Supplementary Material 4. Supplementary Tables 1-9

Supplementary Table 1. Univariate analysis of response to 1-month treatment (HAD specifics & treatment compliance)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Factor |  | Responder | Non-responder | Total | *P*-value\* |
|  | n=109 (37.85%) | n=179 (62.15%) | n=288 (100%) |  |
| HAD specifics | | | | | |
| HAD-A (anxiety) | None | 71 (65.14) | 103 (57.54) | 174 (60.42) | 0.3206 |
| Mild | 26 (23.85) | 46 (25.70) | 72 (25.00) |  |
| Moderate to severe | 12 (11.01) | 30 (16.76) | 42 (14.58) |  |
| HAD-D (depression) | None | 57 (52.29) | 91 (50.84) | 148 (51.39) | 0.8558 |
| Mild | 37 (33.94) | 59 (32.96) | 96 (33.33) |  |
| Moderate to severe | 15 (13.76) | 29 (16.20) | 44 (15.28) |  |
| Treatment compliance | | | | | |
| Timing of the medication | Before breakfast | 107 (98.17) | 173 (96.64) | 279 (96.87) | 0.3257 |
| Before the largest meal | 1 (0.92) | 3 (1.68) | 4 (1.39) |  |
| Before sleep | 1 (0.92) | 0 | 1 (0.35) |  |
| Etc. | 0 | 3 (1.68) | 4 (1.39) |  |
| Consistency in timing of the medication | No | 1 (0.92) | 6 (3.36) | 7 (2.43) | 0.2588 |
| Yes | 108 (99.08) | 173 (96.64) | 281 (97.57) |  |
| Changes in physical activity | Mean±SD | 15.33±98.06 | -4.18±304.33 | 3.20±247.29 | 0.8525 |
| Median | 0.00 | 0.00 | 0.00 |  |
| Min–Max | -270.00–300.00 | -3330.0–700.00 | -3330.0–700.00 |  |
| Sleep habit | Improved | 43 (39.45) | 50 (27.93) | 93 (32.29) | 0.0960 |
| Unchanged | 51 (46.79) | 93 (51.96) | 144 (50.00) |  |
| Worsened | 15 (13.76) | 36 (20.11) | 51 (17.71) |  |
| Diet habit 1 | Improved | 60 (55.05) | 104 (58.10) | 164 (56.94) | 0.3974 |
| Unchanged | 36 (33.03) | 47 (26.26) | 83 (28.82) |  |
| Worsened | 13 (11.93) | 28 (15.64) | 41 (14.24) |  |
| Diet habit 1 - improvement score | Mean±SD | 1.43±0.70 | 1.42±0.75 | 1.43±0.73 | 0.8708 |
| Median | 2.00 | 2.00 | 2.00 |  |
| Min–Max | 0.00–2.00 | 0.00–2.00 | 0.00–2.00 |  |
| Diet habit 2 | Improved | 58 (53.21) | 90 (50.28) | 148 (51.39) | 0.8210 |
| Unchanged | 38 (34.86) | 69 (38.55) | 107 (37.15) |  |
| Worsened | 13 (11.93) | 20 (11.17) | 33 (11.46) |  |
| Diet habit 2 - improvement score | Mean±SD | 1.41±0.70 | 1.39±0.68 | 1.40±0.69 | 0.7253 |
| Median | 2.00 | 2.00 | 2.00 |  |
| Min–Max | 0.00–2.00 | 0.00–2.00 | 0.00–2.00 |  |
| Diet habit 3 | Improved | 54 (49.54) | 90 (50.28) | 144 (50.00) | 0.7579 |
| Unchanged | 39 (35.78) | 68 (37.99) | 107 (37.15) |  |
| Worsened | 16 (14.68) | 21 (11.73) | 37 (12.85) |  |
| Diet habit 3 - improvement score | Mean±SD | 1.35±0.72 | 1.39±0.69 | 1.37±0.70 | 0.7402 |
| Median | 1.00 | 2.00 | 1.50 |  |
| Min–Max | 0.00–2.00 | 0.00–2.00 | 0.00–2.00 |  |
| Diet habit - total score | Mean±SD | 4.19±1.50 | 4.20±1.48 | 4.20±1.48 | 0.9929 |
| Median | 4.00 | 4.00 | 4.00 |  |
| Min–Max | 0.00–6.00 | 0.00–6.00 | 0.00–6.00 |  |
| Alcohol drinking habit | Improved | 17 (15.60) | 37 (20.67) | 54 (18.75) | 0.5558 |
| Unchanged | 87 (79.82) | 135 (75.42) | 222 (77.08) |  |
| Worsened | 5 (4.59) | 7 (3.91) | 12 (4.17) |  |
| Alcohol drinking habit - Improvement | No | 92 (84.40) | 142 (79.33) | 234 (81.25) | 0.2846 |
| Yes | 17 (15.60) | 37 (20.67) | 54 (18.75) |  |
| Smoking habit | Improved | 11 (10.09) | 27 (15.08) | 38 (13.19) | 0.4615 |
| Unchanged | 96 (88.07) | 149 (83.24) | 245 (85.07) |  |
| Worsened | 2 (1.83) | 3 (1.68) | 5 (1.74) |  |
| Smoking habit - Improvement | No | 98 (89.91) | 152 (84.92) | 250 (86.81) | 0.2247 |
| Yes | 11 (10.09) | 27 (15.08) | 38 (13.19) |  |

Values are presented as number (%) unless otherwise indicated.

HAD, hospital anxiety and depression scale; HAD-A, hospital anxiety and depression scale-anxiety; HAD-D, hospital anxiety and depression scale-depression; SD, standard deviation.

Note 2: Diet habit

Diet habit 1 – no meal or drink 2-3 hours before going to bed

Diet habit 2 – small meal and eating slow

Diet habit 3 – avoid caffeine, soft drinks, chocolate, peppermint, tomato, citrus fruits, greasy food, fried foods, and red wine

Note 3: Physical activity

Combined exercise time of at least moderate to severe intensity or more for at least 10 minutes without any resting period.

\*Chi-square test (or Fisher’s exact test) or independent *t*-test.

Supplementary Table 2. Univariate analysis of response to 1-month treatment (past & current medical history)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Factor |  | Responder | Non-responder | Total | *P*-valuea) |
|  | n=109 (37.85%) | n=179 (62.15%) | n=288 (100%) |  |
| **Past medical history** | | | | | |
| **SOC** | | | | | |
| Larynx | (–) | 108 (99.08) | 178 (99.44) | 286 (99.31) | 1.0000 |
| (+) | 1 (0.92) | 1 (0.56) | 2 (0.69) |  |
| Neurovascular | (–) | 108 (99.08) | 179 (100.00) | 287 (99.65) | 0.3785 |
| (+) | 1 (0.92) | 0 | 1 (0.35) |  |
| Mediastinum | (–) | 109 (100.00) | 178 (99.44) | 287 (99.65) | 1.000 |
| (+) | 0 | 1 (0.56) | 1 (0.35) |  |
| Oral cavity | (–) | 109 (100.00) | 178 (99.44) | 287 (99.65) | 1.0000 |
| (+) | 0 | 1 (0.56) | 1 (0.35) |  |
| Ophthalmology | (–) | 108 (99.08) | 179 (100.00) | 287 (99.65) | 0.3785 |
| (+) | 1 (0.92) | 0 | 1 (0.35) |  |
| **PT** | | | | | |
| Arrhythmia | (–) | 109 (100.00) | 178 (99.44) | 287 (99.65) | 1.0000 |
| (+) | 0 | 1 (0.56) | 1 (0.35) |  |
| Cardiac, anatomical defect | (–) | 109 (100.00) | 178 (99.44) | 287 (99.65) | 1.0000 |
| (+) | 0 | 1 (0.56) | 1 (0.35) |  |
| Pulmonary, inflammation | (–) | 108 (99.08) | 179 (100.00) | 287 (99.65) | 0.3785 |
| (+) | 1 (0.92) | 0 | 1 (0.35) |  |
| Pulmonary, malignant tumor | (–) | 109 (100.00) | 178 (99.44) | 287 (99.65) | 1.0000 |
| (+) | 0 | 1 (0.56) | 1 (0.35) |  |
| Thyroid, benign mass | (–) | 109 (100.00) | 178 (99.44) | 287 (99.65) | 1.0000 |
| (+) | 0 | 1 (0.56) | 1 (0.35) |  |
| Larynx benign tumor | (–) | 108 (99.08) | 178 (99.44) | 286 (99.31) | 1.0000 |
| (+) | 1 (0.92) | 1 (0.56) | 2 (0.69) |  |
| Neurovascular disease | (–) | 108 (99.08) | 179 (100.00) | 287 (99.65) | 0.3785 |
| (+) | 1 (0.92) | 0 | 1 (0.35) |  |
| Mediastinal tumor | (–) | 109 (100.00) | 178 (99.44) | 287 (99.65) | 1.0000 |
| (+) | 0 | 1 (0.56) | 1 (0.35) |  |
| Oral cavity, malignant tumor | (–) | 109 (100.00) | 178 (99.44) | 287 (99.65) | 1.0000 |
| (+) | 0 | 1 (0.56) | 1 (0.35) |  |
| Ophthalmologic disease | (–) | 108 (99.08) | 179 (100.00) | 287 (99.65) | 0.3785 |
| (+) | 1 (0.92) | 0 | 1 (0.35) |  |
| **Current medical history** | | | | | |
| **SOC** | | | | | |
| Gastrointestinal | (–) | 102 (93.58) | 164 (91.62) | 266 (92.36) | 0.5411 |
| (+) | 7 (6.42) | 15 (8.38) | 22 (7.64) |  |
| Larynx | (–) | 109 (100.00) | 178 (99.44) | 287 (99.65) | 1.0000 |
| (+) | 0 | 1 (0.56) | 1 (0.35) |  |
| Neurovascular | (–) | 108 (99.08) | 177 (98.88) | 285 (98.96) | 1.0000 |
| (+) | 1 (0.92) | 2 (1.12) | 3 (1.04) |  |
| Neurology | (–) | 104 (95.41) | 171 (95.53) | 275 (95.49) | 1.0000 |
| (+) | 5 (4.59) | 8 (4.47) | 13 (4.51) |  |
| Urogenital | (–) | 106 (97.25) | 171 (95.53) | 277 (96.18) | 0.5427 |
| (+) | 3 (2.75) | 8 (4.47) | 11 (3.82) |  |
| Gynecology | (–) | 107 (98.17) | 177 (98.88) | 284 (98.61) | 0.6350 |
| (+) | 2 (1.83) | 2 (1.12) | 4 (1.39) |  |
| Oral Cavity | (–) | 109 (100.00) | 177 (98.88) | 286 (99.31) | 0.5279 |
| (+) | 0 | 2 (1.12) | 2 (0.69) |  |
| Neuropsychiatry | (–) | 108 (99.08) | 174 (97.21) | 282 (97.92) | 0.4140 |
| (+) | 1 (0.92) | 5 (2.79) | 6 (2.08) |  |
| Allergy | (–) | 109 (100.00) | 175 (97.77) | 284 (98.61) | 0.3010 |
| (+) | 0 | 4 (2.23) | 4 (1.39) |  |
| Breast | (–) | 109 (100.00) | 177 (98.88) | 286 (99.31) | 0.5279 |
| (+) | 0 | 2 (1.12) | 2 (0.69) |  |
| Musculoskeletal | (–) | 106 (97.25) | 172 (96.09) | 278 (96.53) | 0.7472 |
| (+) | 3 (2.75) | 7 (3.91) | 10 (3.47) |  |
| Renal | (–) | 107 (98.17) | 178 (99.44) | 285 (98.96) | 0.5593 |
| (+) | 2 (1.83) | 1 (0.56) | 3 (1.04) |  |
| URI | (–) | 108 (99.08) | 172 (96.09) | 280 (97.22) | 0.2661 |
| (+) | 1 (0.92) | 7 (3.91) | 8 (2.78) |  |
| Cough | (–) | 108 (99.08) | 174 (97.21) | 282 (97.92) | 0.4140 |
| (+) | 1 (0.92) | 5 (2.79) | 6 (2.08) |  |
| Hematology | (–) | 109 (100.00) | 177 (98.88) | 286 (99.31) | 0.5279 |
| (+) | 0 | 2 (1.12) | 2 (0.69) |  |
| Rheumatology | (–) | 109 (100.00) | 178 (99.44) | 287 (99.65) | 1.0000 |
| (+) | 0 | 1 (0.56) | 1 (0.35) |  |
| Ophthalmology | (–) | 108 (99.08) | 177 (98.88) | 285 (98.96) | 1.0000 |
| (+) | 1 (0.92) | 2 (1.12) | 3 (1.04) |  |
| **PT** | | | | | |
| Coronary disease | (–) | 108 (99.08) | 175 (97.77) | 283 (98.26) | 0.6530 |
| (+) | 1 (0.92) | 4 (2.23) | 5 (1.74) |  |
| Arrhythmia | (–) | 108 (99.08) | 177 (98.88) | 285 (98.96) | 1.0000 |
| (+) | 1 (0.92) | 2 (1.12) | 3 (1.04) |  |
| Cardiac, anatomical defect | (–) | 108 (99.08) | 179 (100.00) | 287 (99.65) | 0.3785 |
| (+) | 1 (0.92) | 0 | 1 (0.35) |  |
| Pulmonary, inflammation | (–) | 109 (100.00) | 177 (98.88) | 286 (99.31) | 0.5279 |
| (+) | 0 | 2 (1.12) | 2 (0.69) |  |
| Pulmonary, benign tumor | (–) | 108 (99.08) | 179 (100.00) | 287 (99.65) | 0.3785 |
| (+) | 1 (0.92) | 0 | 1 (0.35) |  |
| Pulmonary, functional disease | (–) | 108 (99.08) | 178 (99.44) | 286 (99.31) | 1.0000 |
| (+) | 1 (0.92) | 1 (0.56) | 2 (0.69) |  |
| Gastrointestinal, functional disease | (–) | 106 (97.25) | 171 (95.53) | 277 (96.18) | 0.5427 |
| (+) | 3 (2.75) | 8 (4.47) | 11 (3.82) |  |
| Gastrointestinal, inflammatory disease | (–) | 105 (96.33) | 175 (97.77) | 280 (97.22) | 0.4823 |
| (+) | 4 (3.67) | 4 (2.23) | 8 (2.78) |  |
| Gastrointestinal, malignant tumor | (–) | 109 (100.00) | 178 (99.44) | 287 (99.65) | 1.0000 |
| (+) | 0 | 1 (0.56) | 1 (0.35) |  |
| Hepatobiliary inflammatory and functional disease | (–) | 108 (99.08) | 176 (98.32) | 284 (98.61) | 1.0000 |
| (+) | 1 (0.92) | 3 (1.68) | 4 (1.39) |  |
| Hepatobiliary, benign tumor | (–) | 109 (100.00) | 178 (99.44) | 287 (99.65) | 1.0000 |
| (+) | 0 | 1 (0.56) | 1 (0.35) |  |
| Pituitary disease | (–) | 108 (99.08) | 179 (100.00) | 287 (99.65) | 0.3785 |
| (+) | 1 (0.92) | 0 | 1 (0.35) |  |
| Bone disorder with calcium disorder | (–) | 106 (97.25) | 176 (98.32) | 282 (97.92) | 0.6763 |
| (+) | 3 (2.75) | 3 (1.68) | 6 (2.08) |  |
| Thyroid, benign tumor | (–) | 108 (99.08) | 177 (98.88) | 285 (98.96) | 1.0000 |
| (+) | 1 (0.92) | 2 (1.12) | 3 (1.04) |  |
| Thyroid, malignant tumor | (–) | 105 (96.33) | 164 (91.62) | 269 (93.40) | 0.1183 |
| (+) | 4 (3.67) | 15 (8.38) | 19 (6.60) |  |
| Thyroid, functional disorder | (–) | 108 (99.08) | 174 (97.21) | 282 (97.92) | 0.4140 |
| (+) | 1 (0.92) | 5 (2.79) | 6 (2.08) |  |
| Larynx, functional disorder | (–) | 109 (100.00) | 178 (99.44) | 287 (99.65) | 1.0000 |
| (+) | 0 | 1 (0.56) | 1 (0.35) |  |
| Neurovascular, structural disease | (–) | 108 (99.08) | 177 (98.88) | 285 (98.96) | 1.0000 |
| (+) | 1 (0.92) | 2 (1.12) | 3 (1.04) |  |
| Cerebrovascular infarct | (–) | 107 (98.17) | 177 (98.88) | 284 (98.61) | 0.6350 |
| (+) | 2 (1.83) | 2 (1.12) | 4 (1.39) |  |
| Neurodegenerative disease | (–) | 107 (98.17) | 179 (100.00) | 286 (99.31) | 0.1424 |
| (+) | 2 (1.83) | 0 | 2 (0.69) |  |
| Neurologic functional disorder | (–) | 107 (98.17) | 173 (96.65) | 280 (97.22) | 0.7145 |
| (+) | 2 (1.83) | 6 (3.35) | 8 (2.78) |  |
| Urogenital, functional disorder | (–) | 108 (99.08) | 176 (98.32) | 284 (98.61) | 1.0000 |
| (+) | 1 (0.92) | 3 (1.68) | 4 (1.39) |  |
| Urogenital inflammation | (–) | 107 (98.17) | 179 (100.00) | 286 (99.31) | 0.1424 |
| (+) | 2 (1.83) | 0 | 2 (0.69) |  |
| Benign prostate hyperplasia | (–) | 108 (99.08) | 174 (97.21) | 282 (97.92) | 0.4140 |
| (+) | 1 (0.92) | 5 (2.79) | 6 (2.08) |  |
| Gynecology, benign tumor | (–) | 107 (98.17) | 177 (98.88) | 284 (98.61) | 0.6350 |
| (+) | 2 (1.83) | 2 (1.12) | 4 (1.39) |  |
| Oral cavity, inflammation | (–) | 109 (100.00) | 177 (98.88) | 286 (99.31) | 0.5279 |
| (+) | 0 | 2 (1.12) | 2 (0.69) |  |
| Depression | (–) | 108 (99.08) | 176 (98.32) | 284 (98.61) | 1.0000 |
| (+) | 1 (0.92) | 3 (1.68) | 4 (1.39) |  |
| Other neuropsychiatry disorder | (–) | 109 (100.00) | 177 (98.88) | 286 (99.31) | 0.5279 |
| (+) | 0 | 2 (1.12) | 2 (0.69) |  |
| Allergy | (–) | 109 (100.00) | 175 (97.77) | 284 (98.61) | 0.3010 |
| (+) | 0 | 4 (2.23) | 4 (1.39) |  |
| Breast malignant mass | (–) | 109 (100.00) | 177 (98.88) | 286 (99.31) | 0.5279 |
| (+) | 0 | 2 (1.12) | 2 (0.69) |  |
| Musculoskeletal inflammatory disease | (–) | 108 (99.08) | 176 (98.32) | 284 (98.61) | 1.0000 |
| (+) | 1 (0.92) | 3 (1.68) | 4 (1.39) |  |
| Degenerative musculoskeletal disease | (–) | 106 (97.25) | 175 (97.77) | 281 (97.57) | 1.0000 |
| (+) | 3 (2.75) | 4 (2.23) | 7 (2.43) |  |
| Renal functional disorder | (–) | 107 (98.17) | 178 (99.44) | 285 (98.96) | 0.5593 |
| (+) | 2 (1.83) | 1 (0.56) | 3 (1.04) |  |
| Upper respiratory infection | (–) | 108 (99.08) | 172 (96.09) | 280 (97.22) | 0.2661 |
| (+) | 1 (0.92) | 7 (3.91) | 8 (2.78) |  |
| Cough | (–) | 108 (99.08) | 174 (97.21) | 282 (97.92) | 0.4140 |
| (+) | 1 (0.92) | 5 (2.79) | 6 (2.08) |  |
| Hematologic disease | (–) | 109 (100.00) | 177 (98.88) | 286 (99.31) | 0.5279 |
| (+) | 0 | 2 (1.12) | 2 (0.69) |  |
| Rheumatic disease | (–) | 109 (100.00) | 178 (99.44) | 287 (99.65) | 1.0000 |
| (+) | 0 | 1 (0.56) | 1 (0.35) |  |
| Ophthalmologic disease | (–) | 108 (99.08) | 177 (98.88) | 285 (98.96) | 1.0000 |
| (+) | 1 (0.92) | 2 (1.12) | 3 (1.04) |  |

SOC, systemic organ class; PT, preferred term.

a)Chi-square test or Fisher’s exact test.

Supplementary Table 3. Univariate analysis of response to 1-month treatment (past & current medication history)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Factor |  | Responder | Non-responder | Total | *P*-valuea) |
|  | n=109 (37.85%) | n=179 (62.15%) | n=288 (100%) |  |
| **Past medication history** | | | | | |
| **AC** | | | | | |
| Gastrointestinal | (–) | 98 (89.91) | 158 (88.27) | 256 (88.89) | 0.6675 |
| (+) | 11 (10.09) | 21 (11.73) | 32 (11.11) |  |
| Systemic acting drugs | (–) | 103 (94.50) | 170 (94.97) | 273 (94.79) | 0.8598 |
| (+) | 6 (5.50) | 9 (5.03) | 15 (5.21) |  |
| Neuropsychiatry | (–) | 107 (98.17) | 171 (95.53) | 278 (96.53) | 0.3283 |
| (+) | 2 (1.83) | 8 (4.47) | 10 (3.47) |  |
| Neurology | (–) | 103 (94.50) | 165 (92.18) | 268 (93.06) | 0.4532 |
| (+) | 6 (5.50) | 14 (7.82) | 20 (6.94) |  |
| Allergy | (–) | 109 (100.00) | 173 (96.65) | 282 (97.92) | 0.0863 |
| (+) | 0 | 6 (3.35) | 6 (2.08) |  |
| Urogenital | (–) | 109 (100.00) | 173 (96.65) | 282 (97.92) | 0.0863 |
| (+) | 0 | 6 (3.35) | 6 (2.08) |  |
| Female hormonal | (–) | 107 (98.17) | 175 (97.77) | 282 (97.92) | 1.0000 |
| (+) | 2 (1.83) | 4 (2.23) | 6 (2.08) |  |
| Musculoskeletal | (–) | 107 (98.17) | 177 (98.88) | 284 (98.61) | 0.6350 |
| (+) | 2 (1.83) | 2 (1.12) | 4 (1.39) |  |
| Salivary gland | (–) | 109 (100.00) | 178 (99.44) | 287 (99.65) | 1.0000 |
| (+) | 0 | 1 (0.56) | 1 (0.35) |  |
| Nutritional supplement | (–) | 106 (97.25) | 173 (96.65) | 279 (96.88) | 1.0000 |
| (+) | 3 (2.75) | 6 (3.35) | 9 (3.13) |  |
| Rheumatology | (–) | 109 (100.00) | 178 (99.44) | 287 (99.65) | 1.0000 |
| (+) | 0 | 1 (0.56) | 1 (0.35) |  |
| Others | (–) | 108 (99.08) | 176 (98.32) | 284 (98.61) | 1.0000 |
| (+) | 1 (0.92) | 3 (1.68) | 4 (1.39) |  |
| **TC** | | | | | |
| Anticoagulant | (–) | 102 (93.58) | 169 (94.41) | 271 (94.10) | 0.7705 |
| (+) | 7 (6.42) | 10 (5.59) | 17 (5.90) |  |
| Vasodilator, anti-angina | (–) | 109 (100.00) | 175 (97.77) | 284 (98.61) | 0.3010 |
| (+) | 0 | 4 (2.23) | 4 (1.39) |  |
| Anti-arrhythmic | (–) | 108 (99.08) | 179 (100.00) | 287 (99.65) | 0.3785 |
| (+) | 1 (0.92) | 0 | 1 (0.35) |  |
| Antitussive | (–) | 108 (99.08) | 176 (98.32) | 284 (98.61) | 1.0000 |
| (+) | 1 (0.92) | 3 (1.68) | 4 (1.39) |  |
| Bronchodilator | (–) | 109 (100.00) | 178 (99.44) | 287 (99.65) | 1.0000 |
| (+) | 0 | 1 (0.56) | 1 (0.35) |  |
| Gastrointestinal protectant | (–) | 105 (96.33) | 170 (94.97) | 275 (95.49) | 0.7722 |
| (+) | 4 (3.67) | 9 (5.03) | 13 (4.51) |  |
| Gastrointestinal, promotility agent | (–) | 106 (97.25) | 172 (96.09) | 278 (96.53) | 0.7472 |
| (+) | 3 (2.75) | 7 (3.91) | 10 (3.47) |  |
| H2 blocker | (–) | 108 (99.08) | 173 (96.65) | 281 (97.57) | 0.2596 |
| (+) | 1 (0.92) | 6 (3.35) | 7 (2.43) |  |
| Proton pump inhibitor | (–) | 104 (95.41) | 171 (95.53) | 275 (95.49) | 1.0000 |
| (+) | 5 (4.59) | 8 (4.47) | 13 (4.51) |  |
| Laxative | (–) | 108 (99.08) | 175 (97.77) | 283 (98.26) | 0.6530 |
| (+) | 1 (0.92) | 4 (2.23) | 5 (1.74) |  |
| Gastrointestinal, spasmolytic | (–) | 109 (100.00) | 178 (99.44) | 287 (99.65) | 1.0000 |
| (+) | 0 | 1 (0.56) | 1 (0.35) |  |
| Antiemetic | (–) | 109 (100.00) | 178 (99.44) | 287 (99.65) | 1.0000 |
| (+) | 0 | 1 (0.56) | 1 (0.35) |  |
| Non-steroidal anti-inflammatory drug | (–) | 106 (97.25) | 177 (98.88) | 283 (98.26) | 0.3703 |
| (+) | 3 (2.75) | 2 (1.12) | 5 (1.74) |  |
| Steroid | (–) | 106 (97.25) | 178 (99.44) | 284 (98.61) | 0.1537 |
| (+) | 3 (2.75) | 1 (0.56) | 4 (1.39) |  |
| Antibiotic | (–) | 109 (100.00) | 174 (97.21) | 283 (98.26) | 0.1606 |
| (+) | 0 | 5 (2.79) | 5 (1.74) |  |
| Acetaminophen | (–) | 108 (99.08) | 178 (99.44) | 286 (99.31) | 1.0000 |
| (+) | 1 (0.92) | 1 (0.56) | 2 (0.69) |  |
| Anti-anxiety, benzodiazepine | (–) | 108 (99.08) | 173 (96.65) | 281 (97.57) | 0.2596 |
| (+) | 1 (0.92) | 6 (3.35) | 7 (2.43) |  |
| Anti-depressant, serotonin-norepinephrine reuptake inhibitor | (–) | 108 (99.08) | 178 (99.44) | 286 (99.31) | 1.0000 |
| (+) | 1 (0.92) | 1 (0.56) | 2 (0.69) |  |
| Anti-depressant, selective serotonin reuptake inhibitor | (–) | 109 (100.00) | 177 (98.88) | 286 (99.31) | 0.5279 |
| (+) | 0 | 2 (1.12) | 2 (0.69) |  |
| Tricyclic antidepressant | (–) | 108 (99.08) | 177 (98.88) | 285 (98.96) | 1.0000 |
| (+) | 1 (0.92) | 2 (1.12) | 3 (1.04) |  |
| Neurology, anticoagulant | (–) | 104 (95.41) | 169 (94.41) | 273 (94.79) | 0.7112 |
| (+) | 5 (4.59) | 10 (5.59) | 15 (5.21) |  |
| Peripheral vasoactive agent | (–) | 109 (100.00) | 177 (98.88) | 286 (99.31) | 0.5279 |
| (+) | 0 | 2 (1.12) | 2 (0.69) |  |
| Neurodegenerative suppressant | (–) | 108 (99.08) | 177 (98.88) | 285 (98.96) | 1.0000 |
| (+) | 1 (0.92) | 2 (1.12) | 3 (1.04) |  |
| Opioid analgesic | (–) | 109 (100.00) | 178 (99.44) | 287 (99.65) | 1.0000 |
| (+) | 0 | 1 (0.56) | 1 (0.35) |  |
| Antiepileptic | (–) | 109 (100.00) | 178 (99.44) | 287 (99.65) | 1.0000 |
| (+) | 0 | 1 (0.56) | 1 (0.35) |  |
| Neuropathic analgesic | (–) | 109 (100.00) | 178 (99.44) | 287 (99.65) | 1.0000 |
| (+) | 0 | 1 (0.56) | 1 (0.35) |  |
| Intra-nasal steroid | (–) | 109 (100.00) | 177 (98.88) | 286 (99.31) | 0.5279 |
| (+) | 0 | 2 (1.12) | 2 (0.69) |  |
| Antihistamine | (–) | 109 (100.00) | 175 (97.77) | 284 (98.61) | 0.3010 |
| (+) | 0 | 4 (2.23) | 4 (1.39) |  |
| Leukotriene inhibitor | (–) | 109 (100.00) | 176 (98.32) | 285 (98.96) | 0.2918 |
| (+) | 0 | 3 (1.68) | 3 (1.04) |  |
| Diuretics | (–) | 107 (98.17) | 178 (99.44) | 285 (98.96) | 0.5593 |
| (+) | 2 (1.83) | 1 (0.56) | 3 (1.04) |  |
| 5α-reductase inhibitor | (–) | 109 (100.00) | 177 (98.88) | 286 (99.31) | 0.5279 |
| (+) | 0 | 2 (1.12) | 2 (0.69) |  |
| Alpha blocker | (–) | 109 (100.00) | 176 (98.32) | 285 (98.96) | 0.2918 |
| (+) | 0 | 3 (1.68) | 3 (1.04) |  |
| Phosphodiesterase-5 inhibitor | (–) | 109 (100.00) | 177 (98.88) | 286 (99.31) | 0.5279 |
| (+) | 0 | 2 (1.12) | 2 (0.69) |  |
| Female hormonal supplement | (–) | 107 (98.17) | 175 (97.77) | 282 (97.92) | 1.0000 |
| (+) | 2 (1.83) | 4 (2.23) | 6 (2.08) |  |
| Anti-hyperlipidemic | (–) | 103 (94.50) | 166 (92.74) | 269 (93.40) | 0.5600 |
| (+) | 6 (5.50) | 13 (7.26) | 19 (6.60) |  |
| Osteoporosis | (–) | 106 (97.25) | 173 (96.65) | 279 (96.88) | 1.0000 |
| (+) | 3 (2.75) | 6 (3.35) | 9 (3.13) |  |
| Muscle relaxant | (–) | 107 (98.17) | 178 (99.44) | 285 (98.96) | 0.5593 |
| (+) | 2 (1.83) | 1 (0.56) | 3 (1.04) |  |
| Sialogogue | (–) | 109 (100.00) | 178 (99.44) | 287 (99.65) | 1.0000 |
| (+) | 0 | 1 (0.56) | 1 (0.35) |  |
| Nutritional supplement | (–) | 106 (97.25) | 173 (96.65) | 279 (96.88) | 1.0000 |
| (+) | 3 (2.75) | 6 (3.35) | 9 (3.13) |  |
| Anti-rheumatic | (–) | 109 (100.00) | 178 (99.44) | 287 (99.65) | 1.0000 |
| (+) | 0 | 1 (0.56) | 1 (0.35) |  |
| Others | (–) | 108 (99.08) | 176 (98.32) | 284 (98.61) | 1.0000 |
| (+) | 1 (0.92) | 3 (1.68) | 4 (1.39) |  |
| **Current medication** | | | | | |
| **AC** | | | | | |
| Pulmonary | (–) | 90 (82.57) | 144 (80.45) | 234 (81.25) | 0.6545 |
| (+) | 19 (17.43) | 35 (19.55) | 54 (18.75) |  |
| Gastrointestinal | (–) | 82 (75.23) | 133 (74.30) | 215 (74.65) | 0.8607 |
| (+) | 27 (24.77) | 46 (25.70) | 73 (25.35) |  |
| Systemic acting drugs | (–) | 97 (88.99) | 157 (87.71) | 254 (88.19) | 0.7438 |
| (+) | 12 (11.01) | 22 (12.29) | 34 (11.81) |  |
| Neuropsychiatry | (–) | 107 (98.17) | 172 (96.09) | 279 (96.88) | 0.4906 |
| (+) | 2 (1.83) | 7 (3.91) | 9 (3.13) |  |
| Neurology | (–) | 102 (93.58) | 163 (91.06) | 265 (92.01) | 0.4448 |
| (+) | 7 (6.42) | 16 (8.94) | 23 (7.99) |  |
| Allergy | (–) | 105 (96.33) | 170 (94.97) | 275 (95.49) | 0.7722 |
| (+) | 4 (3.67) | 9 (5.03) | 13 (4.51) |  |
| Urogenital | (–) | 109 (100.00) | 176 (98.32) | 285 (98.96) | 0.2918 |
| (+) | 0 | 3 (1.68) | 3 (1.04) |  |
| Female hormonal | (–) | 107 (98.17) | 174 (97.21) | 281 (97.57) | 0.7134 |
| (+) | 2 (1.83) | 5 (2.79) | 7 (2.43) |  |
| Musculoskeletal | (–) | 108 (99.08) | 175 (97.77) | 283 (98.26) | 0.6530 |
| (+) | 1 (0.92) | 4 (2.23) | 5 (1.74) |  |
| Nutritional supplement | (–) | 106 (97.25) | 167 (93.30) | 273 (94.79) | 0.1432 |
| (+) | 3 (2.75) | 12 (6.70) | 15 (5.21) |  |
| Rheumatology | (–) | 109 (100.00) | 178 (99.44) | 287 (99.65) | 1.0000 |
| (+) | 0 | 1 (0.56) | 1 (0.35) |  |
| Others | (–) | 108 (99.08) | 172 (96.09) | 280 (97.22) | 0.2661 |
| (+) | 1 (0.92) | 7 (3.91) | 8 (2.78) |  |
| **TC** | | | | | |
| Anticoagulant | (–) | 104 (95.41) | 173 (96.65) | 277 (96.18) | 0.7528 |
| (+) | 5 (4.59) | 6 (3.35) | 11 (3.82) |  |
| Vasodilator, anti-angina | (–) | 109 (100.00) | 177 (98.88) | 286 (99.31) | 0.5279 |
| (+) | 0 | 2 (1.12) | 2 (0.69) |  |
| Anti-arrhythmic | (–) | 107 (98.17) | 179 (100.00) | 286 (99.31) | 0.1424 |
| (+) | 2 (1.83) | 0 | 2 (0.69) |  |
| Mucoactive | (–) | 91 (83.49) | 145 (81.01) | 236 (81.94) | 0.5955 |
| (+) | 18 (16.51) | 34 (18.99) | 52 (18.06) |  |
| Antitussive | (–) | 108 (99.08) | 177 (98.88) | 285 (98.96) | 1.0000 |
| (+) | 1 (0.92) | 2 (1.12) | 3 (1.04) |  |
| Bronchodilator | (–) | 108 (99.08) | 177 (98.88) | 285 (98.96) | 1.0000 |
| (+) | 1 (0.92) | 2 (1.12) | 3 (1.04) |  |
| Gastrointestinal protectant | (–) | 105 (96.33) | 165 (92.18) | 270 (93.75) | 0.1581 |
| (+) | 4 (3.67) | 14 (7.82) | 18 (6.25) |  |
| Gastrointestinal, promotility agent | (–) | 93 (85.32) | 150 (83.80) | 243 (84.38) | 0.7300 |
| (+) | 16 (14.68) | 29 (16.20) | 45 (15.63) |  |
| H2 blocker | (–) | 107 (98.17) | 171 (95.53) | 278 (96.53) | 0.3283 |
| (+) | 2 (1.83) | 8 (4.47) | 10 (3.47) |  |
| Laxative | (–) | 108 (99.08) | 172 (96.09) | 280 (97.22) | 0.2661 |
| (+) | 1 (0.92) | 7 (3.91) | 8 (2.78) |  |
| Gastrointestinal, spasmolytic | (–) | 108 (99.08) | 176 (98.32) | 284 (98.61) | 1.0000 |
| (+) | 1 (0.92) | 3 (1.68) | 4 (1.39) |  |
| Non-steroidal anti-inflammatory drug | (–) | 103 (94.50) | 168 (93.85) | 271 (94.10) | 0.8230 |
| (+) | 6 (5.50) | 11 (6.15) | 17 (5.90) |  |
| Steroid | (–) | 106 (97.25) | 175 (97.77) | 281 (97.57) | 1.0000 |
| (+) | 3 (2.75) | 4 (2.23) | 7 (2.43) |  |
| Antibiotic | (–) | 106 (97.25) | 169 (94.41) | 275 (95.49) | 0.3825 |
| (+) | 3 (2.75) | 10 (5.59) | 13 (4.51) |  |
| Acetaminophen | (–) | 107 (98.17) | 175 (97.77) | 282 (97.92) | 1.0000 |
| (+) | 2 (1.83) | 4 (2.23) | 6 (2.08) |  |
| Anti-anxiety, benzodiazepine | (–) | 108 (99.08) | 173 (96.65) | 281 (97.57) | 0.2596 |
| (+) | 1 (0.92) | 6 (3.35) | 7 (2.43) |  |
| Anti-depressant, serotonin-norepinephrine reuptake inhibitor | (–) | 108 (99.08) | 179 (100.00) | 287 (99.65) | 0.3785 |
| (+) | 1 (0.92) | 0 | 1 (0.35) |  |
| Anti-depressant, selective serotonin reuptake inhibitor | (–) | 109 (100.00) | 177 (98.88) | 286 (99.31) | 0.5279 |
| (+) | 0 | 2 (1.12) | 2 (0.69) |  |
| Tricyclic antidepressant | (–) | 108 (99.08) | 177 (98.88) | 285 (98.96) | 1.0000 |
| (+) | 1 (0.92) | 2 (1.12) | 3 (1.04) |  |
| Neurology, anticoagulant | (–) | 104 (95.41) | 173 (96.65) | 277 (96.18) | 0.7528 |
| (+) | 5 (4.59) | 6 (3.35) | 11 (3.82) |  |
| Peripheral vasoactive agent | (–) | 109 (100.00) | 175 (97.77) | 284 (98.61) | 0.3010 |
| (+) | 0 | 4 (2.23) | 4 (1.39) |  |
| Neurodegenerative suppressant | (–) | 108 (99.08) | 177 (98.88) | 285 (98.96) | 1.0000 |
| (+) | 1 (0.92) | 2 (1.12) | 3 (1.04) |  |
| Opioid analgesic | (–) | 108 (99.08) | 176 (98.32) | 284 (98.61) | 1.0000 |
| (+) | 1 (0.92) | 3 (1.68) | 4 (1.39) |  |
| Antiepileptic | (–) | 109 (100.00) | 178 (99.44) | 287 (99.65) | 1.0000 |
| (+) | 0 | 1 (0.56) | 1 (0.35) |  |
| Neuropathic analgesic | (–) | 108 (99.08) | 179 (100.00) | 287 (99.65) | 0.3785 |
| (+) | 1 (0.92) | 0 | 1 (0.35) |  |
| Intra-nasal steroid | (–) | 107 (98.17) | 176 (98.32) | 283 (98.26) | 1.0000 |
| (+) | 2 (1.83) | 3 (1.68) | 5 (1.74) |  |
| Antihistamine | (–) | 106 (97.25) | 173 (96.65) | 279 (96.88) | 1.0000 |
| (+) | 3 (2.75) | 6 (3.35) | 9 (3.13) |  |
| Leukotriene inhibitor | (–) | 109 (100.00) | 176 (98.32) | 285 (98.96) | 0.2918 |
| (+) | 0 | 3 (1.68) | 3 (1.04) |  |
| Diuretics | (–) | 108 (99.08) | 177 (98.88) | 285 (98.96) | 1.0000 |
| (+) | 1 (0.92) | 2 (1.12) | 3 (1.04) |  |
| 5α-reductase inhibitor | (–) | 109 (100.00) | 177 (98.88) | 286 (99.31) | 0.5279 |
| (+) | 0 | 2 (1.12) | 2 (0.69) |  |
| Alpha blocker | (–) | 109 (100.00) | 177 (98.88) | 286 (99.31) | 0.5279 |
| (+) | 0 | 2 (1.12) | 2 (0.69) |  |
| Phosphodiesterase-5 inhibitor | (–) | 109 (100.00) | 178 (99.44) | 287 (99.65) | 1.0000 |
| (+) | 0 | 1 (0.56) | 1 (0.35) |  |
| Female hormonal supplement | (–) | 107 (98.17) | 174 (97.21) | 281 (97.57) | 0.7134 |
| (+) | 2 (1.83) | 5 (2.79) | 7 (2.43) |  |
| Anti-hyperlipidemic | (–) | 104 (95.41) | 166 (92.74) | 270 (93.75) | 0.3630 |
| (+) | 5 (4.59) | 13 (7.26) | 18 (6.25) |  |
| Osteoporosis | (–) | 106 (97.25) | 170 (94.97) | 276 (95.83) | 0.5448 |
| (+) | 3 (2.75) | 9 (5.03) | 12 (4.17) |  |
| Muscle relaxant | (–) | 108 (99.08) | 175 (97.77) | 283 (98.26) | 0.6530 |
| (+) | 1 (0.92) | 4 (2.23) | 5 (1.74) |  |
| Nutritional supplement | (–) | 106 (97.25) | 167 (93.30) | 273 (94.79) | 0.1432 |
| (+) | 3 (2.75) | 12 (6.70) | 15 (5.21) |  |
| Anti-rheumatic | (–) | 109 (100.00) | 178 (99.44) | 287 (99.65) | 1.0000 |
| (+) | 0 | 1 (0.56) | 1 (0.35) |  |
| Others | (–) | 108 (99.08) | 172 (96.09) | 280 (97.22) | 0.2661 |
| (+) | 1 (0.92) | 7 (3.91) | 8 (2.78) |  |

Values are presented as number (%).

AC, anatomical code; TC, therapeutic code.

a)Chi-square test or Fisher’s exact test.

Supplementary Table 4. Univariate analysis of response to 3-months treatment (HAD specifics & treatment compliance)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Factor |  | Responder | Non-responder | Total | *P*-valuea) |
|  | n=162 (68.35%) | n=75 (31.65%) | n=237 (100%) |  |
| HAD specifics | | | | | |
| HAD-A (anxiety) | Normal | 105 (64.81) | 37 (49.33) | 142 (59.92) | 0.0698 |
| Mild | 37 (22.84) | 23 (30.67) | 60 (25.32) |  |
| Moderate to severe | 20 (12.35) | 15 (20.00) | 35 (14.77) |  |
| HAD-D (depression) | Normal | 88 (54.32) | 35 (46.67) | 123 (51.90) | 0.2360 |
| Mild | 53 (32.72) | 24 (32.00) | 77 (32.49) |  |
| Moderate to severe | 21 (12.96) | 16 (21.33) | 37 (15.61) |  |
| Treatment compliance | | | | | |
| Timing of the medication | Before breakfast | 159 (98.15) | 70 (93.33) | 229 (96.62) | 0.1199 |
| Before the largest meal | 1 (0.62) | 3 (4.00) | 4 (1.69) |  |
| Before sleep | 0 | 0 | 0 |  |
| Etc. | 2 (1.23) | 2 (2.67) | 4 (1.69) |  |
| Consistency in timing of the medication | No | 4 (2.47) | 4 (5.33) | 8 (3.38) | 0.6809 |
| Yes | 158 (97.53) | 71 (94.67) | 229 (96.62) |  |
| Changes in physical activity | Mean±SD | 12.44±152.87 | 18.35±165.16 | 14.31±156.54 | 0.6358 |
| Median | 0.00 | 0.00 | 0.00 |  |
| Min–Max | -840.00–700.00 | -440.00–600.00 | -840.00–700.00 |  |
| Sleep habit | Improved | 55 (33.95) | 20 (26.67) | 75 (31.65) | 0.4258 |
| Unchanged | 81 (50.00) | 39 (52.00) | 120 (50.63) |  |
| Worsened | 26 (16.05) | 16 (21.33) | 42 (17.72) |  |
| Diet habit 1 | Improved | 98 (60.49) | 43 (57.33) | 141 (59.49) | 0.0349 |
| Unchanged | 50 (30.86) | 17 (22.67) | 67 (28.27) |  |
| Worsened | 14 (8.64) | 15 (20.00) | 29 (12.24) |  |
| Diet habit 1 - improvement score | Mean±SD | 1.52±0.65 | 1.37±0.80 | 1.47±0.70 | 0.2973 |
| Median | 2.00 | 2.00 | 2.00 |  |
| Min–Max | 0.00–2.00 | 0.00–2.00 | 0.00–2.00 |  |
| Diet habit 2 | Improved | 84 (51.85) | 40 (53.33) | 124 (52.32) | 0.9777 |
| Unchanged | 58 (35.80) | 26 (34.67) | 84 (35.44) |  |
| Worsened | 20 (12.35) | 9 (12.00) | 29 (12.24) |  |
| Diet habit 2 - improvement score | Mean±SD | 1.40±0.70 | 1.41±0.70 | 1.40±0.70 | 0.8413 |
| Median | 2.00 | 2.00 | 2.00 |  |
| Min–Max | 0.00–2.00 | 0.00–2.00 | 0.00–2.00 |  |
| Diet habit 3 | Improved | 79 (48.77) | 40 (53.33) | 119 (50.21) | 0.6988 |
| Unchanged | 60 (37.04) | 27 (36.00) | 87 (36.71) |  |
| Worsened | 23 (14.20) | 8 (10.67) | 31 (13.08) |  |
| Diet habit 3 - improvement score | Mean±SD | 1.35±0.72 | 1.43±0.68 | 1.37±0.71 | 0.4348 |
| Median | 1.00 | 2.00 | 2.00 |  |
| Min–Max | 0.00–2.00 | 0.00–2.00 | 0.00–2.00 |  |
| Diet habit - total score | Mean±SD | 4.26±1.40 | 4.21±1.58 | 4.24±1.46 | 0.9601 |
| Median | 4.00 | 4.00 | 4.00 |  |
| Min–Max | 0.00–6.00 | 0.00–6.00 | 0.00–6.00 |  |
| Alcohol drinking habit | Improved | 31 (19.14) | 15 (20.00) | 46 (19.41) | 0.9246 |
| Unchanged | 124 (76.54) | 56 (74.67) | 180 (75.95) |  |
| Worsened | 7 (4.32) | 4 (5.33) | 11 (4.64) |  |
| Alcohol drinking habit - Improvement | No | 131 (80.86) | 60 (80.00) | 191 (80.59) | 0.8757 |
| Yes | 31 (19.14) | 15 (20.00) | 46 (19.41) |  |
| Smoking habit | Improved | 21 (12.96) | 13 (17.33) | 34 (14.35) | 0.4284 |
| Unchanged | 139 (85.80) | 60 (80.00) | 199 (83.97) |  |
| Worsened | 2 (1.23) | 2 (2.67) | 4 (1.69) |  |
| Smoking habit - Improvement | No | 21 (12.96) | 13 (17.33) | 34 (14.35) | 0.3720 |
| Yes | 141 (87.04) | 62 (82.67) | 203 (85.65) |  |

Values are presented as number (%) unless otherwise indicated.

Note 1: Sleep habit

Head elevation for 10-15cm during sleep

Note 2: Diet habit

Diet habit 1 – no meal or drink 2-3 hours before going to bed

Diet habit 2 – small meal and eating slow

Diet habit 3 – avoid caffeine, soft drinks, chocolate, peppermint, tomato, citrus fruits, greasy food, fried foods, and red wine.

Note 3: Physical activity

Combined exercise time of at least moderate to severe intensity or more for at least 10 minutes without any resting period.

HAD, hospital anxiety and depression scale; HAD-A, hospital anxiety and depression scale-anxiety; HAD-D, hospital anxiety and depression scale-depression;

SD, standard deviation.

a)Chi-square test (or Fisher’s exact test) or independent *t*-test.

Supplementary Table 5. Univariate analysis of response to 3-months treatment (past & current medical history)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Factor | | Responder | Non-responder | Total | *P*-valuea) |
| n=162 (68.35%) | n=75 (31.65%) | n=237 (100%) |  |
| **Past medical history** | | | | | |
| **SOC** | | | | | |
| Larynx | (–) | 162 (100.00) | 74 (98.67) | 236 (99.58) | 0.3165 |
| (+) | 0 | 1 (1.33) | 1 (0.42) |  |
| Neurovascular | (–) | 161 (99.38) | 75 (100.00) | 236 (99.58) | 1.0000 |
| (+) | 1 (0.62) | 0 | 1 (0.42) |  |
| Mediastinum | (–) | 162 (100.00) | 74 (98.67) | 236 (99.58) | 0.3165 |
| (+) | 0 | 1 (1.33) | 1 (0.42) |  |
| Oral Cavity | (–) | 161 (99.38) | 75 (100.00) | 236 (99.58) | 1.0000 |
| (+) | 1 (0.62) | 0 | 1 (0.42) |  |
| Ophthalmology | (–) | 161 (99.38) | 75 (100.00) | 236 (99.58) | 1.0000 |
| (+) | 1 (0.62) | 0 | 1 (0.42) |  |
| **PT** | | | | | |
| Arrhythmia | (–) | 161 (99.38) | 75 (100.00) | 236 (99.58) | 1.0000 |
| (+) | 1 (0.62) | 0 | 1 (0.42) |  |
| Pulmonary, inflammation | (–) | 161 (99.38) | 75 (100.00) | 236 (99.58) | 1.0000 |
| (+) | 1 (0.62) | 0 | 1 (0.42) |  |
| Pulmonary, malignant tumor | (–) | 161 (99.38) | 75 (100.00) | 236 (99.58) | 1.0000 |
| (+) | 1 (0.62) | 0 | 1 (0.42) |  |
| Larynx, Benign tumor | (–) | 162 (100.00) | 74 (98.67) | 236 (99.58) | 0.3165 |
| (+) | 0 | 1 (1.33) | 1 (0.42) |  |
| Neurovascular, structural disease | (–) | 161 (99.38) | 75 (100.00) | 236 (99.58) | 1.0000 |
| (+) | 1 (0.62) | 0 | 1 (0.42) |  |
| Mediastinum tumor | (–) | 162 (100.00) | 74 (98.67) | 236 (99.58) | 0.3165 |
| (+) | 0 | 1 (1.33) | 1 (0.42) |  |
| Oral cavity, malignant tumor | (–) | 161 (99.38) | 75 (100.00) | 236 (99.58) | 1.0000 |
| (+) | 1 (0.62) | 0 | 1 (0.42) |  |
| Ophthalmology | (–) | 161 (99.38) | 75 (100.00) | 236 (99.58) | 1.0000 |
| (+) | 1 (0.62) | 0 | 1 (0.42) |  |
| **Current medical history** | | | | | |
| **SOC** | | | | | |
| Gastrointestinal | (–) | 149 (91.98) | 68 (90.67) | 217 (91.56) | 0.7361 |
| (+) | 13 (8.02) | 7 (9.33) | 20 (8.44) |  |
| Larynx | (–) | 161 (99.38) | 75 (100.00) | 236 (99.58) | 1.0000 |
| (+) | 1 (0.62) | 0 | 1 (0.42) |  |
| Neurovascular | (–) | 162 (100.00) | 73 (97.33) | 235 (99.16) | 0.0992 |
| (+) | 0 | 2 (2.67) | 2 (0.84) |  |
| Neurology | (–) | 155 (95.68) | 70 (93.33) | 225 (94.94) | 0.5262 |
| (+) | 7 (4.32) | 5 (6.67) | 12 (5.06) |  |
| Urogenital | (–) | 156 (96.30) | 72 (96.00) | 228 (96.20) | 1.0000 |
| (+) | 6 (3.70) | 3 (4.00) | 9 (3.80) |  |
| Gynecology | (–) | 159 (98.15) | 74 (98.67) | 233 (98.31) | 1.0000 |
| (+) | 3 (1.85) | 1 (1.33) | 4 (1.69) |  |
| Neuropsychiatry | (–) | 158 (97.53) | 73 (97.33) | 231 (97.47) | 1.0000 |
| (+) | 4 (2.47) | 2 (2.67) | 6 (2.53) |  |
| Allergy | (–) | 160 (98.77) | 73 (97.33) | 233 (98.31) | 0.5930 |
| (+) | 2 (1.23) | 2 (2.67) | 4 (1.69) |  |
| Breast | (–) | 161 (99.38) | 74 (98.67) | 235 (99.16) | 0.5337 |
| (+) | 1 (0.62) | 1 (1.33) | 2 (0.84) |  |
| Musculoskeletal | (–) | 157 (96.91) | 71 (94.67) | 228 (96.20) | 0.4695 |
| (+) | 5 (3.09) | 4 (5.33) | 9 (3.80) |  |
| Renal | (–) | 160 (98.77) | 75 (100.00) | 235 (99.16) | 1.0000 |
| (+) | 2 (1.23) | 0 | 2 (0.84) |  |
| Upper respiratory infection | (–) | 159 (98.15) | 70 (93.33) | 229 (96.62) | 0.1134 |
| (+) | 3 (1.85) | 5 (6.67) | 8 (3.38) |  |
| Cough | (–) | 159 (98.15) | 73 (97.33) | 232 (97.89) | 0.6528 |
| (+) | 3 (1.85) | 2 (2.67) | 5 (2.11) |  |
| Hematology | (–) | 161 (99.38) | 75 (100.00) | 236 (99.58) | 1.0000 |
| (+) | 1 (0.62) | 0 | 1 (0.42) |  |
| Rheumatology | (–) | 162 (100.00) | 74 (98.67) | 236 (99.58) | 0.3165 |
| (+) | 0 | 1 (1.33) | 1 (0.42) |  |
| Ophthalmology | (–) | 160 (98.77) | 74 (98.67) | 234 (98.73) | 1.0000 |
| (+) | 2 (1.23) | 1 (1.33) | 3 (1.27) |  |
| **PT** | | | | | |
| Cardiac, coronary disease | (–) | 159 (98.15) | 74 (98.67) | 233 (98.31) | 1.0000 |
| (+) | 3 (1.85) | 1 (1.33) | 4 (1.69) |  |
| Arrhythmia | (–) | 160 (98.77) | 74 (98.67) | 234 (98.73) | 1.0000 |
| (+) | 2 (1.23) | 1 (1.33) | 3 (1.27) |  |
| Cardiac, anatomical defect | (–) | 161 (99.38) | 75 (100.00) | 236 (99.58) | 1.0000 |
| (+) | 1 (0.62) | 0 | 1 (0.42) |  |
| Pulmonary, inflammation | (–) | 161 (99.38) | 74 (98.67) | 235 (99.16) | 0.5337 |
| (+) | 1 (0.62) | 1 (1.33) | 2 (0.84) |  |
| Pulmonary, benign tumor | (–) | 161 (99.38) | 75 (100.00) | 236 (99.58) | 1.0000 |
| (+) | 1 (0.62) | 0 | 1 (0.42) |  |
| Pulmonary, functional disease | (–) | 161 (99.38) | 75 (100.00) | 236 (99.58) | 1.0000 |
| (+) | 1 (0.62) | 0 | 1 (0.42) |  |
| Gastrointestinal, functional disease | (–) | 158 (97.53) | 70 (93.33) | 228 (96.20) | 0.1462 |
| (+) | 4 (2.47) | 5 (6.67) | 9 (3.80) |  |
| Gastrointestinal, inflammatory disease | (–) | 156 (96.30) | 73 (97.33) | 229 (96.62) | 1.0000 |
| (+) | 6 (3.70) | 2 (2.67) | 8 (3.38) |  |
| Gastrointestinal, malignant tumor | (–) | 161 (99.38) | 75 (100.00) | 236 (99.58) | 1.0000 |
| (+) | 1 (0.62) | 0 | 1 (0.42) |  |
| Hepatobiliary inflammatory and functional disease | (–) | 159 (98.15) | 74 (98.67) | 233 (98.31) | 1.0000 |
| (+) | 3 (1.85) | 1 (1.33) | 4 (1.69) |  |
| Hepatobiliary, benign tumor | (–) | 161 (99.38) | 75 (100.00) | 236 (99.58) | 1.0000 |
| (+) | 1 (0.62) | 0 | 1 (0.42) |  |
| Pituitary disease | (–) | 161 (99.38) | 75 (100.00) | 236 (99.58) | 1.0000 |
| (+) | 1 (0.62) | 0 | 1 (0.42) |  |
| Bone disorder with calcium disorder | (–) | 158 (97.53) | 74 (98.67) | 232 (97.89) | 1.0000 |
| (+) | 4 (2.47) | 1 (1.33) | 5 (2.11) |  |
| Thyroid, benign tumor | (–) | 159 (98.15) | 75 (100.00) | 234 (98.73) | 0.5535 |
| (+) | 3 (1.85) | 0 | 3 (1.27) |  |
| Thyroid, functional disorder | (–) | 160 (98.77) | 72 (96.00) | 232 (97.89) | 0.3296 |
| (+) | 2 (1.23) | 3 (4.00) | 5 (2.11) |  |
| Larynx, functional disorder | (–) | 161 (99.38) | 75 (100.00) | 236 (99.58) | 1.0000 |
| (+) | 1 (0.62) | 0 | 1 (0.42) |  |
| Neurovascular, structural disease | (–) | 162 (100.00) | 73 (97.33) | 235 (99.16) | 0.0992 |
| (+) | 0 | 2 (2.67) | 2 (0.84) |  |
| Cerebrovascular infarct | (–) | 159 (98.15) | 74 (98.67) | 233 (98.31) | 1.0000 |
| (+) | 3 (1.85) | 1 (1.33) | 4 (1.69) |  |
| Neurodegenerative disease | (–) | 161 (99.38) | 75 (100.00) | 236 (99.58) | 1.0000 |
| (+) | 1 (0.62) | 0 | 1 (0.42) |  |
| Neurologic functional disorder | (–) | 158 (97.53) | 71 (94.67) | 229 (96.62) | 0.2668 |
| (+) | 4 (2.47) | 4 (5.33) | 8 (3.38) |  |
| Urogenital, functional disorder | (–) | 159 (98.15) | 74 (98.67) | 233 (98.31) | 1.0000 |
| (+) | 3 (1.85) | 1 (1.33) | 4 (1.69) |  |
| Urogenital inflammation | (–) | 160 (98.77) | 75 (100.00) | 235 (99.16) | 1.0000 |
| (+) | 2 (1.23) | 0 | 2 (0.84) |  |
| Benign prostate hyperplasia | (–) | 160 (98.77) | 73 (97.33) | 233 (98.31) | 0.5930 |
| (+) | 2 (1.23) | 2 (2.67) | 4 (1.69) |  |
| Gynecology, benign tumor | (–) | 159 (98.15) | 74 (98.67) | 233 (98.31) | 1.0000 |
| (+) | 3 (1.85) | 1 (1.33) | 4 (1.69) |  |
| Depression | (–) | 159 (98.15) | 74 (98.67) | 233 (98.31) | 1.0000 |
| (+) | 3 (1.85) | 1 (1.33) | 4 (1.69) |  |
| Other neuropsychiatry disorder | (–) | 161 (99.38) | 74 (98.67) | 235 (99.16) | 0.5337 |
| (+) | 1 (0.62) | 1 (1.33) | 2 (0.84) |  |
| Allergy | (–) | 160 (98.77) | 73 (97.33) | 233 (98.31) | 0.5930 |
| (+) | 2 (1.23) | 2 (2.67) | 4 (1.69) |  |
| Breast malignant mass | (–) | 161 (99.38) | 74 (98.67) | 235 (99.16) | 0.5337 |
| (+) | 1 (0.62) | 1 (1.33) | 2 (0.84) |  |
| Musculoskeletal inflammatory disease | (–) | 160 (98.77) | 73 (97.33) | 233 (98.31) | 0.5930 |
| (+) | 2 (1.23) | 2 (2.67) | 4 (1.69) |  |
| Degenerative musculoskeletal disease | (–) | 158 (97.53) | 73 (97.33) | 231 (97.47) | 1.0000 |
| (+) | 4 (2.47) | 2 (2.67) | 6 (2.53) |  |
| Renal functional disorder | (–) | 160 (98.77) | 75 (100.00) | 235 (99.16) | 1.0000 |
| (+) | 2 (1.23) | 0 | 2 (0.84) |  |
| Upper respiratory infection | (–) | 159 (98.15) | 70 (93.33) | 229 (96.62) | 0.1134 |
| (+) | 3 (1.85) | 5 (6.67) | 8 (3.38) |  |
| Cough | (–) | 159 (98.15) | 73 (97.33) | 232 (97.89) | 0.6528 |
| (+) | 3 (1.85) | 2 (2.67) | 5 (2.11) |  |
| Hematologic disease | (–) | 161 (99.38) | 75 (100.00) | 236 (99.58) | 1.0000 |
| (+) | 1 (0.62) | 0 | 1 (0.42) |  |
| Rheumatic disease | (–) | 162 (100.00) | 74 (98.67) | 236 (99.58) | 0.3165 |
| (+) | 0 | 1 (1.33) | 1 (0.42) |  |
| Ophthalmologic disease | (–) | 160 (98.77) | 74 (98.67) | 234 (98.73) | 1.0000 |
| (+) | 2 (1.23) | 1 (1.33) | 3 (1.27) |  |

Values are presented as number (%).

SOC, systemic organ class; PT, preferred term.

a)Chi-square test or Fisher’s exact test

Supplementary Table 6. Univariate analysis of response to 3-months treatment (past & current medication history)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Factor | | Responder | Non-responder | Total | *P*-valuea) |
|  | | n=162 (68.35%) | n=75 (31.65%) | n=237 (100%) |  |
| **Past medication history** | | | | | |
| **AC** | | | | | |
| Gastrointestinal | (–) | 145 (89.51) | 62 (82.67) | 207 (87.34) | 0.1408 |
| (+) | 17 (10.49) | 13 (17.33) | 30 (12.66) |  |
| Systemic acting drugs | (–) | 153 (94.44) | 70 (93.33) | 223 (94.09) | 0.7704 |
| (+) | 9 (5.56) | 5 (6.67) | 14 (5.91) |  |
| Neuropsychiatry | (–) | 158 (97.53) | 70 (93.33) | 228 (96.20) | 0.1462 |
| (+) | 4 (2.47) | 5 (6.67) | 9 (3.80) |  |
| Neurology | (–) | 150 (92.59) | 73 (97.33) | 223 (94.09) | 0.2357 |
| (+) | 12 (7.41) | 2 (2.67) | 14 (5.91) |  |
| Allergy | (–) | 160 (98.77) | 72 (96.00) | 232 (97.89) | 0.3296 |
| (+) | 2 (1.23) | 3 (4.00) | 5 (2.11) |  |
| Urogenital | (–) | 161 (99.38) | 73 (97.33) | 234 (98.73) | 0.2360 |
| (+) | 1 (0.62) | 2 (2.67) | 3 (1.27) |  |
| Female hormonal | (–) | 160 (98.77) | 72 (96.00) | 232 (97.89) | 0.3296 |
| (+) | 2 (1.23) | 3 (4.00) | 5 (2.11) |  |
| Musculoskeletal | (–) | 158 (97.53) | 75 (100.00) | 233 (98.31) | 0.3106 |
| (+) | 4 (2.47) | 0 | 4 (1.69) |  |
| Salivary gland | (–) | 162 (100.00) | 74 (98.67) | 236 (99.58) | 0.3165 |
| (+) | 0 | 1 (1.33) | 1 (0.42) |  |
| Nutritional supplement | (–) | 159 (98.15) | 70 (93.33) | 229 (96.62) | 0.1134 |
| (+) | 3 (1.85) | 5 (6.67) | 8 (3.38) |  |
| Rheumatology | (–) | 161 (99.38) | 75 (100.00) | 236 (99.58) | 1.0000 |
| (+) | 1 (0.62) | 0 | 1 (0.42) |  |
| Others | (–) | 159 (98.15) | 75 (100.00) | 234 (98.73) | 0.5535 |
| (+) | 3 (1.85) | 0 | 3 (1.27) |  |
| **TC** | | | | | |
| Vasodilator, anti-angina | (–) | 161 (99.38) | 73 (97.33) | 234 (98.73) | 0.2360 |
| (+) | 1 (0.62) | 2 (2.67) | 3 (1.27) |  |
| Anti-arrhythmic | (–) | 161 (99.38) | 75 (100.00) | 236 (99.58) | 1.0000 |
| (+) | 1 (0.62) | 0 | 1 (0.42) |  |
| Antitussive | (–) | 161 (99.38) | 73 (97.33) | 234 (98.73) | 0.2360 |
| (+) | 1 (0.62) | 2 (2.67) | 3 (1.27) |  |
| Gastrointestinal protectant | (–) | 155 (95.68) | 69 (92.00) | 224 (94.51) | 0.3565 |
| (+) | 7 (4.32) | 6 (8.00) | 13 (5.49) |  |
| Gastrointestinal, promotility agent | (–) | 157 (96.91) | 71 (94.67) | 228 (96.20) | 0.4695 |
| (+) | 5 (3.09) | 4 (5.33) | 9 (3.80) |  |
| H2 blocker | (–) | 159 (98.15) | 71 (94.67) | 230 (97.05) | 0.2119 |
| (+) | 3 (1.85) | 4 (5.33) | 7 (2.95) |  |
| Proton pump inhibitor | (–) | 154 (95.06) | 70 (93.33) | 224 (94.51) | 0.5558 |
| (+) | 8 (4.94) | 5 (6.67) | 13 (5.49) |  |
| Laxative | (–) | 160 (98.77) | 73 (97.33) | 233 (98.31) | 0.5930 |
| (+) | 2 (1.23) | 2 (2.67) | 4 (1.69) |  |
| Gastrointestinal, spasmolytic | (–) | 162 (100.00) | 74 (98.67) | 236 (99.58) | 0.3165 |
| (+) | 0 | 1 (1.33) | 1 (0.42) |  |
| Antiemetic | (–) | 162 (100.00) | 74 (98.67) | 236 (99.58) | 0.3165 |
| (+) | 0 | 1 (1.33) | 1 (0.42) |  |
| Non-steroidal anti-inflammatory drug | (–) | 159 (98.15) | 73 (97.33) | 232 (97.89) | 0.6528 |
| (+) | 3 (1.85) | 2 (2.67) | 5 (2.11) |  |
| Steroid | (–) | 158 (97.53) | 75 (100.00) | 233 (98.31) | 0.3106 |
| (+) | 4 (2.47) | 0 | 4 (1.69) |  |
| Antibiotic | (–) | 161 (99.38) | 72 (96.00) | 233 (98.31) | 0.0948 |
| (+) | 1 (0.62) | 3 (4.00) | 4 (1.69) |  |
| Acetaminophen | (–) | 160 (98.77) | 75 (100.00) | 235 (99.16) | 1.0000 |
| (+) | 2 (1.23) | 0 | 2 (0.84) |  |
| Anti-anxiety, benzodiazepine | (–) | 159 (98.15) | 72 (96.00) | 231 (97.47) | 0.3840 |
| (+) | 3 (1.85) | 3 (4.00) | 6 (2.53) |  |
| Anti-depressant, serotonin-norepinephrine reuptake inhibitor | (–) | 161 (99.38) | 74 (98.67) | 235 (99.16) | 0.5337 |
| (+) | 1 (0.62) | 1 (1.33) | 2 (0.84) |  |
| Anti-depressant, selective serotonin reuptake inhibitor | (–) | 161 (99.38) | 74 (98.67) | 235 (99.16) | 0.5337 |
| (+) | 1 (0.62) | 1 (1.33) | 2 (0.84) |  |
| Tricyclic antidepressant | (–) | 160 (98.77) | 74 (98.67) | 234 (98.73) | 1.0000 |
| (+) | 2 (1.23) | 1 (1.33) | 3 (1.27) |  |
| Neurology, anticoagulant | (–) | 152 (93.83) | 74 (98.67) | 226 (95.36) | 0.1807 |
| (+) | 10 (6.17) | 1 (1.33) | 11 (4.64) |  |
| Peripheral vasoactive agent | (–) | 161 (99.38) | 75 (100.00) | 236 (99.58) | 1.0000 |
| (+) | 1 (0.62) | 0 | 1 (0.42) |  |
| Neurodegenerative suppressant | (–) | 161 (99.38) | 75 (100.00) | 236 (99.58) | 1.0000 |
| (+) | 1 (0.62) | 0 | 1 (0.42) |  |
| Opioid analgesic | (–) | 161 (99.38) | 75 (100.00) | 236 (99.58) | 1.0000 |
| (+) | 1 (0.62) | 0 | 1 (0.42) |  |
| Neuropathic analgesic | (–) | 162 (100.00) | 74 (98.67) | 236 (99.58) | 0.3165 |
| (+) | 0 | 1 (1.33) | 1 (0.42) |  |
| Intra-nasal steroid | (–) | 162 (100.00) | 73 (97.33) | 235 (99.16) | 0.0992 |
| (+) | 0 | 2 (2.67) | 2 (0.84) |  |
| Antihistamine | (–) | 160 (98.77) | 73 (97.33) | 233 (98.31) | 0.5930 |
| (+) | 2 (1.23) | 2 (2.67) | 4 (1.69) |  |
| Leukotriene inhibitor | (–) | 161 (99.38) | 74 (98.67) | 235 (99.16) | 0.5337 |
| (+) | 1 (0.62) | 1 (1.33) | 2 (0.84) |  |
| Diuretics | (–) | 159 (98.15) | 75 (100.00) | 234 (98.73) | 0.5535 |
| (+) | 3 (1.85) | 0 | 3 (1.27) |  |
| Alpha blocker | (–) | 162 (100.00) | 74 (98.67) | 236 (99.58) | 0.3165 |
| (+) | 0 | 1 (1.33) | 1 (0.42) |  |
| Phosphodiesterase-5 inhibitor | (–) | 161 (99.38) | 75 (100.00) | 236 (99.58) | 1.0000 |
| (+) | 1 (0.62) | 0 | 1 (0.42) |  |
| Female hormonal supplement | (–) | 160 (98.77) | 72 (96.00) | 232 (97.89) | 0.3296 |
| (+) | 2 (1.23) | 3 (4.00) | 5 (2.11) |  |
| Anti-hyperlipidemic | (–) | 151 (93.21) | 72 (96.00) | 223 (94.09) | 0.5573 |
| (+) | 11 (6.79) | 3 (4.00) | 14 (5.91) |  |
| Muscle relaxant | (–) | 159 (98.15) | 75 (100.00) | 234 (98.73) | 0.5535 |
| (+) | 3 (1.85) | 0 | 3 (1.27) |  |
| Glucosamine | (–) | 160 (98.77) | 75 (100.00) | 235 (99.16) | 1.0000 |
| (+) | 2 (1.23) | 0 | 2 (0.84) |  |
| Sialogogue | (–) | 162 (100.00) | 74 (98.67) | 236 (99.58) | 0.3165 |
| (+) | 0 | 1 (1.33) | 1 (0.42) |  |
| Nutritional supplement | (–) | 159 (98.15) | 70 (93.33) | 229 (96.62) | 0.1134 |
| (+) | 3 (1.85) | 5 (6.67) | 8 (3.38) |  |
| Anti-rheumatic | (–) | 161 (99.38) | 75 (100.00) | 236 (99.58) | 1.0000 |
| (+) | 1 (0.62) | 0 | 1 (0.42) |  |
| Others | (–) | 159 (98.15) | 75 (100.00) | 234 (98.73) | 0.5535 |
| (+) | 3 (1.85) | 0 | 3 (1.27) |  |
| **Current medication history** | | | | | |
| **AC** | | | | | |
| Gastrointestinal | (–) | 121 (74.69) | 56 (74.67) | 177 (74.68) | 0.9968 |
| (+) | 41 (25.31) | 19 (25.33) | 60 (25.32) |  |
| Systemic acting drugs | (–) | 143 (88.27) | 64 (85.33) | 207 (87.34) | 0.5269 |
| (+) | 19 (11.73) | 11 (14.67) | 30 (12.66) |  |
| Neuropsychiatry | (–) | 157 (96.91) | 72 (96.00) | 229 (96.62) | 0.7104 |
| (+) | 5 (3.09) | 3 (4.00) | 8 (3.38) |  |
| Neurology | (–) | 149 (91.98) | 71 (94.67) | 220 (92.83) | 0.4552 |
| (+) | 13 (8.02) | 4 (5.33) | 17 (7.17) |  |
| Allergy | (–) | 154 (95.06) | 72 (96.00) | 226 (95.36) | 1.0000 |
| (+) | 8 (4.94) | 3 (4.00) | 11 (4.64) |  |
| Urogenital | (–) | 161 (99.38) | 75 (100.00) | 236 (99.58) | 1.0000 |
| (+) | 1 (0.62) | 0 | 1 (0.42) |  |
| Female hormonal | (–) | 160 (98.77) | 71 (94.67) | 231 (97.47) | 0.0816 |
| (+) | 2 (1.23) | 4 (5.33) | 6 (2.53) |  |
| Musculoskeletal | (–) | 160 (98.77) | 73 (97.33) | 233 (98.31) | 0.5930 |
| (+) | 2 (1.23) | 2 (2.67) | 4 (1.69) |  |
| Nutritional supplement | (–) | 155 (95.68) | 68 (90.67) | 223 (94.09) | 0.1446 |
| (+) | 7 (4.32) | 7 (9.33) | 14 (5.91) |  |
| Rheumatology | (–) | 161 (99.38) | 75 (100.00) | 236 (99.58) | 1.0000 |
| (+) | 1 (0.62) | 0 | 1 (0.42) |  |
| Others | (–) | 157 (96.91) | 72 (96.00) | 229 (96.62) | 0.7104 |
| (+) | 5 (3.09) | 3 (4.00) | 8 (3.38) |  |
| **TC** | | | | | |
| Vasodilator, anti-angina | (–) | 161 (99.38) | 74 (98.67) | 235 (99.16) | 0.5337 |
| (+) | 1 (0.62) | 1 (1.33) | 2 (0.84) |  |
| Anti-arrhythmic | (–) | 160 (98.77) | 75 (100.00) | 235 (99.16) | 1.0000 |
| (+) | 2 (1.23) | 0 | 2 (0.84) |  |
| Mucoactive | (–) | 135 (83.33) | 61 (81.33) | 196 (82.70) | 0.7050 |
| (+) | 27 (16.67) | 14 (18.67) | 41 (17.30) |  |
| Antitussive | (–) | 160 (98.77) | 74 (98.67) | 234 (98.73) | 1.0000 |
| (+) | 2 (1.23) | 1 (1.33) | 3 (1.27) |  |
| Bronchodilator | (–) | 160 (98.77) | 75 (100.00) | 235 (99.16) | 1.0000 |
| (+) | 2 (1.23) | 0 | 2 (0.84) |  |
| Gastrointestinal, promotility agent | (–) | 137 (84.57) | 65 (86.67) | 202 (85.23) | 0.6719 |
| (+) | 25 (15.43) | 10 (13.33) | 35 (14.77) |  |
| H2 blocker | (–) | 158 (97.53) | 69 (92.00) | 227 (95.78) | 0.0769 |
| (+) | 4 (2.47) | 6 (8.00) | 10 (4.22) |  |
| Laxative | (–) | 158 (97.53) | 71 (94.67) | 229 (96.62) | 0.2668 |
| (+) | 4 (2.47) | 4 (5.33) | 8 (3.38) |  |
| Gastrointestinal, spasmolytic | (–) | 160 (98.77) | 74 (98.67) | 234 (98.73) | 1.0000 |
| (+) | 2 (1.23) | 1 (1.33) | 3 (1.27) |  |
| Non-steroidal anti-inflammatory drug | (–) | 153 (94.44) | 70 (93.33) | 223 (94.09) | 0.7704 |
| (+) | 9 (5.56) | 5 (6.67) | 14 (5.91) |  |
| Steroid | (–) | 156 (96.30) | 74 (98.67) | 230 (97.05) | 0.4369 |
| (+) | 6 (3.70) | 1 (1.33) | 7 (2.95) |  |
| Antibiotic | (–) | 156 (96.30) | 70 (93.33) | 226 (95.36) | 0.3311 |
| (+) | 6 (3.70) | 5 (6.67) | 11 (4.64) |  |
| Acetaminophen | (–) | 158 (97.53) | 74 (98.67) | 232 (97.89) | 1.0000 |
| (+) | 4 (2.47) | 1 (1.33) | 5 (2.11) |  |
| Anti-anxiety, benzodiazepine | (–) | 158 (97.53) | 73 (97.33) | 231 (97.47) | 1.0000 |
| (+) | 4 (2.47) | 2 (2.67) | 6 (2.53) |  |
| Anti-depressant, serotonin-norepinephrine reuptake inhibitor | (–) | 161 (99.38) | 75 (100.00) | 236 (99.58) | 1.0000 |
| (+) | 1 (0.62) | 0 | 1 (0.42) |  |
| Anti-depressant, selective serotonin reuptake inhibitor | (–) | 161 (99.38) | 74 (98.67) | 235 (99.16) | 0.5337 |
| (+) | 1 (0.62) | 1 (1.33) | 2 (0.84) |  |
| Tricyclic antidepressant | (–) | 159 (98.15) | 75 (100.00) | 234 (98.73) | 0.5535 |
| (+) | 3 (1.85) | 0 | 3 (1.27) |  |
| Peripheral vasoactive agent | (–) | 161 (99.38) | 73 (97.33) | 234 (98.73) | 0.2360 |
| (+) | 1 (0.62) | 2 (2.67) | 3 (1.27) |  |
| Neurodegenerative suppressant | (–) | 161 (99.38) | 75 (100.00) | 236 (99.58) | 1.0000 |
| (+) | 1 (0.62) | 0 | 1 (0.42) |  |
| Opioid analgesic | (–) | 160 (98.77) | 74 (98.67) | 234 (98.73) | 1.0000 |
| (+) | 2 (1.23) | 1 (1.33) | 3 (1.27) |  |
| Neuropathic analgesic | (–) | 161 (99.38) | 75 (100.00) | 236 (99.58) | 1.0000 |
| (+) | 1 (0.62) | 0 | 1 (0.42) |  |
| Intra-nasal steroid | (–) | 159 (98.15) | 73 (97.33) | 232 (97.89) | 0.6528 |
| (+) | 3 (1.85) | 2 (2.67) | 5 (2.11) |  |
| Antihistamine | (–) | 156 (96.30) | 73 (97.33) | 229 (96.62) | 1.0000 |
| (+) | 6 (3.70) | 2 (2.67) | 8 (3.38) |  |
| Leukotriene inhibitor | (–) | 161 (99.38) | 74 (98.67) | 235 (99.16) | 0.5337 |
| (+) | 1 (0.62) | 1 (1.33) | 2 (0.84) |  |
| Diuretics | (–) | 160 (98.77) | 74 (98.67) | 234 (98.73) | 1.0000 |
| (+) | 2 (1.23) | 1 (1.33) | 3 (1.27) |  |
| Phosphodiesterase-5 inhibitor | (–) | 161 (99.38) | 75 (100.00) | 236 (99.58) | 1.0000 |
| (+) | 1 (0.62) | 0 | 1 (0.42) |  |
| Female hormonal supplement | (–) | 160 (98.77) | 71 (94.67) | 231 (97.47) | 0.0816 |
| (+) | 2 (1.23) | 4 (5.33) | 6 (2.53) |  |
| Anti-hyperlipidemic | (–) | 152 (93.83) | 72 (96.00) | 224 (94.51) | 0.7599 |
| (+) | 10 (6.17) | 3 (4.00) | 13 (5.49) |  |
| Osteoporosis | (–) | 156 (96.30) | 70 (93.33) | 226 (95.36) | 0.3311 |
| (+) | 6 (3.70) | 5 (6.67) | 11 (4.64) |  |
| Muscle relaxant | (–) | 160 (98.77) | 73 (97.33) | 233 (98.31) | 0.5930 |
| (+) | 2 (1.23) | 2 (2.67) | 4 (1.69) |  |
| Glucosamine | (–) | 161 (99.38) | 75 (100.00) | 236 (99.58) | 1.0000 |
| (+) | 1 (0.62) | 0 | 1 (0.42) |  |
| Nutritional supplement | (–) | 155 (95.68) | 68 (90.67) | 223 (94.09) | 0.1446 |
| (+) | 7 (4.32) | 7 (9.33) | 14 (5.91) |  |
| Anti-rheumatic | (–) | 161 (99.38) | 75 (100.00) | 236 (99.58) | 1.0000 |
| (+) | 1 (0.62) | 0 | 1 (0.42) |  |
| Others | (–) | 157 (96.91) | 72 (96.00) | 229 (96.62) | 0.7104 |
| (+) | 5 (3.09) | 3 (4.00) | 8 (3.38) |  |

Values are presented as number (%).

AC, anatomical code; TC, therapeutic code.

a)Chi-square test or Fisher’s exact test.

Supplementary Table 7. Univariate comparative analysis between early-responders and late-responders (HAD specifics & treatment compliance)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Factor |  | Early response | Late response | Total | *P*-valuea) |
|  |  | n=92 (56.79%) | n=70 (43.21%) | n=162 (100%) |  |
| HAD specifics | | | | | |
| HAD-A (anxiety) | None | 62 (67.39) | 43 (61.43) | 105 (64.81) | 0.5089 |
| Mild | 21 (22.83) | 16 (22.86) | 37 (22.84) |  |
| Moderate to severe | 9 (9.78) | 11 (15.71) | 20 (12.35) |  |
| HAD-D (depression) | None | 47 (51.09) | 41 (58.57) | 88 (54.32) | 0.5891 |
| Mild | 33 (35.87) | 20 (28.57) | 53 (32.72) |  |
| Moderate to severe | 12 (13.04) | 9 (12.86) | 21 (12.96) |  |
| Treatment compliance | | | | | |
| Timing of the medication | Before breakfast | 91 (98.91) | 68 (97.14) | 159 (98.15) | 0.1852 |
| Before the largest meal | 1 (1.09) | 0 | 1 (0.62) |  |
| Before sleep | 0 | 0 | 0 |  |
| Etc. | 0 | 2 (2.86) | 2 (1.23) |  |
| Consistency in timing of the medication | No | 1 (1.09) | 3 (4.29) | 4 (2.47) | 0.3164 |
| Yes | 91 (98.91) | 67 (95.71) | 158 (97.53) |  |
| Changes in physical activity | Mean±SD | 17.50±102.61 | 5.79±201.40 | 12.44±152.87 | 0.8474 |
| Median | 0.00 | 0.00 | 0.00 |  |
| Min–Max | -270.00–300.00 | -840.00–700.00 | -840.00–700.00 |  |
| Sleep habit | Improved | 36 (39.13) | 19 (27.14) | 55 (33.95) | 0.2141 |
| Unchanged | 44 (47.83) | 37 (52.86) | 81 (50.00) |  |
| Worsened | 12 (13.04) | 14 (20.00) | 26 (16.05) |  |
| Diet habit 1 | Improved | 53 (57.61) | 45 (64.29) | 98 (60.49) | 0.2218 |
| Unchanged | 28 (30.43) | 22 (31.43) | 50 (30.86) |  |
| Worsened | 11 (11.96) | 3 (4.29) | 14 (8.64) |  |
| Diet habit 1 - improvement score | Mean±SD | 1.46±0.70 | 1.60±0.57 | 1.52±0.65 | 0.2514 |
| Median | 2.00 | 2.00 | 2.00 |  |
| Min–Max | 0.00–2.00 | 0.00–2.00 | 0.00–2.00 |  |
| Diet habit 2 | Improved | 51 (55.43) | 33 (47.14) | 84 (51.85) | 0.5599 |
| Unchanged | 30 (32.61) | 28 (40.00) | 58 (35.80) |  |
| Worsened | 11 (11.96) | 9 (12.86) | 20 (12.35) |  |
| Diet habit 2 - improvement score | Mean±SD | 1.43±0.70 | 1.34±0.70 | 1.40±0.70 | 0.3533 |
| Median | 2.00 | 1.00 | 2.00 |  |
| Min–Max | 0.00–2.00 | 0.00–2.00 | 0.00–2.00 |  |
| Diet habit 3 | Improved | 45 (48.91) | 34 (48.57) | 79 (48.77) | 0.6192 |
| Unchanged | 32 (34.78) | 28 (40.00) | 60 (37.04) |  |
| Worsened | 15 (16.30) | 8 (11.43) | 23 (14.20) |  |
| Diet habit 3 - improvement score | Mean±SD | 1.33±0.74 | 1.37±0.68 | 1.35±0.72 | 0.7936 |
| Median | 1.00 | 1.00 | 1.00 |  |
| Min–Max | 0.00–2.00 | 0.00–2.00 | 0.00–2.00 |  |
| Diet habit - total score | Mean±SD | 4.22±1.46 | 4.31±1.34 | 4.26±1.40 | 0.7607 |
| Median | 4.00 | 4.00 | 4.00 |  |
| Min–Max | 1.00–6.00 | 0.00–6.00 | 0.00–6.00 |  |
| Alcohol drinking habit | Improved | 15 (16.30) | 16 (22.86) | 31 (19.14) | 0.5561 |
| Unchanged | 73 (79.35) | 51 (72.86) | 124 (76.54) |  |
| Worsened | 4 (4.35) | 3 (4.29) | 7 (4.32) |  |
| Alcohol drinking habit - Improvement | No | 77 (83.70) | 54 (77.14) | 131 (80.86) | 0.2936 |
| Yes | 15 (16.30) | 16 (22.86) | 31 (19.14) |  |
| Smoking habit | Improved | 10 (10.87) | 11 (15.71) | 21 (12.96) | 0.4564 |
| Unchanged | 80 (86.96) | 59 (84.29) | 139 (85.80) |  |
| Worsened | 2 (2.17) | 0 | 2 (1.23) |  |
| Smoking habit - Improvement | No | 82 (89.13) | 59 (84.29) | 141 (87.04) | 0.3631 |
| Yes | 10 (10.87) | 11 (15.71) | 21 (12.96) |  |

Values are presented as number (%) unless otherwise indicated.

HAD, hospital anxiety and depression scale; HAD-A, hospital anxiety and depression scale-anxiety; HAD-D, hospital anxiety and depression scale-depression; SD, standard deviation.

Note 1: Sleep habit

Head elevation for 10-15cm during sleep

Note 2: Diet habit

Diet habit 1 – no meal or drink 2-3 hours before going to bed

Diet habit 2 – small meal and eating slow

Diet habit 3 – avoid caffeine, soft drinks, chocolate, peppermint, tomato, citrus fruits, greasy food, fried foods, and red wine

Note 3: Physical activity

Combined exercise time of at least moderate to severe intensity or more for at least 10 minutes without any resting period.

a)Chi-square test (or Fisher’s exact test) or independent *t*-test.

Supplementary Table 8. Univariate comparative analysis between early-responders and late-responders (past & current medical history)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Factor | | Early response | Late response | Total | *P*-valuea) |
|  | | n=92 (56.79%) | n=70 (43.21%) | n=162 (100%) |  |
| **Past medical history** | | | | | |
| **SOC** | | | | | |
| Neurovascular | (–) | 91 (98.91) | 70 (100.00) | 161 (99.38) | 1.0000 |
| (+) | 1 (1.09) | 0 | 1 (0.62) |  |
| Oral Cavity | (–) | 92 (100.00) | 69 (98.57) | 161 (99.38) | 0.4321 |
| (+) | 0 | 1 (1.43) | 1 (0.62) |  |
| Ophthalmology | (–) | 91 (98.91) | 70 (100.00) | 161 (99.38) | 1.0000 |
| (+) | 1 (1.09) | 0 | 1 (0.62) |  |
| **PT** | | | | | |
| Arrhythmia | (–) | 92 (100.00) | 69 (98.57) | 161 (99.38) | 0.4321 |
| (+) | 0 | 1 (1.43) | 1 (0.62) |  |
| Pulmonary, inflammation | (–) | 91 (98.91) | 70 (100.00) | 161 (99.38) | 1.0000 |
| (+) | 1 (1.09) | 0 | 1 (0.62) |  |
| Pulmonary, malignant tumor | (–) | 92 (100.00) | 69 (98.57) | 161 (99.38) | 0.4321 |
| (+) | 0 | 1 (1.43) | 1 (0.62) |  |
| Neurovascular, structural disease | (–) | 91 (98.91) | 70 (100.00) | 161 (99.38) | 1.0000 |
| (+) | 1 (1.09) | 0 | 1 (0.62) |  |
| Oral cavity, malignant tumor | (–) | 92 (100.00) | 69 (98.57) | 161 (99.38) | 0.4321 |
| (+) | 0 | 1 (1.43) | 1 (0.62) |  |
| Ophthalmologic disease | (–) | 91 (98.91) | 70 (100.00) | 161 (99.38) | 1.0000 |
| (+) | 1 (1.09) | 0 | 1 (0.62) |  |
| Current medical history | | | | | |
| **SOC** | | | | | |
| Gastrointestinal | (–) | 86 (93.48) | 63 (90.00) | 149 (91.98) | 0.4195 |
| (+) | 6 (6.52) | 7 (10.00) | 13 (8.02) |  |
| Larynx | (–) | 92 (100.00) | 69 (98.57) | 161 (99.38) | 0.4321 |
| (+) | 0 | 1 (1.43) | 1 (0.62) |  |
| Neurology | (–) | 88 (95.65) | 67 (95.71) | 155 (95.68) | 1.0000 |
| (+) | 4 (4.35) | 3 (4.29) | 7 (4.32) |  |
| Urogenital | (–) | 89 (96.74) | 67 (95.71) | 156 (96.30) | 1.0000 |
| (+) | 3 (3.26) | 3 (4.29) | 6 (3.70) |  |
| Gynecology | (–) | 90 (97.83) | 69 (98.57) | 159 (98.15) | 1.0000 |
| (+) | 2 (2.17) | 1 (1.43) | 3 (1.85) |  |
| Neuropsychiatry | (–) | 91 (98.91) | 67 (95.71) | 158 (97.53) | 0.3164 |
| (+) | 1 (1.09) | 3 (4.29) | 4 (2.47) |  |
| Allergy | (–) | 92 (100.00) | 68 (97.14) | 160 (98.77) | 0.1852 |
| (+) | 0 | 2 (2.86) | 2 (1.23) |  |
| Breast | (–) | 92 (100.00) | 69 (98.57) | 161 (99.38) | 0.4321 |
| (+) | 0 | 1 (1.43) | 1 (0.62) |  |
| Musculoskeletal | (–) | 89 (96.74) | 68 (97.14) | 157 (96.91) | 1.0000 |
| (+) | 3 (3.26) | 2 (2.86) | 5 (3.09) |  |
| Renal | (–) | 90 (97.83) | 70 (100.00) | 160 (98.77) | 0.5062 |
| (+) | 2 (2.17) | 0 | 2 (1.23) |  |
| Upper respiratory infection | (–) | 91 (98.91) | 68 (97.14) | 159 (98.15) | 0.5787 |
| (+) | 1 (1.09) | 2 (2.86) | 3 (1.85) |  |
| Cough | (–) | 91 (98.91) | 68 (97.14) | 159 (98.15) | 0.5787 |
| (+) | 1 (1.09) | 2 (2.86) | 3 (1.85) |  |
| Hematology | (–) | 92 (100.00) | 69 (98.57) | 161 (99.38) | 0.4321 |
| (+) | 0 | 1 (1.43) | 1 (0.62) |  |
| Ophthalmology | (–) | 91 (98.91) | 69 (98.57) | 160 (98.77) | 1.0000 |
| (+) | 1 (1.09) | 1 (1.43) | 2 (1.23) |  |
| **PT** | | | | | |
| Coronary disease | (–) | 91 (98.91) | 68 (97.14) | 159 (98.15) | 0.5787 |
| (+) | 1 (1.09) | 2 (2.86) | 3 (1.85) |  |
| Arrhythmia | (–) | 91 (98.91) | 69 (98.57) | 160 (98.77) | 1.0000 |
| (+) | 1 (1.09) | 1 (1.43) | 2 (1.23) |  |
| Cardiac, anatomical defect | (–) | 91 (98.91) | 70 (100.00) | 161 (99.38) | 1.0000 |
| (+) | 1 (1.09) | 0 | 1 (0.62) |  |
| Pulmonary, inflammation | (–) | 92 (100.00) | 69 (98.57) | 161 (99.38) | 0.4321 |
| (+) | 0 | 1 (1.43) | 1 (0.62) |  |
| Pulmonary, benign tumor | (–) | 91 (98.91) | 70 (100.00) | 161 (99.38) | 1.0000 |
| (+) | 1 (1.09) | 0 | 1 (0.62) |  |
| Pulmonary, functional disease | (–) | 91 (98.91) | 70 (100.00) | 161 (99.38) | 1.0000 |
| (+) | 1 (1.09) | 0 | 1 (0.62) |  |
| Gastrointestinal, functional disease | (–) | 90 (97.83) | 68 (97.14) | 158 (97.53) | 1.0000 |
| (+) | 2 (2.17) | 2 (2.86) | 4 (2.47) |  |
| Gastrointestinal, inflammatory disease | (–) | 88 (95.65) | 68 (97.14) | 156 (96.30) | 0.6993 |
| (+) | 4 (4.35) | 2 (2.86) | 6 (3.70) |  |
| Gastrointestinal, malignant tumor | (–) | 92 (100.00) | 69 (98.57) | 161 (99.38) | 0.4321 |
| (+) | 0 | 1 (1.43) | 1 (0.62) |  |
| Hepatobiliary inflammatory and functional disease | (–) | 91 (98.91) | 68 (97.14) | 159 (98.15) | 0.5787 |
| (+) | 1 (1.09) | 2 (2.86) | 3 (1.85) |  |
| Hepatobiliary, benign tumor | (–) | 92 (100.00) | 69 (98.57) | 161 (99.38) | 0.4321 |
| (+) | 0 | 1 (1.43) | 1 (0.62) |  |
| Pituitary disease | (–) | 91 (98.91) | 70 (100.00) | 161 (99.38) | 1.0000 |
| (+) | 1 (1.09) | 0 | 1 (0.62) |  |
| Bone disorder with calcium disorder | (–) | 90 (97.83) | 68 (97.14) | 158 (97.53) | 1.0000 |
| (+) | 2 (2.17) | 2 (2.86) | 4 (2.47) |  |
| Thyroid, benign tumor | (–) | 91 (98.91) | 68 (97.14) | 159 (98.15) | 0.5787 |
| (+) | 1 (1.09) | 2 (2.86) | 3 (1.85) |  |
| Thyroid, functional disorder | (–) | 91 (98.91) | 69 (98.57) | 160 (98.77) | 1.0000 |
| (+) | 1 (1.09) | 1 (1.43) | 2 (1.23) |  |
| Larynx, functional disorder | (–) | 92 (100.00) | 69 (98.57) | 161 (99.38) | 0.4321 |
| (+) | 0 | 1 (1.43) | 1 (0.62) |  |
| Cerebrovascular infarct | (–) | 90 (97.83) | 69 (98.57) | 159 (98.15) | 1.0000 |
| (+) | 2 (2.17) | 1 (1.43) | 3 (1.85) |  |
| Neurodegenerative disease | (–) | 91 (98.91) | 70 (100.00) | 161 (99.38) | 1.0000 |
| (+) | 1 (1.09) | 0 | 1 (0.62) |  |
| Neurologic functional disorder | (–) | 90 (97.83) | 68 (97.14) | 158 (97.53) | 1.0000 |
| (+) | 2 (2.17) | 2 (2.86) | 4 (2.47) |  |
| Urogenital, functional disorder | (–) | 91 (98.91) | 68 (97.14) | 159 (98.15) | 0.5787 |
| (+) | 1 (1.09) | 2 (2.86) | 3 (1.85) |  |
| Urogenital inflammation | (–) | 90 (97.83) | 70 (100.00) | 160 (98.77) | 0.5062 |
| (+) | 2 (2.17) | 0 | 2 (1.23) |  |
| Benign prostate hyperplasia | (–) | 91 (98.91) | 69 (98.57) | 160 (98.77) | 1.0000 |
| (+) | 1 (1.09) | 1 (1.43) | 2 (1.23) |  |
| Gynecology, benign tumor | (–) | 90 (97.83) | 69 (98.57) | 159 (98.15) | 1.0000 |
| (+) | 2 (2.17) | 1 (1.43) | 3 (1.85) |  |
| Depression | (–) | 91 (98.91) | 68 (97.14) | 159 (98.15) | 0.5787 |
| (+) | 1 (1.09) | 2 (2.86) | 3 (1.85) |  |
| Other neuropsychiatry disorder | (–) | 92 (100.00) | 69 (98.57) | 161 (99.38) | 0.4321 |
| (+) | 0 | 1 (1.43) | 1 (0.62) |  |
| Allergy | (–) | 92 (100.00) | 68 (97.14) | 160 (98.77) | 0.1852 |
| (+) | 0 | 2 (2.86) | 2 (1.23) |  |
| Breast malignant mass | (–) | 92 (100.00) | 69 (98.57) | 161 (99.38) | 0.4321 |
| (+) | 0 | 1 (1.43) | 1 (0.62) |  |
| Musculoskeletal inflammatory disease | (–) | 91 (98.91) | 69 (98.57) | 160 (98.77) | 1.0000 |
| (+) | 1 (1.09) | 1 (1.43) | 2 (1.23) |  |
| Degenerative musculoskeletal disease | (–) | 89 (96.74) | 69 (98.57) | 158 (97.53) | 0.6343 |
| (+) | 3 (3.26) | 1 (1.43) | 4 (2.47) |  |
| Renal functional disorder | (–) | 90 (97.83) | 70 (100.00) | 160 (98.77) | 0.5062 |
| (+) | 2 (2.17) | 0 | 2 (1.23) |  |
| Upper respiratory infection | (–) | 91 (98.91) | 68 (97.14) | 159 (98.15) | 0.5787 |
| (+) | 1 (1.09) | 2 (2.86) | 3 (1.85) |  |
| Cough | (–) | 91 (98.91) | 68 (97.14) | 159 (98.15) | 0.5787 |
| (+) | 1 (1.09) | 2 (2.86) | 3 (1.85) |  |
| Hematologic disease | (–) | 92 (100.00) | 69 (98.57) | 161 (99.38) | 0.4321 |
| (+) | 0 | 1 (1.43) | 1 (0.62) |  |
| Ophthalmologic disease | (–) | 91 (98.91) | 69 (98.57) | 160 (98.77) | 1.0000 |
| (+) | 1 (1.09) | 1 (1.43) | 2 (1.23) |  |

Values are presented as number.

SOC, systemic organ class; PT, preferred term.

a)Chi-square test or Fisher’s exact test.

Supplementary Table 9. Univariate comparative analysis between early-responders and late-responders (past & current medication history)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | | Early response | Late response | Total | *P*-valuea) |
| Factor | | n=92 (56.79%) | n=70 (43.21%) | n=162 (100%) |  |
| **Past medication history** | | | | | |
| **AC** | | | | | |
| Gastrointestinal | (–) | 81 (88.04) | 64 (91.43) | 145 (89.51) | 0.4862 |
| (+) | 11 (11.96) | 6 (8.57) | 17 (10.49) |  |
| Systemic acting drugs | (–) | 86 (93.48) | 67 (95.71) | 153 (94.44) | 0.7330 |
| (+) | 6 (6.52) | 3 (4.29) | 9 (5.56) |  |
| Neuropsychiatry | (–) | 90 (97.83) | 68 (97.14) | 158 (97.53) | 1.0000 |
| (+) | 2 (2.17) | 2 (2.86) | 4 (2.47) |  |
| Neurology | (–) | 88 (95.65) | 62 (88.57) | 150 (92.59) | 0.0883 |
| (+) | 4 (4.35) | 8 (11.43) | 12 (7.41) |  |
| Allergy | (–) | 92 (100.00) | 68 (97.14) | 160 (98.77) | 0.1852 |
| (+) | 0 | 2 (2.86) | 2 (1.23) |  |
| Urogenital | (–) | 92 (100.00) | 69 (98.57) | 161 (99.38) | 0.4321 |
| (+) | 0 | 1 (1.43) | 1 (0.62) |  |
| Female hormonal | (–) | 91 (98.91) | 69 (98.57) | 160 (98.77) | 1.0000 |
| (+) | 1 (1.09) | 1 (1.43) | 2 (1.23) |  |
| Musculoskeletal | (–) | 90 (97.83) | 68 (97.14) | 158 (97.53) | 1.0000 |
| (+) | 2 (2.17) | 2 (2.86) | 4 (2.47) |  |
| Nutritional supplement | (–) | 90 (97.83) | 69 (98.57) | 159 (98.15) | 1.0000 |
| (+) | 2 (2.17) | 1 (1.43) | 3 (1.85) |  |
| Rheumatology | (–) | 92 (100.00) | 69 (98.57) | 161 (99.38) | 0.4321 |
| (+) | 0 | 1 (1.43) | 1 (0.62) |  |
| Others | (–) | 91 (98.91) | 68 (97.14) | 159 (98.15) | 0.5787 |
| (+) | 1 (1.09) | 2 (2.86) | 3 (1.85) |  |
| **TC** | | | | | |
| Anticoagulant | (–) | 86 (93.48) | 64 (91.43) | 150 (92.59) | 0.6217 |
| (+) | 6 (6.52) | 6 (8.57) | 12 (7.41) |  |
| Vasodilator, anti-angina | (–) | 92 (100.00) | 69 (98.57) | 161 (99.38) | 0.4321 |
| (+) | 0 | 1 (1.43) | 1 (0.62) |  |
| Anti-arrhythmic | (–) | 91 (98.91) | 70 (100.00) | 161 (99.38) | 1.0000 |
| (+) | 1 (1.09) | 0 | 1 (0.62) |  |
| Antitussive | (–) | 91 (98.91) | 70 (100.00) | 161 (99.38) | 1.0000 |
| (+) | 1 (1.09) | 0 | 1 (0.62) |  |
| Gastrointestinal protectant | (–) | 88 (95.65) | 67 (95.71) | 155 (95.68) | 1.0000 |
| (+) | 4 (4.35) | 3 (4.29) | 7 (4.32) |  |
| Gastrointestinal, promotility agent | (–) | 89 (96.74) | 68 (97.14) | 157 (96.91) | 1.0000 |
| (+) | 3 (3.26) | 2 (2.86) | 5 (3.09) |  |
| H2 blocker | (–) | 91 (98.91) | 68 (97.14) | 159 (98.15) | 0.5787 |
| (+) | 1 (1.09) | 2 (2.86) | 3 (1.85) |  |
| Proton pump inhibitor | (–) | 87 (94.57) | 67 (95.71) | 154 (95.06) | 1.0000 |
| (+) | 5 (5.43) | 3 (4.29) | 8 (4.94) |  |
| Laxative | (–) | 91 (98.91) | 69 (98.57) | 160 (98.77) | 1.0000 |
| (+) | 1 (1.09) | 1 (1.43) | 2 (1.23) |  |
| Non-steroidal anti-inflammatory drug | (–) | 89 (96.74) | 70 (100.00) | 159 (98.15) | 0.2593 |
| (+) | 3 (3.26) | 0 | 3 (1.85) |  |
| Steroid | (–) | 89 (96.74) | 69 (98.57) | 158 (97.53) | 0.6343 |
| (+) | 3 (3.26) | 1 (1.43) | 4 (2.47) |  |
| Antibiotic | (–) | 92 (100.00) | 69 (98.57) | 161 (99.38) | 0.4321 |
| (+) | 0 | 1 (1.43) | 1 (0.62) |  |
| Acetaminophen | (–) | 91 (98.91) | 69 (98.57) | 160 (98.77) | 1.0000 |
| (+) | 1 (1.09) | 1 (1.43) | 2 (1.23) |  |
| Anti-anxiety, benzodiazepine | (–) | 91 (98.91) | 68 (97.14) | 159 (98.15) | 0.5787 |
| (+) | 1 (1.09) | 2 (2.86) | 3 (1.85) |  |
| Anti-depressant, serotonin-norepinephrine reuptake inhibitor | (–) | 91 (98.91) | 70 (100.00) | 161 (99.38) | 1.0000 |
| (+) | 1 (1.09) | 0 | 1 (0.62) |  |
| Anti-depressant, selective serotonin reuptake inhibitor | (–) | 92 (100.00) | 69 (98.57) | 161 (99.38) | 0.4321 |
| (+) | 0 | 1 (1.43) | 1 (0.62) |  |
| Tricyclic antidepressant | (–) | 91 (98.91) | 69 (98.57) | 160 (98.77) | 1.0000 |
| (+) | 1 (1.09) | 1 (1.43) | 2 (1.23) |  |
| Neurology, anticoagulant | (–) | 88 (95.65) | 64 (91.43) | 152 (93.83) | 0.3311 |
| (+) | 4 (4.35) | 6 (8.57) | 10 (6.17) |  |
| Peripheral vasoactive agent | (–) | 92 (100.00) | 69 (98.57) | 161 (99.38) | 0.4321 |
| (+) | 0 | 1 (1.43) | 1 (0.62) |  |
| Neurodegenerative suppressant | (–) | 92 (100.00) | 69 (98.57) | 161 (99.38) | 0.4321 |
| (+) | 0 | 1 (1.43) | 1 (0.62) |  |
| Opioid analgesic | (–) | 92 (100.00) | 69 (98.57) | 161 (99.38) | 0.4321 |
| (+) | 0 | 1 (1.43) | 1 (0.62) |  |
| Antihistamine | (–) | 92 (100.00) | 68 (97.14) | 160 (98.77) | 0.1852 |
| (+) | 0 | 2 (2.86) | 2 (1.23) |  |
| Leukotriene inhibitor | (–) | 92 (100.00) | 69 (98.57) | 161 (99.38) | 0.4321 |
| (+) | 0 | 1 (1.43) | 1 (0.62) |  |
| Diuretics | (–) | 90 (97.83) | 69 (98.57) | 159 (98.15) | 1.0000 |
| (+) | 2 (2.17) | 1 (1.43) | 3 (1.85) |  |
| Phosphodiesterase-5 inhibitor | (–) | 92 (100.00) | 69 (98.57) | 161 (99.38) | 0.4321 |
| (+) | 0 | 1 (1.43) | 1 (0.62) |  |
| Female hormonal supplement | (–) | 91 (98.91) | 69 (98.57) | 160 (98.77) | 1.0000 |
| (+) | 1 (1.09) | 1 (1.43) | 2 (1.23) |  |
| Anti-hyperlipidemic | (–) | 88 (95.65) | 63 (90.00) | 151 (93.21) | 0.2101 |
| (+) | 4 (4.35) | 7 (10.00) | 11 (6.79) |  |
| Osteoporosis | (–) | 90 (97.83) | 69 (98.57) | 159 (98.15) | 1.0000 |
| (+) | 2 (2.17) | 1 (1.43) | 3 (1.85) |  |
| Muscle relaxant | (–) | 90 (97.83) | 69 (98.57) | 159 (98.15) | 1.0000 |
| (+) | 2 (2.17) | 1 (1.43) | 3 (1.85) |  |
| Glucosamine | (–) | 91 (98.91) | 69 (98.57) | 160 (98.77) | 1.0000 |
| (+) | 1 (1.09) | 1 (1.43) | 2 (1.23) |  |
| Nutritional supplement | (–) | 90 (97.83) | 69 (98.57) | 159 (98.15) | 1.0000 |
| (+) | 2 (2.17) | 1 (1.43) | 3 (1.85) |  |
| Anti-rheumatic | (–) | 92 (100.00) | 69 (98.57) | 161 (99.38) | 0.4321 |
| (+) | 0 | 1 (1.43) | 1 (0.62) |  |
| Others | (–) | 91 (98.91) | 68 (97.14) | 159 (98.15) | 0.5787 |
| (+) | 1 (1.09) | 2 (2.86) | 3 (1.85) |  |
| **Current medication history** | | | | | |
| **AC** | | | | | |
| Pulmonary | (–) | 77 (83.70) | 56 (80.00) | 133 (82.10) | 0.5433 |
| (+) | 15 (16.30) | 14 (20.00) | 29 (17.90) |  |
| Gastrointestinal | (–) | 68 (73.91) | 53 (75.71) | 121 (74.69) | 0.7939 |
| (+) | 24 (26.09) | 17 (24.29) | 41 (25.31) |  |
| Systemic acting drugs | (–) | 81 (88.04) | 62 (88.57) | 143 (88.27) | 0.9176 |
| (+) | 11 (11.96) | 8 (11.43) | 19 (11.73) |  |
| Neuropsychiatry | (–) | 90 (97.83) | 67 (95.71) | 157 (96.91) | 0.6529 |
| (+) | 2 (2.17) | 3 (4.29) | 5 (3.09) |  |
| Neurology | (–) | 87 (94.57) | 62 (88.57) | 149 (91.98) | 0.1642 |
| (+) | 5 (5.43) | 8 (11.43) | 13 (8.02) |  |
| Allergy | (–) | 88 (95.65) | 66 (94.29) | 154 (95.06) | 0.7273 |
| (+) | 4 (4.35) | 4 (5.71) | 8 (4.94) |  |
| Urogenital | (–) | 92 (100.00) | 69 (98.57) | 161 (99.38) | 0.4321 |
| (+) | 0 | 1 (1.43) | 1 (0.62) |  |
| Female hormonal | (–) | 91 (98.91) | 69 (98.57) | 160 (98.77) | 1.0000 |
| (+) | 1 (1.09) | 1 (1.43) | 2 (1.23) |  |
| Musculoskeletal | (–) | 91 (98.91) | 69 (98.57) | 160 (98.77) | 1.0000 |
| (+) | 1 (1.09) | 1 (1.43) | 2 (1.23) |  |
| Nutritional supplement | (–) | 90 (97.83) | 65 (92.86) | 155 (95.68) | 0.2406 |
| (+) | 2 (2.17) | 5 (7.14) | 7 (4.32) |  |
| Rheumatology | (–) | 92 (100.00) | 69 (98.57) | 161 (99.38) | 0.4321 |
| (+) | 0 | 1 (1.43) | 1 (0.62) |  |
| Others | (–) | 91 (98.91) | 66 (94.29) | 157 (96.91) | 0.1667 |
| (+) | 1 (1.09) | 4 (5.71) | 5 (3.09) |  |
| **TC** | | | | | |
| Anticoagulant | (–) | 88 (95.65) | 66 (94.29) | 154 (95.06) | 0.7273 |
| (+) | 4 (4.35) | 4 (5.71) | 8 (4.94) |  |
| Vasodilator, anti-angina | (–) | 92 (100.00) | 69 (98.57) | 161 (99.38) | 0.4321 |
| (+) | 0 | 1 (1.43) | 1 (0.62) |  |
| Anti-arrhythmic | (–) | 90 (97.83) | 70 (100.00) | 160 (98.77) | 0.5062 |
| (+) | 2 (2.17) | 0 | 2 (1.23) |  |
| Mucoactive | (–) | 78 (84.78) | 57 (81.43) | 135 (83.33) | 0.5704 |
| (+) | 14 (15.22) | 13 (18.57) | 27 (16.67) |  |
| Antitussive | (–) | 91 (98.91) | 69 (98.57) | 160 (98.77) | 1.0000 |
| (+) | 1 (1.09) | 1 (1.43) | 2 (1.23) |  |
| Bronchodilator | (–) | 91 (98.91) | 69 (98.57) | 160 (98.77) | 1.0000 |
| (+) | 1 (1.09) | 1 (1.43) | 2 (1.23) |  |
| Gastrointestinal protectant | (–) | 88 (95.65) | 66 (94.29) | 154 (95.06) | 0.7273 |
| (+) | 4 (4.35) | 4 (5.71) | 8 (4.94) |  |
| Gastrointestinal, promotility agent | (–) | 78 (84.78) | 59 (84.29) | 137 (84.57) | 0.9309 |
| (+) | 14 (15.22) | 11 (15.71) | 25 (15.43) |  |
| H2 blocker | (–) | 90 (97.83) | 68 (97.14) | 158 (97.53) | 1.0000 |
| (+) | 2 (2.17) | 2 (2.86) | 4 (2.47) |  |
| Laxative | (–) | 91 (98.91) | 67 (95.71) | 158 (97.53) | 0.3164 |
| (+) | 1 (1.09) | 3 (4.29) | 4 (2.47) |  |
| Gastrointestinal, spasmolytic | (–) | 91 (98.91) | 69 (98.57) | 160 (98.77) | 1.0000 |
| (+) | 1 (1.09) | 1 (1.43) | 2 (1.23) |  |
| Antiemetic | (–) | 92 (100.00) | 69 (98.57) | 161 (99.38) | 0.4321 |
| (+) | 0 | 1 (1.43) | 1 (0.62) |  |
| Non-steroidal anti-inflammatory drug | (–) | 86 (93.48) | 67 (95.71) | 153 (94.44) | 0.7330 |
| (+) | 6 (6.52) | 3 (4.29) | 9 (5.56) |  |
| Steroid | (–) | 89 (96.74) | 67 (95.71) | 156 (96.30) | 1.0000 |
| (+) | 3 (3.26) | 3 (4.29) | 6 (3.70) |  |
| Antibiotic | (–) | 90 (97.83) | 66 (94.29) | 156 (96.30) | 0.4041 |
| (+) | 2 (2.17) | 4 (5.71) | 6 (3.70) |  |
| Acetaminophen | (–) | 90 (97.83) | 68 (97.14) | 158 (97.53) | 1.0000 |
| (+) | 2 (2.17) | 2 (2.86) | 4 (2.47) |  |
| Anti-anxiety, benzodiazepine | (–) | 91 (98.91) | 67 (95.71) | 158 (97.53) | 0.3164 |
| (+) | 1 (1.09) | 3 (4.29) | 4 (2.47) |  |
| Anti-depressant, serotonin-norepinephrine reuptake inhibitor | (–) | 91 (98.91) | 70 (100.00) | 161 (99.38) | 1.0000 |
| (+) | 1 (1.09) | 0 | 1 (0.62) |  |
| Anti-depressant, selective serotonin reuptake inhibitor | (–) | 92 (100.00) | 69 (98.57) | 161 (99.38) | 0.4321 |
| (+) | 0 | 1 (1.43) | 1 (0.62) |  |
| Tricyclic antidepressant | (–) | 91 (98.91) | 68 (97.14) | 159 (98.15) | 0.5787 |
| (+) | 1 (1.09) | 2 (2.86) | 3 (1.85) |  |
| Neurology, anticoagulant | (–) | 88 (95.65) | 66 (94.29) | 154 (95.06) | 0.7273 |
| (+) | 4 (4.35) | 4 (5.71) | 8 (4.94) |  |
| Peripheral vasoactive agent | (–) | 92 (100.00) | 69 (98.57) | 161 (99.38) | 0.4321 |
| (+) | 0 | 1 (1.43) | 1 (0.62) |  |
| Neurodegenerative suppressant | (–) | 92 (100.00) | 69 (98.57) | 161 (99.38) | 0.4321 |
| (+) | 0 | 1 (1.43) | 1 (0.62) |  |
| Opioid analgesic | (–) | 91 (98.91) | 69 (98.57) | 160 (98.77) | 1.0000 |
| (+) | 1 (1.09) | 1 (1.43) | 2 (1.23) |  |
| Neuropathic analgesic | (–) | 91 (98.91) | 70 (100.00) | 161 (99.38) | 1.0000 |
| (+) | 1 (1.09) | 0 | 1 (0.62) |  |
| Intra-nasal steroid | (–) | 90 (97.83) | 69 (98.57) | 159 (98.15) | 1.0000 |
| (+) | 2 (2.17) | 1 (1.43) | 3 (1.85) |  |
| Antihistamine | (–) | 89 (96.74) | 67 (95.71) | 156 (96.30) | 1.0000 |
| (+) | 3 (3.26) | 3 (4.29) | 6 (3.70) |  |
| Leukotriene inhibitor | (–) | 92 (100.00) | 69 (98.57) | 161 (99.38) | 0.4321 |
| (+) | 0 | 1 (1.43) | 1 (0.62) |  |
| Diuretics | (–) | 91 (98.91) | 69 (98.57) | 160 (98.77) | 1.0000 |
| (+) | 1 (1.09) | 1 (1.43) | 2 (1.23) |  |
| Phosphodiesterase-5 inhibitor | (–) | 92 (100.00) | 69 (98.57) | 161 (99.38) | 0.4321 |
| (+) | 0 | 1 (1.43) | 1 (0.62) |  |
| Female hormonal supplement | (–) | 91 (98.91) | 69 (98.57) | 160 (98.77) | 1.0000 |
| (+) | 1 (1.09) | 1 (1.43) | 2 (1.23) |  |
| Osteoporosis | (–) | 90 (97.83) | 66 (94.29) | 156 (96.30) | 0.4041 |
| (+) | 2 (2.17) | 4 (5.71) | 6 (3.70) |  |
| Muscle relaxant | (–) | 91 (98.91) | 69 (98.57) | 160 (98.77) | 1.0000 |
| (+) | 1 (1.09) | 1 (1.43) | 2 (1.23) |  |
| Glucosamine | (–) | 91 (98.91) | 70 (100.00) | 161 (99.38) | 1.0000 |
| (+) | 1 (1.09) | 0 | 1 (0.62) |  |
| Nutritional supplement | (–) | 90 (97.83) | 65 (92.86) | 155 (95.68) | 0.2406 |
| (+) | 2 (2.17) | 5 (7.14) | 7 (4.32) |  |
| Anti-rheumatic | (–) | 92 (100.00) | 69 (98.57) | 161 (99.38) | 0.4321 |
| (+) | 0 | 1 (1.43) | 1 (0.62) |  |
| Others | (–) | 91 (98.91) | 66 (94.29) | 157 (96.91) | 0.1667 |
| (+) | 1 (1.09) | 4 (5.71) | 5 (3.09) |  |

Values are presented as number (%).

AC, anatomical code; TC, therapeutic code.

a)Chi-square test or Fisher’s exact test.