**Appendix Table D8. Clinical outcome information – myocardial infarction**

| **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{Collet, 2009 140 /id}  2009  19108880  France  AFIJI | Clopidogrel (75 mg maintenance dose for at least 1 mo) | CYP2C19 \*2 | MI | Recent ischemic symptom with EKG abnormalities in the ST segmen (depression or elevation of at least 0.1 mV)t and a positive troponin measurement as defined locally. | Mean FU = 2.8 yr | Carriers (\*2/\*2 or \*2/\*1)  N = 73 | | N = 10  7.27 events per 100 person-years | HR = 4.57  Adjusted HR = 5.57 | 1.64, 12.53  1.94, 16.01 | 0.001  0.001 | Unadjusted  Adjusted [baseline BMI, smoking status, diabetes status, stent implantation, initial STE MI, use of PPI] | NO | None. |
|  |  |  |  |  |  | Non-carriers (\*1/\*1)  N = 186 | | N = 6  1.58 events per 100 person-years |  |  |  |  |  |  |
| Mega{Mega, 2009 141 /id}  2009  19106084  Multinational  TRITON-TIMI 38 | Clopidogrel 300 mg loading dose, 75 mg maintenance | CYP2C19 | Non-fatal MI | 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 = 10.1% (Kaplan-Meier) | HR = 1.38 | 0.94, 2.02 | NR | ACS subtype (STE or NSTE was used as a stratification factor) | NO | Secondary outcome |
|  |  |  |  |  |  | EM (\*1A/\*1A)  N = 1064 | | NR  Rate = 7.5% (Kaplan-Meier rate) |  |  |  |  |  |  |
| Sibbing{Sibbing, 2009 133 /id}  2009  19193675  Germany  NR | Clopidogrel 600 mg loading dose before stent placement | CYP2C19 \*2 | MI | Thrombolysis in Myocardial Infarction Criteria (TIMI), based on new abnormal Q-wave appearance in the EKG or increase in CK-MB value to three or more times the upper limit of normal; appears to have included NSTE-ACS | 30 days | CYP2C19 \*2 carriers  (\*2/\*2 and \*2/\*1)  N = 680 | | 48 (7%) | HR = 1.15 | 0.82, 1.61 | P = 0.42  [Cox proportional hazards regression; carriers vs. non-carriers] | NO | NO | None |
|  |  |  |  |  |  | CYP2C19 non-carriers (\*1/\*1)  N = 1805 | | 111 (6%) |  |  |  |  |  |  |
|  |  |  | STEMI | NR | 30 days | CYP2C19 \*2 carriers  (\*2/\*2 and \*2/\*1)  N = 680 | | 10 (1%) | HR = 2.96 | 1.20, 7.28 | 0.02  [Cox proportional hazards regression; carriers vs. non-carriers] | NO | NO | None |
|  |  |  |  |  |  | CYP2C19 non-carriers (\*1/\*1)  N = 1805 | | 9 (<1%) |  |  |  |  |  |  |
|  |  |  | NSTE-ACS | NSTE-ACS | 30 days | CYP2C19 \*2 carriers  (\*2/\*2 and \*2/\*1)  N = 680 | | 38 (6%) | HR = 0.99 | 0.68, 1.44 | 0.96  [Cox proportional hazards regression; carriers vs. non-carriers] | NO | NO | None |
|  |  |  |  |  |  | CYP2C19 non-carriers (\*1/\*1)  N = 1805 | | 102 (6%) |  |  |  |  |  |  |
| 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 | MI | Based on TIMI criteria (new abnormal Q-wave appearance in EKG or increase in CK-MB ≥3 x normal) | 30 d | \*17/\*17  N = 76 | | 4 (5.3%) | OR = 1.05 | 0.59, 1.85 | (carriers vs. non-cariers)[logistic regression]  P = 0.61 (across 3 groups) [chi-square test for trend] | NO | NO | Secondary efficacy endpoint |
|  |  |  |  |  |  | \*17/\*1  N = 546 | | 17 (3.1%) |  |  |  |  |  |  |
|  |  |  |  |  |  | \*1/\*1  N = 902 | | 29 (3.2%) |  |  |  |  |  |  |
| Bonello, 2010{Bonello, 2010 45 /id}  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 | ACS | Non–ST-segment elevation acs= clinical symptoms of acute myocardial ischemia within 12 h before admission + at least 1 of the following: a new finding of ST-segment depression >0.05 mV, T-wave inversion >0.3 mV in at least 2 leads, or elevated levels of cardiac markers. | 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%) |  |  |  |  |  |  |
| Yamamoto 2011{Yamamoto, 2011 25 /id}  21168310  Japan  NR | clopidogrel | CYP2C19\*2 or \*3 | Nonfatal myocardial infarction | Nonfatal myocardial infarction | NR | carriers | | 2/62 | NR | NR | NR | NR | NR |  |
|  |  | CYP2C19\*1/\*2 | Myocardial infarction | Myocardial infarction | 21 days | CYP2C19\*1/\*2 | | NR | NR | NR | NR | NR | NR |  |
|  |  | CYP2C19\*1/\*3 | Myocardial infarction | Myocardial infarction | 340 days | CYP2C19\*1/\*3 | | 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 | Repeat MI | Repeat MI | 1 year | CYP2C19\*2 GG | | 680 | N(%)  17 (2.5) | NR | 0.666,  CYP2C19\*2 GG vs \*2 A allele | NR | NR |  |
|  |  | CYP2C19\*2  A allele | Repeat MI | Repeat MI | 1 year | CYP2C19\*2  A allele | | 248 | N(%)  5(2) | NR |  | NR | NR |  |
|  |  | CYP2C19\*2 GG | Repeat MI | Repeat MI | 1 year | CYP2C19\*2 GG | | 565 | N(%)  15 (2.7) | NR | 0.48  CYP2C19\*17 CC vs T allele | NR | NR |  |
|  |  | CYP2C19\*2  A allele | Repeat MI | Repeat MI | 1 year | CYP2C19\*2  A allele | | 363 | N(%)  7 (1.9) | 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 | Non-fatal MI | Non-fatal MI | 15 months | RM vs EM | | 802 | OR=1.38 | 0.94-2.02 | NR | NR | No |  |
|  |  |  | Non-fatal MI | Non-fatal MI | 15 months | EM | | NR | 8.3% | 7.0-9.6 | NR | NR | No |  |
|  |  |  | Non-fatal MI | Non-fatal MI | 15 months | RM | | NR | 11.6% | 8.7-14.8 | 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 | MI | MI | Mean 243.8 days | Non-carrier | | 58 | 2(3.4) | NR | 0.76, Non-carrier vs \*2 carrier | No | No |  |
|  |  |  | MI | MI | Mean 243.8 days | \*2 carrier | | 42 | 1 (2.4) | NR |  | No | No |  |
| Malek 2008{Malek, 2008 167 /id}  18577829  Poland  NR | Clopidogrel and aspirin | CYP2C19 | CV Death or MI | NR | Within 12 months after PCI | | Group 1 | 0 | NR | NR | NR | NR | NR | NR |
|  |  |  |  |  |  | | Group 2 | 1 | NR | NR | NR | NR | NR | NR |
|  |  |  |  |  |  | | Group 3 | 0 | NR | NR | NR | NR | NR | NR |
|  |  |  |  |  |  | | Controls | 5 | NR | NR | NR | NR | NR | NR |
| Luo, 2011{Luo, 2011 18198 /id}22118006 China  NR | LD clopidogrel 300mg and MD 75mg/d and aspirin 300mg LD and MD 100mg/d | CYP2C19  \*1/\*1 | MI | MI | 6 months | | CYP2C19  \*1/\*1 | 67/936 | HR 2.88 | 1.56-8.74 | >0.05  comparing with the next row  chi-square test | NR | NR |  |
|  |  | CYP2C19  \*1/\*2 or \*2/\*2 |  |  |  | | CYP2C19  \*1/\*2 or \*2/\*2 | 115/802 |  |  |  |  |  |  |
| Luo, 2011{Luo, 2011 18198 /id}  22118006  China  NR | LD clopidogrel 300mg and MD 75mg/d and aspirin 300mg LD and MD 100mg/d | CYP2C19  \*1/\*1 | STEMI | STEMI | 6 months | | CYP2C19  \*1/\*1 | 8/936 | HR 3.85 | 1.33-10.05 | >0.05  <omparing with the next row  chi-square test | NR | NR |  |
|  |  | CYP2C19  \*1/\*2 or \*2/\*2 |  |  |  | | CYP2C19  \*1/\*2 or \*2/\*2 | 17/802 |  |  |  |  |  |  |
| Luo, 2011{Luo, 2011 18198 /id}  22118006  China  NR | LD clopidogrel 300mg and MD 75mg/d and aspirin 300mg LD and MD 100mg/d | CYP2C19  \*1/\*1 | NSTEMI | NSTEMI | 6 months | | CYP2C19  \*1/\*1 | 59/936 | HR 2.44 | 1.16-7.13 | <0.05  comparing with the next row  chi-square test | NR | NR |  |
|  |  | CYP2C19  \*1/\*2 or \*2/\*2 |  |  |  | | CYP2C19  \*1/\*2 or \*2/\*2 | 98/802 |  |  |  |  |  |  |
|  |  |  |  |  |  | |  |  |  |  |  |  |  |  |
| Delaney, 2012{Delaney, 2012 18204 /id}  22190063  USA  NR | clopidogrel | CYP2C19\*2 | MI | MI, | 2 years | | CYP2C19\*2 SNP rs4244285 | NR | HR=2.02 | 0.99-4.12 | 0.054 comparing with non carrier of \*2 | No | NR | NR |
|  | clopidogrel | CYP2C19\*17 | MI | MI, | 2 years | | CYP2C19\*17 SNP rs4244285 | NR | HR=0.63 | 0.31-1.29 | 0.207 comparing with non carrier of \*17 | No | NR | NR |
| Nishio, 2012{Nishio, 2012 18214 /id}  22785462  Japan  NR | Clopidogrel and aspirin | TaqMan | MI | NR | Any time during study | | Extensive metabolizer (n=60) | 1 | NR | NR | Across this and next two rows, 0.69 (chi-square test) | NR | NR | NONE |
|  |  |  |  |  |  | | Intermediate metabolizer (n=77) | 1 | NR | NR | NR | NR | NR | NONE |
|  |  |  |  |  |  | | Poor metabolizer (n=23) | 1 | NR | NR | NR | NR | NR | NONE |

AFIJI = Appraisal of risk Factors in young Ischemic patients Justifying aggressive Intervention registry; TRITON-TIMI 38 = Therapeutic Outcomes by Optimizing Platelet Inhibition with Prasugrel-Thrombolysis in Myocardial Infarction.