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Original Article

Randomized trial of efficacy and safety of dornase alfa delivered by eRapid nebulizer in cystic fibrosis patients ☆

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Abstract

Background: Dornase alfa administered via jet nebulizer is indicated as a chronic respiratory medication for cystic fibrosis (CF) patients. Efficacy and safety of dornase alfa via an electronic nebulizer with vibrating membrane technology have not been formally assessed in randomized clinical trials.
Methods: 87 CF patients (≥6 years) were randomized in a crossover study to receive dornase alfa 2.5 mg/d in 2-week periods with the Pari eRapid and Pari LC Plus jet nebulizers. The primary end point was comparison of forced expiratory volume in the first second. Safety, quality of life, and treatment satisfaction/preference were also compared between devices.
Results: Lung function was equivalent between nebulizers. Most domain scores from the Cystic Fibrosis Questionnaire-Revised and Treatment Satisfaction Questionnaire for Medication instruments were similar but patients strongly preferred the eRapid. Mean patient-reported administration times were shorter with the eRapid vs the LC Plus (2.7 vs 10.2 min). Adverse events were similar between devices.
Conclusions: Administration of dornase alfa via the eRapid nebulizer resulted in comparable efficacy and safety, shorter nebulization times, and higher patient preference.

Keywords: Cystic fibrosis; Nebulizers; Dornase alfa

Abbreviations: AE, adverse event; CF, cystic fibrosis; CFQ-R, Cystic Fibrosis Questionnaire Revised; CI, confidence interval; $FEF_{25–75}$, forced expiratory flow in mid-expiratory phase; FEV_1, forced expiratory volume in the first second of expiration; FVC, forced vital capacity; mITT, modified intent-to-treat; QOL, quality of life; SD, standard deviation; TSQM, Treatment Satisfaction Questionnaire for Medication.

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1. Introduction

Cystic fibrosis (CF) is characterized by progressive lung disease due to viscous secretions throughout the sinopulmonary system leading to chronic infection and inflammation. Over the past several decades, survival with CF has increased, possibly due, in part, to the development and increased use of therapeutic agents aimed at reducing infection and inflammation in the CF airway [1–3]. Treatment guidelines for chronic respiratory medications in CF recommend multiple different therapeutic regimens, and patients with CF typically require intensive, lifelong therapy including chest physiotherapy, mucolytics, airway hydrators, anti-inflammatories, and antibiotics [2,4]. The treatment burden in CF is high, and

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daily adherence to lifelong therapies can be challenging as patients struggle to balance treatment time with other activities [3,5,6].

Dornase alfa (Pulmozyme, Genentech, South San Francisco, CA) is a recombinant human deoxyribonuclease I, an enzyme that hydrolyzes the extracellular DNA in sputum of patients with CF in vitro and reduces sputum viscoelasticity [7,8]. In patients with CF, dornase alfa is indicated to improve lung function and reduce the risk of pulmonary exacerbations [8]. Treatment guidelines for chronic respiratory medications in CF patients recommend chronic use of dornase alfa in patients ≥6 years old [2]. Dornase alfa is administered through inhalation of an aerosol mist that is produced by a compressed air-driven nebulizer system [8]. Currently, the US product information for dornase alfa only recommends jet nebulizer/air compressor combinations for delivery of dornase alfa [8].

The eRapid (PARI Respiratory Equipment, Midlothian VA) system (Online Supplement Fig. S1) is a general-purpose electronic nebulizer that uses vibrating membrane technology (eFlow®) [9]. The eRapid device is smaller, lighter, quieter, and more portable than conventional jet nebulizer/air compressor systems [9]. In vitro studies have shown that the eRapid device delivers a comparable dose of dornase alfa with aerosol characteristics similar to that of the Pari LC® Plus jet nebulizer (PARI Respiratory Equipment, Midlothian, VA) [9]. The eRapid device has been studied in 2 European trials [10,11]. In a randomized crossover clinical trial comparing the eRapid device with another conventional device in the delivery of sodium chloride solution, results comparing two week periods of inhalation indicated similar FEV_1 and higher patient satisfaction with eRapid [10]. In another observational trial, CF patients treated with various inhalation therapies who switched from a conventional jet nebulizer to the eRapid for 1 year did not have significant changes in lung function parameters compared to the previous 1-year control period with the conventional nebulizer but total daily inhalation time was reduced by approximately two-thirds with eRapid [11]. eFlow technology is utilized by other devices. For example, in a randomized, open-label, crossover study comparing another nebulizer (also based on eFlow technology and designed for use with a concentrated tobramycin solution) with a conventional nebulizer for the delivery of tobramycin, the time per nebulization was 80% shorter in duration with the eFlow device than with the other nebulizer [12]. These studies showed that inhalation times were reduced and patient satisfaction was higher with eFlow-based devices such as the eRapid compared with a conventional jet nebulizer [10–12]. Although the eRapid device has been available in European and other global markets since 2005, the eRapid device only received 510(k) clearance as a general purpose nebulizer by the US Food and Drug Administration in 2012 [13].

Presented here are the results of IMPART, the first randomized, controlled, crossover study to compare stability of lung function, safety, quality of life, and patient preference when dornase alfa was delivered by eRapid vs a conventional jet nebulizer system (Pari LC Plus) in patients with CF [14].

2. Methods

2.1. Study design

This phase 4, multicenter, randomized, open-label, 2-period crossover study was conducted at 15 US sites (December 2012–June 2013; ClinicalTrials.gov Identifier: NCT01712334; Fig. 1A). After screening, patients received dornase alfa 2.5 mg with the LC Plus jet nebulizer system once daily for a run-in period of 2 weeks before being randomly assigned (1:1) to treatment sequence 1 or 2. Patients in treatment sequence 1 used the eRapid device during treatment period 1 (2 weeks) and the LC Plus nebulizer during treatment period 2 (2 weeks). Patients in treatment sequence 2 used the devices in the reverse order. Patients who were prescribed inhaled antibiotics on a cycled on/off basis (typically 28 days on therapy/28 days off therapy) either administered their inhaled antibiotic continuously for the entire 6-week study or stayed off therapy for 6 weeks. Patients who were on continuous inhaled antibiotics with no "off" period maintained their existing schedule. The study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice. Institutional review boards/ethics committees approved the study for each site. Patients (or legal guardians) provided written informed consent (assent) before any study-related procedures.

2.2. Study population

Patients ≥6 years old with a confirmed diagnosis of CF were included if they had been prescribed dornase alfa once daily for at least 6 months before screening and if they had a forced expiratory volume in the first second of expiration (FEV_1) ≥40% predicted based on the equations of Wang et al. [15] (boys <18 years, girls <16 years) or Hankinson et al. [16] (men ≥18 years, women ≥16 years). Patients were excluded if within 4 weeks before randomization, they had experienced an acute respiratory infection or pulmonary exacerbation, initiated any new chronic respiratory medication (e.g., inhaled corticosteroids, inhaled or oral antibiotics, high-dose ibuprofen, inhaled saline, ivacaftor), or had changes in chest physiotherapy technique or schedule. Patients were also excluded if they were hospitalized within 4 weeks before randomization, had planned hospitalization during the study, or had received organ transplantation.

2.3. Assessments

Pulmonary function testing was performed at screening (day 14), after the 2-week run-in period (day 0), and after the end of each treatment period (days 14 and 28). Patient-reported outcomes were measured at day 0 and at the end of each treatment period with the Cystic Fibrosis Questionnaire Revised (CFQ-R). The Treatment Satisfaction Questionnaire for Medication (TSQM) was administered at the end of each treatment period, and a patient device preference questionnaire was administered at the end of the study (day 28). The CFQ-R assesses the quality of life (QOL) of patients with CF in several domains; the score range for each domain is 0–100 (higher scores reflect better QOL) [17,18]. The

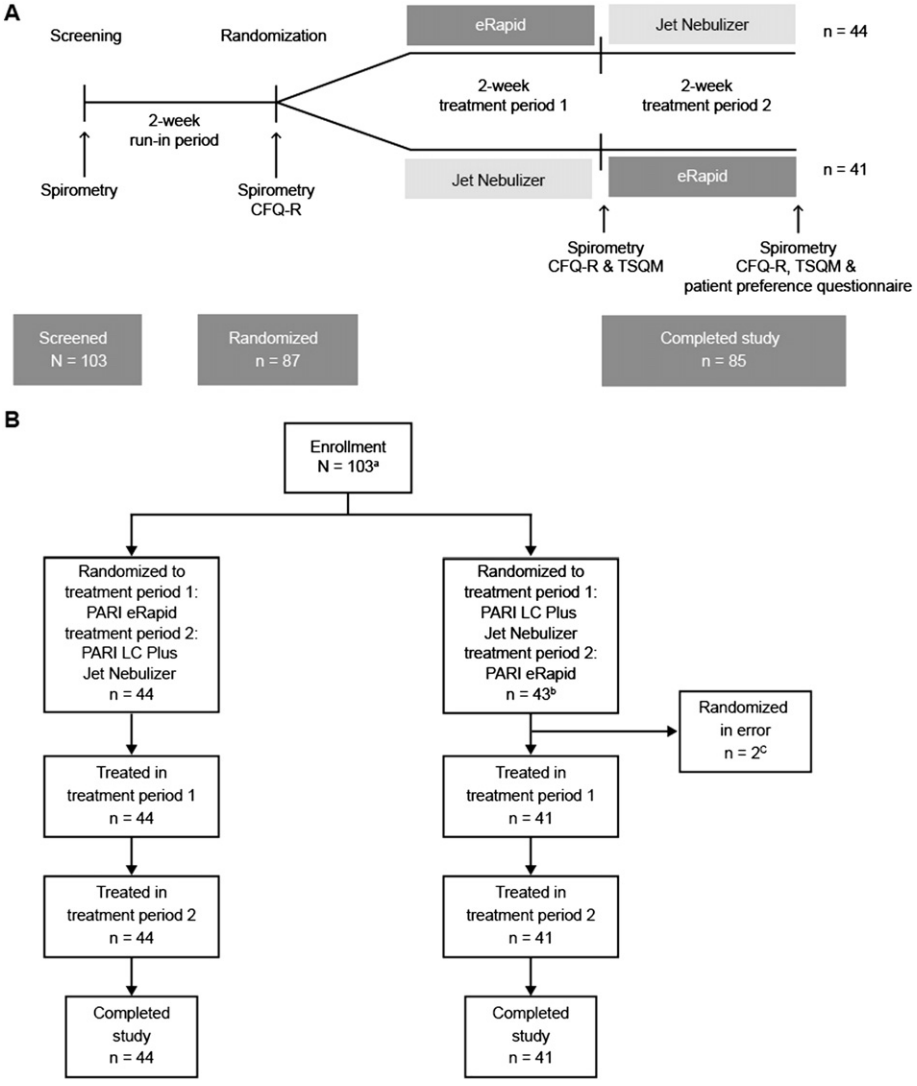

Fig. 1. Study flow. (A) Study design and (B) patient disposition. [a]4 patients who signed informed consent twice (3 of whom were dispensed a nebulizer and entered the run-in period twice) were each counted twice. [b]1 patient who was accidently randomly assigned twice was counted twice. This patient was counted as without post-baseline treatment, and also as having completed the study. [c]Includes a patient who later re-enrolled.

TSQM, version 1.4, was used to measure patients' self-reported treatment satisfaction and was administered only to patients aged ≥14 years [19]. The TSQM is a validated, generic measure of treatment satisfaction that includes 14 items within 4 domains: effectiveness, side effects, convenience, and global satisfaction. The score range for each domain is 0–100 (higher scores reflect better treatment satisfaction). Patient-treatment preference regarding the 2 devices was assessed with self-administered questions for patients ≥14 years old or via an interviewer for patients aged 6–13 years; questions varied depending on age group. Safety was assessed based on frequency and severity of adverse events (AEs) and serious AEs during each treatment period.

2.4. End points

The primary efficacy end point was the percent predicted FEV_1 at the end of each treatment period. Post-hoc subgroup analyses were performed to assess the effect of age or baseline lung function on nebulizer efficacy as measured by FEV_1. Exploratory efficacy end points included the percent predicted forced vital capacity (FVC), percent predicted forced expiratory flow in mid-expiratory phase ($FEF_{25–75}$) and patient-reported outcomes (CFQ-R [days 0, 14, 28]; TSQM [days 14, 28]). The difference in time required to administer dornase alfa with the eRapid nebulizer and the LC Plus nebulizer was reported by patients in a post-hoc analysis.

2.5. Statistical methods and study populations

The primary efficacy analysis was based on bioequivalence principles to compare the mean percent predicted FEV_1 at the end of each treatment period between the eRapid nebulizer and the jet nebulizer. The 2 nebulizers were considered equivalent if the 90% confidence interval (CI) for the ratio of the mean percent predicted FEV_1 values at the end of each treatment period was

between 80% and 125%. The CI for the ratio of the 2 means was calculated using Fieller's theorem [20]. Analyses for the other lung function measures (FVC and $FEF_{25–75}$) were conducted similarly to the primary efficacy analysis. All primary and exploratory efficacy analyses were conducted on the modified intent-to-treat (mITT) population, defined as patients who were randomly assigned and had both baseline and end point FEV_1 values available for both treatment periods. Standard descriptive statistics were used to analyze patient-reported outcome data (CFQ-R, TSQM), and nebulization times. Treatment-preference percentages were calculated on the basis of the total number of respondents to each question. The safety population was defined as patients who were randomly assigned and administered dornase alfa with either nebulizer.

3. Results

3.1. Study population

The study screened 99 unique patients (4 of whom were screened twice as allowed per protocol for a total of 103 patients); 86 were randomly assigned and 85 formed the mITT population (Fig. 1B). Forty-four patients used the eRapid nebulizer in treatment period 1 and the LC Plus jet nebulizer in treatment period 2, and 41 patients used the LC Plus jet nebulizer in treatment period 1 and the eRapid nebulizer in treatment period 2. The mITT and safety populations were the same (n = 85). The average age of patients was 13.6 years (range, 6–44), and most were white (97.6%) (Table 1). Baseline percent predicted FEV_1 was 97.5%, baseline percent predicted FVC was 101.8%, and baseline percent predicted $FEF_{25–75}$ was 92.3%. Concomitant medications and previous and concurrent diseases were similar between treatment sequences. The most common concomitant medications were bronchodilators (94.1% of patients), inhaled antibiotics (38.8%), and inhaled saline (60.0%).

Table 1
Demographics and baseline characteristics.

Characteristic [a]	mITT patients (n = 85)
Age, years	13.6 (6.9); range 6–44
6–13 years, n (%)	50 (58.8)
≥14 years, n (%)	35 (41.2)
Female, n (%)	43 (50.6)
White, n (%)	83 (97.6)
Time since CF diagnosis, years	11.8 (6.4)
Lung function (spirometry)	
FEV_1, L	2.5 (0.9)
FEV_1, % predicted	97.5 (21.8); range 42–148
FVC, L	3.0 (1.1)
FVC, % predicted	101.8 (17.4); range 62–142
$FEF_{25–75}$, L/s	2.7 (1.2)
$FEF_{25–75}$, % predicted	92.3 (37.0); range 18–181
Bronchodilator, n (%) [b]	80 (94.1)
Inhaled antibiotic, n (%) [b]	33 (38.8)
Inhaled saline, n (%) [b]	51 (60.0)

CF = cystic fibrosis; $FEF_{25–75}$ = forced expiratory flow, mid-expiratory phase; FEV_1 = forced expiratory volume in the first second of expiration; FVC = forced vital capacity; mITT = modified intent-to-treat.
[a] Mean (standard deviation), unless noted.
[b] Bronchodilator and inhaled antibiotics and inhaled saline include incidence at baseline and concomitant medications taken during the study.

3.2. Efficacy

The study met its primary efficacy end point (equivalence between the eRapid nebulizer and the LC Plus nebulizer; Table 2). The mean ratio (90% CI) of percent predicted FEV_1 for eRapid/LC Plus jet for either period was 100.9% (99.5%, 102.3%). The 90% CI was contained within the prespecified equivalence boundaries of 80%–125%, satisfying the criteria for equivalence.

Subgroup and sensitivity analyses supported the robustness of the primary efficacy result, demonstrating equivalent FEV_1 outcomes between eRapid and the LC Plus jet nebulizer. Subgroup analysis by age (≥14 and ≥18 years) showed equivalence of the 2 nebulizers (Table 2). For patients who were age ≥14 years, ratio of the means (90% CI) was 101.1% (98.9%, 103.4%). For patients who were age ≥18 years, ratio of the means (90% CI) was 102.5% (99.9%, 105.1%). Subgroup analysis in patients with lower baseline lung function (percent predicted FEV_1 of <90%, <80%, or <70%) also all demonstrated equivalence between the 2 nebulizers (Table 2). The ratio of the means (90% CI) was 98.3% (95.4%, 101.4%), 98.1% (93.8%, 102.6%), and 96.0% (91.5%, 101.2%) for patients with percent predicted FEV_1 of <90%, <80%, or <70%, respectively. Results by treatment sequences are shown in Supplementary Tables 1–3.

Exploratory efficacy analyses for FVC and $FEF_{25–75}$ demonstrated equivalent outcomes for dornase alfa administered using either the eRapid nebulizer or the LC Plus jet nebulizer (Table 2; by treatment sequences, Supplementary Table 4). The ratio of the mean (90% CI) percent predicted FVC was 101.5% (100.3%, 102.7%). The ratio of the mean (90% CI) percent predicted $FEF_{25–75}$ was 101.2% (97.9%, 104.6%).

3.3. Patient-reported outcomes

Eighty-five patients responded to a version of the CFQ-R at the end of each treatment period. For all versions of the CFQ-R, patients reported numerically similar high scores in multiple CFQ-R domains when treated with dornase alfa, regardless of delivery system. There were no apparent differences in most domains of the CFQ-R between nebulizers, or between any nebulizer period and baseline, in any age group or version of the CFQ-R. In particular, mean scores for CFQ-R treatment burden were similar for eRapid and Pari LC Plus jet nebulizers for the ≥14 year age group (57.8 vs 56.8) and the 6–13 year age group (67.1 vs 65.8). Mean CFQ-R respiratory symptom scores were also similar between devices in each age group (77.3 vs 77.9 and 84.0 vs 86.3, respectively).

The TSQM questionnaire was administered to 35 patients aged ≥14 years. Mean TSQM convenience and effectiveness domain scores were numerically higher after treatment using the eRapid than with the LC Plus jet nebulizer (convenience: 76.5 vs 66.5; effectiveness: 76.0 vs 72.9). No difference (mean

Table 2
Efficacy end points in either 2-week period.

	eRapid		Jet nebulizer		Mean ratio eRapid/jet[a]
	Mean (SD), %	Range, %	Mean (SD), %	Range, %	Ratio (90% CI)
FEV_1, % predicted					
Primary end point (n = 85)	**98.1 (22.1)**	**51.5–145.5**	**97.2 (20.7)**	**50.0–142.1**	**100.9 (99.5, 102.3)**
Age group					
≥14 years (n = 35)	87.3 (21.1)	51.5–129.8	86.3 (20.6)	50.0–129.1	101.1 (98.9, 103.4)
≥18 years (n = 13)	76.1 (19.2)	51.5–106.5	74.2 (18.5)	50.0–103.4	102.5 (99.9, 105.1)
Patients with low-baseline lung function					
Baseline FEV_1 <90% (n = 28)	74.7 (14.1)	51.5–99.4	76.0 (14.3)	50.0–99.8	98.3 (95.4, 101.4)
Baseline FEV_1 <80% (n = 19)	67.5 (10.5)	51.5–84.6	68.8 (11.3)	50.0–99.8	98.1 (93.8, 102.6)
Baseline FEV_1 <70% (n = 11)	64.5 (11.0)	51.5–82.2	67.3 (14.5)	50.0–99.8	96.0 (91.5, 101.2)
FVC, % predicted (n = 85)	103.1 (18.4)	64.1–145.1	101.5 (17.0)	66.8–136.6	101.5 (100.3, 102.7)
$FEF_{25–75}$, % predicted (n = 72)	92.2 (38.7)	21.5–210.1	91.1 (36.3)	21.5–174.9	101.2 (97.9, 104.6)

CI = confidence interval; $FEF_{25–75}$ = forced expiratory flow, mid-expiratory phase; FEV_1 = forced expiratory volume in the first second of expiration; FVC = forced vital capacity; SD = standard deviation.
[a] Ratio values were multiplied by 100 to express as a percentage.

score of 100 for both nebulizer systems) was observed in the side effects domain. The global satisfaction domain score was numerically higher with the eRapid vs LC Plus jet nebulizer (mean, 82.1 vs 79.3).

The mean patient-reported administration times were 2.7 min using the eRapid nebulizer, and 10.2 min using the LC Plus jet nebulizer (difference between devices [95% CI], 7.5 min [6.8 min, 8.2 min]).

Patients reported a preference for the eRapid nebulizer. The majority of 6–13 year olds (n = 47) preferred the eRapid (89.4%) to the LC Plus jet nebulizer (8.5%) or had no preference (2.1%). The eRapid was preferred by 90.5% of patients ≥14 years old (n = 21), compared with 4.8% who preferred the LC Plus jet nebulizer, and 4.8% who had no preference. Overall convenience and satisfaction rates were also higher for the eRapid than with the Pari LC Plus jet nebulizer (Table 3).

3.4. Safety

Mean (range) length of exposure to dornase alfa across the 14-day treatment period with the eRapid nebulizer was 13.8 (9–17) days and with the LC Plus jet nebulizer was 13.1 (5–16) days. A similar number of AEs were reported for both nebulizer systems (Table 4). A total of 34 (40.0%) patients experienced at least 1 AE while on study, 18 (21.2%) during treatment with the eRapid and 24 (28.2%) patients with the LC Plus jet nebulizer. AEs were mostly mild to moderate in intensity, there were no serious AEs, and no patients experienced any AEs leading to death, discontinuation, dose reduction, or interruption. There was no effect of treatment sequence on the number of reported AEs. The most common AEs (≥5% overall incidence) reported with eRapid vs LC Plus jet nebulizers were upper respiratory infection (3.5% vs 2.4%), cough (2.4% vs 4.7%), and nasal congestion (2.4% vs 4.7%).

4. Discussion

This study demonstrated that efficacy and safety of dornase alfa delivered by the eRapid electronic nebulizer were comparable with that of a standard jet nebulizer used in patients with CF. Lung function as assessed by FEV_1 was equivalent following administration of dornase alfa between the 2 nebulizer systems. Additionally, a large majority of patients expressed a preference for the use of the eRapid nebulizer.

The 2-week duration for each treatment period was considered sufficient to show efficacy of dornase alfa, based on a previous study that demonstrated consistent increases in FEV_1 that returned to baseline during intermittent 2-week on/off cycling of dornase alfa [21]. Subgroup analyses of FEV_1 in

Table 3
Device preference questions.

Questions[a]	eRapid	Pari LC Plus jet nebulizer
Patients 6–13 years (N = 50), n (%)		
Which device do you like better? (n = 47)[b]	42 (89.4)	4 (8.5)
Why do you like this device better? (N = 46)[c]		
Easier to carry	15 (32.6)	
Easier to use	19 (41.3)	1 (2.2)
Size of device	20 (43.5)	
Nebulization time	41 (89.1)	1 (2.2)
Other	11 (23.9)	2 (4.3)
Patients ≥14 years (N = 35), n (%)		
Taking all things into account, which delivery device do you prefer? (n = 21/21)[b]	19 (90.5)	1 (4.8)
How convenient would it be to use the delivery device away from home?[d] (n = 24/23)	21 (87.5)	14 (60.8)
How convenient is it for you to take care of the delivery device?[d] (n = 22/21)	18 (81.8)	20 (95.2)
How satisfied are you with the portability of the delivery device?[d] (n = 22/21)	21 (95.5)	16 (76.2)

[a] Percentages are based on n, the number of patients with non-missing responses.
[b] One patient had no preference for one device over the other.
[c] >1 choice may be selected.
[d] Responses allowable were "extremely convenient/satisfied", "very convenient/satisfied", "convenient/satisfied", "somewhat convenient/satisfied", "inconvenient/unsatisfied", or "extremely inconvenient/unsatisfied". For the purposes of this table, a rating of "extremely convenient/satisfied", "very convenient/satisfied", "convenient/satisfied", or "somewhat convenient/satisfied" was taken to mean that the patient found the device convenient and/or was satisfied with the device.

Table 4
Safety.

n (%)	During eRapid (N = 85)	During jet nebulizer (N = 85)	Both treatment periods (N = 85)
Patients with any AE, n (%)	18 (21.2)	24 (28.2)	34 (40.0)
Total AEs, n	30	36	66
Patients with any SAE, n (%)	0 (0.0)	0 (0.0)	0 (0.0)
Most common AEs (occurring in >2% of patients), n (%)			
Cough	2 (2.4)	4 (4.7)	6 (7.1)
Nasal congestion	2 (2.4)	4 (4.7)	6 (7.1)
Upper respiratory tract infection	3 (3.5)	2 (2.4)	5 (5.9)
Nasopharyngitis	2 (2.4)	1 (1.2)	3 (3.5)
Abdominal pain, upper	1 (1.2)	1 (1.2)	2 (2.4)
Allergic rhinitis	1 (1.2)	1 (1.2)	2 (2.4)
CF pulmonary exacerbation	0 (0.0)	2 (2.4)	2 (2.4)
Lung hyperinflation	2 (2.4)	0 (0.0)	2 (2.4)
Oropharyngeal pain	1 (1.2)	1 (1.2)	2 (2.4)
Pyrexia	0 (0.0)	2 (2.4)	2 (2.4)
Positive sputum culture	0 (0.0)	2 (2.4)	2 (2.4)
Vomiting	0 (0.0)	2 (2.4)	2 (2.4)

AE = adverse event; CF = cystic fibrosis; SAE = serious adverse event.

older patients (≥14 years of age and ≥18 years of age) and those with lower baseline lung function (based on baseline percent predicted FEV_1 of <90%, <80%, and <70%) were also equivalent and consistent with results of the primary analysis. Other lung function measures, as assessed by FVC and $FEF_{25–75}$, were likewise equivalent between the 2 nebulizer systems. The incidence of AEs was similar between the 2 nebulizer systems and consistent with that of CF disease. There were no serious AEs, deaths, or AEs that led to treatment withdrawal. Overall, these results support the efficacious and safe use of dornase alfa in an eRapid device.

In this study, patients strongly preferred the eRapid nebulizer to the standard jet nebulizer. In younger patients (ages 6–13 years), this preference was attributable to shorter nebulization time, the size of the device, and ease of use. Older patients (≥14 years) noted device portability and convenience for use away from home as reasons for their preference for the eRapid device.

Nonadherence to inhaled therapies for cystic fibrosis remains a significant problem, especially during adolescence, and can influence lung function and health outcomes [22–24]. A survey of patients with CF and their parents found that the most common barriers to treatment adherence were lack of time, forgetfulness, and unwillingness to take treatment in public [25]. Interviews of adolescents with CF and their parents also indicated that time management was a common barrier to adherence to treatment [26]. Patients were less adherent to nebulizer treatments and chest physical therapy than to oral treatments and reported that time pressures did not only involve the actual time spent using a particular therapy, but also related to how patients were able to structure medical care into daily routines. The mean patient-reported nebulization time in the current study was 7.5 min (73%) shorter with the eRapid than with the standard jet nebulizer. In this study, patient preference responses indicate that administration time and convenience are important factors in preferring a particular device. Further studies are warranted to assess whether long-term improvements in adherence can be achieved with use of eRapid.

The main limitations of this study include the open-label design; however, the nature of the devices tested precluded blinding. Also, while 1 month was considered adequate to test the hypothesis of lung function stability, it was not possible to evaluate potential longer-term health outcomes with eRapid use given the short study duration. In addition, because the study included few patients with low lung function (i.e., percent predicted FEV_1 <70%), further studies would be needed to evaluate the eRapid device in those with more advanced stages of lung disease. Finally, use of the eRapid device was not tested in children <6 years of age in the current study. An adaptor allows the use of eRapid in this younger age group; therefore, future studies in children <6 years of age are feasible.

5. Conclusions

Compared with standard jet nebulizer systems, the eRapid system is a more convenient general-purpose electronic nebulizer that is able to deliver dornase alfa with the same efficacy as other devices but with shorter inhalation times. Lung function was comparable in patients with CF when dornase alfa was delivered by eRapid and by a standard jet nebulizer. Patients preferred multiple aspects of treatment delivery using the eRapid nebulizer. Based on the results of this study, use of the eRapid could be considered for patients with CF prescribed dornase alfa as a chronic respiratory medication. These findings plus those of earlier studies [10–12] will help devices using eFlow technology such as the eRapid receive approval from regulatory agencies.

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.jcf.2015.04.003.

Conflicts of interest

Michael Konstan receives compensation from Genentech for co-chairing the scientific advisory group of the Epidemiologic Study of Cystic Fibrosis.

Gregory Sawicki is a consultant for Genentech and serves on the scientific advisory group of the Epidemiologic Study of Cystic Fibrosis.

Will Chou, Karina Raimundo, and Ben Trzaskoma are employed by Genentech and were involved in the study design, the collection, analysis and interpretation of data, the writing of the report, and in the decision to submit the article for publication.

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