**Table 1: Covariate comparisons between trial participants (TP) and non-participants (NP) from neoplastic trialsa**

|  | **Neoplastic disease****(N = 737 each)** |
| --- | --- |
|  | **P** | **NP** | **StDiff** |
| Demographics |  |  |  |
|  Age group |  |  |  |
|  Younger than 18 years | 69 (9.4) | 52 (7.1) | 0.080 |
|  18 to 64 years | 331 (44.9) | 322 (43.7) | 0.025 |
|  65 years and older | 337 (45.7) | 363 (49.2) | -0.069 |
|  Female | 346 (46.9) | 359 (48.7) | -0.035 |
| Medical history: General |  |  |  |
|  Acute respiratory disease | 50 (6.8) | 71 (9.7) | -0.106 |
|  Chronic liver disease | 28 (3.8) | 42 (5.6) | -0.087 |
|  Chronic obstructive lung disease | 33 (4.5) | 58 (7.9) | -0.141 |
|  Depressive disorder | 52 (7.1) | 83 (11.3) | -0.145 |
|  Diabetes mellitus | 97 (13.2) | 132 (17.9) | -0.131 |
|  Gastroesophageal reflux disease | 70 (9.5) | 106 (14.4) | -0.151 |
|  Hyperlipidemia | 136 (18.5) | 188 (25.5) | -0.171 |
|  Hypertensive disorder | 234 (31.8) | 315 (42.7) | -0.227 |
|  Lesion of liver | 142 (19.3) | 81 (11.0) | 0.232 |
|  Obesity | 23 (3.1) | 43 (5.9) | -0.134 |
|  Osteoarthritis | 97 (13.2) | 129 (17.6) | -0.121 |
|  Pneumonia | 52 (7.1) | 90 (12.2) | -0.175 |
|  Renal impairment | 72 (9.8) | 128 (17.3) | -0.221 |
|  Urinary tract infectious disease | 54 (7.3) | 93 (12.6) | -0.178 |
|  Viral hepatitis C | 11 (1.5) | 19 (2.6) | -0.080 |
|  Visual system disorder | 74 (10.0) | 104 (14.1) | -0.125 |
| Medical history: Cardiovascular disease |  |  |  |
|  Atrial fibrillation | 34 (4.6) | 63 (8.6) | -0.162 |
|  Cerebrovascular disease | 31 (4.2) | 45 (6.0) | -0.084 |
|  Coronary arteriosclerosis | 50 (6.8) | 92 (12.4) | -0.192 |
|  Heart disease | 196 (26.6) | 272 (36.9) | -0.223 |
|  Heart failure | 30 (4.1) | 64 (8.7) | -0.189 |
|  Ischemic heart disease | 13 (1.8) | 41 (5.5) | -0.199 |
|  Peripheral vascular disease | 6 (0.8) | 16 (2.2) | -0.113 |
|  Venous thrombosis | 35 (4.7) | 60 (8.1) | -0.141 |
| Medical history: Neoplasms |  |  |  |
|  Hematologic neoplasm | 320 (43.4) | 316 (42.8) | 0.012 |
|  Malignant lymphoma | 169 (22.9) | 174 (23.6) | -0.016 |
|  Malignant neoplastic disease | 737 (100.0) | 736 (99.9)b | 0.015 |
|  Malignant tumor of breast | 101 (13.7) | 121 (16.4) | -0.075 |
|  Malignant tumor of lung | 100 (13.6) | 69 (9.4) | 0.133 |
|  Malignant tumor of urinary bladder | 63 (8.5) | 66 (8.9) | -0.015 |
|  Primary malignant neoplasm of prostate | 68 (9.2) | 65 (8.8) | 0.015 |
| Medication use |  |  |  |
|  Agents acting on the renin-angiotensin system | 171 (23.2) | 201 (27.3) | -0.094 |
|  Antibacterials for systemic use | 419 (56.9) | 461 (62.5) | -0.115 |
|  Antidepressants | 146 (19.8) | 152 (20.7) | -0.022 |
|  Antiepileptics | 160 (21.7) | 172 (23.3) | -0.039 |
|  Antiinflammatory and antirheumatic products | 188 (25.5) | 219 (29.7) | -0.093 |
|  Antineoplastic agents | 273 (37.0) | 341 (46.3) | -0.189 |
|  Antithrombotic agents | 305 (41.4) | 397 (53.9) | -0.251 |
|  Beta blocking agents | 159 (21.6) | 205 (27.9) | -0.145 |
|  Calcium channel blockers | 133 (18.0) | 168 (22.8) | -0.118 |
|  Diuretics | 176 (23.9) | 219 (29.7) | -0.131 |
|  Drugs for acid related disorders | 359 (48.7) | 432 (58.6) | -0.200 |
|  Drugs for obstructive airway diseases | 137 (18.6) | 175 (23.7) | -0.125 |
|  Drugs used in diabetes | 123 (16.7) | 158 (21.4) | -0.121 |
|  Immunosuppressants | 69 (9.4) | 95 (12.9) | -0.111 |
|  Lipid modifying agents | 180 (24.4) | 228 (31.0) | -0.148 |
|  Opioids | 395 (53.6) | 409 (55.5) | -0.038 |
|  Psycholeptics | 358 (48.6) | 361 (49.0) | -0.009 |

aP = participants; NP = non-participants; StDiff = standardized differences; blue highlighted cells refer to covariates that are more prevalent in non-participants than participants (i.e. standardized difference < -0.1) while red highlighted cells refer to covariates that more prominent in participants than non-participants (i.e. standardized difference > 0.1)

bThe estimated percentage is not equal to 100% because one record within the resampling procedure was matched to a participant based on a condition that was listed within the neoplastic disease trial, but that condition was not a neoplastic disease; subsequently, the non-participant was found to not have a code for a neoplastic disorder 365 days prior to his/her index

**Table 2: Covariate comparisons between trial participants (TP) and non-participants (NP) from disorder of digestive system trialsa**

|  | **Disorder of digestive system****(N = 321 each)** |
| --- | --- |
|  | **P** | **NP** | **StDiff** |
| Demographics |  |  |  |
|  Age group |  |  |  |
|  Younger than 18 years | 0 (0.0) | 20 (6.3) | -0.366 |
|  18 to 64 years | 239 (74.5) | 197 (61.3) | 0.284 |
|  65 years and older | 82 (25.5) | 104 (32.4) | -0.152 |
|  Female | 120 (37.4) | 136 (42.3) | -0.100 |
| Medical history: General |  |  |  |
|  Acute respiratory disease | 22 (6.9) | 36 (11.1) | -0.146 |
|  Chronic liver disease | 164 (51.1) | 162 (50.5) | 0.012 |
|  Chronic obstructive lung disease | 16 (5.0) | 26 (8.2) | -0.129 |
|  Depressive disorder | 32 (10.0) | 52 (16.3) | -0.186 |
|  Diabetes mellitus | 56 (17.4) | 79 (24.6) | -0.178 |
|  Gastroesophageal reflux disease | 28 (8.7) | 50 (15.7) | -0.215 |
|  Hyperlipidemia | 33 (10.3) | 65 (20.3) | -0.280 |
|  Hypertensive disorder | 107 (33.3) | 144 (45.0) | -0.241 |
|  Lesion of liver | 164 (51.1) | 131 (40.7) | 0.210 |
|  Obesity | 13 (4.0) | 29 (9.1) | -0.208 |
|  Osteoarthritis | 29 (9.0) | 41 (12.8) | -0.122 |
|  Pneumonia | 10 (3.1) | 29 (9.0) | -0.248 |
|  Renal impairment | 38 (11.8) | 58 (18.1) | -0.177 |
|  Urinary tract infectious disease | 9 (2.8) | 24 (7.4) | -0.210 |
|  Viral hepatitis C | 156 (48.6) | 149 (46.6) | 0.041 |
|  Visual system disorder | 21 (6.5) | 30 (9.3) | -0.103 |
| Medical history: Cardiovascular disease |  |  |  |
|  Atrial fibrillation | 11 (3.4) | 22 (6.8) | -0.154 |
|  Cerebrovascular disease | 11 (3.4) | 16 (5.0) | -0.081 |
|  Coronary arteriosclerosis | 20 (6.2) | 32 (10.1) | -0.141 |
|  Heart disease | 90 (28.0) | 100 (31.3) | -0.072 |
|  Heart failure | 15 (4.7) | 27 (8.4) | -0.150 |
|  Ischemic heart disease | 4 (1.2) | 19 (5.8) | -0.252 |
|  Peripheral vascular disease | 3 (0.9) | 5 (1.7) | -0.070 |
|  Venous thrombosis | 17 (5.3) | 25 (7.9) | -0.105 |
| Medical history: Neoplasms |  |  |  |
|  Hematologic neoplasm | 16 (5.0) | 20 (6.3) | -0.057 |
|  Malignant lymphoma | 2 (0.6) | 7 (2.3) | -0.144 |
|  Malignant neoplastic disease | 157 (48.9) | 152 (47.5) | 0.028 |
|  Malignant tumor of breast | 3 (0.9) | 6 (1.8) | -0.078 |
|  Malignant tumor of lung | 21 (6.5) | 15 (4.7) | 0.077 |
|  Malignant tumor of urinary bladder | 2 (0.6) | 0 (0.0) | 0.110 |
|  Primary malignant neoplasm of prostate | 21 (6.5) | 15 (4.8) | 0.075 |
| Medication use |  |  |  |
|  Agents acting on the renin-angiotensin system | 52 (16.2) | 90 (28.0) | -0.288 |
|  Antibacterials for systemic use | 168 (52.3) | 200 (62.2) | -0.200 |
|  Antidepressants | 71 (22.1) | 73 (22.9) | -0.019 |
|  Antiepileptics | 33 (10.3) | 51 (16.0) | -0.170 |
|  Antiinflammatory and antirheumatic products | 89 (27.7) | 118 (36.7) | -0.194 |
|  Antineoplastic agents | 61 (19.0) | 69 (21.5) | -0.062 |
|  Antithrombotic agents | 142 (44.2) | 168 (52.4) | -0.165 |
|  Beta blocking agents | 87 (27.1) | 109 (33.9) | -0.148 |
|  Calcium channel blockers | 71 (22.1) | 68 (21.2) | 0.021 |
|  Diuretics | 91 (28.3) | 112 (34.8) | -0.141 |
|  Drugs for acid related disorders | 164 (51.1) | 184 (57.3) | -0.125 |
|  Drugs for obstructive airway diseases | 39 (12.1) | 75 (23.5) | -0.301 |
|  Drugs used in diabetes | 86 (26.8) | 94 (29.4) | -0.057 |
|  Immunosuppressants | 64 (19.9) | 45 (13.9) | 0.159 |
|  Lipid modifying agents | 43 (13.4) | 74 (23.1) | -0.252 |
|  Opioids | 175 (54.5) | 189 (58.8) | -0.088 |
|  Psycholeptics | 134 (41.7) | 147 (45.7) | -0.081 |

aP = participants; NP = non-participants; StDiff = standardized differences; blue highlighted cells refer to covariates that are more prevalent in non-participants than participants (i.e. standardized difference < -0.1) while red highlighted cells refer to covariates that more prominent in participants than non-participants (i.e. standardized difference > 0.1)

**Table 3: Covariate comparisons between trial participants (TP) and non-participants (NP) from inflammatory disorder trialsa**

|  | **Inflammatory disorder****(N = 276 each)** |
| --- | --- |
|  | **P** | **NP** | **StDiff** |
| Demographics |  |  |  |
|  Age group |  |  |  |
|  Younger than 18 years | 16 (5.8) | 26 (9.3) | -0.134 |
|  18 to 64 years | 232 (84.1) | 193 (70.0) | 0.339 |
|  65 years and older | 28 (10.1) | 57 (20.7) | -0.294 |
|  Female | 111 (40.2) | 123 (44.6) | -0.089 |
| Medical history: General |  |  |  |
|  Acute respiratory disease | 22 (8.0) | 36 (13) | -0.163 |
|  Chronic liver disease | 147 (53.3) | 146 (52.7) | 0.012 |
|  Chronic obstructive lung disease | 10 (3.6) | 22 (8.1) | -0.191 |
|  Depressive disorder | 29 (10.5) | 44 (15.9) | -0.161 |
|  Diabetes mellitus | 32 (11.6) | 57 (20.8) | -0.252 |
|  Gastroesophageal reflux disease | 13 (4.7) | 31 (11.2) | -0.241 |
|  Hyperlipidemia | 41 (14.9) | 57 (20.6) | -0.150 |
|  Hypertensive disorder | 82 (29.7) | 114 (41.4) | -0.246 |
|  Lesion of liver | 88 (31.9) | 88 (31.8) | 0.001 |
|  Obesity | 11 (4.0) | 26 (9.6) | -0.223 |
|  Osteoarthritis | 24 (8.7) | 35 (12.6) | -0.127 |
|  Pneumonia | 21 (7.6) | 33 (12.1) | -0.150 |
|  Renal impairment | 63 (22.8) | 84 (30.4) | -0.172 |
|  Urinary tract infectious disease | 10 (3.6) | 22 (7.8) | -0.183 |
|  Viral hepatitis C | 147 (53.3) | 141 (51.1) | 0.043 |
|  Visual system disorder | 17 (6.2) | 30 (10.8) | -0.167 |
| Medical history: Cardiovascular disease |  |  |  |
|  Atrial fibrillation | 9 (3.3) | 17 (6.0) | -0.130 |
|  Cerebrovascular disease | 9 (3.3) | 16 (5.7) | -0.115 |
|  Coronary arteriosclerosis | 14 (5.1) | 20 (7.2) | -0.088 |
|  Heart disease | 62 (22.5) | 84 (30.3) | -0.177 |
|  Heart failure | 9 (3.3) | 27 (9.9) | -0.268 |
|  Ischemic heart disease | 5 (1.8) | 18 (6.6) | -0.241 |
|  Peripheral vascular disease | 2 (0.7) | 0 (0.0) | 0.119 |
|  Venous thrombosis | 9 (3.3) | 13 (4.9) | -0.080 |
| Medical history: Neoplasms |  |  |  |
|  Hematologic neoplasm | 0 (0.0) | 0 (0.0) | 0.000 |
|  Malignant lymphoma | 2 (0.7) | 0 (0.0) | 0.119 |
|  Malignant neoplastic disease | 48 (17.4) | 45 (16.2) | 0.033 |
|  Malignant tumor of breast | 2 (0.7) | 0 (0.0) | 0.119 |
|  Malignant tumor of lung | 1 (0.4) | 0 (0.0) | 0.090 |
|  Malignant tumor of urinary bladder | 0 (0.0) | 0 (0.0) | 0.000 |
|  Primary malignant neoplasm of prostate | 1 (0.4) | 0 (0.0) | 0.090 |
| Medication use |  |  |  |
|  Agents acting on the renin-angiotensin system | 49 (17.8) | 74 (26.7) | -0.215 |
|  Antibacterials for systemic use | 140 (50.7) | 165 (59.7) | -0.182 |
|  Antidepressants | 44 (15.9) | 64 (23.1) | -0.183 |
|  Antiepileptics | 17 (6.2) | 42 (15.4) | -0.299 |
|  Antiinflammatory and antirheumatic products | 77 (27.9) | 96 (34.6) | -0.146 |
|  Antineoplastic agents | 24 (8.7) | 27 (9.8) | -0.037 |
|  Antithrombotic agents | 99 (35.9) | 127 (46.0) | -0.207 |
|  Beta blocking agents | 63 (22.8) | 86 (31.2) | -0.189 |
|  Calcium channel blockers | 46 (16.7) | 61 (22.0) | -0.133 |
|  Diuretics | 77 (27.9) | 92 (33.4) | -0.120 |
|  Drugs for acid related disorders | 102 (37.0) | 139 (50.4) | -0.272 |
|  Drugs for obstructive airway diseases | 38 (13.8) | 70 (25.2) | -0.290 |
|  Drugs used in diabetes | 47 (17.0) | 68 (24.6) | -0.188 |
|  Immunosuppressants | 74 (26.8) | 63 (22.8) | 0.092 |
|  Lipid modifying agents | 33 (12.0) | 57 (20.7) | -0.236 |
|  Opioids | 108 (39.1) | 126 (45.6) | -0.131 |
|  Psycholeptics | 69 (25.0) | 98 (35.6) | -0.233 |

aP = participants; NP = non-participants; StDiff = standardized differences; blue highlighted cells refer to covariates that are more prevalent in non-participants than participants (i.e. standardized difference < -0.1) while red highlighted cells refer to covariates that more prominent in participants than non-participants (i.e. standardized difference > 0.1)

**Table 4:** **Trial characteristics, stratified by disease domaina**

|  | **Neoplastic disease****(N = 86)** | **Disorder of digestive system****(N = 31)** | **Inflammatory disorder****(N = 28)** |
| --- | --- | --- | --- |
| Trial Phaseb |  |  |  |
|  Phase 1 | 21 (24.4) | 3 (9.7) | 0 (0.0) |
|  Phase 2 | 43 (50.0) | 17 (54.8) | 13 (46.4) |
|  Phase 3 | 21 (24.4) | 10 (32.3) | 12 (42.9) |
|  Phase 4 | 1 (1.2) | 1 (3.2) | 3 (10.7) |
| Number of Treatment Arms |  |  |  |
|  1 | 30 (34.9) | 9 (29.0) | 7 (25.0) |
|  2 | 28 (32.6) | 10 (32.3) | 11 (39.3) |
|  3 or more | 28 (32.6) | 12 (38.7) | 10 (35.7) |
| Any Mentioned Use of Randomization | 35 (40.7) | 19 (61.3) | 19 (67.9) |
| Any Mentioned Use of Blinding | 14 (16.3) | 10 (32.3) | 8 (28.6) |
| Intervention Model |  |  |  |
|  Single group assignment | 39 (45.3) | 10 (32.3) | 9 (32.1) |
|  Parallel assignment | 41 (47.7) | 21 (67.7) | 19 (67.9) |
|  Other assignment method | 6 (7.0) | 0 (0.0) | 0 (0.0) |
| Industry Sponsor Involvement | 73 (84.9) | 28 (90.3) | 24 (85.7) |
| Use of Data Monitoring Committee | 50 (58.1) | 24 (77.4) | 22 (78.6) |
| Multi-site Trial | 73 (84.9) | 27 (87.1) | 24 (85.7) |
| Overall Trial Enrollmentc |  |  |  |
|  Less than 50 | 24 (27.9) | 7 (22.6) | 5 (17.9) |
|  50 to 499 | 46 (53.5) | 17 (54.8) | 15 (53.6) |
|  500 or more | 16 (18.6) | 7 (22.6) | 8 (28.6) |
| Institution Specific Enrollment |  |  |  |
|  Less than 5 | 17 (19.8) | 6 (19.4) | 6 (21.4) |
|  5 to 19 | 49 (57.0) | 17 (54.8) | 16 (57.1) |
|  20 or more | 20 (23.3) | 8 (25.8) | 6 (21.4) |
| Status |  |  |  |
|  Completed | 33 (38.4) | 19 (61.3) | 17 (60.7) |
|  Recruiting | 15 (17.4) | 2 (6.5) | 1 (3.6) |
|  Active, not recruiting | 28 (32.6) | 3 (9.7) | 3 (10.7) |
|  Terminated, suspended, or withdrawn | 8 (9.3) | 5 (16.1) | 6 (21.4) |
|  Unknown status | 2 (2.3) | 2 (6.5) | 1 (3.6) |

aAll numbers are presented as No. (%) and all groups are mutually exclusive

bFor trials listed as multiple or combination phases, they were analyzed as their latest phase (e.g. “Phase 1/Phase 2” was considered “Phase 2”)

cIf actual enrollment was not available, anticipated enrollment was used