25) and reversible patients (100/25).
- A similar trend was observed for the remaining subgroups, although small populations within some of these subgroups limit interpretation of data.

Figure 1. Pooled annual rate ratios of on-treatment moderate/severe AECOPD vs. VI 25 by subgroup (ITT population)



All = total population; Rev = Reversibility; Smk = Smoking status; CV = cardiovascular history/risk; US = United States of America; EU = European Union; Other Reg 1 = Other Region 1 (Chile, Argentina, Peru, Mexico, Philippines); Other Reg 2 = Other Region 2 (Australia, Canada, South Africa); AA = African American or African Heritage Race; AI = American Indian or Alaska Native Race
*N=818 for VI (Overall); ** Reversibility defined as >200mL and >12% change in FEV_1 post-albuterol; CI = Confidence interval

---

Safety: subgroup analysis

- On-treatment AEs deemed to be drug related were reported in 21%, 17%, 17% and 14% of 50/25, 100/25, 200/25 and VI patients, respectively
  - the AE profile did not markedly differ between the overall population and any specific subgroup (data not shown).
- Pneumonia rates were 27/818 (3%) in patients in the VI group, and 48/820 (6%), 51/806 (6%) and 55/811 (7%), respectively, in the FF/VI 50/25, 100/25 and 200/25 groups.(1)

- All subgroups, with the exception of EU patients, displayed a greater frequency of pneumonia in FF/VI treatment groups compared with VI alone.

- The greatest difference in pneumonia rates between VI and FF/VI patients were observed in the no CV history/risk subgroup: 7/315 (2%) in the VI group; 23/319 (7%), 22/307 (7%) and 23/305 (8%) in the FF/VI 50/25, 100/25 and 200/25 groups, respectively.

- The greatest frequency of pneumonia was observed in the Asian subgroup: 3/42 (7%) in the VI group; 5/40 (13%), 6/42 (14%) and 8/44 (18%) in the 50/25, 100/25 and 200/25 groups, respectively. The majority of patients in the Asian subgroup were of Japanese/East Asian origin.

CONCLUSIONS

- FF/VI once daily reduces the annual rate of moderate/severe exacerbations compared with VI alone in all seven pre-defined subgroups.

- Consistent with previous reports of an association of ICS use with an increased risk of pneumonia,(2) FF/VI treatment was associated with a higher incidence of pneumonia compared with VI alone, a trend that was more pronounced in certain subgroups.

REFERENCES

(1) Dransfield MT, et al. *Lancet Respir Med* 2013; 1:210–223.

(2) Crim C, et al. *Eur Respir J* 2009;34:641–7.

ACKNOWLEDGMENTS

- The presenting author, Mark Dransfield, declares the following real or perceived conflicts of interest during the last 3 years in relation to this presentation: has served as a consultant for Boehringer Ingelheim (BI), GlaxoSmithKline (GSK) and Ikaria. He has received grant funding from the NHLBI for COPD-related research and contracted research funding from Aeris, AstraZeneca, BI, Boston Scientific, Centocor, Forrest, GSK, Ikaria, MedImmune, Otsuka and Pfizer.

- These studies were funded by GlaxoSmithKline (GSK study codes HZC102871 & HZC102970, Clinicaltrials.gov NCT01009463 & NCT01017952).

- Editorial support (in the form of writing assistance, assembling tables and figures, collating author comments, grammatical editing and referencing) was provided by Vikas Sharma, PhD at Gardiner-Caldwell Communications (Macclesfield, UK) and was funded by GlaxoSmithKline.

Presented at the American Thoracic Society Annual Congress, Philadelphia, PA, USA, 17—22 May 2013

POSTER NO. G38

Efficacy of fluticasone furoate (FF)/vilanterol (VI) on lung function in COPD: a pre-specified subgroup analysis

Martinez F(1), Midwinter DA(2), Lettis S(2), Scott-Wilson C(3), Crim CJ(3), Kerwin EM(4)

(1)University of Michigan, Ann Arbor, MI, USA; (2)GlaxoSmithKline, Uxbridge, UK; (3)GlaxoSmithKline, Research Triangle Park, NC, USA; (4)Clinical Research Institute of Southern Oregon, Medford, OR, USA

INTRODUCTION

· FF/VI is a novel ICS/LABA therapy demonstrated to improve lung function in COPD patients when administered once daily at various strengths.(1),(2)

OBJECTIVE

· This pre-specified analysis investigated the effect of FF/VI on lung function from two 24-week studies(1),(2) in seven pre-specified subgroups.

METHODS

· Data from two phase III, multi-center, randomized, double-blind, parallel-group, 24-week studies were pooled.

· FF/VI at strengths of 50/25, 100/25 and 200/25mcg or placebo was dosed once daily in the morning via ELLIPTA™ dry powder inhaler. Other treatment arms (VI 25mcg, FF 100 and 200mcg) are not shown.

· Patients: ≥40 years of age; smoking history ≥10 pack-years; post-bronchodilator FEV_1/FVC ratio ≤0.70; post-bronchodilator FEV_1 ≤70% predicted; score of ≥2 on the modified Medical Research Council Dyspnea scale. Patients were not utilizing ICS or ICS/LABA medications within 4 weeks of study entry, and were not utilizing any LAMA within 1 week and/or any LABA within 48 hours of study entry.

· The present analysis describes the co-primary endpoint of trough FEV_1 (23–24h post-dose) on Day 169; weighted mean FEV_1 (0–4h) on Day 168 was the other co-primary endpoint but is not described here.

· The pre-specified subgroups were: gender; age; reversibility (≥12% and 200mL increase in FEV_1 post-albuterol/salbutamol); smoking status (former vs. current); patient-reported cardiovascular (CV) history/risk (current or past medical history of ≥1 of the following: arrhythmia, cerebrovascular accident, congestive heart failure, coronary artery disease, diabetes mellitus, hypercholesterolemia, hypertension, myocardial infarction); geographic region; race.

RESULTS

Study population and demographics

· 2254 patients were randomized and received at least one dose of study medication (intent-to-treat [ITT] population); 1647 patients completed the studies. Data for 1233 patients are reported here (data for patients in FF and VI monotherapy arms not shown).

Table 1. Patient demographics and screening characteristics (pooled ITT population)

	Placebo (N=412)	FF/VI 50/25 (N=206)	FF/VI 100/25 (N=410)	FF/VI 200/25 (N=205)
Age, years	62.0 (8.47)	62.8 (9.13)	62.1 (8.63)	61.1 (8.67)
Male sex, n (%)	293 (71)	135 (66)	281 (69)	137 (67)
Current smoker, n (%)	220 (53)	111 (54)	220 (54)	112 (55)
Smoking history, pack-years	45.7 (25.4)	44.2 (25.4)	44.7 (24.6)	41.5 (23.4)
CV risk subgroup: yes, n (%)	257 (62)	127 (62)	239 (58)	126 (61)
Reversible subgroup: yes, n (%)	138 (34)	73 (36)	124 (31)	54 (27)
Pre-bronchodilator FEV_1, L	1.31 (0.45)	1.23 (0.47)	1.30 (0.51)	1.33 (0.50)
Post-bronchodilator FEV_1, L	1.48 (0.47)	1.41 (0.50)	1.45 (0.51)	1.46 (0.51)
Percent predicted* post-bronchodilator FEV_1, %	48.4 (12.6)	48.4 (12.7)	48.0 (12.6)	47.1 (12.8)

Values are mean (SD) unless otherwise stated

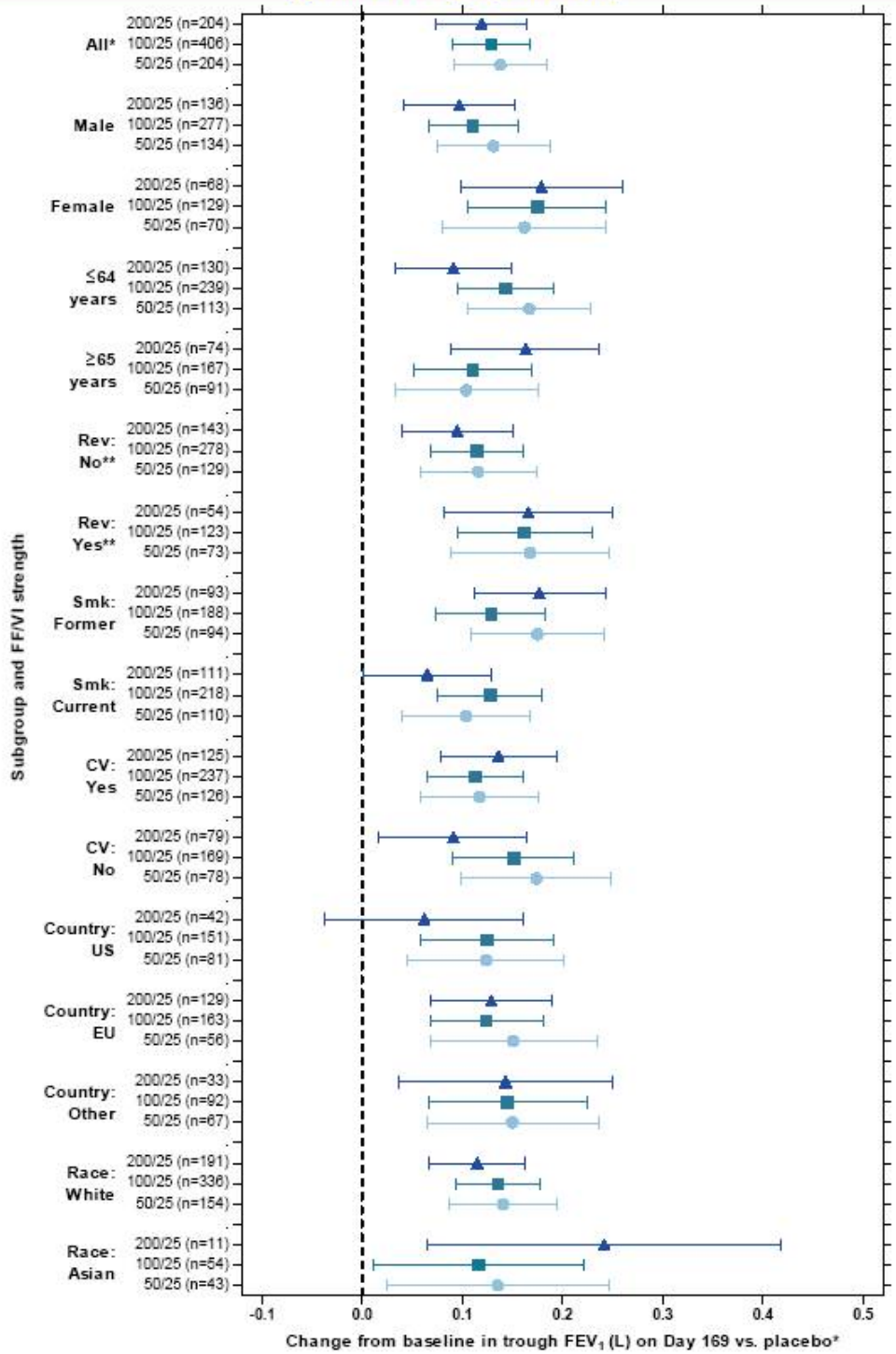
*Reference values were those of NHANES III

RESULTS (cont.)

Efficacy

- FF/VI significantly improved trough FEV_1 compared with placebo in most subgroups (Figure 1)
    - because of the small sample size in the Asian race subgroup, the confidence intervals for treatment comparisons in this subgroup were very wide.
- In all subgroups, FF/VI strengths of 50/25 and 100/25 improved mean trough FEV_1 by 100mL or greater compared with placebo.
- Compared with the placebo group, there were numerically larger improvements in Day 169 trough FEV_1 in reversible patients (~160mL) compared with non-reversible patients (~100mL).
- In most subgroups, FF/VI 200/25 showed no additional numerical improvement in trough FEV_1 compared with FF/VI 100/25. Improvements with FF/VI 50/25 were similar to those with FF/VI 100/25.

Figure 1. Change from baseline trough FEV_1 (L) vs. placebo for different subgroups, Day 169 (pooled ITT population)



*n=407 for placebo (all) **Reversibility defined as >200mL and >12% change in FEV_1 post-albuterol

Note: n = patients in specified group with analyzable data. Race: other races (African American/African; American Indian or Alaskan Native) not shown because of low n in these subgroups

All = total population; Rev = Reversibility; Smk = Smoking status; CV = cardiovascular history/risk - defined as current or past medical history of ≥1 of arrhythmia, cerebrovascular accident, congestive heart failure, coronary artery disease, diabetes mellitus, hypercholesterolemia, hypertension, myocardial infarction; US = United States of America; EU = European Union; Other = Chile, Philippines, Japan/South Korea, Russian Federation, Ukraine

---

Safety

- The most frequently reported adverse events (AEs) were nasopharyngitis, headache, upper respiratory tract infections and candidiasis.
- Candidiasis (including candidiasis, oral candidiasis, oropharyngeal candidiasis and oropharyngitis fungal preferred terms) occurred in 4–10% of patients receiving active treatment compared with 2% receiving placebo.
- Incidence of nasopharyngitis (6–9%) and headache (5–7%) was similar across all treatment groups.

- Upper respiratory tract infections (preferred term) were less frequent in patients receiving FF/VI 200/25mcg or placebo (3%) than in those receiving FF/VI 50/25 or 100/25mcg (7–8%).

- Lower respiratory tract infections (preferred term) were less frequent with active treatment (<1–1%) than placebo (3%).

- On-treatment AEs deemed to be drug related were reported in 12%, 10%, 9% and 8% of patients receiving FF/VI 50/25mcg, 100/25mcg, 200/25mcg and placebo, respectively.

- The AE profile did not differ markedly between the ITT population and any specific subgroup (data not shown).

CONCLUSIONS

- FF/VI once daily at strengths of 50/25 and 100/25mcg improved Day 169 mean trough FEV_1 by 100mL or greater compared with placebo, in all subgroups shown. No further benefit was apparent with FF/VI 200/25mcg.

- None of the baseline characteristics had a notable effect on the efficacy of FF/VI over placebo with respect to trough FEV_1.

- All treatment groups exhibited a broadly similar AE profile.

REFERENCES

(1) Kerwin EM et al. *Respir Med 2013*;107:560–9.
(2) Martinez F et al. *Respir Med 2013*;107:550–9.

ACKNOWLEDGMENTS

- The presenting author, Fernando Martinez, declares the following real or perceived conflicts of interest during the last 3 years in relation to this presentation: Dr. Martinez has participated in advisory boards covering COPD or IPF topics for Able Associates, Actelion, Almirall, Bayer, GSK, Ikaria, Janssen, Medlmmune, Merck, Pearl, Pfizer and Vertex. He has consulted on COPD or IPF topics for American Institute for Research, AstraZeneca, Bayer, Carden Jennings, Cardiomems, Grey Healthcare, HealthCare Research and Consulting, Janssen, Merion, Nycomed/Takeda, and Sudler and Hennessey. He has been a member of steering committees for studies sponsored by Actelion, Centocor, Forest, GlaxoSmithKline, Gilead, Mpex, Nycomed/Takeda. He has participated in Food and Drug Administration mock panels for Boehringer Ingelheim, Forest and GSK. The University of Michigan received funds from the National Institutes of Health for COPD and IPF studies. He has served on speaker's bureaus or in continuing medical education activities sponsored by American College of Chest Physicians, American Lung Association, Astra Zeneca, Bayer, William Beaumont Hospital, Boehringer Ingelheim, Center for Health Care Education, CME Incite, Forest, France Foundation, GlaxoSmithKline, Lovelace, MedEd, MedScape/WebMD, National Association for Continuing Education, Network for Continuing Medical Education, Nycomed/Takeda, Projects in Knowledge, St Luke's Hospital, the University of Illinois Chicago, University of Texas Southwestern, University of Virginia, UpToDate. He has served on DSMBs for Biogen and Novartis. He has received royalties from Castle Connolly and Informa. Both studies were funded by GlaxoSmithKline; GSK study codes HZC112206 and HZC112207; Clinicaltrials.gov NCT01053988 and NCT01054885, respectively.

- Editorial support (in the form of writing assistance, assembling tables and figures, collating author comments, grammatical editing and referencing) was provided by Ian Grieve, PhD and Vikas Sharma, PhD at Gardiner-Caldwell Communications (Macclesfield, UK) and was funded by GlaxoSmithKline.

Presented at the American Thoracic Society Annual Congress, Philadelphia, PA, USA, 17–22 May 2013

Poster No. 42837

The efficacy and safety of umeclidinium/vilanterol compared with tiotropium in COPD

Anzueto A(1), Decramer M(2), Kaelin T(3), Richard N(4), Tabberer M(5), Harris S(4), Church A(4)

(1)University of Texas Health, TX, USA; (2)Respiratory Division, University Hospital, Leuven, Belgium; (3)Lowcountry Lung and Critical Care, Charleston, SC, USA; (4)GlaxoSmithKline, Respiratory, Research Triangle Park, NC, USA; (5)GlaxoSmithKline, Global Health Outcomes, Stockley Park, Uxbridge, UK

INTRODUCTION

- Current guidelines recommend treatment with one or more long-acting bronchodilators for patients with moderate-to-very severe chronic obstructive pulmonary disease (COPD).(1),(2)
- Umeclidinium (UMEC)/vilanterol (VI) is a novel combined long-acting muscarinic antagonist/long-acting β_2 agonist combination bronchodilator in development for the maintenance treatment of COPD.

OBJECTIVES

- To evaluate the efficacy and safety of two once-daily doses of UMEC/VI (62.5/25mcg and 125/25mcg) compared with tiotropium (TIO; 18mcg) and VI (25mcg) monotherapies in patients with COPD.

QUALITATIVE METHODS

Study design and treatment

- Multicenter, randomized, double-blind, active-controlled, parallel-group, double-dummy study (ClinicalTrials.gov: NCT01316900; protocol number: DB2113360).
- Eligible patients ($\geq$40 years, clinically established history of COPD, current or former cigarette smokers with $\geq$10 pack-years, post-bronchodilator forced expiratory volume in 1 second (FEV_1)/forced vital capacity (FVC) <0.7 and predicted FEV_1 $\leq$70%, and modified Medical Research Council dyspnea scale score $\geq$2) were randomized 1:1:1:1 to 24 weeks treatment with UMEC/VI 62.5/25, UMEC/VI 125/25, VI 25, or TIO. Concurrent use of inhaled corticosteroids (ICS) and rescue use of albuterol was allowed.
- Treatments were administered once daily via the Ellipta™ dry powder inhaler or HandiHaler®. All patients were provided with both inhalers each morning, one containing placebo and one active treatment.
- All patients provided written informed consent prior to study participation. The study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. Intention-to-treat (ITT) population (all randomized subjects that took at least one dose of study medication) was the primary population for safety analyses. For efficacy and health outcome analyses, the primary population was the ITT population excluding subjects from Investigator 040688, due to significant deviations from good clinical practice standards.

Endpoints

- *Efficacy:* trough FEV_1 at Day 169 (primary). Additional efficacy and health-related quality of life endpoints included: 0–6h post-dose weighted mean (WM) FEV_1 (secondary); mean transition dyspnea index (TDI) focal score; rescue albuterol use; time to first COPD exacerbation; and St George's Respiratory Questionnaire (SGRQ) score.
- *Safety:* incidence of adverse events (AEs) and serious AEs (SAEs); vital signs; 12-lead electrocardiography (ECG); clinical chemistry; and hematology.

RESULTS

Patient demographics and baseline characteristics

- A total of 1141 patients were enrolled; 843 were included in the ITT population (i.e., randomized and received at least one dose of study medication).
- Patient demographics and baseline characteristics were similar across treatment groups (Table 1).
- ICS use was reported for 44–48% patients across groups.

Efficacy: primary endpoint

- Treatment with UMEC/VI 62.5/25 and 125/25 resulted in statistically significant improvements in least squares mean change from baseline in trough FEV_1 compared with TIO and VI 25 at Day 169 and at all other visit assessments ($p\leq0.008$, Figure 1 and Table 2).

TABLE 1. PATIENT DEMOGRAPHICS AND BASELINE CHARACTERISTICS

	VI 25mcg N=209	UMEC/VI 62.5/25mcg N=212	UMEC/VI 125/25mcg N=214	TIO 18mcg N=208

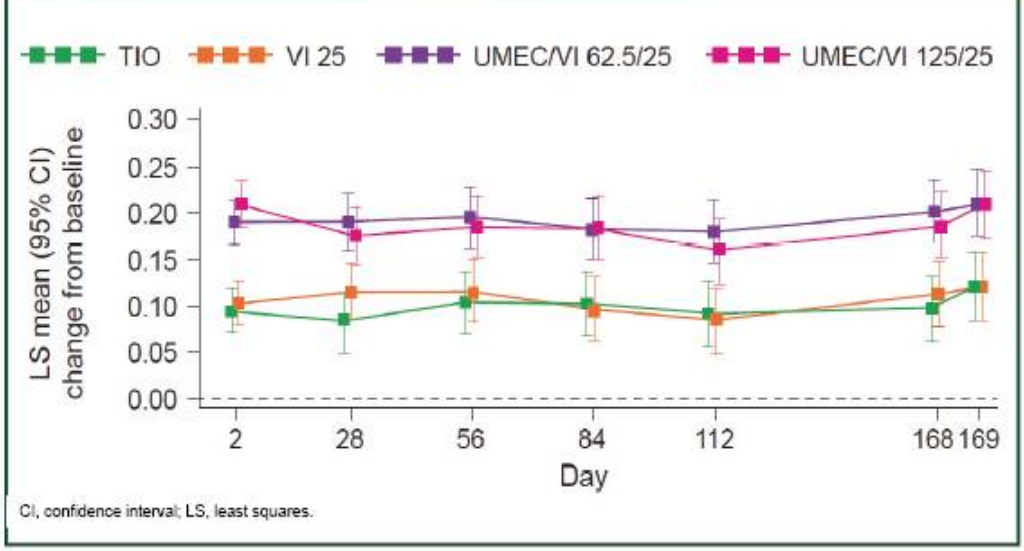
Age, years, mean (SD)	63.2 (9.10)	63.0 (8.67)	62.9 (8.87)	62.6 (9.39)
Sex, n (%)				
Male	143 (68)	148 (70)	151 (71)	140 (67)
Race, n (%)				
White	184 (88)	182 (86)	180 (84)	177 (85)
Smoking status at screening, n (%)				
Current smoker	106 (51)	98 (46)	124 (58)	99 (48)
Smoking pack years, mean (SD)	41.6 (25.36)	44.8 (27.65)	43.5 (24.98)	41.9 (24.44)
Cardiovascular risk factors, n (%)(a)	128 (61)	134 (63)	130 (61)	128 (62)
Pre-bronchodilator FEV_1 (L), mean (SD)	1.327 (0.4967)	1.314 (0.4869)	1.300 (0.4611)	1.298 (0.5021)
Post-albuterol FEV_1 (L), mean (SD)	1.449 (0.4795)	1.441 (0.4745)	1.433 (0.4621)	1.415 (0.5025)
Post-albuterol predicted FEV_1 (%), mean (SD)	47.7 (12.65)	48.0 (12.94)	47.2 (12.79)	47.8 (13.36)
Post-albuterol FEV_1/FVC, mean (SD)	48.173 (10.9416)	47.673 (11.0588)	47.917 (11.4955)	48.342 (11.8678)
Reversible to albuterol, n (%)(b)	52 (25)	57 (27)	61 (29)	217 (26)
ICS use, n (%)(c)				
ICS users	84 (40)	93 (44)	103 (48)	93 (45)

SD, standard deviation.

All values are mean (SD) unless specified otherwise.

(a) Current medical history of angina pectoris, diabetes, hyperlipidemia or hypertension;
(b) reversible defined as an increase in FEV_1 of $\geq$12% and $\geq$0.2L following administration of albuterol;
(c) ICS use was defined as those subjects who were currently taking ICS medications at the screening visit.

FIGURE 1. TROUGH FEV_1 (L)



Efficacy: secondary and other endpoints

- Statistically significant improvements were demonstrated for UMEC/VI 62.5/25 and UMEC/VI 125/25 compared with TIO and VI for 0–6h post-dose WM FEV_1 at Day 168 and at other visits ($p\leq0.006$, Figure 2 and Table 2).

- Improvements in the majority of other lung function analyses were observed when comparing UMEC/VI 62.5/25 or UMEC/VI 125/25 with TIO and VI treatment groups (Table 2).

- On-treatment COPD exacerbations were observed in 8% (VI 25), 7% (UMEC/VI 62.5/25) and 5% (UMEC/VI 125/25, TIO) of patients.

TABLE 2. EFFICACY OUTCOMES

	VI 25mcg N=205	TIO 18mcg N=203
Trough FEV_1 at Day 169, L		
Difference *vs.* monotherapy (95% CI)		
UMEC/VI 62.5/25	0.090‡ (0.039,0.142)	0.090‡ (0.039,0.141)
UMEC/VI 125/25	0.088‡ (0.036,0.140)	0.088‡ (0.036,0.140)
0–6h WM FEV_1 at Day 168, L		
Difference *vs.* monotherapy (95% CI)		
UMEC/VI 62.5/25	0.077‡ (0.025,0.128)	0.074‡ (0.022,0.125)
UMEC/VI 125/25	0.086‡ (0.033,0.138)	0.083‡ (0.031,0.134)
TDI responder at Day 168(a)		
Odds ratio *vs.* monotherapy (95% CI)		

UMEC/VI 62.5/25	1.4 (0.9, 2.0)	0.9 (0.6, 1.3)
UMEC/VI 125/25	1.8‡ (1.2, 2.8)	1.2 (0.8, 1.8)
SGRQ responder at Day 168(b)		
Odds ratio *vs.* monotherapy (95% CI)		
UMEC/VI 62.5/25	0.8 (0.6, 1.3)	0.9 (0.6, 1.3)
UMEC/VI 125/25	1.0 (0.7, 1.5)	1.0 (0.7, 1.6)
Albuterol use at Weeks 1–24, puffs/day		
Difference *vs.* monotherapy (95% CI)		
UMEC/VI 62.5/25	-0.3 (-0.8,0.3)	-0.7‡ (-1.2,-0.1)
UMEC/VI 125/25	-0.2 (-0.8,0.4)	-0.6‡ (-1.2,-0.1)

N=207 for UMEC/VI 62.5/25 and N=208 for UMEC/VI 125/25.

(a) Response was defined as a TDI focal score of at least 1 unit;
(b) response was defined as a SGRQ total score of 4 units below baseline or lower
‡ p-value<0.05.

Safety

- The incidence of AEs was similar across UMEC/VI and VI treatment groups, but lower in the TIO group (Table 3).
- Drug-related dry mouth was observed in ≤1% patients in all treatment groups.
- The incidence of SAEs across treatment groups was 2–7%. The most common SAE was COPD.
- Two deaths occurred in the study (acute cardiac failure in the VI 25 group and cardiac arrest/COPD exacerbation in the UMEC/VI 62.5/25 group). Neither of the deaths were considered to be related to the study drug.
- No clinically meaningful changes in vital signs, ECG parameters, or clinical laboratory parameters were observed for UMEC/VI 62.5/25 or 125/25 compared with monotherapies.

FIGURE 2. WM FEV_1 (L) OVER 0–6h POST-DOSE

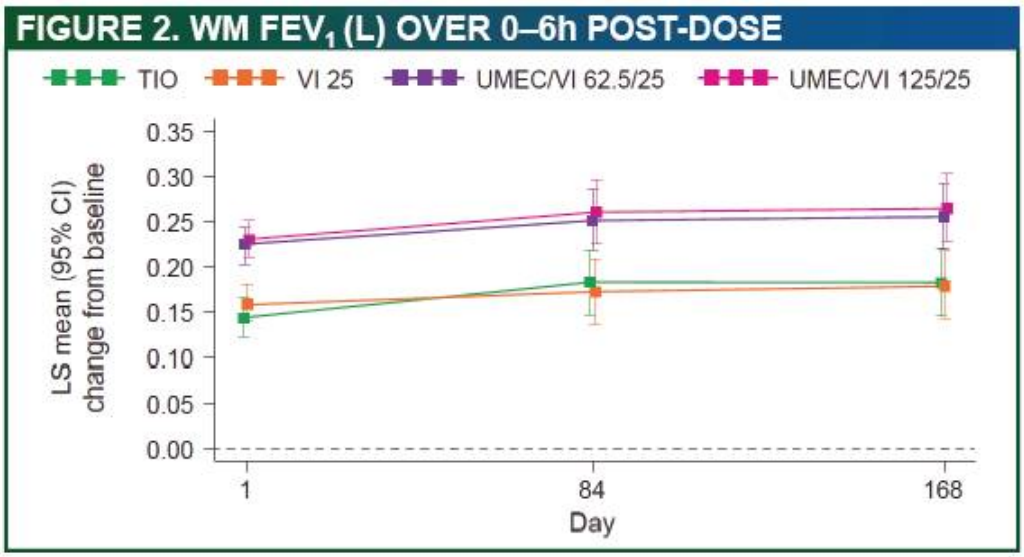


TABLE 3. SUMMARY of AEs AND SAEs

	VI 25mcg N=209	UMEC/VI 62.5/25mcg N=212	UMEC/VI 125/25mcg N=214	TIO 18mcg N=208
Any on-treatment AEs, n	99 (47%)	108 (51%)	94 (44%)	82 (39%)
AEs occurring in ≥3% of patients				
Nasopharyngitis	17 (8%)	21 (10%)	14 (7%)	16 (8%)
Headache	21 (10%)	20 (9%)	14 (7%)	9 (4%)
Upper respiratory tract infection	5 (2%)	8 (4%)	7 (3%)	8 (4%)
Back pain	3 (1%)	10 (5%)	7 (3%)	4 (2%)
Cough	4 (2%)	7 (3%)	7 (3%)	5 (2%)
Oropharyngeal pain	5 (2%)	1 (<1%)	6 (3%)	2 (<1%)
Hypertension	6 (3%)	3 (1%)	3 (1%)	1 (<1%)
Urinary tract infection	2 (<1%)	0	0	6 (3%)
Overall incidence of SAEs	15 (7%)	7 (3%)	5 (2%)	13 (6%)

CONCLUSIONS

- Once-daily dosing with UMEC/VI 62.5/25 and 125/25 improved lung function compared with VI and TIO monotherapy in patients with COPD.
- All treatments were well tolerated and no notable treatment-related changes were observed in vital signs, ECGs, and clinical laboratory parameters.

· The study supports the use of UMEC/VI 62.5/25 and 125/25 as long-term maintenance treatments in COPD.

REFERENCES

(1) GOLD 2013. Available at: http://www.Goldcopd.org/. Last accessed March 2013
(2) Celli BR, Macnee W. Eur Respir J 2004;23:932–46

ACKNOWLEDGEMENTS

· **The presenting author, Antonio Anzueto, has received consultancy and advisory board fees from GlaxoSmithKline, Boehringer Ingelheim, Forest, and AstraZeneca. NR, MT, SH, and AC are employees of GlaxoSmithKline and hold stocks/shares in GlaxoSmithKline.**

· This study was sponsored by GlaxoSmithKline (ClinicalTrials.gov: NCT01316900; protocol number: DB2113360).

· Editorial support (in the form of writing assistance, assembling tables and figures, collating author comments, grammatical editing and referencing) was provided by Yamini Khirwadkar, PhD, at Fishawack Scientific Communications Ltd (UK), and was funded by GlaxoSmithKline.

Presented at the Annual Congress of the American Thoracic Society (ATS), Philadelphia, PA, USA, May 17–22, 2013

Poster No. 42583

Efficacy and safety of once-daily umeclidinium/vilanterol 62.5/25mcg in patients with COPD

Donohue, JF(1), Maleki-Yazdi, MR(2), Kilbride, S (3), Mehta, R(4), Kalberg, C(4), Church, A(4)

(1)University of North Carolina College of Medicine, Chapel Hill, NC, USA; (2)Women's College Hospital, University of Toronto, Ontario, Canada; (3)GlaxoSmithKline, Stockley Park, Uxbridge, UK; (4)GlaxoSmithKline, Research Triangle Park, NC, USA

INTRODUCTION

- Current guidelines recommend treatment with one or more long-acting bronchodilators for patients with moderate-to-very severe chronic obstructive pulmonary disease (COPD).(1),(2)
- Umeclidinium (UMEC)/vilanterol (VI) is a novel long-acting muscarinic antagonist (LAMA)/long-acting β_2-agonist (LABA) combination bronchodilator in development for the maintenance treatment of COPD.

OBJECTIVES

- To evaluate the efficacy and safety of once-daily UMEC/VI 62.5/25 mcg compared with its components (UMEC and VI) and placebo in patients with COPD.

METHODS

Study design and treatments

- Multicenter, randomized, double-blind, placebo-controlled, parallel-group study (ClinicalTrials.gov: NCT01313650; protocol number: DB2113373).
- Key eligibility criteria: ≥40 years of age; clinically established history of COPD; current or former cigarette smokers with ≥10-pack-year smoking history; post-albuterol forced expiratory volume in 1 second (FEV_1)/ forced vital capacity (FVC) <0.7 and predicted FEV_1 ≤70%; and a mMRC dyspnea scale score ≥2.
- Following a 7–14-day run-in, patients were randomized 3:3:3:2 to 24 weeks treatment with UMEC/VI 62.5/25mcg, UMEC 62.5mcg, VI 25mcg or placebo once-daily via the ELLIPTA™ dry powder inhaler. Concurrent use of inhaled corticosteroids (ICS) and rescue albuterol was allowed.
- All patients were required to provide written informed consent prior to study participation. The study was conducted in accordance with the declaration of Helsinki, Good Clinical Practice guidelines, and IRB approval was obtained.

Endpoints

- *Primary efficacy:* trough FEV_1 on Day 169, defined as the mean of the FEV_1 values obtained 23 and 24 hours after dosing on Day 168.
- *Additional efficacy included:* 0–6h post-dose weighted mean (WM) FEV_1; transition dyspnea index (TDI) focal score; St George's Respiratory Questionnaire (SGRQ) score; rescue albuterol use; and time to first COPD exacerbation.
- *Safety:* adverse events (AEs); vital signs; 12-lead electrocardiography (ECG) and 24-h Holter ECG; and clinical chemistry and hematology.
- Plasma pharmacokinetics (PK) were analyzed using population PK methodology.

RESULTS

Patient demographics and baseline characteristics

- A total of 2210 patients were enrolled; 1532 were included in the intention-to-treat (ITT) population (i.e., randomized and received at least one dose of study medication).
- Patient demographics and baseline characteristics were similar across treatment groups (Table 1). ICS use was similar across active treatment groups (51–52%) and placebo (49%).

TABLE 1. PATIENT DEMOGRAPHICS AND BASELINE CHARACTERISTICS

	Placebo N=280	UMEC 62.5 N=418	VI 25 N=421	UMEC/VI 62.5/25 N=413
Age, years	62.2 (9.04)	64.0 (9.16)	62.7 (8.52)	63.1 (8.71)
Sex, n (%)				
Male	195 (70)	298 (71)	285 (68)	305 (74)
Race, n (%)				
White	237 (85)	354 (85)	364 (86)	348 (84)
Patientswith cardiovascular risk factors, n (%)(a)	174 (62)	242 (58)	268 (64)	260 (63)
Post-albuterol % predicted FEV_1	46.7 (12.71)	46.8 (13.39)	48.2 (13.27)	47.8 (13.19)

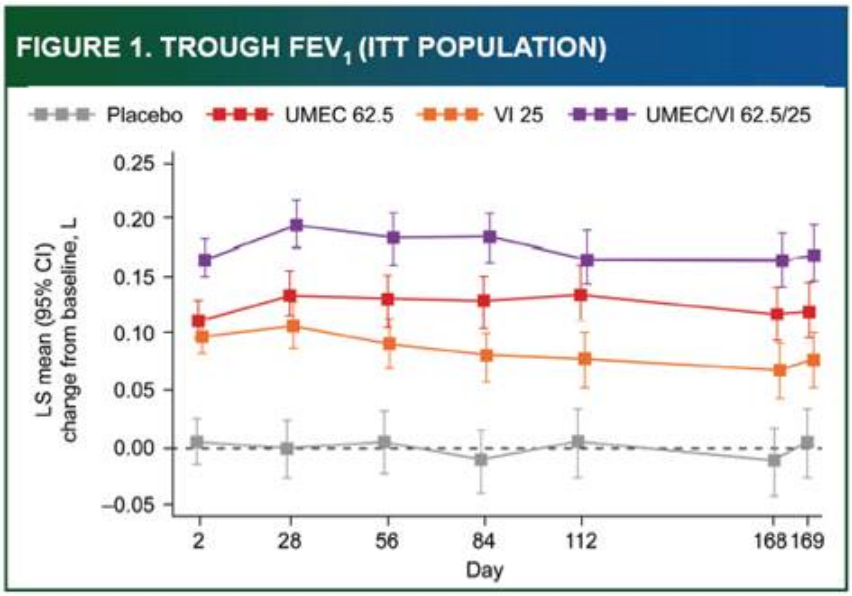
Post-albuterol FEV_1, L	1.355 (0.4629)	1.347 (0.4730)	1.402 (0.5011)	1.425 (0.5426)
Post-albuterol FEV_1/FVC	47.082 (11.4695)	46.775 (11.0696)	47.372 (11.4928)	48.011 (11.4189)
Patients reversible to albuterol(b), n (%)	91 (33)	121 (29)	155 (37)	129 (31)

Values are reported as mean (standard deviation) unless otherwise stated.

(a) Defined as current medical history of angina, myocardial infarction, stroke, diabetes, hypertension, or hyperlipidemia.
(b) Reversible was an increase in FEV1 of ≥12% and ≥200 mL following administration of 4 puffs of albuterol.

Efficacy: Trough FEV_1

- Treatment with UMEC/VI 62.5/25 resulted in statistically significant improvements in trough FEV_1 at Day 169 *vs*. VI, UMEC 62.5 and placebo ($p \leq 0.005$, Table 2). Comparisons at all other visits were statistically significant, except for UMEC/VI 62.5/25 *vs*. UMEC 62.5 at Day 112 (Figure 1). All comparisons of UMEC 62.5 and VI *vs*. placebo were statistically significant ($p<0.001$).



Efficacy: additional endpoints

- Greater improvements in 0–6h post-dose WM FEV_1 were shown for UMEC/VI 62.5/25 *vs*. VI, UMEC 62.5 and placebo ($p<0.001$ for all comparisons at all visits, Figure 2 and Table 2). Both UMEC 62.5 and VI consistently improved 0–6h post-dose WM FEV_1 *vs*. placebo ($p<0.001$, Table 2).

- Greater improvements in TDI focal score, SGRQ score, and rescue albuterol use were shown with UMEC/VI 62.5/25 compared with placebo (Table 2).

- The incidence of COPD exacerbations was lower with UMEC/VI 62.5/25 (7%), UMEC 62.5 (8%), and VI (9%) compared with placebo (13%). Analysis of time to first exacerbation showed that patients on UMEC/VI 62.5/25 had a lower risk of exacerbation *vs*. placebo (hazard ratio: 0.5; 95% CI: 0.3, 0.8 [p=0.004]; corresponding to a risk reduction of 50%).

TABLE 2: EFFICACY ENDPOINT COMPARISONS

(ITT POPULATION)

	UMEC 62.5 (N=418)	**VI 25 (N=421)**	**UMEC/VI 62.5/25 (N=413)**
Through FEV_1 at Day 169, L(a)			
Difference *vs*. placebo	0.115*	0.072*	0.167*
(95% CI)	(0.076, 0.155)	(0.032, 0.112)	(0.128, 0.207)
UMEC/VI 62.5/25 *vs*. monotherapy	0.052†	0.095*	
(95% CI)	(0.017, 0.087)	(0.060, 0.130)	
0-6h WM FEV_1 at Day 168, L(a)			
Difference *vs*. placebo	0.150*	0.122*	0.242*
(95% CI)	(0.110, 0.190)	(0.082, 0.162)	(0.202, 0.282)
UMEC/VI 62.5/25 *vs*. monotherapy	0.092*	0.120*	
(95% CI)	(0.056, 0.127)	(0.084, 0.155)	
TDI focal score at Day 168(a)			
Difference *vs*. placebo	1.0*	0.9*	1.2*
(95% CI)	(0.5, 1.5)	(0.4, 1.4)	(0.7,1.7)
OR *vs*. placebo (95% CI)	1.6 (1.2, 2.3)†	1.5 (1.1, 2.1)‡	2.0 (1.5, 2.8)*
SGRQ score at Day 168			
Difference *vs*. placebo	-4.69*	-5.19*	-5.51*
(95% CI)	(-7.07, -2.31)	(-7.58, -2.80)	(-7.88, -3.13)
OR *vs*. placebo (95% CI)	1.6† (1.2, 2.3)	1.9* (1.3, 2.6)	2.0* (1.4, 2.8)

Rescue albuterol use at weeks 1-24, puffs/day			
Difference *vs.* placebo (95% CI)	-0.3 (-0.8, 0.2)	-0.9* (-1.4, -0.4)	-0.8* (-1.3,-0.3)

(a) Values are differences in least squares mean (95% CI); OR, odds ratio (based on proportion of responders according to outcome measure).
* p≤0.001 vs placebo,
† p≤0.005 vs placebo,
‡ p≤0.05 vs monotherapy. To account for multiplicity across treatment comparisons and endpoints, a step-down closed testing procedure was used.

Safety and pharmacokinetics

- Headache and nasopharyngitis were the most common AEs reported (Table 3). The incidence of dry mouth was low; reported for <1% of patients with UMEC 62.5, VI, and placebo and none treated with UMEC/VI 62.5/25.
- The incidence of serious AEs (SAEs) was similar across treatment groups (3–6%). The most common SAE was COPD.
- Nine deaths were reported (sudden death, COPD exacerbation, and COPD exacerbation/renal failure in VI group; COPD/acute respiratory failure, sudden death, cholecystitis/peritonitis in UMEC 62.5 group; COPD exacerbation/respiratory failure, myocardial infarction, and 'death: undefined cause' in UMEC/VI 62.5/25 group).
- No clinically meaningful treatment-related changes in vital signs, ECG, or clinical laboratory parameters were observed for active treatments compared with placebo.
- There were no differences in the systemic exposure of UMEC 62.5 or VI when administered in combination or as monotherapy. In addition, patient demographics did not influence PK parameters of either compound.

FIGURE 2: 0–6h POST-DOSE WM FEV_1 (ITT POPULATION)

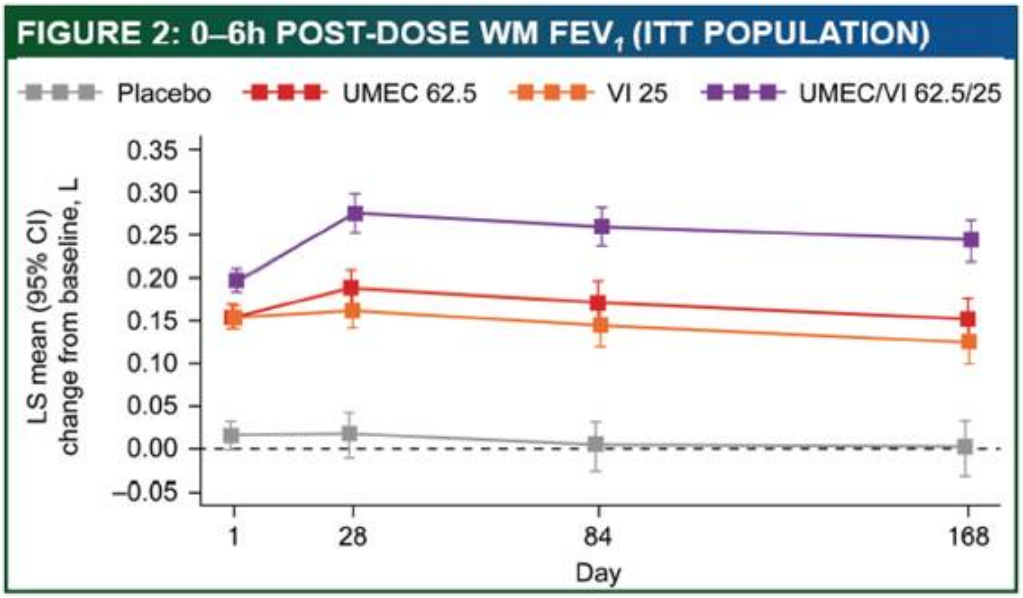


TABLE 3: OVERVIEW OF ADVERSE EVENTS

(ITT POPULATION)

	Placebo N=280	UMEC 62.5 N=418	VI 25 N=421	UMEC/VI 62.5/25 N=413
Any on-treatment AEs, n (%)	130 (46)	216 (52)	204 (48)	212 (51)
AEs reported by ≥3% patients, n (%)				
Headache	26 (9)	32 (8)	25 (6)	35 (8)
Nasopharyngitis	16 (6)	29 (7)	26 (6)	39 (9)
Upper respiratory tract infection	14 (5)	21 (5)	18 (4)	13 (3)
Cough	7 (3)	16 (4)	15 (4)	6 (1)
Oropharyngeal pain	4 (1)	6 (1)	14 (3)	13 (3)
Back pain	7 (3)	8 (2)	7 (2)	13 (3)
Chronic obstructive pulmonary disease	3 (1)	12 (3)	8 (2)	7 (2)
Arthralgia	3 (1)	12 (3)	2 (<1)	4 (<1)

CONCLUSIONS

- Once-daily dosing with UMEC/VI 62.5/25 improved lung function compared with the UMEC and VI monotherapies and placebo in patients with COPD. Other efficacy assessments supported the efficacy of UMEC/VI 62.5/25.
- Safety and tolerability profiles of UMEC/VI 62.5/25 were similar to the monotherapies and placebo.
- This study supports the use of UMEC/VI 62.5/25 as a long-term maintenance treatment for COPD.

REFERENCES

(1) GOLD 2013. Available at: *http://www.Goldcopd.org/* Last accessed March 2013.
(2) Celli BR, Macnee W. *Eur Respir* J 2004; 23:932–946.

ACKNOWLEDGEMENTS

· **JFD and MRM-Y have been consultants for and received research grants from GlaxoSmithKline. SK, CK and AC are employees of GlaxoSmithKline and hold stocks/shares in GlaxoSmithKline.**

· This study was sponsored by GlaxoSmithKline (ClinicalTrials.gov: NCT01313650; protocol number: DB2113373).

· Editorial support was provided by David Griffiths, PhD (in the form of writing assistance, assembling tables and figures, collating author comments, grammatical editing and referencing), from Fishawack Scientific Communications Ltd, funded by GlaxoSmithKline.

Presented at the Annual Congress of the American Thoracic Society (ATS), Philadelphia, PA, USA, May 17–22, 2013