**Supplementary Material 2. Efficacy Endpoints**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Age <65 | | | |  | Age 65-74 | | | | | Age ≥75 | | | | | ANOVA |  |
|  |  | n | Mean | SD | P | \* | n | Mean | SD | p | \* | n | Mean | SD | p | \* | p |  |
| HbA1c (%) | 0M | 148 | 7.76 | 1.50 |  |  | 134 | 7.18 | 1.22 |  |  | 127 | 7.03 | 1.15 |  |  | <0.001 | \*\* |
| 3M | 143 | 7.08 | 1.33 |  |  | 134 | 6.68 | 1.02 |  |  | 120 | 6.54 | 1.09 |  |  | <0.001 | \*\* |
| 6M | 144 | 6.75 | 1.18 |  |  | 129 | 6.42 | 0.94 |  |  | 120 | 6.39 | 0.87 |  |  | 0.005 | \*\* |
| 9M | 134 | 6.74 | 1.19 |  |  | 126 | 6.42 | 1.02 |  |  | 114 | 6.31 | 0.80 |  |  | 0.002 | \*\* |
| 12M | 148 | 6.75 | 1.25 |  |  | 134 | 6.41 | 0.88 |  |  | 127 | 6.32 | 0.81 |  |  | <0.001 | \*\* |
| Δ3M | 143 | -0.72 | 1.02 | 0.000 | \* | 134 | -0.50 | 0.77 | 0.000 | \* | 120 | -0.50 | 0.88 | 0.000 | \* | 0.068 |  |
| Δ6M | 144 | -0.97 | 1.18 | 0.000 | \* | 129 | -0.78 | 1.12 | 0.000 | \* | 120 | -0.69 | 0.99 | 0.000 | \* | 0.092 |  |
| Δ9M | 134 | -1.06 | 1.22 | 0.000 | \* | 126 | -0.77 | 1.17 | 0.000 | \* | 114 | -0.70 | 0.99 | 0.000 | \* | 0.029 | \*\* |
| Δ12M | 148 | -1.01 | 1.21 | 0.000 | \* | 134 | -0.76 | 1.07 | 0.000 | \* | 127 | -0.71 | 0.96 | 0.000 | \* | 0.054 |  |
| Blood glucose (fasting) (mg/dL) | 0M | 59 | 166.95 | 59.61 |  |  | 68 | 142.12 | 47.98 |  |  | 62 | 150.82 | 49.67 |  |  | 0.029 | \*\* |
| 3M | 61 | 138.69 | 48.56 |  |  | 58 | 123.43 | 35.52 |  |  | 47 | 133.19 | 51.02 |  |  | 0.182 |  |
| 6M | 64 | 131.11 | 40.99 |  |  | 54 | 130.06 | 40.48 |  |  | 48 | 122.81 | 29.90 |  |  | 0.481 |  |
| 9M | 57 | 136.33 | 51.20 |  |  | 55 | 121.95 | 32.22 |  |  | 39 | 127.92 | 28.46 |  |  | 0.161 |  |
| 12M | 63 | 133.37 | 35.95 |  |  | 54 | 125.37 | 29.79 |  |  | 50 | 121.94 | 22.68 |  |  | 0.122 |  |
| Δ3M | 43 | -36.79 | 46.35 | 0.000 | \* | 49 | -10.53 | 47.97 | 0.131 |  | 37 | -26.86 | 44.47 | 0.001 | \* | 0.025 | \*\* |
| Δ6M | 46 | -35.28 | 43.43 | 0.000 | \* | 48 | -18.42 | 49.43 | 0.013 | \* | 40 | -28.60 | 49.77 | 0.001 | \* | 0.227 |  |
| Δ9M | 42 | -33.67 | 50.70 | 0.000 | \* | 45 | -17.60 | 41.58 | 0.007 | \* | 32 | -23.22 | 47.28 | 0.009 | \* | 0.271 |  |
| Δ12M | 47 | -34.70 | 47.88 | 0.000 | \* | 45 | -17.16 | 42.96 | 0.010 | \* | 44 | -32.09 | 47.22 | 0.000 | \* | 0.151 |  |
| Blood glucose (postprandial) (mg/dL) | 0M | 62 | 206.35 | 84.01 |  |  | 45 | 193.80 | 70.06 |  |  | 55 | 176.11 | 60.41 |  |  | 0.083 |  |
| 3M | 55 | 169.22 | 68.16 |  |  | 53 | 159.57 | 55.97 |  |  | 54 | 153.28 | 55.13 |  |  | 0.38 |  |
| 6M | 57 | 170.25 | 62.80 |  |  | 55 | 155.53 | 65.52 |  |  | 62 | 153.16 | 57.06 |  |  | 0.274 |  |
| 9M | 57 | 170.19 | 67.71 |  |  | 50 | 156.44 | 55.04 |  |  | 58 | 168.81 | 62.24 |  |  | 0.462 |  |
| 12M | 60 | 156.87 | 47.86 |  |  | 51 | 149.80 | 56.43 |  |  | 60 | 153.75 | 47.60 |  |  | 0.764 |  |
| Δ3M | 45 | -45.40 | 69.57 | 0.000 | \* | 37 | -24.08 | 52.09 | 0.008 | \* | 38 | -20.03 | 67.16 | 0.074 |  | 0.151 |  |
| Δ6M | 46 | -36.07 | 87.00 | 0.007 | \* | 37 | -40.51 | 51.51 | 0.000 | \* | 42 | -20.52 | 50.81 | 0.012 | \* | 0.367 |  |
| Δ9M | 45 | -40.47 | 87.50 | 0.003 | \* | 34 | -36.09 | 62.86 | 0.002 | \* | 39 | -6.38 | 66.37 | 0.552 |  | 0.087 |  |
| Δ12M | 47 | -50.02 | 74.53 | 0.000 | \* | 35 | -36.43 | 76.38 | 0.008 | \* | 44 | -17.98 | 62.88 | 0.065 |  | 0.104 |  |
| TC (mg/dL) | 0M | 64 | 204.47 | 39.49 |  |  | 62 | 202.10 | 33.09 |  |  | 61 | 194.90 | 28.40 |  |  | 0.268 |  |
| 3M | 51 | 196.63 | 32.81 |  |  | 48 | 191.06 | 36.00 |  |  | 45 | 193.20 | 32.21 |  |  | 0.71 |  |
| 6M | 51 | 199.61 | 33.86 |  |  | 49 | 198.82 | 36.98 |  |  | 46 | 188.83 | 28.73 |  |  | 0.221 |  |
| 9M | 44 | 204.11 | 34.38 |  |  | 43 | 188.47 | 29.06 |  |  | 40 | 184.88 | 27.75 |  |  | 0.01 | \*\* |
| 12M | 58 | 198.03 | 35.36 |  |  | 61 | 193.82 | 30.04 |  |  | 66 | 188.79 | 32.68 |  |  | 0.291 |  |
| Δ3M | 45 | -11.73 | 29.64 | 0.011 | \* | 42 | -9.40 | 27.00 | 0.029 | \* | 37 | -2.95 | 15.37 | 0.251 |  | 0.279 |  |
| Δ6M | 48 | -9.27 | 33.75 | 0.063 |  | 43 | -6.95 | 29.67 | 0.132 |  | 38 | -6.24 | 22.30 | 0.093 |  | 0.879 |  |
| Δ9M | 37 | -3.11 | 39.53 | 0.635 |  | 37 | -13.95 | 28.82 | 0.006 | \* | 35 | -12.00 | 18.17 | 0.000 | \* | 0.267 |  |
| Δ12M | 48 | -6.08 | 37.01 | 0.261 |  | 50 | -13.36 | 28.52 | 0.002 | \* | 54 | -7.65 | 25.16 | 0.030 | \* | 0.457 |  |
| LDL-C (mg/dL) | 0M | 123 | 121.43 | 33.76 |  |  | 98 | 120.88 | 28.84 |  |  | 90 | 113.06 | 29.25 |  |  | 0.112 |  |
| 3M | 110 | 116.65 | 29.66 |  |  | 93 | 110.30 | 28.93 |  |  | 74 | 109.14 | 24.59 |  |  | 0.136 |  |
| 6M | 112 | 116.03 | 27.58 |  |  | 93 | 115.17 | 27.15 |  |  | 80 | 106.85 | 23.42 |  |  | 0.041 | \*\* |
| 9M | 100 | 115.93 | 30.11 |  |  | 90 | 111.88 | 29.13 |  |  | 77 | 108.13 | 23.61 |  |  | 0.185 |  |
| 12M | 113 | 112.95 | 25.94 |  |  | 105 | 112.10 | 27.40 |  |  | 91 | 105.79 | 24.33 |  |  | 0.113 |  |
| Δ3M | 106 | -5.72 | 31.49 | 0.064 |  | 78 | -7.10 | 24.06 | 0.011 | \* | 68 | -4.01 | 20.86 | 0.117 |  | 0.785 |  |
| Δ6M | 110 | -6.75 | 32.03 | 0.029 | \* | 82 | -6.33 | 25.09 | 0.025 | \* | 71 | -5.06 | 24.15 | 0.082 |  | 0.922 |  |
| Δ9M | 97 | -5.66 | 32.80 | 0.092 |  | 74 | -10.16 | 27.76 | 0.002 | \* | 70 | -6.59 | 28.83 | 0.060 |  | 0.611 |  |
| Δ12M | 109 | -6.14 | 30.51 | 0.038 | \* | 90 | -6.62 | 25.02 | 0.014 | \* | 82 | -4.96 | 28.27 | 0.116 |  | 0.925 |  |
| HDL-C (mg/dL) | 0M | 133 | 57.76 | 17.16 |  |  | 107 | 57.10 | 14.43 |  |  | 100 | 58.69 | 16.98 |  |  | 0.781 |  |
| 3M | 118 | 56.72 | 14.95 |  |  | 100 | 55.76 | 14.76 |  |  | 84 | 56.05 | 15.62 |  |  | 0.889 |  |
| 6M | 122 | 56.63 | 14.86 |  |  | 104 | 55.85 | 15.49 |  |  | 88 | 56.31 | 14.85 |  |  | 0.928 |  |
| 9M | 109 | 56.39 | 14.99 |  |  | 98 | 55.60 | 14.57 |  |  | 84 | 54.66 | 13.04 |  |  | 0.705 |  |
| 12M | 129 | 56.34 | 15.10 |  |  | 116 | 55.93 | 14.17 |  |  | 105 | 54.63 | 14.12 |  |  | 0.655 |  |
| Δ3M | 112 | -0.94 | 8.19 | 0.225 |  | 86 | -1.30 | 7.05 | 0.092 |  | 72 | -0.98 | 6.70 | 0.219 |  | 0.941 |  |
| Δ6M | 118 | -0.77 | 10.47 | 0.424 |  | 92 | -1.40 | 8.41 | 0.115 |  | 78 | -1.37 | 8.84 | 0.175 |  | 0.864 |  |
| Δ9M | 104 | -1.74 | 9.42 | 0.063 |  | 82 | -0.88 | 8.91 | 0.372 |  | 72 | -1.67 | 8.60 | 0.103 |  | 0.79 |  |
| Δ12M | 123 | -0.69 | 10.49 | 0.467 |  | 98 | -1.38 | 7.72 | 0.080 |  | 89 | -2.24 | 10.65 | 0.051 |  | 0.523 |  |
| TG (mg/dL) | 0M | 139 | 202.57 | 282.53 |  |  | 113 | 157.50 | 99.93 |  |  | 103 | 155.47 | 86.09 |  |  | 0.087 |  |
| 3M | 123 | 173.05 | 193.52 |  |  | 104 | 136.17 | 77.21 |  |  | 87 | 140.31 | 87.34 |  |  | 0.087 |  |
| 6M | 126 | 168.98 | 100.41 |  |  | 107 | 134.93 | 74.94 |  |  | 92 | 147.62 | 87.83 |  |  | 0.013 | \*\* |
| 9M | 112 | 180.95 | 131.81 |  |  | 101 | 148.06 | 95.51 |  |  | 87 | 146.05 | 78.92 |  |  | 0.03 | \*\* |
| 12M | 131 | 169.66 | 154.65 |  |  | 119 | 135.98 | 72.52 |  |  | 109 | 149.06 | 114.69 |  |  | 0.083 |  |
| Δ3M | 118 | -35.75 | 323.56 | 0.232 |  | 90 | -14.69 | 83.19 | 0.097 |  | 78 | -17.94 | 75.07 | 0.038 | \* | 0.751 |  |
| Δ6M | 123 | -36.44 | 271.45 | 0.139 |  | 96 | -16.76 | 86.05 | 0.059 |  | 84 | -10.56 | 64.84 | 0.139 |  | 0.559 |  |
| Δ9M | 108 | -29.56 | 317.47 | 0.335 |  | 87 | -9.64 | 88.58 | 0.313 |  | 78 | -18.68 | 62.53 | 0.010 | \* | 0.801 |  |
| Δ12M | 127 | -35.24 | 305.30 | 0.196 |  | 103 | -26.91 | 93.66 | 0.004 | \* | 95 | -17.51 | 61.11 | 0.006 | \* | 0.809 |  |
| Serum creatinine (mg/dL) | 0M | 136 | 0.70 | 0.18 |  |  | 109 | 0.73 | 0.20 |  |  | 111 | 0.78 | 0.20 |  |  | 0.007 | \*\* |
| 3M | 118 | 0.71 | 0.17 |  |  | 101 | 0.75 | 0.21 |  |  | 97 | 0.82 | 0.19 |  |  | <0.001 | \*\* |
| 6M | 123 | 0.73 | 0.18 |  |  | 104 | 0.75 | 0.20 |  |  | 95 | 0.80 | 0.22 |  |  | 0.019 | \*\* |
| 9M | 112 | 0.71 | 0.15 |  |  | 101 | 0.76 | 0.20 |  |  | 90 | 0.82 | 0.23 |  |  | 0.001 | \*\* |
| 12M | 125 | 0.74 | 0.18 |  |  | 120 | 0.76 | 0.19 |  |  | 113 | 0.82 | 0.22 |  |  | 0.003 | \*\* |
| Δ3M | 111 | 0.00 | 0.11 | 0.775 |  | 85 | 0.03 | 0.10 | 0.004 | \* | 87 | 0.04 | 0.11 | 0.001 | \* | 0.012 | \*\* |
| Δ6M | 118 | 0.01 | 0.11 | 0.443 |  | 93 | 0.03 | 0.12 | 0.005 | \* | 89 | 0.03 | 0.12 | 0.015 | \* | 0.179 |  |
| Δ9M | 106 | 0.01 | 0.11 | 0.241 |  | 88 | 0.05 | 0.11 | 0.000 | \* | 85 | 0.05 | 0.10 | 0.000 | \* | 0.035 | \*\* |
| Δ12M | 118 | 0.03 | 0.11 | 0.010 | \* | 103 | 0.04 | 0.09 | 0.000 | \* | 106 | 0.04 | 0.09 | 0.000 | \* | 0.338 |  |
| Urine Albumin-to-Creatinine Ratio | 0M | 45 | 50.80 | 127.37 |  |  | 30 | 78.06 | 146.32 |  |  | 30 | 119.47 | 428.62 |  |  | 0.524 |  |
| 3M | 34 | 74.43 | 167.16 |  |  | 24 | 23.58 | 33.55 |  |  | 20 | 42.50 | 65.19 |  |  | 0.255 |  |
| 6M | 35 | 38.15 | 146.16 |  |  | 24 | 26.34 | 41.23 |  |  | 27 | 162.13 | 635.35 |  |  | 0.325 |  |
| 9M | 32 | 49.36 | 150.32 |  |  | 24 | 56.59 | 133.76 |  |  | 19 | 203.56 | 815.83 |  |  | 0.414 |  |
| 12M | 38 | 75.18 | 250.40 |  |  | 25 | 45.55 | 110.64 |  |  | 24 | 234.34 | 1012.72 |  |  | 0.437 |  |
| Δ3M | 22 | 2.40 | 20.67 | 0.592 |  | 14 | -4.64 | 26.15 | 0.518 |  | 17 | 0.92 | 21.46 | 0.862 |  | 0.648 |  |
| Δ6M | 23 | -9.34 | 30.13 | 0.151 |  | 17 | -14.49 | 60.20 | 0.336 |  | 23 | 39.32 | 205.43 | 0.369 |  | 0.329 |  |
| Δ9M | 22 | -11.15 | 24.79 | 0.047 | \* | 17 | 14.65 | 52.14 | 0.264 |  | 17 | 65.83 | 292.95 | 0.368 |  | 0.351 |  |
| Δ12M | 28 | 2.41 | 49.32 | 0.798 |  | 16 | 3.76 | 28.44 | 0.604 |  | 22 | 108.19 | 561.84 | 0.377 |  | 0.47 |  |
| Body weight (kg) | 0M | 138 | 72.04 | 14.18 |  |  | 126 | 62.88 | 10.19 |  |  | 122 | 59.93 | 11.74 |  |  | <0.001 | \*\* |
| 3M | 90 | 71.76 | 13.80 |  |  | 71 | 62.77 | 9.79 |  |  | 63 | 59.85 | 11.49 |  |  | <0.001 | \*\* |
| 6M | 94 | 72.62 | 15.04 |  |  | 72 | 63.19 | 9.97 |  |  | 68 | 59.05 | 11.60 |  |  | <0.001 | \*\* |
| 9M | 91 | 72.71 | 15.02 |  |  | 74 | 63.32 | 10.20 |  |  | 62 | 59.27 | 11.21 |  |  | <0.001 | \*\* |
| 12M | 101 | 72.18 | 15.32 |  |  | 78 | 62.33 | 10.30 |  |  | 74 | 59.18 | 11.21 |  |  | <0.001 | \*\* |
| Δ3M | 90 | -0.13 | 1.91 | 0.509 |  | 70 | 0.06 | 1.92 | 0.800 |  | 62 | -0.30 | 1.61 | 0.145 |  | 0.529 |  |
| Δ6M | 94 | 0.00 | 2.55 | 0.987 |  | 71 | -0.31 | 2.18 | 0.229 |  | 67 | -0.55 | 2.23 | 0.048 | \* | 0.343 |  |
| Δ9M | 91 | 0.18 | 3.18 | 0.588 |  | 73 | -0.21 | 2.47 | 0.476 |  | 61 | -0.40 | 2.27 | 0.173 |  | 0.405 |  |
| Δ12M | 101 | 0.02 | 3.50 | 0.960 |  | 78 | -0.20 | 2.94 | 0.541 |  | 73 | -0.57 | 2.14 | 0.025 | \* | 0.435 |  |
| Office SBP (mmHg) | 0M | 144 | 132.90 | 15.54 |  |  | 132 | 135.11 | 16.60 |  |  | 125 | 136.18 | 14.34 |  |  | 0.208 |  |
| 3M | 145 | 131.59 | 13.33 |  |  | 132 | 134.77 | 15.08 |  |  | 123 | 133.21 | 14.90 |  |  | 0.187 |  |
| 6M | 143 | 129.35 | 13.38 |  |  | 129 | 132.76 | 14.52 |  |  | 125 | 134.14 | 15.44 |  |  | 0.019 | \*\* |
| 9M | 143 | 131.64 | 13.73 |  |  | 126 | 131.90 | 15.49 |  |  | 121 | 134.93 | 17.69 |  |  | 0.178 |  |
| 12M | 142 | 131.08 | 15.32 |  |  | 128 | 129.98 | 14.53 |  |  | 125 | 133.49 | 13.87 |  |  | 0.15 |  |
| Δ3M | 142 | -1.04 | 14.10 | 0.380 |  | 131 | -0.42 | 16.22 | 0.768 |  | 121 | -2.41 | 12.56 | 0.037 | \* | 0.535 |  |
| Δ6M | 139 | -3.24 | 16.61 | 0.023 | \* | 128 | -2.39 | 18.82 | 0.153 |  | 123 | -1.92 | 15.11 | 0.162 |  | 0.812 |  |
| Δ9M | 140 | -1.31 | 16.48 | 0.347 |  | 125 | -3.12 | 18.48 | 0.061 |  | 120 | -1.32 | 16.92 | 0.396 |  | 0.632 |  |
| Δ12M | 139 | -2.01 | 16.48 | 0.152 |  | 128 | -4.69 | 16.86 | 0.002 | \* | 123 | -2.33 | 14.53 | 0.077 |  | 0.341 |  |
| Office DBP (mmHg) | 0M | 144 | 79.90 | 10.14 |  |  | 132 | 76.10 | 10.85 |  |  | 125 | 71.60 | 10.25 |  |  | <0.001 | \*\* |
| 3M | 145 | 78.43 | 9.47 |  |  | 132 | 75.75 | 9.99 |  |  | 123 | 70.46 | 10.91 |  |  | <0.001 | \*\* |
| 6M | 143 | 77.08 | 9.57 |  |  | 129 | 73.02 | 9.94 |  |  | 125 | 71.37 | 11.20 |  |  | <0.001 | \*\* |
| 9M | 143 | 78.55 | 9.17 |  |  | 126 | 72.76 | 10.20 |  |  | 121 | 70.32 | 11.46 |  |  | <0.001 | \*\* |
| 12M | 142 | 78.23 | 9.83 |  |  | 128 | 73.28 | 8.63 |  |  | 125 | 71.30 | 11.53 |  |  | <0.001 | \*\* |
| Δ3M | 142 | -1.46 | 9.71 | 0.076 |  | 131 | -0.39 | 8.37 | 0.595 |  | 121 | -0.83 | 8.12 | 0.265 |  | 0.601 |  |
| Δ6M | 139 | -2.64 | 9.97 | 0.002 | \* | 128 | -2.86 | 11.01 | 0.004 | \* | 123 | -0.11 | 9.25 | 0.899 |  | 0.057 |  |
| Δ9M | 140 | -1.51 | 9.93 | 0.073 |  | 125 | -3.41 | 9.69 | 0.000 | \* | 120 | -1.37 | 8.16 | 0.069 |  | 0.154 |  |
| Δ12M | 139 | -1.58 | 10.84 | 0.087 |  | 128 | -2.88 | 9.77 | 0.001 | \* | 123 | -0.24 | 8.78 | 0.759 |  | 0.108 |  |
| Office Pulse rate (bpm) | 0M | 68 | 76.31 | 12.12 |  |  | 66 | 70.23 | 10.01 |  |  | 82 | 73.52 | 11.18 |  |  | 0.007 | \*\* |
| 3M | 65 | 75.45 | 11.18 |  |  | 67 | 69.28 | 9.44 |  |  | 77 | 74.23 | 11.23 |  |  | 0.002 | \*\* |
| 6M | 64 | 74.45 | 10.95 |  |  | 59 | 68.75 | 8.70 |  |  | 77 | 73.45 | 11.71 |  |  | 0.007 | \*\* |
| 9M | 60 | 75.55 | 11.55 |  |  | 63 | 71.03 | 10.67 |  |  | 77 | 73.88 | 12.67 |  |  | 0.098 |  |
| 12M | 61 | 75.69 | 12.39 |  |  | 63 | 68.76 | 9.07 |  |  | 78 | 74.81 | 12.31 |  |  | 0.001 | \*\* |
| Δ3M | 60 | -1.37 | 9.75 | 0.282 |  | 61 | -0.97 | 9.07 | 0.408 |  | 75 | 0.63 | 8.60 | 0.530 |  | 0.398 |  |
| Δ6M | 56 | -1.96 | 9.56 | 0.130 |  | 55 | -1.22 | 9.75 | 0.358 |  | 76 | -0.08 | 8.84 | 0.938 |  | 0.506 |  |
| Δ9M | 55 | -0.95 | 8.00 | 0.385 |  | 56 | 1.32 | 11.25 | 0.383 |  | 74 | 0.27 | 9.03 | 0.798 |  | 0.454 |  |
| Δ12M | 57 | -0.53 | 7.70 | 0.608 |  | 59 | -2.41 | 9.11 | 0.047 | \* | 74 | 0.74 | 9.59 | 0.507 |  | 0.131 |  |

\*p<0.05 vs. Month 0 paired *t*-test, \*\*p<0.05 ANOVA

M: month; TC: total cholesterol; HDL: high-density lipoprotein cholesterol; LDL: low-density lipoprotein cholesterol; SBP: systolic blood pressure; DBP: diastolic blood pressure.