PANDORA GENOMICS

PGxReport™ - Clopidogrel
Drug Sensitivity Assay Results

Detailed information on the genes assessed by this study:

Clinical Background

CYP2C19

- Cytochrome P450 2C19 (CYP2C19) is an isoenzyme of the cytochrome P450 super family that metabolizes and eliminates common prescription drugs, including anti-convulsants, antidepressants, cancer chemotherapy, anti-malaria, anti-ulcer, proton pump inhibitors, and anti-thrombotics (clopidogrel/Plavix®).
- Pharmacogenetic variation leads to inappropriate concentrations of drugs and drug metabolites, which may contribute to toxicity and risk of adverse drug reactions or lack of therapeutic benefit.
- Metabolizer phenotypes can be predicted by the CYP2C19 genotype.
- The clinical impact of the CYP2C19 genotype is influenced by whether a drug is activated (e.g., cyclophosphamide, clopidogrel, tamoxifen) or inactivated (e.g., amitryptiline, escitalopram) by CYP2C19, involvement of other metabolic pathways, and other non-genetic factors (e.g., concomitant medications).

Epidemiology

CYP2C19

- CYP2C19 mutation frequency is dependent on ethnicity. The most common mutations are represented by the *2 and *3 alleles.
- The *2 allele is found in approximately 30% of Asians and 15% of Caucasians and African-Americans.
- The *3 allele is present in approximately 8% of Asians and is rare (<1%) in Caucasians and African-Americans.
- A poor metabolizer phenotype (caused by two non-functional CYP2C19 alleles) is present in 4% of Caucasians, 5% of African-Americans, and up to 25% of Asians.
- The *17 allele is present in approximately 20% of Caucasians and African-Americans, and only 5% of Asians.

Genetics

CYP2C19

- The CYP2C19 gene has nine exons and is located on chromosome 10.
- Inheritance is autosomal recessive.
- Penetrance is drug dependent.

Interpretation

CYP2C19

- If no CYP2C19 mutations are detected, this suggests *1 alleles and normal enzymatic activity.
- If one decreased function or one non-functional CYP2C19 mutation is detected, intermediate-to-normal CYP2C19 enzymatic activity is predicted.
- If two decreased function alleles, or one decreased function and one non-functional allele are detected, intermediate CYP2C19 enzymatic activity is predicted.
- If two non-functional mutations are present on opposite alleles, this predicts low CYP2C19 enzymatic activity and a poor metabolizer phenotype.
  - If a patient is a poor metabolizer (e.g., has the *2 or *3 allele(s)), then alternative therapy options can be considered or alternative dosing. The FDA recommends to be aware that although a higher dose regimen (600 mg loading dose followed by 150 mg once daily) in poor metabolizers increases anti-platelet response, an appropriate dose regimen for poor metabolizers has not been established in a clinical outcome trial.
- Heterozygosity or homozygosity for the increased function *17 allele is associated with increased CYP2C19 activity and an ultra-rapid metabolizer phenotype.
- Genotype results should be interpreted in the context of the individual clinical situation. Consultation with a clinical pharmacy professional is recommended.

Limitations

FIG. 7-8