

Genomics-Guided Clopidogrel Therapy for In-Stent Restenosis: Redefining Precision Medicine in Interventional Cardiology

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ABSTRACT: Coronary artery disease (CAD) remains a leading contributor to global morbidity and mortality, driven by the chronic progression of atherosclerosis and its acute thrombotic complications. Percutaneous coronary intervention (PCI), particularly with drug-eluting stent placement, has revolutionized management yet is still challenged by adverse events such as in-stent restenosis and stent thrombosis. Clopidogrel, a cornerstone oral antiplatelet agent in dual antiplatelet therapy, exhibits substantial interindividual variability in efficacy largely attributable to genetic polymorphisms most notably in the CYP2C19 gene, which governs hepatic prodrug activation. Pharmacogenomics has identified key CYP2C19 LOF alleles (*2, *3 and *17) that predict reduced drug activity and heightened risk for major adverse cardiovascular events (MACE) such as In-stent restenosis following PCI. This review synthesizes current evidence from clinical trials and meta-analyses supporting genotype-guided antiplatelet strategies, explores real-world implementation, and maps the translational pathway from genomic discovery to routine practice. We highlight the barriers and facilitators to adoption including infrastructure, reimbursement, and education as well as future directions involving multi-gene panels, artificial intelligence, and expanded clinical integration. Emphasis is placed on the necessity of individualized care to optimize outcomes in interventional cardiology, with genomics-guided clopidogrel therapy exemplifying the shift from a “one size fits all” approach to precision-guided cardiovascular medicine.

KEYWORDS: Coronary artery disease, atherosclerosis, clopidogrel, pharmacogenomics, CYP2C19, percutaneous coronary intervention, genotype-guided therapy, antiplatelet therapy, precision medicine.

INTRODUCTION

Coronary artery disease (CAD) is a leading cause of morbidity and mortality

worldwide. It develops when the coronary arteries, which supply oxygen-rich blood, nutrients to the heart muscle, become narrowed or blocked due to the

accumulation of atherosclerotic plaque. This plaque is composed of cholesterol, fatty substances, and other cellular debris that build up on the inner walls of the arteries—a process known as atherosclerosis. It does not cause in a sudden manner. The plaque or debris get deposited in the coronary arteries and reduce the supply of blood to the heart muscles. The development of atherosclerosis involves endothelial dysfunction, lipid accumulation, chronic inflammation, and plaque formation, which can eventually rupture and trigger acute coronary syndromes through thrombosis (1).

percutaneous coronary intervention (PCI) it is the first line technique performed for the coronary artery disease. It is a minimally invasive, non-surgical technique employed to relieve the narrowing or obstruction of coronary arteries. By mechanically restoring coronary blood flow, PCI aims to alleviate ischemic symptoms such as angina and reduce the incidence of myocardial infarction, thereby improving clinical outcomes in affected patients. Stent Placement is a technique in PCI in which a mesh wire tube called a stent (often drug-eluting) is placed at the site to keep the artery open and reduce the risk of future narrowing. Compared with bare-metal stents (BMS), drug-eluting stents (DES)-

which incorporate a metallic stent platform with a polymer that releases an antiproliferative drug. Thus DES substantially enhance the efficacy of percutaneous coronary intervention by suppressing neointimal hyperplasia and significantly reducing the incidence of in-stent restenosis (2).

Clopidogrel is an oral antiplatelet agent widely used to reduce the risk of myocardial infarction and stroke particularly in patients with coronary artery disease undergoing percutaneous coronary intervention. It is a prodrug which requires hepatic biotransformation via CYP450 enzymes, including CYP2C19 to generate its active metabolite. This metabolite irreversibly inhibits the platelet P2Y₁₂ ADP receptor, thereby blocking ADP-mediated platelet activation and aggregation for the lifespan of the platelet. The addition of clopidogrel to aspirin-based dual antiplatelet therapy has been shown to reduce the risk of myocardial infarction, stroke, and stent thrombosis in both acute and chronic coronary syndromes. However, interindividual variability in clopidogrel response—largely attributable to genetic polymorphisms affecting drug metabolism remains a significant clinical challenge (3).

Pharmacogenomics, a field at the forefront of precision medicine, recognizes that a

"one size fits all" approach is often inadequate for optimal patient care. By elucidating the genetic factors that influence drug response, pharmacogenomic studies enable more accurate and individualized treatment strategies, thereby improving therapeutic efficacy and safety across diverse patient populations. Genetic variation in the *CYP2C19* gene, specifically the *2 and *3 loss-of-function alleles, result in reduced or absence of enzyme activity, leading to impaired conversion of clopidogrel to its active metabolite. Individuals carrying these alleles exhibit significantly lower levels of the active drug, higher on-treatment platelet reactivity, and consequently an increased risk of major adverse cardiovascular events, particularly following percutaneous coronary intervention (4).

RATIONALE FOR GENOMICS-GUIDED THERAPY

Genetics plays a major role in the drug metabolism in humans. Genetic variability is a key determinant of individual response to antiplatelet with significant clinical implications for patients undergoing percutaneous coronary intervention (PCI). The most prominent genetic contributors are polymorphisms in the *CYP2C19* gene, which encodes the primary enzyme responsible for converting clopidogrel into its active metabolite. Individuals carrying

the *CYP2C19* *2 or *3 loss-of-function alleles exhibit markedly reduced or absent enzyme activity, resulting in lower levels of the active drug, diminished platelet inhibition, and higher on-treatment platelet reactivity. This impaired response increases the risk of major adverse cardiovascular events, including in-stent restenosis and stent thrombosis, despite standard therapy which leads to the coronary artery bypass graft surgery (5).

Beyond *CYP2C19*, additional genetic factors such as variants in *ABCB1* and *POR*—can further modulate clopidogrel absorption and metabolism, contributing to a polygenic effect on drug response. However, the complexity of platelet biology and interindividual differences in drug metabolism mean that a uniform, "one size fits all" approach to antiplatelet therapy may leave a significant subset of patients insufficiently protected against thrombotic complications, underscoring the need for more personalized treatment strategies.

CASE ILLUSTRATION: IN-STENT RESTENOSIS IN CLINICAL PRACTICE

CASE PRESENTATION:

A 67-year-old male with a history of type 2 diabetes mellitus, systemic hypertension, and dyslipidemia-managed for seven years-

presented with complaints of palpitations, generalized tiredness, and tremor. Notably, he denied angina, dyspnoea, diaphoresis, or syncope. He had no history of smoking or alcohol consumption. Five years prior, he had undergone percutaneous transluminal coronary angioplasty (PTCA) with stenting of the right coronary artery (RCA) for chronic stable angina.

On admission, his vital signs were stable (pulse 88/min, SpO₂ 96%, RR 19/min, BP 130/90 mmHg, temperature 97.5°F), and systemic examination was unremarkable. Coronary angiography revealed double vessel disease (DVD) with preserved left ventricular ejection fraction (LVEF 63%). Significant stenoses were noted in the mid left anterior descending (LAD) artery (90–95%), mid left circumflex (LCX) artery (90–95%), and obtuse marginal 1 (OM1, 70%). The previously stented RCA was patent, but there was 30–40% in-stent restenosis (ISR) at the mid RCA.

Given the angiographic findings and history, PCI was performed via a right radial approach, and a drug-eluting stent (DES) was deployed. The patient was prescribed dual antiplatelet therapy (clopidogrel and aspirin), atorvastatin, vitamins B & E, Nicoumalone (for one year), and pantoprazole. He remained clinically stable for four years post-PTCA.

After four years, the patient developed recurrent symptoms of generalized tiredness and palpitations. Subsequent evaluation with ECG and echocardiography revealed a myocardial infarction (MI). Repeat coronary angiography confirmed ISR at the mid RCA and progression of coronary disease. The patient underwent coronary artery bypass grafting (CABG) with four grafts: LIMA to LAD, RSVG to OM1, OM2, and distal RCA. Postoperatively, his regimen included atorvastatin, aspirin, ticagrelor, vitamins B & E, and pantoprazole (6,7).

DISCUSSION AND LEARNING POINTS:

Although drug-eluting stents have significantly reduced ISR rates compared to bare-metal stents, restenosis remains a clinical challenge, particularly in patients with multiple comorbidities.

The role of pharmacogenomic testing plays a major role in above case study. While genetic testing was not performed in this case, it raises important considerations regarding clopidogrel resistance. CYP2C19 loss-of-function alleles are common and can lead to reduced clopidogrel efficacy, potentially contributing to ISR. This case underscores the potential value of pharmacogenomic testing in identifying patients who may benefit from alternative

antiplatelet agents, thus personalizing therapy and potentially improving outcomes (8).

GENETIC DETERMINANTS OF CLOPIDOGREL RESPONSE

Human body consists of several enzymes which plays a major role in the metabolism of several substances. One of the key Enzyme in drug metabolism is cytochrome P450. Based on the combinations of the most common CYP2C19 genetic variants (*1, *2, *3, and *17), individuals can be categorized into distinct metabolizer phenotypes that reflect a gene-dose effect on clopidogrel metabolism and clinical response. Those who carry two LOF alleles such as, (*2/2, *3/3, or *2/*3) are classified as poor metabolisers and exhibit markedly reduced enzymatic activity, leading to insufficient activation of clopidogrel. Individuals with one functional allele and one LOF allele (e.g., *1/*2, *1/*3), as well as those combinations like *2/*17 or *3/*17, are considered intermediate metabolizers with partial reduction in drug activation. The extensive metabolizer or wild type phenotype (*1/*1) represents normal enzymatic function and expected therapeutic response. In contrast, individuals with one or two gain-of-function *17 alleles (*1/*17 or *17/*17) are classified as ultra-rapid metabolizers, characterized by increased enzyme activity

and potentially heightened platelet inhibition. In Indian population the genetic determinants of clopidogrel response are shaped variants in the CYP2C19 gene, especially the *2, *3, and *17 alleles. The *CYP2C19**2 allele is notably prevalent with studies reporting frequencies ranging from about 30 to 46% across various regions of India making it one of the most common loss of function (LOF) alleles in the population. The *17 allele, associated with increased enzyme activity (gain-of-function), shows a prevalence of around 10–19%, varying by region and ethnic group within India (9).

KEY GENETIC VARIANTS:

The CYP2C19 gene is the principal genetic determinant influencing clopidogrel metabolism and response. CYP2C19 encodes the hepatic enzyme responsible for converting clopidogrel into its active metabolite. More than 50 single nucleotide polymorphisms (SNPs) in CYP2C19 have been identified but the most clinically significant are LOF alleles, especially *CYP2C19**2 (c.681G>A, splicing defect) and *CYP2C19**3 (c.636G>A, premature stop codon). These alleles result in non-functional enzymes and impaired clopidogrel activation (10).

Several large meta-analyses have examined the impact of CYP2C19 loss-of-function

alleles on clinical outcomes in patients treated with clopidogrel after PCI, with some studies reporting a significant association while others have found more modest or inconsistent effects. In a landmark meta-analysis by Mega et al., which included 9,685 patients (over 91% of whom underwent PCI and more than half with acute coronary syndromes), carriers of one or two reduced-function CYP2C19 alleles experienced significantly higher rates of major adverse cardiovascular events (MACE), including cardiovascular death, myocardial infarction, or stroke, compared to non-carriers. Specifically, the hazard ratio (HR) for MACE was 1.55 (95% CI, 1.11–2.17; $p=0.01$) for individuals with one reduced-function allele and 1.76 (95% CI, 1.24–2.50; $p=0.002$) for those with two alleles. The risk of stent thrombosis was even more pronounced, with HRs of 2.67 (95% CI, 1.69–4.22; $p<0.0001$) for one allele and 3.97 (95% CI, 1.75–9.02; $p=0.001$) for two alleles.

Beyond CYP2C19, additional genes such as ABCB1 (encoding P-glycoprotein, involved in clopidogrel absorption) and other cytochrome P450 enzymes (e.g., CYP3A4, CYP2B6) may further modulate clopidogrel response, though their impact is less pronounced than CYP2C19 (11).

CLINICAL IMPACT:

Carriers of CYP2C19 LOF alleles exhibit reduced formation of clopidogrel's active metabolite, leading to diminished platelet inhibition and higher on-treatment platelet reactivity. This pharmacogenetic effect translates into a higher risk of adverse cardiovascular events, including stent thrombosis and in-stent restenosis (ISR), particularly after percutaneous coronary intervention (PCI). Meta-analyses and large cohort studies have consistently shown that patients with one or more CYP2C19 LOF alleles have significantly increased rates of major adverse cardiovascular events compared to non-carriers (12).

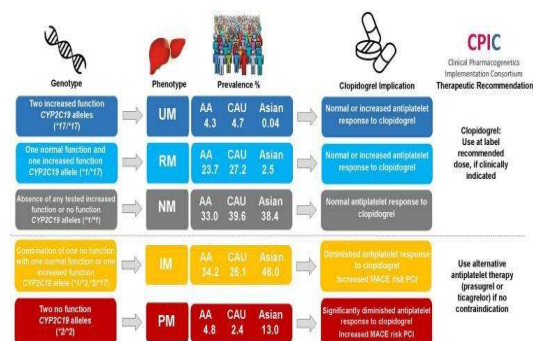
EVIDENCE FOR GENOTYPE-GUIDED ANTIPLATELET THERAPY

MAJOR TRAILS AND META-ANALYSES:

Several landmark studies have evaluated the utility of genotype guided antiplatelet therapy following percutaneous coronary intervention. Vibhu parcha et al, conducted TAILOR-PCI trial that was a large, multi center, randomized study designed to determine whether CYP2C19 genotype-guided selection of P2Y12 inhibitors could reduce ischemic events compared to conventional therapy. In this trial, over 5,000 patients undergoing PCI were assigned to a genotype-guided strategy

(where carriers of CYP2C19 loss-of-function alleles received ticagrelor, and non-carriers received clopidogrel) or to standard clopidogrel therapy. Although the primary composite endpoint (cardiovascular death, myocardial infarction, stroke, stent thrombosis, and severe recurrent ischemia) occurred less frequently in the genotype-guided group (4.0% vs 5.9%), this difference did not reach statistical significance for the prespecified threshold (HR 0.66; P=0.06) (13).

A substantial body of evidence from meta-analyses of randomized controlled trials and observational studies has explored the relationship between CYP2C19 genotype and clinical outcomes in patients treated with clopidogrel. These analyses consistently show that carriers of CYP2C19 loss-of-function (LOF) alleles are at a significantly higher risk of stent thrombosis compared to non-carriers, underscoring the critical role of CYP2C19-mediated metabolism in effective P2Y₁₂ receptor inhibition. The increased risk is primarily driven by higher incidences of cardiovascular death, myocardial infarction, and stroke in these high-risk groups, whereas the association may be less pronounced in stable coronary artery disease populations.



REAL WORLD IMPLEMENTATION:

Real world registry data have demonstrated the feasibility and accuracy of implementing the genomic testing in clinical setting. The studies shown that non laboratory trained staff can successfully perform rapid genotyping with high concordance to standard laboratory methods, enabling timely decision making for antiplatelet selection. For example, the TAILOR-PCI trial incorporated rapid, buccal-based CYP2C19 genotyping, achieving over 99% concordance with reference sequencing and demonstrating that such approaches can be integrated into routine practice (14).

Despite these advances, the adoption of genotype-guided antiplatelet therapy remains variable in clinical practice, influenced by factors such as test availability, cost, and clinician familiarity. As point-of-care technologies and clinical guidelines continue to evolve, broader implementation of personalized antiplatelet

strategies is anticipated, particularly for high-risk populations.

TRANSLATIONAL PATHWAY: FROM DISCOVERY TO PRACTICE

The translational pathway is a journey of genetic discovery into clinical practice. This pathway ensures that advances in genetic research are effectively translated into improved patient care in interventional cardiology. The translational pathway involves a series of coordinated steps.

Genetic Discovery: Identification of CYP2C19 and other relevant gene variants affecting clopidogrel metabolism through genomic studies.

Functional Characterization: Laboratory and clinical studies to determine the impact of these genetic variants on enzyme activity and drug response.

Clinical Association: Observational studies and clinical trials linking genetic variants to outcomes such as stent thrombosis and in-stent restenosis (ISR).

Development of Genotyping Methods: Creation of reliable, rapid, and cost-effective tests for CYP2C19 and other relevant variants.

Clinical Trials of Genotype-Guided Therapy: Randomized controlled trials (e.g., TAILOR-PCI, POPular Genetics)

evaluating the efficacy and safety of genotype-guided antiplatelet therapy.

Regulatory Approval and Guidelines: Inclusion of pharmacogenomic testing recommendations in clinical guidelines and regulatory frameworks.

Implementation in Clinical Practice: Integration of genetic testing into routine care, including point-of-care genotyping and decision-support tools. NABH accreditations can make genetic testing as mandatory in hospitals.

Education and Training: Programs for clinicians and other health care professionals to enhance understanding of the benefits and limitations of genomics-guided therapy.

Future Directions: Expansion to multi-gene panels, rapid testing technologies, and personalized therapeutic algorithms. AI related genomic data and sequencing of genetic data play a vital role in precision treatment.

Finally, continuous monitoring and feedback through real-world registries enable refinement of protocols and assessment of long-term outcomes, while future directions focus on expanding pharmacogenomic panels and enhancing rapid testing capabilities to further personalize antiplatelet therapy. This

translational pathway underscores the systematic progression from genetic discovery to precision-guided clinical care, improving therapeutic efficacy and patient safety in cardiovascular medicine (15).

BARRIERS, FACILITATORS AND FUTURE FRONTIER

Even though strong evidence supporting genotype-guided antiplatelet therapy, there are several barriers hinder its widespread adoption in clinical practice.

1. **Limited infrastructure:** Currently there are limited genomic testing labs are available around India. Many laboratories lack in house genotyping facilities leading to delays in test turnaround and increased logistical complexity.
2. **Integration with Clinical Workflows:** The absence of automated clinical decision support within electronic health records (EHRs) can reduce the sustainability of genotype-guided protocols. Without seamless integration, clinicians may be less likely to order tests or use results in prescribing decisions.
3. **Clinician Awareness and Education:** There is a need for ongoing education to ensure clinicians understand how to interpret genetic test results and apply them to antiplatelet

therapy selection. Gaps in pharmacogenomics knowledge can lead to underutilization of available testing.

4. **Reimbursement and Cost Concerns:** The expense of genetic testing and the lack of clear insurance coverage can make it difficult for many patients to access these tests, especially in hospitals or clinics with limited financial resources.
5. **Patient related factors:** Patient acceptance, understanding and consent for genetic testing may also pose challenges especially in diverse populations with varying health literacy.

Facilitators and Implementations:

Several factors have been shown to promote the successful adoption of genotype-guided antiplatelet therapy. The availability of rapid, on-site genetic testing services with turnaround times as short as one day enables timely clinical decision-making. Embedding pharmacogenomic recommendations within electronic health records (EHRs) and providing point-of-care guidance assist clinicians in interpreting genetic results and translating them into actionable prescribing decisions. Collaboration among multidisciplinary teams—including cardiologists, pharmacists, genetic counsellors, and

nurses—fosters better adherence to protocols and enhances patient education. Institutional support through ongoing education programs and formal endorsement increases clinician confidence and encourages the uptake of pharmacogenomic strategies. Additionally, studies demonstrating the cost-effectiveness of genotype-guided therapy, particularly by preventing adverse events and optimizing drug selection, further support its implementation. Finally, actively involving patients in shared decision-making and clearly communicating the benefits and implications of genetic testing improve patient acceptance and adherence to personalized treatment plans (16).

Ongoing Research and Future Prospects: The fields of pharmacogenomics is an emerging field all over the specialized medicine especially in oncology and cardiology with several promising directions. Technological advancements are making genotyping platforms faster, more affordable, and easier to use, with the development of point-of-care assays that can provide results during the initial patient visit. Applications of pharmacogenomics are also expanding beyond antiplatelet therapy to include a

wide range of cardiovascular drugs, such as anticoagulants, statins, and antihypertensives, with the goal of achieving broader personalization of therapy. Large-scale clinical trials and real-world registry studies, including TAILOR-PCI and POPular Genetics, are underway to evaluate the clinical impact, cost-effectiveness, and best strategies for implementing genotype-guided therapy across diverse populations. As evidence continues to build, professional societies are increasingly integrating pharmacogenomic recommendations into clinical guidelines, which is expected to promote wider adoption. Additionally, research is moving beyond single-gene testing to multi-gene panels and polygenic risk scores, offering the potential for more comprehensive risk assessment and individualized treatment guidance. Artificial intelligence and advanced decision-support tools are being developed to help interpret complex genetic information and combine it with clinical data, providing personalized recommendations at the point of care. Finally, there is a growing focus on global and community-based implementation, with efforts to adapt pharmacogenomic testing for use in community hospitals and low-resource

settings, thereby addressing disparities in access and improving outcomes for a broader range of patients (17).

CONCLUSION

Genomics-guided clopidogrel therapy represents a transformative step toward personalized medicine in interventional cardiology. By identifying patients with CYP2C19 loss-of-function alleles, clinicians can tailor antiplatelet therapy more precisely, reducing the risk of adverse cardiovascular events such as In-stent thrombosis and improving overall treatment outcomes. This pharmacogenomic approach shifts the paradigm from a one-size-fits-all strategy to personalized care, ensuring that each patient receives the most effective and safest therapy based on their genetic profile. Apart from genomic testing, TDM also plays pilot role in personalised medicine. The emerging field of AI needs to be integrated into pharmacogenomics which will be useful in manipulating the results more precisely and cost efficiently.

As genetic testing becomes more accessible and integrated into clinical workflows, the implementation of genotype-guided treatment is poised to enhance decision-making in the

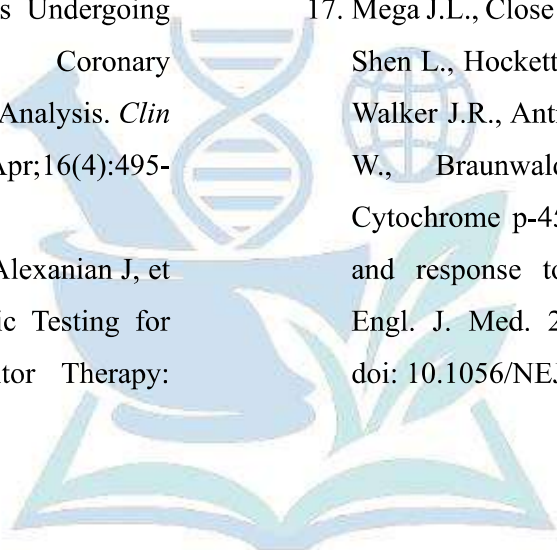
catheterization laboratory and beyond. Continued efforts in clinician education, real-world data collection, and policy development will be critical to overcoming current implementation challenges. Ultimately, embracing precision-guided strategies reinforces the goal of modern cardiology: delivering the right treatment to the right patient at the right time.

REFERENCES

1. Brown SA, Pereira N. Pharmacogenomic Impact of CYP2C19 Variation on Clopidogrel Therapy in Precision Cardiovascular Medicine. *J Pers Med*. 2018;8(1):8.
2. Pereira NL, Farkouh ME, So D, et al. Clopidogrel Pharmacogenetics: State of the Art Review and the TAILOR-PCI Study. *Circ Cardiovasc Interv*. 2018 Feb 1;11(2):e005682.
3. Holmes DR Jr, Dehmer GJ, Kaul S, Leifer D, O’Gara PT, Stein CM. Clopidogrel Pharmacogenetics. *Circ Cardiovasc Interv*. 2019 Nov;12(11):e007811.
4. Ferrero V, Pereira NL, Spertus JA, Cappola TP. Implementing CYP2C19-guided clopidogrel therapy: a scoping

- review. *Pharmacogenomics J.* 2025 Feb;25(1):7.
5. Lee CR, Luzum JA, Sangkuhl K, et al. Clinical Pharmacogenetics Implementation Consortium Guideline for CYP2C19 Genotype and Clopidogrel Therapy: 2022 Update. *Clin Pharmacol Ther.* 2022 Nov;112(5):959-967.
 6. Johnson JA, Cavallari LH. Clinical Pharmacogenetics Implementation Consortium Guidelines for CYP2C19 Genotype and Clopidogrel Therapy: 2022 Update. *Clin Pharmacol Ther.* 2022 Nov;112(5):959-967.
 7. Jiang Y, Jiang C, Wang Q, Wang G, Zhao Y. CYP2C19 variability and clinical outcomes of clopidogrel pharmacotherapy: Updated meta-analyses and perspectives. *Front Pharmacol.* 2025 Jun 19;
 8. Mega JL, Close SL, Wiviott SD, et al. Pharmacogenomics of
 12. Li Q, Fan X, Zhang L, Wang H. Effect of CYP2C19 polymorphism on ischemic outcomes during oral P2Y12 inhibitor treatment: A meta-analysis. *Clin Cardiol.* 2021;44(7):931-939.
 13. Kang J, Kang J-W, Ahn J-M, et al. Clinical Impact of CYP2C19 Genotype on Clopidogrel-Based Antiplatelet Therapy in East Asian
 - clopidogrel: Evidence and perspectives. *Pharmacol Ther.* 2011 Oct;130(3):267-77.
 9. Bagai J, Chewed A, Bavry AA, Holmes DR Jr. CYP2C19 Genetic Testing for Oral P2Y12 Inhibitor Therapy. *Circulation.* 2024 Jan 16.
 10. Klein MD, Williams AK, Lee CR, Stouffer GA. Clinical Utility of CYP2C19 Genotyping to Guide Antiplatelet Therapy in Patients With an Acute Coronary Syndrome or Undergoing Percutaneous Coronary Intervention. *Arterioscler Thromb Vasc Biol.* 2019 Feb 14;39(4):560-567.
 11. Klein MD, Williams AK, Lee CR, Stouffer GA. Clinical Utility of CYP2C19 Genotype-Guided Antiplatelet Therapy in Patients Following Percutaneous Coronary Intervention. *Clin Pharmacol Ther.* 2020 Jul;108(1):208-216.
 - Patients After Drug-Eluting Stent Implantation: A Korean Nationwide Cohort Study. *JACC Cardiovasc Interv.* 2023 Apr 10;16(7):647-657.
 14. Rodrigues-Soares F, Nota A, Silva L, et al. From genes to drugs: CYP2C19 and pharmacogenetics in clinical practice. *Front Pharmacol.* 2024 Feb 14;15:1326776.

15. Sangkuhl K, Swen JJ, Wit FWNM, et al. CYP2C19 Genotype-Guided Antiplatelet Therapy and Clinical Outcomes in Patients Undergoing Percutaneous Coronary Intervention: A Meta-Analysis. *Clin Transl Sci*. 2025; Apr;16(4):495-507.
16. Bagai J, Lukas MA, Alexanian J, et al. CYP2C19 Genetic Testing for Oral P2Y₁₂ Inhibitor Therapy: Current Guidance and Clinical Implications. *Circulation*. 2024 Aug 6;150(6):500-510.
17. Mega J.L., Close S.L., Wiviott S.D., Shen L., Hockett R.D., Brandt J.T., Walker J.R., Antman E.M., Macias W., Braunwald E., et al. Cytochrome p-450 polymorphisms and response to clopidogrel. *N. Engl. J. Med*. 2009;360:354–362. doi: 10.1056/NEJMoa0809171.



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