**Electronic Supplementary Material**

Table 1: Results of monotherapy analysis by OAD

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Patient Characteristics** | **TZD** | | **SU** | **metformin** | **Other\*\*** |
| Number of patients (% ) | 136 (0.58) | | 2,309 (9.77) | 21,166 (89.59) | 15 (0.06) |
| Age (years, SD) | 64.51 (12.44) | | 69.82 (13.19) | 61.96 (12,28) | 63.93 (17.49) |
| Sex (% male) | 55.15 | | 57.73 | 56.59 | 40.00 |
| Lipid lowering therapy (%)\* | 58.09 | | 52.19 | 54.60 | 53.33 |
| Blood pressure tablets (%)\* | 77.94 | | 69.64 | 65.42 | 66.67 |
| **HbA1c (%)** | | | | | |
| Prior to initiation, mean (SD) | 7.81 (0.98) | | 8.20 (1.37) | 8.02 (1.22) | 7.61 (1.55) |
| After initiation, mean (SD) | 7.00 (1.25) | | 7.02 (1.17) | 7.11 (0.98) | 7.27 (0.99) |
| Difference mean (SD)  (*P*-value) | -0.81 (0.19) (<0.001) | | -1.18 (0.06) (<0.001) | -0.91 (0.02) (<0.001) | -0.34 (0.69) (0.633) |
| Gradient prior to initiation | + | | + | + | + |
| Gradient after initiation | - | | - | - | + |
| Combined gradient | + | | + | - | + |
| *P*-value (difference) | <0.001 | | <0.001 | <0.001 | 0.706 |
| **Weight (Kg)** | | | | | |
| Prior to initiation, mean (SD) | 85.45 (18.86) | | 76.90 (17.07) | 92.75 (19.89) | 79.68 (16.01) |
| After initiation, mean (SD) | 87.37 (19.87) | | 78.09 (17.47) | 90.77 (19.90) | 80.25 (15.14) |
| Difference,  mean (SD) (*P*-value) | 1.92 (3.45) (0.579) | | 1.19 (0.94) (0.204) | -1.98 (0.33) (<0.001) | 0.57 (8.99) (0.951) |
| Gradient prior to initiation | - | | - | - | - |
| Gradient after initiation | + | | + | - | - |
| Combined gradient | - | | - | - | - |
| *P*-value (difference) | 0.126 | | 0.002 | 0.078 | 0.998 |
| **SBP** | | | | | |
| Prior to initiation, mean (SD) | 133.90 (15.95) | | 137.38 (18.66) | 139.74 (16.74) | 132.1 (22.21) |
| After initiation, mean (SD) | 132.62 (17.10) | | 137.79 (18.71) | 137.52 (16.65) | 127.8 (15.16) |
| Difference,  mean (SD) (*P*-value) | -1.29 (2.24) (0.565) | | 0.41 (0.68) (0.541) | -2.22 (0.19) (<0.001) | -4.30 (8.50) (0.620) |
| Gradient prior to initiation | - | | - | - | + |
| Gradient after initiation | - | | - | - | - |
| Combined gradient | - | | - | - | - |
| *P*-value (difference) | 0.304 | | 0.946 | 0.699 | 0.925 |
| **TC** | | | | | |
| Prior to initiation, mean (SD) | 4.94 (1.29) | | 4.74 (1.26) | 4.79 (1.15) | 4.47 (0.96) |
| After initiation, mean (SD) | 4.64 (1.14) | | 4.30 (1.05) | 4.27 (0.95) | 4.40 (1.03) |
| Difference,  mean (SD) (*P*-value) | -0.30 (0.23) (0.181) | | -0.44 (0.06) (<0.001) | -0.52 (0.02) (<0.001) | -0.07 (0.49) (0.884) |
| Gradient prior to initiation | - | | - | - | - |
| Gradient after initiation | - | | - | - | - |
| Combined gradient | - | | - | - | - |
| *P*-value (difference) | 0.492 | | 0.753 | 0.003 | <0.001 |
| **Targets** | | | | | |
| Proportion of subjects (mean): | | | | | |
| HbA1c < 7.5% | | 39% | 28% | 27% | 33% |
| Weight decline at last measurement | | 18% | 11% | 18% | 7% |
| SBP < 140 | | 54% | 36% | 37% | 47% |
| TC < 5.0 | | 26% | 28% | 31% | 33% |
| All targets reached | | 2% | 2% | 3% | 0% |
| \* prior to initiation  \*\* patients received acarbose (n=7) and meglitinides [repaglinide or nateglinide] (n=8) | | | | | |

HbA1c, glycated hemoglobin; OAD, oral antidiabetic drug; SBP, systolic blood pressure; SD, standard deviation; SU, sulphonylurea; TC, total cholesterol; TZD, thiazolidinedione.

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Table 2: Results of dual therapy analysis by OAD

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Patient Characteristics** | **metformin + SU** | **SU + metformin** | **metformin + TZD** | **Other combinations\*\*** |
| Number of patients (% ) | 4,001 (55.34) | 1,549 (21.42) | 1,500 (20.75) | 180 (2.49) |
| Age (years, SD) | 62.00 (11.54) | 67.66 (11.54) | 59.66 (10.96) | 69.23 (12.36) |
| Sex (% male) | 60.03 | 62.36 | 59.40 | 59.44 |
| Lipid lowering therapy (%)\* | 81.28 | 74.95 | 82.80 | 74.44 |
| Blood pressure tablets (%)\* | 74.28 | 75.40 | 75.80 | 77.78 |
| **HbA1c (%)** | | | | |
| Prior to initiation, mean (SD) | 8.49 (1.36) | 8.54 (1.23) | 8.35 (1.09) | 8.77 (1.41) |
| After initiation, mean (SD) | 7.37 (1.24) | 7.48 (1.20) | 7.30 (1.18) | 7.46 (0.97) |
| Difference  mean (SD) (*P*-value) | -1.13 (0.04) (<0.001) | -1.06 (0.05) (<0.001) | -1.05 (0.05) (<0.001) | -1.31 (0.16) (<0.001) |
| Gradient prior to initiation | - | + | + | + |
| Gradient after initiation | - | - | - | - |
| Combined gradient | - | - | - | - |
| *P*-value (difference) | <0.001 | <0.001 | <0.001 | <0.001 |
| **Weight (Kg)** | | | | |
| Prior to initiation, mean (SD) | 91.38 (18.61) | 79.84 (15.30) | 96.70  (19.72) | 78.11  (17.10) |
| After initiation,  mean (SD) | 92.66 (19.40) | 79.08 (15.47) | 98.44  (20.51) | 79.40  (17.06) |
| Difference,  mean (SD) (*P*-value) | 1.28 (0.60) (0.033) | -0.76 (0.83) (0.363) | 1.75 (0.99) (0.078) | 1.29 (2.57) (0.618) |
| Gradient prior to initiation | - | + | - | + |
| Gradient after initiation | + | + | + | - |
| Combined gradient | + | + | + | + |
| *P*-value (difference) | 0.469 | 0.331 | 0.311 | 0.479 |
| **SBP** | | | | |
| Prior to initiation, mean (SD) | 136.44 (137.20) | 136.45 (16.84) | 136.14 (14.77) | 135.99  (16.79) |
| After initiation,  mean (SD) | 137.20 (15.90) | 136.78 (17.35) | 135.44 (15.81) | 139.12  (18.35) |
| Difference,  mean (SD) (*P*-value) | 0.76 (0.42) (0.066) | 0.33 (0.74) (0.658) | -0.69 (0.66) (0.287) | 3.21 (2.17) (0.141) |
| Gradient prior to initiation | - | - | - | - |
| Gradient after initiation | - | - | - | - |
| Combined gradient | - | - | - | - |
| *P*-value (difference) | <0.001 | 0.076 | 0.571 | 0.797 |
| **TC** | | | | |
| Prior to initiation, mean (SD) | 4.24 (0.96) | 4.25 (0.82) | 4.17 (0.95) | 4.45 (1.12) |
| After initiation,  mean (SD) | 4.03 (0.92) | 4.00 (0.85) | 4.17 (0.91) | 4.24 (0.88) |
| Difference,  mean (SD) (*P*-value) | -0.21 (0.03) (<0.001) | -0.25 (0.04) (<0.001) | 0.004 (0.05) (0.940) | -0.21 (0.16) (0.181) |
| Gradient prior to initiation | - | - | - | - |
| Gradient after initiation | - | - | - | - |
| Combined gradient | - | - | - | - |
| *P*-value (difference) | 0.004 | 0.598 | 0.168 | 0.699 |
| **Targets** | | | | |
| Proportion of subjects (mean): | | | | |
| HbA1c < 7.5% | 57% | 53% | 56% | 53% |
| Weight decline at last measurement | 31% | 39% | 31% | 34% |
| SBP < 140 | 52% | 53% | 57% | 49% |
| TC < 5.0 | 40% | 42% | 42% | 37% |
| All targets reached | 6% | 7% | 7% | 2% |
| \* prior to initiation  \*\* patients received SU + TZD (n=144), TZD + metformin (n=15), TZD + SU (n=7), meglitinide + metformin (n=7), acarbose + metformin (n=3), metformin + acarbose (n=3), meglitinide + SU (n=1) | | | | |

HbA1c, glycated hemoglobin; OAD, oral antidiabetic drug; SBP, systolic blood pressure; SD, standard deviation; SU, sulphonylurea; TC, total cholesterol; TZD, thiazolidinedione.

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Table 3: Results of triple therapy analysis by OAD

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Patient Characteristics** | **metformin + SU + TZD** | **SU + metformin + TZD** | **metformin +**  **TZD + SU** | **Other combinations\*\*** |
| Number of patients (% ) | 655 (40.63) | 573 (35.55) | 272 (16.87) | 112 (6.95) |
| Age (years, SD) | 59.60 (10.56) | 63.50 (11.13) | 55.93 (10.39) | 65.22 (11.93) |
| Sex (% male) | 62.75 | 65.27 | 70.22 | 65.18 |
| Lipid lowering therapy (%)\* | 84.58 | 80.28 | 89.71 | 80.36 |
| Blood pressure tablets (%)\* | 79.24 | 77.66 | 69.85 | 73.21 |
| **HbA1c (%)** | | | | |
| Prior to initiation, mean (SD) | 8.81 (1.20) | 8.62 (1.13) | 8.68 (1.20) | 8.68 (1.41) |
| After initiation, mean (SD) | 7.76 (1.32) | 7.72 (1.24) | 7.35 (1.29) | 7.51 (1.21) |
| Difference  mean (SD) (*P*-value) | -1.05 (0.07) (<0.001) | -0.90 (0.07) (<0.001) | -1.33 (0.12) (<0.001) | -1.17 (0.18) (<0.001) |
| Gradient prior to initiation | + | + | + | + |
| Gradient after initiation | - | - | - | - |
| Combined gradient | - | - | - | - |
| *P*-value (difference) | <0.001 | <0.001 | <0.001 | 0.002 |
| **Weight (Kg)** | | | | |
| Prior to initiation, mean (SD) | 94.81 (19.47) | 82.22 (15.40) | 99.86  (21.84) | 87.50  (17.55) |
| After initiation,  mean (SD) | 97.69 (20.24) | 84.34 (16.34) | 103.49 (23.58) | 87.24  (18.30) |
| Difference,  mean (SD) (*P*-value) | 2.87 (1.26) (0.022) | 2.12 (1.09) (0.052) | 3.63 (2.27) (0.101) | -0.26 (2.87) (0.928) |
| Gradient prior to initiation | + | + | + | + |
| Gradient after initiation | + | + | - | + |
| Combined gradient | + | + | - | + |
| *P*-value (difference) | 0.349 | 0.161 | 0.213 | 0.894 |
| **SBP** | | | | |
| Prior to initiation, mean (SD) | 137.61 (15.66) | 137.15 (15.09) | 134.69 (13.74) | 136.46  (16.94) |
| After initiation,  mean (SD) | 137.13 (15.90) | 134.80 (16.24) | 134.12 (15.18) | 137.37  (17.47) |
| Difference,  mean (SD) (*P*-value) | -0.48 (0.91) (0.599) | -2.35 (0.97) (0.016) | -0.53 (1.33) (0.690) | 0.92 (2.42) (0.705) |
| Gradient prior to initiation | - | - | - | - |
| Gradient after initiation | - | - | - | + |
| Combined gradient | - | - | - | + |
| *P*-value (difference) | 0.023 | 0.032 | 0<0.001 | 0.287 |
| **TC** | | | | |
| Prior to initiation, mean (SD) | 4.10 (0.87) | 4.05 (0.76) | 4.35 (1.09) | 4.30 (0.84) |
| After initiation,  mean (SD) | 4.21 (0.94) | 4.17 (0.86) | 4.10 (0.99) | 3.99 (0.84) |
| Difference,  mean (SD) (*P*-value) | 0.11 (0.06) (0.068) | 0.12 (0.06) (0.027) | 0.25 (0.11) (0.021) | -0.31 (0.13) (0.016) |
| Gradient prior to initiation | - | - | - | - |
| Gradient after initiation | - | - | + | - |
| Combined gradient | - | - | - | - |
| *P*-value (difference) | 0.235 | 0.96 | 0.047 | 0.671 |
| **Targets** | | | | |
| Proportion of subjects (mean): | | | | |
| HbA1c < 7.5% | 42% | 43% | 58% | 54% |
| Weight decline at last measurement | 24% | 25% | 29% | 37% |
| SBP < 140 | 49% | 54% | 55% | 48% |
| TC < 5.0 | 58% | 62% | 58% | 60% |
| All targets reached | 4% | 5% | 8% | 5% |
| \* prior to initiation  \*\* patients received SU + TZD + metformin (n=62), SU + metformin + acarbose (n=15), TZD + metformin + SU (n=12), metformin + SU + acarbose (n=9), TZD + SU + metformin (n=2), SU + TZD + acarbose (n=2), meglitinide + metformin + TZD (n=2), metformin + TZD + acarbose (n=2), metformin + acarbose + SU (n=2), SU + acarbose + metformin (n=1), metformin + acarbose + TZD (n=1), acarbose + SU + metformin (n=1), acarbose + metformin + SU (n=1) | | | | |

HbA1c, glycated hemoglobin; OAD, oral antidiabetic drug; SBP, systolic blood pressure; SD, standard deviation; SU, sulphonylurea; TC, total cholesterol; TZD, thiazolidinedione.

**Electronic Supplementary Material**

Table 4: Results of insulin therapy analysis by number of OADs

|  |  |  |  |
| --- | --- | --- | --- |
| **Patient Characteristics** | **Single OAD** | **Dual OAD** | **Triple OAD** |
| Number of patients (% ) | 4,464 (99.78) | 3,730 (83.37) | 1,358 (30.35) |
| Age (years, SD) | 61.41 (12.84) | 61.55 (12.21) | 60.96 (11.67) |
| Sex (% male) | 56.96 | 57.59 | 61.05 |
| Lipid lowering therapy (%)\* | 79.29 | 82.09 | 84.9 |
| Blood pressure tablets (%)\* | 81.86 | 83.16 | 83.28 |
| **HbA1c (%)** | | | |
| Prior to initiation, mean (SD) | 9.78 (1.94) | 9.75 (1.85) | 9.82 (1.75) |
| After initiation, mean (SD) | 8.31 (1.58) | 8.34 (1.55) | 8.55 (1.54) |
| Difference  mean (SD) (*P*-value) | -1.47 (0.04) (<0.001) | -1.41 (0.04) (<0.001) | -1.26 (0.06) (<0.001) |
| Gradient prior to initiation | + | + | + |
| Gradient after initiation | - | - | - |
| Combined gradient | - | - | - |
| *P*-value (difference) | <0.001 | <0.001 | <0.001 |
| **Weight (Kg)** | | | |
| Prior to initiation, mean (SD) | 87.12 (19.21) | 87.78 (19.03) | 88.19 (18.87) |
| After initiation,  mean (SD) | 89.24 (19.39) | 89.77 (19.20) | 90.15 (19.10) |
| Difference,  mean (SD) (*P*-value) | 2.12 (0.48) (<0.001) | 1.98 (0.50) (0.001) | 1.96 (0.82) (0.017) |
| Gradient prior to initiation | - | - | + |
| Gradient after initiation | + | + | + |
| Combined gradient | + | + | + |
| *P*-value (difference) | 0.349 | 0.161 | 0.213 |
| **SBP** | | | |
| Prior to initiation, mean (SD) | 135.32 (17.40) | 135.68 (17.22) | 135.32 (17.30) |
| After initiation, mean (SD) | 136.39 (17.89) | 136.76 (17.61) | 137.37 (16.85) |
| Difference,  mean (SD) (*P*-value) | 1.07 (0.39) (0.006) | 1.08 (0.42) (0.009) | 2.05 (0.68) (0.002) |
| Gradient prior to initiation | - | - | - |
| Gradient after initiation | - | - | - |
| Combined gradient | - | - | - |
| *P*-value (difference) | 0.045 | 0.023 | 0.920 |
| **TC** | | | |
| Prior to initiation, mean (SD) | 4.41 (1.19) | 4.39 (1.10) | 4.40 (1.13) |
| After initiation,  mean (SD) | 4.13 (1.05) | 4.12 (1.04) | 4.08 (1.05) |
| Difference,  mean (SD) (*P*-value) | -0.28 (0.03) (<0.001) | -0.27 (0.03) (<0.001) | -0.32 (0.05)  (<0.001) |
| Gradient prior to initiation | - | - | - |
| Gradient after initiation | - | - | - |
| Combined gradient | - | - | - |
| *P*-value (difference) | 0.887 | 0.917 | 0.431 |
| **Targets** | | | |
| Proportion of subjects (mean): | | | |
| HbA1c < 7.5% | 26% | 26% | 21% |
| Weight decline at last measurement | 24% | 25% | 25% |
| SBP < 140 | 52% | 52% | 50% |
| TC < 5.0 | 57% | 60% | 64% |
| All targets reached | 3% | 3% | 1% |
| \* prior to initiation | | | |

HbA1c, glycated hemoglobin; OAD, oral antidiabetic drug; SBP, systolic blood pressure; SD, standard deviation; TC, total cholesterol.

**Electronic Supplementary Material**

Table 5: Summary of patients achieving target by OAD cohort and age

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Monotherapy** | **Dual Therapy** | **Triple Therapy** | **Insulin** |
| **Proportion of subjects (mean):** | | | | |
| **Age <70 years** | | | | |
| HbA1c < 7.5% | 24% | 53% | 43% | 24% |
| Weight decline at last measurement | 17% | 32% | 25% | 24% |
| SBP < 140 | 36% | 56% | 52% | 53% |
| TC < 5.0 | 29% | 40% | 58% | 55% |
| All targets reached | 2% | 6% | 5% | 2% |
| **Age >= 70 years** | | | | |
| HbA1c < 7.5% | 33% | 62% | 56% | 31% |
| Weight decline at last measurement | 17% | 34% | 28% | 24% |
| SBP < 140 | 38% | 47% | 48% | 48% |
| TC < 5.0 | 34% | 43% | 65% | 62% |
| All targets reached | 3% | 6% | 6% | 3% |
| \* prior to initiation | | | | |

HbA1c, glycated hemoglobin; OAD, oral antidiabetic drug; SBP, systolic blood pressure; SD, standard deviation; TC, total cholesterol.