Informatics and Pharmacogenomics

Hamed Abbaszadegan, MD, MBA, FACP, FAMIA
Chief Health Innovation & Informatics Officer
Phoenix VA Health Care System
Clinical Associate Professor of Biomedical Informatics, Internal Medicine, & Pathology
University of Arizona College of Medicine-Phoenix
Learning Objectives

- Formulate structural documentation
- Describe the decision support infrastructure
- Identify intelligent approaches to patients for PGx testing
Clinical Informatics in Healthcare
Structural Documentation

- Formalizes charting
- Allows for standardization
- Creates “back-end” data warehouse storage → Mining
- Most important, allows for Decision Support functionality
A basic pharmacogenomic testing panel was performed as part of the PHASE program. The full test report including individual genotypes and drug-genotype interactions can be found in VistA Imaging under "Pharmacogenomics". A copy of the patient’s full pharmacogenomic report has been provided to them. The following gene phenotype interpretations were identified based on the Clinical Pharmacogenomics Implementation Consortium (CPIC) guidelines using Translational Software.

To learn more about specific drug-genotype interactions, interpreting this report, placing a pharmacogenomic consultation, and other educational materials, please visit: https://vistainc.com/PHASE-provider-SharePoint

Test results:
Genes: CYP2C19
Result: Intermediate metabolizer
Genes: CYP2CS
Result: Normal metabolizer
Genes: CYP2D6
Result: Normal metabolizer
Genes: CYP2A5
Result: Poor metabolizer
Genes: DPD
Result: Normal metabolizer
Genes: SLC10A5
Result: Decreased function
Genes: IDH2
Result: Intermediate or poor metabolizer
Genes: VKORC1
Result: High warfarin sensitivity

Pharmacogenomics results may not be interpretable in patients who are recipients of a liver transplant or who have undergone bone marrow transplant. It is not advisable for these patients to undergo pharmacogenomic testing, instead place a Pharmacogenomics e-consult.

The list below is the current list of CYP Level 1 medications:

- **PHASE 1:**
  - CYP2C19 DECREASED FUNCTION
  - CYP2C9 NORMAL METABOLIZER
  - CYP2C9 DEFICIENT PHENOTYPE
  - CYP2C9 DECREASED FUNCTION
  - CYP2C9 DEFICIENT PHENOTYPE
  - CYP2C9 NORMAL METABOLIZER
  - CYP2C9 NORMAL METABOLIZER
  - CYP2C9 DEFICIENT PHENOTYPE
  - CYP2C9 DEFICIENT PHENOTYPE
  - CYP2C9 NORMAL METABOLIZER
  - CYP2C9 NORMAL METABOLIZER

- **PHASE 2:**
  - CYP2C19 NORMAL METABOLIZER
  - CYP2C9 NORMAL METABOLIZER
  - CYP2C9 NORMAL METABOLIZER
  - CYP2C9 NORMAL METABOLIZER
  - CYP2C9 NORMAL METABOLIZER
  - CYP2C9 NORMAL METABOLIZER
  - CYP2C9 NORMAL METABOLIZER
  - CYP2C9 NORMAL METABOLIZER
  - CYP2C9 NORMAL METABOLIZER
  - CYP2C9 NORMAL METABOLIZER
Structured Consent

VA PHASES: Pharmacogenomics Action for cancer Survivorship

Consent and ordering

- I have discussed the availability of PHASEs pharmacogenomic testing panel with this patient and explained its risks, benefits, and limitations. I have given the patient an opportunity to ask questions regarding pharmacogenomic testing and I have satisfactorily addressed them.

- The patient agrees to have the PHASES pharmacogenomic test panel performed; ordered now via this selection (order will display after template is finished).

- The patient does not agree to have the PHASES pharmacogenomic test panel performed and does not want to be contacted about testing in the future.

- The patient does not want to undergo testing now but agrees to low PHASES staff to contact him/her at a later date to discuss testing further.

I have discussed the availability of PHASEs pharmacogenomic testing panel with this patient and explained its risks, benefits, and limitations. I have given the patient an opportunity to ask questions regarding pharmacogenomic testing and I have satisfactorily addressed them.

The patient agrees to have the PHASES pharmacogenomic test panel performed.

Health Factors: VA PGX PROVIDER EDUCATION (historical) VA PGX TESTING ACCEPTED (historical)
Options: PHARMACOGENETICS PANEL (historical)
Standardized Note
**Assessment/Plan**

**Assessment:**
Pharmacogenetic result interpretation with recommendations: reviewed pharmacogenetic results along with current and immediately planned medications with patient.

Based on the available genes tested, patient is not currently on any medications that would require action.

**Plan:**
No active actionable recommendation at this time.

Future medications will be based on the actionable recommendations below.

**Actionable Recommendations:**

- [ ] **No Action**
  - Please recheck recommendations if new genes are available for testing.
  
  This report is based on the most recent pharmacogenetic testing for this patient. Due to changes in pharmacogenetics reporting and interpretation may occur. In addition, many of these genes will no longer be relevant if this patient has a liver transplant.
Encounter
Drug Dosing Guidance

A medication has potentially reduced efficacy, increased toxicity or the patient has an increased risk for the indicated condition. Guidelines exist for adjusting dosage, increased vigilance or the patient has a moderate risk for the indicated condition.

**Clopidogrel**
*Plavix®*

Reduced Response to Clopidogrel (CYP2C19: Intermediate Metabolizer)

Consider alternative therapy. Examples of alternative drugs: prasugrel (contraindicated in TIA/Stroke patients), ticagrelor, aspirin, aspirin plus dipyridamole.

**Atomoxetine**
*Strattera®*

Possible Atomoxetine Underexposure Leading to Decreased Response (CYP2D6: Normal Metabolizer)

The genotype result indicates that the patient is likely to have an insufficient response due to inadequate drug exposure following standard dosing. Consider the following dosing strategy:

- Initiate treatment at 40 mg/day. increase to 80 mg/day after 3 days and maintain dose.
- If after 2 weeks, optimal clinical response is not observed and adverse events are not present, consider a dose increase to 100 mg/day.
- If after 2 weeks, optimal clinical response is not observed and adverse events are not present, consider therapeutic drug monitoring 1-2 hours post dose. If the plasma concentration is less than 200 ng/ml consider a
Decision Support Infrastructure

- Clinical Reminder Order Checks (CROC)

- Logic:
  - Citalopram:
    - IF the patient is to receive Citalopram AND has genotype results for CYP2C19 AND CYP2D6 available, THEN query phenotypes.
      - IF phenotype is CYP2C19 ultra-rapid phenotype AND CYP2D6 normal or intermediate phenotype THEN CROC will fire when citalopram is ordered.
Select Reminder Order Check Menu Option: GE  Add/Edit Reminder Order Check Items Group
Select Reminder Order Check Items Group by one of the following:

N:  ORDER CHECK ITEMS GROUP NAME
C:  VA DRUG CLASS
D:  DRUG
G:  VA GENERIC
O:  ORDERABLE ITEM
R:  ORDER CHECK RULE
Q:  QUIT

Select Reminder Order Check Items Group by: (N/C/D/G/O/R/Q): N//
Rule Name: VA-LONG QT SYNDROME (RULE)
Display Name: ISSUE: Patient with documented long QT syndrome
Class: National
Sponsor:
Review Date:
Status: Production
Severity: High

Reminder Term: VA-LONG QT SYNDROME (TERM) Reminder Term Status: TRUE

Order Check Text:

* The selected medication is known to also

prolong the QT interval

RECOMMENDATIONS:
- Avoid use if at all possible
- If prescribed, provide close medical observation for arrhythmias
Rule Description:
Clinical Reminder Order Check (CROC) designed in response to NSR #20110211 to warn when ordering a medication known to prolong QT interval for a patient with documented Long QT Syndrome. ---R. Silverman [PBM] Jan 2018, Jun 2018
Interface of Order Check
## Potentially Impacted Medications

<table>
<thead>
<tr>
<th>CATEGORY</th>
<th>DRUG CLASS</th>
<th>STANDARD PRECAUTIONS</th>
<th>USE WITH CAUTION</th>
<th>CONSIDER ALTERNATIVES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anticancer Agents</td>
<td>Fluoropyrimidines</td>
<td>Capetibine (Kolox®)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fluorouracil (Adrucil®)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(topical)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Efudex® (topical)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Thiolpurines</td>
<td>Azathioprine (Azasan®, Imuran®)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mercaptopurine (Purinethol®, Purixan®)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Anticoagulants</td>
<td>Warfarin (Coumadin®)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Antiplatelets</td>
<td>Clopidogrel (Plavix®)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Statins</td>
<td>Simvastatin (Zocor®)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Antiemetics</td>
<td>Ondansetron (Zofran®, Zuplenz®)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infections</td>
<td>Antifungals</td>
<td>Voriconazole (Vfend®)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td>Opioids</td>
<td>Codeine (Codeine, Fioricet® with Codeine)</td>
<td>Codeine, Tramadol (Ultram®)</td>
<td></td>
</tr>
<tr>
<td>Psychotropic</td>
<td>Anti-ADHD Agents</td>
<td>Desipramine (Norpramin®)</td>
<td></td>
<td>Amitriptyline (Elavil®)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fluoxetine (Prozac®, Sarafem®)</td>
<td></td>
<td>Clomipramine (Anafranil®)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fluvoxamine (Luvox®)</td>
<td></td>
<td>Doxepin (Silenor®)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nortriptyline (Pamelor®)</td>
<td></td>
<td>Imipramine (Tofran®)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Paroxetine (Paxil®, Brisdelle®)</td>
<td></td>
<td>Tranylcypromine (Surmontil®)</td>
</tr>
<tr>
<td>Transplantation</td>
<td>Immunosuppressants</td>
<td>Tacrolimus (Prograf®)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Telehealth Instant Connection
Review Results
Let’s Collaborate!

• Lets collaborate!

Hamed.Abbaszadegan@va.gov