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| **Study reference** | **Study characteristics** | **Patient characteristics 2** | **Intervention (I)** | **Comparison / control (C) 3** | **Follow-up** | **Outcome measures and effect size 4** | **Comments** |
| Bremner, 2018 | Type of study: a randomized noninferiority  Study.  Setting and country:  USA  Funding and conflicts of interest: This study was funded by GSK (GSK study CTT200812; ClinicalTrials.gov identifier  NCT02729051). ELLIPTA is owned by or licensed to the GSK group of companies. RB, NB, ASI, C-QZ, and DAL are employees of GSK and hold stocks/shares in  the company. ASI is also an unpaid faculty member at McMaster University,  Canada. PRB has no conflicts of interest to disclose. | Inclusion criteria:  COPD Assessment Test™ (CAT) score ≥ 10 [13, 14];  a post-albuterol/salbutamol FEV1/forced vital capacity ratio  < 0.70; and a post-bronchodilator FEV1 < 50% of predicted  and ≥1 moderate/severe exacerbation in the previous  12 months or a post-bronchodilator FEV1 ≥ 50% to < 80%  of predicted and ≥2 moderate exacerbations or ≥1 severe  exacerbation requiring hospitalization in the previous  12 months.  Exclusion criteria:  a current diagnosis of asthma  (patients with a prior history of asthma were eligible if they  had a current diagnosis of COPD that was the primary cause  of their respiratory symptoms); α1-antitrypsin deficiency; active tuberculosis; other respiratory disorders that were the  primary cause of respiratory symptoms; lung resection surgery  in the previous 12 months; risk factors for pneumonia  (including immunosuppression and neurological disorders  affecting control of the upper airway [e.g. Parkinson’s disease  or myasthenia gravis]; pneumonia and/or moderate/severe  exacerbation that had not resolved at least 14 days prior to  screening; respiratory infections; abnormal findings on chest  X-ray; clinically significant comorbidities; unstable liver or  cardiac disease; and cancer. Patients with a high risk for  pneumonia (e.g. very low body mass index, severely malnourished,  or very low FEV1) were only to be included at  the discretion of the investigator.  N total at baseline:  Intervention: 527  Control: 528  Important prognostic factors2:  *age ± SD:*  *I: 66.7 ± 8.5*  *C: 65.9 ± 8.8*  *Sex:*  *I: 74% M*  *C: 75% M*  Groups comparable at baseline?  Yes | 24 weeks of FF/UMEC/VI 100 μg/62.5 μg/25 μg in a single inhaler and placebo (second inhaler). all treatments/placebo  were delivered using the ELLIPTA inhaler once daily in the morning. | 24 weeks of FF/VI 100 μg/25 μg and UMEC 62.5 μg, in separate inhalers. all treatments/placebo were delivered using the ELLIPTA inhaler once daily in the  morning. | Length of follow-up:  One week after treatment.  Loss-to-follow-up:  Intervention: 6%  Reasons: n.r.  Control: 6%  Reasons: n.r.  Incomplete outcome data:  n.r. | COPD exacerbations rate Defined as the number of exacerbations.  Effect measure: Risk ratio [95% CI]: 0.91 [95% CI: 0.74 to 1.12] in favour of fixed triple therapy.  Mortality n.r.  Quality of life  Defined as the proportion of responders to the SGRQ.  Effect measure: Risk ratio [95% CI]:  0.98 [95% CI 0.97 to 1.10] in favour of fixed triple therapy.  FEV1  Defined as the between treatment difference in FEV1  Effect measure: mean difference [95% CI] 18 mL [95% CI -13 to 50] in favour of fixed triple therapy.  Pneumonia  Defined as the number of participants with pneumonia.  Effect measure: Risk ratio [95% CI]:  Serious adverse events  Defined as the number of serious adverse events.  Effect measure: Risk ratio [95%  **Pneumonia:**  0.67 [0.34 to 1.30] in favour of fixed triple therapy.  **Other SAEs**  0.91 [95% CI 0.64 to 1.30] in favour of fixed triple therapy. | This study showed that single-inhaler FF/UMEC/VI  100 μg/62.5 μg/25 μg was non-inferior to FF/VI 100 μg/  25 μg plus UMEC 62.5 μg based on change from baseline  in trough FEV1 at Week 24 in patients with advanced  COPD. Our findings confirm that single-inhaler triple  therapy with FF/UMEC/VI offers similar efficacy, healthrelated  quality of life, and safety benefits as the same triple  therapy administered using two inhalers. |