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ORIGINAL ARTICLE

## Healthcare resource utilization associated with ivacaftor use in patients with cystic fibrosis

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### ABSTRACT

**Objective:** Ivacaftor was approved in 2012 to treat patients with cystic fibrosis (CF) with specific *CFTR* gene mutations. The objective of this analysis was to analyze the impact of ivacaftor on health resource utilization through analysis of claims data.

**Methods:** Patients diagnosed with CF aged  $\geq 6$  years prescribed ivacaftor between January 1, 2012 and July 31, 2014 with  $\geq 12$  months of continuous insurance coverage prior to and following the prescription were identified. All-cause and CF-specific healthcare resource utilization during the pre- and post-prescription periods and ivacaftor adherence levels were studied.

**Results:** The 79 identified patients had a mean age of 20.8 years, and 54% were female. The proportion of patients with inpatient admissions (all-cause and CF-related) was significantly higher in the pre index compared to post index period ( $p \leq 0.05$ ). Mean ivacaftor medication possession ratio was 0.8 (SD = 0.3), and 73% of patients had a medication possession ratio  $> 0.80$ .

**Limitations:** Only a small number of patients met the inclusion criteria. Additionally, claims data may contain errors or inconsistencies and cannot be used to determine if medications were taken as prescribed.

**Conclusions:** Ivacaftor therapy was associated with significant reductions in hospitalizations along with high rates of adherence to treatment over 12 months.

### ARTICLE HISTORY

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Ivacaftor; Cystic fibrosis; Healthcare resource utilization; Adherence; Medication possession ratio; Pulmonary exacerbation

### Introduction


Cystic fibrosis (CF) is a progressive, genetic disorder affecting nearly 70 000 children and adults across the globe<sup>1,2</sup>. Disease progression, in the form of lung disease and repeated infections, is mainly the result of two mutations in the gene that encodes the cystic fibrosis transmembrane conductance regulator (CFTR) protein, which controls electrolyte transport across cells in the lungs, sweat glands, pancreas, and other tissues. Standard therapies, focused on treating symptoms of the disease and associated with significant treatment burden, include chest physiotherapy, chronic antibiotics, pancreatic enzyme replacement, and nutritional supplements<sup>3</sup>. Ivacaftor was the first drug approved to treat the abnormality in CF caused by *CFTR* mutations.

Ivacaftor potentiates the activity of the CFTR protein, thus addressing the underlying cause of CF<sup>4–6</sup>. Two 48-week randomized, placebo-controlled studies reported improvements in lung function and measures of nutritional health in patients receiving ivacaftor as compared with placebo<sup>1,2</sup>. In the study involving adolescent and adult patients, there was a significant decrease in the number and severity of pulmonary exacerbations (PEX), with patients receiving ivacaftor 55% less likely to have a PEX<sup>1</sup>. This finding is meaningful due to

the importance and impact of PEX on patients' quality-of-life, as well as on the decline in pulmonary function<sup>7–9</sup>. Additionally, patients receiving ivacaftor also experienced fewer hospital days due to PEX as compared to patients receiving placebo<sup>1</sup>. In response to these promising outcomes, the US Food and Drug Administration approved ivacaftor for treatment of patients with CF and a *G551D-CFTR* mutation. Ivacaftor was initially approved for use in the US in 2012, and, as of 2013, ivacaftor has been added to the guidelines for care in patients with CF who have at least one copy of the *G551D-CFTR* mutation, which accounts for  $\sim 4\%$  of patients with CF<sup>10,11</sup>. Following additional successful clinical trials in the relevant patient populations, ivacaftor's approval was expanded to include nine other *CFTR* gene mutations and for use in children aged 2–5; however, the full population indicated to receive treatment with ivacaftor remains a small proportion of patients with CF.

Although the results of the clinical trials are robust, it is important to understand the impact of treatment and adherence in the real-world setting. Insurance claims databases can provide an abundance of data to assess the impact of treatments in clinical practice. Thus, this retrospective cohort study utilized data from a large US claims database to evaluate

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 Supplemental data for this article can be accessed [here](#).

clinical outcomes among commercially insured patients with CF who were treated with ivacaftor. We sought to evaluate real-world healthcare resource utilization and adherence to ivacaftor during the time periods surrounding initiation of ivacaftor treatment.

## Patients and methods

### Data source

This retrospective study used data from the Truven Health *MarketScan Commercial Claims and Encounters* database (MSCCD) for the period January 1, 2012 to July 31, 2014. The MSCCD includes medical and pharmaceutical claims for ~40 million individuals less than 65 years old from over 160 large employers and health plans in the US. The health plans include preferred provider organizations, health maintenance organizations, point-of-service plans, and indemnity plans. Medical claims are linked to retail and mail-order prescription drug claims and person-level enrollment data through the use of unique enrollee identifiers. The database is fully de-identified and complies with the Health Insurance Portability and Accountability Act so that approval from institutional review boards is not considered necessary.

### Patient selection

Patients diagnosed with CF who are at least 6 years old with at least one new claim for ivacaftor (NDC: 51167-0200-02) after January 1, 2012 were eligible for inclusion in the study. Each patient's first claim for ivacaftor between January 1, 2012 and July 31, 2013 was designated as their index date. All patients were required to have a CF diagnostic code (ICD9: 277.0x) on at least one inpatient or two outpatient (at least 30 days apart) claims, as well as continuous enrollment in the database with both medical and pharmaceutical benefits for 12 months before (pre index period) and 12 months after (post index period) the index date.

### Outcome measures

The following patient demographic characteristics were captured at the index date: age, gender, health plan type, and geographic region. Clinical characteristics measured during the 12-month pre index period included specific comorbidities defined by primary or secondary ICD-9 diagnosis codes on any claim generated during the pre-index period and concomitant medications on any claim generated during the pre-index period. Healthcare resource utilization outcomes pre- and post-index date were evaluated on all inpatient admissions, outpatient clinic visits, and outpatient claims, with a sub-set of claims identified as CF-related. CF-related healthcare resource utilization was defined by the presence of a diagnosis code for CF (ICD-9: 277.0x) in the primary position on inpatient claims or in any position on emergency room or outpatient claims. The specific healthcare resource utilization outcome measures included the number and proportion of patients with an inpatient admission, mean number of admissions among patients with an inpatient admission, the

average length of inpatient stay among patients with at least one admission, the mean number of outpatient office visits, and the mean number of outpatient claims. Ivacaftor adherence was assessed in the post period with: the mean number of ivacaftor claims per patient during the post index period, the medication possession ratio (MPR; total days supplied from all ivacaftor refills divided by 365 days of the post-index period), and the overall proportion with a high adherence rate (defined as the proportion of patients with an MPR  $\geq 0.80$ )<sup>12,13</sup>.

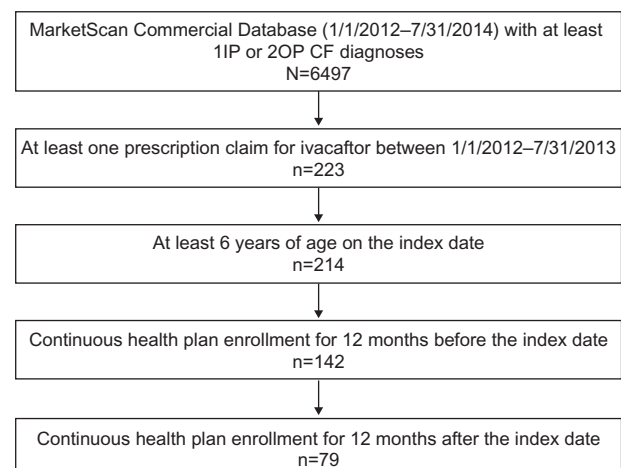
### Statistical analysis

All study outcome measures were summarized using descriptive statistics. Categorical measures were presented as counts and percentages. Continuous measures were presented as means and standard deviations (SD). As this analysis is a comparison between pre- and post-period for the same patient cohort, the two samples are not independent samples. To account for this non-independence, statistical tests of significance for differences across pre- and post-index periods included McNemar's tests for categorical variables and paired *t* tests for continuous variables. A *p*-value  $< 0.05$  was considered significant. All analyses were performed using Treatment Pathways (Truven Health Analytics, Cambridge, MA) and Stata version 12.1 (StataCorp, College Station, TX).

## Results

### Patient identification

A total of 223 patients with at least one prescription claim for ivacaftor between January 1, 2012 and July 31, 2013 were identified. After inclusion criteria were applied, the final study cohort consisted of 79 patients who were at least 6 years old at the index date and with 12 months of pre index and 12 months of post index continuous health plan enrollment (Figure 1).



**Figure 1.** CONSORT diagram showing patient selection. IP, inpatient; OP, outpatient; CF, cystic fibrosis.

**Table 1.** Baseline demographic characteristics.

Demographic characteristic	n = 79
Age, mean (SD)	20.8 (11.8)
Age group, n (%)	
6–11	19 (24.1)
12–17	22 (27.8)
18–34	27 (34.2)
35–54	11 (13.9)
55+	— (0.0)
Female, n (%)	43 (54.4)
Health plan type, n (%)	
Health maintenance organization (HMO)	12 (15.2)
Preferred provider organization (PPO)	48 (60.8)
Point of service (including 'with capitation') (POS)	8 (10.1)
Other/unknown*	11 (13.9)
Geographic region, n (%)	
Northeast	29 (36.7)
North Central	20 (25.3)
South	13 (16.5)
West	16 (20.3)
Unknown/missing data	1 (1.3)

SD, standard deviation.

\*Includes patients insured under exclusive provider organizations, consumer-driven health plans, high-deductible health plans, and those with unknown or missing data.

### Demographic and clinical characteristics

The average age of the study patients was 20.8 (SD =11.8) years, 54% were female, and 36.7%, 25.3%, and 20.3% were from the Northeast, North Central, and Western US Census regions (Table 1). The majority of patients were insured by a preferred provider organization (PPO) (61%), followed by a health maintenance organization (HMO) (15%) and point-of-service (POS) (10%) plan.

The most prevalent clinical characteristics (identified by primary or secondary ICD-9 diagnosis code) on any claim during the pre-index period were sinusitis (35%), non-*Pseudomonas* pulmonary infection (25%), cough (24%), asthma (22%), bronchiectasis (22%), malabsorption (19%), and gastroesophageal reflux disease (18%) (Table 2). The most prevalent concomitant medications identified on claims during the pre-index period were antibiotics (95%), anti-asthmatics (84%), pancreatic enzymes (84%), airway clearance medications (77%), gastrointestinal medications (49%), tobramycin inhalation solution (43%), and nutrition medications (27%) (Table 2 and Supplementary Table S1).

### Healthcare resource utilization and medication adherence

A significant decrease was observed in the proportion of patients with at least one CF-related inpatient admission during the 12 months after ivacaftor initiation compared to the 12 months prior (19.0% pre index vs 6.3% post index;  $p=0.041$ ), corresponding to a 66.9% reduction (Table 3). While the percentage of patients with a CF-related admission decreased following ivacaftor initiation, among those patients with at least one hospital admission there were no significant differences pre- vs post-initiation of ivacaftor in either average number of admissions with an admitting diagnosis of CF per patient (1.6 pre index vs 1.2 post index) or average total hospital days (13.8 days pre index vs 7.8 days post index) (Table 3). A significant decrease was also observed in the proportion

**Table 2.** Clinical characteristics and medications within the 12-month pre-index period.

Clinical characteristic	n = 79
Respiratory diagnosis,* n (%)	
Aspergillosis	3 (3.8)
Asthma	17 (21.5)
Bronchiectasis	17 (21.5)
Cough	19 (24.1)
Nasal polyp	4 (5.1)
Pulmonary infection	22 (27.8)
<i>Pseudomonas</i>	11 (13.9)
Non- <i>Pseudomonas</i>	20 (25.3)
Sinusitis	28 (35.4)
GI/hepatic diagnosis,* n (%)	
Biliary tract disorder	1 (1.3)
GERD	14 (17.7)
Intestinal obstruction	2 (2.5)
Malabsorption	15 (19.0)
Nausea/vomiting	3 (3.8)
Pancreatitis	1 (1.3)
Pancreatic insufficiency†	66 (83.5)
Other diagnosis,* n (%)	
Depression	1 (1.3)
Diabetes, type I	5 (6.3)
Diabetes, type II	8 (10.1)
Hypertension	2 (3.5)
Renal insufficiency	1 (1.3)
Medication,‡ n (%)	
Airway clearance	61 (77.2)
Anti-allergy	15 (19.0)
Anti-asthma	66 (83.5)
Antibiotic	75 (94.9)
Anti-depressant/anti-anxiety	5 (6.3)
Anti-inflammatory	8 (10.1)
Birth control	6 (7.6)
Endocrine	12 (15.2)
Pancreatic enzymes	66 (83.5)
Gastrointestinal	39 (49.4)
Nutrition	21 (26.6)
Pain relief	8 (10.1)
Dornase alfa	58 (73.4)
Tobramycin inhalation solution	34 (43.0)
Other	10 (12.6)

GI, gastrointestinal; GERD, gastroesophageal reflux disease; NDC, National Drug Code.

\*Clinical characteristics as identified by primary or secondary ICD-9 diagnosis code on any claim generated during the pre-index period.

†Reported based on prescription claims for pancreatic enzymes during the pre-index period.

‡Medications as identified by a NDC code on any claim generated during the pre-index period.

of patients with an all-cause inpatient admission (32.9% pre index vs 16.5% post index;  $p=0.021$ ). This corresponds to a 49.9% reduction in the proportion of patients with an inpatient admission. Finally, 21 patients had a decrease in all-cause inpatient admissions, while 11 patients had an increase, and one patient had no change in the 12 months after initiation of ivacaftor. For CF-related inpatient admissions, 15 patients had a decrease, while five had an increase in the 12 months after initiation of ivacaftor. A sensitivity analysis was conducted using 6-month pre- and post-index periods, which resulted in a larger sample size ( $n=106$ ), and the results found were consistent.

The average number of ivacaftor claims per patient in the 12-month post index period was 8.8 (SD =3.6) (Table 4). The majority of patients (73%) were adherent to ivacaftor therapy (MPR >0.80), and the average MPR of all patients in the study was 0.8 (SD =0.3). Patients with single-month supply claims for ivacaftor ( $n=63$ ) had an average MPR of 0.8 (SD =0.3), while those with multi-month claims for ivacaftor ( $n=16$ ) had

**Table 3.** Healthcare resource utilization.

Healthcare resource utilization	Pre-index	Post-index	<i>p</i> -value
Patients with an all-cause inpatient admission, <i>n</i> (%)	26 (32.9)	13 (16.5)	0.021
Number of admissions among all patients, mean (SD)	0.5 (1.0)	0.3 (0.9)	0.055
Number of admissions among patients with an admission, mean (SD)	1.6 (1.1)	1.9 (1.4)	0.175
Average total hospital days per patient, mean (SD)	13.1 (17.9)	12.8 (14.8)	0.846
Patients with inpatient admissions with admitting diagnosis of CF, <i>n</i> (%)	15 (19.0)	5 (6.3)	0.041
Number of admissions among all patients, mean (SD)	0.3 (0.7)	0.1 (0.3)	0.017
Number of admissions among patients with an admission, mean (SD)	1.6 (0.9)	1.2 (0.4)	—**
Average total hospital days per patient, mean (SD)	13.8 (14.2)	7.8 (5.2)	—**
Number of all-cause outpatient claims per patient, mean (SD)	52.8 (68.6)	47.5 (68.9)	0.155
Number of all-cause outpatient office visits per patient, mean (SD)	8.8 (7.3)	8.2 (7.2)	0.266
Number of CF-related outpatient claims per patient*, mean (SD)	36.1 (46.3)	31.5 (48.9)	0.124
Number of CF-related outpatient office visits, mean (SD)	5.4 (3.9)	4.7 (4.2)	0.111
Number of pulmonary function tests per patient, <i>n</i> (%)	75 (94.9)	74 (93.7)	1.000

SD, standard deviation; CF, cystic fibrosis.

\*All outpatient services include physician office and other visits, as well as services such as laboratory and radiology (i.e. all outpatient services excluding emergency room visits).

\*\*No patient with a pre-index admission had a post-index admission and visa versa.

**Table 4.** Ivacaftor treatment characteristics during the post-index period.

Treatment characteristics	<i>n</i> = 79
Number of ivacaftor claims per patient, mean (SD)	8.8 (3.6)
MPR,* mean (SD)	0.8 (0.3)
Patients with single-month supply claims,† mean (SD)	0.8 (0.3)
Patients with multi-month supply claims,‡ mean (SD)	0.9 (0.2)
MPR >0.80, <i>n</i> (%)	58 (73.4)

SD, standard deviation; MPR, medication possession ratio.

\*MPR was calculated as the sum of the day's supply as listed on each adjudicated ivacaftor claim divided by the total number of days in the post index period (365).

†*n* = 63 for patients with average day's supply between 28–35.‡*n* = 16 for patients with average day's supply between 51–90.

an average MPR of 0.9 (SD =0.2). The distribution of MPR deciles can be seen in Figure 2.

## Discussion

This retrospective, observational study demonstrates that real-world ivacaftor use from January 2012 through July 2014 is associated with adherence higher than that seen with other chronic CF medications and reduced healthcare resource utilization. Using administrative claims data from commercially insured patients with CF in the US, this study demonstrates statistically significant lower rates of all-cause and CF-related inpatient hospitalizations in the 12 months following the initiation of ivacaftor therapy compared with the 12 months prior. In total, following ivacaftor initiation there was a 50% reduction in the proportion of patients with an all-cause inpatient admission and a 67% reduction in the proportion of inpatient admissions where CF was listed as the admitting diagnosis. It is important to note that a CF diagnosis code was listed as a primary or secondary diagnosis code on all all-cause inpatient admissions, and a respiratory-related code (ICD9: 460-519) was the primary diagnosis in 64% of instances where CF was a secondary diagnosis on the inpatient admission.

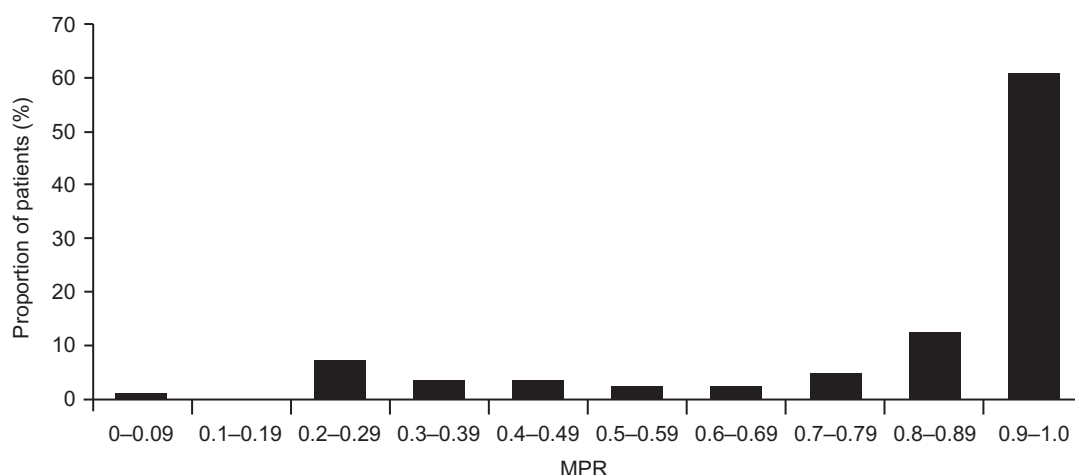
The pre-index hospitalization rates and lengths of stay observed in this analysis are consistent with rates reported in the general CF literature from studies of multiple CF populations<sup>7,11,14,15</sup>. A UK study of resource utilization rates reported that 57% of patients with CF had at least one inpatient stay for a PEx, with an average length of stay of 9.2 days; one-half of those patients required continuation of intravenous antibiotic after discharge for an additional mean of 4.9 days<sup>7</sup>.

Inpatient hospitalizations in a French study were reported among 26% and 30% for patients during 2000 and 2003, respectively<sup>14</sup>. Another resource utilization study including US and Canadian patients with CF reported that nearly a quarter (22.4%) of patients required at least one hospitalization over the 48-week study period, of which 85.8% were related to CF<sup>15</sup>. Although these are lower than the 35% rate of PEx reported in the 2013 US Cystic Fibrosis Foundation Patient Registry (CFFPR)<sup>11</sup>, the US registry does not distinguish between PEx that require hospitalization and those that do not. Further, while these studies may have had differing criteria for identification of inpatient stays and for PEx analyzed, the similarity in results reported suggests consistency in CF care. The average number of days of hospitalizations for PEx per year was 19.1 days, with an additional 11.9 days of home intravenous treatment annually.

Certain categories of healthcare resource utilization were not statistically significantly different in the post index period: for instance, while the mean number of CF-related outpatient claims trended lower than in the pre-index period (5.4 pre-index vs 4.7 post-index; *p* = 0.111), there was no statistical significance observed in this small sample size study. Larger sample sizes and longer observation time may be needed to confirm or refute this trend. CF Foundation clinical care guidelines recommend that patients aged 6 or older visit their care center at least 4 times per year, which is reflected in the CF-related outpatient visit results<sup>16</sup>. These results reflect continued best practices for specialized CF care.

Overall, clinical characteristics reported in this analysis are consistent with those reported in the CFFPR; this includes similar rates of sinusitis (35% vs 30%), asthma (22% vs 26%), diabetes (16% vs 20%), and depression (1% vs 4%). Medication use is also comparable between this analysis and the CFFPR: for example, 84% of patients received pancreatic enzymes compared with 87% of patients in the CFFPR, and dornase alfa usage was 73% compared with 85% in the CFFPR<sup>11</sup>. Drug classification for concomitant medications was conducted based on therapeutic class, which may be different from the intended use in patients with CF.

Pulmonary exacerbations often require hospitalization, are associated with loss of lung function, markedly impact quality-of-life, and are associated with increased mortality<sup>7–9,17</sup>.



**Figure 2.** Medication possession ratio by deciles. MPR, medication possession ratio; total days supplied from all ivacaftor refills divided by 365 days of the post-index period.

In a randomized, double-blind, placebo-controlled phase 3 study, ivacaftor taken orally twice a day showed a 55% reduction in the risk of PEx ( $p=0.001$ ) over a 48-week period as compared with placebo. Furthermore, patients treated with ivacaftor experienced significantly fewer hospitalization days due to a PEx (3.92 vs 4.15;  $p=0.028$ )<sup>1</sup>. A separate longitudinal observational cohort study by Rowe *et al.*<sup>18</sup> assessed hospitalizations before and after a group of patients with CF initiated ivacaftor treatment. During the 6 months prior to starting ivacaftor, 27% of patients had an inpatient hospitalization, whereas only 8% had a hospitalization during the 6 months after ivacaftor initiation (difference =19.1%; 95% confidence interval [CI]=10.8–27.5;  $p<0.001$ ). Additionally, the total number of hospitalizations in the 6 months following ivacaftor initiation declined by 16.3% (95% CI =8.1–24.4;  $p<0.001$ ), as compared with the 6 months prior. Consistent with these findings, results of our current analysis also show that initiation of ivacaftor therapy is associated with lower rates of healthcare resource utilization, specifically inpatient hospitalizations, in patients with CF.

Poor adherence to standard-of-care regimens may play a major role in increasing the cost of healthcare in patients with CF, and thus ensuring high rates of adherence is a goal of therapy<sup>19</sup>. Aggressive CF treatment plans that incorporate increasingly complicated, time-consuming daily regimens have led to challenges to adherence and disease self-management<sup>20,21</sup>. Multiple studies have documented low adherence to treatment routines in CF<sup>21–31</sup>. Barriers to adherence include perceived lack of efficacy, time management, and developmental challenges during the transition into adulthood<sup>21–24</sup>. Among adolescents and young adults with CF, adherence to chest airway clearance has been estimated to be 40–47%, while adherence to dietary recommendations is even lower, at ~20%<sup>25</sup>. Additionally, a study assessing the impact of medication adherence on lung function among patients with CF reported that adherence to chronic pulmonary medication averages close to 50%, with a range from 35–75%<sup>26</sup>. Furthermore, the authors concluded that patients with CF with low adherence (MPR <50%) had the highest probability of suffering a PEx event<sup>27</sup>. These low levels of adherence among patients with CF are similar to those

reported for patients suffering from other chronic diseases where numerous reviews have found adherence rates to cluster around 50%<sup>28–31</sup>. In our study, adherence to ivacaftor exceeded reported adherence estimates from other studies of other chronic CF therapies, potentially due to several factors, including oral administration and high perceived treatment benefit among patients. Future work directed to those with low adherence is needed to understand drivers.

This analysis is limited by the small number of patients who met the inclusion criteria and initiated treatment with ivacaftor during the study period. At that time, ivacaftor was approved for treatment in patients with at least one *G551D-CFTR* mutation, which had a prevalence in the US of 4.4% according to the 2013 CFFPR<sup>11</sup>. However, the sensitivity analysis which assessed a sample with shorter follow-up period found consistent results. Additionally, some patients included in the analysis may have received ivacaftor during clinical trials prior to January 1, 2012, since the use of ivacaftor in a clinical trial would not appear in an insurance claims database. As a result, some patients may have received ivacaftor during the pre-index period, potentially biasing their pre-index healthcare resource utilization. Despite this possibility of pre-index ivacaftor use, the analysis shows significant reductions in all-cause and CF-related inpatient admissions. Further, the decision to hospitalize a patient is driven by the patient's clinician and may vary by center and region as well as other factors. Second, the analysis was conducted using healthcare claims data, which are collected for billing purposes and may be prone to data coding limitations and data entry error. The prevalence of co-morbid conditions, for instance, may differ from clinical trial or registry analyses due to differences in disease coding and/or reporting. Additionally, claims data do not include certain clinical characteristics such as lung function measurements, limiting the ability to assess impact on such physiologic outcomes. Third, adherence with therapy was estimated using outpatient pharmacy claims during the study period. Although office-administered medications indicate that therapy is actually given, it cannot be assumed that medications obtained in the outpatient pharmacy are taken by patients as prescribed. Additionally, this data does not capture written prescriptions

that went unfilled. Finally, the claims data only included patients with commercial insurance in the US who received ivacaftor during the study period, thus the results may not be generalizable to individuals without insurance coverage or those with government subsidized insurance plans, which tend to include individuals in the US with lower socioeconomic status. Additionally, the results may not be generalizable to individuals who received ivacaftor after the study period, as a result of the expanded indication into patients with additional *CFTR* mutations.

Ivacaftor, a precision medicine for an orphan disease, is mutation-specific and indicated for a small percentage of patients with CF (~5% of patients with CF). The objective of this study was to evaluate the clinical outcomes among commercially insured patients with CF who were treated with ivacaftor to assess the real-world treatment benefits in healthcare resource utilization, and was not designed to analyze the costs of medical care. Improvements in clinical outcomes, such as the reductions in hospitalizations demonstrated in this study, are important for assessment of therapeutic value along with the wider social value and other considerations, particularly in the case of orphan diseases like CF where the overall cost of treatment regimens can be high<sup>32,33</sup>. Future studies could expand the value assessment of ivacaftor therapy in several ways, including longer term clinical outcomes, health-related quality-of-life, impact on the patients' families and broader society, along with the associated costs.

## Conclusions

In this real-world, US-based claims database, ivacaftor therapy was associated with significant reductions in hospitalizations among a geographically diverse group of patients with CF. A majority of patients demonstrated adherence rates >80% to ivacaftor therapy. Although these findings should be interpreted with the knowledge that certain clinical parameters and biometric information are not captured in insurance claims data, the presented findings are consistent with previously reported results from clinical trials and observational studies, and suggest that ivacaftor treatment has benefits to patients outside the clinical trial setting<sup>1-3,12,13</sup>.

## Transparency

### Declaration of funding

This study was funded by Vertex Pharmaceuticals Incorporated, and conducted by Truven Health Analytics, Cambridge, MA, USA.

### Declaration of financial/other relationships

MB and BL are employees of Truven Health Analytics, who were paid by Vertex Pharmaceuticals Incorporated for this study and for the development of this manuscript. ES, LO, and DP are employees of Vertex Pharmaceuticals Incorporated and may own stock or stock options in that company. JSW was a former employee of Vertex Pharmaceuticals Incorporated. GS and JSW have received consultant fees and their institutions have received financial support from Vertex Pharmaceuticals

Incorporated for study participation. JME peer reviewers on this manuscript have no relevant financial or other relationships to disclose.

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