**Appendix Table E109. Phenotypic test details in studies assessing the predictive ability of miscellaneous platelet function tests in patients with ischemic heart disease**

| **Author, year [ref]**  **UID**  **Country**  **Study Name** | **Test/Device name**  **Device category Device name & manufacturer\*** | **Agonist used** | **Sample Collection and Procurement**  **Anticoagulant used**  **Interval between clopidogrel doses and blood sampling (in days)**  **Interval between sampling and testing (in days):** | **Grouping of Phenotypes\*\* [Definition]** | **Rational for the grouping of phenotypes reported (Yes/No)**  **[short description]** | **Frequency of phenotypes** |
| --- | --- | --- | --- | --- | --- | --- |
| Smit,  2010  20889993  Netherlands  ON-TIME-2 | Fe induced platelet aggregation  (FIPA)  Sysmex K4500  Sysmex, Kobe, Japan | AISI  434 low carbon stainless steel | whole blood; collected before PCI  Citrate  (0.109 M)  NR  Clopidogrel came first  NR | quartiles 1-4 | Not explicitly reported | quartiles 1 162 (25%)  quartiles 2 162 (25%)  quartiles 3 162 (25%)  quartiles 4 162 (25%) |
| Dziewierze,  2005  15815794  Poland  NR | Platelet aggregation inhibition  Plateletworks with Sysmex K800  Helena Laboratory | ADP | blood samples were collected at baseline and 3, 6, 12 , 24 hours from the initial loading dose of clopidogrel  3.2% natrium citrate  baseline and 3, 6, 12 , 24 hours  15 minutes | DPAI≤10% non-responder  DPAI>10% responder | not explicitly reported. | DPAI≤10% non-responder; N=7  DPAI>10% responder; N=24 |
| Breet,  2010  20179285  Netherlands  POPULAR | Plateletworks  NR  (Helena Laboratories,  Beaumont, Texas). | ADP | NR  K3-EDTA and tubes containing diphenylalanyl-Lprolyl-  L-arginine chloromethyl ketone  (PPACK[50 μmol/L]  NR  2 hours | plateletworks <80.5  plateletworks >=80.5 | Based on ROC curves | plateletworks <80.5; n=344  plateletworks >=80.5; n=262 |
| Breet,  2010  20179285  Netherlands  POPULAR | IMPACT-R  IMPACT-R  Matis Medical Inc, Beersel, Belgium | ADP | Before heparinization  3.2% citrate  NR  2 hours | High OTPR ≤2  Normal OTPR >2 | Based on ROC curves | High OTPR ≤2 (n = 296)  Normal OTPR >2 (n = 609) |
| Mobley,  2004  14969622  USA  NONE | NR/Optical platelet aggregation  Dual Channel Aggregometer  Chrono-Log Corp., Havertown, Pennsylvania  &  Thromboelastograph  Hemoscope Corporation, Niles, Illinois  &  Optical platelet aggregation  Ichor Plateletworks  Helena Laboratories, Beaumont,  Texas | ADP | NR  Heparin for Chronolog; Reptilase and factor XIIIa for TEG; Citrate for Ichor  Sampling done before and after clopidogrel (but interval NR)  NR | Nonresponders (failure of clopidogrel inhibition)  defined as <10% reduction from baseline averaging results from all 3 analyzers  Responders  ≥10% reduction from baseline averaging results from all 3 analyzers | Not explicitly stated | Nonresponders  15/50 (30%)  Responders  35/50 (70%) |
| Mobley,  2004  14969622  USA  NONE | Optical platelet aggregation  Ichor Plateletworks  Helena Laboratories, Beaumont,  Texas | ADP | NR  citrate  Sampling done before and after clopidogrel (but interval NR)  NR | Nonresponders  Responders | Not explicitly stated | Nonresponders  15/50 (30%)  Responders  35/50 (70%) |
| Lindvall,  2009  19477870  Sweden  None | Aggregometry  NR  Plateletworks Helena Lab, Beaumont, TX, USA | 20 uM ADP | Blood samples were drawn from the radial arterial cannula before and after administration of a bolus of two million kallikrein inhibiting units (KIU) [of aprotinin]; measurements done just before and just after aprotinin given, with both measurements taken long after clopidogrel given  EDTA  Mean (SD) interval between last clopidogrel dose and surgery (with blood sampling occurring just before start of surgery) 63.7± 28 hours; median, 72 hours; IQR, 29.5-78 hours  Testing done immediately after sampling | Clopidogrel nonresponse (>90% aggregation)  Clopidogrel response (≤90% aggregation) | literature published | Clopidogrel nonresponse (>90% aggregation); 4 (27%)  Clopidogrel response (≤90% aggregation); 11 (73%) |
| Gurbel, 2003  12714161  USA  No | P-selectin expression  Flow cytometry  Parmingen, San Diego, California | ADP 200 umol/liter | Blood was collected immediately before clopidogrel administration (baseline), and at 1, 5, and 30 days after stenting.  3.8% trisodium citrate  at 0, 1, 5, 30 days  NR | Nonresponder (change from baseline of <10%)  Responder (change from baseline of <10%) | Not explicitly reported | Nonresponder (change from baseline of <10%):  P-selectin expression: 9/38 (24%)  P-selectin expression: 29 of 38 (76%) |
| Kim, 2010  20449634  Korea  NR | turbidimetry-based optical detection device  VerifyNowP2Y12 assay  NR  &  LTA ADP  AggRam  aggregometer  Helena Laboratories Corp., Beaumont, TX | 20 μmol/L ADP for VerifyNow  &  5 and 20 μmol/L ADP | Blood was drawn into a Greiner Bio-One 3.2% citrate Vacuette tube  sodium citrate 3.2%  clopidogrel- naı¨ve patients received a 300-mg loading-dose (LD) of clopidogrel at least 12 h before procedure, and blood sampling was performed after insertion of the arterial sheath. In the case of patients who were already on chronic clopidogrel therapy, blood sampling was performed at the catheterization lab without clopidogrel LD  60 minutes | VerifyNow  PRU<240  PRU≥240  LTA: Aggregation <50%  Aggregation ≥50% | Based on literature | VerifyNow  PRU<240 n=512  PRU≥240 n=546  Aggregation <50%: NR  Aggregation ≥50%: NR |
| Kalantzi, 2012  21806493  Greece  NR | CD40L, PMP,  FACS  Calibur flow cytometer (Becton-Dickinson, San Jose,  CA) | ADP | Citrated blood samples were collected after the patient’s presentation at the emergency room  before clopidogrel administration (baseline), as well as at 5- and 30-days after clopidogrel loading.  citrate  5 days  30 days | nonresponder  VASP PRI >50%  responder  VASP PRI <50% | reference 15, 23 | non-responder n=12  responder n=28 |
| Siller-matula, 2012  22260716  PEGASUS-PCI | CPA, Impact R  Cone and platelet analyzer  DiaMed, Cressier, Switzerland | 2uM ADP | Blood samples from patients  were obtained from the arterial sheath (6F) in the catheterization  laboratory directly post-PCI and at least 5 min after  intravenous infusion of aspirin.  3.8% sodium citrate  NR  performed up to 24 h after blood sampling | Clopidogrel  non-responder  according to MEA (≥ 48 U)  Clopidogrel responder  according to MEA  (< 48 U)  n = 321 (80%) | ref 16, 28 | non-responder  n = 81 (20%)  responder  n = 321 (80%) |
| Saad, 2012  22146578  Egypt  NR | Flow Cytometry  EPICS-XL PROFILE II Coulter flow cytometer  Beckman Coulter, Inc., Fullerton, CA | ADP (5 μM/L) | Peripheral blood samples before PCI 6 hrs after clopodigrel  3.8% trisodium citrate  0.25 days (6hours)  NR | best cutoff value of posttreatment platelet  reactivity to predict ischemic events | ROC analysis | NR |
| Lakkis, 2001  11458412  USA  NR | ICHOR platelet works | ADP 20uM | Blood samples were collected 5 min before tirofiban or abciximab was started, and at 30 min, 4 hr, 12 hr during the infusion, and 2 hr after termination of either infusion.  EDTA  30 mins, 3h, 12h,2h  NR | NR (continuous) | NR | NR |

ADP= adenosine 5'-diphosphate; Ag= aggregation; PGE1=prostaglandin; ROC=receiver operating characteristic; AUC=area under the curve; IPA= inhibition of platelet aggregation; LTA= light transmission aggregometry; MEA= multiple electrode platelet aggregometry; PFA= platelet function analysis; TEG=thromboelastography; sTEG=short thromboelastography; VASP = vasodilator-stimulated phosphoprotein; VASP-FCT=vasodilator-stimulated phosphoprotein flow cytometry; CEPI=collagen-epinephrine ; CADP=collagen-ADP; CT=closure times; HCPR=high on-clopidogrel platelet reactivity; PCI = percutaneous coronary intervention; RPA= residual platelet aggregation; GP= glycoprotein; HRP=high platelet reactivity; NPR=normal on-treatment platelet reactivity; HPPR= high post-treatment platelet reactivity; MPA= maximum platelet aggregation; RPR= residual platelet reactivity; OTPR=on-treatment platelet reactivity; DPAI= degree of platelet aggregation inhibition; PRU=P2Y12 reaction units; CRP=C-reaction protein; PRI=platelet reactivity index; LR=low responder; IQR=interquartile range; AA= arachidonic acid; LD=loading dose; MD=maintain dose; SD=standard deviation; NR=not reported