Critical error rates with the ELLIPTA inhaler compared with other dry-powder inhalers in patients with COPD: an open-label, low-intervention clinical study

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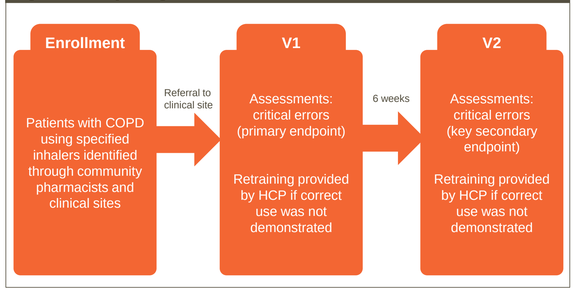
Aims

- Combinations of inhaled corticosteroids (ICS), long-acting β_2-agonists (LABAs), and long-acting muscarinic antagonists (LAMAs) are recommended for chronic obstructive pulmonary disease (COPD) maintenance therapy.[1]
- Errors in inhaler use, particularly critical errors (inhaler errors leading to no or significantly reduced medication being inhaled), may reduce treatment efficacy.[2,3]
- The types of inhaler used, the number of inhalers used, and the extent of training received from healthcare professionals (HCPs)[1,4] have an impact on inhaler error rates.
- The ELLIPTA inhaler, a dry-powder inhaler (DPI) able to deliver the ICS/LAMA/LABA regimen fluticasone furoate/umeclidinium/vilanterol (FF/UMEC/VI) in a single dose, is associated with fewer critical errors than other commonly used DPIs and metered-dose inhalers.[5,6]
- We conducted the current study to assess critical error rates with the ELLIPTA inhaler versus other commonly used DPIs, alone and in combination before and after receipt of error correction, where needed, from a HCP in a low-intervention setting.

Methods

- This open-label, low-intervention clinical study was carried out at 13 centers in the Netherlands (n=9) and the United Kingdom (n=4) from June 2017 to March 2018.
- Enrolled patients were ≥40 years of age with a physician's diagnosis of COPD and had received one of the following DPIs alone or in combination with a LAMA-only inhaler (ELLIPTA UMEC or HandiHaler tiotropium [TIO]) for ≥3 months prior to inclusion
  - ELLIPTA FF/VI (100/25µg) or UMEC/VI (62.5/25µg)
  - Turbuhaler budesonide/formoterol (BUD/FOR [160/45µg])
  - DISKUS fluticasone propionate/salmeterol (FP/SAL [500/50µg])
  - Breezhaler indacaterol/glycopyrronium (IND/GLY [85/43µg])
  - LAMA-only inhaler (HandiHaler TIO [18µg] or ELLIPTA UMEC [62.5µg]).
- The study comprised two visits (V1 and V2) (**Figure 1**).
- The primary endpoint was the percentage of patients making ≥1 critical error at V1 for each DPI tested (prior to retraining).
- The key secondary endpoint was the proportion of patients making ≥1 critical error at V2 for each single DPI tested (6 weeks after retraining, if needed).
- Single DPIs and DPI combinations were assessed for each endpoint; analyses were conducted from the perspective of the primary inhaler (ICS/LABA, LAMA or LAMA/LABA for patients using a single DPI and the ICS/LABA inhaler if using two DPIs).
- Correct use and inhaler errors were assessed against a checklist for each DPI; checklists were based on the steps outlined in the appropriate patient information leaflet, review of the literature, and further review of these lists by external experts.
- Primary and secondary endpoints were analyzed using a logistic regression model, with treatment options as fixed effects and adjusting for the covariate of time on DPI.
- Post-hoc sensitivity analyses were performed as time on DPI was confounded with DPI type; patients were likely to have used ELLIPTA for less time than older DPIs.
- All odds ratios (ORs) reported herein are from post-hoc sensitivity analyses due to the confounding issue described.

Figure 1. Study design



Results

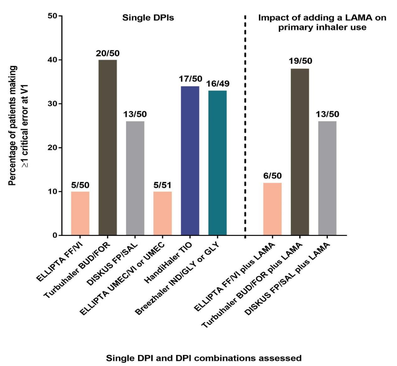
Patient demographics and clinical characteristics

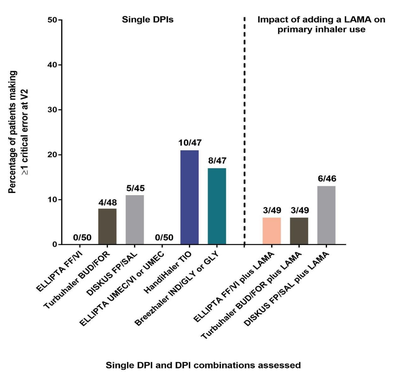
- Overall, 461 patients were screened and 450 were enrolled into one of nine DPI cohorts (the intent-to-treat [ITT] population).
- Demographic and clinical characteristics were similar across DPI cohorts, with a mean age of 67.2 years (standard deviation 9.8); 54% of the ITT population was male.

Critical errors with the primary inhaler at V1

- For the ICS/LABA inhalers, the number of patients making ≥1 critical error at V1 was 5/50 (10%) with ELLIPTA FF/VI, 20/50 (40%) with Turbuhaler BUD/FOR, and 13/50 (26%) with DISKUS FP/SAL (**Figure 2a**)
  - the odds of a patient making ≥1 critical error was 5.56 times greater with Turbuhaler BUD/FOR (95% confidence interval [CI]: 1.93–16.01; p=0.001) and 2.98 times greater with DISKUS FP/SAL (95% CI: 1.00–8.88; p=0.050) than with ELLIPTA FF/VI.
- For the LAMA and LAMA/LABA inhalers, the number of patients making ≥1 critical error at V1 was 5/51 (10%) with ELLIPTA UMEC/VI or UMEC, 17/50 (34%) with HandiHaler TIO, and 16/49 (33%) with Breezhaler IND/GLY or GLY (**Figure 2a**)
  - the odds of a patient making ≥1 critical error was 4.42 times greater with HandiHaler TIO (95% CI: 1.52–12.83; p=0.006) and 4.17 times greater with Breezhaler IND/GLY or GLY (95% CI: 1.42–12.18; p=0.009) than with ELLIPTA UMEC/VI or UMEC.
- Addition of a LAMA inhaler had minimal effect on critical error rates with the primary ICS/LABA inhalers at V1; the number of patients making ≥1 critical error was 6/50 (12%) with ELLIPTA FF/VI, 19/50 (38%) with Turbuhaler BUD/FOR, and 13/50 (26%) with DISKUS FP/SAL (**Figure 2a**).

Figure 2. Percentage of patients making ≥1 critical error at (a) V1 baseline assessment and (b) V2 after training 6 weeks later





LAMA represents ELLIPTA UMEC or HandiHaler TIO.

Critical errors with the primary inhaler at V2

- For the ICS/LABA inhalers, the number of patients making ≥1 critical error at V2 fell to zero for ELLIPTA FF/VI, 4/48 (8%) with Turbuhaler BUD/FOR, and 5/45 (11%) with DISKUS FP/SAL (**Figure 2b**)
  - the odds of a patient making ≥1 critical error was 10.21 times greater with Turbuhaler BUD/FOR (95% CI: 0.52–200.90; p=0.126) and 13.72 times greater with DISKUS FP/SAL (95% CI: 0.72–263.13; p=0.082) than with ELLIPTA FF/VI.
- For the LAMA and LAMA/LABA inhalers, the number of patients making ≥1 critical error at V2 fell to zero with ELLIPTA UMEC/VI or UMEC, 10/47 (21%) with HandiHaler TIO, and 8/47 (17%) with Breezhaler IND/GLY or GLY (**Figure 2b**)
  - the odds of a patient making ≥1 critical error was 28.28 times greater with HandiHaler TIO (95% CI: 1.56–512.53; p=0.024) and 21.74 times greater with Breezhaler IND/GLY or GLY (95% CI: 1.18–399.54; p=0.038) than with ELLIPTA UMEC/VI or UMEC.
- Addition of a LAMA inhaler had minimal effect on critical error rates with the primary ICS/LABA inhalers at V2; the number of patients making ≥1 critical error was 3/49 (6%) with ELLIPTA FF/VI, 3/49 (6%) with Turbuhaler BUD/FOR, and 6/46 (13%) with DISKUS FP/SAL (**Figure 2b**).

Conclusions

- In a low-intervention setting, patients with COPD were less likely to make critical errors when using the ELLIPTA inhaler for maintenance therapy than the other ICS/LABA, LAMA or LAMA/LABA DPIs assessed during this study; lower critical error rates may lead to improved medication receipt for patients using ELLIPTA.
- Addition of a LAMA inhaler had little effect on critical error rates with the primary ICS/LABA inhalers and error rates remained lowest with ELLIPTA when a LAMA was added.
- The profound effect of albeit 'verbal' training during this study also highlights the importance of thorough instruction and training, provided by the HCP, to ensure patients understand how to take their medication.

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Disclosures

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