**TABLE 1 Primary Efficacy Outcome by Baseline Diabetes-related Factors and Select Background Antihyperglycemic Therapy**

|  | **Ticagrelor (N = 9619)** | | **Placebo (N = 9601)** | |  | | |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Characteristic** | **Number of Patients** | **Patients with events (%)** | **Number of Patients** | **Patients with events (%)** | **Hazard Ratio (95% CI)** | **P value** | **Pinteraction** | **Risk Difference**  **(95% CI)**  **[%]** | **P value** | **Pinteraction** |
| Duration of type 2 diabetes mellitus at baseline (years) |  |  |  |  |  |  | 0.8660 |  |  | 0.8745 |
| ≤5 | 2462 | 157 (6.4%) | 2426 | 169 (7.0%) | 0.91 (0.74, 1.14) | 0.4189 |  | -0.6% (-2.0%, 0.8%) | 0.4225 |  |
| >5 to 10 | 2353 | 146 (6.2%) | 2461 | 182 (7.4%) | 0.84 (0.68, 1.05) | 0.1208 |  | -1.2% (-2.6%, 0.2%) | 0.1091 |  |
| >10 to 15 | 1944 | 170 (8.7%) | 1949 | 173 (8.9%) | 0.99 (0.80, 1.23) | 0.9477 |  | -0.1% (-1.9%, 1.6%) | 0.9100 |  |
| >15 to 20 | 1293 | 100 (7.7%) | 1250 | 116 (9.3%) | 0.84 (0.64, 1.10) | 0.2067 |  | -1.5% (-3.7%, 0.6%) | 0.1765 |  |
| >20 | 1561 | 163 (10.4%) | 1511 | 177 (11.7%) | 0.88 (0.71, 1.09) | 0.2371 |  | -1.3% (-3.5%, 0.9%) | 0.2746 |  |
| Baseline HbA1c (%) |  |  |  |  |  |  | 0.5027 |  |  | 0.5212 |
| ≤6 | 1263 | 86 (6.8%) | 1285 | 76 (5.9%) | 1.16 (0.85, 1.57) | 0.3549 |  | 0.9% (-1.0%, 2.8%) | 0.3724 |  |
| >6 to 7 | 3301 | 209 (6.3%) | 3259 | 241 (7.4%) | 0.86 (0.71, 1.04) | 0.1119 |  | -1.1% (-2.3%, 0.2%) | 0.0967 |  |
| >7 to 8 | 2334 | 184 (7.9%) | 2449 | 215 (8.8%) | 0.90 (0.74, 1.10) | 0.3177 |  | -0.9% (-2.5%, 0.7%) | 0.2722 |  |
| >8 to 9 | 1227 | 108 (8.8%) | 1163 | 122 (10.5%) | 0.84 (0.65, 1.09) | 0.1891 |  | -1.7% (-4.1%, 0.7%) | 0.1658 |  |
| >9 to 10 | 633 | 51 (8.1%) | 615 | 75 (12.2%) | 0.64 (0.45, 0.92) | 0.0144 |  | -4.1% (-7.5%, -0.8%) | 0.0185 |  |
| >10 | 625 | 77 (12.3%) | 596 | 67 (11.2%) | 1.10 (0.79, 1.52) | 0.5748 |  | 1.1% (-2.5%, 4.7%) | 0.5948 |  |

**Table 2 Primary Safety Outcome in the THEMIS Cohort by Baseline Diabetes-related Factors and Select Background Antihyperglycemic Therapy**

|  | **Ticagrelor (N = 9562)** | | **Placebo (N = 9531)** | |  | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Characteristic** | **Number of Patients** | **Patients with events (%)** | **Number of Patients** | **Patients with events (%)** | **Hazard Ratio (95% CI)** | **p-value** | **Pinteraction** |
| Duration of type 2 diabetes mellitus at baseline (years) |  |  |  |  |  |  | 0.9793 |
| ≤5 | 2445 | 47 (1.9%) | 2406 | 25 (1.0%) | 2.04 (1.26, 3.32) | 0.0039 |  |
| >5 to 10 | 2343 | 49 (2.1%) | 2444 | 21 (0.9%) | 2.75 (1.65, 4.59) | 0.0001 |  |
| >10 to 15 | 1931 | 43 (2.2%) | 1933 | 18 (0.9%) | 2.72 (1.57, 4.72) | 0.0004 |  |
| >15 to 20 | 1287 | 32 (2.5%) | 1244 | 19 (1.5%) | 1.88 (1.07, 3.32) | 0.0291 |  |
| >20 | 1550 | 35 (2.3%) | 1501 | 16 (1.1%) | 2.39 (1.32, 4.32) | 0.0039 |  |
| Baseline HbA1c (%) |  |  |  |  |  |  | 0.4982 |
| ≤6 | 1260 | 27 (2.1%) | 1281 | 12 (0.9%) | 2.55 (1.29, 5.04) | 0.0069 |  |
| >6 to 7 | 3276 | 81 (2.5%) | 3237 | 36 (1.1%) | 2.56 (1.73, 3.78) | <.0001 |  |
| >7 to 8 | 2324 | 41 (1.8%) | 2437 | 23 (0.9%) | 2.13 (1.28, 3.55) | 0.0037 |  |
| >8 to 9 | 1221 | 25 (2.0%) | 1152 | 17 (1.5%) | 1.56 (0.84, 2.89) | 0.1561 |  |
| >9 to 10 | 629 | 20 (3.2%) | 613 | 3 (0.5%) | 6.91 (2.05, 23.26) | 0.0018 |  |
| >10 | 624 | 8 (1.3%) | 593 | 7 (1.2%) | 1.15 (0.42, 3.16) | 0.7920 |  |

**Table 3 Net Clinical Benefit in the THEMIS Cohort by Baseline Diabetes-related Factors and Select Background Antihyperglycemic Therapy**

|  | **Ticagrelor (N = 9619)** | | **Placebo (N = 9601)** | |  | | |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Characteristic** | **Number of Patients** | **Patients with events (%)** | **Number of Patients** | **Patients with events (%)** | **Hazard Ratio (95% CI)** | **P value** | **Pinteraction** | **Risk Difference**  **(95% CI)**  **[%]** | **P value** | **Pinteraction** |
| Duration of type 2 diabetes mellitus at baseline (years) |  |  |  |  |  |  | 0.8042 |  |  | 0.7950 |
| ≤5 | 2462 | 198 (8.0%) | 2426 | 213 (8.8%) | 0.92 (0.75, 1.11) | 0.3746 |  | -0.7% (-2.3%, 0.8%) | 0.3541 |  |
| >5 to 10 | 2353 | 187 (7.9%) | 2461 | 234 (9.5%) | 0.84 (0.69, 1.02) | 0.0738 |  | -1.6% (-3.2%, 0.0%) | 0.0590 |  |
| >10 to 15 | 1944 | 222 (11.4%) | 1949 | 211 (10.8%) | 1.07 (0.88, 1.29) | 0.5109 |  | 0.6% (-1.4%, 2.6%) | 0.5751 |  |
| >15 to 20 | 1293 | 147 (11.4%) | 1250 | 152 (12.2%) | 0.95 (0.76, 1.19) | 0.6684 |  | -0.8% (-3.3%, 1.7%) | 0.5388 |  |
| >20 | 1561 | 214 (13.7%) | 1511 | 228 (15.1%) | 0.90 (0.75, 1.08) | 0.2596 |  | -1.4% (-3.9%, 1.1%) | 0.2807 |  |
| Baseline HbA1c (%) |  |  |  |  |  |  | 0.4620 |  |  | 0.4920 |
| ≤6 | 1263 | 117 (9.3%) | 1285 | 107 (8.3%) | 1.12 (0.86, 1.45) | 0.4038 |  | 0.9% (-1.3%, 3.1%) | 0.4416 |  |
| >6 to 7 | 3301 | 273 (8.3%) | 3259 | 306 (9.4%) | 0.89 (0.75, 1.05) | 0.1533 |  | -1.1% (-2.5%, 0.3%) | 0.1171 |  |
| >7 to 8 | 2334 | 249 (10.7%) | 2449 | 276 (11.3%) | 0.96 (0.81, 1.13) | 0.6077 |  | -0.6% (-2.4%, 1.2%) | 0.5173 |  |
| >8 to 9 | 1227 | 142 (11.6%) | 1163 | 145 (12.5%) | 0.93 (0.74, 1.17) | 0.5446 |  | -0.9% (-3.5%, 1.7%) | 0.5292 |  |
| >9 to 10 | 633 | 73 (11.5%) | 615 | 96 (15.6%) | 0.72 (0.53, 0.97) | 0.0333 |  | -4.1% (-7.9%, -0.3%) | 0.0386 |  |
| >10 | 625 | 88 (14.1%) | 596 | 82 (13.8%) | 1.02 (0.76, 1.38) | 0.8733 |  | 0.3% (-3.6%, 4.2%) | 0.9341 |  |

**Table 4 Net Clinical Benefit in the THEMIS-PCI Cohort by Baseline Diabetes-related Factors and Select Background Antihyperglycemic Therapy**

|  | **Ticagrelor (N = 5558)** | | **Placebo (N = 5596)** | |  | | |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Characteristic** | **Number of Patients** | **Patients with events (%)** | **Number of Patients** | **Patients with events (%)** | **Hazard Ratio (95% CI)** | **P value** | **Pinteraction** | **Risk Difference**  **(95% CI)**  **[%]** | **P value** | **Pinteraction** |
| Duration of type 2 diabetes mellitus at baseline (years) |  |  |  |  |  |  | 0.7634 |  |  | 0.7625 |
| ≤5 | 1374 | 107 (7.8%) | 1392 | 125 (9.0%) | 0.86 (0.67, 1.12) | 0.2581 |  | -1.2% (-3.3%, 0.9%) | 0.2727 |  |
| >5 to 10 | 1383 | 101 (7.3%) | 1446 | 152 (10.5%) | 0.70 (0.54, 0.89) | 0.0047 |  | -3.2% (-5.3%, -1.1%) | 0.0030 |  |
| >10 to 15 | 1157 | 125 (10.8%) | 1139 | 122 (10.7%) | 1.02 (0.79, 1.30) | 0.9035 |  | 0.1% (-2.4%, 2.6%) | 0.9464 |  |
| >15 to 20 | 760 | 77 (10.1%) | 722 | 86 (11.9%) | 0.86 (0.63, 1.17) | 0.3371 |  | -1.8% (-5.0%, 1.4%) | 0.2813 |  |
| >20 | 881 | 109 (12.4%) | 894 | 132 (14.8%) | 0.82 (0.64, 1.06) | 0.1275 |  | -2.4% (-5.6%, 0.8%) | 0.1461 |  |
| Baseline HbA1c (%) |  |  |  |  |  |  | 0.3236 |  |  | 0.3096 |
| ≤6 | 702 | 62 (8.8%) | 744 | 72 (9.7%) | 0.90 (0.64, 1.26) | 0.5387 |  | -0.8% (-3.8%, 2.1%) | 0.5876 |  |
| >6 to 7 | 1940 | 132 (6.8%) | 1929 | 184 (9.5%) | 0.71 (0.57, 0.89) | 0.0031 |  | -2.7% (-4.5%, -1.0%) | 0.0022 |  |
| >7 to 8 | 1380 | 149 (10.8%) | 1419 | 166 (11.7%) | 0.94 (0.76, 1.18) | 0.5989 |  | -0.9% (-3.2%, 1.4%) | 0.4731 |  |
| >8 to 9 | 687 | 75 (10.9%) | 675 | 80 (11.9%) | 0.91 (0.67, 1.25) | 0.5758 |  | -0.9% (-4.3%, 2.4%) | 0.6093 |  |
| >9 to 10 | 363 | 41 (11.3%) | 360 | 55 (15.3%) | 0.72 (0.48, 1.08) | 0.1137 |  | -4.0% (-8.9%, 1.0%) | 0.1254 |  |
| >10 | 348 | 49 (14.1%) | 330 | 42 (12.7%) | 1.10 (0.73, 1.67) | 0.6391 |  | 1.4% (-3.8%, 6.5%) | 0.6527 |  |

**Supplementary Table 1 Primary Efficacy Outcome in the THEMIS-PCI Cohort by Baseline Diabetes-related Factors and Select Background Antihyperglycemic Therapy**

|  | **Ticagrelor (N = 5558)** | | **Placebo (N = 5596)** | |  | | |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Characteristic** | **Number of Patients** | **Patients with events (%)** | **Number of Patients** | **Patients with events (%)** | **Hazard Ratio (95% CI)** | **P value** | **Pinteraction** | **Risk Difference**  **(95% CI)**  **[%]** | **P value** | **Pinteraction** |
| Duration of type 2 diabetes mellitus at baseline (years) |  |  |  |  |  |  | 0.8623 |  |  | 0.8707 |
| ≤5 | 1374 | 88 (6.4%) | 1392 | 98 (7.0%) | 0.90 (0.68, 1.20) | 0.4883 |  | -0.6% (-2.5%, 1.2%) | 0.5438 |  |
| >5 to 10 | 1383 | 79 (5.7%) | 1446 | 116 (8.0%) | 0.71 (0.54, 0.95) | 0.0205 |  | -2.3% (-4.2%, -0.5%) | 0.0174 |  |
| >10 to 15 | 1157 | 101 (8.7%) | 1139 | 100 (8.8%) | 1.00 (0.76, 1.32) | 0.9918 |  | -0.1% (-2.4%, 2.3%) | 1.0000 |  |
| >15 to 20 | 760 | 51 (6.7%) | 722 | 63 (8.7%) | 0.77 (0.54, 1.12) | 0.1748 |  | -2.0% (-4.7%, 0.7%) | 0.1720 |  |
| >20 | 881 | 85 (9.6%) | 894 | 103 (11.5%) | 0.82 (0.62, 1.09) | 0.1750 |  | -1.9% (-4.7%, 1.0%) | 0.2173 |  |
| Baseline HbA1c (%) |  |  |  |  |  |  | 0.9268 |  |  | 0.9043 |
| ≤6 | 702 | 51 (7.3%) | 744 | 52 (7.0%) | 1.03 (0.70, 1.51) | 0.8871 |  | 0.3% (-2.4%, 2.9%) | 0.8388 |  |
| >6 to 7 | 1940 | 106 (5.5%) | 1929 | 139 (7.2%) | 0.76 (0.59, 0.98) | 0.0312 |  | -1.7% (-3.3%, -0.2%) | 0.0292 |  |
| >7 to 8 | 1380 | 114 (8.3%) | 1419 | 130 (9.2%) | 0.92 (0.71, 1.18) | 0.4914 |  | -0.9% (-3.0%, 1.2%) | 0.4215 |  |
| >8 to 9 | 687 | 59 (8.6%) | 675 | 67 (9.9%) | 0.86 (0.61, 1.22) | 0.3950 |  | -1.3% (-4.4%, 1.7%) | 0.4016 |  |
| >9 to 10 | 363 | 25 (6.9%) | 360 | 43 (11.9%) | 0.56 (0.34, 0.92) | 0.0213 |  | -5.1% (-9.3%, -0.8%) | 0.0218 |  |
| >10 | 348 | 40 (11.5%) | 330 | 35 (10.6%) | 1.09 (0.69, 1.71) | 0.7236 |  | 0.9% (-3.8%, 5.6%) | 0.8066 |  |

**Supplementary Table 2 Primary Safety Outcome in the THEMIS-PCI Cohort by Baseline Diabetes-related Factors and Select Background Antihyperglycemic Therapy**

|  | **Ticagrelor (N = 5536)** | | **Placebo (N = 5564)** | |  | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Characteristic** | **Number of Patients** | **Patients with events (%)** | **Number of Patients** | **Patients with events (%)** | **Hazard Ratio (95% CI)** | **p-value** | **Pinteraction** |
| Duration of type 2 diabetes mellitus at baseline (years) |  |  |  |  |  |  | 0.6323 |
| ≤5 | 1368 | 26 (1.9%) | 1384 | 15 (1.1%) | 1.93 (1.02, 3.65) | 0.0420 |  |
| >5 to 10 | 1376 | 27 (2.0%) | 1435 | 12 (0.8%) | 2.62 (1.33, 5.17) | 0.0055 |  |
| >10 to 15 | 1152 | 26 (2.3%) | 1132 | 12 (1.1%) | 2.43 (1.23, 4.83) | 0.0108 |  |
| >15 to 20 | 760 | 15 (2.0%) | 720 | 12 (1.7%) | 1.38 (0.64, 2.95) | 0.4070 |  |
| >20 | 877 | 17 (1.9%) | 890 | 10 (1.1%) | 1.97 (0.90, 4.31) | 0.0885 |  |
| Baseline HbA1c (%) |  |  |  |  |  |  | 0.7259 |
| ≤6 | 702 | 16 (2.3%) | 742 | 7 (0.9%) | 2.70 (1.11, 6.57) | 0.0282 |  |
| >6 to 7 | 1933 | 41 (2.1%) | 1921 | 24 (1.2%) | 1.95 (1.18, 3.22) | 0.0095 |  |
| >7 to 8 | 1373 | 22 (1.6%) | 1411 | 15 (1.1%) | 1.71 (0.89, 3.30) | 0.1094 |  |
| >8 to 9 | 686 | 12 (1.7%) | 671 | 9 (1.3%) | 1.44 (0.61, 3.42) | 0.4082 |  |
| >9 to 10 | 363 | 11 (3.0%) | 360 | 1 (0.3%) | 11.64 (1.50, 90.12) | 0.0188 |  |
| >10 | 348 | 5 (1.4%) | 330 | 5 (1.5%) | 1.05 (0.30, 3.61) | 0.9429 |  |