Clinical Efficacy of ELLIPTA vs. DPI in Children Aged 5–11 Years with Moderate to Severe Asthma


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.2–5 Evidence on the type of inhaler children can use when compared to adults is also limited,6 and also that they have similar rates of correct use.7–9 Errors are much more likely to occur in the handling of the inhaler technique, which is important to ensure adequate drug delivery into the airways,8 can be affected by age and type of inhaler device.10

Study population

In total, 228 children were screened. Of these, 12 children were screening failures; 2 children were screening failures due to lack of compliance with the criteria (n=4), withdrew based on the clinician’s decision (n=2), and were withdrawn for personal reasons (n=2). The remaining 216 children were randomized and performed at least one MDI use, of which 12% (n=26) were home, 30% (n=65) were used in the doctor’s office, 5% (n=11) were used at home, and 5% (n=11) were used at home and in the doctor’s office.

Study 206934 design

Multicenter, single-arm, stratified, open-label, randomized, placebo controlled study (NCT03249651). Children (5–7 and 8–11 years of age) continued their usual inhaler medication, were trained, and required to demonstrate correct placebo DPI dry powder inhaler (DPI) use at Visit 1 (V1). A healthcare provider (HP) provided this training with reference to the ELLIPTA DPI instructions for Use.11

ELLIPTA DPI was used once daily for 2 weeks at all home. Returning to the clinic, children were randomized 1:1 to inhaled salbutamol (91.4 μg) using the ELLIPTA DPI (n=111) or placebo DPI (n=111). The study period was 6 weeks. Each child used their allocated DPI at home for 2 weeks, and an HP performed the assessment of the correct use of the DPI at the next visit.

Study 206934 endpoints

Co-primary endpoints were the percentage of children from each age group who correctly used the ELLIPTA DPI on their first attempt (primary endpoint) and the percentage of those demonstrating correct use in each age group who rated the ELLIPTA DPI as easy to use at Visit 2 (study end).

Secondary efficacy and exploratory endpoints, and safety were also assessed.

Study 206934 statistical analyses

Population, secondary and exploratory endpoints, and safety data were assessed in the population (all screened patients who received at least one dose of study medication). For the primary endpoint, the modified intent-to-treat (mITT) population (all screened patients who received at least one dose of study medication and received the exposure at randomization) was analyzed. All study endpoints were 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 208132)

An existing adult questionnaire12 was adapted for children aged 5–11 years. Each response item was modified to make it “easy,” “very easy,” or “difficult,” or “very difficult” to a binary response (items rated “hard” or “easy”).13 A questionnaire was developed for children matched with caregivers assistance; children 8–11 years of age completed the questionnaire independently.

An ELLIPTA inhalator 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, 222 children were screened. Of these, 12 children were screening failures; 2 children were screening failures due to lack of compliance with the criteria (n=4), withdrew based on the clinician’s decision (n=2), and were withdrawn for personal reasons (n=2). The remaining 210 children were randomized and performed at least one MDI use, of which 12% (n=26) were home, 30% (n=65) were used in the doctor’s office, 5% (n=11) were used at home, and 5% (n=11) were used at home and in the doctor’s office.

The ITT population included 222 participants of which 123 (56%) 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 usual asthma therapy (maintenance/relief), compared to 7% (n=16) who were using a DPI.

There were 221 children in the mITT population; one child in the 8–11 year group completed Visit 1 but withdrew before study completion.

Co-primary results

All children at Visit 2, most children aged 5–7 years (n=118; 92% [CI 84, 97], and 5–7 years and 8–11 years (n=154; 93% [CI 90, 96]) demonstrated correct use of the ELLIPTA DPI without assistance from a caregiver on the first attempt. Of the children, 92% (95% CI 87, 95), 88% (95% CI 80, 95) and 77% (95% CI 68, 85) rated the DPI as easy to use on their first attempt and in their second attempt with caregiver assistance and as, of these 222 participants, 96% (n=216) rated the ELLIPTA DPI as easy to use at Visit 2 (Figure 1).

Table 1. Summary of errors made with ELLIPTA DPI at Visit 1 and on the first attempted ITT endpoint

<table>
<thead>
<tr>
<th>Attempt</th>
<th>(n)</th>
<th>Prop (%)</th>
<th>5–7 years stratum (n=154) % (100)</th>
<th>8–11 years stratum (n=68) % (100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>V1 1st attempt</td>
<td>114</td>
<td>90 (84, 97)</td>
<td>101 (94, 99)</td>
<td>7 (94, 99)</td>
</tr>
<tr>
<td>V1 2nd attempt</td>
<td>114</td>
<td>90 (84, 97)</td>
<td>101 (94, 99)</td>
<td>7 (94, 99)</td>
</tr>
</tbody>
</table>

Secondary efficacy and exploratory endpoints

At Visit 1 all 11 (n=222) successfully demonstrated correct use of the ELLIPTA DPI, taking between 1 to 5 attempts. After initial training from an HCP, 94% (n=207) were successful in all children with 99% (n=220) children aged 5–7 years demonstrated correct use after their first attempt.

At Visit 2 96% of all participants (n=216) demonstrated correct use of the ELLIPTA DPI on their first attempt without caregiver assistance and, of these 222 participants, 96% (n=216) rated the ELLIPTA DPI as easy to use (Figure 1).

Correct use and ease-of-use exploratory endpoints are summarized in Table 2.

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

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>(n)</th>
<th>Correct use</th>
<th>Ease of use</th>
<th>5–7 years stratum (n=154) % (100)</th>
<th>8–11 years stratum (n=68) % (100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>V2 1st attempt</td>
<td>114</td>
<td>90 (84, 97)</td>
<td>99 (94, 99)</td>
<td>7 (94, 99)</td>
<td></td>
</tr>
<tr>
<td>V2 2nd attempt</td>
<td>114</td>
<td>90 (84, 97)</td>
<td>99 (94, 99)</td>
<td>7 (94, 99)</td>
<td></td>
</tr>
</tbody>
</table>

Conclusions

ELLIPTA DPI was reported as “easy” to use by the majority (85%) of children in both age strata who demonstrated correct use of the ELLIPTA DPI at Visit 2 (study end).

Most children (92%) 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.

For those that is easier to use could be learned by patients with asthma, thereby improving overall adherence to therapy and, ultimately, improving asthma control.

References


