**Supplemental Data**

**Supplemental Table 1. Changes in HbA1c, Body Weight, and Systolic BP for the Overall Populations and Latin American Subgroups of the PBO-Controlled Studies at Week 26\***

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Overall Population** | | | | | | | | | | | | |
|  | **Monotherapy10** | | | | **Add-on to MET18** | | | **Add-on to MET + SU19** | | | | | |
|  | **PBO**  **(n = 192)** | | **CANA**  **100 mg**  **(n = 195)** | **CANA**  **300 mg**  **(n = 197)** | **PBO**  **(n = 183)** | **CANA**  **100 mg**  **(n = 368)** | **CANA**  **300 mg**  **(n = 367)** | **PBO**  **(n = 156)** | | **CANA**  **100 mg**  **(n = 157)** | | **CANA**  **300 mg**  **(n = 156** | |
| HbA1c, n | 189 | | 191 | 194 | 181 | 365 | 360 | 150 | | 155 | | 152 | |
| Baseline, % | 8.0 (1.0) | | 8.1 (1.0) | 8.0 (1.0) | 8.0 (0.9) | 7.9 (0.9) | 8.0 (0.9) | 8.1(0.9) | | 8.1 (0.9) | | 8.1 (0.9) | |
| Change, % | 0.14 (0.07) | | –0.77 (0.07) | –1.03 (0.06) | –0.17 (0.06) | –0.79 (0.04) | –0.94 (0.04) | –0.13 (0.08) | | –0.85 (0.08) | | –1.06 (0.08) | |
| Difference vs PBO (95% CI) |  | | −0.91  (−1.09, −0.73)† | −0.16  (−1.34,  –0.99)† |  | −0.62  (−0.76, −0.48)† | −0.77  (−0.91,  –0.64)† |  | | −0.71  (−0.90,  –0.52)† | | −0.92  (−1.11,  –0.73)† | |
| Body weight, n | 190 | | 192 | 194 | 181 | 365 | 360 | 150 | | 156 | | 154 | |
| Baseline, kg | 87.5 (19.4) | | 85.9 (21.5) | 86.9 (20.6) | 86.7 (22.5) | 88.7 (22.3) | 85.4 (20.7) | 90.8 (22.5) | | 93.5 (22.4) | | 93.5 (22.1) | |
| Change, kg | –0.5 (0.2) | | –2.5 (0.2) | –3.4 (0.2) | –1.1 (0.2) | –3.3 (0.2) | –3.6 (0.2) | –0.8 (0.3) | | –1.9 (0.3) | | –2.5 (0.3) | |
| Change, % | –0.6 (0.2) | | –2.8 (0.2) | –3.9 (0.2) | –1.2 (0.3) | –3.7 (0.2) | –4.2 (0.2) | –0.7 (0.3) | | –2.1 (0.3) | | –2.6 (0.3) | |
| Difference vs PBO (95% CI) |  | | −2.2  (−2.9, –1.6)† | −3.3  (−4.0, –2.6)† |  | −2.5  (−3.1, –1.9)† | −2.9  (−3.5, –2.3)† |  | | −1.4  (−2.1, –0.7)† | | −2.0  (−2.7, –1.3)† | |
| Systolic BP, n | 190 | | 192 | 195 | 181 | 365 | 360 | 150 | | 156 | | 154 | |
| Baseline, mmHg | 127.7 (13.7) | | 126.7  (12.5) | 128.5  (12.7) | 128.0  (12.7) | 128.0  (12.7) | 128.7  (13.0) | 130.1  (13.7) | | 130.4  (13.5) | | 130.8  (12.8) | |
| Change, mmHg | 0.4 (0.8) | | –3.3 (0.8) | –5.0 (0.8) | 1.5 (0.8) | –3.8 (0.6) | –5.1 (0.6) | –2.7 (1.0) | | –4.9 (1.0) | | –4.3 (1.0) | |
| Difference vs PBO (95% CI) |  | | −3.7  (−5.9, –1.6)† | −5.4  (−7.6, –3.3)† |  | −5.4  (−7.3, –3.4)† | −6.6  (−8.5, –4.7)† |  | | −2.2  (−4.7, 0.2)‡ | | −1.6  (−4.1, 0.9)‡ | |
|  | **Latin American subgroup** | | | | | | | | | | | | |
|  | **Monotherapy** | | | | **Add-on to MET** | | | | **Add-on to MET + SU** | | | | |
| Characteristic | **PBO**  **(n = 37)** | **CANA**  **100 mg**  **(n = 41)** | | **CANA**  **300 mg**  **(n = 38)** | **PBO**  **(n = 40)** | **CANA**  **100 mg**  **(n = 80)** | **CANA**  **300 mg**  **(n = 79)** | | **PBO**  **(n = 26)** | | **CANA**  **100 mg**  **(n = 23)** | | **CANA**  **300 mg**  **(n = 27)** |
| HbA1c, n | 37 | 41 | | 38 | 40 | 80 | 76 | | 26 | | 23 | | 26 |
| Baseline, % | 8.0 (0.9) | 8.2 (1.0) | | 8.1 (1.1) | 8.0 (0.9) | 7.9 (0.9) | 8.0 (0.9) | | 8.3 (1.2) | | 8.3 (0.8) | | 8.4 (1.2) |
| Change, % | 0.27 (0.15) | –1.10 (0.14) | | –1.02 (0.15) | –0.37 (0.13) | –0.98 (0.10) | –1.05 (0.10) | | –0.44 (0.18) | | –1.24 (0.20) | | –1.51 (0.19) |
| Difference vs PBO (95% CI) |  | −1.37  (−1.79, −0.96)§ | | −1.29  (−1.71, −0.87)§ |  | −0.61  (−0.90, −0.32)§ | −0.68  (−0.97,  − 0.39)§ | |  | | −0.81  (−1.30,  −0.32)§ | | −1.07  (−1.55,  −0.60)§ |
| Body weight, n | 37 | 41 | | 38 | 40 | 80 | 76 | | 26 | | 23 | | 27 |
| Baseline, kg | 79.0 (20.3) | 75.7 (16.1) | | 73.8 (17.5) | 77.1 (15.2) | 77.4 (17.9) | 77.3 (18.2) | | 70.0 (17.8) | | 73.2 (15.0) | | 73.2 (12.4) |
| Change, kg | 0.3 (0.4) | –2.2 (0.3) | | –3.0 (0.4) | –1.0 (0.5) | –2.7 (0.4) | –2.9 (0.4) | | –0.1 (0.4) | | –1.4 (0.4) | | –1.4 (0.3) |
| Change, % | 0.5 (0.5) | –2.9 (0.5) | | –3.7 (0.5) | −1.4 (0.6) | –3.5 (0.5) | –3.9 (0.5) | | 0.1 (0.5) | | –1.8 (0.5) | | –2.0 (0.5) |
| Difference vs PBO (95% CI) |  | −3.3  (−4.7,−2.0)§ | | −4.1  (−5.5,−2.7)§ |  | −2.1  (−3.4,−0.7)§ | −2.5  (−3.8,−1.2)§ | |  | | −1.9  (−3.2, −0.6)§ | | −2.1  (−3.4, −0.9)§ |
| Systolic BP, n | 37 | 41 | | 38 | 40 | 80 | 76 | | 26 | | 23 | | 27 |
| Baseline, mmHg | 127.0  (14.9) | 121.0  (11.8) | | 124.0  (13.8) | 125.3  (12.3) | 124.4  (13.4) | 124.5  (13.7) | | 134.5  (12.6) | | 127.9  (12.9) | | 129.9  (14.3) |
| Change, mmHg | 2.1 (1.8) | –4.2 (1.7) | | –8.2 (1.8) | 2.2 (1.9) | –2.9 (1.4) | –4.8 (1.4) | | –5.1 (1.9) | | –5.0 (2.0) | | –9.6 (1.9) |
| Difference vs PBO (95% CI) |  | −6.3  (−11.3, –1.4)§ | | −10.3  (−15.3,−5.3)§ |  | −5.1  (−9.2, −1.1)§ | −7.0  (−11.1,−2.9)§ | |  | | 0.2  (−5.0, 5.3)§ | | −4.4  (−9.4,0.5)§ |

BP, blood pressure; PBO, placebo; MET, metformin; SU, sulfonylurea; CANA, canagliflozin; CI, confidence interval; SD, standard deviation; LS, least squares; SE, standard error; NS, not significant.

\*Data are mean (SD) baseline and LS mean change (SE) from baseline.

†*P* <0.001 versus PBO.

‡*P* = NS versus PBO.

§Statistical comparisons were not performed in the post hoc analysis of patients from Latin America.

**Supplemental Table 2. Changes in HbA1c, Body Weight, and Systolic BP for the Overall Populations and Latin American Subgroups of the Active-Controlled Studies at Week 52\***

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Overall Population** | | | | | | | |
|  | **Add-on to MET vs SITA18** | | | **Add-on to MET vs GLIM16** | | | **Add-on to MET + SU vs SITA21** | |
|  | **SITA**  **100 mg**  **(n = 366)** | **CANA**  **100 mg**  **(n = 368)** | **CANA**  **300 mg**  **(n = 367)** | **GLIM**  **(n = 482)** | **CANA**  **100 mg**  **(n = 483)** | **CANA**  **300 mg**  **(n = 485)** | **SITA**  **100 mg**  **(n = 378)** | **CANA**  **300 mg**  **(n = 377)** |
| HbA1c, n | 354 | 365 | 360 | 473 | 478 | 474 | 365 | 374 |
| Baseline, % | 7.9 (0.9) | 7.9 (0.9) | 8.0 (0.9) | 7.8 (0.8) | 7.8 (0.8) | 7.8 (0.8) | 8.1 (0.9) | 8.1 (0.9) |
| Change, % | –0.73 (0.05) | –0.73 (0.05) | –0.88 (0.05) | –0.81 (0.04) | –0.82 (0.04) | –0.93 (0.04) | –0.66 (0.05) | –1.03 (0.05) |
| Difference vs SITA/GLIM (95% CI) |  | 0.00  (−0.12, 0.12)† | −0.15  (−0.27,  –0.03)‡ |  | −0.01  (−0.11, 0.09)† | −0.12  (−0.22,  –0.02)‡ |  | −0.37  (−0.50,  –0.25)‡ |
| Body weight, n | 355 | 365 | 360 | 478 | 479 | 480 | 367 | 375 |
| Baseline, kg | 87.6 (20.9) | 88.7 (22.3) | 85.4 (20.7) | 86.6 (19.8) | 86.8 (20.0) | 86.6 (19.3) | 89.6 (23.1) | 87.6 (23.2) |
| Change, kg | –1.2 (0.2) | –3.3 (0.2) | –3.7 (0.2) | 0.7 (0.2) | –3.7 (0.2) | –4.0 (0.2) | 0.1 (0.2) | –2.3 (0.2) |
| Change, % | –1.3 (0.2) | –3.8 (0.2) | –4.2 (0.2) | 1.0 (0.2) | –4.2 (0.2) | –4.7 (0.2) | 0.3 (0.2) | –2.5 (0.2) |
| Difference vs SITA/GLIM (95% CI) |  | −2.4  (−3.0, –1.8)§ | −2.9  (−3.4, –2.3)§ |  | −5.2  (−5.7, –4.7)§ | −5.7  (−6.2, –5.1)§ |  | −2.8  (−3.3, –2.2)§ |
| Systolic BP, n | 355 | 365 | 360 | 480 | 479 | 480 | 367 | 375 |
| Baseline, mmHg | 128.0  (13.5) | 128.0  (12.7) | 128.7  (13.0) | 129.5  (13.5) | 130.0  (12.4) | 130.0  (13.8) | 130.1  (14.0) | 131.2  (13.2) |
| Change, mmHg | –0.7 (0.6) | –3.5 (0.6) | –4.7 (0.6) | 0.2 (0.6) | –3.3 (0.6) | –4.6 (0.6) | 0.9 (0.7) | –5.1 (0.7) |
| Difference vs SITA/GLIM (95% CI) |  | −2.9  (−4.5, –1.3)§ | −4.0  (−5.6, –2.4)§ |  | −3.5  (−4.9, –2.1)| | −4.8  (−6.2, –3.4) | |  | −5.9  (−7.6, –4.2)§ |
|  | **Latin American subgroup** | | | | | | | |
|  | **Add-on to MET vs SITA** | | | **Add-on to MET vs GLIM** | | | **Add-on to MET + SU vs SITA** | |
| Characteristic | **SITA**  **100 mg**  **(n = 81)** | **CANA**  **100 mg**  **(n = 80)** | **CANA**  **300 mg**  **(n = 79)** | **GLIM**  **(n = 51)** | **CANA**  **100 mg**  **(n = 52)** | **CANA**  **300 mg**  **(n = 52)** | **SITA**  **100 mg**  **(n = 80)** | **CANA**  **300 mg**  **(n = 76)** |
| HbA1c, n | 79 | 80 | 76 | 51 | 52 | 52 | 78 | 76 |
| Baseline, % | 7.9 (0.8) | 7.9 (0.9) | 8.0 (0.9) | 8.0 (0.7) | 7.9 (0.8) | 7.7 (0.6) | 8.0 (0.9) | 7.9 (1.0) |
| Change, % | –0.72 (0.11) | –0.94 (0.12) | –0.93 (0.11) | –0.86 (0.13) | –0.95 (0.12) | –1.10 (0.13) | –0.77 (0.12) | –1.21 (0.13) |
| Difference vs SITA/GLIM (95% CI) |  | −0.22  (−0.48, 0.05)¶ | −0.21  (−0.48,  0.06)¶ |  | −0.10  (−0.44,  0.24)¶ | −0.24  (−0.59, 0.10)¶ |  | −0.45  (−0.69,  −0.20)¶ |
| Body weight, n | 80 | 80 | 76 | 51 | 52 | 52 | 78 | 76 |
| Baseline, kg | 77.0 (16.4) | 77.4 (17.9) | 77.3 (18.2) | 81.7 (14.1) | 79.3 (17.2) | 79.4 (14.1) | 79.6 (18.7) | 79.1 (16.7) |
| Change, kg | –0.5 (0.4) | –2.7 (0.4) | –3.2 (0.4) | 1.4 (0.5) | –2.5 (0.5) | –3.2 (0.5) | 0.6 (0.5) | –2.1 (0.5) |
| Change, % | –0.6 (0.5) | –3.6 (0.5) | –4.3 (0.5) | 1.6 (0.6) | –3.3 (0.6) | –4.0 (0.6) | 0.8 (0.6) | –2.6 (0.7) |
| Difference vs SITA/GLIM (95% CI) |  | −3.0  (−4.2,−1.8)¶ | −3.7  (−4.9,−2.4)¶ |  | −4.9  (−6.4,−3.3)¶ | −5.5  (−7.1,−4.0)¶ |  | −3.4  (−4.6, −2.1)¶ |
| Systolic BP, n | 80 | 80 | 76 | 51 | 52 | 52 | 78 | 76 |
| Baseline, mmHg | 123.8  (14.1) | 124.4  (13.4) | 124.5  (13.7) | 130.8  (12.7) | 128.2  (12.9) | 129.2  (14.0) | 128.3  (13.9) | 132.0  (12.4) |
| Change, mmHg | –0.6 (1.5) | –3.8 (1.5) | –4.5 (1.5) | –1.3 (1.5) | –3.4 (1.5) | –6.3 (1.5) | 3.0 (2.4) | –2.6 (2.5) |
| Difference vs SITA/GLIM (95% CI) |  | −3.2  (−6.7, 0.3)¶ | −4.0  (−7.5,−0.5)¶ |  | −2.1  (−6.2, 2.0)¶ | −5.0  (−9.1,−1.0)¶ |  | −5.7  (−10.5, −0.8)¶ |

BP, blood pressure; MET, metformin; SITA, sitagliptin; GLIM, glimepiride; SU, sulfonylurea; CANA, canagliflozin; CI, confidence interval; SD, standard deviation; LS, least squares; SE, standard error.

\*Data are mean (SD) baseline and LS mean change (SE) from baseline.

†CANA demonstrated non-inferiority to SITA/GLIM; upper limit of the 95% CI was less than the prespecified margin of 0.3%.

‡CANA demonstrated superiority to SITA/GLIM; upper limit of the 95% CI <0.0%.

§*P* <0.001 versus SITA/GLIM.

|Statistical comparisons were not performed (not prespecified).

¶Statistical comparisons were not performed in the post hoc analysis of patients from Latin America.