ORIGINAL ARTICLE

# Effectiveness of Fluticasone Furoate–Vilanterol for COPD in Clinical Practice

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## ABSTRACT

### BACKGROUND

Evidence for the management of chronic obstructive pulmonary disease (COPD) comes from closely monitored efficacy trials involving groups of patients who were selected on the basis of restricted entry criteria. There is a need for randomized trials to be conducted in conditions that are closer to usual clinical practice.

### METHODS

In a controlled effectiveness trial conducted in 75 general practices, we randomly assigned 2799 patients with COPD to a once-daily inhaled combination of fluticasone furoate at a dose of 100 μg and vilanterol at a dose of 25 μg (the fluticasone furoate–vilanterol group) or to usual care (the usual-care group). The primary outcome was the rate of moderate or severe exacerbations among patients who had had an exacerbation within 1 year before the trial. Secondary outcomes were the rates of primary care contact (contact with a general practitioner, nurse, or other health care professional) and secondary care contact (inpatient admission, outpatient visit with a specialist, or visit to the emergency department), modification of the initial trial treatment for COPD, and the rate of exacerbations among patients who had had an exacerbation within 3 years before the trial, as assessed in a time-to-event analysis.

### RESULTS

The rate of moderate or severe exacerbations was significantly lower, by 8.4% (95% confidence interval, 1.1 to 15.2), with fluticasone furoate–vilanterol therapy than with usual care (P=0.02). There was no significant difference in the annual rate of COPD-related contacts to primary or secondary care. There were no significant between-group differences in the rates of the first moderate or severe exacerbation and the first severe exacerbation in the time-to-event analyses. There were no excess serious adverse events of pneumonia in the fluticasone furoate–vilanterol group. The numbers of other serious adverse events were similar in the two groups.

### CONCLUSIONS

In patients with COPD and a history of exacerbations, a once-daily treatment regimen of combined fluticasone furoate and vilanterol was associated with a lower rate of exacerbations than usual care, without a greater risk of serious adverse events. (Funded by GlaxoSmithKline; Salford Lung Study ClinicalTrials.gov number, NCT01551758.)

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Guidelines on the management of chronic obstructive pulmonary disease (COPD) are based on numerous randomized, controlled trials of efficacy, which are usually generated for registration purposes.[1] However, these trials have included patients who were selected with the use of strict criteria and were closely monitored, and therefore the results have limited relevance to everyday clinical practice.[2] To counter this, it has been proposed that integrated comparative effectiveness trials involve more representative patients and be conducted in much less restricted environments.[3-5]

The Salford Lung Study was designed to evaluate the effectiveness and safety of the once-daily inhaled combination of fluticasone furoate and vilanterol (fluticasone furoate–vilanterol) as compared with existing maintenance therapy (usual care) in a large, real-world population of patients with COPD in conditions of normal care. The trial was initiated before the approval of fluticasone furoate–vilanterol in the United Kingdom and was conducted in and around Salford, United Kingdom, a community served mainly by a single hospital with an established electronic health record (EHR) system that connects primary and secondary care. This setting permits the unobtrusive observation of patients for effectiveness and safety monitoring, blended into routine clinical care.[6]

## Methods

### Patients

Between March 13, 2012, and October 23, 2014, we recruited patients who were 40 years of age or older, had received a documented diagnosis of COPD from a general practitioner, and had had one or more COPD exacerbations in the previous 3 years. Patients had to be taking regular maintenance inhaler therapy, defined as the use of one or more long-acting bronchodilators; inhaled glucocorticoids, alone or in combination with a long-acting bronchodilator; or a combination of inhaled glucocorticoids, a long-acting beta-agonist (LABA), and a long-acting muscarinic antagonist (LAMA). There were no restrictions regarding smoking history or spirometric values. Among the few exclusion criteria were an exacerbation within the previous 2 weeks and long-term use of oral glucocorticoids. Details of the trial design and the analysis approach have been published previously.[7,8]

Patients were recruited in primary care practices by the health care professionals who provided their normal, everyday care. All the patients provided written informed consent. The trial was conducted in accordance with the International Conference on Harmonisation Good Clinical Practice guidelines and the provisions of the 2008 Declaration of Helsinki. The trial protocol was approved by the National Research Ethics Service Committee North West, Greater Manchester South. The protocol, including the statistical analysis plan, is available with the full text of this article at NEJM.org.

### Trial Design

This prospective, 12-month, open-label, parallel-group, randomized trial was conducted in 75 general practices in Salford and South Manchester, United Kingdom. Randomization was performed by means of a centralized randomization service, with stratification according to baseline maintenance therapy and presence or absence of a COPD exacerbation in the previous 12 months. Participants were assigned, in a 1:1 ratio, to receive one of two treatments: combination therapy with 100 μg of fluticasone furoate and 25 μg of vilanterol (Relvar [in Europe] or Breo [in the United States], GlaxoSmithKline), administered once daily as a dry powder through an inhaler (Ellipta, GlaxoSmithKline) (the fluticasone furoate–vilanterol group); or the continuation of usual care as determined by the general practitioner (the usual-care group). Patients who were randomly assigned to fluticasone furoate–vilanterol and had been previously treated with two long-acting bronchodilators and an inhaled glucocorticoid were allowed to continue taking a LAMA in addition to fluticasone furoate–vilanterol.

At the first trial visit, patients were offered participation and provided written informed consent. Within 1 to 60 days after the first visit, patients were randomly assigned to receive fluticasone furoate–vilanterol or to continue their usual maintenance therapy. (The 2 full months was the result of being able to use planned appointments in order to make the trial as close to normal practice as possible.) Trial staff trained the patients in each treatment group in the correct inhaler techniques and dosing, obtained baseline information on disease duration, smoking status, lung function, and concomitant medical history, and performed baseline assessments

of COPD symptoms with the use of the COPD Assessment Test (CAT)[9] and of quality of life with the use of the European Quality of Life–5 Dimensions (EQ-5D) questionnaire.[10] Spirometric findings were evaluated according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD), with airflow limitation present when the ratio of the forced expiratory volume in 1 second ($FEV_1$) to forced vital capacity was less than 0.7. Severity was graded according to the level of $FEV_1$.

If at months 3, 6, and 9 patients had had no contact with their general practice within the previous 8 weeks, they were contacted by telephone by a trial team member to assess any serious adverse events or nonserious adverse drug reactions; there was no additional intervention at these assessments. At 12 months, trial staff met the patients to make a final assessment of outcomes. Thus, most patients had contact with trial staff only at recruitment, at the baseline visit, and at 12 months.

To preserve the real-world nature of the trial, the patients' experience was as close to everyday clinical practice care as possible. The key investigators in the trial were the general practitioners, who could choose the appropriate therapy according to their clinical opinion, and treatments were dispensed by community pharmacies in the usual way. Patients could switch from fluticasone furoate–vilanterol to usual care, but patients in the usual-care group were not permitted to switch to the fluticasone furoate–vilanterol group. All the general practitioners and pharmacy staff received training regarding Good Clinical Practice guidelines as well as training in trial procedures and trial medications as appropriate to their roles.[8]

### OUTCOME MEASUREMENTS

The primary outcome was the mean annual rate of moderate or severe exacerbations, defined as any worsening of respiratory symptoms that led to treatment with antibiotic agents or systemic glucocorticoids (or both), to hospital admission, or to scheduled or unscheduled hospital visits. The primary outcome was assessed in the primary effectiveness analysis population, which was a subgroup of the entire trial population that included patients who had undergone randomization, received a prescription of the trial medication (e.g., fluticasone furoate–vilanterol or, in the usual-care group, a COPD-controller medication), and had had one or more exacerbations in the preceding year. All the secondary outcomes were analyzed in the entire trial population (i.e., all the patients who underwent randomization and received a prescription of the trial medication) and included the rate of first exacerbation, as assessed in a time-to-event analysis, and the annual rates of primary and secondary health care contacts. Other outcomes included the CAT score and the EQ-5D questionnaire results. Except for exacerbations, modification to trial medication, CAT score, EQ-5D questionnaire, and demographic characteristics, data were collected in real time with the use of an integrated primary and secondary care EHR that was developed by NorthWest EHealth (NWEH). EHR data for the primary outcome were independently verified by the research team (general practitioner, research nurse, or research doctor).

### SAFETY EVALUATION

Safety outcomes included serious adverse events of pneumonia (defined as pneumonia, which was prespecified as an adverse event of special interest), the frequency and type of other serious adverse events, and adverse drug reactions. Adverse events of special interest were defined a priori as groups of events of interest that were considered to be possibly related to inhaled glucocorticoids or LABAs. Safety monitoring was performed by means of continuous real-time monitoring of the patients' EHRs with the use of the linked NWEH database system and by means of telephone contact every 3 months (unless another contact occurred). Investigators reported serious adverse events and adverse drug reactions on electronic case-report forms, which were continuously monitored by near–real-time data monitoring and a dedicated clinical safety team. Cause of death was not adjudicated but was assigned by the primary investigator for all fatal events.

### TRIAL OVERSIGHT

The Salford Lung Study team sought scientific advice by means of a joint consultation process with the National Institute for Health and Care Excellence and the Medicines and Healthcare Products Regulatory Agency. Informal advice was sought from the National Research Ethics Service Committee North West, Greater Manchester South, United Kingdom, before the formal ethics application.

The trial was designed by the sponsor and the academic partners. The sponsor and NWEH collected the data. Statistical analyses were performed by a contract research organization on behalf of, and with oversight by, employees of the sponsor. All the authors had full access to the data and vouch for the accuracy and completeness of all the data and analyses and for the fidelity of the trial to the protocol. The first draft of the manuscript was written jointly by the primary academic and senior authors, and all the authors worked collaboratively to prepare the final content and made the decision to submit the manuscript for publication. Editorial support was provided by a medical writer, paid by the sponsor.

### STATISTICAL ANALYSIS

Sample-size calculations were based on the primary outcome (mean annual rate of moderate or severe exacerbations). We calculated that 2238 patients would need to be enrolled for the trial to have 80% power to detect a relative change of 12% in the mean annual rate of moderate or severe exacerbations between the fluticasone furoate–vilanterol group and the usual-care group, assuming a mean rate of 2.3 exacerbations in the usual-care group, as estimated on the basis of a retrospective analysis of historical data from patients from the Salford area who underwent randomization at the time of the protocol amendment[11] that were collected from the linked NWEH database. Calculations were based on a negative binomial regression, with a dispersion rate of 0.7, and used a two-sided 5% significance level. All the analyses were conducted according to the intention-to-treat principle (see the Supplementary Appendix, available at NEJM.org).

## RESULTS

### TRIAL POPULATION

Of 3161 patients with COPD who were screened, 2802 underwent randomization (see the Supplementary Appendix). Three patients in the fluticasone furoate–vilanterol group never took the trial medication, so the overall trial population consisted of 2799 patients. Of these, 2269 patients (81%) had one or more moderate or severe exacerbations in the year before the trial and made up the primary effectiveness analysis population (Table 1). In the overall trial population, 1291 patients in the fluticasone furoate–vilanterol group and 1309 in the usual-care group completed the trial; in the primary effectiveness analysis population, 1051 patients in the fluticasone furoate–vilanterol group and 1056 in the usual-care group completed the trial.

In the primary effectiveness analysis population, 276 patients (12%) were taking a LABA, a LAMA, or both (35 patients were taking both) at the time of randomization. A total of 762 patients (34%) were receiving inhaled glucocorticoids, a combination of inhaled glucocorticoids and a LABA, or a combination of inhaled glucocorticoids and a LAMA; 119 of these patients were using inhaled glucocorticoids as monotherapy. A total of 1231 patients (54%) were receiving combination triple therapy with inhaled glucocorticoids, a LABA, and a LAMA.

Overall, 47% of the patients reported having had two or more moderate COPD exacerbations in the year before entry; 7% reported having had one or more severe exacerbations. A total of 22% of the patients had a diagnosis of asthma recorded. More than three quarters of the patients (77%) had coexisting conditions (Table 1).

In the fluticasone furoate–vilanterol group, 342 patients (24%) modified their medication regimen; 302 of these patients (22%) switched back to their previous care, of whom 54 (4%) switched back because of a need for better control. In the usual-care group, 160 patients (11%) modified their medication regimen, including 114 (8%) who had a need for better control.

### PRIMARY OUTCOME

In the primary effectiveness analysis population, the rate of moderate or severe exacerbations was 1.74 exacerbations per year in the fluticasone furoate–vilanterol group, as compared with 1.90 per year in the usual-care group, indicating an 8.4% (95% confidence interval [CI], 1.1 to 15.2) lower rate in the fluticasone furoate–vilanterol group (P=0.02) (Fig. 1A). This finding was confirmed in the entire trial population, in which the rate of moderate or severe exacerbations was 1.50 exacerbations per year in the fluticasone furoate–vilanterol group, as compared with 1.64 per year in the usual-care group, indicating an 8.4% (95% CI, 1.4 to 14.9) lower rate in the fluticasone furoate–vilanterol group (P=0.02). In patients with COPD of GOLD grade 1 or 2 at baseline (GOLD grade 1, indicating mild disease, is

**Table 1. Characteristics of the Participants at Baseline.***

| Characteristic | Entire Trial Population (N=2799) | Usual Care (N=1403) | Fluticasone Furoate–Vilanterol (N=1396) | Primary Effectiveness Analysis Population (N=2269) |
|---|---|---|---|---|
| Age — yr | 67±10 | 67±10 | 67±10 | 67±10 |
| Female sex — no. (%) | 1369 (49) | 671 (48) | 698 (50) | 1122 (49) |
| Body-mass index† | 28±6 | 28±6 | 28±7 | 28±6 |
| Current smoking — no. (%) | 1289 (46) | 666 (47) | 623 (45) | 1046 (46) |
| Postbronchodilator $FEV_1$ — liters | 1.62±0.64 | 1.62±0.65 | 1.62±0.64 | 1.59±0.64 |
| No. of exacerbations during the 12 mo before randomization | 2.01±1.99 | 2.04±2.08 | 1.98±1.90 | 2.48±1.93 |
| Coexisting condition — no. (%) | | | | |
| Any | 2145 (77) | 1076 (77) | 1069 (77) | 1758 (77) |
| Cardiac condition | 720 (26) | 367 (26) | 353 (25) | 588 (26) |
| Vascular condition | 1363 (49) | 675 (48) | 688 (49) | 1095 (48) |
| Asthma | 609 (22) | 293 (21) | 316 (23) | 512 (23) |
| Diabetes | 438 (16) | 208 (15) | 230 (16) | 353 (16) |

* Plus–minus values are means ±SD. There were no significant differences between the treatment groups in any of the baseline characteristics. The primary effectiveness analysis population was a subgroup of the entire trial population that included patients who had undergone randomization, received a prescription of the trial medication, and had had one or more exacerbations in the preceding year. Additional details on the baseline characteristics are provided in Table S1 in the Supplementary Appendix. $FEV_1$ denotes forced expiratory volume in 1 second.
† The body-mass index is the weight in kilograms divided by the square of the height in meters.

defined as an $FEV_1$ ≥80% of the predicted value, and GOLD grade 2, indicating moderate disease, as an $FEV_1$ ≥50% and <80% of the predicted value, both in the presence of a ratio of $FEV_1$ to forced vital capacity of <0.7), the rate of exacerbations was 1.50 exacerbations per year in the fluticasone furoate–vilanterol group, as compared with 1.71 per year in the usual-care group, indicating a 12.1% (95% CI, 1.0 to 21.9) lower rate in the fluticasone furoate–vilanterol group.

Fig. 1B shows the percent change in the rate of moderate or severe exacerbations between the groups in the primary effectiveness analysis population, stratified according to prerandomization treatment; the interaction of treatment with strata was not significant (P=0.29). The treatment difference was significant among patients in the primary effectiveness population whose randomization stratum and prerandomization treatment included an inhaled glucocorticoid and a LABA (1.87 exacerbations per year among 927 patients in the fluticasone furoate–vilanterol group vs. 2.03 exacerbations per year among 908 patients in the usual-care group), with an 8.0% (95% CI, 0.11 to 15.4) lower rate in the fluticasone furoate–vilanterol group (P=0.047).

### SECONDARY OUTCOMES

There was no significant difference in the rate of first moderate or severe exacerbation in the time-to-event analysis in the entire trial population (hazard ratio with fluticasone furoate–vilanterol vs. usual care, 0.93; 95% CI, 0.85 to 1.02). Similarly, there was no significant difference in the rate of severe exacerbations between the fluticasone furoate–vilanterol group and the usual-care group (0.09 and 0.08 exacerbations per year, respectively; the rate with fluticasone furoate–vilanterol was higher by 9.7% [95% CI, –16.9 to 44.7]; P=0.52) or in the rate of first severe exacerbation in the time-to-event analysis (hazard ratio, 1.27; 95% CI, 0.98 to 1.66; P=0.08).

There was no significant difference between the fluticasone furoate–vilanterol group and the usual-care group in the annual rate of COPD-related contact with primary care; the rate was 1.7% (95% CI, –5.1 to 8.0) lower in the fluticasone furoate–vilanterol group than in the usual-

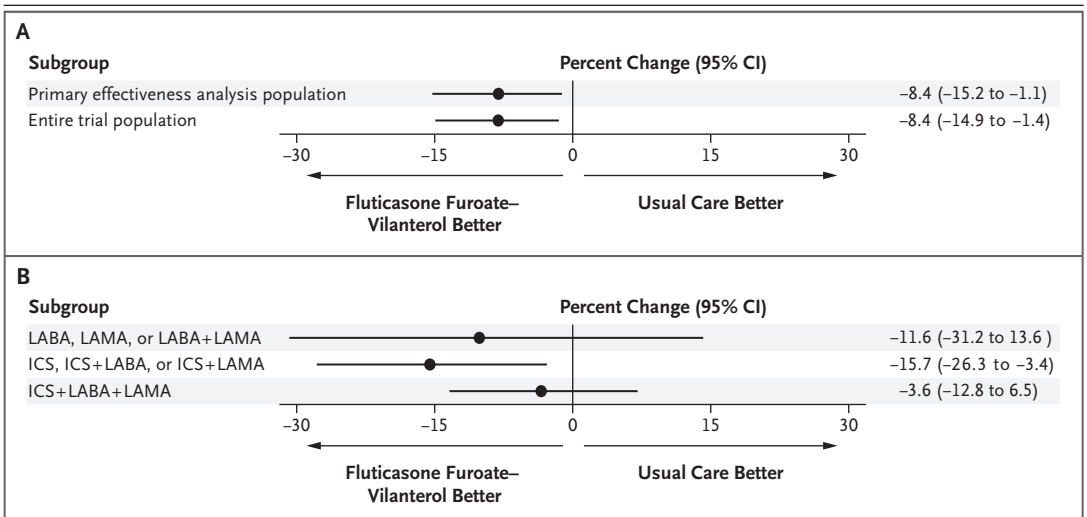


**Figure 1. Treatment Effect on Moderate or Severe Exacerbations.**

Shown is the effect of the combination of 100 μg of fluticasone furoate and 25 μg of vilanterol, as compared with usual care, on the rate of moderate or severe exacerbations. Percent-change estimates and 95% confidence intervals are shown. Panel A shows the primary-outcome analysis and the sensitivity analysis in the entire trial population. Panel B shows risk reductions stratified according to maintenance treatment at randomization for the primary effectiveness analysis population, which was a subgroup of the entire trial population that included patients who had undergone randomization, received a prescription of the trial medication, and had had one or more exacerbations in the preceding year. ICS denotes inhaled glucocorticoid, LABA long-acting beta-agonist, and LAMA long-acting muscarinic antagonist.

care group. The annual rate of all primary care contacts was slightly higher (12.3%; 95% CI, 5.4 to 19.6) in the fluticasone furoate–vilanterol group than in the usual-care group. There were no significant differences in the rate of secondary health care contacts.

In an analysis that was based on the entire trial population, 596 of 1317 patients (45%) in the fluticasone furoate–vilanterol group had a decrease in their CAT score by 2 or more points (indicating an improvement in COPD-related health status), as compared with 481 of 1325 patients (36%) in the usual-care group (odds ratio in favor of fluticasone furoate–vilanterol, 1.51; 95% CI, 1.28 to 1.77; P<0.001). There was no significant between-group difference in the change from baseline in the EQ-5D score. Results in the primary effectiveness analysis population were similar to those that were based on the entire trial population.

### SAFETY

The incidence of serious adverse events during treatment was similar in the fluticasone furoate–vilanterol group and the usual-care group (with events occurring in 404 patients [29%] and 383 patients [27%], respectively). There was no notable difference between the two groups with regard to any adverse event of special interest (Table 2). A total of 94 patients (7%) in the fluticasone furoate–vilanterol group had one or more serious adverse events listed as pneumonia, as compared with 83 (6%) in the usual-care group (incidence ratio, 1.1; 95% CI, 0.9 to 1.5). For the comparison of the fluticasone furoate–vilanterol group with the usual-care group, there was a trend toward a higher mean number of serious adverse events of pneumonia in the stratum receiving a treatment regimen without an inhaled glucocorticoid at randomization (mean annual rate, 3.01 hospitalizations; 95% CI, 0.97 to 9.33) than in the strata receiving an inhaled glucocorticoid at randomization (P=0.10 for the interaction of treatment with baseline maintenance therapy in the analysis across the three strata). A total of 13 patients (1%) in each group had an event of pneumonia (adverse event of special interest) with a fatal outcome. A total of 45 patients in the fluticasone furoate–vilanterol group and 30 in the usual-care group died dur-

ing the trial; reported causes of fatal events are listed in the Supplementary Appendix. One patient in each group died from a serious adverse event that was recorded as being related to the trial medication (pneumonia in 1 patient in the usual-care group, and pulmonary embolism and deep-vein thrombosis in 1 in the fluticasone furoate–vilanterol group). No subgroups with a higher risk of a serious adverse event of pneumonia in the fluticasone furoate–vilanterol group than in the usual-care group were identified.

## DISCUSSION

The Salford Lung Study on COPD was a large, randomized, comparative effectiveness trial conducted in a population that was intended to represent that seen in everyday clinical practice. We found that a simple, once-daily treatment with an inhaled combination of fluticasone furoate and vilanterol was superior to usual care by the patient's general practitioner with regard to the frequency of moderate or severe exacerbations and was not associated with a significantly higher risk of serious adverse events.

The combination of fluticasone furoate and vilanterol has been shown previously to result in lower rates of exacerbations of COPD than vilanterol alone in conventional randomized, controlled trials of efficacy.[12] However, this trial shows that broad populations of patients with COPD benefit from treatment with fluticasone furoate–vilanterol, and the findings differ from those of efficacy trials in which fluticasone furoate–vilanterol was associated with outcomes that were similar to those with the twice-daily combination of fluticasone propionate and salmeterol.[13] We found no excess number of serious adverse events of pneumonia in the overall comparisons, but as expected, we found a trend toward a greater number of serious adverse events of pneumonia with fluticasone furoate–vilanterol than with a treatment regimen consisting of bronchodilators only.[14] Also, we cannot rule out a higher incidence of mild pneumonia with fluticasone furoate–vilanterol than with usual care.

The strength of the trial derives from its innovative design. It took place in a single urban area, with primary and secondary care connected through an EHR, integrated with a new data recording system to enable the collection of a trial-relevant data set that contained more than 3 million lines of data for all the effectiveness and safety outcomes. After randomization, a patient was contacted by telephone only as a safety check on three occasions over a period of 12 months, and only then if there had been no health care contact within a 3-month period. All treatment was carried out by the usual caregivers, while patients were simultaneously monitored remotely with the use of the EHR for the early detection of safety events.

This comparative effectiveness trial needs careful interpretation. Although randomized, the trial was an open-label trial, which could potentially have introduced bias, although we made all efforts to have the treatment experience be similar for all the patients, by giving them similar initial training on the use of the inhaler, having them obtain their prescriptions from the general prac-

**Table 2. Serious Adverse Events of Special Interest during Treatment in the Entire Trial Population.***

| Event | Usual Care (N=1403) | Fluticasone Furoate–Vilanterol (N=1396) |
|---|---|---|
| | *number (percent)* | |
| Cardiovascular event | | |
| Any event | 107 (8) | 108 (8) |
| Cardiac arrhythmia | 54 (4) | 52 (4) |
| Cardiac failure | 28 (2) | 28 (2) |
| Cardiac ischemia | 33 (2) | 34 (2) |
| Hypertension | 1 (<1) | 0 |
| Stroke | 25 (2) | 21 (2) |
| Pneumonia | 83 (6) | 94 (7) |
| Lower respiratory tract infection, excluding pneumonia | 58 (4) | 64 (5) |
| Decreased bone mineral density and associated fracture | 45 (3) | 45 (3) |
| Effects on glucose level | 16 (1) | 23 (2) |
| Hypersensitivity | 10 (1) | 10 (1) |
| Effects on potassium level | 2 (<1) | 2 (<1) |
| Glucocorticoid-associated eye disease | 2 (<1) | 2 (<1) |
| Local effects from glucocorticoids | 1 (<1) | 0 |

* Serious adverse events of special interest during treatment that were associated with the known pharmacologic action of inhaled glucocorticoids or long-acting beta-agonists were identified with the use of standardized *Medical Dictionary for Regulatory Activities* (MedDRA), version 18.1, queries (SMQs) and sponsor-defined special interest terms when no SMQ was available. The grouping of events was defined according to standard MedDRA groups, if available.

titioner, having them collect the medication at their usual pharmacy, and so forth. However, the unblinded trial is the likely reason for the larger degree of switching of treatment over the first 3 months of the trial in the fluticasone furoate–vilanterol group than in the usual-care group. Patients switched to familiar treatment, despite fewer changes that were due to treatment failure in the fluticasone furoate–vilanterol group than in the usual-care group (i.e., need for better control). It should be noted that approximately 50% of the patients were taking triple therapy despite well-preserved lung function. A considerable proportion of patients had a diagnosis of asthma recorded. We do not believe that all these patients had an asthma–COPD overlap syndrome[15]; instead, the finding could indicate that some patients with COPD received a diagnosis of asthma early in the course of their COPD. This situation would usually have led to exclusion from COPD efficacy studies. Most of the general practitioners also took part in the Salford Lung Study involving patients with asthma[16] and thus had no incentive to include patients with current asthma in this trial.

Our findings challenge the automatic transfer of findings from efficacy studies to clinical guidelines or everyday clinical practice. For any new treatment, safety and efficacy randomized, controlled trials are essential, but they are carried out in carefully selected populations, from which patients with coexisting conditions are excluded, and represent less than 10% of patients with COPD.[2] Frequent face-to-face monitoring ensures high adherence to therapy and good inhaler technique. This comparative effectiveness trial that was conducted in a population of patients with COPD was largely unsupervised over the yearlong period, which allowed important factors in usual clinical care, such as adherence, frequency of dosing, and persistence of good inhaler technique, to come into play.

In conclusion, patients in general practice who had a diagnosis of COPD and a heightened risk of exacerbations had a benefit with simple, once-daily inhaled combination treatment with fluticasone furoate and vilanterol, without an additional risk of serious adverse events. Future effectiveness studies are likely to influence clinical guidelines, not only for COPD but for many other chronic diseases.

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