Characteristics of Patients with Cystic Fibrosis Using Twice vs Once Daily Dornase Alfa Regimens

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INTRODUCTION

- Dornase alfa reduces the risk of respiratory infections and improves pulmonary function in patients with cystic fibrosis (CF).[1]
- The recommended dosage is once-daily (QD), although certain CF patients may benefit from a twice-daily (BID) regimen.[2] Real-world prescribing patterns may not be consistent with dosing recommended on the package insert.
- Little is known about how patients treated with QD vs. BID regimens differ.
- The objective of this analysis was to examine the characteristics of patients who use twice versus once daily dosing.

METHODS

Study Design

- Retrospective descriptive analysis of de-identified commercial insurance claims data.
- Study examined characteristics of patients with CF (ICD-9-CM: 277.0x) on BID vs. QD dornase alfa in the identification (ID) period (1/1/2009 – 10/31/2011).

Patient Identification

- We compared patients starting BID use to those with continuous use of QD dornase alfa. The first fill of either BID or QD use in the identification (ID) period was defined as the index date.
- Patients not continuously enrolled for 3 months before (baseline) or 1 year after (follow-up) the index date were excluded.
- New users of a regimen were those with no evidence of that regimen during baseline.

Study Measures

- Patient demographics and baseline comorbidities, as measured by the Charlson Comorbidity Index (CCI) (a commonly used measure of overall level of illness validated for use in insurance claims data),[3] were compared between study groups.
- Respiratory exacerbations were reported for the baseline period and the first 3 months of follow-up.
  - Exacerbations were defined as CF-related (claims with a primary diagnosis of CF) hospitalizations, ED visits, or use of IV/oral antibiotics.
- Treatment exposure was measured in the follow-up period.

Statistical Analysis

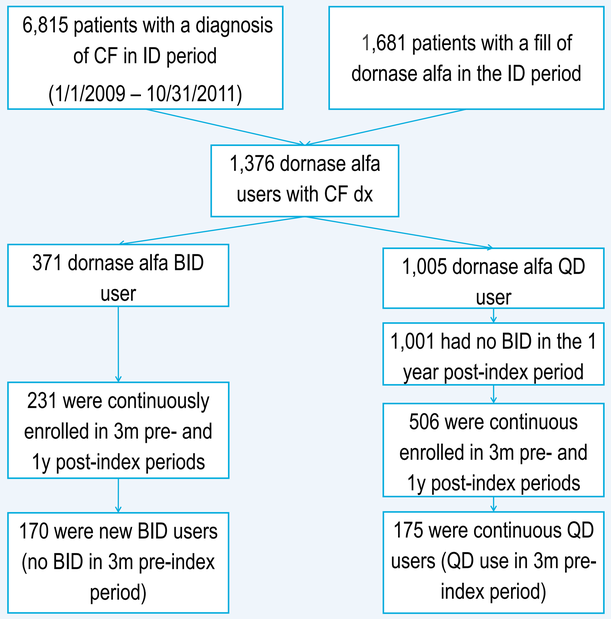
- Means and standard deviations (SD) were reported for continuous variables, and counts and percentages for categorical variables.
- All measures were reported with stratification by new BID users and continuous QD users.
- Since BID dosing may be required in older patients, analyses were repeated for the subset ≥ 21 years old .

RESULTS

Patient Demographics

- We identified 170 new BID and 175 continuous QD users **(Figure 1)**.
- BID users had mean (SD) age 24 (14.1) vs. 15.5 years (11.5, P<.001) for QD users **(Table 1)**.
- Gender and geographic region distribution were similar between groups.

Figure 1. Patient Identification



BID: twice-daily; QD: once-daily.

Table 1. Patient Demographics and Comorbidities

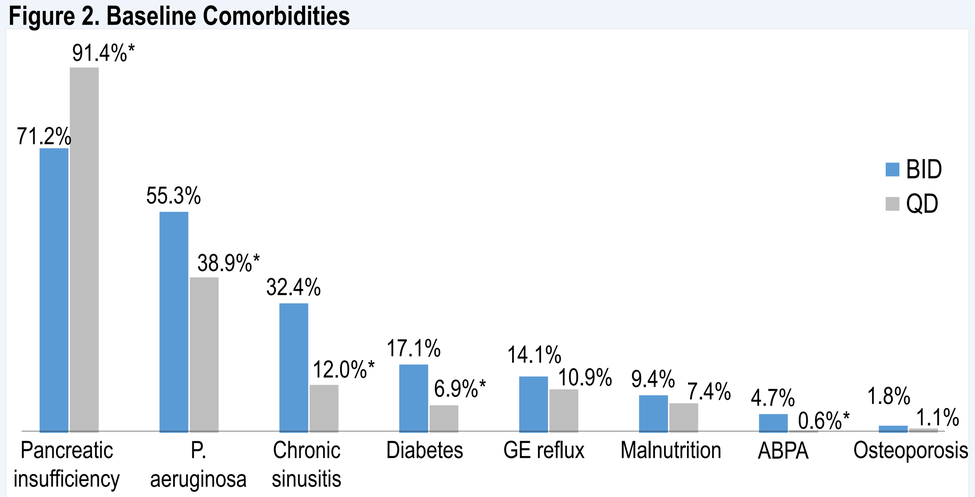
	New BID Users N = 170	Continuous QD Users N = 175	*P* Value
Age, mean years (SD)	24.0 (14.1)	15.5 (11.5)	<.001
Age, year, n (%)			<.001
<21	81 (47.6)	138 (78.9)	
21+	89 (52.4)	37 (21.1)	
Female, n (%)	81 (47.6)	87 (49.7)	0.701
Charlson Comorbidity Index, mean (SD)	1.8 (1.8)	1.1 (1.5)	<.001
Comorbidities associated with CF, n (%)	159 (93.5)	167 (95.4)	0.439
Pancreatic insufficiency	121 (71.2)	160 (91.4)	<.001
P. aeruginosa[a]	94 (55.3)	68 (38.9)	0.002
Chronic sinusitis	55 (32.4)	21 (12.0)	<.001
Diabetes mellitus	29 (17.1)	12 (6.9)	0.003
Gastroesophageal (GE) reflux	24 (14.1)	19 (10.9)	0.359
Malnutrition or failure to thrive	16 (9.4)	13 (7.4)	0.507
Allergic bronchopulmonary aspergillosis (ABPA)	8 (4.7)	1 (0.6)	0.018[b]
Osteoporosis	3 (1.8)	2 (1.1)	0.681[b]

BID: twice-daily; QD: once-daily; CF: Cystic Fibrosis.
[a] Pseudomonas aeruginosa infection or treatment with aminoglycoside or quinolone.
[b] Fisher's exact Chi-square test.

Presence of Comorbidity

- BID users had a CCI of 1.8 (1.8) vs. 1.1 (1.5) for QD users (P<0.001) **(Table 1)**.
- BID users had statistically significant higher rates of pseudomonas infection, chronic sinusitis, diabetes, and ABPA, but a statistically significantly lower rate of pancreatic insufficiency **(Table 1; Figure 2)**.

Figure 2. Baseline Comorbidities



GE: Gastroesophageal; ABPA: Allergic bronchopulmonary aspergillosis.
* P<0.05.

Exacerbations

- At baseline, exacerbation rates were 69.4% (BID) and 61.7% (QD, *P*=0.133), and the mean (SD) number of exacerbations was 2.4 (3.5) and 1.4 (1.7, *P*<0.001) for BID and QD, respectively **(Table 2)**.
- During 3 months of follow-up, exacerbation rates decreased to 62.4% in the new BID users and increased to 66.9% in the continuing QD group (*P*=0.382),
- The mean number of exacerbations was 2.2 (4.2) in BID users and 1.4 (1.6, *P*=0.021) in QD users **(Table 3)**.

Table 2. Respiratory Exacerbations[a] in Baseline

	New BID Users N = 170	Continuous QD Users N = 175	P Value
Any respiratory exacerbations[a], n (%)	118 (69.4)	108 (61.7)	0.133
No. of respiratory exacerbations, mean (SD)	2.4 (3.5)	1.4 (1.7)	<.001

[a] Any medical claim for: inpatient hospitalization or ED visit with primary diagnosis of CF, hemoptysis, pneumothorax, acute asthma, acute respiratory infection, pneumonia and influenza, acute respiratory failure or pulmonary insufficiency, or bronchospasm, or any pharmacy claim for oral antibiotics (except oral azithromycin), or IV antibiotics.

Table 3. Respiratory Exacerbations[a] in First 3 Months of Follow-up

	New BID Users N = 170	Continuous QD Users N = 175	P Value
Any respiratory exacerbations[a], n (%)	106 (62.4)	117 (66.9)	0.382
No. of respiratory exacerbations, mean (SD)	2.2 (4.2)	1.4 (1.6)	0.021

[a] Any medical claim for: inpatient hospitalization or ED visit with primary diagnosis of CF, hemoptysis, pneumothorax, acute asthma, acute respiratory infection, pneumonia and influenza, acute respiratory failure or pulmonary insufficiency, or bronchospasm, or any pharmacy claim for oral antibiotics (except oral azithromycin), or IV antibiotics.

Treatment Exposure

- Annual mean (SD) days supply filled was 132.5 (109.9) for BID and 286.6 (91.3) for QD (*P*<0.001).

Findings were generally similar for the subgroup ≥ 21 years old (n=126); results not shown.

CONCLUSION

- At baseline, BID dornase alfa users were older than QD users and had higher Charlson Comorbidity Index as well as higher rates of pseudomonas, chronic sinusitis, diabetes, and ABPA. They had a lower rate of pancreatic insufficiency.
- Between-group differences exacerbation rates were not statistically significant, however, new BID users did have a numerical drop in exacerbation rate after initiating therapy, while QD users had an increase. Rates were not adjusted for baseline between-group differences.
- Overall exposure to QD treatment was about twice as long as BID treatment. The reason for this finding is unclear.
- Sample size was too small for definitive conclusions about the ≥ 21 year old population.

References

1. Genentech, Inc. "Highlights of Prescribing Information for Pulmozyme (dornase alfa)," 2014.
2. Genentech, Inc. "Highlights of Prescribing Information for Pulmozyme (dornase alfa)," 2014.
3. Deyo RA, et al. *J Clin Epidemiol*. 1992;45(6):613-619

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