

Cost Analysis of COPD Exacerbations and Cardiovascular Events in SUMMIT

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Chronic obstructive pulmonary disease (COPD) is a major clinical and economic burden; it is the third-leading cause of death in the United States.^{1,2} Often coexisting with other comorbid diseases, the morbidity and mortality of COPD cost the United States an estimated \$49.9 billion in 2010, of which approximately 60% was attributed to direct costs.³ These costs are primarily driven by COPD exacerbations and hospitalizations (related to COPD or comorbid disease), which account for 50% to 75% of direct costs.⁴

Of the comorbidities commonly seen in patients with COPD, the most clinically significant is cardiovascular (CV) disease. Individuals with COPD have an increased risk of CV-related hospitalization and/or mortality compared with those without COPD.⁵⁻⁸ In patients with COPD, more deaths are caused by CV disease (eg, coronary heart disease, stroke) than by respiratory-related COPD effects,^{9,10} and the increased hospitalization and emergency visit rates associated with comorbid CV disease in COPD result in costs that are 2.5 times higher than in patients with COPD without CV comorbidities.¹¹ Therefore, treatments that reduce the incidence of COPD exacerbations and CV events may have the potential for generating cost savings and reducing the economic burden of COPD.

Limited evidence is available on the impact of COPD treatment on CV events and mortality, and current guidelines from the Global Initiative for Chronic Obstructive Lung Disease recommend that patients' COPD and comorbid CV diseases be treated independently.¹² Results from secondary analyses of 2 large-scale clinical trials suggest that COPD maintenance therapies consisting of inhaled corticosteroid/long-acting β_2 agonist (ICS/LABA) combinations may reduce patients' risk of CV events and respiratory and CV-related mortality.^{13,14}

The Study to Understand Mortality and Morbidity in COPD (SUMMIT) was a prospective, randomized, phase 3 trial that compared the efficacy of once-daily ICS/LABA fluticasone furoate/vilanterol 100 mcg/25 mcg (FF/VI) combination therapy, and its individual components FF 100 mcg once-daily monotherapy and VI 25 mcg once-daily monotherapy, versus placebo on mortality in patients

ABSTRACT

OBJECTIVES: The Study to Understand Mortality and Morbidity in COPD (SUMMIT) trial compared the efficacy of once-daily fluticasone furoate/vilanterol (FF/VI) with placebo, FF monotherapy, and VI monotherapy on mortality in patients with moderate chronic obstructive pulmonary disease (COPD) and a history/increased risk of cardiovascular (CV) disease. We conducted a post hoc economic analysis using data from SUMMIT to evaluate the economic benefits of treating these patients with COPD and CV risk.

STUDY DESIGN: Patients (aged 40-80 years, with ≥ 10 pack-years' smoking history and a risk of CV events) were randomized (1:1:1:1) to receive placebo, FF 100 mcg, VI 25 mcg, or FF/VI 100 mcg/25 mcg.

METHODS: This was a post hoc economic analysis to assess the rates and associated costs of the composite end point (acute COPD exacerbations and revascularization/CV composite events) in the SUMMIT trial from a US healthcare payer perspective.

RESULTS: Overall, 16,485 patients were evaluated; of these, 5246 (31.8%) experienced an on-treatment composite end point event (28.5% experienced a COPD exacerbation, 4.2% experienced a CV event, and 2.0% underwent a revascularization procedure). The mean estimated 1-year on-treatment combined end point cost was highest for placebo and lowest for FF/VI (\$4220 vs \$3482, respectively). The reductions in cost versus placebo were significant for all active treatments ($P < .0001$). The likelihood of experiencing an on-treatment combined end point event was lower for patients treated with FF/VI versus placebo (hazard ratio, 0.81; $P < .001$).

CONCLUSIONS: One-year combined end point event costs were significantly lower for all active treatments versus placebo. Clinicians and payers may be able decrease costs by effectively managing patients' COPD in those with CV risk.

Am J Manag Care. 2019;25(11):e320-e325

with moderate COPD and a heightened risk of CV disease.¹⁵ The primary end point of SUMMIT was the incidence of all-cause mortality, which was unaffected by combination FF/VI therapy or the individual components compared with placebo.¹⁵ Outcomes assessed in the SUMMIT trial included the rate of moderate and severe COPD exacerbations¹⁵ and the number of patients experiencing a first composite CV event (CV death, myocardial infarction, stroke, unstable angina, or transient ischemic attack). All active treatments significantly reduced moderate and severe exacerbations versus placebo (all $P < .025$), whereas no differences were observed in composite CV events.¹⁵

This post hoc analysis used patient-level event data from the SUMMIT trial to examine the combined economic burden of acute COPD exacerbations and CV events and to evaluate the costs (US\$) associated with these events, stratified by treatment (FF/VI, FF monotherapy, VI monotherapy, and placebo) from a US payer perspective. The primary objective of our analysis was to evaluate the incremental costs related to the combined end point (COPD exacerbation or revascularization/CV event) between treatment cohorts. Our secondary objectives were to evaluate the likelihood of experiencing the combined end point between treatment cohorts and to quantify the incremental number of events related to the combined end point between treatment cohorts.

METHODS

Study Design

This was a retrospective, post hoc economic analysis of within-trial acute COPD exacerbation and CV event data from the SUMMIT trial, conducted from the US payer perspective. The SUMMIT trial was a multicenter, randomized, double-blind, placebo-controlled, event-driven, international clinical trial of FF/VI in patients with COPD with heightened CV risk (ClinicalTrials.gov identifier, NCT01313676; GSK study number, HZC113782). Details of the main SUMMIT study design have been reported previously.^{15,16}

The SUMMIT trial was conducted in accordance with Good Clinical Practice guidelines and the Declaration of Helsinki and was approved by local ethics committees. All patients provided written informed consent. Employees of the study sponsor were involved in the design and data interpretation of this economic analysis and had the right to approve or disapprove the publication of the finished manuscript.

Study Population

Patients included in the SUMMIT trial were aged 40 to 80 years, with a clinical diagnosis of moderate COPD, a smoking history of 10 or more pack-years, a postbronchodilator forced expiratory volume in 1 second between 50% and 70% of the predicted value, and a

TAKEAWAY POINTS

In patients with moderate chronic obstructive pulmonary disease (COPD) and cardiovascular (CV) risk, once-daily fluticasone furoate/vilanterol (FF/VI) was associated with significantly lower rates and costs of combined COPD exacerbations and revascularization/CV events versus placebo, FF monotherapy, and VI monotherapy. COPD exacerbations were more frequent than CV events (28.5% vs 4.2% experienced an event, respectively).

- ▶ Cost savings were driven by differences in rates of exacerbations, particularly severe exacerbations.
- ▶ The exacerbation reduction with FF/VI led to annual per-patient savings of \$738 versus placebo (17% cost reduction).
- ▶ Minimizing exacerbation rates in patients with COPD and CV risk with effective maintenance therapy can lead to significant cost savings.

history of or an increased risk of CV disease. Detailed inclusion and exclusion criteria have previously been reported.¹⁵

In total, 16,485 patients were randomized (1:1:1:1) to 1 of 4 once-daily inhaled treatments: placebo, FF 100 mcg, VI 25 mcg, or FF/VI 100 mcg/25 mcg. Exacerbation definitions were predetermined in the study protocol and were consistent across the study, and CV events were adjudicated centrally. Therefore, differences in treatment patterns and healthcare systems within the US payer system were minimized, ensuring consistency in the imputation of costs across combined end point events.

Efficacy Data

For this economic analysis, efficacy data on acute COPD exacerbations and revascularization/CV composite events were taken from the SUMMIT intent-to-treat (ITT) efficacy population.¹⁵ COPD exacerbation data were captured for both moderate exacerbations, defined as requiring treatment with antibiotics and/or systemic corticosteroids, and severe exacerbations, defined as requiring hospitalization. CV events for the SUMMIT composite end point (major adverse CV events) were adjudicated by an independent clinical end point committee for each patient for whom an event was recorded.¹⁶ Efficacy data were captured while patients were on treatment. For COPD exacerbations, this was defined as the time from initiation of study treatment until 1 day after the end of treatment, whereas for CV events and revascularization this extended until 7 days after the end of treatment.

Evaluation of Costs

Unit costs for acute COPD exacerbations, revascularization, and CV events were applied to the events observed in the SUMMIT trial, allowing a within-trial comparison of the associated costs between treatment cohorts. Unit costs were taken from a retrospective database analysis using a large, nationally representative commercial claims database (Optum Clinformatics; data on file, GlaxoSmithKline: GSK DOF#2016N306416_00) for COPD exacerbations and from the Truven Health MarketScan Research databases for CV events. COPD and CV disease were defined using *International Classification of Diseases, Ninth Edition, Clinical Modification (ICD-9-CM)* diagnosis codes; history of CV disease included arrhythmia, angina, acute myocardial

TABLE 1. Baseline Patient Demographic Characteristics

Characteristic	Total N = 16,485 (100.0%)	FF/VI 100/25 n = 4121 (25.0%)	FF 100 n = 4135 (25.1%)	VI 25 n = 4118 (25.0%)	Placebo n = 4111 (24.9%)
Age in years, mean (SD)	65.2 (7.9)	65.3 (8.0)	65.0 (8.0)	65.2 (7.7)	65.2 (7.9)
Age category in years, n (%)					
<55	1639 (9.9)	416 (10.1)	430 (10.4)	385 (9.3)	408 (9.9)
55-64	5745 (34.8)	1404 (34.1)	1459 (35.3)	1467 (35.6)	1415 (34.4)
65-74	7020 (42.6)	1749 (42.4)	1726 (41.7)	1771 (43.0)	1774 (43.2)
≥75	2081 (12.6)	552 (13.4)	520 (12.6)	495 (12.0)	514 (12.5)
Male, n (%)	12,289 (74.5)	3112 (75.5)	3053 (73.8)	3053 (74.1)	3071 (74.7)
Race, n (%)					
White	13,357 (81.0)	3332 (80.9)	3358 (81.2)	3339 (81.1)	3328 (81.0)
African American	258 (1.6)	69 (1.7)	62 (1.5)	67 (1.6)	60 (1.5)
Asian	2723 (16.5)	679 (16.5)	683 (16.5)	680 (16.5)	681 (16.6)
Other	147 (0.9)	41 (1.0)	32 (0.8)	32 (0.8)	42 (1.0)
Hispanic or Latino ethnicity, n (%)	1183 (7.2)	298 (7.2)	304 (7.4)	291 (7.1)	290 (7.1)
Residing in United States, n (%)	2590 (15.7)	647 (15.7)	647 (15.6)	650 (15.8)	646 (15.7)

FF 100 indicates fluticasone furoate 100 mcg; FF/VI 100/25, fluticasone furoate 100 mcg/vilanterol 25 mcg; VI 25, vilanterol 25 mcg.

infarction, congestive heart failure, stroke, pulmonary embolism, and other codes for CV disease. All costs were valued in 2015 US dollars.

Statistical Analyses

To account for variable patient follow-up periods, the censored cost data method of Bang and Tsiatis using inverse probability weighting (IPW) was used to estimate mean costs.¹⁷

The 1-year costs of combined on-treatment acute COPD exacerbations and revascularization/composite CV events were calculated using the number of events per patient, obtained from the trial, and the unit cost per event (for moderate or severe events, as appropriate), obtained from claims database analyses.

A Cox proportional hazards model was used to evaluate between-treatment differences in the risk of experiencing a combined end point event while on treatment. Poisson regression models were used to estimate and compare the mean rates of events, and the incremental differences in rates, for each active treatment cohort versus placebo.

To estimate the uncertainty in the estimates of the mean costs, bootstrapping was performed using 1000 random samples for each treatment cohort. These used the same sample size as the original treatment cohort and calculated 1000 estimates for mean cost for each treatment cohort using IPW. The 95% CIs around the mean costs for each treatment cohort were subsequently estimated as the 2.5th and 97.5th percentiles of these bootstrap means.

Incremental cost differences between each active treatment cohort and placebo, and corresponding 95% CIs, were computed and compared statistically using independent *t* tests among the bootstrap-generated means.

Descriptive statistics (mean, SD, median, and percentiles for continuous measures; frequency distributions for categorical variables) were used to characterize the study sample. All analyses

were done using SAS version 9.4 (SAS Institute; Cary, North Carolina) and STATA version 13.0 (StataCorp; College Station, Texas).

RESULTS

Patient Characteristics

All 16,485 patients in the SUMMIT ITT efficacy population were included in this analysis. Patient demographic characteristics at baseline are presented in **Table 1**. Overall, the majority of patients (77.4%) were aged 55 to 74 years; patients were predominantly male (74.5%) and most were white (81.0%). Each treatment cohort represented approximately 25% of the total ITT population (Table 1).

The numbers of patients experiencing each type of event are shown in **Table 2**. Overall, approximately one-third (31.8%) of patients experienced an event while on treatment. COPD exacerbations were the most frequent events, experienced by 28.5% of patients, whereas CV composite events were experienced by 4.2% of patients overall (4.2% each in the FF/VI and placebo groups, 3.9% in the FF group, and 4.4% in the VI group). Approximately 2% of patients in each treatment group underwent a revascularization procedure. Sudden death was the most frequent specific CV event, experienced by 64 (1.6%) patients in both the FF/VI and VI groups, 54 (1.3%) patients in the FF group, and 65 (1.6%) patients in the placebo group. The incidence of other specific CV events was also similar across the groups (Table 2).

Exacerbation/CV Event Composite Costs by Treatment

The unit costs per event used in this cost analysis are displayed in Table 2. After imputation, the mean 1-year, on-treatment, combined acute COPD exacerbation and revascularization/composite CV event cost estimates were \$3482 in the FF/VI cohort, \$3518 in the FF cohort, \$3639 in the VI cohort, and \$4220 in the placebo cohort (**Figure 1**).

TABLE 2. On-Treatment Events and Unit Cost per Event

	Total N= 16,485 (100.0%) n (%)	FF/VI 100/25 n = 4121 (25.0%) n (%)	FF 100 n = 4135 (25.1%) n (%)	VI 25 n = 4118 (25.0%) n (%)	Placebo n = 4111 (24.9%) n (%)	Unit Cost per Event (\$), mean (SD)
Any event	5246 (31.8)	1214 (29.5)	1348 (32.6)	1328 (32.3)	1356 (33.0)	NC
COPD exacerbation	4704 (28.5)	1075 (26.1)	1232 (29.8)	1176 (28.6)	1221 (29.7)	–
Moderate exacerbation	3911 (23.7)	874 (21.2)	1040 (25.2)	993 (24.1)	1004 (24.4)	2273 (9113)
Severe exacerbation	1293 (7.8)	300 (7.3)	321 (7.8)	316 (7.7)	356 (8.7)	35,916 (44,701)
Revascularization procedure ^a	324 (2.0)	87 (2.1)	82 (2.0)	78 (1.9)	77 (1.9)	61,702 (67,195)
CV composite event	688 (4.2)	174 (4.2)	161 (3.9)	180 (4.4)	173 (4.2)	NC
Myocardial infarction	181 (1.1)	47 (1.1)	46 (1.1)	46 (1.1)	42 (1.0)	25,013 (26,475)
Unstable angina	84 (0.5)	19 (0.5)	16 (0.4)	22 (0.5)	27 (0.7)	20,785 (30,362)
Stroke	130 (0.8)	33 (0.8)	33 (0.8)	31 (0.8)	33 (0.8)	17,897 (17,659)
Transient ischemia attack	34 (0.2)	7 (0.2)	7 (0.2)	12 (0.3)	8 (0.2)	8999 (4548)
Sudden death ^b	247 (1.5)	64 (1.6)	54 (1.3)	64 (1.6)	65 (1.6)	1650 (3891)
Other CV death ^c	30 (0.2)	8 (0.2)	7 (0.2)	10 (0.2)	5 (0.1)	42,165 (68,646)
Procedural death ^d	2 (0.0)	0 (0.0)	1 (0.0)	0 (0.0)	1 (0.0)	61,075 (86,272)

COPD indicates chronic obstructive pulmonary disease; CV, cardiovascular; FF 100, fluticasone furoate 100 mcg; FF/VI 100/25, fluticasone furoate 100 mcg/vilanterol 25 mcg; ICD-9-CM, International Classification of Diseases, Ninth Edition, Clinical Modification; NC, not calculated; VI 25, vilanterol 25 mcg.

^aHeart revascularization, including percutaneous transluminal coronary angioplasties and coronary artery bypass grafts (ICD-9-CM procedure codes 00.66, 36.0X, 36.1X, 36.2X, 36.3X). Cost for revascularization events was calculated within 30 days post event date and included inpatient, outpatient, and drug costs; events were identified using inpatient files.

^bA sudden CV death was defined as an event with both an ICD-9-CM code for a CV disease event (ICD-9-CM diagnosis codes 427.XX, 401.XX-402.XX, 404.XX, 410.XX-414.XX, 428.XX, 429.XX) and an ICD-9-CM code for sudden death (ICD-9-CM diagnosis codes 798.1, 798.2, 798.9), using both inpatient and outpatient files. Cost for sudden death was calculated based on the claims of the event; events were identified using both inpatient and outpatient files.

^cOther CV death was defined as CV disease events (ICD-9-CM diagnosis codes 391-398, 401-405, 410-415, 415.1, 416, 417, 420-438, 440-444, 446-448, 451-459) with discharge to death (DSTATUS: 20-29).

^dProcedural death (cardiac surgery-related) was defined as events of operations on the CV system (ICD-9-CM procedure codes 35.XX, 36.XX, 37.XX, 38.XX, 39.XX) as well as coded for discharge to death (DSTATUS: 20-29). Cost for procedural death and other CV death events was calculated based on the claim of the event and only considered inpatient costs; events were identified using inpatient files.

The reduction in mean costs versus placebo was significant for all active treatment cohorts ($P < .0001$) (Figure 1). Median 1-year cost estimates were \$3472 for FF/VI, \$3522 for FF, \$3636 for VI, and \$4207 for placebo.

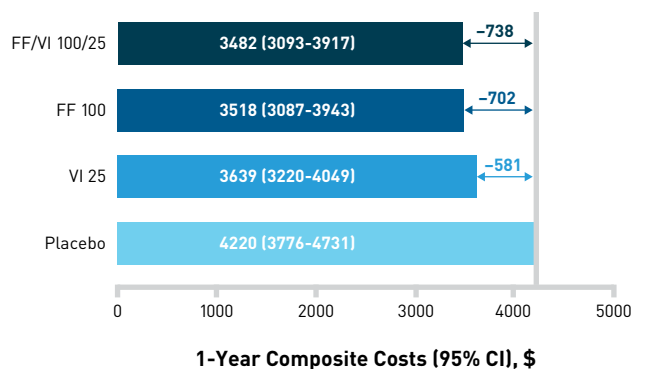
Exacerbation/CV Event Risk by Treatment

A total of 5246 (31.8%) patients experienced an on-treatment combined end point event. These events were less common in the FF/VI arm (29.5% had an event) compared with the placebo arm (33.0% had an event) (Table 3). The likelihood of experiencing a first combined end point event was significantly lower for patients in the FF/VI arm versus placebo (hazard ratio [HR], 0.81), versus FF monotherapy (HR, 0.85), and versus VI monotherapy (HR, 0.87), corresponding to reductions in risk of 19.2%, 14.7%, and 13.0%, respectively (all $P < .001$) (Table 3). No statistically significant difference in risk was observed between FF and VI monotherapies and placebo (Table 3).

Difference in Event Rates by Treatment Cohort

Overall, patients had a mean of 0.35 on-treatment combined end point events annually. This mean was lowest in the FF/VI cohort (0.29 events), similar between the FF and VI cohorts (0.35 and 0.36 events, respectively), and highest in the placebo cohort (0.39 events). Rate ratios for combined end point events were significantly lower for all active treatments versus placebo (Figure 2).

FIGURE 1. Mean On-Treatment Combined COPD Exacerbation and Revascularization/CV Composite Costs per Year



	Difference vs Placebo (95% CI), \$	P
FF/VI 100/25	-738 [-758 to -719]	<.0001
FF 100	-702 [-721 to -682]	<.0001
VI 25	-581 [-600 to -561]	<.0001

COPD indicates chronic obstructive pulmonary disease; CV, cardiovascular; FF 100, fluticasone furoate 100 mcg; FF/VI 100/25, fluticasone furoate 100 mcg/vilanterol 25 mcg; VI 25, vilanterol 25 mcg.

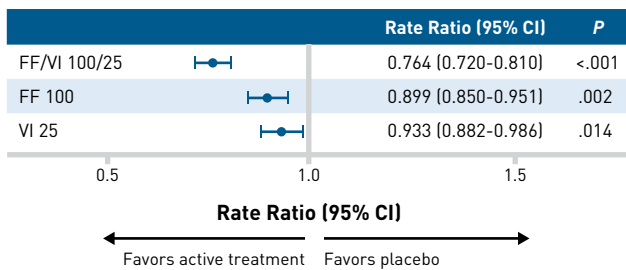
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TABLE 3. Risk of a First On-Treatment COPD Exacerbation, Revascularization, or Composite CV Event

Characteristics	FF/VI 100/25 n = 4121 (25.0%)	FF 100 n = 4135 (25.1%)	VI 25 n = 4118 (25.0%)	Placebo n = 4111 (24.9%)
COPD exacerbation, revascularization, or composite CV event, n (%)	1214 (29.5)	1348 (32.6)	1328 (32.3)	1356 (33.0)
FF/VI 100/25 vs component				
Hazard ratio (95% CI)	-	0.85 (0.79-0.92)	0.87 (0.81-0.94)	0.81 (0.75-0.87)
P	-	<.001	<.001	<.001
Reduction in risk of event	-	14.7%	13.0%	19.2%
Component vs placebo				
Hazard ratio (95% CI)	0.81 (0.75-0.87)	0.95 (0.88-1.02)	0.93 (0.86-1.00)	-
P	<.001	.163	.053	-
Reduction in risk of event	19.2%	5.2%	7.2%	-

COPD indicates chronic obstructive pulmonary disease; CV, cardiovascular; FF 100, fluticasone furoate 100 mcg; FF/VI 100/25, fluticasone furoate 100 mcg/vilanterol 25 mcg; VI 25, vilanterol 25 mcg.

FIGURE 2. Combined End Point Event Rate Ratios: Active Treatments Versus Placebo



FF 100 indicates fluticasone furoate 100 mcg; FF/VI 100/25, fluticasone furoate 100 mcg/vilanterol 25 mcg; VI 25, vilanterol 25 mcg.

DISCUSSION

COPD with comorbid CV disease represents a major clinical and economic burden,¹⁸ and treatments that reduce COPD exacerbations and CV events may offer cost savings. In this post hoc cost-effectiveness analysis of data from the SUMMIT trial, patients with COPD in the active treatment arms (FF/VI, FF monotherapy, or VI monotherapy) had significantly lower on-treatment costs versus those on placebo; these costs were lowest in the FF/VI cohort. The risk of experiencing an acute COPD exacerbation or revascularization/CV composite event was significantly lower in patients receiving FF/VI compared with all other treatments, and a significant difference was not observed between patients receiving FF or VI monotherapy and those receiving placebo.

Because no notable between-treatment differences were observed in the incidence of revascularization or CV events, the cost savings of the active treatments were driven mainly by reductions in COPD exacerbation rates, in particular severe exacerbations, relative to placebo. Although the differences between the numbers of

patients experiencing a severe exacerbation were fairly small (7.3% of patients on FF/VI vs 8.7% on placebo), the substantial costs associated with a severe exacerbation (\$35,916 per event) resulted in significant differences in 1-year per-patient costs. Differences in the numbers of moderate exacerbations were more pronounced (21.2% of patients on FF/VI vs 24.4% on placebo). However, the relatively low costs of moderate exacerbations (\$2273 per event) restricted their impact on per-patient cost savings. These findings correspond to the results of a study investigating costs of COPD care from the Spanish National Health Service perspective, which estimated that although only 16% to 19% of the exacerbations experienced by the examined patients were severe, they accounted for 32% to 37% of the total costs.¹⁹

Consistent with our findings in patients with COPD at risk of a CV event, treatment cost analyses conducted in US managed care databases of patients with COPD without CV risk have also demonstrated that intervention with a range of maintenance therapies is effective in reducing rates of hospitalizations due to COPD exacerbations and, accordingly, healthcare resource utilization costs.²⁰⁻²² The magnitude of the reduction in exacerbation rates/hospitalizations and treatment costs in different studies may vary depending on the prescribed maintenance treatments under comparison, and differences in end point events should also be taken into consideration.

Economic analyses within clinical trials are growing in favor and can be a useful tool for decision makers due to their timeliness and high internal validity.²³ Recently, a cost analysis of the Lung Function and Quality of Life Assessment in Chronic Obstructive Pulmonary Disease with Closed Triple Therapy (FULFIL) trial from Lipson et al was performed using similar methodology to that of our analysis, although from a UK payer perspective.²⁴ During the trial, patients recorded their unscheduled COPD-related healthcare contacts in a paper diary. The number of visits for each type of contact and the number of days spent in hospital were aggregated, then multiplied by unit costs to generate average annual costs for each treatment arm.

In an analysis of healthcare resource utilization in the Salford Lung Study in COPD (SLS), FF/VI was shown to offer significant cost savings versus patients' usual care in an everyday clinical setting.²⁵ In SLS, FF/VI provided a statistically significant reduction in moderate-to-severe exacerbations versus usual care²⁶; however, no between-treatment differences were observed in terms of severe exacerbations. Subsequently, there were no differences in COPD-related secondary care/hospitalization costs between FF/VI and usual care.²⁵

SUMMIT was the first COPD outcome trial that focused on a population with CV comorbidity, as well as the first to include a

prespecified secondary outcome of composite CV disease events in such a cohort. CV disease is a common comorbidity in the general COPD population; within the SLS population, which was selected to give an accurate representation of patients in UK clinical practice, 26% of participants had a cardiac condition.¹⁵ Nonetheless, our within-trial comparison of the associated costs between treatment cohorts provides useful cost-effectiveness data, with savings resulting from the reduction in COPD exacerbations observed during treatment with once-daily FF/VI. Although the results are therefore not fully applicable outside of the SUMMIT trial, US payer-specific costs were applied to improve the generalizability. Additionally, variability around the cost estimates was determined using bootstrapping, which may address uncertainties in the cost estimates from a payer perspective.

Limitations

This study had several limitations. The results were obtained for patients meeting the SUMMIT inclusion criteria and may not be generalizable to a real-world population with greater variation in comorbidities and disease severity. The unit cost of COPD exacerbations, revascularization procedures, and composite CV events may not accurately reflect the cost of treating such events for all patients, as the cost data were derived from a population that included Medicare Advantage patients and therefore may not be reflective of fee-for-service costs. Although exacerbation definitions were standardized and CV events were adjudicated across the study, these may not be reflective of what happens within the US healthcare environment. There was also a lack of sensitivity testing on some factors that might have affected outcomes, such as sex differences, and exacerbation rates were low. Limitations inherent to the use of administrative claims data (such as miscoding or underreporting of diagnoses) are applicable to the computation of event costs used in the analysis.

CONCLUSIONS

In this economic analysis of a large, multicountry clinical trial, the 1-year combined acute COPD exacerbation and revascularization/CV composite event costs were significantly lower for all of the active treatment arms when compared with placebo. Clinicians and payers may be able decrease the cost of COPD care by managing COPD effectively in patients with CV risk. ■

Acknowledgments

Editorial support (in the form of writing assistance, assembling tables and figures, collating author comments, grammatical editing, and referencing) was provided by David Mayes, MChem, at Gardiner-Caldwell Communications (Macclesfield, England), and was funded by GlaxoSmithKline plc.

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Source of Funding: This study (HO-15-15547) was funded by GlaxoSmithKline plc; SUMMIT (HZC113782/NCT01313676) was funded by GlaxoSmithKline plc.

Author Disclosures: Drs Stanford and Bogart were employees of the pharmaceutical company GlaxoSmithKline plc during the study. Drs Coutinho and

Eaddy and Ms Yu are employees of Xcenda, a healthcare consulting company that received research funds from GlaxoSmithKline plc for conducting the within-trial economic analysis.

Authorship Information: Concept and design (RHS, ADC); acquisition of data (RHS, ADC, MB); analysis and interpretation of data (RHS, ADC, ME, BY, MB); drafting of the manuscript (RHS, ADC, ME, BY, MB); critical revision of the manuscript for important intellectual content (RHS, ADC, ME, BY, MB); and statistical analysis (ADC).

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