**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.