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 19, 2014**

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 19, 2014 at the American Thoracic Society (ATS) 2014 International Conference held in San Diego, California, GlaxoSmithKline (GSK) presented posters containing information from Phase 3 studies of umeclidinium/vilanterol (UMEC/VI) and a Phase 3 study of ELLIPTA®, the new dry powder inhaler. ANORO™ ELLIPTA® is the proprietary name for UMEC/VI. ANORO™ ELLIPTA® is a combination of two bronchodilators, a long-acting beta$_2$ agonist (LABA) and an anticholinergic in a single inhaler. UMEC/VI has been developed under the 2002 LABA collaboration between Glaxo Group Limited and Theravance, Inc. The posters are filed as Exhibits 99.1 to 99.3 to this report and are incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit	Description
Exhibit 99.1	Bronchodilator response to the long-acting bronchodilator combination of umeclidinium/vilanterol across subgroups of patients with COPD
Exhibit 99.2	Cardiovascular safety of umeclidinium/vilanterol in COPD: results from eight randomized clinical trials
Exhibit 99.3	A randomized controlled trial comparing two dry powder inhalers: more patients with COPD prefer ELLIPTA compared to DISKUS based on inhaler-specific attributes

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 19, 2014

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

EXHIBIT INDEX

Exhibit No.	Description
99.1	Bronchodilator response to the long-acting bronchodilator combination of umeclidinium/vilanterol across subgroups of patients with COPD
99.2	Cardiovascular safety of umeclidinium/vilanterol in COPD: results from eight randomized clinical trials
99.3	A randomized controlled trial comparing two dry powder inhalers: more patients with COPD prefer ELLIPTA compared to DISKUS based on inhaler-specific attributes

Exhibit 99.1

Poster Board No. 411

Bronchodilator response to the long-acting bronchodilator combination of umeclidinium/vilanterol across subgroups of patients with COPD

MeiLan K. Han(1), Chris Kalberg(2), Jean Brooks(3), Alison Church(2)

(1)Division of Pulmonary Medicine, University of Michigan, Ann Arbor, MI, USA; (2)GlaxoSmithKline, Respiratory and Immuno-Inflammation, Research Triangle Park, NC, USA; (3)GlaxoSmithKline, Stockley Park, Uxbridge, UK

INTRODUCTION

- Long-acting muscarinic antagonists (LAMAs) and long-acting β2-agonists (LABAs) have distinct and complementary mechanisms of action to improve bronchodilation.
- The fixed-dose combination of the LAMA umeclidinium (UMEC) and the LABA vilanterol (VI) (ANORO™ ELLIPTA™) has been shown to produce statistically significant improvements in lung function compared with UMEC or VI monotherapy, in patients with chronic obstructive pulmonary disease (COPD).(1)–(3)
- ANORO™ ELLIPTA™ is an approved maintenance treatment for COPD in the US. It is not indicated for treatment of asthma.
- This evaluation reports findings from the subgroup analyses of trough forced expiratory volume in 1 second (FEV_1) from Phase III studies conducted for UMEC/VI.

METHODS

Subgroup analyses

- Pre-specified subgroup analyses were conducted using integrated data (N=4713) from four 24-week, multicenter, randomized, placebo- or active-controlled studies (ClinicalTrials.gov: NCT01316900; protocol number: DB2113360; ClinicalTrials.gov: NCT01313637, protocol number: DB2113361; ClinicalTrials.gov: NCT01313650, protocol number: DB2113373; ClinicalTrials.gov: NCT01316913, protocol number: DB2113374).
- Subgroups were defined based on gender, age, disease severity (GOLD stage), smoking status, inhaled corticosteroid (ICS) use, and bronchodilator reversibility (defined as an increase in FEV_1 from baseline of ≥12% and 200 mL following 4 puffs of albuterol at screening), geographical region, and treatment naivety.
  - Race (White vs. non-White) was included as a post-hoc analysis.
- Trough FEV_1 at Day 169 (Week 24) was the primary efficacy endpoint in each study and was defined as the mean of FEV_1 values obtained 23 h and 24 h after dosing on Day 168 (Week 24 visit).

Patients

- Males and females ≥40 years of age with with a diagnosis of COPD; current or former cigarette smokers with ≥10-pack-year smoking history; post-albuterol FEV_1/forced vital capacity <0.7 and predicted FEV_1 ≤70% of normal; and a modified Medical Research Council dyspnea scale score ≥2.

Treatments

- Eligible patients were randomized to the following once-daily treatments:
  - In Study 1 (ClinicalTrials.gov identifier: NCT01313650), patients were randomized (3:3:3:2) to UMEC/VI 62.5/25 mcg (delivering 55/22 mcg), UMEC 62.5 mcg (delivering 55 mcg), VI 25 mcg (delivering 22 mcg), or placebo.(1)
  - In Study 2 (ClinicalTrials.gov: NCT01313637) patients were randomized (3:3:3:2) to UMEC/VI 125/25 mcg (delivering 113/22 mcg), UMEC 125 mcg (delivering 113 mcg), VI 25 mcg or placebo.(2)
  - In Studies 3 and 4 (ClinicalTrials.gov: NCT01316900 and ClinicalTrials.gov: NCT01316913) patients were randomized 1:1:1:1 to UMEC/VI 125/25 mcg, UMEC/VI 62.5/25 mcg, tiotropium bromide (TIO) 18 mcg, and either VI 25 (Study 3) or UMEC 125 mcg (Study 4).(4)
- All medications (except TIO) were administered using the ELLIPTA™ inhaler.
- TIO was administered via the Handihaler®.

RESULTS

- For all patients (intent-to-treat [ITT] analysis) UMEC/VI 125/25 mcg and UMEC/VI 62.5/25 mcg provided significantly greater improvements from baseline in trough FEV_1 at Day 169 compared with placebo (0.216 and 0.199 L, respectively; both $p<0.001$).
- Results for the subgroups analysis were consistent with the ITT analysis: both UMEC/VI 125/25 mcg and UMEC/VI 62.5/25 mcg provided statistically significant improvements in trough FEV_1 at Day 169 compared with placebo across subgroups (Table 1).
- Improvements compared with placebo for the White (84%) and non-White (16%) subgroups were 0.217 L and 0.208 L respectively with UMEC/VI 125/25 mcg and 0.190 L and 0.235 L respectively with UMEC/VI 62.5/25 mcg, reflecting the results from the overall analysis.
- The magnitude of improvement over placebo in trough FEV_1 at Day 169 was similar for UMEC/VI 125/25 mcg and UMEC/VI 62.5/25 mcg across subgroups with the exception of a larger response with UMEC/VI 125/25 mcg compared with UMEC/VI 62.5/25 mcg in the subgroup of patients demonstrating bronchodilator reversibility at screening (Table 1 and Figure 1).

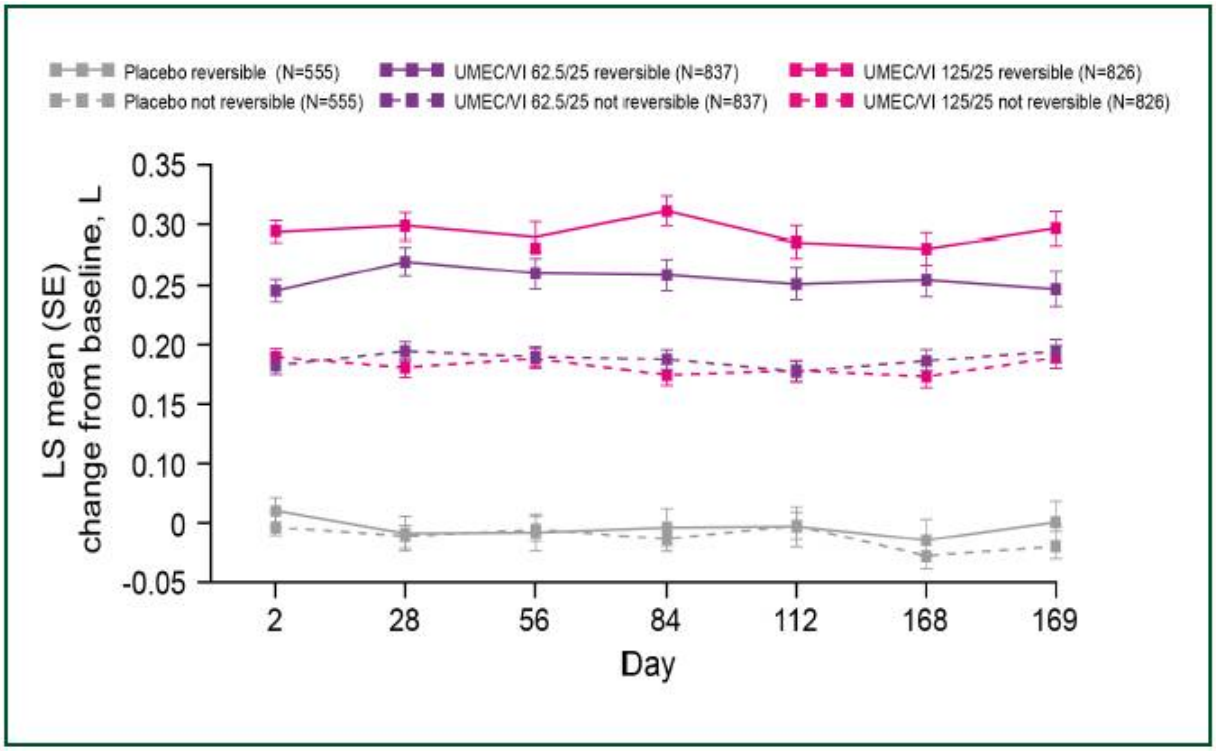
TABLE 1. LS MEAN TREATMENT DIFFERENCE FROM PLACEBO IN TROUGH FEV_1 AT DAY 169 (L, [95% CI]; ITT POPULATION)

Subgroup (% patients)		UMEC/VI 62.5/25 mcg (N=837)	UMEC/VI 125/25 mcg (N=826)
Gender	Male (68)	0.201* (0.167, 0.236)	0.221* (0.186, 0.256)
	Female (32)	0.193*	0.204*

		(0.142, 0.243)	(0.154, 0.254)
Age, years(a)	<64 (55)	0.184* (0.143, 0.224)	0.233* (0.192, 0.274)
	65-74 (35)	0.224* (0.178, 0.270)	0.204* (0.158, 0.250)
	75-84 (10)	0.191* (0.107, 0.274)	0.177* (0.091, 0.262)
COPD severity(b)	GOLD II (46)	0.204* (0.163, 0.246)	0.237* (0.195, 0.279)
	GOLD III/IV (54)	0.193* (0.155, 0.232)	0.199* (0.160, 0.238)
Smoking status	Current (49)	0.209* (0.170, 0.249)	0.237* (0.197, 0.277)
	Former (51)	0.186* (0.145, 0.227)	0.193* (0.151, 0.234)
ICS user	Yes (49)	0.198* (0.157, 0.238)	0.205* (0.164, 0.246)
	No (51)	0.200* (0.161, 0.240)	0.228* (0.188, 0.267)
Bronchodilator reversibility	Yes (69)	0.225* (0.174, 0.276)	0.282* (0.231, 0.333)
	No (31)	0.188* (0.154, 0.221)	0.181* (0.147, 0.216)
Geographical region	US (25)	0.212* (0.155, 0.269)	0.272* (0.213, 0.330)
	European Union (41)	0.188* (0.142, 0.233)	0.207* (0.167, 0.248)
	Other (34)	0.181* (0.131, 0.231)	0.179* (0.125, 0.234)
Treatment naïvety	Treatment naïve(c) (33)	0.211* (0.163, 0.259)	0.239* (0.189, 0.289)
	Not treatment naïve (67)	0.193* (0.158, 0.228)	0.205* (0.170, 0.240)

CI, confidence interval; GOLD, Global initiative for chronic Obstructive Lung Disease classification; ICS, inhaled corticosteroid; LS, least squares *p≤0.001 vs placebo (n=555); Analysis used a repeated measures model with terms for study, treatment, smoking status at screening, baseline FEV_1 (mean of 30 min and 5 min pre-dose on Day 1), Day, geographical region, subgroup (if not already included), and Day by baseline, Day by treatment, subgroup by treatment and subgroup by Day by treatment interactions. (a) <1% of subjects were ≥85 years of age and were not included in the analysis; (b)Gold II = 50% ≤ FEV_1 <80% predicted'; GOLD III = 30% ≤ FEV_1 <50% predicted; GOLD IV = FEV_1 <30% predicted; (c)no use of COPD medications apart from short-acting bronchodilators in the 30 days prior to screening.

FIGURE 1. TROUGH FEV_1 (L) IN PATIENTS REVERSIBLE AND NOT REVERSIBLE TO ALBUTEROL



CONCLUSIONS

- UMEC/VI 125/25 mcg and 62.5/25 mcg once daily provide statistically significant improvements over placebo in lung function irrespective of gender, age, race, disease severity, smoking status, ICS use, bronchodilator reversibility, geographical region, and treatment naivety.

- In patients reversible to bronchodilator therapy at screening, improvements were greater with UMEC/VI 125/25 mcg than with UMEC/VI 62.5/25 mcg.

REFERENCES

(1) Donohue J, *et al*. *Respir Med* 2013;107:1538–46.
(2) Celli B, *et al*. *Chest* 2014;[Epub ahead of print].
(3) Anzueto AR, *et al*. Presented at Annual Congress of the ATS, May 17–22, 2013, Philadelphia, PA, USA.
(4) Decramer M, *et al*. Presented at Annual Congress of the ERS, September 7–11, 2013, Barcelona, Spain.

ACKNOWLEDGMENTS

- The presenting author, MKH has been a consultant for and received research grants from GlaxoSmithKline. CK, JB and AC are employees of GlaxoSmithKline and hold stocks/shares in GlaxoSmithKline.

- This study was funded by GlaxoSmithKline (ClinicalTrials.gov: NCT01316900; protocol number: DB2113360; ClinicalTrials.gov: NCT01313637, protocol number: DB2113361; ClinicalTrials.gov: NCT01313650, protocol number: DB2113373; ClinicalTrials.gov: NCT01316913, protocol number: DB2113374).

- Editorial support (in the form of writing assistance, assembling tables and figures, collating author comments, grammatical editing and referencing) was provided by Joanne Parker and Afia Akram, at Fishawack Indicia Ltd, funded by GlaxoSmithKline.

Presented at the Annual Congress of the American Thoracic Society (ATS), San Diego, CA, USA, May 16–21, 2014

Exhibit 99.2

Poster Board No. 415

Cardiovascular safety of umeclidinium/vilanterol in COPD: results from eight randomized clinical trials

Gerald Naccarelli(1), John Finkle(2), Bikramjit Chopra(3), Jean Brooks(3), Stephanie Harris(4), Alison Church(4)

(1)Penn State Heart and Vascular Institute, Milton S. Hershey Medical Center, Penn State University, Hershey, PA, USA; (2)GlaxoSmithKline, Upper Providence, Collegeville, PA, USA;
(3)GlaxoSmithKline, Stockley Park, Uxbridge, Middlesex, UK; (4)GlaxoSmithKline, Respiratory and Immuno-Inflammation, Research Triangle Park, NC, USA

INTRODUCTION

- Concerns have been raised around the cardiovascular (CV) safety of long-acting muscarinic antagonists (LAMAs) and long-acting b-agonists (LABAs) in patients with chronic obstructive pulmonary disease (COPD).(1), (2)
- Umeclidinium (UMEC)/vilanterol (VI) (ANORO™ ELLIPTA™) is an approved maintenance treatment for COPD in the US. It is not indicated for treatment of asthma.

OBJECTIVES

- To assess the CV safety of once-daily UMEC/VI in patients with COPD.

METHODS

- Major adverse CV events (MACE) and CV adverse events of special interest (AESI) were assessed in a pooled analysis of patients with COPD enrolled in Phase III efficacy and safety studies of UMEC/VI 125/25 mcg (delivering 113/22 mcg), UMEC/VI 62.5/25 mcg (delivering 55/22 mcg), UMEC 62.5 mcg (delivering 55 mcg), UMEC 125 mcg (delivering 113 mcg), VI 25 mcg (delivering 22 mcg), or active-comparator (tiotropium [TIO] via Handihaler®) (**Table 1**).

MACE analysis (Studies 1–8)

- MACE evaluations were divided into ‘broad’ (planned) and ‘narrow’ (post hoc) analyses and included:
  - Broad MACE analysis included all the Medical Dictionary for Regulatory Activities (MedDRA) preferred terms (PTs) in the ‘Myocardial infarction (MI)’ and ‘Other ischemic heart disease’ standardized MedDRA queries (SMQs).
  - Narrow MACE analysis specified the preferred terms of ‘acute MI’ and ‘MI only’
  - Both analyses included adjudicated CV death and non-fatal stroke in addition to the terms listed above.

AESI analysis (Studies 1–4, and 7)

- CV AESI are presented from the four 24-week primary efficacy studies and a 52-week long-term safety study.
  - CV AESI categories were: acquired long QT interval, cardiac arrhythmias, cardiac failure, cardiac ischemia, hypertension, sudden death, and stroke.
  - Appropriate SMQs or MedDRA Higher Level Terms (HLTs) were used to define AE terms.
    - When MedDRA SMQs or HLTs were not available, an appropriate selection of MedDRA PTs were used.

RESULTS

Patients

- Overall, 6156 patients (2615 subject years [SY]) were included in the MACE analyses and 5295 patients (2315 SY) in the CV AESI analysis.

MACE analyses

- A similar or lower number of patients experienced an event with UMEC/VI or their monotherapy components compared with placebo in both the broad and narrow MACE analyses (broad: UMEC/VI or their monotherapy components 9–22 [1–2%] patients vs 20 [2%] patients for placebo; narrow: UMEC/VI or their monotherapy components 2–8 [<1%] patients vs 7 patients [<1%] for placebo; **Table 2**).
- Exposure-adjusted incidence rates (i.e. number of subjects with an event per 1000 SY of exposure) were lower in both the broad and narrow analyses for UMEC/VI or their monotherapy components than for placebo (broad: UMEC/VI treatment 31.2–44.5 vs 54.3 for placebo; narrow: UMEC/VI or their monotherapy components 9.9–18.1 vs 19.0 for placebo; **Table 2**).
- Incidence of CV death, non-fatal stroke, non-fatal cardiac ischemia, and non-fatal MI were low and similar across all treatment groups including placebo(≤1%).
- There was a small numerical imbalance in exposure-adjusted incidence of non-fatal MI (UMEC/VI 125/25 mcg, 5.2; UMEC/VI 62.5/25 mcg, 7.4; placebo, 2.7 patients with events/1000-patient-years) based on the low actual number of MIs (UMEC/VI 125/25 mcg, 3; UMEC/VI 62.5/25 mcg, 3; placebo, 1).
  - This was not observed for non-fatal cardiac ischemia.

TABLE 1. SUMMARY OF CLINICAL STUDIES

Study	Number of patients (Intent-to-treat population)	Study design
Primary efficacy studies(3)-(5)		
Study 1: DB2113361/NCT01313637	1489	24-week, double-blind, placebo-control, parallel-group

Study 2: DB2113373/NCT01313650	1532	24-week, double-blind, placebo-control, parallel-group
Study 3: DB2113360/NCT01316900	843	24-week, blinded, active-control, parallel-group
Study 4: DB2113374/NCT01316913	869	24-week, blinded, active-control, parallel-group
Exercise/lung function studies(6)		
Study 5: DB2114417/NCT01328444	348	12-week, double-blind, placebo-control, crossover
Study 6: DB2114418/NCT01323660	307	12-week, double-blind, placebo-control, crossover
Long-term safety study(7)		
Study 7: DB2113359/NCT01316887	562	52-week, double-blind, parallel-group, placebo-control
UMEC monotherapy study(8)		
Study 8: AC4115408/NCT01387230	206	12-week, double-blind, parallel-group, placebo-control

TABLE 2. SUMMARY OF MACE (STUDIES 1–8)(a)

	Placebo N=1053 SY=369	UMEC/VI 62.5/25 N=1124 SY=408	UMEC/VI 125/25 N=1330 SY=573	UMEC 62.5 N=576 SY=202	UMEC 125 N=1016 SY=449	VI 25 N=1174 SY=441	TIO N=423 SY=173
Number of patients (%)							
Number of patients with events per 1000 SY of exposure							
Broad MACE	20 (2) **54.3**	15 (1) **36.8**	22 (2) **38.4**	9 (2) **44.5**	14 (1) **31.2**	17 (1) **38.5**	6 (1) **34.7**
Narrow MACE	7 (<1) **19.0**	5 (<1) **12.3**	6 (<1) **10.5**	2 (<1) **9.9**	7(<1) **15.6**	8(<1) **18.1**	1 (<1) **5.8**
Adjudicated CV death(b)	2 (<1) **5.4**	2 (<1) **4.9**	0 **0**	0 **0**	1 (<1) **2.2**	2 (<1) **4.5**	0 **0**
Non-fatal stroke(c)	4 (<1) **10.9**	0 **0**	3 (<1) **5.2**	1 (<1) **4.9**	2 (<1) **4.5**	4 (<1) **9.1**	1 (<1) **5.8**
Non-fatal cardiac ischemia(d)	14 (1) **38.0**	13 (1) **31.9**	19 (1) **33.2**	8 (1) **39.5**	11 (1) **24.5**	12 (1) **27.2**	5 (1) **28.9**
Non-fatal MI(e)	1 (<1) **2.7**	3 (<1) **7.4**	3 (<1) **5.2**	1 (<1) **4.9**	4 (<1) **8.9**	2 (<1) **4.5**	0 **0**
Total MACE, number of events							
Total MACE, n (broad)	22	16	22	11	15	18	6
Total MACE, n (narrow)	8	5	6	2	7	8	1

(a)DB2113361; DB2113373; DB2113360; DB2113374; DB2114417; DB2114418; DB2113359; AC4115408, subjects in crossover studies were counted once under each treatment received; (b)Independently adjudicated; (c)The following MedDRA SMQ contributed to the non-fatal stroke AESI category: central nervous system haemorrhages and cerebrovascular conditions SMQ; (d)The following MedDRA SMQs contributed to non-fatal cardiac ischemia: Myocardial Infarction SMQ; Other Ischaemic Heart Disease SMQ. (e)The following MedDRA PTs contributed to non-fatal MI: MI and acute MI.

CV AESI

- In the 6-month studies, small imbalances in the incidence of any CV AESI was noted in some of the active treatment groups compared with placebo. However, incidence in the UMEC/VI 125/25 mcg group was similar and had a lower exposure adjusted rate than the placebo group (**Table 3**).
    - Incidence of cardiac arrhythmia, cardiac failure, cardiac ischemia, and hypertension was low; small differences in exposure-adjusted incidence rates were observed.
    - Stroke was reported in <1% of patients across all treatment groups including placebo.

TABLE 3. CV AESI (STUDIES 1–4, 6-MONTH STUDIES)(a)

	Placebo N=555 SY=208	UMEC/VI 62.5/25 N=842 SY=346	UMEC/VI 125/25 N=832 SY=336	UMEC 62.5 N=418 SY=168	UMEC 125 N=629 SY=249	VI 25 N=1034 SY=411	TIO N=423 SY=173
Number of patients (%)							
Number of patients with events per 1000 SY of exposure							
Any CV AESI	40 (7) **192.7**	70 (8) **202.4**	55 (7) **163.6**	41 (10) **244.2**	52 (8) **208.9**	95 (9) **231.0**	27 (6) **156.0**
Acquired long QT	0 **0**	0 **0**	2 (<1) **5.9**	1 (<1) **6.0**	0 **0**	0 **0**	0 **0**
Cardiac arrhythmias	18 (3) **86.7**	24 (3) **69.4**	19 (2) **56.5**	20 (5) **119.1**	20 (3) **80.4**	46 (4) **111.9**	9 (2) **52.0**
Cardiac failure	6 (1) **28.9**	11 (1) **31.8**	11 (1) **32.7**	7 (2) **41.7**	7 (1) **28.1**	12 (1) **29.2**	5 (1) **28.9**
Cardiac ischemia	5 (<1) **24.1**	11 (1) **31.8**	12 (1) **35.7**	7 (2) **41.7**	5 (<1) **20.1**	12 (1) **29.2**	4 (<1) **23.1**
Hypertension	11 (2) **53.0**	25 (3) **72.3**	17 (2) **50.6**	12 (3) **71.5**	21 (3) **84.4**	29 (3) **70.5**	11 (3) **63.6**
Sudden death	0 **0**	0 **0**	0 **0**	0 **0**	0 **0**	1 (<1) **2.4**	0 **0**
Stroke	2 (<1) **9.6**	1 (<1) **2.9**	1 (<1) **3.0**	1 (<1) **6.0**	1 (<1) **4.0**	3 (<1) **7.3**	1 (<1) **5.8**

(a)DB2113361; DB2113373; DB2113360; DB2113374

- In the long-term safety study, the incidence of any CV AESI was lower for UMEC 125 mcg and UMEC/VI 125/25 mcg (22% and 15%) compared with placebo (23%) (**Table 4**).
  - Incidence of cardiac arrhythmias was lower in the UMEC/VI 125/25 mcg group compared with UMEC 125 mcg and placebo (12% vs 17% and 16%).
  - Incidence of cardiac ischemia was lower in the UMEC/VI 125/25 mcg and UMEC 125 mcg group compared with placebo (2% vs 4%).
  - Incidence of hypertension was lower in UMEC/VI 125/25 mcg and UMEC 125 mcg compared with placebo (4% and 3% vs 6%).
- No additive effects were observed with combination treatment compared with the individual components and no dose response was evident between either UMEC/VI or UMEC doses.

TABLE 4. CV AESI (STUDY 7, LONG-TERM SAFETY)(a)

	Placebo N=109 SY=80	UMEC/VI 125/25 N=226 SY=177	UMEC 125 N=227 SY=167
Number of patients (%) **Number of patients with events per 1000 SY of exposure**			
Any CV AESI	25 (23) **311.0**	34 (15) **192.6**	49 (22) **293.1**
Acquired long QT	0 **0**	0 **0**	0 **0**
Cardiac arrhythmias	17 (16) **211.5**	26 (12) **147.3**	39 (17) **233.3**
Cardiac failure	1 (<1) **12.4**	2 (<1) **11.3**	4 (2) **23.9**
Cardiac ischemia	4 (4) **49.8**	4 (2) **22.7**	4 (2) **23.9**
Hypertension	7 (6) **87.1**	8 (4) **45.3**	6 (3) **35.9**
Sudden death	0 **0**	0 **0**	0 **0**
Stroke	0 **0**	0 **0**	1 (<1) **6.0**

(a)DB2113359

CONCLUSIONS

- No increased risk of MACE was observed with active treatments versus placebo
- Overall, the number of cardiac ischemia events were low with inconsistent small imbalances appearing in some studies but not others.
- No evidence of dose response for either UMEC/VI or UMEC and no additive effect with combination treatment over individual components was observed.
- No clinically-relevant increase in CV events was apparent with UMEC/VI, UMEC or VI compared with placebo.

REFERENCES

(1) Singh S *et al*. *JAMA.* 2008;300:1439–50.
(2) Gershon A, *et al*. *JAMA Intern Med.* 2013;173:1175–85.
(3) Celli B, *et al*. *CHEST.*. 2014 [Epub ahead of print].
(4) Donohue J, *et al*. *Respir Med.* 2013;107:1538–46.
(5) DeCramer M, *et al*. *Lancet Resp Med*. In press.
(6) Maltais F, *et al*. Submitted.
(7) Donohue J, *et al*. Submitted.
(8) Trivedi R, *et al*. *Eur Resp J* 2014;43:72–81.

ACKNOWLEDGMENTS

- The presenting author, Gerald Naccarelli, declares the following real or perceived conflicts of interest during the last 3 years in relation to this presentation: consultancies for Xention, Daiichi-Sankyo, Biosense Webster, Janssen, Otsuka Pharmaceutical, Bristol-Myers Squibb, GlaxoSmithKline, Boehringer-Ingelheim, Pfizer, sanofi aventis, and Forest. JF, BC, JB, SH, and AC are employees of GlaxoSmithKline and hold stocks/shares in GlaxoSmithKline.

· The studies described in this presentation were funded by GlaxoSmithKline.

· Editorial support in the form of writing assistance, assembling tables and figures, collating author comments, grammatical editing, and referencing was provided by Joanne Parker of Fishawack Indicia Ltd and was funded by GlaxoSmithKline.

Presented at the Annual Congress of the American Thoracic Society (ATS), San Diego, CA, USA, May 16–21, 2014

A randomized controlled trial comparing two dry powder inhalers: more patients with COPD prefer ELLIPTA compared to DISKUS based on inhaler-specific attributes

POSTER #PA145

Suyong Yun Kirby(1), Chang-Qing Zhu(2), Edward Kerwin(3), Richard Stanford(1), George Georges(1)

(1)GlaxoSmithKline, Research Triangle Park, NC, USA; (2)GlaxoSmithKline, Stockley Park, UK; (3)Clinical Research Institute of Southern Oregon, PC, Medford, Oregon, USA

INTRODUCTION

Virtually all of the maintenance treatments for chronic obstructive pulmonary disease (COPD) are delivered using inhaler technology. Patient preference for an inhaler is an important factor when deciding on maintenance treatment as it may impact compliance with therapy. This study compares patient preference of an existing dry powder inhaler (DISKUS™) and a novel dry powder inhaler (ELLIPTA™) based on several inhaler specific attributes. It also examines the preference for a once-daily versus a twice-daily dosing regimen.

OBJECTIVES

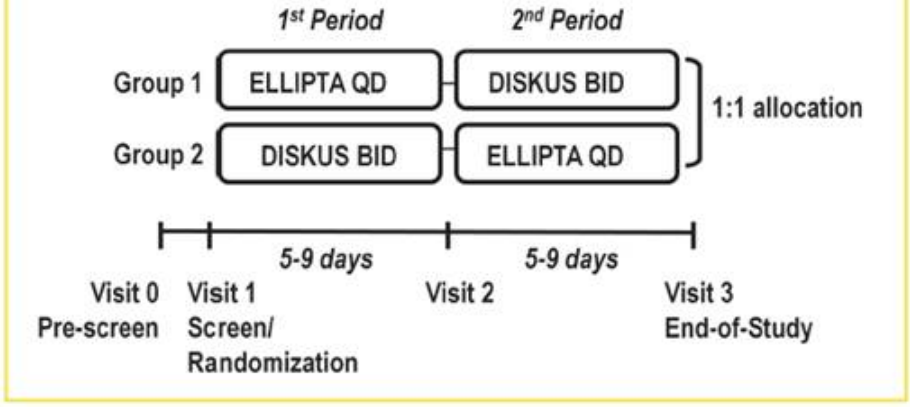
- The primary objective of this study was to evaluate whether more subjects with COPD prefer the ELLIPTA inhaler to the DISKUS inhaler based on the size of the numbers on the dose counter.

- The secondary objective was to evaluate the subject's preference for these two inhalers based on the number of steps needed to take the COPD medication and the size of the inhaler.

METHODS

- This is a multicenter (United States), randomized, open-label, crossover study. Patients with COPD who had not used ELLIPTA or DISKUS within 6 months from screening were randomized to use ELLIPTA placebo inhaler once daily followed by DISKUS placebo inhaler twice daily, or vice versa, each for approximately one week (Figure 1). Subjects were allowed to continue their existing prescribed COPD maintenance treatment throughout the study. At the end of the study, patients answered 7 questions to evaluate their preference of inhaler attributes and preferred dosing regimen.

Figure 1. Study Schematic



- Subject's preference was analyzed using Cochran-Mantel-Haenszel test accounting for sequence of inhaler use and order of response options presented (ELLIPTA then DISKUS or vice versa). A step-down testing approach (primary to secondary) and Hochberg (across secondary endpoints) were applied for multiple comparisons. Safety assessments included adverse events (AEs) and COPD exacerbations.

RESULTS

Subject Disposition and Baseline Characteristics

This study was conducted from 28 May to 15 July, 2013. A total of 314 subjects were screened, of which 287 subjects (Intent-to-Treat [ITT] population) were randomized. Two subjects in the ITT Population were excluded from the Per-Protocol (PP) Population as they were unable to complete the preference questions due to AEs that led to withdrawal during Period 1. Two hundred eighty three subjects completed the study. Four subjects withdrew prematurely: 3 due to adverse events (AEs) and one due to a COPD exacerbation.

The demographics and baseline characteristics of the study population were representative of a general COPD population (Table 1).

Table 1. Demographics and Baseline Characteristics

Demographics / Baseline Characteristics	ITT Population N=287
Male sex, n (%)	153 (53)

Age, years	64.7 (9.74)
Body mass index, kg/m^2	28.2 (6.34)
Duration of COPD, n (%)	
≥1 to <5 years	94 (33)
≥5 years to <10 years	97 (34)
≥10 years	96 (33)
Years smoked	41.3 (9.94)
Smoking pack years	56.5 (27.02)

Values are mean (SD) unless otherwise stated

Exposure and Inhaler Use Compliance

Table 2. Exposure and Inhaler Use Compliance

	ELLIPTA N=287	DISKUS N=285
Exposure, days	7.2 (0.99)	7.2 (1.17)
Compliance rate (%)	105.6 (16.29)	96.1 (18.45)
Compliance category, n (%)		
<80%	2 (<1)	24 (8)
≥80 to ≤120%	263 (92)	252 (88)
>120%	21 (7)	9 (3)

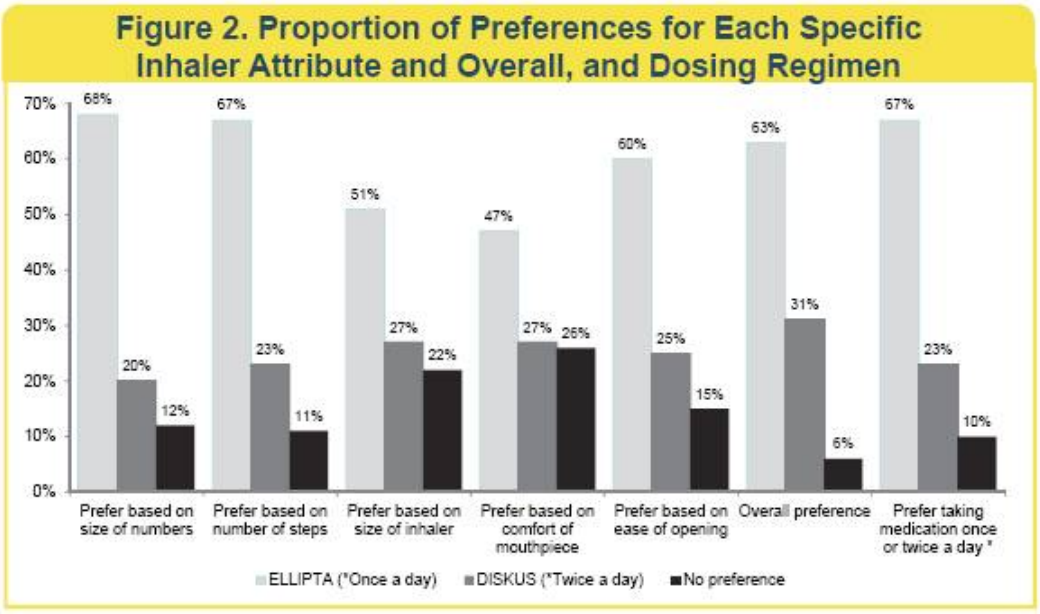
Values are mean (SD) unless otherwise stated

COPD Medications

Concurrent COPD medications used most frequently during the study were salbutamol (58%), tiotropium bromide (39%), budesonide + formoterol fumarate (23%), oxygen (15%), and salbutamol sulphate + ipratropium bromide (11%). Fluticasone propionate and salmeterol + fluticasone propionate were used by 7 and 4 subjects, respectively; they were the hydrofluoroalkane aerosol formulations administered via metered dose inhaler.

Inhaler and Dosing Regimen Preference

A statistically significant larger proportion of subjects preferred ELLIPTA over DISKUS for each of the 5 specific attributes and overall, and preferred a once-daily over a twice-daily dosing regimen (p<0.001 for each comparison).



Safety

· Overall, AEs were reported for 36 subjects (Table 3).

Table 3. Adverse Events Occurring in a Total of More than One Subject

	Number (%) of Subjects		
Adverse event	ELLIPTA N=287	DISKUS N=285	Total N=287
Any AE	23 (8)	14 (5)	36 (13)

Headache	2 (<1)	5 (2)	7 (2)
Back pain	3 (1)	0	3 (1)
Diarrhea	2 (<1)	0	2 (<1)
Dry mouth	1 (<1)	1 (<1)	2 (<1)
Neck pain	1 (<1)	1 (<1)	2 (<1)
Conjunctivitis	0	2 (<1)	2 (<1)

- No deaths were reported during this study.
- Three subjects experienced a total of 5 non-fatal serious AEs (SAEs) [one subject with deep vein thrombosis, esophageal candidiasis, and metastases to liver; one subject with bronchitis; and one subject with vertebrobasilar insufficiency]. The first two subjects were withdrawn due to SAEs. The subject with vertebrobasilar insufficiency remained on study. One additional subject was withdrawn due to a non-serious wrist fracture.
- Two subjects experienced COPD exacerbations and withdrew prematurely from the study (one noted as withdrawn due to an AE).

CONCLUSIONS

- More patients with COPD prefer the ELLIPTA over DISKUS inhaler based on five specific inhaler attributes and overall.
- More patients with COPD prefer to take their COPD medication once daily versus twice daily.
- Safety in subjects with COPD using both placebo inhalers was consistent with health conditions observed in patients with COPD in general.

ACKNOWLEDGMENTS

- The presenting author, S Yun Kirby, is employed by and holds stock in GlaxoSmithKline.
- This research was funded by GlaxoSmithKline (GSK study number RLV116669; ClinicalTrials.gov Identifier, NCT01868009).
- Editorial support (grammatical editing, graphical support) was provided by David Cutler, PhD at Gardiner-Caldwell Communications (Macclesfield, UK) and was funded by GlaxoSmithKline.

Presented at the American Thoracic Society Annual Congress, San Diego, CA, USA, 16–21 May 2014