Appendix Table E31. Phenotypic test details in studies assessing the predictive ability of VerifyNow in patients with ischemic heart disease

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| --- | --- | --- | --- | --- | --- | --- |
| **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**  |
| Cotton, 2010{Cotton, 2010 75 /id}20406238UKNR | VerifyNowVerifyNowAccumetrics, San Diego, CA, USA) | ADP | After discarding 5 mL, arterial sheath blood was drawn into vacutainer R tubes and analyzed using the Verify-Now system containing sodium citrate0.109 M NRNR | PRU≤240PRU >240 | Based on previous literature | PRU≤240PRU >240 |
| Angiolillo, 2007{Angiolillo, 2008 180 /id}18312754USAOPTIMUS | VerifyNow P2Y12VerifyNow P2Y12 | ADP | 2 to 4 hours after antiplatelet therapy intakeNR2 to 4 hours after antiplatelet therapy intakeNR | P2Y12 inhibition ≥50%P2Y12 inhibition <50% | Not explicitly reported. | P2Y12 inhibition ≥50%: n=17 (50%)P2Y12 inhibition <50%: n=17 (50%) |
| Breet, 2010{Breet, 2010 86 /id}20179285NetherlandsPOPULAR | VerifyNowP2Y12assayAccumetrics,SanDiego,California | ADP | NRGreiner tubesNRWithin 2 hours after blood collection. | Verify now P2Y12 <236Verify now P2Y12 ≥ 236 | Based on ROC curves | Verify now P2Y12 <236: n=646Verify now P2Y12 ≥236: n=406 |
| Kim, 2010{Kim, 2010 241 /id}20449634KoreaNR | turbidimetry-based optical detection deviceVerifyNowP2Y12assayNR | 20 μmol/L ADP | Blood was drawn into a Greiner Bio-One 3.2% citrate Vacuette tubesodium 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 LD60 minutes | PRU<240PRU≥240 | Based on literature | PRU<240 n=512PRU≥240 n=546 |
| Ko, 2011{Ko, 2011 26 /id}21315223KoreaNR | turbidimetric-based optical detection systemVerifyNow P2Y12 AssayAccumetrics | ADP | Before PCI; 8 and 24 hrs after PCIlepirudin (25 μg/mL)5 days (clopidogrel came first)0.125 days (Within 3 hrs)  | Hyporesponsiveness to clopidogrel (PRU≥ 274)Normal responsiveness to clopidogrel (PRU<274) | For identification of PRU cutoff, ROC curve analysis that presented the highest sum of sensitivity and specificity was used | Hyporesponsiveness to clopidogrel (PRU≥ 274): 121 (54.5)Normal responsiveness to clopidogrel (PRU<274): 101 (45.5) |
| Campo, 2010{Campo, 2010 58 /id}2095132010 sites in Italy, Belgium, France, Sprain3T/2R trial | VerifyNowP2Y12assayNRAccumetrics,SanDiego,California | NR | NRNRNRNR | Full responder (%PI≥40% full responder)Poor responder (%PI<40 poor responder ) | Based on literature | Full responder (%PI≥40% full responder ): N=289Poor responder (%PI<40 poor responder ): N=179 |
| Campo, 2011{Campo, 2011 13 /id}21679849ItalyNR | VerifyNowP2Y12assayNRAccumetrics,SanDiego,California | NR | NRNRAll samples obrtained after clopidogrel started; Blood samples were drawn at baseline (just before PCI and administration of interventional therapy) and at 1 and 6 months after PCI.NR | Clopidogrel poor response (PRU value ≥235) at baselineClopidogrel full response (PRU <235) at baselineEnhanced response (PRU ≤85) at 1 moNormal response (PRU 86-238) at 1 moPoor response (≥239) at 1 month | For PRU≥235 vs <235: Based on literature For enhanced, normal, poor: best cutoffs from ROC curves done in current study | Clopidogrel poor response (PRU value ≥235) at baseline, 107 (36%)Clopidogrel full response (PRU <235) at baseline, 193 (64%)Enhanced response (PRU ≤85) at 1 mo, 75 (25%)Normal response (PRU 86-238) at 1 mo, 185 (62%)Poor response (≥239) at 1 mo, 40 (13%) |
| Cuisset, 2008{Cuisset, 2008 168 /id}18549843BelgiumNR | VerifyNow P2Y12VerifyNow P2Y12NR | PGE1+ADP | Before PCI NR0.5 days (≥12 hrs)Clopidogrel came firstNR | Quartile 1 (nonresponders) percent inhibition P2Y12 <15%Quartile 2-4 (responders) percent inhibition P2Y12 ≥15% | Not explicitly reported. | Quartile 1 (nonresponders) percent inhibition P2Y12 <15%: 32 (25%)Quartile 2-4 (responders) percent inhibition P2Y12 ≥15%: 90 (75%) |
| de\_Miguel\_Castro, 2009{de Miguel, 2009 136 /id}19232185SpainNR | VerifyNowVerifyNow® analyzerAccumetrics Inc., San Diego, California | NR | Before angiography3.2% sodium citrateNR [clopidogrel came first]0.04 (1 hr) | Post treatment platelet reactivity ≤ 175Post treatment platelet reactivity >175Quartile 1 (<115 PRU)Quartile 2 (115 -164 PRU) Quartile 3 (165 -206 PRU) Quartile 4 ( >206 PRU) | Not explicitly reported. | Post treatment platelet reactivity ≤ 175: 97 (60.2%)Post treatment platelet reactivity >175: 64 (39.8%) Quartile 1 (<115 PRU): 40 (25%)Quartile 2 (115 -164 PRU): 40 (25%)Quartile 3 (165 -206 PRU): 40 (25%)Quartile 4 ( >206 PRU):41 (25%) |
| Gladding, 2008{Gladding, 2008 149 /id}19463375New ZealandSecondary (but not subgroup) analysis of PRINC (Plavix Response in Coronary Intervention) Trial | Agglutination plus light transmittanceVerifyNow point-of-care rapid platelet function analyzer (RPFA) and its P2Y12 cartridgeAccumetrics Ltd., San Diego, California | ADP, 20 mmol/l[published as mmol but must be umol?] | Arterial blood was sampled through a 6-F femoral sheath and transferred immediately; collection tubes were inverted 4 times to mix the anticoagulant and left at ambient temperature (24°C)3.2% citratePlatelet function was tested at baseline, 2, 4, and 7 h from10 mins | 600 mg Clopidogrel:Nonresponse (inhibition <10%) at 7 hrResponse (inhibition >=10%) at 7 hr1200 mg ClopidogrelNonresponse (inhibition <10%) at 7 hrResponse (inhibition >=10%) at 7 hr | Not explicitly reported. | 600 mg ClopidogrelNonresponse (inhibition <10%) at 7 hr: 6/26 (26%) Response (inhibition >=10%) at 7 hr: 20/26 (77%)1200 mg ClopidogrelNonresponse (inhibition <10%) at 7 hr:2/37 (5%)Response (inhibition >=10%) at 7 hr:35/37 (95%) |
| Huczek, 2011{Huczek, 2011 239 /id}21443410PolandNR | VerifyNow/ turbidoaggregometryVerifyNow P2Y12 assayAccumetrics Inc., San Diego, CA | ADP (with prostaglandinE1 to reduce the nonspecific binding for ADP toP2Y1 receptor) | Venous blood sample after clopidogrel3.2% sodium citrate0.5 ± 0.1 days (12± 2 hours); Clopidogrel came first NR | low platelet reactivity (PRU≤150) - first Medium platelet reactivity (PRU = 151-209High platelet reactivity (PRU ≥210) – Third tertile | Not explicitly reported. | low platelet reactivity (PRU≤150) - first tertile - 124 (33.2%)Medium platelet reactivity (PRU = 151-209) - Second tertile - 124 (33.2%)High platelet reactivity (PRU ≥210) – Third tertile-124 (33.2%) |
| Kim, 2011{Kim, 2011 5 /id}21786434South KoreaCiLostazol administration before pErcutaneous coronAry intervention for Reduction of periprocedural myonecrosis trial (CLEAR trial) | VerifyNow P2Y12NRAccumetrics Inc., San Diego, CA | NR | Samples were obtained by antecubital venipunture using a 23-gauge syringe, and the initial 3 to 4 mm of blood was discarded. The second samples were collected in 4.5-mL plastic tubes for rapid platelet-function assay3.2% citrateVenous blood samples were drawn immediately after randomization (baseline, before clopidogrel), before PCI (7 days later after pre-treatment with clopidogrel), and 6 and 24 hours after PCI. NR | clopidogrel resistance (% inhibition <20%)normal response to clopidogrel (% inhibition ≥20%)  | Based on literature | clopidogrel resistance (% inhibition <20%): 37/110 (34%)normal response to clopidogrel (% inhibition ≥20%): 73/110 (66%) |
| Lee, 2009{Lee, 2009 230 /id}20049136South KoreaNR | VerifyNow P2Y12 assayNRNR | NR | samples were collected from the vein following PCI. Sampling was done in the hospital for patients who were continually hospitalized during this period or during the first follow-up for patients who had been discharged. 3.2% citratesamples were collected after PCI and 5 days after initiating regular administration of clopidogrel (75 mg)Within 8 hours | Clopidogrel low response (<20% inhibition)Clopidogrel normal response (≥20% inhibition) | Based on literature | Clopidogrel low response (<20% inhibition): 95 (40%)Clopidogrel normal response (≥20% inhibition):142 (60%) |
| Mangiacapra, 2010{Mangiacapra, 2010 83 /id}20298992ItalyNR | VerifyNow/optical turbidimetryVerifyNow P2Y12 assayAccumetrics, San Diego, California | 20-µmol adenosine diphosphate, | Before PCI3.2% sodium citrateNR [Clopidogrel came first]NR | high platelet reactivity PRU value ≥240not high platelet reactivity | Based on literature | high platelet reactivity PRUvalue ≥240: 78 (31.2%)Not high platelet reactivity: 172 (68.8%) |
| Mangiacapra, 2010{Mangiacapra, 2010 94 /id}20129566BelgiumNR | VerifyNow/optical turbidimetryVerifyNow P2Y12 assayAccumetrics, San Diego, California | 20-µmol adenosine diphosphate, | Before PCI3.2% sodium citrateNR [Clopidogrel came first]NR | High platelet reactivity (HPR) - PRU value ≥240 unitsNormal platelet reactivity - PRU value <240 units | Not explicitly reported. | High platelet reactivity (HPR) - PRU value ≥240 units: 101 (30%)Normal platelet reactivity - PRU value <240 units: 237 (70%) |
| Mangiacapra, 2010{Mangiacapra, 2010 65 /id}20723634ItalyNR | VerifyNow/optical turbidimetryVerifyNow P2Y12 assayAccumetrics, San Diego, California | 20-µmol adenosine diphosphate, | Before PCI3.2% sodium citrateNR [Clopidogrel came first]NR | high platelet reactivity PRUvalue ≥240not high platelet reactivity | Based on literature | high platelet reactivity PRUvalue ≥240: 77 (27%)not high platelet reactivity: 208 (73%) |
| Marcucci, 2009{Marcucci, 2009 144 /id}19118249ItalyNR | VerifyNow/optical turbidimetryVerifyNow P2Y12 assayAccumetrics, San Diego, California | ADP | 24 hours after600-mg clopidogrel loadingsodium citrate 0.109 mol/L1 day [clopidogrel came first]NR | high residual platelet reactivity (PRU ≥ 240)No residual platelet reactivity (PRU < 240) high residual platelet reactivity (PRU ≥ 235)No residual platelet reactivity (PRU < 235)PRU quartiles Quartile 1 ≤129Quartile 2 130-195Quartile 3 196-257Quartile 4 ≥258  | ROC analysis; posttreatment PRU that provided the greatest sum of sensitivity and specificity. | high residual platelet reactivity (PRU ≥ 240): 219 (32.1%)No residual platelet reactivity (PRU < 240): 464 (67.9%) high residual platelet reactivity (PRU ≥ 235): 231 (33.8%)No residual platelet reactivity (PRU < 235): 452 (66.2%) PRU quartiles Quartile 1 ≤129: 171 (25%)Quartile 2 130-195: 171 (25%)Quartile 3 196-257: 171 (25%)Quartile 4 ≥258: 170 (25%)  |
| Patti, 2008{Patti, 2011 22 /id}18804738ItalyARMYDA-PRO (Antiplatelettherapy for Reduction of MYocardial Damage duringAngioplasty-Platelet Reactivity Predicts Outcome) | VerifyNow/optical turbidimetryVerifyNow P2Y12 assayAccumetrics, San Diego, California | NR (ADP and PGE1 as per Ref 8) | Before PCI & 8 and 24 hrs after intervention NR0.25 days between clopidogrel dose & sampling in 120 pts; the other 40 were on chronic clopidogrel therapy NR | First QuartileSecond QuartileThird QuartileFourth Quartile | Not explicitly reported for quartile classification;For identification of PRU cutoff, ROC curve analysis that presented the highest sum of sensitivity and specificity was used. | First Quartile: 40 (25)Second Quartile:40 (25)Third Quartile: 40 (25)Fourth Quartile: 40 (25) |
| Patti, 2011{Patti, 2011 22 /id}21256470ItalyAntiplatelet Therapy for Reduction of Myocardial Damage During Angioplasty (ARMYDA)–Bleeding Study (ARMYDA-BLEEDS) | VerifyNow P2Y12 assayNRAccumetrics, Inc., San Diego, California | NR | NRNRDose came first; reactivity tested immediately before PCI and at 8 and 24 hours after interventionNR | PRU quartiles at baseline (before PCI): 1 (lowest PRU, which = highest inhibtion)234Also ROC-curve-based threshold PRU>189 (low inhibition) PRU< or = 189 (high inhibition) | Not explicitly reported for quartiles; for cutoff at 187, authors did an ROC analysis in this study | PRU quartiles at baseline (before PCI): 1 (lowest PRU, which = highest inhibtion): 77 (25%)2: 77 (25%)3: 77 (25%)4: 79 (25%)Also ROC-curve-based threshold PRU>189 (low inhibition): NRPRU< or = 189 (high inhibition): NR |
| Price, 2011{Price, 2011 23 /id}21406646USAGauging Responsiveness with A VerifyNow assay—Impact on Thrombosis And Safety (GRAVITAS) | VerifyNow P2Y12 test/turbidoaggregometryVerifyNow P2Y12 testAccumetrics, San Diego, California | NR | 12 to 24 hoursafter PCI; outcomes and repeat measurements at 30 days and 6 months NR0.5-1 day (12-24 hrs)Clopidogrel came first NR | High on-treatment reactivity (PRU≥230)Not High On-Treatment Reactivity (PRU<230) | Based on literature | High on-treatment reactivity (PRU≥230): 1105 (65.3%)Not High On-Treatment Reactivity (PRU<230): 586 (34.7%) |
| Price, 2008{Price, 2008 174 /id}18263931USANR | VerifyNow P2Y12 assay NRAccumetrics Inc | 20-µmol adenosine diphosphate, | Whole blood was obtained at the time of catheterization prior to anticoagulant therapy in patients on previous clopidogrel therapy and by phlebotomy 12 h after PCI 3.2% sodiumWhole blood was obtained by phlebotomy 12 h after PCI and a 600 mg clopidogrel loading dose in patients who were clopidogrel naiveNR | Low reactivity (PRU<235) High reactivity (PRU≥235) | ROC analysis | Low reactivity (PRU<235): 258High reactivity (PRU≥235): 122 |
| Saw, 2008{Saw, 2008 242 /id}19463380CanadaBRIEF-PCI | VerifyNow P2Y12 assay NRAccumetrics Inc | ADP | Whole blood samples 3.2% sodium citrateNRNR | Low-responder (Clopidogrel low-responders were defined as those belonging to the lowest quartile of platelet inhibition)- <19%Responder ≥19% | Not explicitly reported. | Low-responder (Clopidogrel low-responders were defined as those belonging to the lowest quartile of platelet inhibition): 51 (24.4)responder: 147 (70.3) |
| Valgimigli, 2009{Valgimigli, 2009 244 /id}1952833710 sites in Europe (Italy, Belgium, France, Spain)Tailoring Treatment With Tirofiban in Patients Showing Resistance to Aspirin and/or Resistance to Clopidogrel (3T/2R) study | VerifyNow P2Y12 assay NRAccumetrics Inc | NR | NRNRClopidogrel loading dose (300 or 600 mg) 2-6 hr before PCI except in those who’d been on clopidogrel for at least 7 days previously at a dose of 75 mg/dayNR | Clopidogrel nonresponders (<40% inhibition)Dual (clopidogrel and aspirin) nonrespondersAspirin nonresponder | Not explicitly reported | Clopidogrel nonresponders (<40% inhibition): 147Dual (clopidogrel and aspirin) nonresponders: 26Aspirin nonresponder: 136For groups above, denominator unclear no % not given. The Ns sum to 309 patients but 54 were withdrawn—group affiliation not given. Total of 263 enrolled in the end. |
| Vavuranakis, 2011{Vavuranakis, 2011 245 /id}21712606GreeceNR | VerifyNow system/turbidoaggregometry VerifyNow P2Y12 systemAccumetrics, SanDiego, CA, USA | NR | Whole blood ; prior to catheterization 0.2 ml buffered 3.2% sodium citrate solutionNR[clopidogrel came first]0.01 ± 0.007 (15±1 min after collection) | NR | ROC analysis to predicts the presence of Large ThrombusBurden | NR |
| Breet, 2011{Breet, 2011 15 /id}21478385The NetherlandsPOPular | VerifyNow NRNR | ADP | NRK3-EDTA NR2h | No HCPR (VerifyNow)With HCPR and Dual HCPR (VerifyNow)Cutoff: 236 P2Y12 reaction units | Based on literature | No HCPR (VerifyNow): 280With HCPR and dual HPR (VerifyNow): 168 |
| Suh, 2011{Suh, 2011 33 /id}21232664KoreaCILON-T | VerifyNow/turbidometric aggregationNRNR | 20uM ADP and 22nM PGE1 | NRNRNR2h | low PRU 0-164Middle PRU 165-264High PRU ≥ 265 | ROC analysis | low PRU 0-164:<16%Middle PRU 165-264:16-36%High PRU ≥ 265:>36% |
| Price, 2011{Price, 2011 18182 /id}21875913USAGauging Responsiveness with A VerifyNow assay—Impact on Thrombosis And Safety (GRAVITAS) | VerifyNow P2Y12 test/turbidoaggregometryVerifyNow P2Y12 testAccumetrics, San Diego, California | NR | 12 to 24 hoursafter PCI; outcomes and repeat measurements at 30 days and 6 months NR0.5-1 day (12-24 hrs)Clopidogrel came firstNR | High on-treatment reactivity at 30 days (PRU≥208)Not high on-treatment reactivity at 30 days (PRU<208)High on-treatment reactivity at 30 days (PRU≥230)Not high on-treatment reactivity at 30 days (PRU<230) | Based on literature | Not high on-treatment reactivity (PRU<208): 1156(45.3%)High On-Treatment Reactivity (PRU≥208): 1397 (54.7%)Not high on-treatment reactivity (PRU<230): 1105 (56.7%)High On-Treatment Reactivity (PRU≥230): 586 (43.3%) |
| Park, 2011 {Park, 2011 1 /id} 22152948KoreaNR | VerifyNow P2Y12NRNR | ADP | NRNRNR24 to 48 h post-PCI | HTPR was defined by a PRU value>235 and/or a % inhibition <15%.  | Based on literature | High n=1660normal n=1189 |
| Park, 2011{Park, 2011 18181 /id}21880289KoreaCROSS-VERIFY | VerifyNow P2Y12NRNR | NR | NRNRNRNR | high OPR (HOPR) : ≥235 PRU | Based on literature | HOPR: n=407 No HOPR: n=402 |
| Mangiacapra, 2012{Mangiacapra, 2012 18179 /id}22440493Italy & BelgiumARMYDA-PROVE | VerifyNow system/turbidoaggregometryVerifyNow P2Y12 systemAccumetrics, SanDiego, CA, USA | NR | Whole blood; prior to catheterization3.2% sodium citrateNR[clopidogrel came first]NR | Low platelet reactivity (LPR) (PRU ≤178) to predict bleeding eventsNormal platelet reactivity NPR (PRU between ≥179 and ≤238)High platelet reactivity (HPR) (PRU ≥239) to predict ischemic events | ROC analysis | LPR (PRU ≤178) : n = 248 [33.9%]NPR (PRU between ≥179 and ≤238): n = 244 [33.3%]HPR (PRU ≥239: n = 240 [32.8%] |
| Yu, 2012 {Yu, 2012 18231 /id}22787468KoreaNR | VerifyNow NR(Accumetrics Inc., San Diego, CA, USA | ADP | 12 to 24 hours post- PCI3.2% sodium citrateclopidogrel received at least 6 hours before PCINR | responder (PRU>235-240)low responder | Ref 11, 21, 22 | responder n=186low responder n=77 |
| Jin, 2012 {Jin, 2012 18230 /id} KoreaNR | VerifyNow P2Y12 point-of care assayNR(Accumetrics Inc., San Diego, CA, USA | 20 μmol of ADP | NRNRblood sample obtained at the time of discharge and run with 60 minutes while patients was taking MD clopidogrel | no HPRHPR | Not explicitly reported. | no HPR N=127HPR N=54 |
| Saraf, 2010{Saraf, 2010 18234 /id}20447533UKNR | VerifyNow P2Y12 point-of care assayNR(Accumetrics Inc., San Diego, CA, USA | ADP | NRsodium citrate 0.109 mol/LNRNR | PRU≥240PRU<240 | Based on literature | PRU≥240 = NRPRU<240 = NR |
| Ari, 2011{Ari, 2012 18246 /id}21239075TurkeyEFFICIENT | VerifyNow P2Y12 | 20mM ADP | blood samples were drawn before PCI3.2% sodium citrate3 days 30 min to 4 hours  | clopidogrel resistance inhibition <40% | NR | platelet inhibition <40%=94platelet inhibition ≥40%=98 |
| Gaglia, 2012{Gaglia, 2011 18244 /id}21919956USANR | VerifyNow P2Y12 | 20 µM ADP | 6 hours following a loadingdose of clopidogrel3.2% sodium citrate6 hours6 and 24 hours following PCI | PRU>235 PRI≤235 | Based on literature | PRU>235: 54 PRI≤235: 146 |
| Codner, 2012{Codner, 2012 18241 /id}22534051IsraelNR | VerifyNow P2Y12 | 20 µM ADP & prostaglandin E1 22 nmol | NR3.2% citrateNR1 hr | PRU>235 PRI≤235 | Based on literature | PRU>235: 22 PRI≤235: 35 |

\*If more than one test, use separate rows

\*\*E.g., nonresponsive vs. responsive to clopidogrel, high vs. low platelet reactivity,