**Table: Primary and secondary outcomes**

| Parameter | FCM (N = 24) | | | Placebo (N = 24) | | | P value |
|---|---|---|---|---|---|---|---|
| | Baseline | Week 1 | Week 8 | Baseline | Week 1 | Week 8 | |
| **Oxygenation** | | | | | | | |
| Resting $SpO_2$, % | 94.1 ± 0.5 | 94.5 ± 0.4 | 93.7 ± 0.5 | 94.7 ± 0.3 | 94.4 ± 0.4 | 94.9 ± 0.3 | 0.93 |
| Mean nocturnal $SpO_2$, % | 91.8 ± 0.5 [a] | 92.3 ± 0.4 [a] | 92.0 ± 0.4 [a] | 92.0 ± 0.5 [b] | 92.3 ± 0.4 [b] | 92.2 ± 0.5 [b] | 0.32 |
| Nocturnal $SpO_2$ < 90%, % | 14.7 ± 5.1 [a] | 14.6 ± 3.9 [a] | 13.8 ± 4.4 [a] | 16.4 ± 5.5 [b] | 15.5 ± 5.1 [b] | 15.8 ± 5.3 [b] | 0.94 |
| Oxygen desaturation index, $h^{-1}$ | 8.0 ± 1.9 [a] | 7.3 ± 2.2 [a] | 7.8 ± 2.7 [a] | 6.4 ± 1.2 [b] | 6.7 ± 1.2 [b] | 7.5 ± 1.1 [b] | 0.56 |
| Capillary $PO_2$, kPa | 9.35 ± 0.24 [b] | 9.14 ± 0.26 [b] | 9.19 ± 0.23 [b] | 9.37 ± 0.25 [a] | 9.27 ± 0.23 [a] | 9.04 ± 0.17 [a] | 0.52 |
| Capillary $SO_2$, % | 94.6 ± 0.4 [b] | 94.4 ± 0.4 [b] | 94.4 ± 0.4 [b] | 94.6 ± 0.4 [a] | 94.4 ± 0.3 [a] | 94.1 ± 0.3 [a] | 0.64 |
| **6-minute walk test** | | | | | | | |
| Distance, m | 330 ± 18 | 343 ± 19 | 354 ± 19 | 335 ± 20 [b] | 337 ± 22 [b] | 345 ± 22 [b] | 0.02 |
| $SpO_2$ change, % | −4.1 ± 0.8 | −4.1 ± 0.8 | −4.3 ± 1.0 | −5.6 ± 1.4 [b] | −5.0 ± 1.2 [b] | −5.2 ± 1.4 [b] | 0.91 |
| Heart rate change, $min^{-1}$ | 18.4 ± 3.4 | 14.0 ± 3.2 | 19.3 ± 3.6 | 17.7 ± 3.0 [b] | 18.1 ± 3.5 [b] | 17.5 ± 3.8 [b] | 0.50 |
| **Symptom & quality of life scores[1]** | | | | | | | |
| BODE score | 3.5 ± 0.4 [a] | 3.3 ± 0.4 [a] | 3.4 ± 0.4 [a] | 3.5 ± 0.4 [c] | 3.5 ± 0.4 [c] | 3.5 ± 0.4 [c] | 0.22 |
| COPD Assessment Test™ | 14.5 ± 1.3 | 14.8 ± 1.6 | 16.6 ± 1.5 | 16.5 ± 1.5 | 15.5 ± 1.6 | 18.3 ± 1.5 | 0.97 |
| St. George Respiratory Questionnaire total score | 41.8 ± 3.2 | 39.8 ± 3.2 | 41.5 ± 3.1 | 46.1 ± 3.5 | 44.9 ± 3.7 | 47.9 ± 3.7 | 0.06 |
| Modified MRC dyspnea scale | 1.9 ± 0.2 | 1.5 ± 0.2 | 1.8 ± 0.2 | 2.0 ± 0.2 | 2.0 ± 0.2 | 2.0 ± 0.2 | 0.008 |
| Dyspnea-12 score | 9.0 ± 1.4 | 9.5 ± 1.6 | 10.9 ± 1.6 | 10.1 ± 1.5 | 10.5 ± 1.7 | 11.1 ± 1.6 | 0.43 |
| Fatigue severity score | 33.0 ± 3.2 | 31.0 ± 2.8 | 32.0 ± 2.6 | 39.8 ± 3.3 | 37.6 ± 3.4 | 41.1 ± 3.1 | 0.13 |
| Hospital Anxiety and Depression Score – Anxiety score | 4.3 ± 0.8 | 4.7 ± 0.9 | 4.5 ± 0.9 | 5.4 ± 0.8 | 5.3 ± 0.8 | 5.1 ± 0.8 | 0.31 |
| Hospital Anxiety and Depression Score – Depression score | 4.2 ± 0.5 | 4.2 ± 0.6 | 3.8 ± 0.5 | 5.9 ± 0.8 | 5.8 ± 0.7 | 5.7 ± 0.7 | 0.89 |
| Visual analogue scales | | | | | | | |
| Dyspnea | 28.3 ± 4.1 | 32.1 ± 5.1 | 27.6 ± 4.4 | 32.4 ± 4.9 | 39.7 ± 5.2 | 33.8 ± 4.9 | 0.56 |
| Cough | 28.6 ± 5.2 | 34.4 ± 5.4 | 34.6 ± 5.6 | 31.3 ± 5.7 | 30.6 ± 5.3 | 29.9 ± 4.6 | 0.25 |
| Sputum production | 24.9 ± 5.3 | 21.4 ± 4.1 | 27.5 ± 4.9 | 21.2 ± 4.7 | 24.9 ± 4.8 | 25.6 ± 4.1 | 0.48 |
| Sputum purulence | 18.9 ± 4.5 [c] | 17.1 ± 4.2 [c] | 17.7 ± 4.7 [c] | 24.4 ± 5.9 [c] | 19.6 ± 4.2 [c] | 26.0 ± 4.5 [c] | 0.43 |

| Parameter | FCM (N = 24) | | | Placebo (N = 24) | | | P value |
|---|---|---|---|---|---|---|---|
| | Baseline | Week 1 | Week 8 | Baseline | Week 1 | Week 8 | |
| **Spirometry** | | | | | | | |
| $FEV_1$, L | 1.08 ± 0.10 [a] | 1.04 ± 0.09 [a] | 1.07 ± 0.09 [a] | 1.25 ± 0.07 | 1.27 ± 0.08 | 1.27 ± 0.08 | 0.12 |
| $FEV_1$, % of predicted | 43.6 ± 3.3 [a] | 42.3 ± 3.2 [a] | 43.1 ± 3.0 [a] | 46.0 ± 3.1 | 46.3 ± 3.3 | 46.5 ± 3.4 | 0.13 |
| $FEV_1$/FVC, % | 40.4 ± 2.2 [a] | 41.3 ± 2.2 [a] | 41.0 ± 2.1 [a] | 39.8 ± 2.2 | 39.2 ± 2.3 | 39.3 ± 2.1 | 0.24 |
| **Echocardiography** | | | | | | | |
| Tricuspid regurgitant jet measured, n (%) | 8 (33.3) | 8 (33.3) | 6 (25.0) | 7 (29.2) | 7 (29.2) | 6 (25.0) | — |
| Trans-tricuspid pressure gradient, mmHg | 28.8 ± 1.8 [d] | 26.8 ± 1.1 [d] | 28.2 ± 1.0 [d] | 35.2 ± 3.0 [d] | 35.8 ± 3.1 [d] | 36.9 ± 5.1 [d] | 0.09 |

*All data are reported as mean ±SE. Statistical analysis was performed by linear mixed effects modelling; P values are given for the fixed effect of "status post FCM infusion". $FEV_1$: forced expiratory volume in one second, FVC: forced vital capacity, FCM: ferric carboxymaltose.*

*[1] Scale ranges: BODE 0–10, COPD Assessment Test™ 0–40, Dyspnea-12 score 0–36, Fatigue severity score 9–63, Hospital Anxiety and Depression Score 0–21, Likert scale 1–7, modified MRC scale 0–4, St. George Respiratory Questionnaire 0–100, visual analogue scales 0–100. For all scores a lower value is better.*

*[a–d] Descriptive data (mean ±SE) are reported for participants with a valid measurement at each time point ([a] n = 23, [b] n = 22, [c] n = 21, [d] n = 6); cases with partially missing data were excluded. Cases with missing data were still included in the linear mixed effects model.*