**Table S1** Pulmonary medication use at baseline (treated set)

|  |  |
| --- | --- |
| Pulmonary medication class, n (%) | Study |
| 1222.37(n = 151) | 1222.38(n = 157) |
| LAMA monotherapy | 30 (19.9) | 30 (19.1) |
| LABA monotherapy | 8 (5.3) | 3 (1.9) |
| LABA/ICS and no LAMA | 11 (7.3) | 23 (14.6) |
| LAMA/ICS and no LABA | 1 (0.7) | 1 (0.6) |
| LAMA/LABA and no ICS | 15 (9.9) | 4 (2.5) |
| LAMA/LABA/ICS triple therapy | 39 (25.8) | 23 (14.6) |

LAMA: long-acting muscarinic antagonist; LABA: long-acting β2-agonist; ICS: inhaled corticosteroid

**Table S2** Arithmetic mean, geometric mean and median endurance times after 6 weeks (full analysis set)

|  |  |  |
| --- | --- | --- |
|  | Study 1222.37 | Study 1222.38 |
|  | Adjusted arithmetic mean, s (SE)a | Adjusted geometric mean, s (SE)b | Median, s | Adjusted arithmetic mean, s (SE)a | Adjusted geometric mean, s (SE)b | Median, s |
| Placebo | 448.1 (16.7) | 369.8 (11.9) | 394 | 405.2 (17.0) | 354.3 (12.1) | 346 |
| Olodaterol 5 µg | 492.0 (16.5) | 421.6 (13.5) | 427 | 469.6 (17.2) | 396.3 (13.7) | 397 |
| Olodaterol 10 µg | 494.2 (16.7) | 420.7 (13.6) | 445 | 444.9 (17.2) | 391.5 (13.6) | 380 |

aCalculated based on a mixed effects repeated measures model on original scale; bcalculated based on back-transformation of mean estimated with a mixed effects repeated measures model on log10-transformed data
SE: standard error

**Table S3** Geometric mean (SE) endurance time after 6 weeks by GOLD (full analysis set)

|  |  |  |
| --- | --- | --- |
| Study | GOLD 2 | GOLD 3/4 |
|  | Patients, n | Adjusted geometric mean (SE) endurance time, s | Improvement compared to placebo, % | Patients, n | Adjusted geometric mean (SE) endurance time, s | Improvement compared to placebo, % |
| 1222.37 Placebo Olodaterol 5 µg  Olodaterol 10 µg | 919493 | 410.5 (24.3)455.9 (26.8)462.3 (27.3) | 11.112.6 | 45 4643 | 288.7 (24.3)348.2 (29.1)335.2 (28.5) | 20.616.1 |
| 1222.38 Placebo Olodaterol 5 µg  Olodaterol 10 µg | 105103102 | 372.7 (18.7)412.2 (20.8)412.3 (20.9) | 10.610.6 | 403737 | 305.5 (24.7)350.0 (29.0)338.2 (28.0) | 14.610.7 |

GOLD: Global initiative for chronic Obstructive Lung Disease; SE: standard error

**Table S4** Peak expiratory flow outcomes at 6 weeks (full analysis set)

|  |  |  |
| --- | --- | --- |
| Treatment | Planned time, min | Adjusted mean (SE) difference from placebo after 6 weeks, L/s |
| Study 1222.37 Olodaterol 5 µg Olodaterol 10 µg Olodaterol 5 µg Olodaterol 10 µg | -0.30 (pre-dose/trough)60 (post-dose) | 0.32 (0.06)a0.30 (0.06)a0.59 (0.06)a0.62 (0.06)a |
| Study 1222.38 Olodaterol 5 µg Olodaterol 10 µg Olodaterol 5 µg Olodaterol 10 µg | -0.30 (pre-dose/trough)60 (post-dose) | 0.28 (0.06)c0.29 (0.06)d0.58 (0.07)c0.55 (0.07)d |

an = 137; bn = 136; cn = 143; dn = 139
*p* < 0.0001 for all
SE: standard error

**Fig. S1** Hierarchical testing order: each test was considered confirmatory only if all of the previous tests were positive



**Fig. S2** Participant flow in (a) Study 1222.37 and (b) Study 1222.38
QD: once daily



**Fig. S3.** Exercise endurance time after 6 weeks for (a) Study 1222.37 and (c) Study 1222.38. Log10-transformation of exercise endurance time after 6 weeks for (b) Study 1222.37 and (d) Study 1222.38 (full analysis set)

