# Practical Use of ELLIPTA, a Once-Daily, Dry Powder Inhaler for Children With Asthma

**Poster No. 071**

Sutton L[1], Halverson P[2], Liem J[3], Collison K[1], Heyes L[4], Jain R[1], Rees J[5], Lenney W[6,7], Sharma R[6]

[1]GlaxoSmithKline plc., Research Triangle Park, NC, US; [2]Allergy and Asthma, Minneapolis, MN, US; [3]Joel Liem Medicine Professional Corporation, Windsor, ON, Canada; [4]Respiratory Medical Franchise, GlaxoSmithKline plc., Brentford, UK; [5]GlaxoSmithKline plc., Stockley Park, UK; [6]GlaxoSmithKline plc., Brentford, UK; [7]Keele University, Keele, UK.

## Background

- While inhalers are the mainstay of asthma treatment for patients of all ages,[1] 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 contrasting results, with suggestions that children have lower rates of correct use when compared to adults[2,3] and also that they have similar rates of correct use.[4]
- Correct inhaler technique, which is important to ensure appropriate drug delivery into the airways,[5] can be affected by age and type of inhaler device.[6,7]

## Methods

### Study 206924 design

- Multicenter, single-arm, stratified, open-label, randomized, placebo study (NCT03478657). Children (5–7 and 8–11 years of age), continuing their usual inhaled asthma medication, were trained in, and required to demonstrate, correct placebo ELLIPTA dry powder inhaler (DPI) use at their first clinic visit (maximum of 5 attempts). A healthcare provider (HCP) provided this training with reference to the ELLIPTA DPI Instructions for Use.[8]
- ELLIPTA DPI was used once daily for 28±2 days at home. Returning to the clinic, children were randomized 1:1 to a modified ease-of-use questionnaire from Study 208129 (NCT03315572) and rated ELLIPTA DPI use as “easy” or “hard”. Caregivers (parents/guardians) also completed a questionnaire assessing ELLIPTA DPI features.
- Children were asked to demonstrate correct DPI use after questionnaire completion (maximum of 2 attempts).

### Study 206924 endpoints

- Co-primary efficacy endpoints were the percentage of children from each age group who correctly used the ELLIPTA DPI after their first attempt, and the percentage of those demonstrating correct use in each age group who rated the ELLIPTA DPI as “easy” to use (both at Visit 2 [study end]).
- Secondary efficacy and exploratory endpoints, and safety were also assessed.

### Study 206924 statistical analyses

- Population, secondary and exploratory endpoints, and safety data were assessed in the intent-to-treat (ITT) population (all screened patients who received ≥1 dose of placebo).
- Efficacy analyses (co-primary and most secondary endpoints) were performed in the modified ITT (mITT) population (all screened patients who received 1 dose of placebo study treatment and received the ease-of-use questionnaire at randomization).
- All study endpoints evaluated the percentage of children or parents/guardians who met the endpoint criteria. Two way 95% confidence intervals (CIs) for these percentages were calculated using the exact binomial distribution.

### Questionnaire validation (study 208129)

- An existing adult questionnaire[9] was adapted for children aged 5–11 years. Each response item was modified from a Likert scale (items rated “very easy”, “easy”, “difficult”, or “very difficult”) to a bivariate response (items rated “hard” or “easy”). The questionnaire for children 5–7 years of age was completed with caregiver assistance; children 8–11 years of age completed the questionnaire independently.
- An ELLIPTA inhalation trainer device, used in helping children develop a proper inhalation technique for optimal drug delivery to the lungs, was also used.

## Results

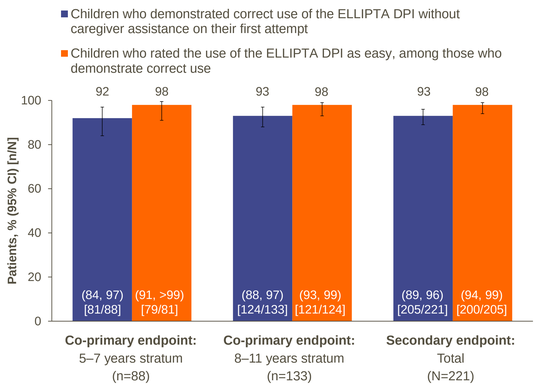
### Study populations

- In total, 232 children were screened. Of these, 10 children were screening failures: did not meet the inclusion criteria (n=4); withdrawal based on a physician’s decision (n=4); and voluntary withdrawal (n=2).
- The ITT population comprised 222 participants, of which 129 (58%) were white, 133 (60%) were male, and the mean (standard deviation) age was 8.3 (2.0) years.
  - Of 222 participants, 88% of 222 participants (n=196) were using a metered-dose inhaler (MDI) for the delivery of their main asthma therapy (maintenance and/or rescue), compared to 7% (n=16) who were using a DPI.
- There were 221 children in the mITT population: one child in the 8–11 years age group completed Visit 1 but withdrew before study completion.

### Co-primary efficacy endpoints

- At Visit 2, most children aged 5–7 years (n=81/88; 92% [95% CI 84%, 97%]) and 8–11 years (n=124/133; 93% [95% CI 88%, 97%]) demonstrated correct use of the ELLIPTA DPI without assistance from a caregiver on the first attempt. Of these, the majority of children aged 5–7 years (n=79/81; 98% [95% CI 91%, >99%]) and 8–11 years (n=121/124; 98% [95% CI 93%, 99%]) rated the ELLIPTA DPI as “easy” to use (**Figure 1**).

### Figure 1. Co-primary and secondary endpoints at Visit 2 (mITT population)




The 95% CI for the percentages are calculated using the exact binomial distribution

CI, confidence interval; DPI, dry powder inhaler; mITT, modified Intent-to-Treat

### Secondary efficacy and exploratory endpoints

- At Visit 1, all participants (N=222) successfully demonstrated correct use of the ELLIPTA DPI, taking between 1 to 5 attempts. After initial training from an HCP, 24% (n=21/88) of children aged 5−7 years and 50% (n=67/134) of children aged 8−11 years demonstrated correct use after their first attempt.
- At Visit 1, a higher percentage of children aged 5–7 years (51%, n=45/88) demonstrated a critical error (an error that was likely to significantly inhibit delivery of the prescribed dose of medication to the patient) on their first attempt at correct use, compared with children aged 8–11 years (25%, n=34/134). Inhaler technique errors are summarized in **Table 1**.
- At Visit 2, 93% of all participants (n=205/221) demonstrated correct use of their ELLIPTA DPI on their first attempt without caregiver assistance and, of these 205 participants, 98% (n=200/205) rated the ELLIPTA DPI as “easy” to use (**Figure 1**).
- Correct use and ease-of-use exploratory endpoints are summarized in **Table 2**.

### Table 1. Summary of errors made with ELLIPTA DPI at Visit 1 and on the first attempt (ITT population)

| Attempt 1, n (%) | 5–7 years stratum (n=88) | 8–11 years stratum (n=134) | Total (N=222) |
|---|---|---|---|
| Children demonstrating correct use | 21 (24) | 67 (50) | 88 (40) |
| Children who did not demonstrate correct use | 67 (76) | 67 (50) | 134 (60) |
| **Reasons for incorrect use*** | | | |
| **Child did not slide the cover completely down to expose the mouthpiece until a “click” is heard** | 3 (4) | 4 (6) | 7 (5) |
| **Child shook the inhaler** | 4 (6) | 7 (10) | 11 (8) |
| Child did not breathe out (exhales) while holding the inhaler away from their mouth | 33 (49) | 31 (46) | 64 (48) |
| **Child breathed into the mouthpiece** | 34 (51) | 19 (28) | 53 (40) |
| **Child did not place mouthpiece between lips and close lips firmly around it** | 21 (31) | 13 (19) | 34 (25) |
| Child did not take one long steady breath in through their 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 holds 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) |

*Percentage for individual, incorrect use reasons are calculated based on number of participants who did not demonstrate correct use

Participants could be counted more than once depending on the reasons for incorrect use
Critical errors are in **bold text**

DPI, dry powder inhaler; ITT, Intent-to-Treat

### Safety

- A total of 29 adverse events (AEs) were reported. One AE of cough was related to treatment (placebo), and no serious AEs or deaths were reported.

### Table 2. Correct use and ease-of-use exploratory endpoints at Visit 2 (mITT population)

| Exploratory endpoints, n (%) [95% CI] | 5–7 years stratum (n=88) | 8–11 years stratum (n=133) | Total (N=221) |
|---|---|---|---|
| **Correct use** | | | |
| Children demonstrating correct use of the ELLIPTA DPI with or without caregiver assistance on first or second attempt | 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 | 2 (2) [<1, 8] | 1 (1) [<1, 4] | 3 (1) [<1, 4] |
| **Ease-of use** | | | |
| Children who rate 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 rate 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 inhaler if their child’s current daily inhaled medication(s) were available in this device | 84 (95) [89, 99] | 124 (93) [88, 97] | 208 (94) [90, 97] |

95% CI for the percentages are calculated using the exact binomial distribution

CI, confidence interval; DPI, dry powder inhaler; mITT, modified Intent-to-Treat

## Conclusions

- ELLIPTA DPI was reported as “easy” to use by the majority (98%) of children in both age strata who demonstrated correct use of the ELLIPTA DPI at Visit 2 (study end).
- Most children (93%) used the inhaler correctly at Visit 2 without caregiver assistance.
- Training on correct inhaler technique by HCPs, together with caregiver supervision, resulted in decreased handling errors for most children.
- An inhaler that is easier to use could be favored by patients with asthma, thereby improving overall adherence to therapy and, ultimately, improving asthma control.

## References

1. GINA. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention. 2019. www.ginasthma.org.
2. Capanoglu M, et al. *J Asthma* 2015;52(8):838–45.
3. Kamps AW, et al. *Acta Paediatr* 2002;91(2):159–63.
4. Goren A, et al. *Pediatr Pulmonol* 1994;18(2):77–80.
5. Lavorini F, et al. *Respir Med* 2008;102:593–604.
6. van der Palen J, et al. *Int J Chron Obstruct Pulmon Dis* 2018;13:2515–23.
7. Melani AS, et al. *Respir Med* 2011;105(6):930–8.
8. GlaxoSmithKline plc. Arnuity ELLIPTA IFU. 2014. https://www.arnuity.com/about-arnuity/how-to-use-arnuity.html.
9. Matza LS, et al. *Value Health* 2013;16(4):461–79.

## Acknowledgements and disclosures

- The authors declare the following real or perceived conflicts of interest during the last 3 years in relation to this presentation: LS is an employee of and holds shares in GlaxoSmithKline plc. KC, RJ, LH, JR, and RS are also employees of and shareholders in GlaxoSmithKline plc. WL was an employee of GlaxoSmithKline plc. at the time of the study. PH and JL have nothing to disclose.
- This study was funded by GlaxoSmithKline plc. (study numbers 206924 [NCT03478657] and 208921 [NCT03315572]).
- Trademarks are owned by or licensed to the GlaxoSmithKline plc. group of companies.
- Editorial support (in the form of writing assistance, assembling tables and figures, collating author comments, grammatical editing, and referencing) was provided by Kirsty Millar, MSc, of Gardiner–Caldwell Communications, Macclesfield, UK, and was funded by GlaxoSmithKline plc.

**Presented at the American Academy of Allergy, Asthma and Immunology Annual Meeting, Philadelphia, PA, USA, March 13–16, 2020**

Please find the online version of this poster by scanning the QR code or via http://tago.ca/AAAAI_9