**Appendix Table E69. Results from studies assessing the ability of Multiplate Analyzer to predict myocardial infarction 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)** |
| Ko, 2011{Ko, 2011 26 /id}  21315223  Korea  NR | Multiple Electrode Platelet Aggregometry (MEA-ADP) | Periprocedural MI | Postprocedural ↑ of troponin or CK-MB >3 times the 99th percentile of the ULN in patients with normal baseline levels (or >3 times in pts with elevated baseline levels). | From PCI to 30 days | 30 days | MI+ | NR | NR | NR | NR | NR | NR | AUC=0.419; P=0.310  (Fig2d) | Multiple Electrode Platelet Aggregometry (MEA-ADP) |
| 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 | Myocardial infarction | according to TIMI  criteria | 30 days | Low Responders (>416 aggregation units\*min) | Myocardial infarction | 12 (3.7%) | OR=1.16 | 0.61-2.21 | P=0.64  (low vs normal responder)  [log rank] | NO | NR | Secondary |
|  |  |  |  |  |  | Normal Responders (≤416 aggregation units\*min) |  | 41 (3.2%) |  |  |  |  |  |  |
|  |  |  | Myocardial infarction | according to TIMI  criteria | 6 months | Low Responders (>416 aggregation units\*min) | Myocardial infarction | 17 (5.2%) | OR=1.4 | 0.8-2.4 | P=0.25  (low vs normal responder)  [log rank] | NO | NR | Secondary |
|  |  |  |  |  |  | Normal Responders (≤416 aggregation units\*min) |  | 49 (3.8%) |  |  |  |  |  |  |
|  |  |  | MI >24 h post-PCI | according to TIMI  criteria | 30 days | Low Responders (>416 aggregation units\*min) | MI >24 h post-PCI | 5 (1.5%) | OR=4.02 | 1.28-12.63 | P=0.02  (low vs normal responder)  [log rank] | NO | NR | Secondary |
|  |  |  |  |  |  | Normal Responders (≤416 aggregation units\*min) |  | 5 (0.4%) |  |  |  |  |  |  |
|  |  |  | Q-wave MI | according to TIMI  criteria | 30 days | Low Responders (>416 aggregation units\*min) | Q-wave MI | 5 (1.5%) | OR=4.99 | 1.53-16.29 | P=0.008  (low vs normal responder)  [log rank] | NO | NR | Secondary |
|  |  |  |  |  |  | Normal Responders (≤416 aggregation units\*min) |  | 4 (0.3%) |  |  |  |  |  |  |
| Schulz, 2010{Schulz, 2010 67 /id}  20691843  Germany  NR | Clopidogrel 75 mg/d + Aspirin 100 mg/d | MEA by Multiplate analyzer | MI | according to Thrombolysis in  Myocardial Infarction criteria | 1 year | Low responder | MI | 17 (5.3%) | HR=1.3 | 0.7-2.2 | 0.378  (low vs normal)  Chisquare | NO | NR | Secondary outcome |
|  |  |  |  |  |  | Normal responder |  | 43 (4.1%) |  |  |  |  |  |  |
|  |  |  | Q‑wave MI | according to Thrombolysis in  Myocardial Infarction criteria | 1 year | Low responder | Q‑wave MI | 8 (2.5%) | HR=4 | 1.5-10.7 | 0.005  (low vs normal)  Chisquare | NO | NR | Secondary outcome |
|  |  |  |  |  |  | Normal responder |  | 8 (0.6%) |  |  |  |  |  |  |
| Freynhofer, 2011{Freynhofer, 2011 1 /id}  21614416  Austria  NR | 300 or 600mg LDClopidogrel and maintain dose 75 mg+aspirin 100mg | MEA | STEMI |  |  | High reactivity/poor response |  | 0 | OR=0.3 (calculate) | 0-6.7 | NR | NR | NR | Fig 1 |
|  |  |  |  |  |  | Low reactivity/good response |  | 3 |  |  |  |  |  | Fig 1 |
| Eshtehardi 2010{Eshtehardi, 2010 78 /id}  20435201  Switzerland  NR | 600 mg LD Clopidogrel+500 mg aspirin | Aggregometry | PCI-related MI | peak CK-MB >3x ULN if baseline troponin was normal, and >20% increase of  CK or CK-MB postprocedure in case of elevated baseline  Troponin [ref 25] | Within 30 days after PCI | Clopidogrel low response | PCI-related MI | 2 (6.1%) | NR | NR | 0.039 across this and next 3 rows (Fisher’s exact or chi-square) | NR | NR | NONE |
|  |  |  |  |  |  | Aspirin low response |  | 3 (8.8%) |  |  |  |  |  |  |
|  |  |  |  |  |  | Dual low response |  | 5 (26.3%) |  |  |  |  |  |  |
|  |  |  |  |  |  | Normal response |  | 9 (6.8%) |  |  |  |  |  |  |
|  |  |  | MI | new Q waves ≥0.4-sec duration in at least 2 contiguous leads on ECG with or without elevate CK or CK-MB; In the absence of pathologic Q waves, an elevation of CK levels >3x ULN with elevated CK-MB or troponin I or T level | after the periprocedural period | Clopidogrel low response |  | 0 |  |  | 0.004 across this and next three rows (Fisher’s exact or chi-square) |  |  |  |
|  |  |  |  |  |  | Aspirin low response |  | 0 |  |  |  |  |  |  |
|  |  |  |  |  |  | Dual low response |  | 2 (10.5%) | OR=6.6 (calculated) | 0.6-74.8 |  |  |  |  |
|  |  |  |  |  |  | Normal response |  | 1 (0.8%) |  |  |  |  |  |  |
| Ivandic, 2009{Ivandic, 2009 125 /id}  19359538  Germany  NR | Clopidogrel600mg LD+aspires 0.5g | Aggregometry | STEMI | ST-elevation myocardial infarction | 30days or later after PCI | Responders (n=163) | ST-elevation myocardial infarction | 1 (0.6%) | Relative risk vs. previous row, 8.58 | 0.56-131.65 | NR | NR | NR |  |
|  |  |  |  |  |  | Dual nonresponders (n=19) |  | 1 (5.3%) |  |  |  |  |  |  |
| 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 | Periprocedural MI | Increase in hs-TnT to >three times the upper reference limit (>39 ng/L) for those with preprocedural hs-TnT levels within the normal range  In those with elevated preprocedural hs-TnT, a further elevation of hs-TnT >39 ng/L | 3 days | High on treatment platelet reactivity >468 AU\*min  n=95 | HTPR | 13 | OR (calculated)= 1.13 | 0.53-2.42 | P=0.23  (HTPR vs normal)  [Fisher’s exact] | No | NR |  |
|  |  |  |  |  |  | normal platelet reactivity  ≤468 AU\*min  n=155 |  | 19 |  |  |  |  |  |  |
| Sibbing, 2012{Sibbing, 2012 18239 /id}  22682553  Germany  ISAR-REACT 4 | LD: 600 mg of clopidogrel and 500 mg aspirin MD: clopidogrel 75 mg x 12 months and aspirin 100 mg twice daily for an indefinite period | MEA | Any recurring MI in pts on Abciximab Plus UFH | Any recurring MI | 30 days | high on-treatment platelet reactivity  >468 AU\*min  n=96 | Any recurring MI | 8 | OR(calculated)=1.4 | 0.53-3.6 | P=0.5  (HTPR vs normal)  [Cox regression] | No | NR |  |
|  |  |  |  |  |  | normal platelet reactivity  ≤468 AU\*min  n=178 |  | 11 |  |  |  |  |  |  |
|  |  |  | Any recurring MI in pts on Bivalirudin | Any recurring MI | 30 days | high on-treatment platelet reactivity  >468 AU\*min  n=109 | Any recurring MI | 22 | OR(calculated)=5.5 | 2.3-12.8 | P<0.001  (HTPR vs normal)  [Cox regression] | No | NR |  |
|  |  |  |  |  |  | normal platelet reactivity  ≤468 AU\*min  n=181 |  | 8 |  |  |  |  |  |  |
|  |  |  | Large MI in pts on Abciximab Plus UFH | Large | 30 days | high on-treatment platelet reactivity  >468 AU\*min  n=96 | large MI | 4 | OR(calculated)=1.5 | 0.4-5.7 | P=0.55  (HTPR vs normal)  [Cox regression] | No | NR |  |
|  |  |  |  |  |  | normal platelet reactivity  ≤468 AU\*min  n=178 |  | 5 |  |  |  |  |  |  |
|  |  |  | Large MI in pts on Bivalirudin | Large MI | 30 days | high on-treatment platelet reactivity  >468 AU\*min  n=109 | large mi | 12 | OR(calculated)=7.3 | 2.1-26.6 | P<0.001  (HTPR vs normal)  [Cox regression] | No | NR |  |
|  |  |  |  |  |  | normal platelet reactivity  ≤468 AU\*min  n=181 |  | 3 |  |  |  |  |  |  |