**Appendix Table E33. Results from studies assessing the ability of VerifyNow to predict death 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)** |
| Breet, 2010{Breet, 2010 86 /id}  20179285  Netherlands  POPULAR | maintaining Clopidogrel 75 mg daily +aspirin 80-100mg daily | VerifyNow P2Y12 | Death | death, | 1-year | High OTPR | Death | 9/406  (2.2) | OR=1.60 | 0.63-4.08 | 0.32  (high OTPR vs Normal OTPR)  [logistic regression] | No | NR |  |
|  |  |  |  |  |  | Normal  OTPR |  | 9/646  (1.4) |  |  |  |  |  |  |
| Kim, 2010{Kim, 2010 241 /id}  20449634  Korea  NR | 300-600mg LD and 75 mg maintain dose clopidogrel | VerifyNow P2Y12 (PRU) | cardiac death | cardiac death | 6 months | <240 | cardiac death | 0.2% | OR=3.85 | 0.46-32.12 | 0.258  (≥240 vs <240)  [logistic regression] | NR | NR |  |
|  |  |  |  |  |  | ≥240 |  | 0.9% |  |  |  |  |  |  |
| Campo, 2010{Campo, 2010 58 /id}  20951320  10 sites in Italy, Belgium, France, Sprain  3T/2R trial | Clopidogrel LD 300 or 600 mg or maintaining 75mg daily | VerifyNowP2Y12 | Death | Death | 1-year | Full responder | Death | 5/289 (1.7) | NR | NR | 0.4  (poor vs full responder)  [log rank] | NR | NR | Figure 4 and figure 5, KM curve for 1-year primary end point |
|  |  |  |  |  |  | Poor responder |  | 4/179 (2.2) | OR (calculate)=1.30 | 0.3-4.9 | P=0.737 (poor responder vs full responder)  [Fisher’s exact test] |  |  |  |
| Campo, 2011{Campo, 2011 13 /id}  21679849  Italy  NR | Clopidogrel + aspirin | VerifyNow | Death | NR | 1 yr | Poor response at baseline (N=107) | Death | 3 | OR (calculated)=1.83 | 0.4-9.2 | P=0.67  (poor responder at baseline vs full responder)  [Fisher’s exact test] | NR | NR | NO |
|  |  |  |  |  |  | Full response at baseline (n=193) |  | 3 |  |  |  |  |  |  |
|  | Clopidogrel + aspirin | VerifyNow | Death | Death | 1 yr | Poor response at 1 mo (n=40) |  | 5 | OR (calculated)=37 | 4.2-326 | P=0.0002  (poor responder at 1 month vs full responder)  [Fisher’s exact test] | NR | NR | NR |
|  |  |  |  |  |  | Full response at 1 mo (n=260) |  | 1 |  |  |  |  |  |  |
| Kim, 2011{Kim, 2011 5 /id}  21786434  South Korea  CiLostazol administration before pErcutaneous coronAry intervention for Reduction of periprocedural myonecrosis trial (CLEAR trial) | Clopidogrel+aspirin | VerifyNow | Cardiac death |  | 6 months | Clopidogrel resistance |  | 0/37 (0%) |  |  | NS  (resistance vs normal response)  [chi-square statistics or Fisher ’s exact test] |  |  |  |
|  |  |  |  |  |  | Normal response |  | 1/73 (1%) |  |  |  |  |  |  |
| Lee, 2009{Lee, 2009 230 /id}  20049136  South Korea  NR | 600 mg clopidogrel + 300 mg aspirinLD & in pts with DES, 100 mg aspirin +75 mg clopidogrel | VerifyNow | Cardiac death | Cardiac death |  | Normal response |  | 1 (0.7%) |  |  | 0.344 (low vs normal response)  [chi-square or Fisher’s exact] |  |  |  |
|  |  |  |  |  |  | Low response |  | 2 (2.1%) |  |  |  |  |  |  |
| Marcucci, 2009{Marcucci, 2009 144 /id}  19118249  Italy  NR | clopidogrel 600 mg LD + 75 mg MD & ASA 500 mg IV LD + 100-325 mg MD | VerifyNow | Cardiovascular death | Cardiovascular death | 12 months | high residual platelet reactivity (PRU≥240) | Cardiovascular death | 13 (5.9) | HR=2.38 | 1.15–5.2 | P=0.031  (RPR vs no RPR)  [cox regression] | NO | NR |  |
|  |  |  |  |  |  | No residual platelet reactivity (PRU<240) |  | 11 (2.4) |  |  |  |  |  |  |
|  |  |  |  |  | 12 months | high residual platelet reactivity (PRU≥240) | Cardiovascular death | 13 (5.9) | HR=2.55 | 1.08–6.07 | P=0.034  (RPR vs no RPR)  [cos regression] | YES;  cardiovascular risk factors, renal failure, left ventricular ejection fraction <40%, multivessel disease, total stent length, bifurcation lesions, number of lesions treated, type of stent used, and use of glycoprotein IIb/IIIa inhibitors | NR |  |
|  |  |  |  |  |  | No residual platelet reactivity (PRU<240) |  | 11 (2.4) |  |  |  |  |  |  |
|  |  |  | Survival free from Cardiovascular death | Survival free from Cardiovascular death | 12 months | high residual platelet reactivity (PRU≥240) | Survival free from Cardiovascular death | NR | NR | NR | P=0.02  (RPR vs no RPR)  Log rank test | NO | NR |  |
|  |  |  |  |  |  | No residual platelet reactivity (PRU<240) |  | NR |  |  |  |  |  |  |
|  |  |  | Cardiovascular death | Cardiovascular death | 12 months | high residual platelet reactivity (PRU≥235) | Cardiovascular death | NR | HR=2.37 | 1.06–5.3 | P=0.035  (RPR vs no RPR)  [cox regression] | NO | NR |  |
|  |  |  |  |  |  | No residual platelet reactivity (PRU<235) |  | NR |  |  |  |  |  |  |
|  |  |  | Cardiovascular death | Cardiovascular death**Error! Bookmark not defined.** | 12 months | high residual platelet reactivity (PRU≥235) | Cardiovascular death | NR | HR=2.41 | 1.01–5.72 | P=0.046  (RPR vs no RPR)  [cox regression] | YES;  cardiovascular risk factors, renal failure, left ventricular ejection fraction <40%, multivessel disease, total stent length, bifurcation lesions, number of lesions treated, type of stent used, and use of glycoprotein IIb/IIIa inhibitors | NR |  |
|  |  |  |  |  |  | No residual platelet reactivity (PRU<235) |  | NR |  |  |  |  |  |  |
| Price, 2011{Price, 2011 23 /id}  21406646  USA  Gauging Responsiveness with A VerifyNow assay—Impact on Thrombosis And Safety (GRAVITAS) | Clopidogrel 75 mg/d MD+ Aspirin 75-162 mg/d MD | VerifyNow | Cardiovascular death | Cardiovascular death83 | 6 months | High on-treatment reactivity was  defined (PRU≥230) | Cardiovascular death | 8 (0.7%) | HR=1.42 | 0.38-5.36 | P=0.60  (high vs not high)  [log-rank test stratified by acute coronary syndromes status] | NO | NR | Secondary analysis |
|  |  |  |  |  |  | Not High On-Treatment Reactivity (PRU<230) |  | 3 (0.5%) |  |  |  |  |  |  |
|  | Clopidogrel 75 mg/d MD+ Aspirin 75-162 mg/d MD | VerifyNow | All cause death | All cause death | 6 months | High on-treatment reactivity was  defined (PRU≥230) | All cause death | 10 (0.9%) | HR=1.34 | 0.42-4.28 | P=0.62  (high vs not high)  [log-rank test stratified by acute coronary syndromes status] | NO | NR | Secondary analysis |
|  |  |  |  |  |  | Not High On-Treatment Reactivity (PRU<230) |  | 4 (0.7%) |  |  |  |  |  |  |
| Price, 2008{Price, 2008 174 /id}  18263931  USA  NR | Clopidogrel LD 600 mg and maintaining 75mg daily | VerifyNow P2Y12 assay | CV death | Cardiovascular death | 6-months | Lower reactivity | CV death | 0/209 | NR | NR | 0.04 comparing with the following row | NR | NR |  |
|  |  |  |  |  |  | High reactivity |  | 3/108 (2.8) |  |  |  |  |  |  |
|  | Clopidogrel LD 600 mg and maintaining 75mg daily | VerifyNow P2Y12 assay | CV death | Cardiovascular death | 6-months follow-up with a minimal of 3 months post-procedure | Lower reactivity | CV death | 0/252 | NR | NR | 0.04 comparing with the following row | NR | NR |  |
|  |  |  |  |  |  | High reactivity |  | 3/121  (2.5) |  |  |  |  |  |  |
|  |  |  |  |  |  | Total |  | 3/373 (0.8) |  |  |  |  |  |  |
| Breet, 2011{Breet, 2011 15 /id}  21478385  The Netherlands  POPular | Clopidogrel LD 300 or 600mg or maintaining 75 mg daily | VerifyNow | Death | Death | 1 year | HCPR(high on-clopidogrel platelet reactivity) or dual HPR | Death, | 6/168 | OR (calculate)=3.6 | 0.9-14.6 | P=0.07  (HCPR(high on-clopidogrel platelet reactivity) or dual HPR vsLow CPR+ or low PR)  [Fisher’s exact test] | NR | NR |  |
|  |  |  |  |  |  | Low CPR + Low PR |  | 3/280 |  |  |  |  |  |  |
| Park, 2011 {Park, 2011 1 /id} 22152948  Korea  NR | clopidogrel LD 300 or 600 mg>=12h before PCI, MD 75mg/day  aspirin LD 200mg, MD 100-200 mg/day | VerifyNow | death | death | 2-year | HTPR (PRU >235 and/or a % inhibition <15%) | death | high 40/1660  (2) | HR=1.10 | 0.69-1.75 | 0.71  comparing with normal  cox proportional model | NR | NR |  |
|  |  |  |  |  |  |  |  | normal  32/1189  (2) |  |  |  |  |  |  |
| Park, 2011{Park, 2011 18181 /id}  21880289  Korea  CROSS-VERIFY | clopidogrel LD 300 or 600 mg, MD 75mg/day; aspirin MD 100 mg/day | VerifyNow | Cardiac death | Cardiac death | 1 year | high OPR (HOPR) ≥275 PRU  n=247 | Cardiac death | 3 (1.2%) | NR | NR | P=0.299  (HOPR vs no HOPR)  [log rank test] | NR | NR |  |
|  |  |  |  |  |  | No HOPR <275 PRU  n=562 |  | 3 (0.5%) |  |  |  |  |  |  |
| Mangiacapra, 2012{Mangiacapra, 2012 18179 /id}  22440493  Italy & Belgium  ARMYDA-PROVE | Clopidogrel LD: 600 mg loading dose ≥6 h before PCI or 75 mg/d x 5 days  Clopidogrel MD: 75 mg/d from 4 weeks to 12 months  Aspirin 80-100 mg/day | VerifyNow | Death | Death | 30 days | Low PR (PRU ≤178)  n = 248 | Death | 1 (0.4%) | NR | NR | NS  [Fisher’s exact test] | No | NR |  |
|  |  |  |  |  |  | Normal PR (PRU between ≥179 and ≤238)  n = 244 |  | 1 (0.4%) |  |  |  |  |  |  |
|  |  |  |  |  |  | High PR (PRU ≥239)  n = 240 |  | 1 (0.4%) |  |  |  |  |  |  |
| Jin, 2012 {Jin, 2012 18230 /id} Korea  NR | 600mg clopidogrel and 300 mg aspirin LD, 75 mg clopidogrel and 100 mg aspirin as MD | VerifyNow P2Y12 | cardiovascular death | cardiovascular death, | 12 months | no HPR (<282PRU) | cardiovascular death, | 4/127=3.1% | HR=3.84 | 1.04-14.22 | 0.044comparing with HPR  cox-model | **yes** | **No** |  |
|  |  |  |  |  |  | HPR (≥282PRU) | cardiovascular death, | 6/54=11.1% |  |  |  |  |  |  |
| Yu, 2012 {Yu, 2012 18231 /id}  22787468  Korea  NR | LD 300mg aspirin and 300 mg clopidogrel, | VerifyNow P2Y12 | cardiac death | cardiac death | 12 months | responder  n=109 | cardiac death | 2/109=1.8% | OR=3.6 | 0.17-76.14 | 0.234  comparing with low responder  chi square test or Fisher’s exact test | **No** | **No** | **no** |
|  |  |  |  |  |  | low responder n=77 |  | 0/77=0 |  |  |  |  |  |  |
| Gaglia, 2012{Gaglia, 2011 18244 /id}  21919956  USA  NR | LD: 600 mg loading clopidogrel or 75-mg for 5 days  MD: Aspirin + clopidogrel 75 mg for 1 month in patients with BMS and 12 months in patients receiving DES | VerifyNow | death | death | 3 days | HPR with PRU>235  n=54 | HPR | 0 | OR (calculated)=2.7 | NR | 0.6  (HPR vs NPR)  [Fishers exact test] | No | NR |  |
|  |  |  |  |  |  | NPR with PRU>235  n=146 |  | 0 |  |  |  |  |  |  |