

About 4% To 30% Patients Do Not Respond Adequately To Clopidogrel

This results in higher risk for myocardial infarction, stent thrombosis, or stroke due to insufficient clopidogrel-induced platelet inhibition.

Clopidogrel, a prodrug, is primarily metabolized by CYP2C19 enzyme to an active form.

This gene is responsible for metabolism of many drugs including clopidogrel, voriconazole and proton-pump inhibitors. Variations in this gene are associated with poor response to clopidogrel and increased cardiovascular morbidity and mortality.



Genetic variants of CYP2C19 associated with altered CYP2C19 activity have been identified and are relatively common in most populations.



Individuals with loss of function (LOF) variants of CYP2C19, CYP2C19*2 or CYP2C19*3 (~20 to 60% of the population carry at least one LOF copy), are at increased risk for thrombotic cardiovascular events due to decreased drug efficacy. In contrast, the fast (ultra-rapid) metabolizing variant CYP2C19*17 (in ~20% to 30% of the population) is associated with increased drug activation and increased risk of bleeding.



The USFDA has recommended to use caution in poor metabolizers before prescribing clopidogrel. Use of alternative anti-platelet therapy or alternative dosing strategy of clopidogrel in CYP2C19 poor metabolizers has also been recommended.

AyuGen Biosciences Pvt Ltd performs molecular genetic testing to detect presence of common genetic changes (or variations) in cytochrome P450 2C19 (CYP2C19) gene.

Indications for CYP2C19 polymorphism testing

Testing is recommended in acute coronary syndrome patients who are being considered for clopidogrel based antiplatelet therapy or who are already on this medication.

Sample requirements and laboratory testing for CYP2C19 genotypes.

The preferred sample is 3ml blood in EDTA tube
Test Result & Turn around time - 5 days

PATIENT CLASSIFICATION BASED ON CYP2C19 GENOTYPING TEST

| Patient Classification | CYP2C19 Genotypes | Clinical Implication |
|--------------------------|----------------------|--|
| Ultra-rapid metabolizer | *1/*17, *17/*17 | Normal Clopidogrel dosing |
| Extensive metabolizer | *1/*1 | |
| Intermediate metabolizer | *1/*2, *1/*3, *2/*17 | Alternative anti-platelet therapy or alternative dosing strategy |
| Poor metabolizer | *2/*2, *2/*3, *3/*3 | |

Reference- SA Scott et al Clinical Pharmacogenetics Implementation Consortium Guidelines for CYP2C19 Genotype and Clopidogrel Therapy: 2013 Update Clinical pharmacology & Therapeutics | VOLUME 94 NUMBER 3 | SEPTEMBER 2013

Please contact on 020- 2553 8990 or 0942311 8990 for sample collection or further information.

AyuGen Biosciences Pvt. Ltd., 562/1 Shivajinagar, Pune 411005, Maharashtra, India

References:

1. Sibbing D, Koch W, Gebhard D, Schuster T, Braun S, Stegherr J, Morath T, Schömig A, von Beckerath N, Kastrati A. Cytochrome 2C19*17 Allelic Variant, Platelet Aggregation, Bleeding Events, and Stent Thrombosis in Clopidogrel-Treated Patients With Coronary Stent Placement. *Circulation*. 2010 Feb;121(4):512-8.
2. Shuldiner AR, O'Connell JR, Bliden KP, Gandhi A, Ryan K, Horenstein RB, Damcott CM, Pakyz R, Tantry US, Gibson Q, Pollin TI, Post W, Parsa A, Mitchell BD, Faraday N, Herzog W, Gurbel PA. Association of cytochrome P450 2C19 genotype with the antiplatelet effect and clinical efficacy of clopidogrel therapy. *JAMA* 2009 Aug 26;302(8):849-57.
3. Bonello L, Palot-Bonello N, Armero S, Camoin-Jau L, Paganelli F. Impact of loading dose adjustment on platelet reactivity in homozygotes of the 2C19 2 loss of function polymorphism. *Int J Cardiol*. 2009 Aug 25.
4. Sibbing D, Stegherr J, Latz W, Koch W, Mehilli J, Dörrler K, Morath T, Schömig A, Kastrati A, von Beckerath N. Cytochrome P450 2C19 loss-of-function polymorphism and stent thrombosis following percutaneous coronary intervention. *Eur Heart J*. 2009 Apr;30(8):916-22.
5. Mega JL, Close SL, Wiviott SD, Shen L, Hockett RD, Brandt JT, Walker JR, Antman EM, Macias W, Braunwald E, Sabatine MS. Cytochrome p-450 polymorphisms and response to clopidogrel. *N Engl J Med*. 2009 Jan 22;360(4):354-62.
6. Simon T, Verstuyft C, Mary-Krause M, Quteineh L, Drouot E, Méneveau N, Steg PG, Ferrières J, Danchin N, Becquemont L; French Registry of Acute ST-Elevation and Non-ST-Elevation Myocardial Infarction (FAST-MI) Investigators. Genetic determinants of response to clopidogrel and cardiovascular events. *N Engl J Med*. 2009 Jan 22;360(4):363-75.