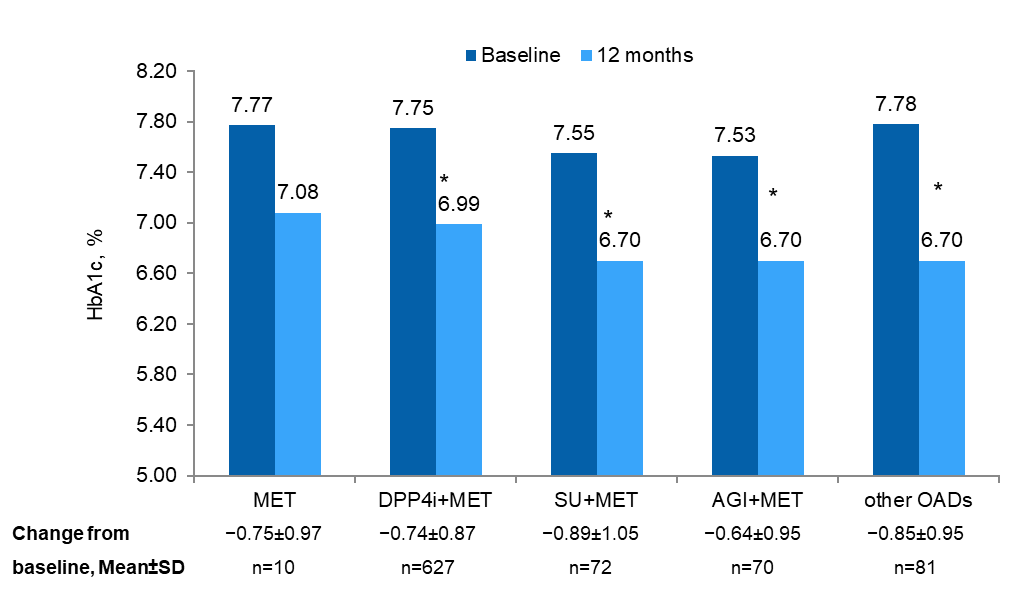
**Figure S1.** Change in HbA1c by OAD class and visit



\*p<0.0001 versus baseline

AGI, alpha-glucosidase inhibitor; DPP-4i, dipeptidyl peptidase-4 inhibitor; HbA1c, glycated hemoglobin; MET, metformin; OAD, oral anti-diabetes drug; SD, standard deviation; SU, sulfonylurea

**Table S1.**Summary statistics of patient characteristics by visit (eligible patients)

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Baseline** | **Month 12** | **Month 24** |
| **HbA1c, %** | 7.72±0.54 | 6.95±0.82 | N/A |
| **Body weight, kg** | 78.70±13.60 | 79.26±13.80 | 78.63±13.64 |
| **BMI, kg/m2** | 29.78±4.66 | 29.98±4.79 | 29.84±4.77 |
| **Vital signs** |  |  |  |
| **Pulse rate, bpm** | 75.64±6.97 | 75.35±6.43 | 74.83±6.21 |
| **Systolic blood pressure, mm Hg** | 134.11±15.33 | 132.73±14.41 | 130.84±14.43 |
| **Diastolic blood pressure, mm Hg** | 77.74±7.39 | 76.62±6.95 | 76.07±7.29 |

BMI, body mass index; bpm, beats per minute; HbA1c, glycated hemoglobin; N/A, not applicable

**Table S2.** DSC-R domains: summary statistics by visit and OAD class

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Score** | **Visit** | **All OADs**  **(N=860)** | **p-value\*** | **MET**  **(n=10)** | **DPP-4i+MET**  **(n=627)** | **SU+MET**  **(n=72)** | **AGI+MET**  **(n=70)** | **Other**  **OADs (n=81)** |
| **Psychological fatigue score** | Baseline | 1.0±1.00 | - | 1.4±1.46 | 1.0±0.98 | 1.0±0.95 | 1.2±1.14 | 0.9±1.02 |
| Month 12 | 0.9±0.93 | 0.0011 | 1.0±1.73 | 0.9±0.95 | 0.8±0.77 | 1.0±0.88 | 0.7±0.97 |
| Month 24 | 0.9±0.92 | 0.0173 | 1.0±1.73 | 0.8±0.92 | 0.9±0.94 | 0.8±0.77 | 0.8±0.95 |
| **Psychological cognitive function score** | Baseline | 0.7±0.85 | - | 1.1±1.33 | 0.7±0.84 | 0.7±0.74 | 0.9±0.93 | 0.6±0.87 |
| Month 212 | 0.6±0.77 | 0.1494 | 0.8±1.44 | 0.6±0.79 | 0.8±0.75 | 0.7±0.76 | 0.6±0.66 |
| Month 24 | 0.6±0.74 | 0.0157 | 0.8±1.44 | 0.6±0.77 | 0.8±0.70 | 0.5±0.67 | 0.4±0.55 |
| **Neuropathic pain score** | Baseline | 0.6±0.83 | - | 0.6±1.31 | 0.6±0.81 | 0.6±0.76 | 0.9±1.04 | 0.6±0.80 |
| Month 12 | 0.5±0.71 | 0.3936 | 0.6±0.63 | 0.5±0.69 | 0.7±0.68 | 0.8±0.89 | 0.5±0.73 |
| Month 24 | 0.5±0.69 | 0.3037 | 0.6±0.96 | 0.5±0.67 | 0.7±0.74 | 0.7±0.75 | 0.5±0.73 |
| **Neuropathic sensory function score** | Baseline | 0.7±0.86 | - | 0.8±1.08 | 0.7±0.82 | 0.7±0.82 | 1.1±1.07 | 0.6±0.87 |
| Month 12 | 0.7±0.74 | 0.1510 | 0.3±0.35 | 0.6±0.72 | 0.8±0.73 | 0.9±0.88 | 0.7±0.76 |
| Month 24 | 0.6±0.72 | 0.1667 | 0.6±0.88 | 0.6±0.69 | 0.8±0.75 | 0.9±0.75 | 0.7±0.82 |
| **Cardiovascular symptoms score** | Baseline | 0.6±0.74 | - | 0.6±0.59 | 0.6±0.69 | 0.6±0.81 | 1.0±0.91 | 0.6±0.77 |
| Month 12 | 0.6±0.65 | 0.1487 | 0.4±0.72 | 0.6±0.62 | 0.7±0.78 | 0.8±0.69 | 0.5±0.66 |
| Month 24 | 0.6±0.64 | 0.0955 | 0.4±0.72 | 0.6±0.60 | 0.8±0.82 | 0.6±0.71 | 0.6±0.69 |
| **Ophthalmological function score** | Baseline | 0.6±0.80 | - | 1.0±1.52 | 0.5±0.74 | 0.6±0.82 | 1.0±0.99 | 0.6±0.89 |
| Month 12 | 0.5±0.71 | 0.0560 | 0.5±0.92 | 0.5±0.70 | 0.7±0.63 | 0.9±0.83 | 0.4±0.65 |
| Month 24 | 0.5±0.66 | 0.0191 | 0.0±0.00 | 0.5±0.68 | 0.7±0.61 | 0.6±0.63 | 0.4±0.57 |
| **Hypoglycemia score** | Baseline | 0.7±0.92 | - | 1.0±1.25 | 0.7±0.90 | 0.8±0.80 | 1.1±0.95 | 0.7±1.01 |
| Month 12 | 0.6±0.76 | 0.0010 | 0.9±1.54 | 0.6±0.76 | 0.7±0.68 | 0.7±0.77 | 0.5±0.73 |
| Month 24 | 0.6±0.75 | 0.0022 | 0.9±1.54 | 0.6±0.76 | 0.8±0.75 | 0.5±0.60 | 0.4±0.70 |
| **Hyperglycemia score** | Baseline | 1.0±0.89 | - | 0.9±0.92 | 0.9±0.89 | 0.9±0.86 | 1.5±0.85 | 1.0±0.90 |
| Month 12 | 0.7±0.75 | <0.0001 | 0.3±0.43 | 0.6±0.75 | 0.8±0.70 | 1.0±0.77 | 0.7±0.73 |
| Month 24 | 0.6±0.69 | <0.0001 | 0.3±0.43 | 0.6±0.68 | 0.8±0.66 | 0.8±0.74 | 0.7±0.68 |
| **Total DSC-R score** | Baseline | 0.7±0.68 | - | 0.9±1.05 | 0.7±0.63 | 0.7±0.69 | 1.1±0.86 | 0.7±0.70 |
| Month 12 | 0.6±0.59 | <0.0001 | 0.6±0.91 | 0.6±0.57 | 0.8±0.64 | 0.9±0.68 | 0.6±0.57 |
| Month 24 | 0.6±0.56 | <0.0001 | 0.5±0.91 | 0.6±0.54 | 0.8±0.69 | 0.7±0.57 | 0.6±0.54 |

Data are expressed as mean±SD

\*Changes versus baseline

AGI, alpha-glucosidase inhibitor; DPP-4i, dipeptidyl peptidase-4 inhibitor; DSC-R, Diabetes Symptom Checklist-Revised; MET, metformin; OAD, oral anti-diabetes drug; SU, sulfonylurea

**Table S3.** EQ-5D dimensions: summary statistics by visit and OAD class

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **Baseline** | | | | | | **Month 12** | | | | | |
|  |  | **MET**  **(n=10)** | **DPP-4i+MET (n=627)** | **SU+MET (n=72)** | **AGI+MET (n=70)** | **Other OADs**  **(n=81)** | **All OADs (N=860)** | **MET**  **(n=4)** | **DPP-4i+MET (n=551)** | **SU+MET (n=63)** | **AGI+MET (n=64)** | **Other OADs**  **(n=81)** | **All OADs (N=756)** |
| **Mobility** | **None** | 5 | 407 | 42 | 37 | 49 | 540 (63.7) | 1 | 352 | 43 | 41 | 47 | 484 (66.9) |
| **Some** | 4 | 210 | 30 | 32 | 32 | 308 (36.3) | 2 | 172 | 16 | 22 | 26 | 238 (32.9) |
| **Extreme** | - | - | - | - | - | - | 0 | 2 | 0 | 0 | 0 | 2 (0.3) |
| **Self-care** | **None** | 8 | 551 | 63 | 56 | 72 | 750 (88.4) | 2 | 462 | 54 | 56 | 63 | 637 (88.1) |
| **Some** | 1 | 64 | 9 | 13 | 8 | 95 (11.2) | 1 | 59 | 5 | 7 | 10 | 82 (11.3) |
| **Extreme** | 0 | 2 | 0 | 0 | 1 | 3 (0.4) | 0 | 4 | 0 | 0 | 0 | 4 (0.6) |
| **Usual activities** | **None** | 8 | 516 | 58 | 57 | 69 | 708 (83.6) | 2 | 432 | 54 | 54 | 61 | 603 (83.4) |
| **Some** | 1 | 92 | 14 | 11 | 10 | 128 (15.1) | 1 | 84 | 5 | 9 | 11 | 110 (15.2) |
| **Extreme** | 0 | 9 | 0 | 1 | 1 | 11 (1.3) | 0 | 9 | 0 | 0 | 1 | 10 (1.4) |
| **Pain/discomfort** | **None** | 4 | 340 | 42 | 29 | 39 | 454 (53.5) | 1 | 317 | 46 | 30 | 38 | 432 (59.8) |
| **Some** | 5 | 262 | 29 | 35 | 40 | 371 (43.8) | 2 | 199 | 12 | 33 | 35 | 281 (38.9) |
| **Extreme** | 0 | 15 | 1 | 5 | 2 | 23 (2.7) | 0 | 9 | 1 | 0 | 0 | 10 (1.4) |
| **Anxiety/depression** | **None** | 4 | 399 | 48 | 36 | 41 | 528 (62.3) | 1 | 366 | 48 | 29 | 47 | 491 (67.8) |
| **Some** | 5 | 194 | 21 | 28 | 36 | 284 (33.5) | 2 | 143 | 10 | 27 | 22 | 204 (28.2) |
| **Extreme** | 0 | 23 | 3 | 5 | 4 | 35 (4.1) | 0 | 17 | 1 | 7 | 4 | 29 (4.0) |

Data are expressed as n or n (%)

AGI, alpha-glucosidase inhibitor; DPP-4i, dipeptidyl peptidase-4 inhibitor; EQ-5D, EuroQol 5 dimensions; MET, metformin; OAD, oral anti-diabetes drug; SU, sulfonylurea

**Table S4.**TSQM-9: summary statistics by visit and OAD class (eligible patients)

|  |  | **Baseline**  **(N=860)** | **Month 12**  **(N=756)** | | **Month 24**  **(N=664)** | |
| --- | --- | --- | --- | --- | --- | --- |
| **Score** | **Score** | **p-value\*** | **Score** | **p-value\*** |
| **MET** | **Effectiveness** | 62.4±12.04 | 72.2±25.46 | 0.4226 | 77.8±19.25 | 0.5000 |
| **Convenience** | 69.8±12.76 | 61.1±9.62 | 1.0000 | 68.5±3.21 | 0.5000 |
| **Global satisfaction** | 56.5±15.61 | 58.3±16.02 | 1.0000 | 71.3±19.51 | 0.5063 |
| **DPP-4i+MET** | **Effectiveness** | 67.7±16.07 | 74.8±18.06 | <0.0001 | 77.8±17.83 | <0.0001 |
| **Convenience** | 75.1±15.77 | 79.2±14.52 | <0.0001 | 80.4±13.80 | <0.0001 |
| **Global satisfaction** | 62.6±17.63 | 72.3±18.17 | <0.0001 | 74.6±18.49 | <0.0001 |
| **SU+MET** | **Effectiveness** | 63.5±15.81 | 71.5±12.28 | <0.0001 | 78.2±16.32 | <0.0001 |
| **Convenience** | 69.7±14.11 | 75.2±12.45 | 0.0020 | 78.7±14.63 | 0.0197 |
| **Global satisfaction** | 56.0±13.75 | 66.9±12.99 | <0.0001 | 73.4±18.93 | <0.0001 |
| **AGI+MET** | **Effectiveness** | 62.6±15.03 | 63.9±13.56 | 0.1587 | 66.1±10.34 | 0.0126 |
| **Convenience** | 68.3±11.56 | 70.0±9.70 | 0.2104 | 68.7±9.86 | 0.7534 |
| **Global satisfaction** | 52.1±16.78 | 60.1±13.58 | 0.0004 | 61.8±12.81 | <0.0001 |
| **Other OADs** | **Effectiveness** | 60.4±14.01 | 67.0±14.10 | 0.0011 | 68.1±12.42 | 0.0001 |
| **Convenience** | 70.0±13.71 | 69.6±13.00 | 0.6897 | 71.9±11.01 | 0.5779 |
| **Global satisfaction** | 54.7±16.35 | 60.9±16.60 | 0.0005 | 64.0±15.49 | <0.0001 |

Data are expressed as mean±SD

\*Change versus baseline

AGI, alpha-glucosidase inhibitor; DPP-4i, dipeptidyl peptidase-4 inhibitor; MET, metformin; OAD, oral anti-diabetes drug; SU, sulfonylurea; TSQM-9, Treatment Satisfaction Questionnaire of Medication-9

**Table S5.** Number of patients with adverse reaction by SOC

|  | **N=860** |
| --- | --- |
| **At least one adverse drug reaction** | 24 (2.79) |
| **Gastrointestinal disorders** | 14 (1.63) |
| **Investigations** | 4 (0.47) |
| **Skin and subcutaneous tissue disorders** | 3 (0.35) |
| **Ear and labyrinth disorders** | 1 (0.12) |
| **Immune system disorders** | 1 (0.12) |
| **Musculoskeletal and connective tissue disorders** | 1 (0.12) |
| **Nervous system disorders** | 1 (0.12) |
| **Respiratory, thoracic and mediastinal disorders** | 1 (0.12) |

Data are expressed as n (%) of eligible patients with at least one adverse reaction

SOC, system organ class