**SUPPLEMENTARY MATERIAL**

**Ticagrelor or Prasugrel in Patients with Acute Coronary Syndromes and Diabetes Mellitus**

**Running Title: Prasugrel vs. Ticagrelor in ACS Patients with Diabetes**

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**Table S1. Angiographic and Data\***

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Characteristic | Diabetes (n=888) | | | No diabetes (n=3114) | | |
| Ticagrelor (n=460) | Prasugrel (n=428) | P value | Ticagrelor (n=1542) | Prasugrel  (n=1572) | P value |
| Access site |  |  | 0.716 |  |  | 0.987 |
| Femoral artery | 287(62.4) | 279 (65.2) |  | 957 (62.1) | 980 (62.3) |  |
| Radial artery | 171 (37.2) | 147 (34.3) |  | 577 (37.4) | 584 (37.2) |  |
| Other | 2 (0.4) | 2 (0.5) |  | 8 (0.5) | 8 (0.5) |  |
| Number of diseased coronary arteries |  |  | 0.748 |  |  | 0.760 |
| No obstructive CAD | 30 (6.5) | 25 (5.8) |  | 140 (9.0) | 139 (8.8) |  |
| One-vessel disease | 103 (22.4) | 85 (19.9) |  | 498 (32.3) | 496 (31.6) |  |
| Two-vessel disease | 115 (25.0) | 115 (26.9) |  | 405 (26.3) | 440 (28.0) |  |
| Three-vessel disease | 212 (46.1) | 203 (47.4) |  | 499 (32.4) | 497 (31.6) |  |
| Left ventricular ejection fraction\*\* | 50.0±12.1 | 50.4±12.2 | 0.628 | 52.1±11.0 | 52.5±10.8 | 0.324 |

Data are counts (proportion; %) or mean ±standard deviation. CAD indicates coronary artery disease.

\*Angiographic data are not available for 4 patients with diabetes (1 in the prasugrel group and 3 in the ticagrelor group) and 10 patients without diabetes (4 in the prasugrel group and 6 in the ticagrelor group).

\*\*Left ventricular ejection fraction was not available in 34 patients with diabetes (18 patients in the prasugrel and 16 patients in the ticagrelor group) and 176 patients without diabetes (91 patients in the prasugrel and 85 patients in the ticagrelor grpoup)

**Table S2. Procedural Characteristics**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Characteristic | Diabetes (n=743) | | | No diabetes (n=2632) | | |
| Ticagrelor  (n=376) | Prasugrel (n=367) | P value | Ticagrelor  (n=1299) | Prasugrel (n=1333) | P value |
| Target vessel |  |  | 0.694 |  |  | 0.718 |
| Left main coronary artery | 8 (2.1) | 9 (2.4) |  | 28 (2.2) | 29 (2.2) |  |
| LAD coronary artery | 171 (45.5) | 157 (42.8) |  | 575 (44.3) | 561 (42.0) |  |
| Left circumflex coronary artery | 73 (19.4) | 67 (18.3) |  | 272 (20.9) | 278 (20.9) |  |
| Right coronary artery | 117 (31.1) | 122 (33.2) |  | 403 (31.0) | 446 (33.5) |  |
| Bypass graft | 7 (1.9) | 12 (3.3) |  | 21 (1.6) | 19 (1.4) |  |
| Complex lesion (type B2/C) | 221 (58.8) | 228 (62.1) | 0.391 | 757 (58.3) | 779 (58.4) | 0.963 |
| More than 1 lesion treated | 131 (34.8) | 144 (39.2) | 0.244 | 438 (33.7) | 460 (34.5) | 0.699 |
| TIMI flow grade before the intervention |  |  | 0.105 |  |  | 0.185 |
| 0 | 120 (31.9) | 110 (30.0) |  | 471 (36.3) | 474 (35.6) |  |
| 1 | 34 (9.1) | 28 (7.6) |  | 93 (7.2) | 127 (9.5) |  |
| 2 | 73 (19.4) | 99 (27.0) |  | 288 (22.2) | 287 (21.5) |  |
| 3 | 149 (39.6) | 130 (35.4) |  | 447 (34.4) | 445 (33.4) |  |
| TIMI flow grade after the intervention |  |  | 0.627 |  |  | 0.217 |
| 0 | 4 (1.1) | 1 (0.3) |  | 13 (1.0) | 15 (1.1) |  |
| 1 | 2 (0.5) | 3 (0.8) |  | 7 (0.5) | 4 (0.3) |  |
| 2 | 10 (2.7) | 11 (3.0) |  | 40 (3.1) | 26 (2.0) |  |
| 3 | 360 (95.7) | 352 (95.9) |  | 1239 (95.4) | 1288 (96.6) |  |
| Type of intervention |  |  |  |  |  |  |
| Drug-eluting stent | 332 (88.3) | 331 (90.2) | 0.475 | 1165 (89.7) | 1211 (90.8) | 0.347 |
| Bare-metal stent | 1 (0.3) | 5 (1.4) | 0.119 | 3 (0.2) | 3 (0.2) | >0.999 |
| Bioresorbable vascular scaffold | 20 (5.3) | 20 (5.5) | 0.999 | 79 (6.1) | 76 (5.7) | 0.740 |
| Drug-eluting balloon | 12 (3.2) | 8 (2.2) | 0.532 | 24 (1.9) | 19 (1.4) | 0.484 |
| Plain balloon angioplasty | 13 (3.2) | 11 (3.0) | 0.999 | 44 (3.4) | 34 (2.6) | 0.250 |
| Maximal stent diameter (mm) | 3.1 ± 0.5 | 3.1 ± 0.5 | 0.740 | 3.2 ± 0.5 | 3.2 ± 0.5 | 0.575 |
| Total stented length (mm) | 32.1 ± 18.0 | 30.6 ± 17.0 | 0.277 | 30.4 ± 16.5 | 30.2 ± 17.0 | 0.821 |
| Successful PCI | 364 (96.8) | 361 (98.4) | 0.254 | 1276 (98.2) | 1300 (97.5) | 0.264 |
| Periprocedural antithrombotic medication |  |  |  |  |  |  |
| Aspirin | 336 (89.4) | 329 (89.6) | 0.995 | 1166 (89.8) | 1202 (90.2) | 0.775 |
| Unfractionated heparin | 363 (96.5) | 346 (94.3) | 0.193 | 1217 (93.7) | 1249 (93.7) | >0.999 |
| Low molecular weight heparin | 17 (4.5) | 13 (3.5) | 0.623 | 57 (4.4) | 52 (3.9) | 0.595 |
| Bivalirudin | 19 (5.1) | 32 (8.7) | 0.067 | 106 (8.2) | 109 (8.2) | >0.999 |
| GPIIb/IIIa inhibitor | 46 (12.2) | 37 (10.1) | 0.415 | 173 (13.3) | 161 (12.1) | 0.370 |

Data are counts (proportions; %) or mean ± standard deviation.

GPIIb/IIIa indicates glycoprotein IIb/IIIa; LAD, left anterior descending; PCI, percutaneous coronary intervention; TIMI, Thrombolysis in Myocardial Infarction

**Table S3. Diagnosis and Drug Therapy at Discharge\***

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Characteristic | Diabetes (n=875) | | | No diabetes (n=3078) | | |
| Ticagrelor (n=452) | Prasugrel (n=423) | P value | Ticagrelor (n=1523) | Prasugrel (n=1555) | P value |
| Final diagnosis – no. (%) |  |  | 0.984 |  |  | 0.655 |
| Unstable angina | 50 (11.9) | 47 (12.0) |  | 139 (9.9) | 126 (8.9) |  |
| NSTEMI | 211 (50.1) | 194/386 (49.5) |  | 623 (44.2) | 632 (44.5) |  |
| STEMI | 160 (38.0) | 151/386 (38.5) |  | 646 (45.9) | 662 (46.6) |  |
| Therapy at discharge – no. (%) |  |  |  |  |  |  |
| Aspirin | 432 (95.6) | 402 (95.0) | 0.828 | 1434 (94.2) | 1476 (94.9) | 0.394 |
| Ticagrelor | 361 (79.9) | 3 (0.7) | <0.001 | 1241 (81.5) | 11 (0.7) | <0.001 |
| Prasugrel | 8 (1.8) | 342 (80.9) | <0.001 | 13 (0.9) | 1254 (80.6) | <0.001 |
| Clopidogrel† | 22 (4.9) | 32 (7.6) | 0.129 | 68 (4.5) | 85 (5.5) | 0.232 |
| Oral anticoagulant drugs | 20 (4.4) | 22 (5.2) | 0.705 | 62 (4.1) | 78 (5.0) | 0.241 |
| Beta blocking agents | 385 (85.2) | 365 (86.3) | 0.709 | 1256 (82.5) | 1280 (82.3) | 0.948 |
| ACE inhibitor/ARB | 395 (87.4) | 377 (89.1) | 0.489 | 1264 (83.0) | 1313 (84.4) | 0.300 |
| Statin | 414 (91.6) | 396 (93.6) | 0.312 | 1396 (91.7) | 1435 (92.3) | 0.570 |

Data are counts (proportions; %)

ACE indicates angiotensin-converting enzyme; ARB, angiotensin receptor blocker; NSTEMI, non-ST-segment elevation myocardial infarction;

STEMI, ST-segment elevation myocardial infarction

\*shown for patients discharged alive;

† most frequent reason for switching to clopidogrel was indication for oral anticoagulation

**Table S4.** Timing of occurrence of definite or probable stent thrombosis and myocardial infarction

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Time** | Diabetes (n=892) | | No diabetes (n=3124) | |
| Ticagrelor (n=463) | Prasugrel (n=429) | Ticagrelor (n=1548) | Prasugrel (n=1576) |
| Definite or probable stent thrombosis |  |  |  |  |
| ≤24 hours | 1 | 2 | 7 | 2 |
| >24 hours to 30 days | 1 | 5 | 10 | 8 |
| >30 days to 1 year | 4 | 2 | 3 | 1 |
| Total number | 6 | 9 | 20 | 11 |
| Myocardial infarction |  |  |  |  |
| ≤24 hours | 4 | 4 | 17 | 7 |
| >24 hours to 30 days | 4 | 5 | 20 | 7 |
| >30 days to 1 year | 18 | 19 | 33 | 18 |
| Total number | 26 | 28 | 70 | 32 |

Data are number of events

**Table S5. Antithrombotic Medication After Discontinuation of Study Drug During Follow-up\***

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Drug | Diabetes (n=116) | | | No diabetes (n=326) | | |
| Ticagrelor (n=63) | Prasugrel (n=53) | P value | Ticagrelor (n=180) | Prasugrel (n=146) | P value |
| Ticagrelor – no. (%) | 0 | 6 (11.3) | 0.008 | 0 | 8 (5.5) | 0.001 |
| Prasugrel – no. (%) | 10 (15.9) | 0 | 0.002 | 25 (13.9) | 0 | <0.001 |
| Clopidogrel – no. (%) | 33 (52.4) | 27 (50.9) | >0.999 | 86 (47.8) | 79 (54.1) | 0.305 |
| Oral anticoagulation – no. (%) | 15 (23.8) | 12 (22.6) | >0.999 | 25 (13.9) | 32 (21.9) | 0.008 |
| Other | 16 (25.4) | 15 (28.3) | 0.887 | 62 (33.6) | 49 (34.4) | 0.960 |

Data are counts (proportions; %)

Oral anticoagulation is also given in combination with a P2Y12 inhibitor

\*Shown for patients discharged alive



**Supplementary Figure 1.** One-Year Cumulative Incidences and Hazard Ratios with 95% confidence Interval [CI] of the Primary Endpoint of Death, Myocardial Infarction, or Stroke in Subgroups of Patients with diabetes mellitus. CABG=coronary artery bypass graft; CI=confidence interval; NSTEMI=non-ST-segment elevation myocardial infarction; PCI=percutaneous coronary intervention; Pint=P for interaction; STEMI=ST-segment elevation myocardial infarction.

\* The risk estimates (hazard ratios with 95% confidence interval) are obtained from the Cox proportional hazard model after adjustment for the participating center and stratification according to the clinical presentation (acute coronary syndrome with or without ST-segment elevation) and with the interaction term entered into the model. The completeness of baseline data (denominators in the events/total ratio) is shown in Table 1.

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**Supplementary Figure 2.** One-Year Cumulative Incidences and Hazard Ratios with 95% Confidence Interval [CI] of the Primary Endpoint of Death, Myocardial Infarction, or Stroke in Subgroups of Patients without diabetes mellitus. CABG=coronary artery bypass graft; CI=confidence interval; NSTEMI=non-ST-segment elevation myocardial infarction; PCI=percutaneous coronary intervention; Pint=P for interaction; STEMI=ST-segment elevation myocardial infarction.

\* The risk estimates (hazard ratios with 95% confidence interval) are obtained from the Cox proportional hazard model after adjustment for the participating center and stratification according to the clinical presentation (acute coronary syndrome with or without ST-segment elevation) and with the interaction term entered into the model. The completeness of baseline data (denominators in the events/total ratio) is shown in Table 1.