**SUPPLEMENTAL MATERIAL**

**Effectiveness of extrafine single inhaler triple therapy in chronic obstructive pulmonary disease in Germany – real world evidence of the non-interventional TriOptimize study**

Christian Gessner1

Frederik Trinkmann2,3

Sanaz Bahari Javan4

Raimund Hövelmann4

Valentina Bogoevska4

George Georges5

Elena Nudo6

Carl-Peter Criée7

1Pneumologische Praxis Leipzig, Universitätsklinikum Leipzig, Institut für Klinische Immunologie, Leipzig, Germany;

2Pneumology and Critical Care Medicine, Thoraxklinik at University Hospital Heidelberg, Translational Lung Research Center Heidelberg (TLRC), Member of German Center for Lung Research (DZL), Heidelberg, Germany;

3Department of Biomedical Informatics at the Center for Preventive Medicine and Digital Health Baden-Württemberg (CPD-BW), University Medical Center Mannheim, Medical Faculty Mannheim, Heidelberg University, Germany;

4Department of Medical Affairs, Chiesi GmbH, Hamburg, Germany;

5Corporate R&D, Chiesi USA Inc., Cary, North Carolina, USA;

6 Global Medical Affairs, Chiesi Farmaceutici S.p.A., Parma, Italy;

7Department of Sleep and Respiratory Medicine, Evangelical Hospital Goettingen-Weende, Bovenden, Germany

**Supplemental Table 1.** Comorbidities stratified by prior COPD treatment

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **ICS+LABA+LAMA**  **n (%)** | **ICS/LABA**  **n (%)** | **LAMA/LABA**  **n (%)** | **Total**  **n (%)** |
| At least one comorbidity | 1186 (79.4) | 458 (74.6) | 319 (71.7) | 1963 (76.9) |
| Asthma non-allergic | 241 (16.1) | 101 (16.4) | 16 (3.6) | 358 (14.0) |
| Asthma allergic | 128 (8.6) | 68 (11.0) | 12 (2.7) | 208 (8.1) |
| Type II diabetes mellitus | 208 (13.9) | 98 (15.9) | 51 (11.4) | 357 (14.0) |
| Arterial hypertension | 765 (51.1) | 288 (46.5) | 213 (47.7) | 1266 (49.4) |
| Coronary heart disease | 250 (16.8) | 87 (14.1) | 81 (18.2) | 418 (16.4) |
| ICS Inhaled Corticosteroid; LABA: Long-acting β2-agonists; LAMA: Long-acting muscarinic antagonists; SD: Standard Deviation; | | | | |

**Supplemental Table 2.** Patients with concomitant medication at least once during the study

|  |  |
| --- | --- |
|  | **n(%)** |
| Related to adverse event | 15 (0.6) |
| Rescue medication | 1,698 (64.7) |
| Other medication\* | 1,284 (49.0) |
| Beta-blocking agents, selective | 461 (17.6) |
| ACE-inhibitors, plain | 352 (13.4) |
| Platelet aggregation inhibitors excl. Heparin | 326 (12.4) |
| HMG CoA reductase inhibitors | 311 (11.9) |
| Angiotensin II receptor blockers (ARBs), plain | 287 (10.9) |
| Proton pump inhibitors | 287 (10.9) |
| Sulfonamides, plain | 266 (10.1) |
| \*Other concomitant medication was coded according to the WHO Drug Dictionary  including the Anatomical Therapeutic Chemical (ATC) classification system. Only other concomitant medications (ATC level 4) which were taken by ≥ 10% of the patients are shown. | |

**Supplemental Table 3.** Total CAT score in categories stratified by GOLD group at baseline

|  | | **GOLD A n (%)** | **GOLD B n (%)** | **GOLD C n (%)** | **GOLD D n (%)** |
| --- | --- | --- | --- | --- | --- |
| Baseline | CAT < 10 | 23 (18.3) | 52 (4.6) | 40 (9.4) | 23 (2.9) |
| CAT 10 – 20 | 58 (46.0) | 495 (43.7) | 138 (32.5) | 269 (33.7) |
| CAT 21 – 30 | 44 (34.9) | 489 (43.1) | 200 (47.1) | 378 (47.4) |
| CAT > 30 | 1 (0.8) | 98 (8.6) | 47 (11.1) | 128 (16.0) |
| Month 6 | CAT < 10 | 23 (25.0) | 129 (15.0) | 53 (15.8) | 50 (9.0) |
| CAT 10 – 20 | 44 (47.8) | 413 (48.0) | 159 (47.5) | 207 (37.4) |
| CAT 21 – 30 | 24 (26.1) | 260 (30.2) | 110 (32.8) | 242 (43.8) |
| CAT > 30 | 1 (1.1) | 58 (6.7) | 13 (3.9) | 54 (9.8) |
| Restricted to patients with available data for total CAT score at baseline or Month 6 and GOLD group at baseline  CAT: COPD Assessment Test; GOLD: Global Initiative for Chronic Obstructive Lung Disease | | | | | |

**Supplemental Table 4.** CAT responders stratified by GOLD group at baseline

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | | **GOLD A**  **n (%)** | **GOLD B**  **n (%)** | **GOLD C**  **n (%)** | **GOLD D**  **n (%)** |
| CAT responder | | | | | |
|  | Yes | 41 (45.1) | 499 (58.6) | 210 (64.0) | 263 (47.8) |
|  | No | 50 (54.9) | 352 (41.4) | 118 (36.0) | 287 (52.2) |
| Restricted to patients with available data for CAT response at Month 6 and GOLD group at baseline  CAT: COPD Assessment Test; GOLD: Global Initiative for Chronic Obstructive Lung Disease | | | | | |

**Supplemental Table 5.** Total CAT score stratified by GOLD group at baseline

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **GOLD A** | | **GOLD B** | | **GOLD C** | | **GOLD D** | |
|  | N | Mean ± SD | N | Mean ± SD | N | Mean ± SD | N | Mean ± SD | |
| Baseline | 126 | 16.9 ± 7.3 | 1134 | 21.0 ± 7.0 | 425 | 21.3 ± 7.8 | 798 | 23.0 ± 7.4 | |
| Month 6 | 92 | 15.1 ± 7.2 | 860 | 17.9 ± 7.8 | 335 | 17.7 ± 7.3 | 553 | 20.9 ± 7.9 | |
| Month 6 - Baseline | 91 | -1.4 ± 5.8 | 851 | -2.9 ± 6.5 | 328 | -3.7 ± 6.1 | 550 | -1.9 ± 6.5 | |
| Restricted to patients with available data for total CAT score at baseline or Month 6 and GOLD group at baseline  CAT: COPD Assessment Test; GOLD: Global Initiative for Chronic Obstructive Lung Disease | | | | | | | | |

**Supplemental Table 6.** Average change of lung function parameters between baseline and after 6 months of treatment stratified by prior COPD treatment

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **ICS+LABA+LAMA** | | | **ICS/LABA** | | | | **LAMA/LABA** | | | | **Total** | | |
|  | N | Mean ± SD |  | N | Mean ± SD |  | N | | Mean ± SD |  | N | | Mean ± SD |  | |
| FVC (L) | 618 | 0.04 ± 0.5 |  | 250 | 0.12 ± 0.5 | \* | 256 | | 0.04 ± 0.5 |  | 1124 | | 0.06 ± 0.5 | \* | |
| IC (L) | 463 | 0.00 ± 0.6 |  | 163 | 0.08 ± 0.6 |  | 198 | | 0.03 ± 0.6 |  | 824 | | 0.02 ± 0.6 |  | |
| FEV1 (mL) | 621 | 38.8 ± 290.2 | \* | 256 | 134.3± 405.7 | \* | 278 | | 15.8 ± 350.3 |  | 1155 | | 54.4 ± 336.1 | \* | |
| FEV1 (L) | 621 | 0.04 ± 0.3 | \* | 256 | 0.13 ± 0.4 | \* | 278 | | 0.02 ± 0.4 |  | 1,155 | | 0.05 ± 0.3 | \* | |
| sRtot (kPa\*s) | 495 | -0.16 ± 1.4 | \* | 184 | -0.53 ± 1.3 | \* | 184 | | -0.09 ± 1.6 |  | 863 | | -0.23 ± 1.4 | \* | |
| TLC (L) | 466 | 0.00 ± 1.0 |  | 184 | -0.06 ± 1.1 |  | 178 | | 0.17 ± 1.0 | \* | 828 | | 0.02 ± 1.0 |  | |
| RV (L) | 348 | 0.00 ± 0.8 |  | 132 | -0.35 ± 0.8 | \* | 132 | | -0.08 ± 0.9 |  | 612 | | -0.10 ± 0.9 | \* | |
| Lung function test was performed without prior bronchospamolysis  \* p-value (t-test) <0.05  FEV1: Forced Expiratory Volume (in 1 second); FVC: Forced Vital Capacity; IC: Inspiratory Capacity; ICS: Inhaled Corticosteroid; LABA: Long-acting β2-agonists; LAMA: Long-acting muscarinic antagonists; sR: Specific breathing resistance; R: Breathing Resistance; RV: Residual Volume; TLC: Total Lung Capacity | | | | | | | | | | | | | | | |

**Supplemental Table 7.** Average change of lung function parameters between baseline and after 6 months of treatment stratified by prior GOLD group at baseline

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **GOLD A** | | | **GOLD B** | | | **GOLD C** | | | **GOLD D** | | | |
|  | N | Mean ± SD |  | N | Mean ± SD |  | N | Mean ± SD |  | | N | Mean ± SD |  |
| FVC (L) | 53 | 0.02 ± 0.44 |  | 507 | 0.04 ± 0.48 |  | 197 | 0.06 ± 0.44 | \* | | 328 | 0.08 ± 0.5 | \* |
| IC (L) | 41 | -0.01 ± 0.40 |  | 381 | 0.01 ± 0.62 |  | 118 | 0.06 ± 0.54 |  | | 250 | 0.01 ± 0.49 |  |
| FEV1 (mL) | 53 | 31.7 ± 361.5 |  | 537 | 51.9 ± 367.0 | \* | 199 | 70.8 ± 342.4 | \* | | 329 | 46.9 ± 268.5 | \* |
| FEV1 (L) | 53 | 0.03 ± 0.36 |  | 537 | 0.05 ± 0.37 | \* | 199 | 0.07 ± 0.34 | \* | | 329 | 0.05 ± 0.27 | \* |
| sRtot (kPa\*s) | 43 | -0.03 ± 0.71 |  | 374 | -0.16 ± 1.31 |  | 151 | -0.38 ± 1.46 |  | | 278 | -0.26 ± 1.66 |  |
| TLC (L) | 42 | -0.01 ± 0.95 |  | 367 | 0.02 ± 1.04 |  | 137 | -0.05 ± 0.95 |  | | 250 | 0.03 ± 1.06 |  |
| RV (L) | 40 | 0.08 ± 0.78 |  | 287 | -0.09 ± 0.88 |  | 94 | -0.16 ± 0.71 |  | | 164 | -0.14 ± 0.86 |  |
| Lung function test was performed without prior bronchospamolysis  \* p-value (t-test) <0.05  FEV1: Forced Expiratory Volume (in 1 second); FVC: Forced Vital Capacity; IC: Inspiratory Capacity; ICS: Inhaled Corticosteroid; LABA: Long-acting β2-agonists; LAMA: Long-acting muscarinic antagonists; sR: Specific breathing resistance; R: Breathing Resistance; RV: Residual Volume; TLC: Total Lung Capacity | | | | | | | | | | | | | |

|  | **Adherence at baseline, n (%)** | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| **Adherence 6 months after switch to efSITT** | **Poor** | | **Moderate** | | **Good** | |
| **Poor (TAI ≤ 45)** | 62 | (31.6) | 21 | (7.3) | 38 | (4.0) |
| **Moderate (TAI 46 – 49)** | 48 | (24.5) | 80 | (27.9) | 89 | (9.3) |
| **Good (TAI = 50)** | 86 | (43.9) | 186 | (64.8) | 828 | (86.7) |
| For 611patients data were assessed at baseline but not at month 6 | | | | | | |

**Supplemental Table 8.** Adherence according to TAI at baseline and 6 months after switch to efSITT

