**APPENDIX**

Table 1. Mean values of self-rated QoL and the three domains (i.e. somatic comorbidities, cognitive functioning and neuropsychiatric symptoms (NPS)) over time

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Baseline  | 1y FU  | 2y FU  | 3y FU  |
| **EQ-5D, M (SD)** | N = 301 | N = 235 | N = 220 | N = 186 |
| VAS total score | 69.4 (15.6) | 72.6 (14.0) | 71.6 (13.9) | 71.7 (15.0) |
| **Cognitive tests, M (SD)** | N = 265-313 | N = 215-245 | N = 198-222 | N = 169-191 |
| VLT (immediate recall) | -1.1 (1.2) | -0.5 (1.3) | -0.9 (1.4) | -0.6 (1.5) |
| Fluency | -0.7 (0.8) | -0.7 (0.9) | -0.8 (1) | -0.8 (1) |
| TMT-A | -0.5 (1.4) | -0.4 (1.5) | -0.4 (1.6) | -0.3 (1.7) |
| TMT-B | -0.7 (1.5) | -0.6 (1.4) | -0.6 (1.5) | -0.5 (1.6) |
| SCWT 1-2 † | -1.1 (1.4) | -1.1 (1.5) | -1.1 (1.5) | -1.2 (1.7) |
| SCWT interference ‡ | -0.7 (1.7) | -0.7 (1.8) | -0.7 (1.8) | -0.6 (1.8) |
| LDST | -0.5 (1.1) | -0.4 (1.2) | -0.4 (1.2) | -0.4 (1.3) |
| MMSE§ | 26.9 (2.6) | 27.0 (2.7) | 26.5 (3.2) | 26.4 (3.6) |
| **Neuropsychiatric symptoms, N (%)** | N = 307-308 | N = 224 | N = 209 | N = 193-195 |
| NPI  |  |  |  |  |
|  Delusions | 18 (6.0) | 6 (2.7) | 6 (2.9) | 5 (2.9) |
|  Hallucinations | 11 (3.6) | 4 (1.8) | 5 (2.4) | 3 (1.7) |
|  Agitation | 61 (20.2) | 33 (14.9) | 26 (12.7) | 28 (16.1) |
|  Depression | 122 (40.4) | 60 (27.1) | 56 (27.3) | 50 (28.7) |
|  Anxiety | 84 (27.8) | 41 (18.6) | 27 (13.2) | 24 (13.8) |
|  Euphoria | 29 (9.6) | 16 (7.2) | 7 (3.4) | 5 (2.9) |
|  Apathy | 132 (43.7) | 76 (34.4) | 65 (31.7) | 61 (35.1) |
|  Disinhibition | 51 (16.9) | 34 (15.4) | 23 (11.2) | 25 (14.4) |
|  Irritability | 156 (51.7) | 84 (38.0) | 79 (38.5) | 68 (39.1) |
|  Aberrant motor behavior | 35 (11.6) | 35 (15.8) | 19 (9.3) | 12 (6.9) |
|  Nighttime behavior disturbances | 82 (27.2) | 40 (18.1) | 32 (15.6) | 36 (20.7) |
|  Appetite and eating abnormalities | 62 (20.5) | 44 (19.9) | 31 (15.1) | 27 (15.5) |
| GDS-15 ¶ |  |  |  |  |
|  Self-reported depression | 63 (20.9) | 31 (14.0) | 30 (14.6) | 26 (14.9) |
| **CIRS categories, N (%)** | N = 315 | N = 246-249 | N = 224 | N = 207-208 |
| Cardiac | 92 (29.2) | 67 (27.2) | 61 (27.4) | 61 (29.5) |
| Vascular | 144 (45.7) | 110 (44.7) | 98 (43.9) | 92 (44.4) |
| Hematopoietic | 12 (3.8) | 6 (2.4) | 12 (5.4) | 7 (3.4) |
| Respiratory | 74 (23.5) | 47 (19.1) | 44 (19.7) | 39 (18.8) |
| Eyes, ears, nose | 54 (17.1) | 38 (15.4) | 50 (22.4) | 36 (17.4) |
| Upper digestive tract | 48 (15.2) | 23 (9.3) | 27 (12.1) | 27 (13.0) |
| Lower digestive tract | 28 (8.9) | 19 (7.7) | 20 (9.0) | 15 (7.2) |
| Liver | 20 (6.3) | 10 (4.1) | 10 (4.5) | 13 (6.3) |
| Kidneys | 15 (4.8) | 9 (3.7) | 6 (2.7) | 6 (2.9) |
| Urogenital | 57 (18.1) | 42 (17.1) | 45 (20.2) | 37 (17.9) |
| Neuromuscular | 40 (12.7) | 41 (16.7) | 42 (18.8) | 41 (19.8) |
| Neurological | 75 (23.8) | 42 (17.1) | 48 (21.5) | 52 (25.1) |
| Endocrine | 49 (15.6) | 36 (14.6) | 31 (13.9) | 30 (14.5) |

N = numbers available. Neuropsychological test scores are presented as z-scores computed using normative means. # computed for those with at least five neuropsychological tests present.

Abbreviations: VAS = Visual Analogue Scale; VLT = Verbal Learning Test; TMT-A = Trail Making Test part A; TMT-B = Trail Making Test part B; SCWT = Stroop Color Word Test; LDST = Letter Digit Substitution Test; MMSE: Mini Mental State Examination; NPI: Neuropsychiatric Inventory; GDS-15: Geriatric Depression Scale-15 items; CIRS: Cumulative Illness Rating Scale.

† SCWT 1–2, average of Stroop Color Word Test card 1 + 2; ‡ SCWT interference index = Stroop Color Word Test card 3 divided by the average of Stroop Color Word Test card 1 + 2; § raw score; ¶ a cut-off score of 6/15 or higher was used;

Table 2. Predicted mean scores of QoL over the course of the study period by status of baseline determinants

|  |  |
| --- | --- |
|  | Time |
|  | Baseline |  | FU1 |  | FU2 |  | FU3 |
|  | Absent | Present |  | Absent | Present |  | Absent | Present |  | Absent | Present |
| *Cognition* |  |  |  |  |  |  |  |  |  |  |  |
| *-* |  |  |  |  |  |  |  |  |  |  |  |
| *Somatic comorbidities* |  |  |  |  |  |  |  |  |  |  |  |
| Eyes/ears/nose comorbidities | 62.1 | 59.2 |  | 67.7 | 65.3 |  | 65.4 | 65.0 |  | 58.8 | 63.1 |
| Lower digestive tract comorbidities | 63.3 | 58.0\* |  | 67.7 | 65.3 |  | 67.0 | 63.4 |  | 65.4 | 56.6\*\* |
| *Neuropsychiatric symptoms* |  |  |  |  |  |  |  |  |  |  |  |
| Agitation  | 59.6 | 61.7 |  | 67.1 | 65.9\* |  | 68.4 | 62.0 |  | 64.5 | 57.4\*\* |
| Appetite and eating abnormalities | 62.9 | 58.4\* |  | 64.9 | 68.1 |  | 65.1 | 65.2 |  | 61.8 | 60.0 |
| Nighttime behavior disturbances | 62.7 | 58.5\*\* |  | 67.1 | 65.9 |  | 64.8 | 65.5 |  | 62.8 | 58.5 |
| Self-reported depression | 67.6 | 53.7\*\* |  | 72.6 | 60.4\*\* |  | 69.4 | 61.0\*\* |  | 67.1 | 54.8\*\* |

Based on random intercept analyses adjusted for age at baseline, sex, education and study center. Predicted mean scores are estimated marginal means of time by group. Key: FU = follow-up. \* *p* < 0.05, \*\* *p* < 0.01 between subjects with baseline determinants present vs. absent