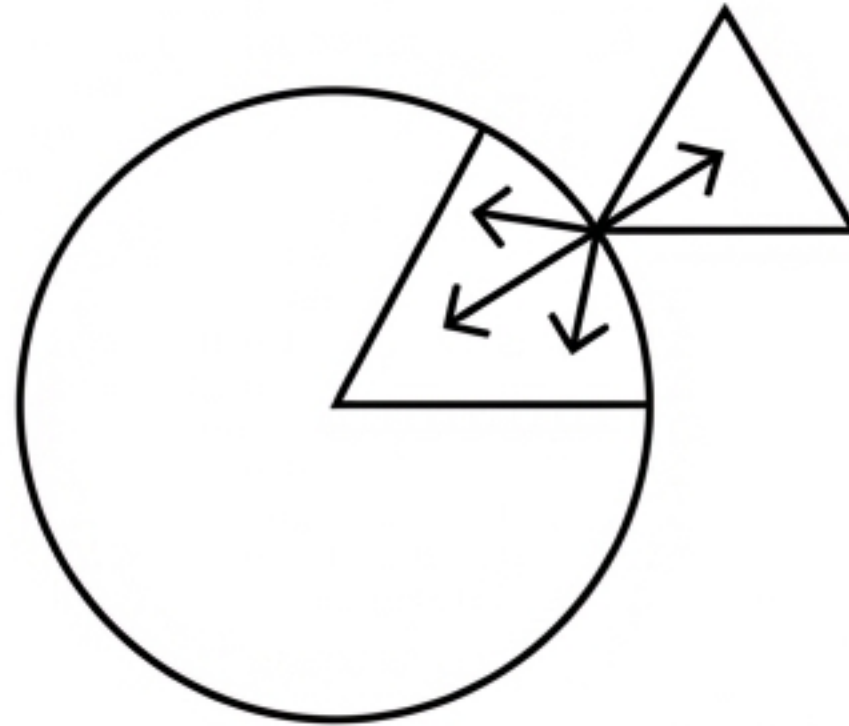


CYP2C19 PHARMACOGENETICS

A Clinical Field Guide



Interpreting Clopidogrel (Plavix) Resistance and Dosing Strategies.

Designed for rapid reference in clinical settings. This guide translates genetic markers into actionable prescribing decisions.

The Clinical Indication

Clopidogrel (Plavix) is a prodrug, meaning it requires liver metabolism to become active. Efficacy varies significantly based on the patient's genetic profile.

Primary Indication: To verify efficacy when a patient is prescribed Clopidogrel monotherapy.

Visual Translation

اصلی ترین indication چک کردن:
اگر بیمار فقط روی پلاویگی باشد

Translated Insight: Main indication for checking: if patient is only on Plavix.

How to Write the Request

Lab Requisition Form

<input type="checkbox"/> _____	<input type="checkbox"/> _____	<input type="checkbox"/> _____
<input type="checkbox"/> _____	<input type="checkbox"/> _____	<input type="checkbox"/> _____
<input type="checkbox"/> _____	<input type="checkbox"/> _____	<input type="checkbox"/> _____
<input type="checkbox"/> _____	<input type="checkbox"/> _____	<input type="checkbox"/> _____
<input type="checkbox"/> _____	<input type="checkbox"/> _____	<input type="checkbox"/> _____
<i>Please check CYP2C19 resistance mutations to clopidogrel</i>		
<input type="checkbox"/> _____	<input type="checkbox"/> _____	<input type="checkbox"/> _____
<input type="checkbox"/> _____	<input type="checkbox"/> _____	<input type="checkbox"/> _____
<input type="checkbox"/> _____	<input type="checkbox"/> _____	<input type="checkbox"/> _____
<input type="checkbox"/> _____	<input type="checkbox"/> _____	<input type="checkbox"/> _____
<input type="checkbox"/> _____	<input type="checkbox"/> _____	<input type="checkbox"/> _____

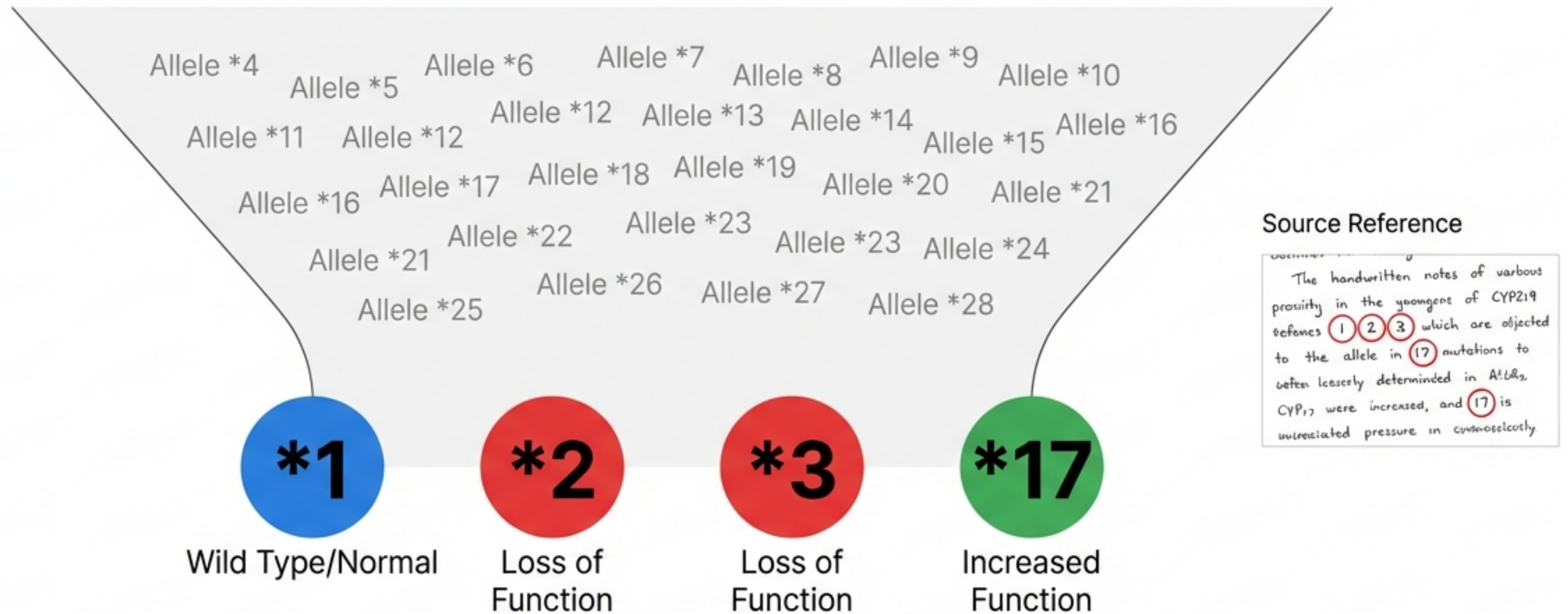
How to write a request for laboratory:

Please check CYP2C19 resistance mutations to clopidogrel

Directive: Use specific language to avoid administrative ambiguity.

The Genetic Scope: CYP2C19

From 28 possibilities to the 4 that matter.

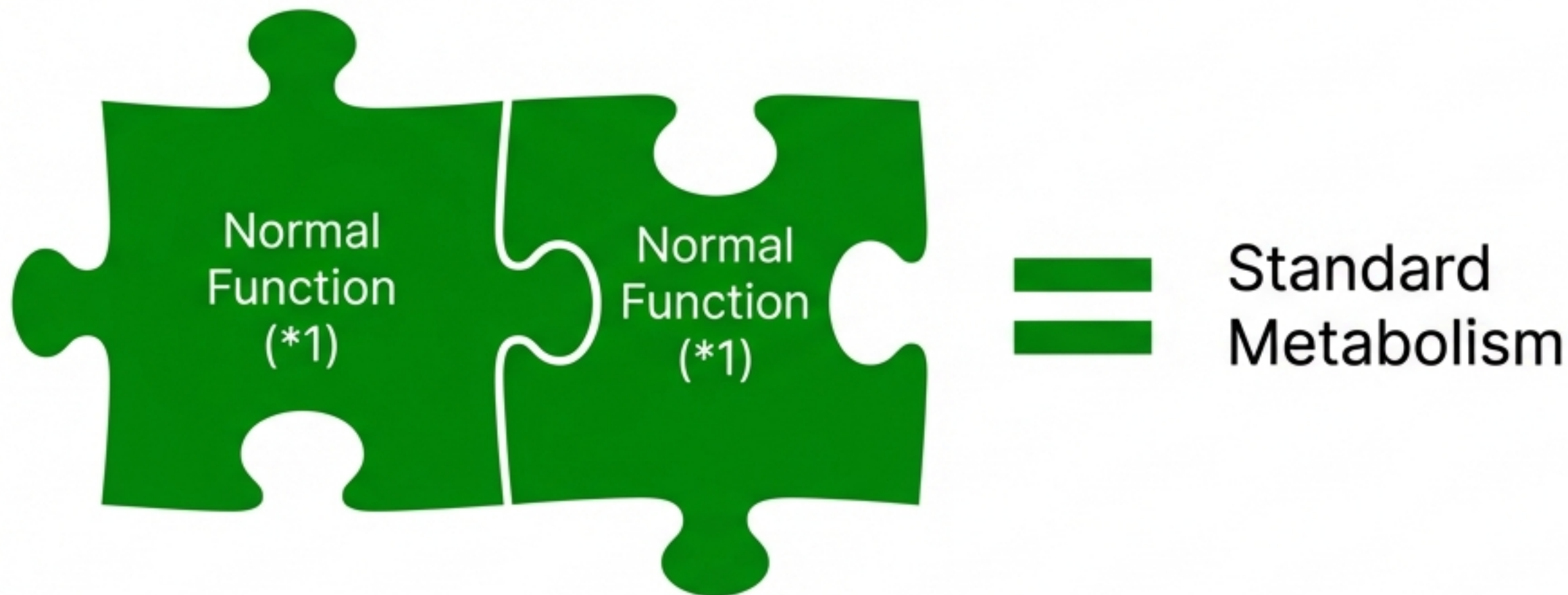


We focus exclusively on these mutations to determine Clopidogrel resistance.

TYPE A: EXTENSIVE METABOLIZER

Genotype: *1/*1

The Wild Type Standard



Mechanism:

Normal enzyme function.
Matches standard population baseline.

Clinical Action:

STANDARD DOSE. The drug is effective at normal levels.

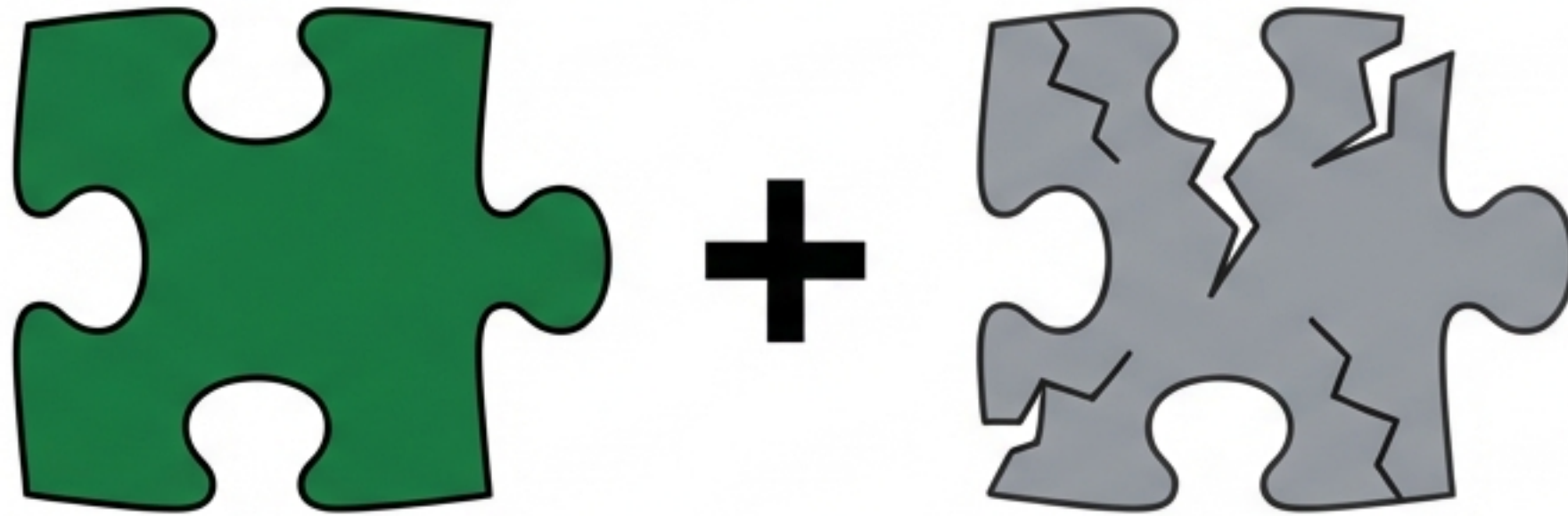
Source Reference

wild type : extensive metabolism

کسانی که فنوتیپ استاندارد دارند و دوز استاندارد می‌دهند

Genotypes: *1/*2, *1/*3, *2/*17, *3/*17

Decreased Function



Normal Function (*1) /
Fast Function (*17)

Loss-of-Function
Allele (*2, *3)

= Reduced Activity

- **Key Insight:** Patient possesses at least one *2 or *3 allele.
- **Clinical Consequence:** **RESISTANT / CAUTION.** Functional efficacy is reduced.

Source Reference

$\left. \begin{array}{l} 1/2 \\ 1/3 \\ 2/17 \\ 3/17 \end{array} \right\} \Rightarrow$ عملکرد را کم می کنند و عملاً
جزو مقاوم حساب می شود

TYPE C: POOR METABOLIZER

Genotypes: *2/*2, *2/*3, *3/*3

Loss of Function



Loss of Function
(*2 or *3)



Loss of Function
(*2 or *3)



**NO
METABOLISM**

Mechanism: Double hit of resistance.

Clinical Consequence: HIGH RESISTANCE. Clopidogrel will not be metabolized into its active form. Do not use standard approach.

Source Reference

Poor metabolizer = loss of function

*2/2
2/3
3/3* \implies *فقدان الوظيفة
loss of function = ضيق*

Poor metabolizer reference note

TYPE D: ULTRA-RAPID METABOLIZER

Genotypes: *17/*17, *1/*17

Increased Hemorrhage Risk



Hyper-function
(*17) present

+



Accelerated
Activity

=

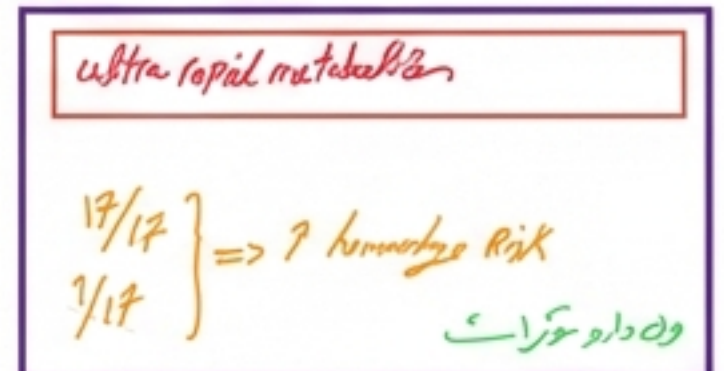
**Accelerated
Activity**

Mechanism: Hyper-function of the enzyme.

Clinical Consequence: EFFECTIVE BUT RISKY. The drug works, but there is a statistically increased hemorrhage risk.

Note: Standard dose is often maintained, but monitoring is required.

Source Reference



IBM Plex Mono Medium

Anatomy of a Lab Result

Clinical data

Requested for Plavix genotype –based dose adjustment.

Specimen

Whole blood in EDTA tube

Method

DNA was extracted using QIAamp DNA Blood Mini. Allele Specific PCR was performed for amplification of human CYP2C19*2, CYP2C19*3 and CYP2C19*17 by ABI Veriti instrument, Sequencing of CYP2C19*2, CYP2C19*3 and CYP2C19*17 were performed via Pyromark Q96 instrument and analysed to detect Polymorphism.

Test Result

SNP	RESULT
CYP2C19 681G>A (*2)	G/G
CYP2C19 636G>A (*3)	G/G
CYP2C19 -806C>T (*17)	C/C

Interpretation

- CYP2C19 genotype : *1/*1
- Extensive metabolizer.
- Standard or normal Clopidogrel dose recommended.

Cautions

Test results should be interpreted in context of clinical findings, sampling, and other laboratory data. If results obtained do not match other clinical or laboratory findings, please contact the laboratory for possible interpretation. Misinterpretation of results may occur if the information provided is inaccurate or incomplete. Every molecular test has a 0.5-1 % error rate. This is due to rare molecular events and factors related to the preparation and analysis of samples.

If specimen has not been collected in Partolab we won't accept any responsibility of patient's identity because improper labeling, handling and storage or delayed delivery may cause inaccurate or false results.

Interpretation Logic:

The absence of mutations 681G>A (*2) and 636G>A (*3) confirms the Wild Type status.

Target SNPs identified via PCR

Allele status determination

Final Genotype Calculation

Clinical Interpretation

Clinical Decision Matrix

CYP2C19 Allele Analysis for Clopidogrel Optimization

Extensive Metabolizer	*1/*1	Standard Dose. Drug is effective.
Intermediate Metabolizer	*1/*2, *1/*3, *2/*7, *2/*17, *3/*17	Resistant. Reduced efficacy. Consider alternatives.
Poor Metabolizer	*2/*2, *2/*3, *3/*3	High Resistance. Loss of function. Drug ineffective.
Ultra-Rapid Metabolizer	*17/*17, *1/*17	Effective / Risk. Works well, but monitor for bleeding.