

# Treatment Patterns Among Patients With Cystic Fibrosis Using Twice Daily Dornase Alfa Regimen

Michael S. Broder, MD, MSHS<sup>1</sup>; Eunice Chang, PhD<sup>1</sup>; Sheila R. Reddy, PhD, RPh<sup>1</sup>; Karina Raimundo, MS<sup>2</sup>

<sup>1</sup> Partnership for Health Analytic Research, LLC, Beverly Hills, CA, USA; <sup>2</sup> Genentech, Inc., South San Francisco, CA USA

## BACKGROUND & OBJECTIVE

- Use of dornase alfa, a mucolytic agent, reduces risk of respiratory infection and helps pulmonary function in cystic fibrosis (CF) patients.
- Since FDA approval in 1993, dornase alfa has become one of the most commonly prescribed medications for patients with CF.<sup>1</sup>
- Recommended dosage of dornase alfa is once-daily (QD), although data from pivotal clinical trials suggest twice-daily (BID) use may be beneficial for patients  $\geq 21$  years who have a relatively small effect with QD use.<sup>2</sup>
- We set out to examine the extent of BID dornase alfa use among CF patients in a real-world setting, which is currently unknown.

## METHODS

- Retrospective analysis of US insurance claims data that examined patients with CF (ICD-9-CM: 277.0x) who initiated BID dornase alfa regimens in the identification (ID) period (1/1/2009 – 10/31/2011).
- Index date defined as the first fill date of BID use in the ID period.
- Exclusion criteria: patients not continuously enrolled in the 3 months before or 1 year after index; patients who had a BID dispensing in the pre-index period.

### Measures

- Baseline characteristics were measured in 3 months before the index date.
- BID treatment uptake, duration, and discontinuation in the year following index.
  - Treatment duration was calculated as time to discontinuation (gap in BID use of  $> 60$  days after completion of previous BID fill) of the index BID regimen.
- For reference, respiratory exacerbations were also measured 3 months before and after the index date, defined as one of the following:
  - Hospitalization or ED visits with primary diagnosis of CF.
  - A medical claim with an ICD-9-CM code for: hemoptysis (786.3); pneumothorax (512.xx); acute asthma (493.01/02, 493.11/12, 493.21/22, 493.91/92); acute resp. infection (460.xx–466.xx); pneumonia and influenza (480.xx–488.xx); acute resp. failure or pulmonary insufficiency (518.81/82); or bronchospasm (519.11).
  - A pharmacy claim for any antibiotics: oral (except azithromycin) and IV.

### Statistical Analysis

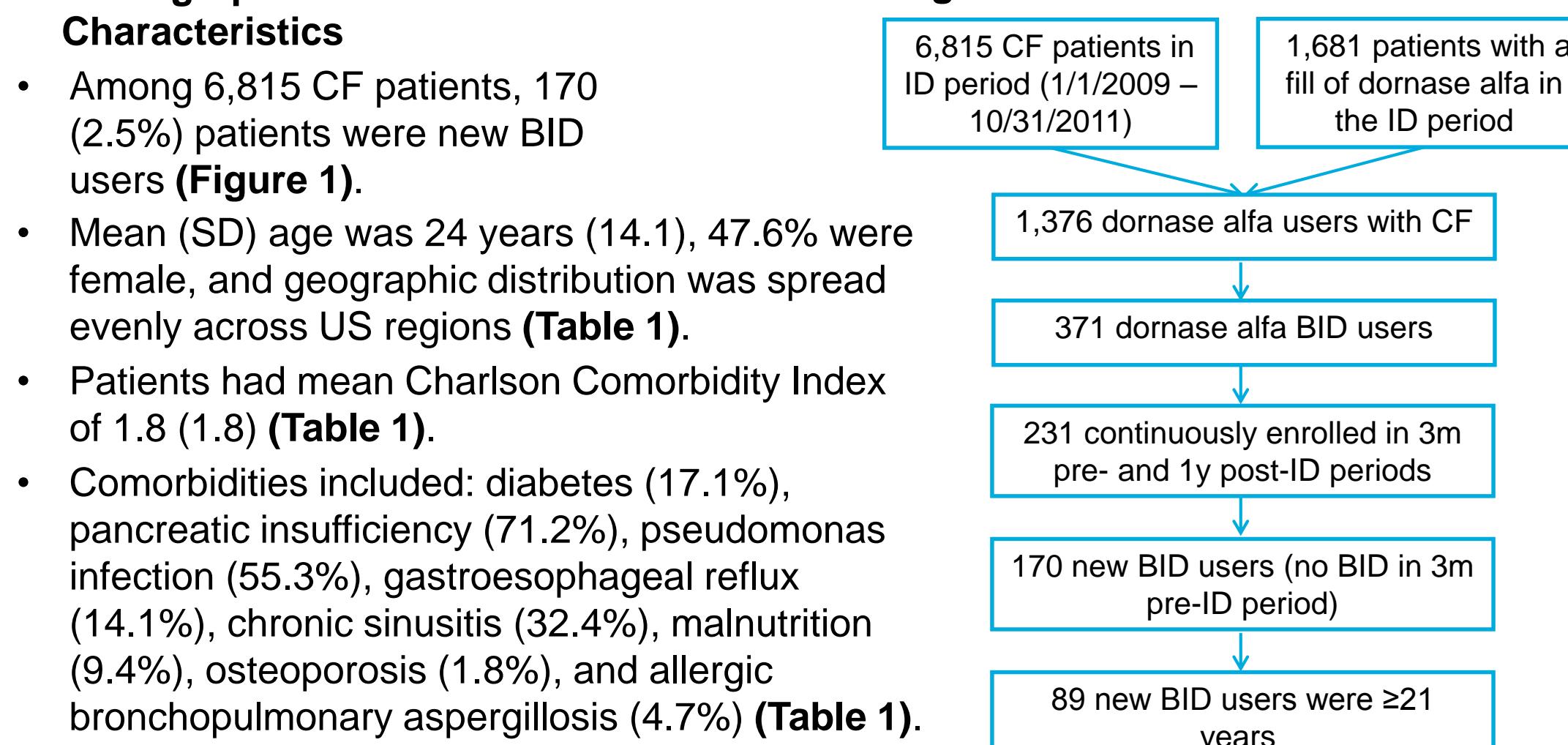
- We evaluated patterns of use by plotting medication dispensed over time. Each color represented a different regimen (BID, QD, QD & BID, and no use). Graphical results were reported in aggregate and for each patient.
- The analysis was repeated for patients  $\geq 21$  years old (n=89).
- All data transformations and analyses were performed using SAS® version 9.4.

## RESULTS

### Demographics and Patient Characteristics

- Among 6,815 CF patients, 170 (2.5%) patients were new BID users (**Figure 1**).
- Mean (SD) age was 24 years (14.1), 47.6% were female, and geographic distribution was spread evenly across US regions (**Table 1**).
- Patients had mean Charlson Comorbidity Index of 1.8 (1.8) (**Table 1**).
- Comorbidities included: diabetes (17.1%), pancreatic insufficiency (71.2%), pseudomonas infection (55.3%), gastroesophageal reflux (14.1%), chronic sinusitis (32.4%), malnutrition (9.4%), osteoporosis (1.8%), and allergic bronchopulmonary aspergillosis (4.7%) (**Table 1**).

**Figure 1. Patient Identification**



**Table 1. Patient Demographics and Comorbidities**

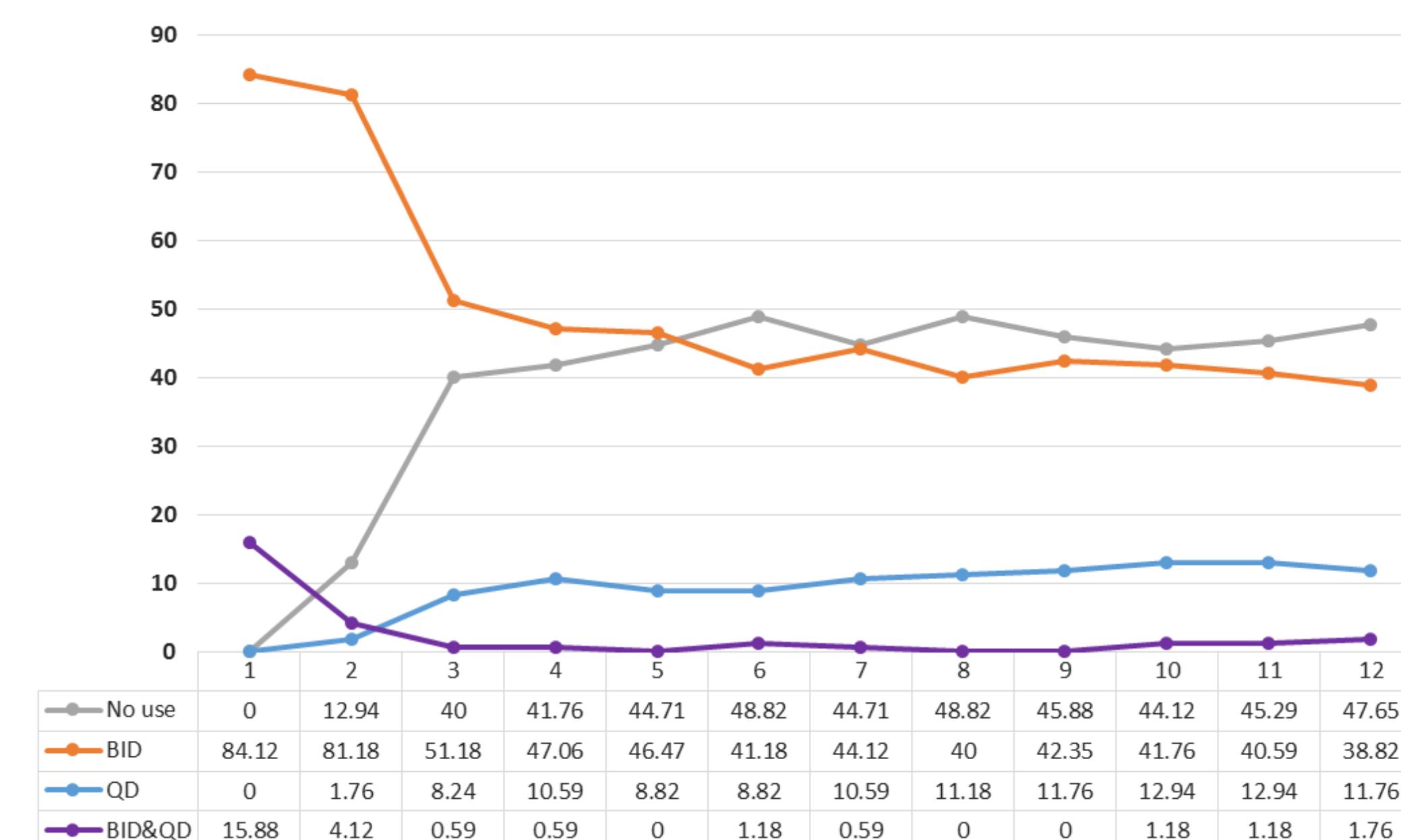
|  | BID New Users<br>N = 170 |
|--|--------------------------|
| Age, mean years (SD)                       | 24.0 (14.1)              |
| Age, year, n (%)                           |                          |
| <21  | 81 (47.6)                |
| 21+  | 89 (52.4)                |
| Female                                     | 81 (47.6)                |
| Charlson Comorbidity Index, mean (SD)      | 1.8 (1.8)                |
| Comorbidities associated with CF, n (%)    | 159 (93.5)               |
| Diabetes mellitus                          | 29 (17.1)                |
| Pancreatic insufficiency                   | 121 (71.2)               |
| Pseudomonas aeruginosa pulmonary infection | 94 (55.3)                |
| Gastroesophageal reflux                    | 24 (14.1)                |
| Chronic sinusitis                          | 55 (32.4)                |
| Malnutrition or failure to thrive          | 16 (9.4)                 |
| Osteoporosis                               | 3 (1.8)                  |
| Allergic bronchopulmonary aspergillosis    | 8 (4.7)                  |

## RESULTS

### BID Dornase Alfa Utilization

- Patients initiating BID use received on average 4.2 (3.1) BID fills, corresponding to mean days supply of 132.5 (109.9; results not shown).
- Under half of patients (41.2%) continued BID for 6 months with 38.8% on the regimen at 1 year (**Figures 2 & 3**).

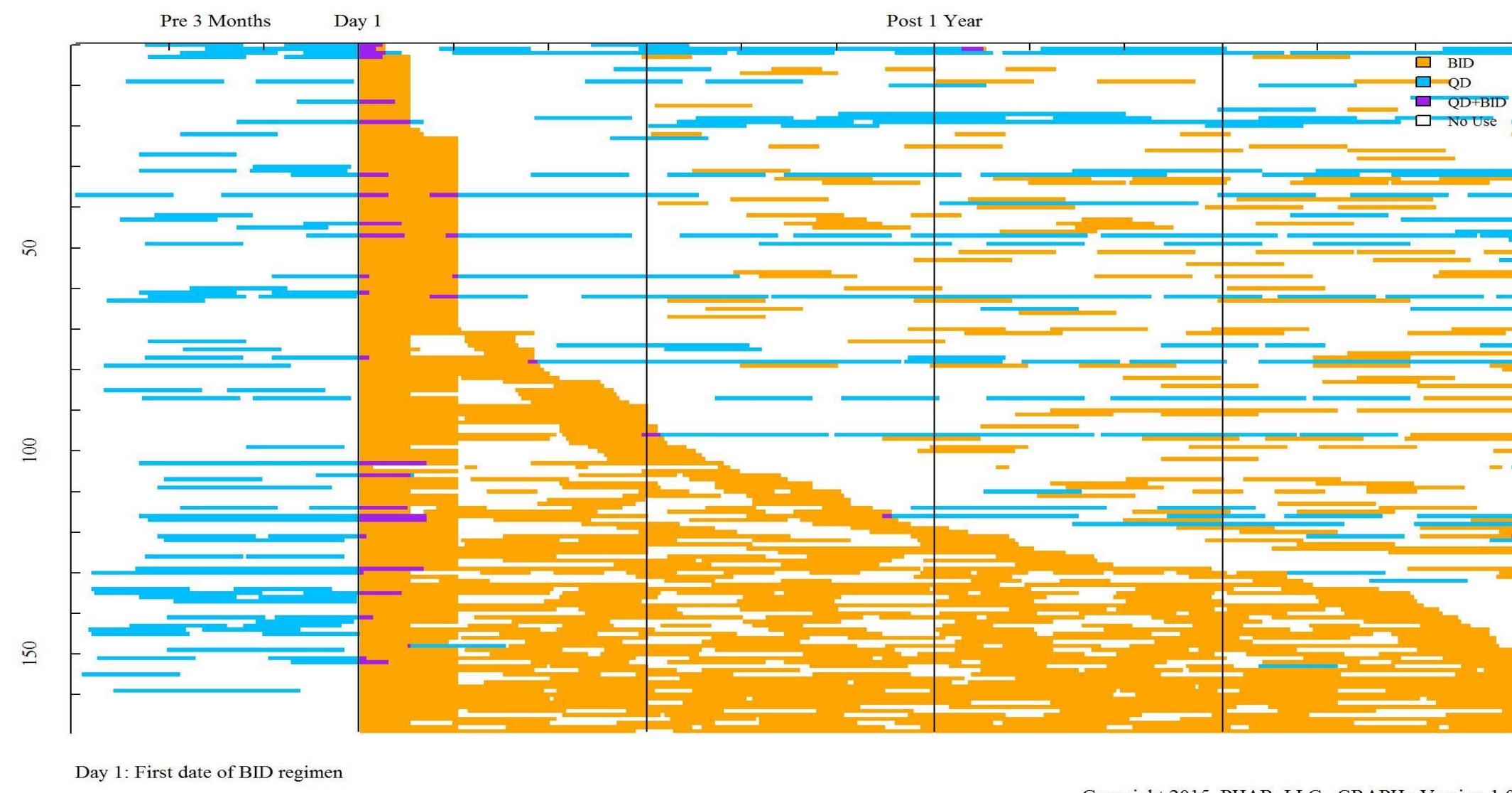
**Figure 2: Monthly Dornase Alfa Use Following Initiation of BID Regimen (N = 170)**



### Respiratory Exacerbations

- Clinically, 3-month pre-index exacerbation rates were 69.4% for BID users, with a mean of 2.4 (3.5) exacerbations/patient. Exacerbation rates at 3 months post-index dropped 10.2% to 62.4%, with a mean of 2.2 (4.2) exacerbations/patient.
- Trend towards reduction in respiratory exacerbations in the post BID initiation period, however, observation period and sample size were small (**Table 2**).

**Figure 3. Dornase Alfa Use for Each Patient Initiating BID Regimen (N=170)**



**Table 2. Respiratory Exacerbations Before and After Initiating BID Regimen**

| BID New Users<br>N = 170                    |            |
|---|------------|
| Before BID initiation (3-month pre-index)   |            |
| Any respiratory exacerbations, n (%)        | 118 (69.4) |
| No. of respiratory exacerbations, mean (SD) | 2.4 (3.5)  |
| After BID initiation (3-month post-index)   |            |
| Any respiratory exacerbations, n (%)        | 106 (62.4) |
| No. of respiratory exacerbations, mean (SD) | 2.2 (4.2)  |

## LIMITATIONS

- Our treatment patterns analysis was based on dispensing data as reported on pharmacy claims, which may not reflect how the medication was actually used.
- Results may not be generalizable to uninsured individuals or to those with other types of insurance not included in this database.

## CONCLUSION

- On average, patients continued BID use for about 4 months before switching to QD or stopping. Most patients discontinued BID use by month 6, with a further drop over the remainder of the year.
- Some patients may benefit from BID dornase alfa use for a period of time.
- This study suggests that physicians and patients practice appropriate BID use, without need for health plan management to restrict access to higher doses of dornase alfa.

## REFERENCES

- Wagener JS. Curr Opin Pulm Med Nov 2012; 18(6):609-14.
- Genentech, Inc., "Highlights of Prescribing Information for Pulmozyme® (dornase alfa)."