



# The evaluation of the correct use and ease-of use of the ELLIPTA DPI in children with asthma

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## Abstract

**Rationale:** Asthma studies show many children use inhalers incorrectly even after instruction. For two age groups of children with asthma, we determined the proportions who used the once-daily ELLIPTA dry-powder inhaler (DPI) correctly, and who found it easy to use.

**Methods:** This was a multicenter, single-arm, stratified, open-label, placebo study (NCT03478657). Children aged 5–7 and 8–11 years were trained in, and required to demonstrate, correct placebo ELLIPTA DPI use at their first clinic visit. The inhaler was used at home once daily for 28 ± 2 days. On returning to the clinic, children were randomized to an age-appropriate, ease-of-use questionnaire that had been developed and validated previously, and which rated the inhaler as “easy” or “hard” to use. Following questionnaire completion, children were then asked to demonstrate correct inhaler use. Correct use and ease-of use were assessed in each age group (co-primary endpoints) and overall (secondary endpoints).

**Results:** Of 222 enrolled children, 221 completed the study. Among children aged 5–7 years, 92% ( $n = 81/88$ ) demonstrated correct ELLIPTA use on their first attempt, compared with 93% ( $n = 124/133$ ) aged 8–11 years. Of these children, 98% (5–7 years:  $n = 79/81$ ; 8–11 years:  $n = 121/124$ ) rated the inhaler easy to use. Overall, 93% ( $n = 205/221$ ) demonstrated correct inhaler use on their first attempt, and 98% ( $n = 200/205$ ) rated it easy to use.

**Conclusion:** ELLIPTA DPI was used correctly and easily by most children on their first attempt without additional training.

## KEYWORDS

dry-powder inhaler, questionnaire, technique

## 1 | INTRODUCTION

Asthma, the most prevalent chronic disease in children worldwide, is characterized by variable symptoms of wheeze, shortness of breath, chest tightness, and/or cough.<sup>1</sup> In 2016, approximately 8.3% of children in the United States were reported to have asthma.<sup>2</sup> While inhalers are the mainstay of asthma treatment for all ages,<sup>1</sup> studies on the correct use and ease-of use of inhalers in children are limited.

Evidence comparing the rates of correct inhaler use in children to that in adults is not widely available and has produced conflicting results; some studies suggest that children have lower rates of correct use when compared with adults,<sup>3,4</sup> while others report similar rates of correct use for both groups.<sup>5</sup> Correct inhaler technique, which is important to ensure appropriate drug delivery into the airways,<sup>6</sup> can be affected by age and type of inhaler.<sup>7,8</sup> Studies of inhaler use in children would thus be of benefit to clinicians when helping to decide on treatment choice for their patients.

Our study evaluated the correct use and ease-of use of a placebo ELLIPTA dry powder inhaler (DPI) in children with asthma aged 5–11 years, who continued to receive their usual asthma treatment and who were naïve to the use of the ELLIPTA DPI.

## 2 | METHODS

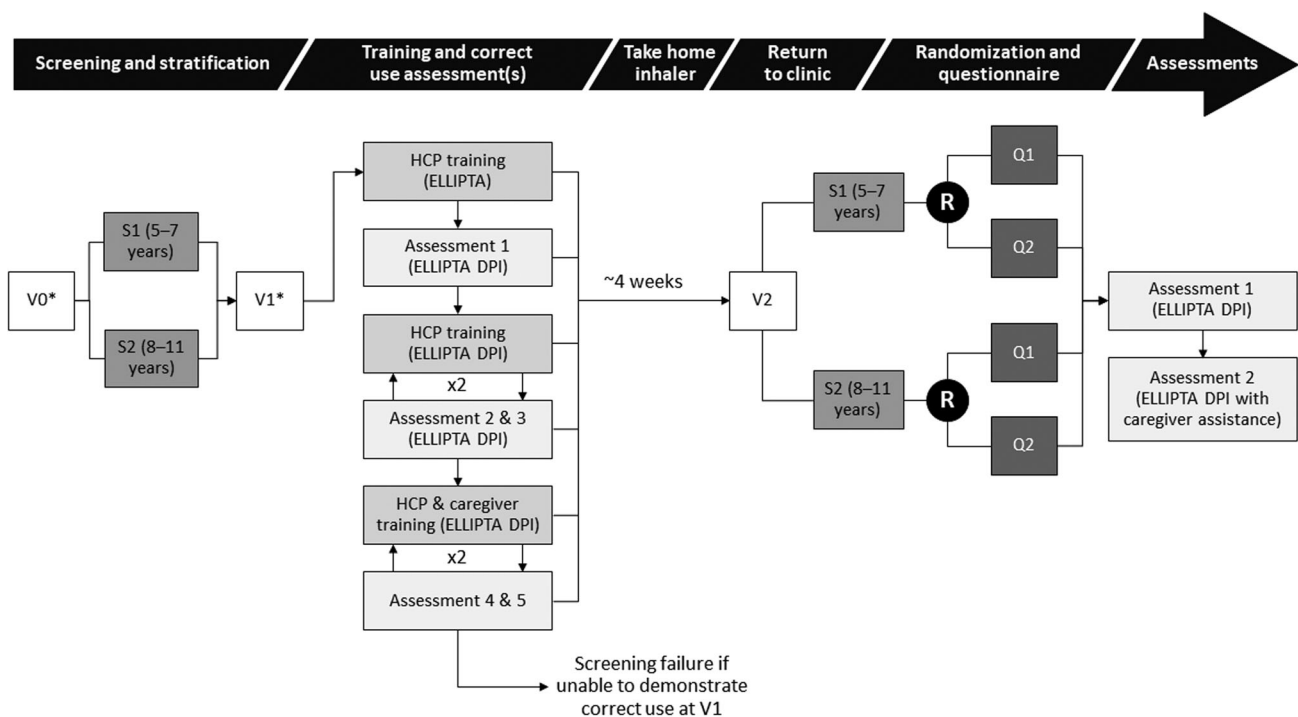
### 2.1 | Study design

This was a multicenter, single-arm, stratified, open-label, 28-day placebo study of children with asthma aged 5–11 years, conducted at

a total of 19 sites across the US ( $n = 15$ ) and Canada ( $n = 4$ ) between June and December 2018 (NCT03478657). The study design is shown in Figure 1. On the first day of screening (Visit 0), children were stratified into two age groups: those aged 5–7 years and those aged 8–11 years. Written, informed consent was obtained from all parents or guardians (caregivers) and written assent was obtained from all participants at Visit 0, along with information on participant medical history, demographics, and current asthma therapy. At Visit 1, all children were instructed in the correct use of the ELLIPTA DPI by a healthcare professional (HCP) trained in the use of the ELLIPTA DPI. They were then asked to use the inhaler unaided; if they were unable to use it correctly, the HCP could provide instructions twice more and the caregiver could assist with two further attempts. Any child who failed to demonstrate correct use after five attempts was excluded from the study. Visit 0 and Visit 1 could take place on the same day.

Children were given a placebo ELLIPTA DPI to take home for the duration of the study ( $28 \pm 2$  days) and were asked to inhale through it once daily at approximately the same time each day (children continued to use their usual prescribed asthma medications). The child's caregiver noted the date and time of each inhalation, and the study investigator was responsible for the documentation of any adverse events (AEs) or serious adverse events (SAEs).

Ease-of use and correct use were both assessed at the final study visit (Visit 2). Ease-of use was assessed using a validated, modified, printed questionnaire for children that was adapted from an existing adult questionnaire<sup>9</sup> (Appendix A) in a previous study on questionnaire validation (NCT03315572; details on the Methodology and Results of the questionnaire validation study are provided in



**FIGURE 1** Study design. \*Visit 0 (screening) and Visit 1 can take place on the same day.

DPI, dry powder inhaler; HCP, healthcare professional; Q, questionnaire (version A or B); R, randomization; S, age stratum; V, study visit

Appendix B). Upon their return to the clinic, children were randomized 1:1 using an Interactive Web Response System to receive Version A or Version B of a modified ease-of-use questionnaire, which was completed before the correct-use assessment. Each version of the questionnaire included the same questions, but with response options in the alternative order as a means of limiting response bias from children or their caregivers: Version A ranked responses from “easy” to “hard,” and Version B ranked responses from “hard” to “easy.” The questionnaire for children 5–7 years of age (Appendix C) was completed with caregiver assistance, whereas children aged 8–11 years independently completed the questionnaire (Appendix D). Caregivers also completed one of two versions of a questionnaire (Appendix E) that assessed various features of the ELLIPTA DPI. In the questionnaire validation study only, an ELLIPTA DPI inhalation trainer tool was used by children to indicate whether they had sufficient inspiratory flow to correctly activate the inhaler. Further details on the development and validation of the study questionnaire are provided in Appendix B.

Correct use was assessed by an HCP who made reference to a checklist developed from the ELLIPTA instructions for use.<sup>10</sup> During the correct-use assessment, children did not receive assistance from their caregiver or the HCP on their first attempt; however, they were allowed another attempt with assistance from their caregiver if they were unable to use the inhaler correctly. The number of inhalations taken by the child during the study was also recorded at Visit 2.

The study protocol, any amendments, the informed consent, and other information that required pre-approval were reviewed and approved by a national, regional, or investigational center ethics committee or institutional review board, in accordance with the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use, Good Clinical Practice, and applicable country-specific requirements, including US 21 Code of Federal Regulations 312.3(b) for constitution of independent ethics committees. The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki.

## 2.2 | Inclusion and exclusion criteria

Children, 5–11 years of age with at least 6 months of diagnosed asthma and who were using a maintenance and/or rescue inhaler, were eligible for inclusion in the study. Additionally, eligible children must have been naïve to the ELLIPTA DPI, that is, they had not previously been prescribed an ELLIPTA DPI or received any training in its correct use. Informed, written consent from at least one caregiver and informed permission from the child ( $\geq 7$  years of age) were required before study entry. Children with a diagnosis of other respiratory disorders, or who had a history of an asthma exacerbation within the previous 3 months, were excluded. Children with a diagnosis of psychiatric or psychological disorders were also excluded, as were those whose caregiver had a medical condition that could have affected their ability to take part in the study. All concomitant medications being taken at enrollment, or during the study, were recorded.

## 2.3 | Study endpoints

The co-primary efficacy endpoints were the percentage of children from each age group who correctly used the ELLIPTA DPI at Visit 2 after their first attempt, and the percentage of those from each age group demonstrating correct use who rated the ELLIPTA DPI as easy to use at Visit 2. Secondary efficacy endpoints were: the percentage of children from each age group who correctly used the ELLIPTA DPI after initial training from an HCP at Visit 1; the percentage of children from each age group who made at least one critical error with the ELLIPTA DPI after initial training from an HCP at Visit 1; the percentage of children from both age groups combined who demonstrated correct use of the ELLIPTA DPI on their first attempt without caregiver assistance, and of those, the percentage who rated the ELLIPTA DPI as easy to use, both at Visit 2. A critical error was defined as an error that was likely to significantly inhibit delivery of the prescribed dose of medication to the patient, determined according to an HCP who was trained in the use of the ELLIPTA DPI.

Exploratory (ease-of use and correct use) endpoints included the percentage of children from both age groups combined who made at least one critical error during use of the ELLIPTA DPI after initial training from an HCP at Visit 1; the percentage of children from each age group who made at least one critical error during use of the ELLIPTA DPI at Visit 2; the number of children and the number of caregivers who found it easy to tell how many doses remained in the ELLIPTA DPI at Visit 2; the number of children from both age groups combined who showed correct ELLIPTA DPI use on their first or second attempt with assistance from their caregiver at Visit 2; and the likelihood that a caregiver would request their child's medication in the ELLIPTA DPI if the formulation was available (after Visit 2). Safety (AEs and SAEs) was also assessed, including the incidence of asthma exacerbations.

## 2.4 | Statistical analyses

Three analysis populations were defined: all participants enrolled, which included all children whose caregiver had signed the informed consent form (the accompanying assent had been acquired from the child where appropriate); the intent-to-treat (ITT) population, comprising all children who were screened and received at least one dose of study medication (placebo); and the modified ITT (mITT) population, which included children who were screened and received one dose of study medication (placebo), and who were randomized to a version of the ease-of-use questionnaire at Visit 2. The ITT population was used for analysis of all population data, some secondary and exploratory endpoint analyses, and safety. The mITT population was used for analysis of the co-primary endpoints and most secondary and exploratory efficacy endpoints. For all study endpoints, two-sided 95% confidence interval (CI) for the percentages were calculated using the exact binomial distribution. Statistical analyses were performed using SAS software, version 9.4.

The planned sample size (generated using PASS, version 12,<sup>11</sup> and quality-checked using SAS software) for the study was 200

(comprising  $n = 80$  children aged 5–7 years [stratum 1], and  $n = 120$  aged 8–11 years [stratum 2]). Assuming that 80% of participants in each stratum would demonstrate correct inhaler use, a total sample size of 200 participants ( $n = 80$  [stratum 1];  $n = 120$  [stratum 2]) would produce a two-sided 95% CI equal to the sample proportion of correct use  $(80\%) \pm 9.28$  and  $\pm 7.51$  percentage points, in each stratum, respectively. In addition, assuming that 80% of participants in both strata would demonstrate correct use and would evaluate the ELLIPTA DPI as easy to use at Visit 2, a total sample size of 160 ( $n = 64$  [stratum 1];  $n = 96$  [stratum 2]) would produce a 95% CI equal to the sample proportion  $(80\%) \pm 10.42$ , and  $\pm 8.44$  percentage points. CIs were calculated via the Exact (Clopper–Pearson) formula, which uses the binomial probabilities directly.

### 3 | RESULTS

#### 3.1 | Study populations

In total, 232 children were screened: 10 were screening failures due to not meeting the inclusion criteria ( $n = 4$ ), withdrawal based on a physician's decision ( $n = 4$ ), or voluntary withdrawal ( $n = 2$ ) (Supporting Information E-Figure 1). Thus, 222 children were recruited to the study, which exceeded the planned sample size of 200 participants.

The ITT population comprised all 222 children, of whom 58% ( $n = 129$ ) were white; 60% ( $n = 133$ ) were male, and the mean (standard deviation [SD]) age was 8.3 (2.0) years. Of 222 children, 77% ( $n = 171$ ) were receiving maintenance therapy either with or without a rescue inhaler, and 23% ( $n = 51$ ) were receiving rescue medication only; 88% of children ( $n = 196$ ) were using a metered-dose inhaler for the delivery of their main current maintenance and/or rescue asthma therapy, compared to 7% ( $n = 16$ ) who were using a non-ELLIPTA DPI (Table 1). Mean (SD) exposure to study treatment was 28.6 (1.34) days in children 5–7 years of age, and 28.2 (2.13) days in children 8–11 years of age.

There were 221 children in the mITT population: one child in the 8–11 years age group completed Visit 1 but withdrew from the study before Visit 2.

#### 3.2 | Co-primary endpoints

For the co-primary endpoints at Visit 2, 92% ( $n = 81/88$ ; 95% CI: 84%, 97%) of children aged 5–7 years, and 93% ( $n = 124/133$ ; 95% CI: 88%, 97%) of children aged 8–11 years demonstrated correct use of the ELLIPTA DPI without assistance from a caregiver on the first attempt. Of the children who could use the ELLIPTA DPI correctly on their first attempt ( $N = 205$ ), 98% ( $n = 79/81$ ; 95% CI: 91%, >99%) of children aged 5–7 years and 98% ( $n = 121/124$ ; 95% CI: 93%, 99%) of children aged 8–11 years rated the ELLIPTA DPI as easy to use (Table 2).

**TABLE 1** Demographic characteristics of children (ITT population)

	5–7 years stratum (N = 88)	8–11 years stratum (N = 134)	Total (N = 222)
Age, mean (SD), years	6.1 (0.8)	9.7 (1.1)	8.3 (2.0)
Male, n (%)	47 (53)	86 (64)	133 (60)
Height, mean (SD), cm	120.5 (8.0)	142.3 (10.0)	133.7 (14.2)
Weight, mean (SD), kg	24.7 (7.0)	42.4 (14.3)	35.4 (14.8)
BMI, mean (SD), kg/m <sup>2</sup>	16.8 (3.2)	20.5(4.8)	19.0 (4.6)
Race, n (%)			
Asian	7 (8)	13 (10)	20 (9)
Black or African American	24 (27)	37 (28)	61 (27)
White	53 (60)	76 (57)	129 (58)
Other/multiple	4 (5)	8 (6)	12 (5)
Main current asthma therapy, n (%)			
Maintenance ± rescue, n (%)	70 (80)	101 (75)	171 (77)
Rescue only	18 (20)	33 (25)	51 (23)
Main current asthma therapy delivery system, n (%)			
Non-ELLIPTA DPI	2 (2)	14 (10)	16 (7)
MDI	78 (89)	118 (88)	196 (88)
Other <sup>a</sup>	8 (9)	2 (1)	10 (5)

Abbreviations: BMI, body mass index; DPI, dry-powder inhaler; ITT, intent-to-treat; MDI, metered-dose inhaler; SD, standard deviation.

<sup>a</sup>Includes nebulizer, pill, and tablet, etc.

#### 3.3 | Secondary efficacy and exploratory endpoints

For the secondary efficacy endpoints at Visit 1, 24% ( $n = 21/88$ ; 95% CI: 15%, 34%) of children aged 5–7 years and 50% ( $n = 67/134$ ; 95% CI: 41%, 59%) of children aged 8–11 years demonstrated correct use of the ELLIPTA DPI on their first attempt, after initial instruction from an HCP. Overall, 40% ( $n = 88/222$ ; 95% CI: 33%, 46%) of children correctly used the inhaler on their first attempt, and 64% ( $n = 143/222$ ) did not demonstrate a critical error on their first attempt. Fifty-one percent ( $n = 45/88$ ; 95% CI: 40%, 62%) of children 5–7 years of age demonstrated a critical error on their first attempt at Visit 1, compared with 25% ( $n = 34/134$ ; 95% CI: 18%, 34%) of children in the 8–11 years age group. All children in the ITT population ( $N = 222$ ) were able to demonstrate correct use of the ELLIPTA DPI, with a small proportion of children (2%,  $n = 5/222$ ) requiring the maximum of five attempts to demonstrate correct use. No children demonstrated a critical error on their fifth attempt. Inhaler errors at Visit 1, on the first attempt, are summarized in Table 3.

**TABLE 2** Co-primary and secondary endpoints at Visit 2 (mITT population)

n (%) [95% CI] <sup>a</sup>	Co-primary endpoints		Secondary endpoint
	5–7 years stratum (N = 88)	8–11 years stratum (N = 133)	Total (N = 221)
Children who demonstrated correct use of the ELLIPTA DPI without caregiver assistance on their first attempt	81 (92) [84, 97]	124 (93) [88, 97]	205 (93) [89, 96]
Children who rated the use of the ELLIPTA DPI as easy, among those who demonstrated correct use at Visit 2 <sup>b</sup>	79 (98) [91, >99]	121 (98) [93, 99]	200 (98) [94, 99]

Abbreviations: CI, confidence interval; DPI, dry powder inhaler; mITT, modified intent-to-treat.

<sup>a</sup>95% CI calculated using exact binomial distribution.

<sup>b</sup>Percentage calculated as (number of participants who rate the ELLIPTA as easy/number of participants who demonstrate correct use on their first attempt) × 100.

For the secondary efficacy endpoints at Visit 2, 93% of all children ( $n = 205/221$ ; 95% CI: 89%, 96%) demonstrated correct use of their ELLIPTA DPI on their first attempt without caregiver assistance and, of these children, 98% ( $n = 200/205$ ; 95% CI: 94%, 99%) rated the ELLIPTA DPI as easy to use (Table 2). For the exploratory endpoints at Visit 2, 100% ( $N = 133$ ; 95% CI: 97%, 100%) of children aged 8–11 years found it easy to tell how many doses were left in the ELLIPTA DPI, compared with 84% ( $n = 74/88$ ; 95% CI: 75%, 91%) of children aged 5–7 years (Table 4). All children ( $N = 221$ ; 95% CI: 98%, 100%) demonstrated correct use of the ELLIPTA DPI after either one or two attempts, with only 8% ( $n = 7/88$ ; 95% CI: 3%, 16%) aged 5–7 years and 7% ( $n = 9/133$ ; 95% CI: 3%, 12%) aged 8–11 years requiring caregiver assistance on their second attempt. Very low proportions of children made critical errors at Visit 2 (Table 4).

Ninety-four percent ( $n = 208/221$ ; 95% CI: 90%, 97%) of caregivers responded that they would be likely or very likely to request the ELLIPTA DPI from their child's doctor if their child's current asthma medication was available in this formulation, while 98% ( $n = 217/221$ ; 95% CI: 95%, >99%) responded that it was easy or very easy to tell how many doses were left in the ELLIPTA DPI (Table 4).

### 3.4 | Safety findings

A total of 29 AEs were reported. One AE of cough was related to treatment (placebo). The most common AE was viral upper respiratory tract infection ( $n = 5$ ), followed by gastrointestinal disorders (any event, including vomiting;  $n = 4$ ), and upper respiratory tract infection, cough, and injury (all  $n = 3$ ) (Table 5). No SAEs or deaths were reported.

**TABLE 3** Summary of errors (plain text) and critical errors (underlined text) made with the ELLIPTA DPI at Visit 1 and on the first attempt (ITT population)

Attempt 1	5–7 years stratum (N = 88)	8–11 years stratum (N = 134)	Total (N = 222)
Children demonstrating correct use, $n$ (%)	21 (24)	67 (50)	88 (40)
Children who did not demonstrate correct use, $n$ (%)	67 (76)	67 (50)	134 (60)
<b>Reasons for incorrect use, <math>n</math> (%)<sup>a</sup></b>			
<u>Child did not slide the cover completely down to expose the mouthpiece until a “click” was heard</u>	3 (4)	4 (6)	7 (5)
<u>Child shook the inhaler</u>	4 (6)	7 (10)	11 (8)
Child did not breathe out (exhale) while holding the inhaler away from his/her mouth	33 (49)	31 (46)	64 (48)
<u>Child breathed into the mouthpiece</u>	34 (51)	19 (28)	53 (40)
<u>Child did not place mouthpiece between lips and close lips firmly around it</u>	21 (31)	13 (19)	34 (25)
Child did not take one long steady breath in through his/her mouth	28 (42)	15 (22)	43 (32)
Child blocked the air vent with fingers	11 (16)	8 (12)	19 (14)
Child did not remove inhaler from his/her mouth and held his/her breath	19 (28)	14 (21)	33 (25)
Child did not breathe out slowly and gently	23 (34)	12 (18)	35 (26)
Child did not close the inhaler completely	11 (16)	8 (12)	19 (14)

Note: Participants could be counted more than once depending on the reasons for incorrect use. Checklist items for correct use were based on the steps outlined in the ELLIPTA instructions for use.<sup>10</sup>

Abbreviations: DPI, dry powder inhaler; ITT, intent-to-treat.

<sup>a</sup>Percentage for individual incorrect use reasons were calculated based on number of participants who did not demonstrate correct use.

**TABLE 4** Correct use and ease-of use exploratory endpoints at Visit 2 (mITT population)

n (%) [95% CI] <sup>a</sup>	5–7 years stratum (N = 88)	8–11 years stratum (N = 133)	Total (N = 221)
Exploratory endpoints: correct use			
Children demonstrating correct use of the ELLIPTA DPI with or without caregiver assistance on their first or second attempt at Visit 2	88 (100) [96, 100]	133 (100) [97, 100]	221 (100) [98, 100]
Children demonstrating correct use of the ELLIPTA DPI with caregiver assistance on their second attempt	7 (8) [3, 16]	9 (7) [3, 12]	16 (7) [4, 11]
Children who made ≥1 critical error during the use of the ELLIPTA DPI at Visit 2	2 (2) [<1, 8]	1 (1) [<1, 4]	3 (1) [<1, 4]
Exploratory endpoints: ease-of use			
Children who rated the ability to tell how many doses are remaining in the ELLIPTA DPI as easy	74 (84) [75, 91]	133 (100) [97, 100]	207 (94) [90, 96]
Caregivers who rated the ability to tell how many doses are remaining in the ELLIPTA as easy or very easy	86 (98) [92, >99]	131 (98) [95, >99]	217 (98) [95, >99]
Caregivers who would be likely or very likely to ask their doctor for the ELLIPTA DPI if their child's current daily inhaled medication was available in this type of inhaler	84 (95) [89, 99]	124 (93) [88, 97]	208 (94) [90, 97]

Abbreviations: CI, confidence interval; DPI, dry powder inhaler; mITT, modified intent-to-treat.

<sup>a</sup>95% CI calculated using exact binomial distribution.

## 4 | DISCUSSION

Our study showed that the majority of children could correctly use the ELLIPTA DPI on their first attempt without caregiver assistance, and nearly all reported that they found it easy to use. This is

**TABLE 5** Summary of AEs (ITT population)

System organ class preferred term, n (%)	Total (N = 222)
Any event	29 (13)
Infections and infestations (any event)	16 (7)
Viral upper respiratory tract infection	5 (2)
Upper respiratory tract infection	3 (1)
Otitis media acute	2 (<1)
Pharyngitis streptococcal	2 (<1)
Respiratory, thoracic, and mediastinal disorders (any event)	5 (2)
Cough	3 (1)
Gastrointestinal disorders (any event)	4 (2)
Vomiting	2 (<1)
Injury, poisoning, and procedural complications (any event)	3 (1)
Nervous system disorders (any event)	2 (<1)
Headache	2 (<1)

Note: Only AEs occurring for at least two participants are included.

Abbreviations: AE, adverse event; ITT, intent-to-treat.

consistent with ease-of-use studies of the ELLIPTA DPI conducted in adults with chronic obstructive pulmonary disease or asthma.<sup>7,12–16</sup>

Our results are also comparable to the findings of other pediatric studies of inhaler use<sup>3–5</sup> that have shown correct training by study staff, together with caregiver supervision, is likely to help decrease handling errors. In a similar manner, studies in adults have demonstrated that patients can benefit from training by HCPs.<sup>14,15</sup> Assistance from caregivers during the study period may have also helped children retain knowledge of correct inhaler use, although this was not monitored. The ELLIPTA DPI was shown to be safe for use by children in this study, with no children making any critical errors after two attempts at Visit 2. Our findings support the use of ELLIPTA DPI in pediatric patients with asthma. Fluticasone furoate (delivered via ELLIPTA DPI) has previously demonstrated improvements to lung function in pediatric patients with asthma,<sup>17</sup> and is approved for the treatment of patients ≥5 years of age in the US.<sup>10</sup> Research into the use of fluticasone furoate/vilanterol combination therapy, also delivered via ELLIPTA DPI, is ongoing.

Generating adequate inspiratory flow is important in ensuring sufficient drug delivery to the lungs. Use of the ELLIPTA inhalation trainer in the questionnaire validation study did suggest that children had sufficient inspiratory flow to correctly activate the ELLIPTA DPI. The ELLIPTA inhalation trainer was not used in our study, which presents a potential limitation. However, we did find that high proportions of children could demonstrate correct use of the ELLIPTA DPI, with only five children requiring as many as five attempts to demonstrate correct use during the first study visit. Without

sufficient inspiratory flow, the ELLIPTA DPI could not have been correctly activated or used, and so our findings were consistent with the idea that children had adequate inspiratory flow to correctly activate the inhaler. Use of an inhalation trainer, or a similar tool, may be useful if a patient's ability to inhale sufficiently is in doubt—for example, in younger patients or in those who require additional instruction before demonstrating correct use—but further study would be required to investigate this.

A particular strength of our study was the large population size; these data could help pediatricians, respiratory nurses, and other clinicians when recommending treatment options for children aged 5–11 years with asthma. A high proportion of children rated the ELLIPTA DPI as easy to use, and most caregivers responded that if their child's current asthma medication was available in the ELLIPTA DPI, they would be likely or very likely to request it from their child's doctor. This has potential implications for child inhaler preference and resulting improvements in adherence with an easy-to-use inhaler, but further study would be required to confirm this. An additional strength of our study was the use of a questionnaire modified for children that allowed a study design similar to that used in studies with adults (correct use and ease-of use assessment at Visit 2). A literature review by Kalton and Schuman<sup>18</sup> discusses the possible effects of question structure and survey format on response bias—a phenomenon observed when study participants may tend to favor the first or last response presented to them over other options. By randomizing participants to two versions of a questionnaire with response options presented in alternative orders (“easy” to “hard” and “hard” to “easy”), we potentially reduced the effects of response bias on our results, and obtained a more balanced view of participant experience with the ELLIPTA DPI than we would have if all responses had been presented in the same order.

Despite the data demonstrating that the ELLIPTA DPI was easy to use, and that it was used correctly by nearly all the children studied, a possible limitation of our study was the absence of comparator inhalers, which the children surveyed may or may not have found easier to use than the ELLIPTA DPI. Future pediatric studies including the ELLIPTA DPI and different inhaler types would be of interest when considering inhaler preference in children.

## 5 | CONCLUSION

Using modified ease-of-use questionnaires for children with asthma, the once-daily ELLIPTA DPI was reported as easy to use, with most children using it correctly. Since ease-of use affects patient preference, an inhaler that is easier to use could improve overall adherence to therapy and, ultimately, improve asthma control.

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### DISCLOSURES

Andy Preece, Renu Jain, Jamie Rees, Philippe Bareille and Raj Sharma are employees of and shareholders in GlaxoSmithKline plc. Richard H. Stanford was an employee of GlaxoSmithKline plc. at the time of the study and is now an employee of AESARA. Kathryn Collison, Warren Lenney and Logan Heyes were employees of GlaxoSmithKline plc. at the time of the study. Philip Halverson and Joel Liem have nothing to disclose.

### AUTHOR CONTRIBUTIONS

Philip Halverson and Joel Liem contributed to acquisition of data. Kathryn Collison, Logan Heyes, Renu Jain, Warren Lenney, Raj Sharma, Jamie Rees, Andy Preece, Philippe Bareille, and Richard Stanford contributed to study conception and/or design, and data analysis and/or interpretation. All authors contributed to writing and critically revising the manuscript for important intellectual content.

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#### SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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