CARDIOVASCULAR PHARMACOGENOMICS

MAXIMIZE EFFICACY AND MINIMIZE ADVERSE EVENTS OF COMMON CV THERAPIES
WHAT IS PHARMACOGENOMICS, AND WHY IS IT IMPORTANT?

The drugs available today to treat cardiovascular disease are powerful agents that work as intended in most patients. Yet, in some people, a particular drug at the standard dose might not work well enough or may even trigger a serious adverse reaction. This can be due to genetic causes, which often play an important role in a patient’s predisposition to experiencing adverse drug reactions or therapeutic failure.

The science of pharmacogenomics studies how a patient’s specific DNA sequences influence his or her response to medications.

Some individuals are prone to drug toxicity or inefficacy with the use of standard doses. Therefore, the timely delivery of pharmacogenomic information (or drug-gene interaction warnings) helps maximize efficacy and minimize adverse events.

RANGE OF DRUG RESPONSE PHENOTYPES FOR GENES THAT METABOLIZE COMMON CARDIOVASCULAR DRUGS

<table>
<thead>
<tr>
<th>CYP2C19</th>
<th>CYP3A4</th>
<th>CYP2C9</th>
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<tbody>
<tr>
<td>Poor Metabolizer</td>
<td>Intermediate Metabolizer</td>
<td>Extensive Metabolizer</td>
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By using a patient’s unique genetic makeup as a factor when prescribing a drug, physicians are able to ensure the right drug at the right dose at the right time to maximize treatment effectiveness while avoiding potentially life-threatening side effects.

CARDIOVASCULAR DRUGS WITH WELL-ESTABLISHED PHARMACOGENOMIC ASSOCIATIONS

<table>
<thead>
<tr>
<th>DRUG NAME</th>
<th>BRAND NAME</th>
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</thead>
<tbody>
<tr>
<td>Clopidogrel</td>
<td>Plavix</td>
</tr>
<tr>
<td>Warfarin</td>
<td>Coumadin</td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>Lipitor</td>
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<tr>
<td>Simvastatin</td>
<td>Zocor</td>
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<tr>
<td>Lovastatin</td>
<td>Mevacor, Altoprev</td>
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</tbody>
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24/7 CLINICAL SUPPORT AND BILLING SOLUTIONS

- Our pharmacogenomics testing is full-service. We encourage clients to call and speak with one of our laboratory directors or genetic counselors, free of charge, should they have questions.
- Mayo Laboratory Inquiry answers all calls personally, 24 hours a day, every day. We resolve more than 99% of inquiries with a single phone call.
- Dedicated support teams located in your region offer support on any laboratory matter.
- Our service and logistics experts guide you through reimbursement or other billing-related questions, including third-party billing and prior authorization.

Telephone 855-516-8404
Email rstmmlcardiology@mayo.edu
PHARMACOGENOMICS TESTING FOR CLOPIDOGREL

WHY SHOULD I ORDER?
- Cytochrome P450 2C19 (encoded by the gene CYP2C19) is a liver enzyme that participates in the activation of the anticoagulant clopidogrel.
- It is estimated that 2% to 14% of the U.S. population are poor metabolizers.1
- Poor, and to some extent, intermediate metabolizers may not effectively convert clopidogrel to its active form. As a result, clopidogrel may be less effective in inhibiting platelet activity in those people who may remain at risk for heart attack, stroke, and cardiovascular death.

FEATURED TEST
- Clopidogrel (Mayo ID: 2C19B)
  Variant analysis of the CYP2C19 gene
  USEFUL FOR
  - Predicting anticoagulation response to clopidogrel.
  - Identifying patients who may be at risk for altered metabolism of drugs that are modified by CYP2C19.

RESEARCH IN SUPPORT OF CLOPIDOGREL TESTING2
- Post PCI-genotyping implemented in 2012, performed for 412 patients.
- Coronary events reduced significantly for patients with CYP2C19 loss of function (LOF) variants who received alternative therapy.

ADDITIONAL PHARMACOGENOMICS TESTING
- Warfarin Sensitivity Genotype (Mayo ID: WARFB)
  Variant analysis of the CYP2C9 and VKORC1 genes
  USEFUL FOR
  Identifying patients who may require warfarin dosing adjustments including:
  - Patients who have previously been prescribed warfarin and have required multiple dosing adjustments to maintain the international normalized ratio (INR) in the target range.
  - Patients with a history of thrombosis or bleeding when taking warfarin.
  - Patients being started on warfarin.

- Atorvastatin, Simvastatin, Lovastatin (Mayo ID: 3A4B)
  Variant analysis of the CYP3A4 gene
  USEFUL FOR
  - Determining therapeutic strategies for drugs that are metabolized by CYP3A4, including atorvastatin, simvastatin and lovastatin.
TAP INTO THE EXPERTISE OF MAYO CLINIC

The Personalized Genomics Laboratory (PGL) performs genetic screening to aid clinicians in drug selection and treatment (pharmacogenomics), assessment of cardiovascular-based genetic disorders, and immune competence and reconstitution.

The staff of PGL uses many different methods and technologies, including DNA extraction, robotics, fluidic micro arrays, real-time PCR, Sanger DNA sequencing, and next-generation sequencing, to obtain patient results in a timely and efficient manner.

FOR MORE INFORMATION ABOUT CARDIOVASCULAR TESTING, VISIT
MayoMedicalLaboratories.com/cardiology

REFERENCES