**Appendix Table E49. Phenotypic test details in studies assessing the predictive ability of VASP 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**  |
| Freynhofer, 2011{Freynhofer, 2011 1 /id}21614416AustriaNR | Flow cytometric analysis of VASP phosphorylation Platelet VASP kitBiocytex, Marseille, France | ADP | Venous blood samples along with the routine blood samples were collected via atraumatic venipuncture of the forearm into coagulation tubesbuffered sodium citrate 3.2%6-24 h (morning) after PCI48 hours after blood collection | VASP result: PRI≤60.2% (low reactivity, good response)VASP result: PRI>60.2% (high reactivity, poor response) | ROC curve (area under the ROC-curve was 0.683 (p=0.014) for the platelet reactivity index (PRI) calculated from median fluorescence intensities (FI) with an optimal cut-off at 60.2% PRI.) | VASP result: PRI≤60.2% (low reactivity, good response): 114/300 (38%)VASP result: PRI>60.2% (high reactivity, poor response): 186/300 (62%) |
| Siller-Matula,2009{Siller-Matula, 2009 234 /id}19135705AustriaNR | Flow cytometric analysis of VASP phosphorylation Platelet VASP kitBiocytex, Marseille, France | Adenosine diphosphate(ADP), prostaglandin (PGE1) | 1st blood sample: in catheterization laboratory, after PCI and after 250 mg IV aspirin ; 2nd blood sample: 20‑24 hours after PCI3.8% citrateNR; Clopidogrel came first0.04 days (1 hour) | Platelet reactivity index ≥ 69% by VASP (? Low efficiency)Platelet reactivity index <69% by VASP | Based on normal ranges as reported by manufacturer | Platelet reactivity index ≥ 69% by VASP (? Low efficiency): 8 (27%)Platelet reactivity index <69% by VASP: 22 (63%) |
| Blindt, 2007{Blindt, 2007 189 /id}18064332 GermanyNR | Flow cytometric analysis of VASP phosphorylationNRBiocytex, Marseille, France | 10 µM ADP | blood samples were obtained 72–96 h after stent placementCitrate Interval at least 8 days.NR | VASP-platelet reactivity indices (VASP-PRI) > 48%VASP-platelet reactivity indices (VASP-PRI) < 48% | ROC curve revealed VASP PRI <48% be the best cut-off | VASP-platelet reactivity indices (VASP-PRI) > 48%: NRVASP-platelet reactivity indices (VASP-PRI) < 48%: NR |
| Kalantzi, 2011{Kalantzi, 2011 19 /id}21255245GreeceNR | Flow cytometric analysis of VASP phosphorylationNRBiocytex, Marseille, France | ADP | Pre-clopidogrel, 5 days after clopidogrel, 30 days after clopidogrelCitrate5 days; the pre-clopidogrel sampling was not used for estimation of responder statusNR | Non-responders (VASP platelet reactivity index [PRI] ≥50%)Responders (VASP PRI < 50%) | Based on literature; Proposed previously [Ref #6] and also associated with adverse clinical outcome [ref #4] | Non-responders (VASP platelet reactivity index [PRI] ≥50%): 46 (75.4%)Responders (VASP PRI < 50%): 15 (24.6%) |
| Siller-Matula, 2010{Siller-Matula, 2010 89 /id}19943879AustriaNR | Flow cytometric analysis of VASP phosphorylationNRBiocytex, Marseille, France | ADP | Blood samples obtained from arterial sheath3.8% citrateDose first (clopidogrel loading dose given at least 2 hr before PCI); Samples taken directly after PCI and at least 5 min after IV aspirin dose (250 mg).NR | Clopidogrel responders (PRI<42%)Clopidogrel nonresponders (PRI≥42%) | ROC optimal cutoffs for prediction of definite stent thrombosis at 6 m, as done in this study | Clopidogrel responders (PRI<42%): 154 (37%)Clopidogrel nonresponders (PRI≥42%): 262 (64%) |
| Bjelland, 2010{Bjelland, 2010 42 /id}20727659NorwayNR | Dual flow cytometryPLT VASP/P2Y12Biocytex, France | ADP | Whole blood; Day 1 and Day 3 after clopidogrel administrationcitrateDay 1: Median 21 hrs [IQR: 17.5-27.5]Day 1: Median 68 hrs [IQR: 63-72]NR | Satisfactory clopidogrel effect (Platelet reactivity index <0.5)Unsatisfactory clopidogrel effect (Platelet reactivity index ≥0.5) | Based on literature | Satisfactory clopidogrel effect (Platelet reactivity index <0.5): 0 (0%)Unsatisfactory clopidogrel effect (Platelet reactivity index ≥0.5): 25 (100%) |
| Bonello, 2007{Bonello, 2007 199 /id}17488353FranceNR | VASPPlatelet VASP kitsDiagnostica Stago,Asnieres, France | ADP and/or prostaglandin E1 (PGE1) | Blood samples for PRI testing were drawn before PCI and at least 24 h after clopidogrel loading dose and aspirin3.8% trisodium citrate24 hours 24 hours | Quintile 1 (<47%) vs Quintile 2-4 | 70% is normal range using ROC curve. | Quintile 1 (<47%) : 29vs Quintile 2-4: 115 |
| Djukanovic, 2008{Djukanovic, 2008 163 /id}18719318SerbiaNR | Flow cytometric analysis of VASP phosphorylation Platelet VASP kitDiagnostica Stago (Biocytex), Asnières, France | PGE1 and ADP | Whole blood; Collection time NR0.129 M sodium citrateNRNR | At Day 2:Rapid response (Platelet reactivity index ≤50% at 2 days)Not rapid response (Platelet reactivity index >50% at 2 days) At Day 7:Good responders (Platelet reactivity index ≤50% at Day 7): NR (Difficult to extract from Fig 2B)Bad responders (Platelet reactivity index >50% at Day 7) | Based on literature | Rapid response (Platelet reactivity index ≤50% at 2 days): 7/17 (41.2%)Not rapid response (Platelet reactivity index >50% at 2 days): 10/17 (58.8%) Good responders (Platelet reactivity index ≤50% at Day 7): NR (Difficult to extract from Fig 2B)Bad responders (Platelet reactivity index >50% at Day 7): NR (Difficult to extract from Fig 2B) |
| El Ghannudi, 2011{El, 2011 3 /id}21524751France NR | Flow cytometric analysis of VASP phosphorylation Platelet VASP kitDiagnostica Stago (Biocytex), Asnières, France | ADP | Whole blood samples were drawn by venous puncture0.129 M sodium citrateBlood taken at least 6 h after clopidogrel, mean interval ~24 h, and range 12-120 hSent to Alsace laboratory for VASP immediately after sample obtained but interval NR | Non-diabetic responders (NDM-R) (PRI <61%)Non-diabetic low responders (NDM-LR) (PRI≥61%)Diabetic responders (DM-R) (PRI<61%)Diabetic low responders (DM-LR) (PRI≥61%)[NB outcome data available for only 429 of the 436 (98.4%) but NR why]Also some data reported for groups with cutoff at 60%, not 61%, but no explanation given | Based on literature (Ref 7) | Non-diabetic responders (NDM-R) (PRI <61%) 177 (64.8%)Non-diabetic low responders (NDM-LR) (PRI≥61%) 96 (35.2%)Diabetic responders (DM-R) (PRI<61%) 85 (52.1%)Diabetic low responders (DM-LR) (PRI≥61%) 78 (47.9%) |
| El Ghannudi, 2010{El, 2010 74 /id}20630458FranceNR | Flow cytometric analysis of VASP phosphorylation Platelet VASP kitDiagnostica Stago (Biocytex), Asnières, France | ADP | Blood samples drawn at least 6 h after a loading dose (300 or 600 mg) of clopidogrel. 0.129 mol/L sodium Citrate 6 h after a loading dose (300 or 600 mg) of clopidogrel. NR | Low responder (PRI≥61%)Responder (PRI≥61%) | Based on an ROC curve from data on subjects in this study | Low responder (PRI≥61%): N=184Responder (PRI≥61%): N=277 |
| Morel, 2011{Morel, 2011 187 /id}21251579FranceNR | Flow cytometric analysis of VASP phosphorylation Platelet VASP kitDiagnostica Stago (Biocytex), Asnières, France | prostaglandin E1 (PGE1) or ADP | after PCI0.129 M sodium citrate0.25 (6 hours after loading dose)NR [It is reported that the samples were sent off immediately for analysis] | Low responders (PRI≥ 61%)Normal responders (PRI<61%) By Quartile:Quartile 1 (<40.30%)Quartile 2 (40.30%–55.83%)Quartile 3 (55.84%–70.25%)Quartile 4 (>70.25%) | Single PRI cutoff based on literature; quartile cutoffs not explicitly reported | Low responders (PRI≥ 61%): 173 (40%)Normal responders (PRI<61%): 260 (60%)Quartile 1 (<40.30%): 108 (25%)Quartile 2 (40.30%–55.83%): 108 (25%)Quartile 3 (55.84%–70.25%):108 (25%)Quartile 4 (>70.25%): 109 (25%) |
| Palmerini, 2010{Palmerini, 2010 81 /id}19604542ItalyDOUBLE | VASP PhosprylationVASP kitBiocytex, Marseille, France | ADP 20 µmol/L | 1-2 hrs after ingestion of last clopidogrel dose done at baseline, 1 week and 1 monthCitrateNR [clopidogrel] 0.02 [30 minutes] | Poor responders (PRI>50%) in clopidogrel 75 mg groupNormal responders (PRI between 30-50%) in clopidogrel 75 mg group Poor responders (PRI>50%) in clopidogrel 150 mg groupNormal responders (PRI between 30-50%) in clopidogrel 150 mg group | Based on literature | Poor responders (PRI>50%) in clopidogrel 75 mg group: 21 (87.5%)Normal responders (PRI between 30-50%) in clopidogrel 75 mg group : 3 (12.5%)Poor responders (PRI>50%) in clopidogrel 150 mg group: 20 (83.3%)Normal responders (PRI between 30-50%) in clopidogrel 150 mg group: 4 (16.7%) |
| Schafer, 2011{Schafer, 2011 11 /id}21655677GermanyNR | Flow cytometric analysis of VASP phosphorylation Platelet VASP/P2Y12 kitBiocytex, Marseille, France | ADP | NRNR24 hours after loading with 600 mg clopidogrelNR | PRI >50% (suboptimal inhibition; impaired clopidogrel responsiveness)PRI≤ 50% 14 (26%)PRI quartiles: <51%, 51-58%, 59-71%, and >71%PRI >57%PRI ≤57% | >50% vs. </=50% was based on literature 57% threshold based on ROC analysis in present study | PRI >50% (suboptimal inhibition; impaired clopidogrel responsiveness): 40 (74%)PRI≤50%: 14 (26%)PRI quartiles: <51%, 51-58%, 59-71%, and >71%: Frequency NRPRI >57%: 40 (74%)PRI ≤57%: 14 (26%) |
| Frere, 2007{Frere, 2007 193 /id}17938809FranceNR | Flow cytometric analysis of VASP phosphorylation Platelet VASP/P2Y12 kitBiocytex, Marseille, France | PGE1 and ADP | before the PCI at least 12 h after the loading dose of clopidogrel and aspirin, and before administration of tirofiban if needed.3.8% trisodium citrate After 12hours after the loading dose of clopidogrel With 1 hour | VASP PRI ≥ 53%VASP PRI < 53% | As per the ROC curve created using data from study subjects | VASP PRI ≥ 53%: 13/106 (12.3%)VASP PRI < 53%: 1/89 (1.1%) |
| Kalantzi, 2012{Kalantzi, 2012 18174 /id} 21806493GreeceNR | VASPVASP/P2Y12 kit (BioCytex, Marseille,France) | ADP 2.5, 5 and 10uMADPADP | Citrated blood samples were collected after the patient’s presentation at the emergency roombefore clopidogrel administration (baseline), as well as at 5- and 30-days after clopidogrel loading. citrate5 days 30 days | nonresponderVASP PRI >50%responder VASP PRI <50% | reference 15, 23 | nonresponder n=12responder n=28 |
| Siller-matula, 2012{Siller-Matula, 2012 18177 /id}22260716AustriaPEGASUS-PCI | VASPPlatelet VASP; BioCytex,Marseille, France | ADP | Blood samples from patientswere obtained from the arterial sheath (6F) in the catheterizationlaboratory directly post-PCI and at least 5 min afterintravenous infusion of aspirin.3.8% sodium citrate NRperformed up to 24 h after blood sampling | Clopidogrelnon-responderaccording to MEA (≥ 48 U)Clopidogrel responderaccording to MEA(< 48 U)n = 321 (80%) | ref 16, 28 | non-respondern = 81 (20%)respondern = 321 (80%) |
| Tselepis, 2011 {Tselepis, 2011 1 /id}22008470GreeceNR | VASPFACS Calibur flow cytometerBecton Dickinson, san Jose, CA, USAVASP/P2Y12 kit (BioCytex, Marseille,France)  | ADP+PGE1 (prostaglandin E1)  | Blood samples were obtained from all patients before clopidogrel loading (baseline) as well as at 5 and 30 days afterwards. NR0, 5 and 30 days3h after blood sampling | clopidogrel responders PRI 50% as cutoff | reference 21 | clopidogrel responder n=57non-responder n=17 |
| Gaglia, 2012{Gaglia, 2011 18244 /id}21919956USANR | VASPFACS Calibur flow cytometerBecton Dickinson, san Jose, CA, USAVASP/P2Y12 kit (BioCytex, Marseille,France)  | ADP+PGE1 (prostaglandin E1)  | 6 hours following a loadingdose of clopidogrel3.2% sodium citrate6 hours6 and 24 hours following PCI | PRI>50% PRI≤50% | Based on literature | PRI>50%: 79 PRI≤50%: 121 |
| Cuisset, 2011{Cuisset, 2011 18245 /id}21872198FranceNR | VASPPlatelet VASP; BioCytex,Marseille, France | ADP | ≥12 hours after the loading dose of aspirin and clopidogrel3.8% trisodium citrate12 hrsNR | PRI>50% PRI≤50% | NR | PRI>50%: 331PRI≤50%: 358 |

\*If more than one test, use separate rows

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

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;