**Appendix Table E73. Results from studies assessing the ability of Multiplate Analyzer to predict bleeding events in patients with ischemic heart disease**

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author,year**  **UID**  **Country**  **Study name** | **Treatment** | **Phenotypic Test Used [index test]** | **Clinical Outcome** | **Outcome Definition** | **Timing of measurement** | **Index test result: category (e.g., HPR+) – ONE ROW PER PHENOTYPE GROUP** | **Outcome status (e.g., bleeding or no bleeding)** | **No. with outcome status within phenotype group** | **Comparative metric (OR, RR, HR)** | **95% CI** | **P (between which groups?)**  **[statistical test]** | **Adjusted?**  **[YES/NO/NR]**  **If YES, for what factors?** | **Procedures for multiple comparisons [YES, NO, NR]** | **Comments (e.g., additional data in figures)** |
| Sibbing 2010{Sibbing, 2010 88 /id}  19943882  Sibbing 2010{Sibbing, 2010 73 /id}  20633826  Germany  NR | Clopidogrel: 600 mg LD + 150 mg/day clopidogrel for 3 days + 75 mg/day clopidogrel MD & Aspirin: 500 mg IV LD + 100 mg aspirin (twice per day) MD | MEA | in-hospital major bleed | As per Thrombolysis in Myocardial Infarction  (TIMI) criteria -TIMI major bleeding | 30 days | Enhanced Responders (<188 aggregation units\*min) | in-hospital major bleed | 21/975 (2.2%) | Sensitivity: 0.62  Specificity: 0.62  AUC=0.61 | 0.51-0.7 | P=0.017 for ROC | NR | NR | Primary |
|  |  |  |  |  |  | Remaining patients - Not enhanced responders (≥188 aggregation units\*min) |  | 13/1558 (0.8%) |  |  |  |  |  |  |
|  |  |  | in-hospital major bleed | As per Thrombolysis in Myocardial Infarction  (TIMI) criteria -TIMI major bleeding | 30 days | Enhanced Responders (<188 aggregation units\*min) | in-hospital major bleed | 21/975 (2.2%) | OR=2.6 | 1.3-5.2 | P=0.005  (enhanced vs remaining responder)  [llogistic regression ] | NO | NR | Primary |
|  |  |  |  |  |  | Remaining patients - Not enhanced responders (≥188 aggregation units\*min) |  | 13/1558 (0.8%) |  |  |  |  |  |  |
|  |  |  | in-hospital major bleed | As per Thrombolysis in Myocardial Infarction  (TIMI) criteria -TIMI major bleeding | 30 days | Enhanced Responders (<188 aggregation units\*min) | in-hospital major bleed | 21/975 (2.2%) | OR=3.5 | 1.6-7.3 | P=0.001  (enhanced vs remaining responder)  [multiple logistic regression ] | YES;  age, body mass index, diabetes, renal failure, presence of an MI at admission, treatment at admission with aspirin, a thienopyridine, a statin or a coumarin derivate, use of abciximab, use of intra-aortic balloon pumping, number of lesions treated and complex lesions (defined as type B2/C lesions according to AHA/ACC lesions morphology). | NR | Primary |
|  |  |  |  |  |  | Remaining patients - Not enhanced responders (≥188 aggregation units\*min) |  | 13/1558 (0.8%) |  |  |  |  |  |  |
|  |  |  | in-hospital major bleed | As per Thrombolysis in Myocardial Infarction  (TIMI) criteria -TIMI major bleeding | 30 days | Enhanced responder (AUC≤188) (N=975) | Yes bleeding | NR /975(2.2%) | NR | NR | 0.018 across this and next two rows of enhanced, normal and low responders |  |  | Data for this outcome are %s in Fig. 1—can be obtained by digitizing |
|  |  |  |  |  |  | Normal responder (AUC189-467) (N=1130) | Yes bleeding | NR/1130 |  |  | 0.72 between noral and low responder |  |  |  |
|  |  |  |  |  |  | Low responder (AUC≥468) (N=428) | Yes bleeding | NR/428 |  |  |  |  |  |  |
|  |  |  | in-hospital minor bleed | As per Thrombolysis in Myocardial Infarction  (TIMI) criteria -TIMI minor bleeding | 30 days | Enhanced Responders (<188 aggregation units\*min) | in-hospital minor bleed | 55/975 (5.6%) | OR=1.1 | 0.8-1.5 | P=0.68  (enhanced vs remaining responder)  [logistic regression | NO | NR | Primary |
|  |  |  |  |  |  | Remaining patients - Not enhanced responders (≥188 aggregation units\*min) |  | 82/1558 (5.3%) |  |  |  |  |  |  |
|  |  |  | Bleeding Composite | TIMI major and minor bleeding | 30 days | Enhanced Responders (<188 aggregation units\*min) | in-hospital major and minor bleed | 76/975 (7.8%) | OR=1.3 | 0.95-1.8 | P=0.1  (lenhanced vs remaining responder)  [logistic regression ] | NO | NR | Primary |
|  |  |  |  |  |  | Remaining patients - Not enhanced responders (≥188 aggregation units\*min) |  | 95/1558 (6.1%) |  |  |  |  |  |  |
| Sibbing 2009{Sibbing, 2009 135 /id}  19264241  Sibbing 2010{Sibbing, 2010 100 /id}  20062919  Germany  NR | Clopidogrel: 600 mg LD + 150 mg/day clopidogrel for 3 days + 75 mg/day clopidogrel MD & Aspirin: 500 mg IV LD + 100 mg aspirin (twice per day) MD | MEA | Thrombolysis In Myocardial Infarction  (TIMI) major bleeding | TIMI criteria | 30 days | High Responders (Quintile 1 ≤124 AU\*min) | Thrombolysis In Myocardial Infarction  (TIMI) major bleeding | 4/318 (1.3%) | OR=1.8  (calculated) | 0.6-5.9 | P=0.32 between quintile 1 and 2-5  [Chi square] | NO | NR | Safety |
|  |  |  |  |  |  | Normal Responders and low responders (Quintile 2 -5) |  | 9/1290 (0.7%) |  |  |  |  |  |  |
|  |  |  | Thrombolysis In Myocardial Infarction  (TIMI) minor bleeding | TIMI criteria | 30 days | High Responders (Quintile 1 ≤124 AU\*min) | Thrombolysis In Myocardial Infarction  (TIMI) minor bleeding | 10/318 (3.1%) | OR=1.3 (calculated) | 0.6-2.7 | P=0.45 between high responder and remaining  [Chi square] | NO | NR | Safety |
|  |  |  |  |  |  | Normal Responders and low responders (Quintile 2 -5) |  | 31/1290 (2.4%) |  |  |  |  |  |  |
| Schulz 2010{Schulz, 2010 67 /id}  20691843  Germany  NR | Clopidogrel 75 mg/d + Aspirin 100 mg/d | MEA by Multiplate analyzer | In-hospital TIMI major bleeding | defined according to Thrombolysis in  Myocardial Infarction criteria | 1 year | Low responder | In-hospital TIMI major bleeding | 1 (0.3%) | HR=0.3 | 0.01-2.4 | 0. 460  (low vs normal)  Cox proportional hazards model | NO | NR | Secondary outcome |
|  |  |  |  |  |  | Normal responder |  | 12 (0.9%) |  |  |  |  |  |  |
| Siller-matula, 2012{Siller-Matula, 2012 1 /id}22260716  PEGASUS-PCI | clopidogrel LD 600mg, MD 75mg | MEA | TIMI major bleeding | TIMI major bleeding | 12-month | non-responder | TIMI major bleeding | 0/81 (0) | HR=0  OR=1.17(calculated) | 0-33  0.009-2.84 | NR | yes,CY  P2C19\*2 carrier status,BMI, CRP levels,DM, age, renal failure(creatine clearance<60mg mL,MI,sex,PPI | NR |  |
|  |  |  |  |  |  | responder |  | 11/321(4) |  |  |  |  |  |  |
| Gerotziafas, 2012{Gerotziafas, 2012 18243 /id}  22311629  Greece  NR | aspirin  100 mg and clopidogrel 75 mg once daily | MEA | Bleeding |  | 90 days | High platelet reactivity MEA >50U  n=3 | HPR | 0 | OR (calculated)= 29.6 | NR | P=0.1  (HPR vs normal)  [Fisher’s exact] | No | NR |  |
|  |  |  |  |  |  | normal platelet reactivity  n=103 |  | 0 |  |  |  |  |  |  |
| Johnston, 2012{Johnston, 2012 18242 /id}  22465351  New Zealand  NR | aspirin ≥300 mg at and clopidogrel  ≥300 mg and/or aspirin (≥75 mg) and clopidogrel (≥75 mg) | MEA | Bleeding |  | 3 days | High on treatment platelet reactivity >468 AU\*min  n=95 | HTPR | 0 | OR (calculated)=1.63 | NR | P=0.81  (HTPR vs normal)  [Fisher’s exact] | No | NR |  |
|  |  |  |  |  |  | normal platelet reactivity  ≤468 AU\*min  n=155 |  | 0 |  |  |  |  |  |  |