**Appendix Table E35. Results from studies assessing the ability of VerifyNow to predict stent thrombosis 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)** |
| Breet, 2010{Breet, 2010 86 /id}20179285NetherlandsPOPULAR | maintaining Clopidogrel 75 mg daily +aspirin 80-100mg daily | VerifyNow P2Y12 | Stent thrombosis  | Stent thrombosis  | 1-year  | High OTPR | Stent thrombosis  | 8/406 (2.0) | OR=2.58 | 0.84-7.93 | <0.09 | No  | NR |  |
|  |  |  |  |  |  | Normal OTPR |  | 5/646 (0.8) |  |  |  |  |  |  |
| Kim, 2010{Kim, 2010 241 /id}20449634KoreaNR | 300-600mg LD and 75 mg maintain dose clopidogrel  | VerifyNow P2Y12 (PRU) | stent thrombosis  | stent thrombosis | 6 months |  <240 | stent thrombosis | 1.0% | OR=2.92 | 0.98-8.7 | 0.044 | NR | NR |  |
|  |  |  |  |  |  | ≥240 |  | 2.8% |  |  |  |  |  |  |
| Campo, 2010{Campo, 2010 58 /id}2095132010 sites in Italy, Belgium, France, Sprain3T/2R trial | Clopidogrel LD 300 or 600 mg or maintaining 75mg daily | VerifyNowP2Y12 | Definite ST  | Definite ST | 1-year  | Full responder | Definite ST | 2/289 (0.6) | NR | NR | 0.3 | NR | NR |  |
|  |  |  |  |  |  | Poor responder |  | 3/179 (1.7) |  |  |  |  |  |  |
|  | Clopidogrel LD 300 or 600 mg or maintaining 75mg daily | VerifyNowP2Y12 | Definite/probable ST  | Definite/probable ST | 1-year  | Full responder | Definite/probable ST | 3/289 (1) | NR | NR | 0.1 | NR | NR |  |
|  |  |  |  |  |  | Poor responder |  | 5/179 (2.8) |  |  |  |  |  |  |
| Campo, 2011{Campo, 2011 13 /id}21679849ItalyNR | Clopidogrel + aspirin | VerifyNow | Stent thrombosis |  |  | Poor response at baseline (N=107) |  | 2 | OR (calculate)=1.82 | NR | P=0.62(poor response vs full response)[Fisher’s exact test] |  |  |  |
|  |  |  |  |  |  | Full response at baseline (n=193) |  | 2 |  |  |  |  |  |  |
|  | Clopidogrel + aspirin | VerifyNow | Stent thrombosis | xx |  | Poor response at 1 mo (n=40) |  | 3 | OR (calculate)=21 | NR | P=0.008(poor response vs full response)[Fisher’s exact test] |  |  |  |
|  |  |  |  |  |  | Full response at 1 mo (n=260) |  | 1 |  |  |  |  |  |  |
| Kim, 2011{Kim, 2011 5 /id}21786434South KoreaCiLostazol administration before pErcutaneous coronAry intervention for Reduction of periprocedural myonecrosis trial (CLEAR trial) | Clopidogrel+aspirin | VerifyNow | Stent thrombosis |  | 6 mo | Clopidogrel resistance |  | 1/37 (3%) |  |  | NS vs. next row (chi-square statistics or Fisher ’s exact test) |  |  |  |
|  |  |  |  |  |  | Normal response |  | 1/73 (1%) |  |  |  |  |  |  |
| Lee, 2009{Lee, 2009 230 /id}20049136South KoreaNR | 600 mg clopidogrel + 300 mg aspirinLD & in pts with DES, 100 mg aspirin +75 mg clopidogrel | VerifyNow  | Definitie stent thrombosis | in-stent thrombosis on coronary angiography | 6 mo after stenting | Normal response | YES event | 0 (0%) | NR | NR | 0.014 vs. next row (chi-square or Fisher’s exact) | NR | NR | NONE |
|  |  |  |  |  |  | Low response |  | 4 (4.2%) |  |  |  |  |  |  |
|  |  |  | Probable stent thrombosis | MI confirmed around the area of stent insertion or in cases in which death due to an unknown cause occurred within 30 days post-PCI |  | Normal response |  | 0 (0%) |  |  |  |  |  |  |
|  |  |  |  |  |  | Low response |  | 0 (0%) |  |  |  |  |  |  |
|  |  |  | Possible stent thrombosis | idiopathic sudden death within 30 days post-PCI |  | Normal response |  | 0 (0%) |  |  |  |  |  |  |
|  |  |  |  |  |  | Low response |  | 0 (0%) |  |  |  |  |  |  |
|  |  |  | Acute stent thrombosis |  | within 24 hours after stenting | Normal response |  | 0 (0%) |  |  |  |  |  |  |
|  |  |  |  |  |  | Low response |  | 1 (1.0%) |  |  |  |  |  |  |
|  |  |  | Subacute stent thrombosis |  | Within 1 day after stenting | Normal response |  | 0 (0%) |  |  |  |  |  |  |
|  |  |  |  |  |  | Low response |  | 1 (1.0%) |  |  |  |  |  |  |
|  |  |  | Late stent thrombosis |  | Within 1 mo after stenting | Normal response |  | 0 (0%) |  |  |  |  |  |  |
|  |  |  |  |  |  | Low response |  | 2 (2.1%) |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Price, 2011{Price, 2011 23 /id}21406646USAGauging Responsiveness with A VerifyNow assay—Impact on Thrombosis And Safety (GRAVITAS) | Clopidogrel 75 mg/d MD+ Aspirin 75-162 mg/d MD | VerifyNow | Stent thrombosis | Stent thrombosis | 6 months | High on-treatment reactivity wasdefined (PRU≥230) | Stent thrombosis | 8 (0.7%) | HR=2.16 | 0.46-10.19 | P=0.31(high vs not high)[log-rank test stratified by acute coronary syndromes status] | NO | NR | Secondary analysis |
|  |  |  |  |  |  | Not High On-Treatment Reactivity (PRU<230) |  | 2 (0.3%) |  |  |  |  |  |  |
| Price, 2008{Price, 2008 174 /id}18263931USANR | Clopidogrel LD 600 mg and maintaining 75mg daily | VerifyNow P2Y12 assay | Stent thrombosis | Stent thrombosis | 6-months | Lower reactivity | Stent thrombosis | 0/209 | NR | NR | 0.004 comparing with the following row  | NR | NR |  |
|  |  |  |  |  |  | High reactivity  |  | 5/108 (4.6) |  |  |  |  |  |  |
|  |  |  |  |  |  | Total  |  | 5/317 (1.6) |  |  |  |  |  |  |
|  | Clopidogrel LD 600 mg and maintaining 75mg daily | VerifyNow P2Y12 assay | Stent thrombosis | Stent thrombosis | 6-months follow-up with a minimal of 3 months post-procedure | Lower reactivity | Stent thrombosis | 0/252 | NR | NR | 0.004 comparing with the following row  | NR | NR |  |
|  |  |  |  |  |  | High reactivity  |  | 5/121 (4.1) |  |  |  |  |  |  |
|  |  |  |  |  |  | Total  |  | 5/373(1.3) |  |  |  |  |  |  |
| Breet, 2011{Breet, 2011 15 /id}21478385The NetherlandsPOPular | Clopidogrel LD 300 or 600mg or maintaining 75 mg daily | VerifyNow | ST | ST | 1 year | HCPR(high on-clopidogrel platelet reactivity) or dual HPR | ST | 2/168 | OR (calculate)=3.53 | NR | P=0.3(HCPR(high on-clopidogrel platelet reactivity) or dual HPR vsLow CPR+ or low PR)[Fisher’s exact test] | NR | NR |  |
|  |  |  |  |  |  | Low CPR + normal PR |  | 1/280 |  |  |  |  |  |  |
| Park, 2011 {Park, 2011 1 /id} 22152948KoreaNR | clopidogrel LD 300 or 600 mg>=12h before PCI, MD 75mg/dayaspirin LD 200mg, MD 100-200 mg/day | VerifyNow | stent thrombosis | definite, probable, or possible  | 2-year | HTPR (PRU >235 and/or a % inhibition <15%) | stent thrombosis | high 13/1660(0.8) | HR=0.72 | 0.34-1.51 | 0.38comparing with normal Cox proportional model  | NR | NR |  |
|  |  |  |  |  |  |  |  | normal15/1189(0.8) |  |  |  |  |  |  |
| Park, 2011{Park, 2011 18181 /id}21880289KoreaCROSS-VERIFY | clopidogrel LD 300 or 600 mg, MD 75mg/day; aspirin MD 100 mg/day | VerifyNow | stent thrombosis | Definite or probable  | 1 year | high OPR (HOPR) ≥235 PRUn=407 | stent thrombosis | NR | NR | NR | P=0.060(HOPR vs no HOPR)Log rank test | NR | NR |  |
|  |  |  |  |  |  | No HOPR <235 PRUn=402 |  | NR |  |  |  |  |  |  |
|  | clopidogrel LD 300 or 600 mg, MD 75mg/day; aspirin MD 100 mg/day | VerifyNow | stent thrombosis | Definite or probable  | 1 year | high OPR (HOPR) ≥275 PRUn=247 | stent thrombosis | 5(2%) | OR=5.79 (calculated) | 1.11-30.0 | P=0.018(HOPR vs no HOPR)Log rank test | NR | NR |  |
|  |  |  |  |  |  | No HOPR <275 PRUn=562 |  | 2 (0.4%) |  |  |  |  |  |  |
|  |  |  | Definite stent thrombosis | Definite stent thrombosis | 1 year | high OPR (HOPR) ≥275 PRUn=247 | Definite stent thrombosis | 2 (0.8%) | OR=2.29(calculated) | 0.32-16.32 | P=0.395(HOPR vs no HOPR)Log rank test | NR | NR |  |
|  |  |  |  |  |  | No HOPR <275 PRUn=562 |  | 2 (0.4%) |  |  |  |  |  |  |
|  |  |  | Probable stent thrombosis | probable stent thrombosis  | 1 year | high OPR (HOPR) ≥275 PRUn=247 | Probable stent thrombosis | 3(1.2%) | OR=16.1 (calculated) | 0.83-312.96 | P=0.009(HOPR vs no HOPR)Log rank test | NR | NR |  |
|  |  |  |  |  |  | No HOPR <275 PRUn=562 |  | 0 (0%) |  |  |  |  |  |  |
|  |  |  | stent thrombosis | Definite or probable  | 1 year | Hyporesponders <5% inhibition of platelet aggregation n=195 | stent thrombosis | 5(2.6%) | OR=8.05 (calculated) | 1.55-41.84 | P=0.003(hypo-vs normal responders)Log rank test | NR | NR | Supp fig 5 has incorrect information on N at risk |
|  |  |  |  |  |  | responders ≥5% inhibition of platelet aggregation n=614 |  | 2 (0.3%) |  |  |  |  |  |  |
| Mangiacapra, 2012{Mangiacapra, 2012 18179 /id}22440493Italy & BelgiumARMYDA-PROVE | Clopidogrel LD: 600 mg loading dose ≥6 h before PCI or 75 mg/d x 5 daysClopidogrel MD: 75 mg/d from 4 weeks to 12 monthsAspirin 80-100 mg/day | VerifyNow | Stent thrombosis | Stent thrombosis | 30 days | Low PR (PRU ≤178)n = 248  | Stent thrombosis | 0(0%) | NR | NR | P=0.013[Fisher’s exact test] | No | NR |  |
|  |  |  |  |  |  | Normal PR (PRU between ≥179 and ≤238) n = 244 |  | 0(0%) | OR=0.22(calculated) | 0.012-4.11 | normal vs others |  |  |  |
|  |  |  |  |  |  | High PR (PRU ≥239)n = 240 |  | 4 (1.7%) |  |  |  |  |  |  |
| Jin, 2012 {Jin, 2012 18230 /id}22682702 KoreaNR | 600mg clopidogrel and 300 mg aspirin LD, 75 mg clopidogrel and 100 mg aspirin as MD | VerifyNow P2Y12 | stent thrombosis | stent thrombosis | 12 months | no HPR  | stent thrombosis | 3/127=2.4% | HR=2.43 | 0.48-12.45 | 0.286 comparing with HPRcox-model | **yes** | **No** |  |
|  |  |  |  |  |  | HPR | stent thrombosis | 3/54=5.6% |  |  |  |  |  |  |
| Yu, 2012 {Yu, 2012 18231 /id}22787468KoreaNR | LD 300mg aspirin and 300 mg clopidogrel, | VerifyNow P2Y12 | stent thrombosis | stent thrombosis | 12 months | respondern=109 | stent thrombosis | 4/109=3.7% | OR=1.43(calculated) | 0.26-8.0 | 0.68 comparing with low responderchi square test or Fisher’s exact test | **No** | **No** | **No** |
|  |  |  |  |  |  | low responder n=77 |  | 2/77=2.6% |  |  |  |  |  |  |
| Gaglia, 2012{Gaglia, 2011 18244 /id}21919956USANR | 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 | stent thrombosis | stent thrombosis | 3 days | HPR with PRU>235n=54 | HPR | 0 | OR (calculated)=2.7 | NR | 0.6(HPR vs NPR)[Fishers exact test] | No | NR |  |
|  |  |  |  |  |  | NPR with PRU>235n=146 |  | 0 |  |  |  |  |  |  |