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Impact of Lumacaftor/Ivacaftor on Pulmonary Exacerbation Rates in Members with Cystic Fibrosis in a Medicaid Population

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BACKGROUND

- Although cystic fibrosis (CF) affects multiple organ systems throughout the body, pulmonary disease is the leading cause of morbidity and mortality among patients with CF. It has been shown that forced expiratory volume in one second (FEV_1) levels and pulmonary exacerbation (PEx) rates are predictors of survival and thus remain important targets when evaluating the benefit of new CF therapies.[1]
- In randomized trials, lumacaftor/ivacaftor (LUM/IVA) led to statistically significant absolute improvements in FEV_1, as well as reductions in PEx rates, hospitalizations, and use of intravenous antibiotics.[2]
- Two observational studies demonstrated the real-world effectiveness of LUM/IVA in improving pulmonary outcomes; however, higher rates of adverse events and discontinuation rates occurred compared with randomized trials. To our knowledge, there is no published data evaluating real-world outcomes for Medicaid patients receiving this therapy.[3,4]

OBJECTIVE

To compare CF PEx rates pre- and post-initiation of LUM/IVA in one state's Medicaid program.

METHODS

This retrospective, observational cohort study utilized pharmacy and medical claims and prior authorization data.

Enrollment

- Members of one state's fee-for-service (FFS) and managed Medicaid plan with ≥ 1 pharmacy claim for LUM/IVA between July 2, 2015 (Food and Drug Administration-approval date) and September 30, 2016.
- **Inclusion criteria:**
  - Age ≥ 6 years
  - Diagnosis of CF and homozygous for the *F508del* mutation
- **Exclusion criteria:**
  - Medicaid was secondary payer
  - Any break in Medicaid coverage during the study period

Outcomes

- The date of the first pharmacy claim for LUM/IVA was defined as the index date. Data was collected six months pre- and post-index date.
- Demographic data collected included gender, age, baseline CF medications, and complications of CF.
- The primary outcome was annualized rate of PEx per member pre- and post-index date.
  - PEx was defined as any combination of claims for the following events: CF PEx or respiratory infection ICD-10 code related to (1) an emergency room (ER) visit or (2) inpatient hospitalization or (3) pharmacy claim for an oral or intravenous antibiotic (excluding macrolides).
  - A gap of ≥ 7 days between events was considered a new PEx event.
- Secondary outcomes included the annualized days of PEx per member and a breakdown of the number and type of events that corresponded to each PEx pre- and post-LUM/IVA initiation.
- A subgroup analysis was performed for adherent members (calculated as proportion of days covered [PDC] ≥ 0.8).

Statistical Analysis

- Descriptive statistics were used to report demographics and outcomes.
- Chi-square and paired t-test were used to test for significance among categorical and continuous variables, respectively.

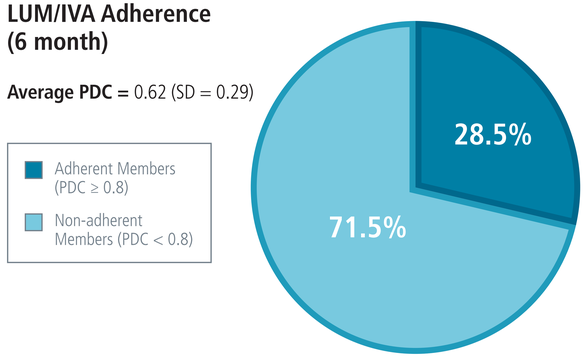
RESULTS

Member Demographics	N=21
Gender (# female)	<11*
Age, in years, at treatment initiation (mean, range)	20.1, 12 - 51
Number of CF medications at baseline (mean, standard deviation [SD])	3.5, 2.1
Members receiving respiratory medications, excluding respiratory antibiotics (%)	81.8
Members receiving respiratory antibiotics (%)	59.1
Members receiving gastrointestinal medications (%)	68.2
Complications of cystic fibrosis (%)†	
0	0
1	14.3
2	19.0
≥ 3	66.7

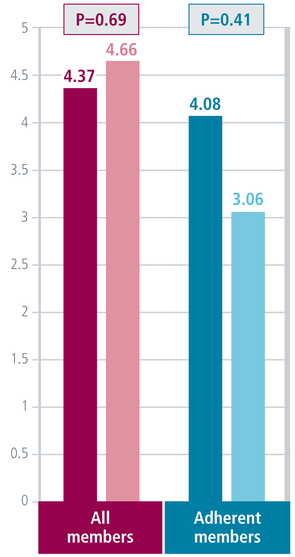
* Not reportable due to cell size <11.
† Complications include: allergic bronchopulmonary aspergillosis, arthritis, anxiety disorder, cancer, depression, diabetes, gall stones, gastroesophageal reflux disease, hearing loss, hepatic stenosis, hypertension, kidney disease, liver disease, nasal polyps, osteopenia/osteoporosis, pancreatic disease, peptic ulcer disease, renal failure (requiring dialysis), and sinus disease[5]

LUM/IVA Adherence (6 month)

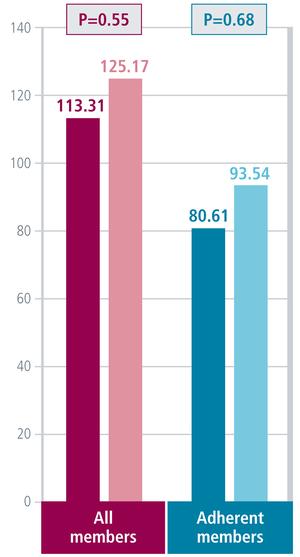
Average PDC = 0.62 (SD = 0.29)



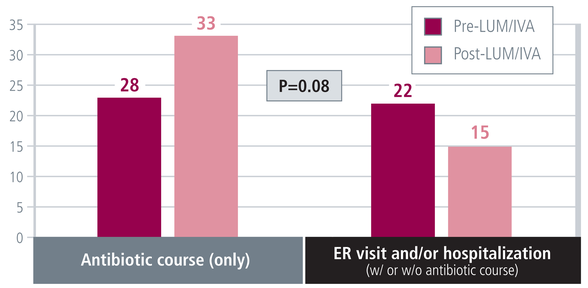
Annualized PEx Rate



Annualized Days of PEx



Number and type of events corresponding to each PEx



DISCUSSION

There was no statistically significant difference in the annualized rate of PEx and days of PEx per member in the pre-LUM/IVA period compared to the post-LUM/IVA period.

- Among adherent members, the annualized rate of PEx decreased in the post-LUM/IVA period compared to the pre-LUM/IVA period. Annualized days of PEx per member marginally increased. However, these changes were not considered to be significant.

Type of PEx associated with antibiotic courses (only) increased in the post-LUM/IVA period compared to the pre-LUM/IVA period. Conversely, PEx associated with at least one ER visit or hospitalization decreased during this period.

Non-adherence to LUM/IVA was commonly observed in our study population, which for some members may be indicative of treatment discontinuation. This finding is consistent with other real-world outcomes studies demonstrating that approximately 17% to 40% of patients discontinue treatment due to adverse events.[3,4]

LIMITATIONS

- Using claims data to define PEx is not validated.
- Due to its small sample size, this study was not powered to show a difference in the primary endpoint.
- Pharmacy claims are not a true measure of patient adherence to a medication in the outpatient setting, and data was not available to identify inpatient medication administration.
- Clinical parameters, such as pulmonary function data, were not available.

CONCLUSIONS

- This claims analysis did not find a statistically significant difference in the rate of PEx after initiation of LUM/IVA in a real-world cohort of CF patients in a Medicaid program, although numerical improvement was observed in a subset of adherent members.
- Further investigation is warranted to better understand LUM/IVA medication use patterns in this population and impact on disease state.
- Our findings support that interventions to improve adherence to CF treatments may represent a strategy for a payer to improve health outcomes for their members.

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DISCLOSURES/ACKNOWLEDGMENTS

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