Appendix D. Appendix Tables for Key Question 1

**Appendix Table D1. Descriptive characteristics of studies reporting analytic validity information for CYP2C19 assays**

| **Author****Year****Country****PMID** | **Patient population** | **Assays evaluated (agonist)****[brand name, manufacturer]** | **Test timing** | **Study design for the assessment of analytic validity** | **Sample size** | **Results** |
| --- | --- | --- | --- | --- | --- | --- |
| Shuldiner2009USA19706858 | Patients undergoing nonemergent PCI; those with MI within 48 h were excluded. | TaqMan SNP assay(rs4244285, rs4986893, rs56337013, rs12248560, corresponding to \*2, \*3, \*5, \*17, respectively)[Applied Biosystems, Foster City, CA] | Not clear  | Repeat genotyping of samples | Not reported (for the subset of duplicate samples) | Genotype concordance rate >98% |
| Sibbing2009Germany19193675 | Patients undergoing PCI in a single center; patients included in the study were selected among those participating in a set of randomized trials of abciximab | TaqMan assay(rs4244285, corresponding to \*2)[ABI Prism Sequence Detector 7000, Applied Biosystems] | Blood was obtained after diagnostic angiography and before PCI; timing of genetic analysis was not clear | Repeat genotyping of samples (20% of all genotyped samples; selection NR) | 20% of 2485 = 497 | “All repeated experiments revealed identical results when compared with the initial genotype” |
| Sibbing2011Germany21527445 | Patients undergoing PCI in a single center; patients included in the study were selected among those participating in a prospective trial (blood for genotyping was available for 95% of the study participants) | TaqMan assay(rs4244285, corresponding to \*2)[ABI Prism Sequence Detector 7000, Applied Biosystems] | Blood was obtained after diagnostic angiography and before PCI; timing of genetic analysis was not clear | Repeat genotyping of samples (20% of all genotyped samples; selection NR) | 20% of 1524 = 305 | “Repeat genotyping revealed identical results”, the call rate was 100% |
| Trenk2011Germany21685174 | Patients undergoing elective coronary stent placement after pre-treatment with 600 mg of clopidogrel and aspirin (≥100 mg per day for at least 5 days) in a single center; patients were participants in the EXCELSIOR study | For CYP2C19 \*2 (rs4244285): PCR using the Drug Metabolism Genotyping Assay (Applied Biosystems, Frankfurt, Germany)†For CYP2C19 \*17 (rs12248560): TaqMan assay[Applied Biosystems, Foster City, CA] | Not clear | Repeat genotyping of samples | Not reported (for the subset of duplicate samples) | Concordance rate = 100% |
| Sibbing2010Germany20083681 | Patients with CAD undergoing PCI in a single center; patients included in the study were selected among those participating in a prospective study (blood for genotyping was available for 95% of the study participants) | TaqMan assay(rs12248560, corresponding to \*7)[ABI Prism Sequence Detector 7000, Applied Biosystems, Foster City, CA] | Blood was obtained directly before PCI; timing of genetic analysis was not clear | Repeat genotyping of samples (20% of all genotyped samples; selection NR) | 20% of 1524 = 305 | “Repeat genotyping revealed identical results” |
| Siller-Matula2012Austria22260716PAGASUS-PCI | Consecutive patients with coronary artery disease undergoing PCI with stent placement at least 2h post-loading with clopidogrel 600 mg; 99% received DES | TaqMan Drug Metabolism Genotyping Assay(rs12248560, corresponding to \*17)[ABI Prism Sequence Detector 7000, Applied Biosystems, Foster City, CA]Real-time allelic discrimination assay(rs4244285, corresponding to \*2)[ABI Prism Sequence Detector 7000, Applied Biosystems, Foster City, CA]Sequencing(did not report if both variants were evaluated)[BigDye Terminator v. 3.1 sequencing kit and 3130xl Genetic Analyzer, Applied Biosystems, Foster City, CA] | Blood samples were obtained in the catheterization laboratory directly post-PCI | Sequencing of randomly selected samples among those analyzed using allelic discrimination techniques | Not reported (for the subset of samples genotyped with both methods) | “No discrepancies were observed” |
| Namazi2012Iran22265638 | Patients undergoing elective PCI with DES placement in a single center; all patients received a loading dose of clopidogrel (600 mg) at least 24h pre-PCI and all patients had received aspiring for ≥ 7d pre-PCI | PCR-RFLP(rs4244285 and rs4986893, corresponding to \*2 and \*3, respectively)[additional information NR]Direct sequencing[additional information NR] | Samples were obtained at baseline, 2h post-loading, and 24h and 30d post-PCI | Sequencing of randomly selected samples among those analyzed with PCR RFLP | Not reported (for the subset of samples genotyped with both methods) | Sequencing analysis “confirmed” the results of PCR-RFLP analysis |
| Delaney2012USA22190063 | Patients started on clopidogrel post-MI and/or PCI; samples were obtained from participants in the BioVU DNA biobank linked to de-identified health records | TaqMan(rs4244285, rs4986893, rs28399504; rs12248560, corresponding to \*2, \*3, \*4, \*17, respectively)[Applied Biosystems, Foster City, CA] | Samples obtained “during routine clinical care and about to be discarded” | Repeat genotyping of samples | Not reported (for the subset of duplicate samples) | “Concordance >98% between duplicates”; call rates >95%; 1 sample excluded because of poor genotyping efficiency; \*3 and \*4 polymorphisms were excluded from subsequent analysis because they were very rare (\*4 observed only in 5 subjects; \*3 not polymorphic in the study population)  |
| Bhatt2012Multinational22450429CHARISMA | Patients with manifest atherothrombotic disease (coronary, cerebrovascular, or peripheral arterial) or with multiple risk factors for atherothrombotic disease randomized to clopidogrel+aspirin or placebo + aspirin; patients were participants in the genetics substudy of the CHARISMA randomized trial | PCR-RFLP(rs4244285, corresponding to \*2)[additional information NR]TaqMan allelic discrimination assay (rs4986893, corresponding to \*3)[additional information NR] | Samples obtained from the available population [additional information NR] | Repeat genotyping of randomly selected samples | 11% of 4862 patients with adequate DNA recovered = 535 samples (4924 patients provided blood) | “No errors were identified in the replicates”; “missingness was <2% for all SNPs” |
| Roberts2012Canada22464343RAPID GENE | Patients undergoing PCI for NSTE-ACS or stable angina; all patients were treated with 600 mg clopidogrel ≥24h pre-PCI | Point-of-care genotyping(rs4244285, corresponding to \*2)[Spartan RX CYP2C19 device, Spartan Biosciences, Ottawa, ON, Canada]Direct sequencing(rs4244285, corresponding to \*2)[ABI PRISM dye terminator method; Applied Biosystems, Foster City, CA] | Screening for \*2 variants was performed at the time of randomization; \*2 status was also investigated with the Spartan device and sequencing 1w post-PCI | Genotyping of samples using both methods | 187 patients with complete followup | 1 sample had discrepant results (\*2 carrier by Spartan RX but non-carrier by sequencing)Analytic sensitivity of Spartan RX using sequencing as the reference standard = 100% (95% CI 92.3%, 100%)Analytic specificity of Spartan RX using sequencing as the reference standard = 99.3% (95% CI 96.3%, 100%)Conclusive rate = 93.6% |
| Mega2011USA22088980ELEVATE-TIMI 56 | Patients with known cardiovascular disease on clopidogrel maintenance therapy | Pyrosequencing(\*2 allele)[additional information NR]Nucleic acid research-use only assay(\*2 allele)[Nanosphere Verigene 2C19/CBS assay, additional information NR] | At the time of study enrollment | Genotyping of samples using both methods | 333 patients successfully genotyped (of 335 enrolled) | “Results were confirmed for CYP2C19\*2 status” |

†Information on the genotyping assay was extracted from Trenk et al. 2008 (PMID = 18482659) **Abbreviations:** h = hour; MI = myocardial infarction; PCI = percutaneous coronary intervention; PMID = PubMed identification number.