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, 2012**

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.

Today at the American Thoracic Society International Conference in San Francisco, California, GlaxoSmithKline (GSK) presented three posters containing information from Phase 1, Phase 2a and Phase 3a studies with RELOVAIR™. RELOVAIR™ is a once-daily inhaled corticosteroid (ICS)/long-acting beta-agonist (LABA) combination treatment, comprising fluticasone furoate and vilanterol (FF/VI), currently in development for the treatment of patients with chronic obstructive pulmonary disease (COPD) and patients with asthma, under the LABA collaboration agreement between GSK and Theravance, Inc. (the "Company"). GSK also presented a poster on a Phase 2a study of a once-daily long-acting muscarinic antagonist (LAMA)/LABA dual bronchodilator GSK573719 ('719)/VI, an investigational combination medicine being developed under the LABA collaboration between GSK and the Company, for the treatment of patients with COPD. The four 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	A repeat dose, double-blind, placebo-controlled 'Through QT/QTc study' to assess the cardiac safety of fluticasone furoate (FF) and vilanterol (VI) administered in combination
Exhibit 99.2	The effect of fluticasone furoate (FF) alone and in combination with vilanterol (VI) on the early asthmatic response 23h after dosing in patients with mild persistent asthma: results from a 28-day randomized, controlled, crossover study

Exhibit 99.3	Effect of fluticasone furoate (FF)/vilanterol (VI) administered once daily on 24h pulmonary function in patients with COPD: a randomized, three-way, incomplete block, crossover study
Exhibit 99.4	Safety and tolerability of the GSK573719/vilanterol combination 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, 2012

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

EXHIBIT INDEX

Exhibit	Description
Exhibit 99.1	A repeat dose, double-blind, placebo-controlled 'Through QT/QTc study' to assess the cardiac safety of fluticasone furoate (FF) and vilanterol (VI) administered in combination
Exhibit 99.2	The effect of fluticasone furoate (FF) alone and in combination with vilanterol (VI) on the early asthmatic response 23h after dosing in patients with mild persistent asthma: results from a 28-day randomized, controlled, crossover study
Exhibit 99.3	Effect of fluticasone furoate (FF)/vilanterol (VI) administered once daily on 24h pulmonary function in patients with COPD: a randomized, three-way, incomplete block, crossover study
Exhibit 99.4	Safety and tolerability of the GSK573719/vilanterol combination in patients with COPD

Poster No. D3

A repeat dose, double-blind, placebo-controlled 'Thorough QT/QTc study' to assess the cardiac safety of fluticasone furoate (FF) and vilanterol (VI) administered in combination

Rodger Kempsford,(1) Ann Allen,(2) Kathryn Kelly,(3) Parminder Saggu,(4) Courtney Crim(5)

GlaxoSmithKline R&D: (1)Respiratory Medicines Development Centre and (2)Clinical Pharmacology Modelling & Simulation, Stevenage, UK; (3)Clinical Pharmacology Science & Study Operations, Uxbridge, UK; (4)Quantitative Sciences, Uxbridge, UK; (5)Respiratory Medicines Development Center, Research Triangle Park, NC, USA

INTRODUCTION

- A combination of the novel inhaled corticosteroid FF and long-acting beta$_2$ adrenoceptor agonist VI (FF/VI) is currently under development as a once-daily inhaled treatment for asthma and COPD.
- Beta$_2$ adrenoceptor agonists can prolong the electrocardiogram (ECG) QTc interval, particularly at supra-therapeutic doses.
- This study was conducted to comply with United States and European regulatory requirements that all new non-antiarrhythmic drugs must be assessed for potential effects on cardiac conduction in a 'Thorough QT/QTc study'.(1)

OBJECTIVES

Primary

- To demonstrate the lack of effect of FF/VI (200/25mcg) on the QTc interval (Fridericia's correction; QTcF) compared with placebo after 7 days' dosing. This represented the highest FF/VI dose administered in phase III studies in asthma and COPD.

Secondary

- To estimate the effect of FF/VI (800/100mcg) on the QTcF interval compared with placebo after 7 days' dosing. This FF/VI dose represented four-times the highest dose administered in phase III studies in asthma and COPD.
- To estimate the effect of FF/VI (200/25 and 800/100mcg) on the QTc interval (individual correction; QTci) compared with placebo after 7 days' dosing.
- To estimate the effect of single dose oral moxifloxacin (400mg; positive control for assay sensitivity) on the QTcF interval compared with placebo after 7 days' dosing.

METHODS

- This was a single center, randomized, double-blind (single-blind moxifloxacin), four-way crossover study in healthy male and female non-smoking subjects.
- Subjects each received:
  - inhaled FF/VI (200/25mcg) for 7 days + placebo tablet (Day 7 only)
  - inhaled FF/VI (800/100mcg) for 7 days + placebo tablet (Day 7 only)
  - inhaled placebo for 7 days + placebo tablet (Day 7 only)
  - inhaled placebo for 7 days + moxifloxacin 400mg tablet (Day 7 only).
- Continuous ECG data (Mortara H12+ [12-lead; 1000Hz]) was collected on Day –1 (0–12h; period 1) and on Day 7 (0–24h; periods 1–4).
- Subjects remained on bed rest in a semi-supine position for 30min pre-dose to 4h post-dose and were then placed on bed rest in the supine or semi-supine position for at least 30min prior to each remaining time point.
- QTc values were calculated as the mean of 15 ECG complexes (five ECG complexes from each of three 10-second recordings approximately 1min apart). Each subject's ECGs were analyzed by the same blinded independent cardiologist.
- QTcF (msec) was calculated as $QT/(R\text{-}R)^{1/3}$.
- Each individual's QTci correction factor was determined from 0–12h Holter ECGs collected pre-treatment (Day –1 treatment period 1), pre-treatment (Day 1 periods 1–4) and on placebo (total = 72 ECG readings [24 time points in triplicate]).
- QTc data were analyzed as the mean time-matched difference from placebo in change from baseline. A clinically significant effect was defined as where the upper bound of the upper 90% confidence interval (CI) for this difference exceeded 10msec at any time point.(1)
- Adverse events (AEs) and laboratory safety screens were recorded throughout the study.

RESULTS

Table 1. Demographics (N=85).

Characteristic	Value
Mean age, years: median (range)	28.0 (18–65)
Gender (M/F): n (%)	49/36 (58/42)
Height, cm: mean (SD)	170 (9)
Weight, kg: mean (SD)	69 (11)
Race: n (%)	
White — White/Caucasian/European Heritage	60 (71)
African American/African Heritage	9 (11)
Asian — Central/South Asian Heritage	10 (12)
Asian — Japanese/East Asian/South East Asian Heritage	4 (5)
African American/African Heritage and White	1 (1)
Asian and White	1 (1)

SD = standard deviation

Pharmacodynamics

- At an FF/VI dose of 200/25mcg there was a lack of effect on QTcF or QTci: all time-matched mean differences in change from baseline from placebo were <5msec with all upper 90% CIs <10msec (Figure 1).

- At an FF/VI dose of 800/100mcg (representing four times the proposed therapeutic FF/VI dose of 200/25mcg), there was no clinically significant effect on QTcF (all upper 90% CIs were <10msec) at any time point except 30min post-dose where the upper 90% CI exceeded 10msec but with a mean value <10msec (mean [90% CI]: 9.6msec [7.2, 12.0]).

- At an FF/VI dose of 800/100mcg there was no clinically significant effect on QTci: all time-matched mean differences in change from baseline from placebo were <5msec with all upper 90% CIs <10msec (Figure 1). There was no marked difference in 0–24h QTci for FF/VI 200/25mcg and 800/100mcg (Figure 1) suggesting that QTci more effectively corrected for heart rate than QTcF.

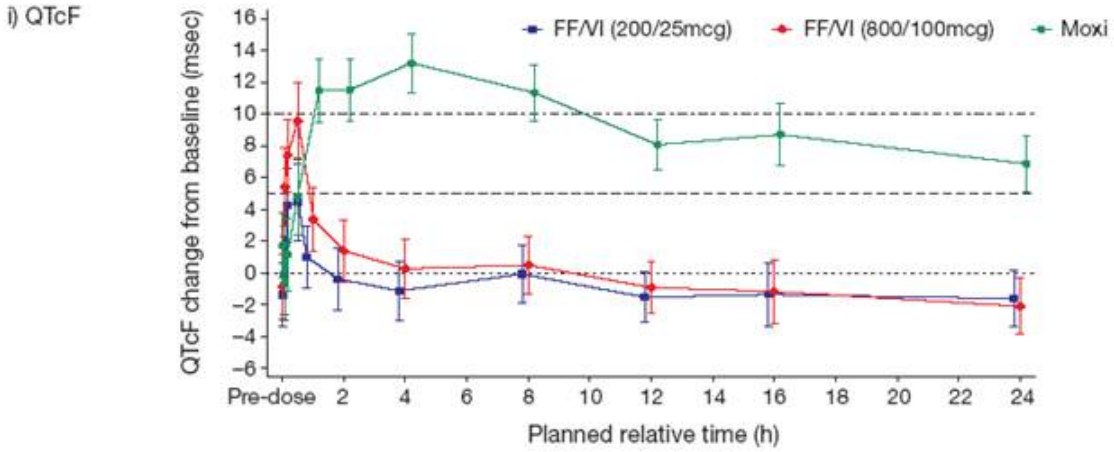
- Categorical analysis showed that there were no QTcF values >450msec after either FF/VI 200/25mcg or 800/100mcg (Table 2). There were no QTcF increases from baseline of >30msec after FF/VI 200/25mcg and only three subjects (4%) had an increase from baseline of between 30–60msec (Table 3).

- Assay sensitivity was confirmed: moxifloxacin (400mg) prolonged both QTcF and QTci time-matched mean differences in change from baseline from placebo >10msec at 1–8h post-dose (Figure 1). The magnitude of the effect was comparable for QTcF and QTci and was also similar to that reported previously.(2) Moxifloxacin was also associated with increases in QTcF as indicated by categorical analysis (Tables 2 and 3).

- Heart rate changes were seen after both doses of FF/VI. Maximum heart rate (0–4h mean difference from placebo [90% CI]) was 3.9bpm [2.7, 5.1] and 12.4bpm [11.2, 13.6] following administration of FF/VI 200/25mcg and 800/100mcg, respectively. Weighted mean heart rate (0–4h mean difference from placebo [90% CI]) was 2.6bpm [1.6, 3.5] and 7.5bpm [6.6, 8.5] following administration of FF/VI 200/25mcg and 800/100mcg, respectively. Peak effects on heart rate were seen at 10min after dosing with FF/VI, which correlated with the VI C_{max} at 5–10min. Maximum and weighted mean heart rate (0–4h mean difference from placebo [90% CI]) following moxifloxacin 400mg were 0.3 bpm [–0.9, 1.6] and 1.1bpm [0.2, 2.1], respectively.

- All treatments were well tolerated; there were no AEs that led to withdrawal. The frequency (%) of AEs was higher for the FF/VI 800/100mcg (61%) and moxifloxacin (58%) treatment regimens compared with FF/VI 200/25mcg (47%) and placebo (42%) treatment regimens (Table 4). The most frequent AE was headache, which had a similar frequency across all treatment regimens (18–23%). FF/VI 800/100 was associated with a higher incidence of palpitations (15%), dizziness (10%) and tremor (8%) compared with placebo or FF/VI 200/25mcg. Single-dose moxifloxacin administration was associated with nausea (11%).

Figure 1. QTcF and QTci on Day 7 (0–24h) following administration of FF/VI and moxifloxacin. Adjusted mean change from baseline (difference from placebo [90% CI]).



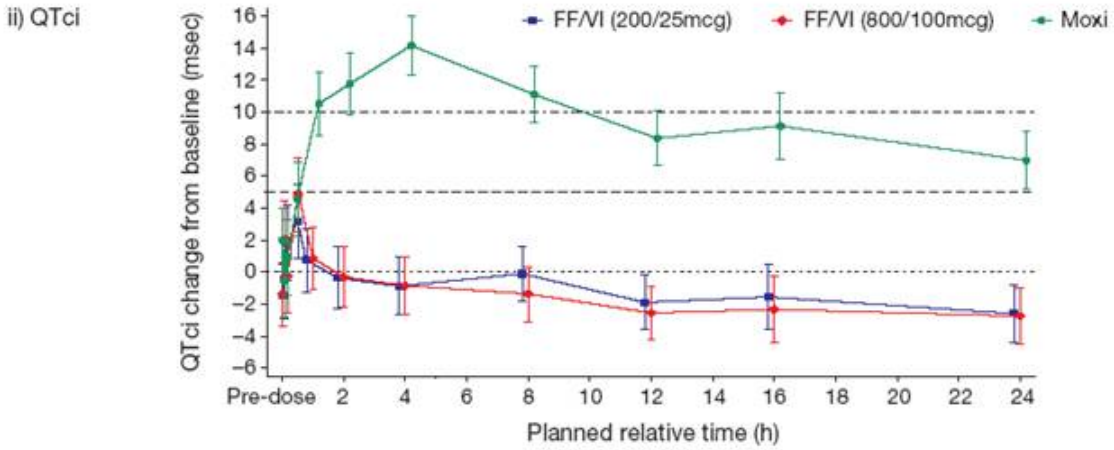


Table 2. QTcF categorical analysis: absolute values (0–24h post-dose; Day 7).

	QTcF maximum post-dose (msec)			
Treatment	**≤450 n (%)**	**>450–480 n (%)**	**>480–500 n (%)**	**>500 n (%)**
FF/VI 200/25mcg	73 (100)	0	0	0
FF/VI 800/100mcg	73 (100)	0	0	0
Placebo	73 (100)	0	0	0
Moxifloxacin 400mg	69 (95)	4 (5)	0	0

Per protocol population

Table 3. Categorical QTcF analysis: change from baseline (0–24h post-dose; Day 7).

	QTcF maximum change from baseline (msec)		
Treatment	**≤30 n (%)**	**>30–60 n (%)**	**≥60 n (%)**
FF/VI 200/25mcg	73 (100)	0	0
FF/VI 800/100mcg	70 (96)	3 (4)	0
Placebo	73 (100)	0	0
Moxifloxacin 400mg	61 (84)	12 (16)	0

Per protocol population

Table 4. Most frequent AEs (≥3% in any treatment group).

Adverse event	**Placebo**	**FF/VI 200/25mcg**	**FF/VI 800/100mcg**	**Moxifloxacin 400mg**
N	84	81	80	79
Any event	34 (42)	38 (47)	49 (61)	46 (58)
Headache	18 (21)	19 (23)	17 (21)	14 (18)
Palpitations	2 (2)	1 (1)	12 (15)	4 (5)
Dizziness	1 (1)	1 (1)	8 (10)	3 (4)
Nausea	0	1 (1)	2 (3)	9 (11)
Dysmenorrhea	2 (2)	3 (4)	4 (5)	3 (4)
Anxiety	0	2 (2)	5 (6)	0
Oropharyngeal pain	1 (1)	1 (1)	6 (8)	0
Tremor	0	2 (2)	6 (8)	0
URTI	1 (1)	3 (4)	2 (3)	3 (4)
Diarrhea	1 (1)	2 (2)	0	3 (4)
Pre-syncope	1 (1)	0	2 (3)	3 (4)

Abdominal pain	1 (1)	1 (1)	0	3 (4)
Dry mouth	0	3 (4)	1 (1)	1 (1)
Fatigue	0	1 (1)	4 (5)	1 (1)
Contact dermatitis	3 (4)	0	0	0

URTI = upper respiratory tract infection

CONCLUSIONS

- At the proposed highest therapeutic dose of FF/VI (200/25mcg) there was a lack of effect on the QTc interval as measured by either QTcF or QTci. All time-matched mean differences from placebo (0–24h) were <5msec with no upper 90% CI values greater than 10msec.

- At a four-fold multiple of the FF/VI therapeutic dose (800/100mcg) there was a small, predictable and transient effect on QTcF during the 1st hour after dosing. The upper 90% CI exceeded 10msec at one time-point (30min) after dosing. All mean differences from placebo were <10msec.

- At a four-fold multiple of the FF/VI therapeutic dose (800/100mcg) there was a lack of effect on QTci. All time-matched mean differences from placebo (0–24h) were <5msec with no upper 90% CI values greater than 10msec. There were no marked differences in QTci between FF/VI 200/25mcg and 800/100mcg.

REFERENCES

(1) ICH Harmonised Tripartite Guideline, May 2005. Available at: http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E14/Step4/E14_Guideline.pdf.

(2) Stylianou A, Roger K, Stephens K. A statistical assessment of QT data following placebo and moxifloxacin dosing in thorough QT studies. J Biopharmaceutical Statistics 2008;18:502–16.

ACKNOWLEDGMENTS

- This study was sponsored by GlaxoSmithKline (ClinicalTrials.gov: NCT01209026; HZA102936).
- R. Kempsford is an employee of GlaxoSmithKline.
- The clinical phase of this study was conducted by Hammersmith Medicines Research, London NW10 7EW, UK.
- Editorial support (in the form of copy-editing) was provided by Geoff Weller, PhD, at Gardiner-Caldwell Communications and was funded by GlaxoSmithKline.

Presented at the Annual Conference of the American Thoracic Society (ATS), San Francisco, CA, USA, May 18–23 2012

Poster No. K6

The effect of fluticasone furoate (FF) alone and in combination with vilanterol (VI) on the early asthmatic response 23h after dosing in patients with mild persistent asthma: results from a 28-day, randomized, controlled, crossover study

Oliver A(1), Quinn D(2), Goldfrad C(3), van Hecke B(4)*, Ayer J(1), Boyce M(4)

(1)GlaxoSmithKline Respiratory and Immuno-Inflammation Medicines Development Centre, Uxbridge, UK; (2)P3 Research, Wellington, New Zealand; (3)Quantitative Sciences Division, GlaxoSmithKline, Uxbridge, UK; (4)Hammersmith Medicines Research Ltd, London, UK. *Present Address: GSK Medicines Research Unit, Prince of Wales Hospital, Randwick, Australia

INTRODUCTION

- There is a need for preventative asthma maintenance therapy that provides lasting bronchoprotection against allergen provocation.
- An allergic response (AR) comprises two temporal events in a sensitized patient(1)
  - early AR (EAR): starts ~20min after allergen exposure with a rapid decline in lung function that recovers within 2–3h
  - late AR (LAR): a subsequent, less acute decline in lung function which starts 2–4h post exposure, is most severe at 8–12h and may not be fully recovered by 24h.
- The EAR is an important clinical event in sensitized asthma patients as it can result in significant lung function decline, albeit of a relatively short duration, and act as a precursor to the more sustained LAR.(2)
- FF, a novel inhaled once-daily corticosteroid, is being developed as a monotherapy for asthma(3)–(7) and in combination with VI (FF/VI), a novel inhaled once-daily long-acting $beta_2$ agonist(8) (LABA) for the management of asthma and COPD.

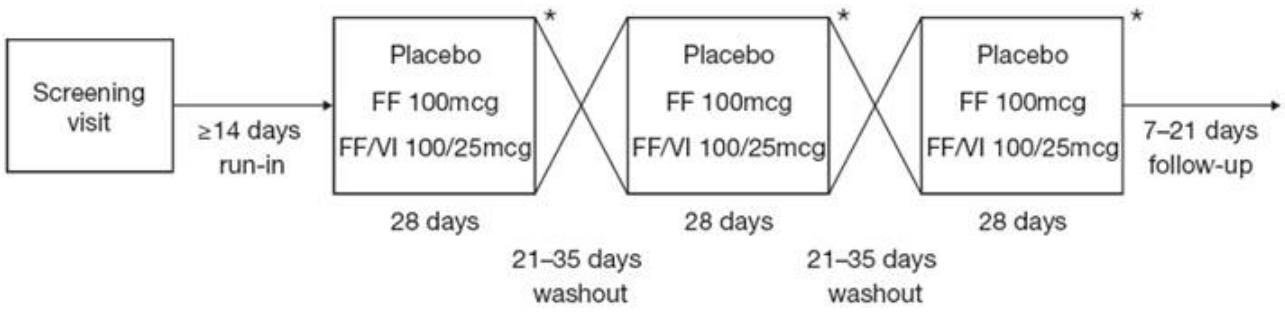
OBJECTIVES

- To assess the effect of FF and FF/VI vs placebo on the EAR at the trough of dosing (i.e. 22–23h post-dose).
- To determine any additional effect of FF/VI vs FF on the EAR at the trough of dosing.

METHODS

- Multicenter, randomized, double-blind, placebo-controlled, three-period crossover study. A schematic of the study design is shown in Figure 1.
- Patients were aged 18–65 years with mild asthma. Figure 1. Study design.

Figure 1. Study design.



*Inhaled allergen challenge 22–23h after final dose

- In addition, patients needed to demonstrate
  - methacholine challenge PC_{20} <8mg/mL at screening or within last 6 months, or previous AMP PC_{20} <60mg/mL, or histamine PC_{20} <8mg/mL within last 6 months
  - positive skin prick test (wheal ≥3mm vs neg. control) to ≥1 allergens (house dust mite, grass pollen, and cat hair) at screening or within 12 months of screening
  - EAR to inhaled allergen with a fall in FEV1 of ≥20% 5–30min after the final concentration of allergen (grass pollen, house dust mite or cat dander/hair) at screening.
- EAR was stimulated by inhaled allergen challenge ~23h post-dose, at an average time of 16:47h.

Efficacy endpoints and safety measures

- Primary: weighted mean (wm) change from post-saline baseline in FEV_1 between 0–2h after allergen challenge (22–23h post-treatment) on Day 29.

· Secondary endpoints: maximum % decrease and minimum absolute change from prechallenge (Day 29) baseline in FEV_1 between 0–2h; and incidence of treatment-related adverse events (AEs).

RESULTS

· 52 patients were randomized (intent-to-treat [ITT] population); 50 (96%) completed the study.

· Table 1 shows baseline demographic characteristics and lung function at screening.

Table 1. Patient baseline demographics and lung function at screening (ITT population).

Demographics	
Age(%)	
18–40 years	71
41–65 years	29
Female (%)	35
BMI, kg/m^2, mean (range)	25.94 (18.9-33.6)
White race (%)	92
Lung function	
Pre-bronchodilator FEV_1, L, mean (SD)	3.52 (0.713)
Pre-bronchodilator FEV_1 % predicted, mean (SD)	89.71 (8.848)

BMI = body mass index; SD = standard deviation

Efficacy

· FEV_1 increased from Day 1 to Day 29 with FF/VI and FF (Figure 2a).

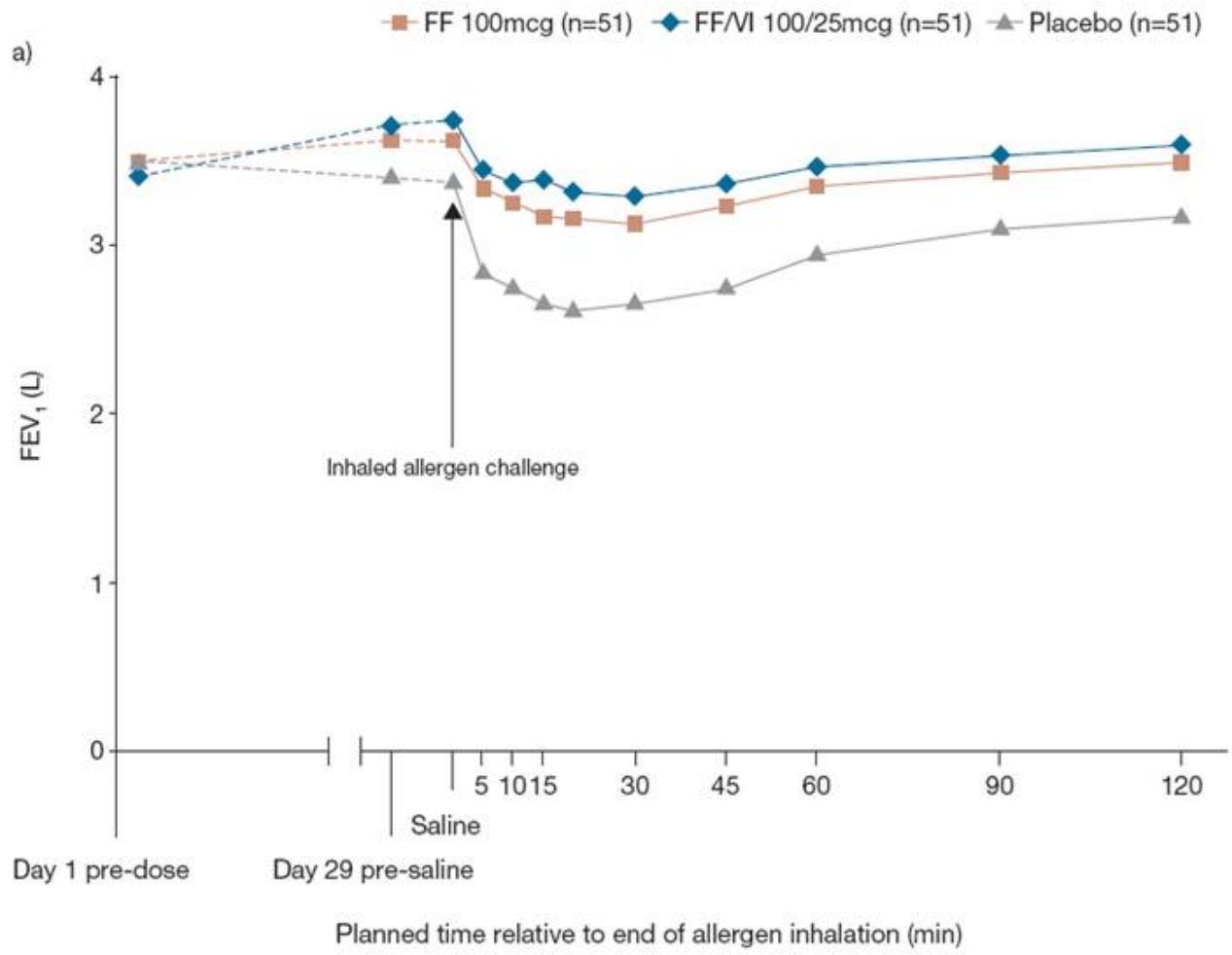
· Both FF 100mcg and FF/VI 100/25mcg attenuated the decline in FEV_1 following allergen challenge versus placebo (Figure 2; Table 2).

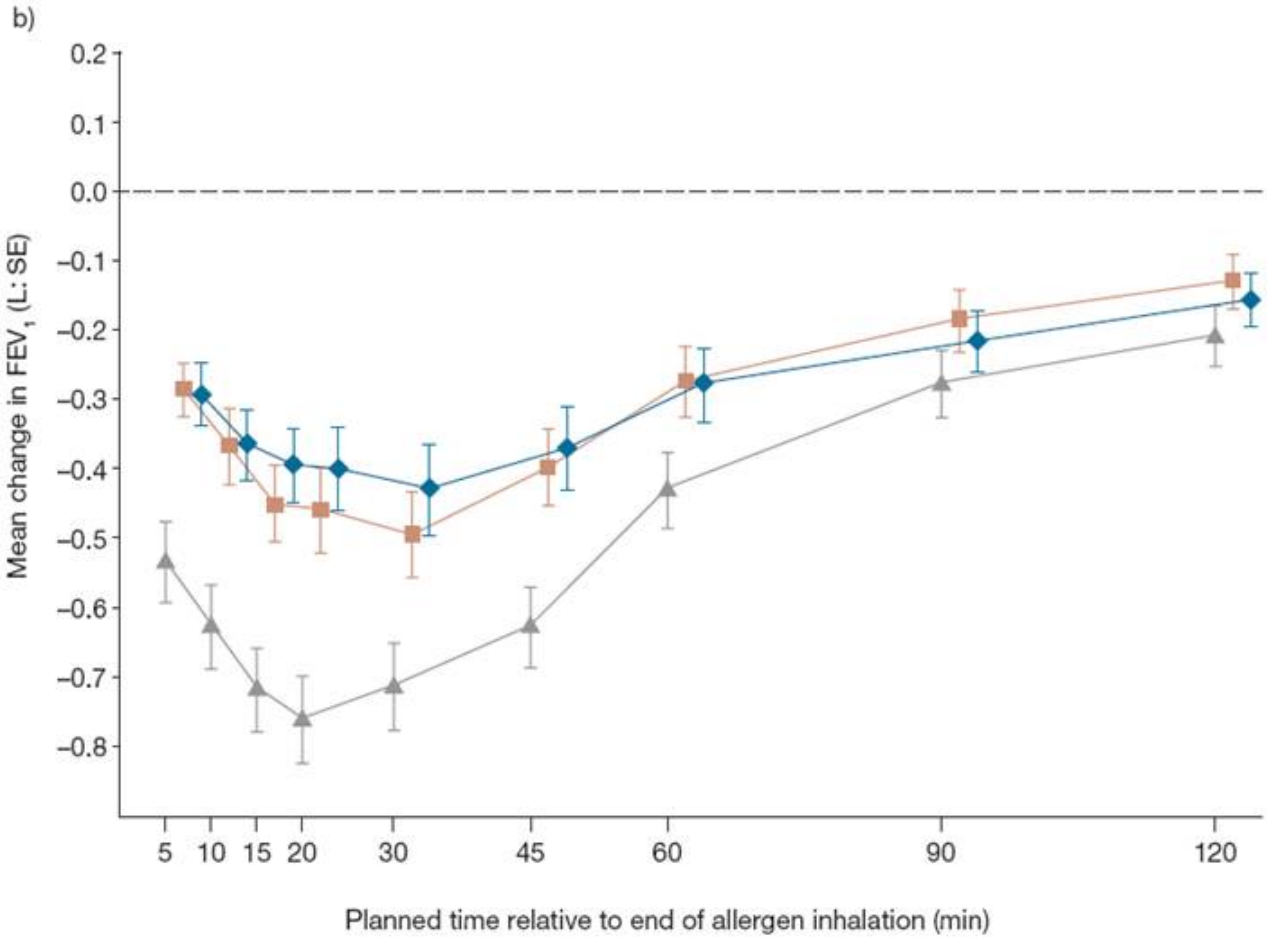
Table 2. Statistical analysis of treatment differences in change from post-saline baseline (ITT population).

	Treatment difference wmFEV_1 (L)	95% CI
FF – placebo	0.162	0.087, 0.237
FF/VI – placebo	0.145	0.069, 0.222
FF/VI – FF	–0.017	–0.091, 0.057
Max. percent decrease in FEV_1		
FF – placebo	10.951	8.053, 13.848
FF/VI – placebo	11.785	8.849, 14.721
FF/VI – FF	0.834	–2.010, 3.678
Max. absolute decrease in FEV_1 (L)		
FF – placebo	0.330	0.232, 0.429
FF/VI – placebo	0.331	0.231, 0.431
FF/VI – FF	0.001	–0.096, 0.097

Efficacy endpoints were analyzed using a mixed-effects analysis of covariance (ANCOVA) model, with fixed effects of treatment, period, subject-level baseline, period-level baseline, country, sex and age and subject fitted as a random effect
CI = confidence interval; wm = weighted mean

Figure 2. Time course (a) of mean absolute FEV_1 and (b) change in mean FEV_1 from post-saline baseline (ITT population): allergen challenge initiated at an average time of 16:47h.





Safety

· Overall incidence of AEs was similar between groups (Table 3).

Table 3. Most common(a) on-treatment AEs (ITT population).

N (%)	Placebo (n=51)	FF 100mcg (n=51)	FF/VI 100/25mcg (n=51)
Any on-treatment AE	20 (39)	22 (43)	18 (35)
Headache	9 (18)	11 (22)	5 (10)
Oropharyngeal pain	2 (4)	2 (4)	2 (4)
Nasopharyngitis	3 (6)	2 (4)	0
Cough	1 (2)	3 (6)	0
Chest discomfort	3 (6)	0	0
Mouth ulceration	0	2 (4)	2 (4)
Nausea	2 (4)	2 (4)	0
Dysphonia	0	2 (4)	2 (4)
Hot flush	0	0	2 (4)
Seasonal allergy	0	2 (4)	0

(a)≥3% of patients, any treatment group

CONCLUSIONS

- FF 100mcg and FF/VI 100/25mcg inhaled once daily over 28 days provided significant and clinically relevant bronchoprotection against the EAR relative to placebo in patients with mild asthma.

- That this protection is provided at the trough of dosing suggests true 24-h protection, and also suggests that FF 100mcg or FF/VI 100/25mcg has the potential to reduce symptoms associated with environmental allergens throughout the day in people with atopic asthma.

REFERENCES

(1) Gauvreau GM, et al. Contrib Microbiol 2007;14:21–32;
(2) O'Byrne PM. Allergy Asthma Immunol Res 2009;1:3–9;
(3) Busse WW, et al. Thorax 2012;67:35–41;
(4) Bleecker ER, et al. Eur Respir J 2010;36(Suppl. 54):204s;
(5) Bateman ED, et al. Respir Med 2012;106:642–50;
(6) Woodcock A, et al. Respir Res 2011;12:160;
(7) Woodcock A, et al. Respir Res 2011;12:132;
(8) Lötvall J, et al. Eur Resp J 2012;Feb 23 [Epub ahead of print].

ACKNOWLEDGMENTS

- This study was sponsored by GlaxoSmithKline. ClinicalTrials.gov: NCT01128569; protocol number: HZA113090.
- Amanda Oliver, Caroline Goldfrad and Jonathan Ayer are shareholders and employees of GlaxoSmithKline. Dean Quinn, Benjamin van Hecke and Malcolm Boyce have no conflict of interest. Benjamin van Hecke was employed by Hammersmith Research Ltd at the time of this study.
- Editorial support (in the form of writing assistance, assembling tables and figures, collating author comments, grammatical editing and referencing) was provided by Lisa Moore at Gardiner-Caldwell Communications and was funded by GlaxoSmithKline.

Presented at the Annual Conference of the American Thoracic Society (ATS), San Francisco, California, USA, May 18–23, 2012

Poster No. D69

Effect of fluticasone furoate (FF)/vilanterol (VI) administered once daily on 24h pulmonary function in patients with COPD: a randomized, three-way, incomplete block, crossover study

Boscia JA,(1) Pudi KK,(2) Zvarich MT,(3) Sanford L,(4) Crim C(3)

(1)CU Pharmaceutical Research, Union, SC, USA; (2)Upstate Pharmaceutical Research, Greenville, SC, USA; (3)Respiratory Medicines Development Center, GlaxoSmithKline, Research Triangle Park, NC, USA; (4)Quantitative Sciences Division, GlaxoSmithKline, Uxbridge, UK

INTRODUCTION

- Available inhaled corticosteroid/long-acting beta$_2$ agonist (ICS/LABA) combinations for COPD require twice-daily administration.
- Once-daily treatment could improve adherence and simplify treatment in chronic diseases such as COPD.(1)
- VI, an inhaled LABA with 24-h activity,(2) provides clinically relevant 24-h improvement in lung function in COPD.(3) FF is an ICS still active at 24h with demonstrated efficacy in asthma.(4)–(8)
- The combination FF/VI is being developed in a new dry powder inhaler (DPI) for the treatment of COPD(9) and asthma with the potential for once-daily dosing.

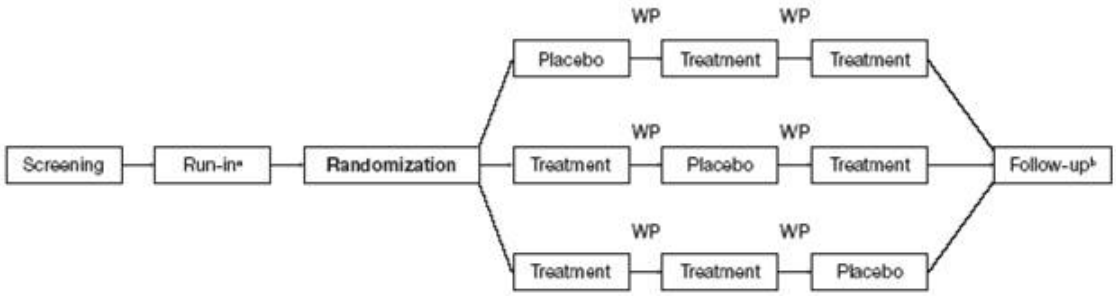
OBJECTIVES

- To evaluate the 24-h spirometric effect of FF/VI compared with placebo in patients with COPD.

METHODS

- Phase III, multicenter, randomized, double-blind, placebo-controlled, incomplete block, crossover study.
- Eligible patients were aged ≥40 years, had COPD, a post-bronchodilator FEV_1 of ≤70% predicted, FEV_1/FVC ratio of ≤0.70, current or prior history of ≥10 pack-years of cigarette smoking, and a score of ≥2 on the Modified Medical Research Council (mMRC) Dyspnea 0–4 Scale.
- A schematic of the study design is shown in Figure 1. Each treatment was inhaled once a day in the morning using a new DPI.

Figure 1. Study schematic.



Treatment was FF/VI 50/25mcg, FF/VI 100/25mcg, FF/VI 200/25mcg.
Each patient received two of three doses of FF/VI and placebo.

(a) Run-in period was 2 weeks; during this time all patients received placebo to establish a stable baseline. Each treatment period lasted 28 days.
(b) Follow-up was 7 days after the last treatment day.
WP = washout period (each 2 weeks).

Efficacy endpoints and safety measures

- Primary: time-adjusted (weighted mean) area under the FEV_1-vs-time curve over 24h at the end of each 28-day treatment period (Period Days 28–29)
  - analysis was performed using a mixed model with period, dose regimen, period baseline FEV_1 and mean baseline FEV_1 fitted as fixed effects and subject as a random coefficient.
- Secondary (1) 0–25h serial FEV_1 at Period Days 28–29
  - analysis was the same as used for primary analysis but with the addition of a categorical fixed effect for nominal time relative to dosing on Period Day 28 and a dose regimen by time interaction term.
- Secondary (2) change from treatment period baseline in trough FEV_1 (Period Day 29)
  - analysis was the same as used for the primary analysis.
- Safety assessments: incidence of adverse events (AEs), pneumonias and exacerbations; vital signs; QTc calculated by Fridericia formula (QTcF); heart rate; clinical laboratory evaluations, including serum glucose and potassium levels; oropharyngeal examinations; and 0–24h serum cortisol at Period Days 28–29.

RESULTS

- Fifty-four patients were randomized; all received at least one dose of study drug (intent-to-treat [ITT] population) and 78% completed all three treatment periods and follow-up.
- Table 1 shows patient demographic characteristics and screening lung function.

Table 1. Patient demographics and lung function at screening (ITT population).

Variable	Total (N=54)
Age, years	57.9 (9.24)
Female, n (%)	29 (54)
Race, n (%)	
White/Caucasian/European heritage	48 (89)
African American/African heritage	6 (11)
Smoking status at screening, n (%)	
Current smoker	45 (83)
Former smoker	9 (17)
Duration of COPD, n (%)	
<1 year	6 (11)
≥1 to <5 years	19 (35)
≥5 to <10years	17 (31)
≥10 years	12 (22)
Type of COPD, n (%)	
Chronic bronchitis(a)	35 (65)
Emphysema(a)	34 (63)
Patients with ≥1 exacerbation in the 12 months prior to screening, n (%)	
Requiring oral/systemic corticosteroids and/or antibiotics (but not involving hospitalization)	4 (7)
Requiring hospitalization	4 (7)
Dyspnea score on mMRC Dyspnea Scale, n (%)	
2	29 (54)
3	24 (44)
4	1 (2)
COPD medication taken at screening, n (%)	
Any COPD medication	36 (67)
Short-acting beta$_2$ agonist	34 (63)
Long-acting anticholinergic	5 (9)
Short-acting anticholinergic	5 (9)
Oxygen	2 (4)
ICS + LABA(b)	1 (2)
Lung function at screening	
Post-bronchodilator % predicted FEV_1	49.8 (10.61)
Post-bronchodilator FEV_1/FVC, %	52.9 (9.52)
Percent reversibility FEV_1(c)	8.8 (16.97)
FEV_1 reversibility, mL(c)	90.7 (227.12)
Patients with reversible(d) FEV_1, n (%)	14 (26)

Data presented as mean (SD) unless otherwise stated
(a)Patients could select both chronic bronchitis and emphysema;
(b)salmeterol xinafoate plus fluticasone propionate;
(c)N=53;
(d)Reversibility was defined as an increase in FEV_1 of ≥12% and ≥200mL following administration of albuterol/salbutamol

SD = standard deviation

Efficacy

- All three strengths of FF/VI demonstrated significantly higher 0–24h weighted mean FEV_1 than placebo over Period Days 28–29. The effect was not ICS-dose related; adjusted mean improvements in FEV_1 for FF/VI compared with placebo were 220–236mL (all p<0.001; Figure 2).
- Adjusted mean improvements against placebo in change from period baseline serial FEV_1 measures (Period Days 28–29) were observed at each timepoint and with each strength of FF/VI over the 0–25h period (147–301mL; p<0.001 vs placebo; Figure 3a and 3b), indicating sustained bronchodilation.
- Analysis of change from period baseline in trough FEV_1 at the end of the 28-day treatment periods showed both statistically and clinically significantly greater values for all three strengths of FF/VI compared with placebo (adjusted mean improvements, 177–211mL; all p<0.001; Figure 4).

Figure 2. Weighted mean treatment differences from placebo in 0–24h weighted mean FEV_1 (L) over Period Days 28–29 (ITT population).

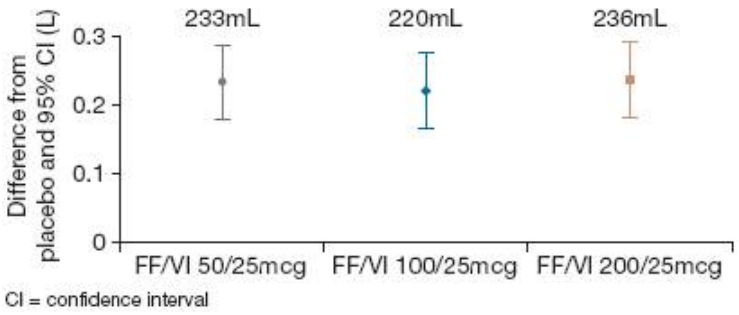


Figure 3. (a) Adjusted mean and (b) adjusted mean treatment differences from placebo for change from period baseline in serial 0–25h FEV_1 (L) over Period Days 28–29 (ITT population).

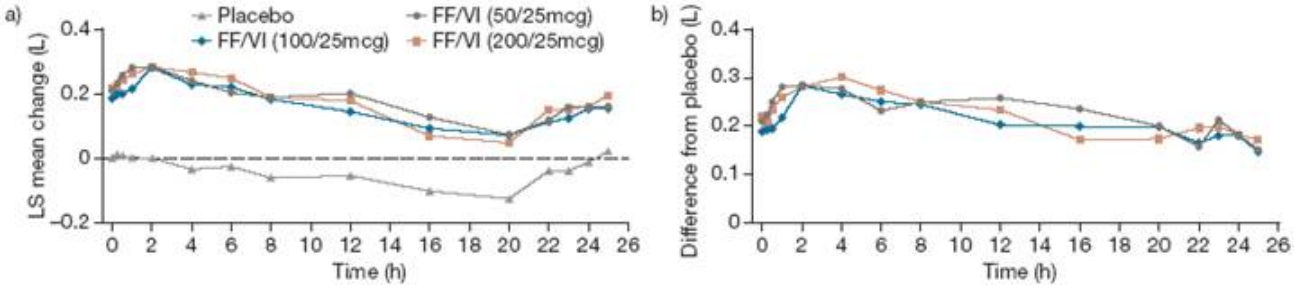
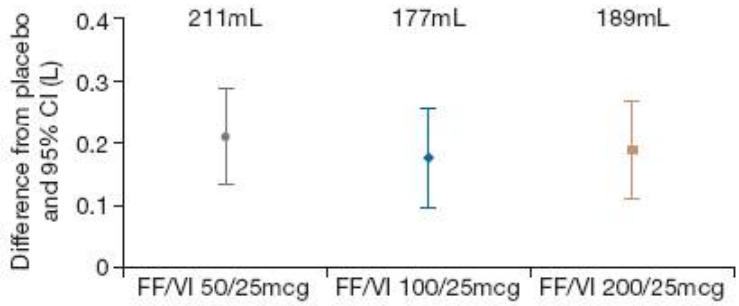


Figure 4. Adjusted mean differences from placebo in change from period baseline in trough FEV_1 (L) at Period Day 29 (ITT population).



Safety

- FF/VI was well tolerated; the number of on-treatment AEs was low in each FF/VI group and was not ICS-dose dependent (3–4 [10–12%] with FF/VI; 2 [4%] with placebo) (Table 2).
- Two serious AEs were reported: one during the first washout period after treatment with placebo and one during the second washout period after treatment with FF/VI 50/25mcg (Table 2); neither was considered to be treatment related.
- No pneumonias were reported.
- No significant effects on vital signs, QTcF, heart rate, serum glucose or serum potassium levels were reported.
- Four cases of possible candidiasis were identified: one produced a positive culture (pre-FF/VI 200/25mcg treatment; period baseline assessment).
- Mean serum cortisol levels over Period Days 28–29 with FF/VI were similar to placebo (Figure 5). No significant effects on 0–24h weighted mean serum cortisol were seen (LS geometric mean ratio FF/VI to placebo 0.89–0.98; p=NS).

Figure 5. Raw geometric means for serial serum cortisol over Period Days 28–29 (nmol/L) (ITT population).

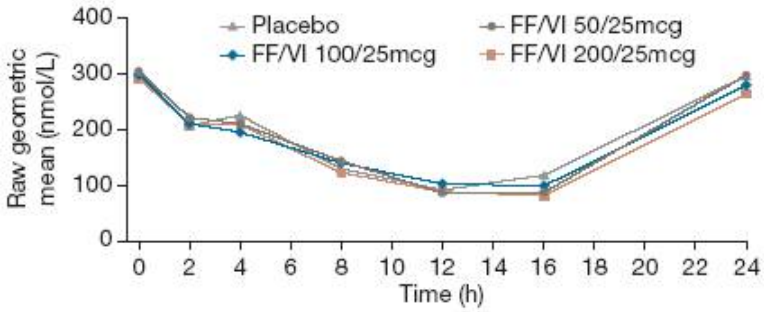


Table 2. Summary of AEs(a) reported by at least one patient in any treatment group (ITT population).

Variable	Placebo (N=51)	FF/VI 50/25mcg (N=34)	FF/VI 100/25mcg (N=33)	FF/VI 200/25mcg (N=31)

AEs on treatment, n (%)	**2 (4)**	**4 (12)**	**4 (12)**	**3 (10)**
Infections and infestations				
Cellulitis	0	0	1 (3)	0
Rhinitis	0	0	1 (3)	0
Sinusitis	0	1 (3)	0	0
Upper respiratory tract infection	0	0	1 (3)	0
Urinary tract infection	1 (2)	0	0	0
Respiratory, thoracic and mediastinal disorders				
Epistaxis	0	1 (3)	0	0
Nasal congestion	0	1 (3)	0	0
Oropharyngeal pain	1 (2)	0	0	0
Pharyngeal inflammation	0	0	0	1 (3)
Postnasal drip	1 (2)	0	0	0
Gastrointestinal disorders				
Diarrhea	0	0	1 (3)	0
Vomiting	0	0	1 (3)	0
Injury, poisoning and procedural complications				
Caustic injury	0	0	0	1 (3)
Musculoskeletal and connective tissue disorders				
Muscle spasms	0	0	0	1 (3)
Nervous system disorders				
Headache	0	1 (3)	0	0
Vascular disorders				
Raynaud’s phenomenon	0	1 (3)	0	0
AEs during washout, n (%)	**3 (6)**	**4 (12)**	0	**1 (3)**
Musculoskeletal and connective tissue disorders				
Neck pain	1 (2)	1 (3)	0	0
CREST syndrome	0	1 (3)	0	0
Infections and infestations				
Upper respiratory tract infection	1 (2)	1 (3)	0	0
Nervous system disorders				
Headache	1 (2)	0	0	0
Transient ischemic attack	0	1 (3)(b)	0	0
Gastrointestinal disorders				
Nausea	0	1 (3)(b)	0	0
Metabolism and nutrition disorders				
Hyponatremia	0	1 (3)(b)	0	0
Vascular disorders				
Hypertension	0	0	0	1 (3)
AEs leading to permanent withdrawal from study, n (%)	0	**1 (3)**(b)	0	0
Serious AEs, n (%)	**1 (2)**	**1 (3)**(b)	0	0

(a)AEs defined by the Medical Dictionary for Regulatory Activities: one patient could report more than one AE
(b)This was a single patient who experienced a serious AE of transient ischemic attack (with previous history of strokes), accompanied by AEs of nausea and hyponatremia, which occurred during the second washout period and led to withdrawal from treatment
During the run-in period, prior to randomization, one patient reported an upper respiratory tract infection; this AE was not considered to be treatment related

CONCLUSIONS

· FF/VI inhaled once daily in the morning for 28 days produced significant improvements in pulmonary function with a prolonged (>24h) duration of action and was well tolerated, supporting once-daily dosing in patients with COPD.

REFERENCES

(1) Saini SD, et al. Am J Manag Care 2009;15:e22–e33.
(2) Morrison V, et al. Am J Respir Crit Care Med 2010;181:A4453.
(3) Hanania NA, et al. Chest 2012 Jan 12 [Epub ahead of print].
(4) Busse WW, et al. Thorax 2012;67:35–41.

(5) Bleecker ER, et al. Eur Respir J 2010;36(Suppl. 54):204s.
(6) Bateman ED, et al. Resp Med 2012;106:642–650.
(7) Woodcock A, et al. Respir Res 2011;12:160.
(8) Woodcock A, et al. Respir Res 2011;12:132.
(9) Lötvall J, et al. BMJ Open 2012;2:e000370.

ACKNOWLEDGMENTS

· This study was sponsored by GlaxoSmithKline. ClinicalTrails.gov: NCT01072149; protocol number: HZC110946.

· Joseph A Boscia (presenting author) is on the speakers' bureau of GlaxoSmithKline and was a principal investigator in this clinical trial, which was sponsored by GlaxoSmithKline and administered by his employer CU Pharmaceutical Research.

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

Presented at the Annual Conference of the American Thoracic Society (ATS), San Francisco, California, USA, May 18–23, 2012

Poster No. D68

Safety and tolerability of the GSK573719/vilanterol combination in patients with COPD

Feldman G(1), Walker R(2), Brooks J(3), Mehta R(4), Crater G(5)

(1)S. Carolina Pharmaceutical Research, Spartanburg, USA; (2)Greenville Pharmaceutical Research, Greenville, USA; (3)GlaxoSmithKline, Uxbridge, UK; (4)GlaxoSmithKline, Research Triangle Park, USA; (5)GlaxoSmithKline, Mississauga, Canada

INTRODUCTION

- Bronchodilators are central to the pharmacological management of chronic obstructive pulmonary disease (COPD) symptoms. Treatment with long-acting bronchodilators, a beta$_2$ agonist (LABA) or a muscarinic antagonist (LAMA), has been shown to be more effective than a short-acting bronchodilator.(1)
- Long-acting bronchodilators, however, may increase the risk of cardiovascular side effects such as tachycardia and prolongation of the QTc interval.(2)–(4)
- Combination therapy with different classes of pharmacological agents has the potential to increase efficacy and decrease the risk of side effects, compared with increasing the dose of a single bronchodilator when symptoms are not adequately controlled.(1)
- GSK573719 (umeclidinium, UMEC) is an investigational inhaled LAMA currently in development as a once-daily combination product with vilanterol (GW642444, VI), an investigational, potent and selective LABA, for treatment of COPD.
- Previous studies of UMEC(5)–(6) and VI(7) monotherapies in healthy volunteers and in patients with COPD(8)–(12) have demonstrated that both treatments are well tolerated and have favorable safety profiles.
- This was the first clinical study conducted to evaluate the safety and tolerability of the UMEC/VI combination in patients with COPD.

OBJECTIVES

- Evaluate the safety, tolerability, pharmacodynamics (PD), and pharmacokinetics (PK) of repeat inhaled doses of UMEC/VI (500/25mcg) administered once daily for 28 days in patients with COPD.

METHODS

Study population

- Males and females $\geq$40 years of age with an established clinical history of COPD, a history of smoking $\geq$10 packs of cigarettes a year, a post-albuterol/salbutamol forced expiratory volume in 1 second (FEV_1)/forced vital capacity (FVC) ratio of $\leq$0.70 and a post-albuterol/salbutamol FEV_1 of $\leq$0.80 of predicted normal values.
- Patients were excluded if they had a current diagnosis of asthma, alpha1-antitrypsin deficiency, or an abnormal 12-lead electrocardiogram (ECG) that resulted in an active medical problem or had clinically significant abnormalities from 24-h Holter ECG monitoring at screening, or had used oral corticosteroids, antibiotics, or had been hospitalized due to exacerbation of COPD or a lower respiratory tract infection within 3 months prior to screening.

Study design and treatment

- Multicenter, randomized, placebo-controlled, double-blind, parallel-group study at four centers in the USA from January 14 2010 to April 20 2010 (ClinicalTrials.gov: NCT01039675; protocol number: DB2113120).
- Patients who met the eligibility criteria completed a run-in period of 5–8 days. Following the run-in period, patients who met the randomization criteria received 4 weeks of treatment with a 7-day follow-up.
- Patients were randomized 4:1 to UMEC/VI (500/25mcg) or placebo administered via a novel dry powder inhaler
  - this ratio provided 90% power to demonstrate the non-inferiority of UMEC/VI to placebo in terms of weighted mean pulse rate assuming at least 36 patients in the UMEC/VI group and 9 patients in the placebo group completed the study.

Endpoints

- Primary: weighted mean pulse rate during 0–6h post dose on Day 28.
- Secondary: weighted mean pulse rate during 0–6h post dose on Days 1 and 14; and maximum and minimum pulse rate during 0–6h post dose on Days 1, 14 and 28.
- Blood pressure, ECG, 24-h Holter monitoring, adverse events (AEs), incidence of COPD exacerbations, spirometry, hematology, biochemistry, urinalysis, and PK were assessed.

RESULTS

Demographics

- 77 patients were screened, 51 were randomized (intent-to-treat population [ITT]), 44 completed the study

- seven patients prematurely withdrew from the study: 2 AEs (swollen tongue and upper abdominal pain); 2 lack of efficacy(exacerbation); 1 lost to follow-up; 1 investigator discretion; 1 withdrew consent.

· Baseline patient characteristics and screening lung function are shown in **Table 1.**

Safety endpoints

Pulse rate

· The adjusted mean changes from baseline in weighted mean pulse rate during 0–6h post dose on Day 28 (primary endpoint) were similar between UMEC/VI and placebo (–0.5 beats per min [bpm]; 95% confidence interval [CI]: –5.5, 4.5; **Figure 1**)
  · UMEC/VI was non-inferior to placebo as the upper confidence limit was below the prespecified non-inferior limit of 10bpm.

· The adjusted mean changes from baseline in weighted mean pulse rate during 0–6h post dose on Day 1 were similar for UMEC/VI (–0.6bpm) and placebo (–1.2bpm). On Day 14, the values were 3.1bpm (UMEC/VI) and –1.7bpm (placebo).

· The adjusted mean treatment differences between UMEC/VI and placebo in maximum pulse rate during 0–6h post dose were small
  · 2.0bpm (95% CI: –3.7, 7.6) on Day 1; 4.8bpm (95% CI: –1.8, 11.3) on Day 14, and –1.3bpm (95% CI: –6.9, 4.3) on Day 28 (**Figure 2a**).

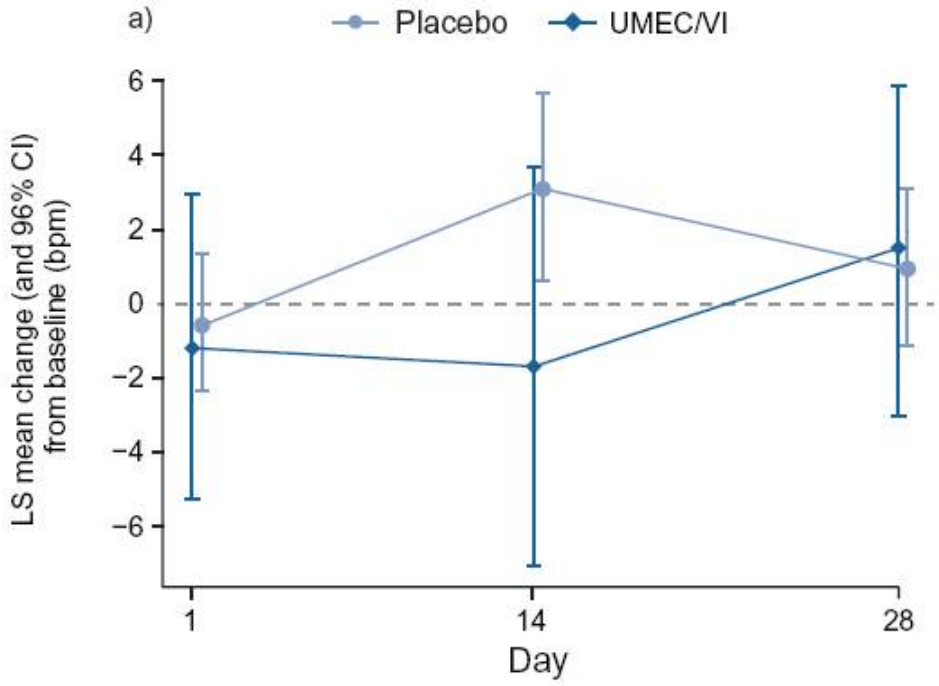
· The adjusted mean treatment differences between UMEC/VI and placebo in minimum pulse rate during 0–6h post dose were also small
  · 0.3bpm (95% CI: –4.3, 5.0) on Day 1; 4.0bpm (95% CI: –2.3, 10.2) on Day 14, and 1.7bpm (95% CI: –3.6, 7.1) on Day 28 (**Figure 2b**).

TABLE 1: BASELINE DEMOGRAPHICS AND SCREENING LUNG FUNCTION (ITT POPULATION)

	Placebo (n=9)	UMEC/VI (500/25mcg) (n=42)
Age		
Mean (SD)	58.7 (9.77)	59.2 (9.48)
Range	42-69	40-83
Female, n (%)	2 (22)	18 (43)
Tobacco history, n (%)		
Current smoker	7 (78)	24 (57)
Former smoker	2 (22)	18 (43)
Smoking pack-years		
Mean (SD)	75.7 (44.70)	58.4 (25.98)
Range	22-148	14-133
Race, n (%)		
White	8 (89)	36 (86)
African American/African Heritage	1 (11)	6 (14)
Screening lung function		
Post-bronchodilator FEV_1 (L)	1.642 (0.4558)	1.482 (0.5840)
Post-bronchodilator percent predicted FEV_1 (%)	50.58 (15.609)	48.37 (15.376)
Percent reversibility FEV_1 (%)	5.05 (9.178)	8.54 (11.015)
Post-bronchodilator FEV_1/FVC (L)	0.523 (0.127)	0.540 (0.123)

SD = standard deviation

FIGURE 1: CHANGE FROM BASELINE IN 0–6H WEIGHTED MEAN PULSE RATE (ITT POPULATION)



Analyses were performed using a repeated measures model with covariates of baseline pulse rate, sex, age, smoking status, treatment day, and day by treatment and day by baseline interactions
LS = least squares

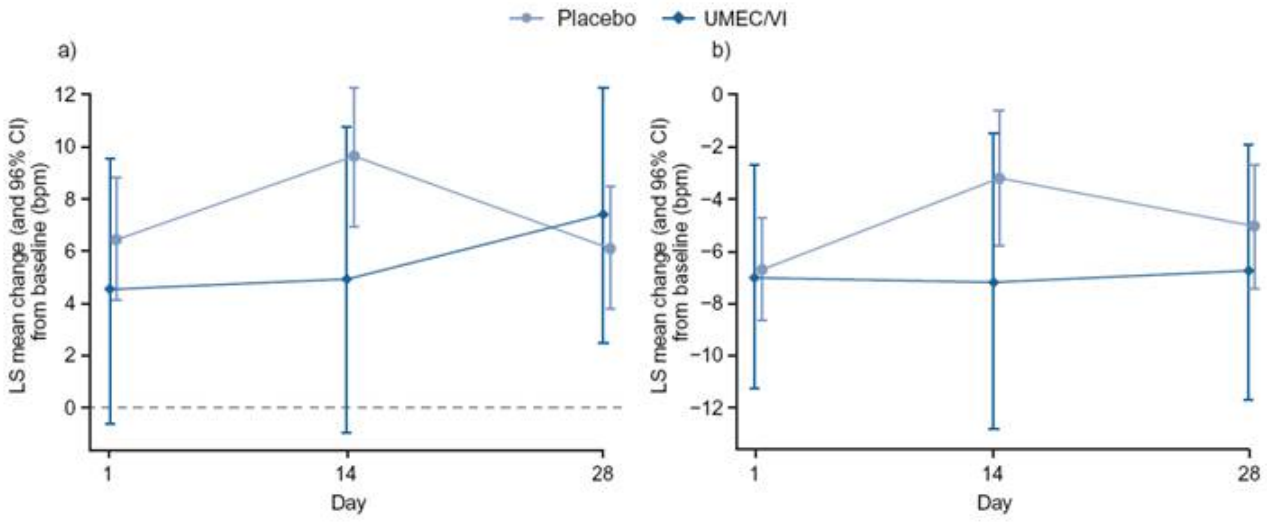
Blood pressure, ECG, and clinical laboratory assessments

- No clinically significant differences were observed for blood pressure and minimum and maximum heart rate.
- At screening, no patient had an abnormal clinically significant finding in 24-h Holter ECG assessments. At Day 28, 86% of patients on UMEC/VI and 89% of patients on placebo had no change or insignificant changes, while 11% of patients in each treatment group had clinically significant unfavorable changes.
- The proportion of patients receiving UMEC/VI with clinically significant unfavorable changes from baseline in the 12-lead ECG finding at any time post baseline was low and comparable with placebo (29% vs 22%).
- No clinically significant difference was observed between UMEC/VI and placebo in the change from baseline in 0–6h maximum QTcF.
- No clinically relevant treatment effects were noted in any laboratory assessments.

AEs

- A greater proportion of patients receiving UMEC/VI reported AEs than patients receiving placebo (26% vs 11%; **Table 2**).
- No single AE was reported in more than one patient; no serious AEs were reported.

FIGURE 2. CHANGE FROM BASELINE IN 0–6H MAXIMUM AND MINIMUM PULSE RATES (ITT POPULATION)



Analyses were performed using a repeated measures model with covariates of baseline pulse rate, sex, age, smoking status, treatment day, and day by treatment and day by baseline interactions

TABLE 2: REPORTED ON-TREATMENT ADVERSE EVENTS (ITT POPULATION)

Most common AE, n (%)	Placebo (n=9)	UMEC/VI (500/25mcg) (n=42)
Any on-treatment AE	1 (11)	11 (26)

Sinusitis	1 (11)	1 (2)
Gastroenteritis	0	1 (2)
Upper abdominal pain	0	1 (2)(a)
Dry mouth	0	1 (2)
Nausea	0	1 (2)
Swollen tongue	0	1 (2)
Cough	0	1 (2)
Dyspnea	0	1 (2)
Pleurisy	0	1 (2)
Allergic rhinitis	0	1 (2)
Gout	0	1 (2)
Hypokalemia	0	1 (2)
Abnormal dreams	0	1 (2)
Anxiety	0	1 (2)
Cholelithiasis	0	1 (2)
Muscle strain	0	1 (2)
Rash	0	1 (2)
Any post-treatment AE	1 (11)	0
Any treatment-related AEs	0	1 (2)(b)
AEs leading to withdrawal or discontinuation of study medication	0	3 (7)
Upper abdominal pain(c)	0	1 (2)
Swollen tongue	0	1 (2)
Pleurisy(c)	0	1 (2)

(a)AE was reported as right upper quadrant pain
(b)One patient reported treatment-related AEs of abnormal dreams, swollen tongue and dry mouth
(c)Not considered related to study treatment

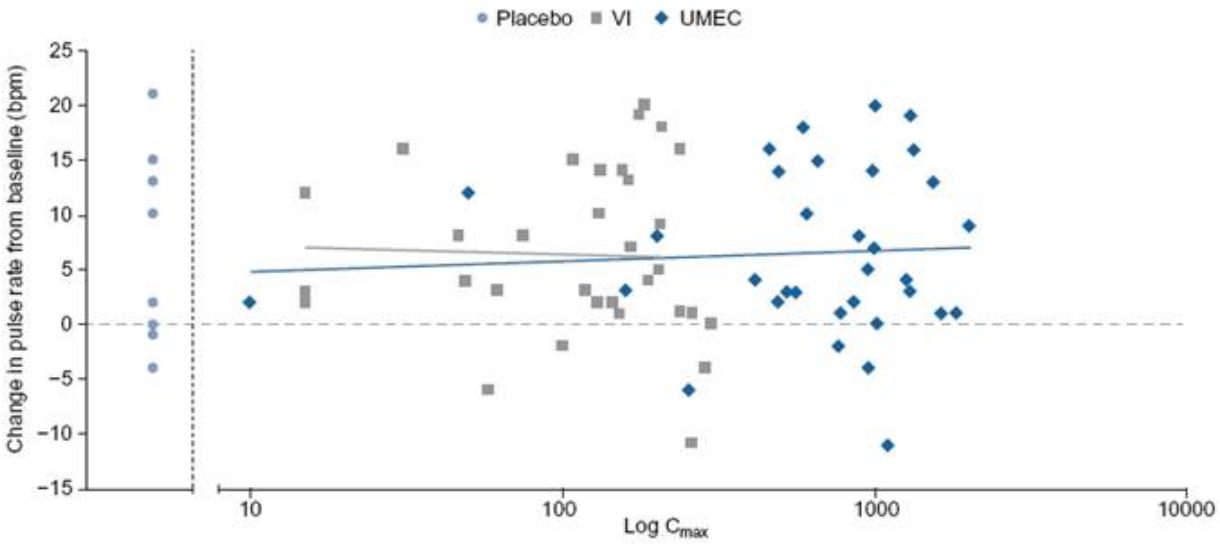
COPD exacerbation
· Three patients receiving UMEC/VI had a COPD exacerbation
  · lack of efficacy was reported by the investigator as the cause of two exacerbations; these patients were withdrawn from the study
  · an upper respiratory infection other than the common cold was the cause of the other exacerbation
  · all three patients were treated with antibiotics and corticosteroids.

Spirometry

· Greater improvements were observed for UMEC/VI compared with placebo for change from baseline for both trough FEV_1 and serial FEV_1 over 0–6h post dose
  · raw mean change from baseline in trough FEV_1 on Day 29 with UMEC/VI was 163mL and with placebo was 9mL
  · increases in serial FEV_1 from baseline occurred on Day 1 at 1h, 3h, and 6h (Day 1: 194–265mL), and on Days 14 and 28 at pre-dose, 1h, 3h and 6h (Day 14: 155–271mL; Day 28: 160–273mL) with UMEC/VI.

PK/PD analysis
· Both UMEC and VI were rapidly absorbed (median time to maximum plasma concentration [t_{max}] ~6min for both drugs) following single and repeat doses of UMEC/VI. No accumulation for area under the curve (AUC) or maximum plasma concentration (C_{max}) on Day 28 vs Day 1 was observed.
· No relationship between steady-state C_{max} and change from baseline in pulse rate on Day 28 was observed for UMEC or VI (**Figure 3**). Furthermore, the level of change on Day 28 with active treatment was similar to that observed with placebo.

FIGURE 3: INDIVIDUAL CHANGE FROM BASELINE IN PULSE RATE VS MAXIMUM PLASMA CONCENTRATION (C_{MAX}) ON DAY 28(a) (PK POPULATION)



(a)Linear regression: UMEC C_{max} vs change in baseline pulse rate, Y=0.95X + 3.70
r^2=0.0034; VI C_{max} vs change in baseline pulse rate, Y=–0.696X + 7.79 r^2=0.00115

CONCLUSIONS

- The UMEC/VI (500/25mcg) combination administered once daily for 28 days in patients with moderate-to-very severe COPD was not associated with any clinically significant effects on pulse rate, blood pressure, heart rate or incidence of AEs relative to placebo.

- Both UMEC and VI showed rapid absorption followed by a quick decline in plasma concentration indicating rapid distribution and elimination. No association between steady-state C_{max} and change from baseline in pulse rate occurred for either UMEC or VI.

- The safety profile of UMEC/VI demonstrated in this study further supports the development of this once-daily LAMA/LABA combination as a COPD therapy.

REFERENCES

(1) GOLD. Global Strategy for Diagnosis, Management, and Prevention of COPD – updated December 2011. Available at:www.goldcopd.org. Last accessed 24 April 2012.
(2) Spiriva (tiotropium) prescribing information. http://bidocs.boehringer-ingelheim.com/BIWebAccess/ViewServlet.ser?docBase=renetnt&folderPath=/Prescribing+Information/Pls/Spiriva/Spiriva.pdf. Last accessed 24 April 2012.
(3) Serevent (salmeterol) prescribing information. http://us.gsk.com/products/assets/us_serevent_diskus.pdf. Last accessed 24 April 2012.
(4) Arcapta (indacaterol) prescribing information. http://www.pharma.us.novartis.com/product/pi/pdf/arcapta.pdf. Last accessed 24 April 2012.
(5) Cahn A, et al. Eur Resp J 2011;38(Suppl. 55):723s.
(6) Mehta R, et al. Eur Resp J 2011;38(Suppl. 5):723s.
(7) Kempsford RD, et al. Am J Respir Crit Care Med 2010;181:A446.
(8) Decramer M, et al. Eur Resp J 2011;38(Suppl. 55):150s.
(9) Kelleher D, et al. Eur Resp J 2011;38(Suppl. 55):140s.
(10) Mehta R, et al. Eur Resp J 2011;38(Suppl. 55):138s.
(11) Kempsford RD, et al. Am J Respir Crit Care Med 2010;181:A4447.
(12) Hanania N, et al. Chest 2012. Epub ahead of print.

ACKNOWLEDGMENTS

- This study was sponsored by GlaxoSmithKline.
- GF and RW received funds as Principal Investigators in this clinical trial sponsored by GlaxoSmithKline.
- Editorial support (in the form of writing assistance, assembling tables and figures, collating author comments, grammatical editing and referencing) was provided by Tara N Miller, PhD at Gardiner-Caldwell Communications (Lyndhurst, NJ) and was funded by GlaxoSmithKline.

Presented at the Annual Conference of the American Thoracic Society (ATS), San Francisco, California, USA, May 18–23, 2012