**Appendix Table D7. Clinical outcome information – mortality**

| **Author,year**  **UID**  **Country**  **Study name** | **Treatment** | **Genetic Test Used [index test]** | **Clinical Outcome** | **Outcome Definition** | **Timing of measurement** | **Genotype groups** | **No. with outcome status within phenotype group** | **Comparative metric** | **95% CI** | **P (between which groups?)**  **[statistical test]** | **Statistical Adjustment**  **[If YES, for what factors?]** | **Procedures for multiple comparisons** | **Comments** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Collet, 2009{Collet, 2009 140 /id}  19108880  France  AFIJI | Clopidogrel (75 mg maintenance dose for at least 1 mo) | CYP2C19 \*2 | CV death | Death with a demonstrable cardiovascular cause or any death not clearly attributable to non-cardiovascular cause. | Mean FU = 2.8 yr | Carriers (\*2/\*2 or \*2/\*1)  N = 73 | 2  1.45 events per 100 person-years | HR = 5.74  Adjusted HR = NON EVALUABLE (small number of events) | 0.52, 63.48  NA | 0.10  NA | Unadjusted  NA | NO | None. |
|  |  |  |  |  |  | Non-carriers (\*1/\*1)  N = 186 | 1  0.26 events per 100 person-years |  |  |  |  |  |  |
| Giusti, 2009{Giusti, 2009 134 /id}  19268736  Italy  RECLOSE | Aspirin (loading dose = 325 mg; maintenance dose = 325 mg per day) and clopidogrel (loading dose = 600 mg; 75 mg maintenance). | CYP2C19\*2 | Cardiac mortality | NR | Maximum FU of 6 mo | \*2/\*2 or \*2/\*1  N = 247 | 10 (4%) | NR | NR | 0.037 (chi square test) | NO | NO | Component of composite secondary outcome |
|  |  |  |  |  |  | \*1/\*1  N = 525 | 8 (1.5%) |  |  |  |  |  |  |
| Mega, 2009{Mega, 2009 141 /id}  19106084  Multinational  Genetics substudy of TRITON-TIMI 38 [Therapeutic Outcomes by Optimizing Platelet Inhibition with Prasugrel-Thrombolysis in Myocardial Infarction] | Clopidogrel 300 mg loading dose, 75 mg maintenance | CYP2C19 | Death from cardiovascular causes | NR; all outcomes were adjudicated by a committee unaware of group assignments | Up to 15 mo (maximum duration of treatment on trial) | IM or PM (1/\*2A, \*1A/\*3, \*1A/\*4, \*1A/\*8, \*2A/\*2A, \*2A/\*3, \*2A/\*4, \*2A/\*5A, \*2A/\*8)  N = 395 | NR  Rate = 2.0% (Kaplan-Meier) | HR = 4.79 | 1.40, 16.37 | NR | ACS subtype (STE or NSTE was used as a stratification factor) | NO | Secondary outcome |
|  |  |  |  |  |  | EM (\*1A/\*1A)  N = 1064 | NR  Rate = 0.4% (Kaplan-Meier rate) |  |  |  |  |  |  |
| Sibbing, 2009{Sibbing, 2009 133 /id}  19193675  Germany  NR | Clopidogrel 600 mg loading dose before stent placement | CYP2C19 \*2 | Death | NR | 30 days | CYP2C19 \*2 carriers  (\*2/\*2 and \*2/\*1)  N = 680 | 5 (<1%) | HR = 0.83 | 0.30, 2.26 | 0.71  [Cox proportional hazards regression; carriers vs. non-carriers] | NO | NO | None |
|  |  |  |  |  |  | CYP2C19 non-carriers (\*1/\*1)  N = 1805 | 16 (1%) |  |  |  |  |  |  |
| Sibbing, 2010{Sibbing, 2010 95 /id}  20083681  Germany  Part of a prospective study of the Multiplate analyzer | Clopidogrel 600 mg loading dose; clopidogrel 75 mg (1/d) and aspirin 100 mg (2/d) maintenance. | CYP2C19 \*17 | Mortality | Death within 30 days | 30 d | \*17/\*17  N = 76 | 1 (1.3%) | OR = 0.87 | 0.23, 3.31 | (carriers vs. non-cariers)[logistic regression]  P = 0.84 (across 3 groups) [chi-square test for trend] | NO | NO | Secondary efficacy endpoint |
|  |  |  |  |  |  | \*17/\*1  N = 546 | 2 (0.4%) |  |  |  |  |  |  |
|  |  |  |  |  |  | \*1/\*1  N = 902 | 5 (0.6%) |  |  |  |  |  |  |
| Bonello{Bonello, 2010 45 /id}  2010  20708365  France  NR | All patients received oral LDs of 250 mg aspirin and 600 mg clopidogrel at least 6 h before the first VASP index measurement | CYP2C19 | Death | Death | In hospital | Wild-type  N = 277 | 0 (0%) | NR | NR | NS | NR | NR | None |
|  |  |  |  |  |  | Heterozygotes 2C19\*2  N = 123 | 0 (0%) |  |  |  |  |  |  |
|  |  |  |  |  |  | Homozygotes 2C19\*2  N = 11 | 0 (0%) |  |  |  |  |  |  |
| Malek{Malek, 2010 43 /id}  2010  20924183  Poland  NR | Aspirin + clopidogrel | CYP2C19\*2 | All cause mortality | All cause mortality | 4 years | \*2/\*2 or \*2/\*1  N = 56 | 10 (17.9%); count calculated based on proportion | HR = 1.9 | 0.9, 4.0 | 0.09 [noncarrier  Vs. carrier of \*2; Kaplan-Meier] | NR | NR | curve in figure 1b |
|  |  |  |  |  |  | \*2 noncarriers  N = 205 | 20 (9.8%); count calculated based on proportion |  |  |  |  |  |  |
| Yamamoto 2011{Yamamoto, 2011 25 /id}  21168310  Japan  NR | clopidogrel | CYP2C19\*2 or \*3 | Cardiovascular death | Cardiovascular death | 74 days | Carriers  N = 61 | 1 () | NR | NR | NR | NR | NR |  |
|  |  | CYP2C19\*2/\*2 | Cardiovascular death | Cardiovascular death | NR | CYP2C19\*2/\*2 | NR | NR | NR | NR | NR | NR |  |
| Tiroch, 2010{Tiroch, 2010 62 /id}  20826260  Germany  NR | aspirin (100mg twice daily) and clopidogrel ( 75mg once Daily) | CYP2C19\*2 GG | Death | Death | 1 year | CYP2C19\*2 GG  N = 680 | 54 (7.9) | NR | NR | 0.08, CYP2C19\*2 GG vs \*2 A allele | NR | NR |  |
|  |  | CYP2C19\*2  A allele | Death | Death | 1 year | CYP2C19\*2  A allele  N = 248 | 11 (4.4) | NR | NR |  | NR | NR |  |
|  |  | CYP2C19\*17 CC | Death | Death | 1 year | CYP2C19\*17 CC  N = 565 | 34 (6) | NR | NR | 0.203  CYP2C19\*17 CC vs T allele | NR | NR |  |
|  |  | CYP2C19\*17 T allele | Death | Death | 1 year | CYP2C19\*17 T allele  N = 363 | 30 (8.3) | NR | NR |  | NR | NR |  |
| Sorich, 2010{Sorich, 2010 49 /id}  20492467  707 sites in 30 countries  Substudy of TRITON-TIMI 38 | 300-mg loading dose and 75-mg daily maintenance dose | CYP2C19 | CV death | CV death | 15 months | RM( with one or two reduced function alleles)  vs  EM( no reduced function allele )  N = 802 | 4.2% | OR=4.79 | 1.4-16.37 | NR | NR | No |  |
|  |  |  | CV death, | CV death, | 15 months | EM | 0.9% |  | 0.3-1.7 | NR | NR | No |  |
|  |  |  | CV death, | CV death, | 15 months | RM | NR |  | 2.2-6.1 | NR | NR | No |  |
| Sawada, 2010{Sawada, 2010 36 /id}  21099121  Japan  NR | loading dose of clopidogrel (300 mg) and maintenance dose of clopidogrel (75 mg/day) and aspirin (100 mg/day) | CYP2C19 | Death | Death | Mean 243.8 days | Non-carrier | 58 | 0 (0%) | NR | 0.87, Non-carrier vs \*2 carrier | No | No |  |
|  |  |  | Death | Death | Mean 243.8 days | \*2 carrier | 42 | 1 (2.4%) | NR | NO | NO | NO |  |
| Campo  2011{Campo, 2011 185 /id}  21679849  Italy  NR | Clopidogrel + aspirin | TaqMan | Death | All cause death | 1 mo to 1 yr after PCI | \*2 noncarriers | 4 (1.8%) | NR | NR | NR | NR | NO |  |
|  |  |  |  |  |  | \*2 carriers | 2 (2.5%) | NR | NR |  |  |  |  |
|  |  |  |  |  |  | \*17 noncarriers | 5 (2.5%) | NR | NR |  |  |  |  |
|  |  |  |  |  |  | \*17 carriers | 1 (1.0%) | NR | NR |  |  |  |  |
| Luo, 2011  22118006  {Luo, 2011 1 /id}  China  NR | LD clopidogrel 300mg and MD 75mg/d and aspirin 300mg LD and MD 100mg/d | CYP2C19  \*1/\*1 | cardiac death | cardiac death | 6 months | CYP2C19  \*1/\*1 | 6/936 | HR 0.95 | 0.45-2.36 | >0.05  comparing with the next row  chi-square test | NR | NR |  |
|  |  | CYP2C19  \*1/\*2 or \*2/\*2 |  |  |  | CYP2C19  \*1/\*2 or \*2/\*2 | 5/802 |  |  |  |  |  |  |
| Delaney, 2011{Delaney, 2012 7 /id}  22190063  USA  NR | clopidogrel | CYP2C19\*2 | death | death | 2 years | CYP2C19\*2 SNP rs4244285 | NR | HR=1.76 | 0.57-5.37 | 0.323 comparing with non carrier of \*2 | No | NR | NR |
|  | clopidogrel | CYP2C19\*17 | death | death | 2 years | CYP2C19\*17 SNP rs4244285 | NR | HR=1.62 | 0.69-3.81 | 0.267 comparing with non carrier of \*17 | No | NR | NR |
| Chen, 2012{Chen, 2012 18221 /id}  22071359  China  NR | Clopidogrel and aspirin | TaqMan | CV death | Within the 1-yr followup period | NR | \*2/\*2 (n=57) | 6 | Vs. \*1/\*1:  Unadjusted HR 5.733  Adjusted HR 6.321 | For unadjusted, 1.502-21.884  For adjusted, 2.081-19.205 | For unadjusted, 0.011 (K-M)  For adjusted, 0.001 (logistic regression) | For adjusted: adjusted for age, sex, DM, smoking, drug use, stenting, and ACS vs. stable angina | NR | NONE |
|  |  |  |  |  |  | \*1/\*2 (n=291) | 9 | Vs. \*1/\*1:  Unadjusted HR 1.258  Adjusted HR 1.303 | For unadjusted, 0.386-4.102  For adjusted, 0.478-3.548 | For unadjusted, 0.704 (K-M)  For adjusted, 0.605 (logistic regression) | For adjusted: adjusted for age, sex, DM, smoking, drug use, stenting, and ACS vs. stable angina |  |  |
|  |  |  |  |  |  | \*1/\*1 (n=306) | 7 | NA | NA | NA | NA |  |  |
|  |  |  | Death from any cause | Within the 1-yr followup period | NR | \*2/\*2 (n=57) | 6 | Vs. \*1/\*1:  Unadjusted HR 4.086  Adjusted HR 4.794 | For unadjusted, 1.115-14.461  For adjusted, 1.683-13.659 | For unadjusted, 0.029 (K-M)  For adjusted, 0.003 (logistic regression) | For adjusted: adjusted for age, sex, DM, smoking, drug use, stenting, and ACS vs. stable angina | NR | NONE |
|  |  |  |  |  |  | \*1/\*2 (n=291) | 10 | Vs. \*1/\*1:  Unadjusted HR 1.053  Adjusted HR 1.089 | For unadjusted, 0.368-3.016  For adjusted, 0.437-2.713 | For unadjusted, 0.923 (K-M)  For adjusted, 0.855 (logistic regression) | For adjusted: adjusted for age, sex, DM, smoking, drug use, stenting, and ACS vs. stable angina |  |  |
|  |  |  |  |  |  | \*1/\*1 (n=306) | 9 | NA | NA | NA | NA |  |  |
| Nishio, 2012{Nishio, 2012 18214 /id}  22785462  Japan  NR | Clopidogrel and aspirin | TaqMan | Death | NR | Any time during study | Extensive metabolizer (n=60) | 1 | NR | NR | Across this and next two rows, 0.24 (chi-square test) | NR | NR | NONE |
|  |  |  |  |  |  | Intermediate metabolizer (n=77) | 2 | NR | NR |  | NR | NR | NONE |
|  |  |  |  |  |  | Poor metabolizer (n=23) | 2 | NR | NR |  | NR | NR | NONE |
|  |  |  | Cardiac death | NR |  | Extensive metabolizer (n=60) | 0 | NR | NR | Across this and next two rows, 0.34 (chi-square test) | NR | NR | NONE |
|  |  |  |  |  |  | Intermediate metabolizer (n=77) | 2 (the same 2 as classified just above in this group) | NR | NR |  | NR | NR | NONE |
|  |  |  |  |  |  | Poor metabolizer (n=23) | 0 | NR | NR |  | NR | NR | NONE |
| Goodman, 2012{Goodman, 2012 18213 /id}  22261200  Multi-country  PLATO | Clopidogrel 300-mg loading dose, 75-mg daily maintenance  dose | CYP2C19 \*2 | All cause mortality | death | 12 months | CYP2C19 loss-of-function carriers (\*2 through \*8) on a PPI  n=434 | 11 (2.5%) | HR= 1.67 | 1.03–2.71 | NR | no | NR |  |
|  |  |  |  |  |  | non carriers of CYP2C19 loss-of-function allele or not taking a PPI  n=2418 | 24 (1%) |  |  |  |  |  |  |