**Appendix Table E54. Results from studies assessing the ability of VASP to predict major adverse cardiovascular events in patients with ischemic heart disease**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **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)** |
| Freynhofer, 2011{Freynhofer, 2011 1 /id}21614416AustriaNR | Clopidogrel+aspirin | VASP | MACE | MACE included: 1) definite and probable ST according to the ARC-definition; 2) cardiovascular death, defined as death associated with ACS, significant arrhythmia, or congestive heart failure; and 3) non-fatal STEMI (STEMI: acute onset of prolonged typical ischaemic chest pains, ST-segment elevation of at least 1 mm in 2 or more contiguous electrocardiogram leads and increased biomarkers of myocardial necrosis) | 6 mo | PRI>60.2% (high reactivity, poor response)N=186 | MACE | 8.1% | NR | NR | NR | NR | NR | Get n’s from Fig 1 (pasted in on last page of this form) |
|  |  |  |  |  |  | VASP result: PRI≤60.2% (low reactivity, good response)N=114 |  | 0.9% | Relative risk reduction= 89%  |  | 0.007 (>60.2 vs ≤60.2) |  |  | Get n’s from Fig 1 (pasted in on last page of this form) |
|  |  |  |  |  |  | Cutoff 60.2% |  |  | AUC 0.683 | NR | 0.014 |  |  | ROC curves in Fig 2 |
| Bonello, 2007{Bonello, 2007 199 /id}17488353FranceNR | clopidogrel LD 300-mg followed by 75 mg daily | VASP | MACE | Cardiovascular death, ischemic stroke, recurrent ACS, and repeated revascularization either by coronary angioplasty or bypass surgery | 6-month | Quintile 1N=28 | MACE | 0 | NR | NR | NR | NR | NR |  |
|  |  |  |  |  |  | Quintiles 2-5N=144 |  | 21(14.5) | OR (calculated)= 0.1 | NR | P= 0.11(Q2-5 vs Q1)[Fisher's exact] | NR | NR |  |
| El Ghannudi 2011{El, 2011 3 /id}21524751France NR | Clopidogrel + aspirin | VASP | MACE | Not explicitly defined | 9 months | non-diabetic responders (NDM-R) (PRI <61%) |  | 15 (15.8%) |  |  | 0.26 across all 4 phenotypic groups with 61% cutoff (log-rank test) |  |  |  |
|  |  |  |  |  |  | non-diabetic low responders (NDM-LR) (PRI≥61%) |  | 23 (13.1%) | HR 1.06  | 0.55–2.03 | 0.87 (univariate analysis) |  |  |  |
|  |  |  |  |  |  | PRI > 50% (LR to clopidogrel) in patients without diabetes |  |  | HR 1.15  | 0.60–2.21 | 0.67 (univariate analysis) |  |  |  |
|  |  |  |  |  |  | diabetic responders (DM-R) (PRI<61%) |  | 12 (14.1%) |  |  |  |  |  |  |
|  |  |  |  |  |  | diabetic low responders (DM-LR) (PRI≥61%) |  | 17 (23%) | HR 2.01 | 0.96–4.23 | 0.06 (univariate analysis) |  |  |  |
|  |  |  |  |  |  | Same as just above |  |  | HR 2.44 | 1.10–5.39 | 0.027 (multivariate analysis) |  |  |  |
|  |  |  |  |  |  | PRI > 50% (LR to clopidogrel) in patients with diabetes |  |  | HR 1.28 | 0.59–2.77 | 0.52 (univariate analysis) |  |  |  |
| El Ghannudi, 2010{El, 2010 74 /id}20630458FranceNR | Clopidogrel LD 300 or 600mg | VASP | MACE  | MACE | 9 months | Low responders | MACE | 35/178(19.7) | NR | NR | 0.06(low responders vs responders) | NR | NR |  |
|  |  |  |  |  |  | responders |  | 22/275 (13.1) |  |  |  |  |  |  |
|  | Clopidogrel LD 300 or 600mg | VASP PRI | MACE  | MACE  | 9 months  | PRI≥61% | MACE  | NR | HR=1.54 | 0.97-2.46 | 0.07(low responders vs responders)[Cox regression] | No  | NR |  |
|  |  |  |  |  |  | PRI≥50% | MACE | NR | HR=1.36 | 0.83-2.22 | 0.22(low responders vs responders)[Cox regression] | No  | NR |  |
|  |  |  |  |  |  | PRI≥69% | MACE | NR | HR=1.14 | 0.67-1.92 | 0.64(low responders vs responders)[Cox regression] | No  | NR |  |
| Morel, 2011{Morel, 2011 187 /id}21251579FranceNR | clopidogrel 300-600 mg LD | VASP | MACE | all-cause mortality, nonfatal myocardial infarction, or target lesion revascularization | mean 9±2 months | low responders (PRI≥ 61%) | MACE | 35 (20.2%) | HR=1.54 | 0.96-2.45 | P=0.069(low vs normal)[Cox regression] | NO | NR | Secondary |
|  |  |  |  |  |  | normal responders (PRI<61%) |  | 36 (13.8%) |  |  |  |  |  |  |
|  | clopidogrel 300-600 mg LD | VASP | MACE | all-cause mortality, nonfatal myocardial infarction, or target lesion revascularization | mean 9±2 months | low responders (PRI≥ 61%) | MACE | 35 (20.2%) | HR=2.36 | 1.35-4.15 | P=0.003(low vs normal)[Cox regression] | YES;Planned PCI; Drug-eluting stent; | NR | Secondary |
|  |  |  |  |  |  | normal responders (PRI<61%) |  | 36 (13.8%) |  |  |  |  |  |  |
|  | clopidogrel 300-600 mg LD | VASP | MACE | all-cause mortality, nonfatal myocardial infarction, or target lesion revascularization | mean 9±2 months | Quartile 1 (<40.30%) | MACE | 5 (15.2%) | NR | NR | P=0.019(low vs normal)fishers exact | NO | NR | Secondary |
|  |  |  |  |  |  | Quartile 2 (40.30%–55.83%) |  | 3 (10%) |  |  |  |  |  |  |
|  |  |  |  |  |  | Quartile 3 (55.84%–70.25%) |  | 9 (31%) |  |  |  |  |  |  |
|  |  |  |  |  |  | Quartile 4 (>70.25%) |  | 7 (24.1%) |  |  |  |  |  |  |
| Schafer,2011{Schafer, 2011 11 /id}21655677GermanyNR | Clopidogrel | VASP | combined cardiovascular endpoint consisting of cardiac death, nonfatal myocardial infarction, stent thrombosis, ischaemic stroke, and urgent target vessel revascularisation | NR | 12 mo | <51% PRI (n is NR) | YES event | 2 | NR | NR | NR | NR | NR | NR |
|  |  |  |  |  |  | 51-58% PRI (n is NR) |  | 2 | NR | NR | NR | NR | NR | NR |
|  |  |  |  |  |  | 59-71% PRI (n is NR) |  | 6 | NR | NR | NR | NR | NR | NR |
|  |  |  |  |  |  | >71% PRI (n is NR) |  | 5 | NR | NR | NR | NR | NR | NR |
|  |  |  |  |  |  | >57% |  | 5/40 (12%) [per data in rest of table, s/b 12, not 5 [see Table 2 in paper]) | HR = 4.3 | 1.3-9.9 | 0.0136 (>57% vs ≤ 57%)[log rank] | NR | NR | K-M curve given in Fig. 2B |
|  |  |  |  |  |  | </=57% |  | 6/14 (41.4%) [per data in rest of table, s/b 3, not 6 [see Table 2 in paper]) | NR | NR | NR | NR | NR | K-M curve given in Fig. 2B |
|  |  |  |  |  |  |  |  |  | AUC 0.69 | 0.53-0.86 | 0.027 |  |  | ROC curve in Fig. 2A |
| Frere, 2007{Frere, 2007 193 /id}17938809FranceNR | 600 mg loading dose of clopidogrel and maintaining 75mg daily  | VASP | CV event | CV death, acute or subacute stent thrombosis, recurrent ACS and stroke | 30 days after PCI | ≥53% N=106 | CV event | 13 (12.3%)  | AUC: 0.73±0.08OR (calculated)= 12.3 | NR | P= 0.017(>53 vs ≤ 53%)[Fisher's exact] | NR | NR | NR |
|  |  |  |  |  |  | <53%N=89 | CV event | 1 (1.1%) |  |  |  |  |  |  |