Inhalation parameters in patients with asthma using albuterol electronic multi-dose dry powder inhaler

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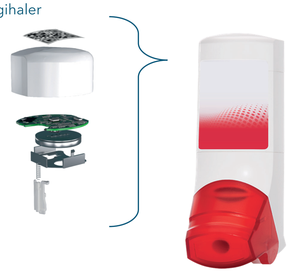
Rationale and objective

- Inhalation therapy for asthma treatment is reliant on correct inhaler technique for optimal deposition of medication, although errors are common.[1,2]
- ProAir Digihaler (albuterol 90 µg/dose; **Figure 1**) is an electronic multi-dose dry powder inhaler (eMDPI) designed with an integrated electronic module that accurately records objective information on inhaler usage and parameters, and can be used by patients and healthcare professionals to monitor inhaler technique.[3]
- The objective of this analysis was to describe inhaler technique and potentially clinically relevant patterns of inhaler use during the study.

Figure 1 ProAir Digihaler

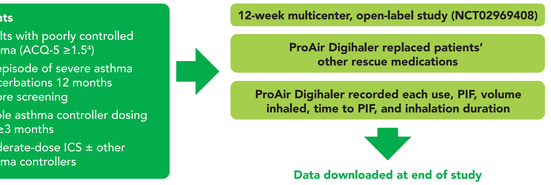


Methods

Study design

- Data were gathered from a 12-week, open-label study assessing inhalation parameter changes in adult patients with asthma (NCT02969408) conducted between February 2017 and February 2018.
- For rescue therapy, patients used ProAir Digihaler (albuterol 90 µg/dose) as needed.
- Digihaler passively recorded time and date of albuterol use and inhalation parameters: peak inspiratory flow (PIF), inhalation volume, inhalation duration, and time to PIF.
- Data were downloaded from inhalers and analyzed at the end of the study (**Figure 2**).

Figure 2 Study design



ACQ-5, Asthma Control Questionnaire-5; ICS, inhaled corticosteroids; PIF, peak inspiratory flow.

Results

- A total of 360 patients completed the study with ≥1 valid inhalation from Digihaler and were included in the analysis; of these, 64 patients experienced a total of 78 exacerbations.
- Inhalation parameters varied both over the duration of the study, and during a single day.
- **Table 1** shows demographics and inhalation characteristics for patients enrolled in the study.

Table 1 Baseline demographics and inhalation characteristics of patients with ≥1 valid inhalation

	Full study period		10 days prior to an exacerbation
	Patients without exacerbation(s), (n=296)	Patients with exacerbation(s), (n=64)	Patients with exacerbation(s), (n=64)
Mean age, years (range)	49.5 (18.0–82.0)	52.0 (25.0–87.0)	52.0 (25.0–87.0)
Females, n (%)	235 (79.4)	55 (85.9)	55 (85.9)
Mean PIF, L/min (SD)	73.18 (20.3)	73.37 (23.1)	71.78 (23.2)
Mean inhalation volume, L (SD)	1.45 (0.75)	1.44 (0.70)	1.44 (0.77)
Mean inhalation duration, seconds (SD)	1.62 (0.88)	1.60 (0.79)	1.61 (0.83)
Mean time to PIF, seconds (SD)	0.55 (0.41)	0.56 (0.43)	0.58 (0.46)

PIF, peak inspiratory flow; SD, standard deviation.

- Instances of very low PIF (<18 L/min) or no inhalations (patients opening and closing the cap without an inhalation) occurred in 12.7% of inhalation events.
- Inhaler event definitions are shown in **Table 2**.

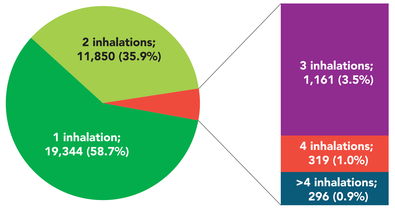
Table 2 Inhaler event definitions

Event status
Very low inhalation flow (PIF <18 L/min) or no inhalation (opening and closing the cap)
Low inhalation flow (PIF 18–29 L/min)
PIF 30–59 L/min
PIF 60–119 L/min
PIF 120–199 L/min
Air vent block (PIF ≥200 L/min)
Unexpected multiple inhalations recorded as one event*

*i.e. >1 inhalation prior to cap closure. PIF, peak inhalation flow

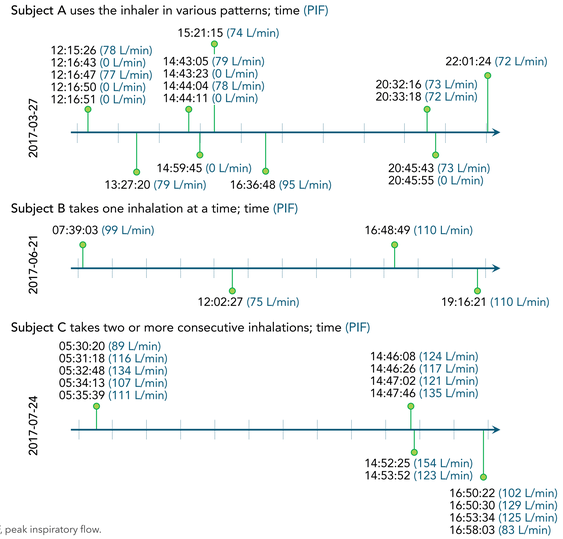
- Overall, 58.9% of episodes included a single inhalation per episode of use, and 35.8% included two inhalations (**Figure 3**).
  - An episode is defined as a series of inhaler events with a time interval no longer than 60 seconds between consecutive events.

Figure 3 Episodes of inhaler use with one or more inhalations



- Various patterns of inhaler use were identified, including patterns that may potentially be clinically important (**Figure 4**).

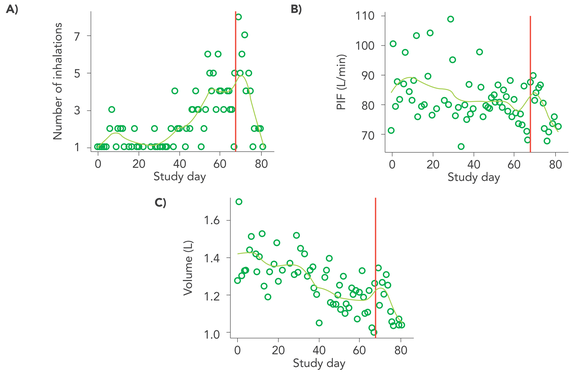
Figure 4 Patterns of inhaler use identified during the study



PIF, peak inspiratory flow.

- In some patients, prior to the exacerbations, the inhalation parameters changed consistently with a clinical deterioration: increase in the number of inhalations, decrease in PIF, and decrease in inhalation volume (**Figure 5**).

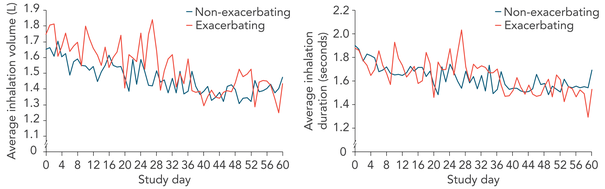
Figure 5 Example of an individual patient's changes in inhalation parameters preceding an exacerbation; A) increase in number of inhalations, B) decrease in daily PIF, C) decrease in daily inhalation volume



The red vertical line represents a confirmed asthma exacerbation. PIF, peak inspiratory flow.

- On average, gradual decreases in inhalation volume and inhalation duration were seen in both exacerbators and non-exacerbators (**Figure 6**).

Figure 6 Decreases in inhalation volume and duration during the study



Conclusions

- Inhalation parameters recorded by ProAir Digihaler may indicate inhaler technique deterioration or changes in underlying airway physiology preceding an exacerbation.
- These data support prior evidence that patient inhaler technique wanes within days of standard-of-care inhaler training.[5,6]
- The data could help identify patients at risk of exacerbations who might benefit from intervention from a mobile application monitoring technique or further instruction or intervention, potentially supporting improved asthma management.

Presented at: AAAAI 2020, Philadelphia, Pennsylvania, USA; March, 13–16 2020

Disclosures: GS, LG, MR, TL, TH, RB, and MD are employees of Teva Pharmaceuticals. Some authors may own stock from the respective companies they work for. RP has received grants from Boehringer Ingelheim and personal fees from Grifols, Sunovion, and Teva Pharmaceuticals. NF declares no conflict of interest.

Acknowledgments: Medical writing support was provided by Melanie Francis, of Zoetic Science (an Ashfield company, part of UDG Healthcare plc), and was funded by Teva Branded Pharmaceutical Products R&D Inc.

Role of the funding source: Funding was provided by Teva Branded Pharmaceutical Products R&D Inc. Teva employees were involved in the study design, data collection and analysis, and in the writing of this manuscript. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

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