Implementing Personalized Medicine in a Community Health System: The Mission Health Experience

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Division of Practice Advancement and Clinical Education
UNC Eshelman School of Pharmacy
Mission Health

• Non-profit rural health care system in Western North Carolina
  – Regional tertiary care referral center (763 beds)
  – Six affiliate hospitals (+400 beds)
  – Over 500 directly employed physicians and advanced practitioners
  – Mission Health is certified in more than 50 medical specialties and sub-specialties
  – Serve ~1 million residents across 18 counties

• Highly rated
  – Watson Health: 15 Top Health Systems in 6 of past 7 years
  – Seven Centers of Excellence: Cancer, Heart, Mission Children’s Hospital, Neurosciences, Orthopedics, Trauma and Women’s Health
Current PM Team/Services

**Personalized Medicine Team:**
- VP, Jonathan Bailey, MHA
- Former Director, Lynn Dressler, Dr.P.H.
- Interim Director and Clinical Pharmacist, Gillian Bell, PharmD
- Coordinator: Paige Krug, B.S.
- Research Nurse: Pearl Abernathy, RN (part time)
- Trainees: Students, Residents, Fellows

**Program Services**
- Education/training/resource
- Meeting/exceeding national guidelines for tumor markers, including QI studies
- PGx testing for drugs with boxed warnings; CDS alerts
- Clinical consultation
  - Personalized Medicine Clinic
  - Consults for cancer genomic profiling
- Clinical research
  - Pilot study in primary care, supportive care in cancer pts
Clinical Implementation at Mission Health

- **2014**: Assessment of drug use, planning
- **2015**: Codeine Alerts Dec 2015
- **2016**: Primary Care Pilot Study Sept 2016
- **2017**: Pilot study in Supportive Care August 2017
- **2018**: TPMT and mercaptopurine May 2018

- **PM Clinic April 2016**: HLA-B and carbamazepine March 2017
- **Updated codeine and tramadol alerts May 2018**: PACE pilot study July 2018
- **HLA-B and abacavir Nov 2018**: Palliative care pilot study Nov 2018
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Palliative care pilot study Nov 2018
Personalized Medicine Clinic Visits

- **Goal:** Provide mechanism for clinicians to refer patients needing specialized visits to discuss the implications pharmacogenomics tests and to counsel on results if tests are indicated.

- **Structure**
  - Clinic appointments to discuss testing and to review results
  - Uses existing infrastructure at the Fullerton Genetics Center
  - Multidisciplinary team: Pharmacist, medical geneticist, genetic counselors (as needed)
  - Patient must be referred by clinician

- **Patient Takeaways**
  - Better understanding of how genetics impacts medication response
  - Summary report to take home and use anywhere
Personalized Medicine Clinic Visits

Visit 1:
- Ensure realistic expectations of pharmacogenomic testing; provide the info needed for value based decision
- PharmD meets with patient/family first
- PharmD takes detailed medication history
- PharmD/MD discuss the risks, limitations, opportunities and cost of PGx testing
- If decision made to test, buccal swab obtained and sent to lab for panel analysis

Visit 2:
- Ensure patient/family understands how pharmacogenomics can impact current/future medication selection; with patient/family, determine which clinicians will receive interpretative report
- PharmD/MD creates summary and to help review pharmacogenomic results with patient/family
- PharmD works with referring provider and patient to interpret & apply results, and, if appropriate, recommend drug management changes
Personalized Medicine Clinic Visits

• Challenges:
  – Scheduling within an existing clinic
  – Creating new documentation in the EHR
  – Process for receiving and denying referrals
  – Advertising new service
  – Patients with unrealistic expectations
  – Sustaining momentum
  – Reimbursement
    • For initial visit, bill on face to face time with the physician
    • For the follow-up, PharmD sees patient and bills the lowest level (99211) regardless of time spent
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Mission PM Pilot Study in Primary Care

• Most primary care physicians do not have comfort level or knowledge to ordering, interpreting, and applying results of pharmacogenomics testing

• Unless tests are ordered early on (in primary care), information is not available when needed

• Target patient population: >65yo, with Medicare, taking multiple drugs, one of which is a PGx high-risk drug

• Opportunity to address logistics, familiarity and use of these new genetic tests when cost of test and education is not a barrier
Mission PM Pilot Study in Primary Care

- Research participants included primary care physicians (PCPs) and eligible patients
- PCPs agreed to participate in 2 CME education sessions, complete pre- and post-testing surveys and a brief post-testing interview
- Education/training provided by the Personalized Medicine clinical pharmacist
- Eligible patients were ≥ 65 yo, on Medicare, and taking ≥ 4 prescription drugs, where at least 1 drug was a high evidence drug-gene interaction
- Patients agreed to a cheek swab for testing, and pre- and post-testing surveys
- Testing was covered by a grant from the NC Biotechnology Center
- Study approved by the Mission IRB
For PCPs
• Pre-testing surveys included 41 questions regarding perspective, knowledge and barriers relevant to PGx testing in their practice
• Post-testing surveys included several identical questions to previous survey and additional questions regarding process
• Phone interviews were only conducted with MDs about experience with testing and feasibility

For Patients:
• Pre-testing surveys were completed at the time of the consent process
• Post-testing surveys were completed at least 3 months after PGx testing results were complete

Analysis
• Comparisons between groups made using Fisher’s exact test
• Items reported on a Likert scale [strongly agree (SA); agree (A); neutral (N); disagree (D); strongly disagree (SD)] were often collapsed into 2 categories (SA/A vs others)
• Not all respondents answered all questions
Panel Testing and Interpretation

• Commercially available PGx panel testing was performed by two reference laboratories

• Genes included (not complete list): CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, CYP3A4, CYP3A5, F2, F5, OPRM1, SLC6A4, SLCO1B1, VKORC1

• The PM clinical pharmacist provided a clinical summary of relevant PGx results for each patient and recommendations for changing drug, dose or other considerations
• 51 patients and 4 physicians from 3 practices enrolled in the study
  • 49 patients completed the post-testing surveys and were included in analysis
• Prior to the study, none of the physicians had ordered a PGx test
• Overall, 97% of all patients had genetic variations that could affect prescribing and 29% of patients had variations that could affect current medications
## Patient Demographics

<table>
<thead>
<tr>
<th>Variable</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex:</strong></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>28 (57.1%)</td>
</tr>
<tr>
<td>Male</td>
<td>21 (42.9%)</td>
</tr>
<tr>
<td><strong>Age:</strong></td>
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<tr>
<td>65-69</td>
<td>14 (28.6%)</td>
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<tr>
<td>70-79</td>
<td>33 (67.3%)</td>
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<tr>
<td>80+</td>
<td>2 (4.1%)</td>
</tr>
<tr>
<td><strong>Race:</strong></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>49 (100%)</td>
</tr>
<tr>
<td><strong>Education:</strong></td>
<td></td>
</tr>
<tr>
<td>No college, Some college/Degree, Post graduate</td>
<td></td>
</tr>
<tr>
<td></td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>23</td>
</tr>
<tr>
<td></td>
<td>15</td>
</tr>
<tr>
<td><strong>Health Status (Pre-test survey):</strong></td>
<td></td>
</tr>
<tr>
<td>Excellent/Very Good/Good</td>
<td>27</td>
</tr>
<tr>
<td>Fair/Poor</td>
<td>22</td>
</tr>
<tr>
<td>Pre-survey Question</td>
<td>Response</td>
</tr>
<tr>
<td>-----------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Before this study, where have you heard the term “Personalized Medicine”?</td>
<td>67%: Never heard</td>
</tr>
<tr>
<td></td>
<td>26%: TV, Mag, Internet, Newspaper</td>
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<tr>
<td></td>
<td>12%: MD</td>
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<tr>
<td></td>
<td>6%: Other</td>
</tr>
<tr>
<td>Why did you decide to participate in study? (top 3 reasons)</td>
<td>71%: Believe results will help me</td>
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<tr>
<td></td>
<td>71%: Interested in learning how my genes affect my drug response</td>
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<tr>
<td></td>
<td>57%: My MD/Nurse suggested it</td>
</tr>
<tr>
<td>Have you ever stopped taking a prescription medicine because of the side effects?</td>
<td>67%: Yes</td>
</tr>
<tr>
<td></td>
<td>30%: No</td>
</tr>
<tr>
<td>My health, at present, depends on my medicines</td>
<td>97%: SA/A</td>
</tr>
<tr>
<td></td>
<td>3%: Uncertain</td>
</tr>
</tbody>
</table>
**Patient responses: pre- vs. post-testing surveys**

<table>
<thead>
<tr>
<th>Question</th>
<th>Pre-testing</th>
<th>Post-testing</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Certain responses to drugs could be predicted by my genetic makeup</td>
<td>SA/A: 67% Uncertain: 33%</td>
<td>SA/A: 82% Uncertain: 18.4%</td>
<td>P&lt;0.01</td>
</tr>
<tr>
<td>PM testing could help me/my MD understand a previous bad drug response</td>
<td>SA/A: 67% Uncertain: 29%</td>
<td>SA/A: 88% Uncertain: 10%</td>
<td>P=0.02</td>
</tr>
<tr>
<td>PM testing could help me/my MD understand what drugs are better to treat my condition</td>
<td>SA/A: 80% Uncertain: 18%</td>
<td>SA/A: 92% Uncertain: 0</td>
<td>P=0.01</td>
</tr>
<tr>
<td>PM Testing could help me and my family understand our likelihood of developing cancer.</td>
<td>SA/A: 60% Uncertain: 39%</td>
<td>SA/A: 49% Uncertain: 31% SD/D: 20%</td>
<td>P=.05</td>
</tr>
<tr>
<td>PM testing is similar to other tests my MD orders</td>
<td>SA/A: 22% Uncertain: 45% SD/D: 33%</td>
<td>SA/A: 22% Uncertain: 22% SD/D: 53%</td>
<td>P=0.13</td>
</tr>
</tbody>
</table>
PCP responses: pre- vs. post-testing surveys

<table>
<thead>
<tr>
<th>Question</th>
<th>Pre-testing Response</th>
<th>Post-testing Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>I am comfortable with my knowledge of PGx</td>
<td>Disagree: 100%</td>
<td>SA/A: 100%</td>
</tr>
<tr>
<td>Top 4 barriers to PGx testing in practice</td>
<td>• Lack of expertise</td>
<td>• How to integrate results in EMR</td>
</tr>
<tr>
<td></td>
<td>• Lack of comfort applying results</td>
<td>• How to utilize results over time to manage patients medication</td>
</tr>
<tr>
<td></td>
<td>• Out of pocket expense</td>
<td>• Out of pocket expense</td>
</tr>
<tr>
<td></td>
<td>• Lack of reimbursement for testing</td>
<td>• Lack of reimbursement for testing</td>
</tr>
</tbody>
</table>
Physician interviews

Question 1: What did you gain by being in this study?
• “Awareness that this [PGx] is out there, it is not the future, it is now.”
• “[I have] more comfort in interpreting and applying results for future [drug/medication] use.”
• “[I have a] better understanding of the pharmacogenetics [in general] and the limits of the testing
• “So many PGx related meds are ID [infectious disease] or cancer, it was a good experience to gain a better understanding of which drugs are related to my [primary care] practice.”;

Question 2: How did this impact workflow? Anything stand out as great?
• All agreed that the testing did not significantly impact workflow
• Unanimous agreement that the interpretative summaries provided by PM Pharmacist were very helpful
Physician interviews

Question 3: What clinical value did participating in this study bring to you or your practice?

• “Allowing good conversations between physician and patients” and “[how the test results] could impact future care”

• “provided a competitive edge” [for the practice]"

• [since many of my patients] “google stuff before coming into the office; I love responding to these questions”

• “doing it [pre-emptive testing] for every young patient [diagnosed with depression] would be awesome”

• “ if a patient has a bad response right off the bat [to an anti-depressant] we may lose them to follow-up.”
Considerations for current medications

- Consider changing current med to an alternative (n=3)
  - CYP2C19 and clopidogrel, tricyclic antidepressants
  - CYP2D6 and opioid pain medications
- Consider changing dose of current medication (n=4)
  - CYP2C19 and proton pump inhibitor
- Monitor for side effects/efficacy due to gene-drug-drug interaction (n=8)
  - CYP2C9 inhibitor in CYP2C9 intermediate metabolizer on celecoxib
  - CYP1A2 inducer in CYP1A2 rapid metabolizer on duloxetine
Conclusions

- **Providing PGx testing in a busy primary care practice is feasible**
  - Pre-study barriers included lack of confidence in interpreting test results, convincing evidence, and clinical guidelines
  - Post-study reported barriers changed to include more logistical concerns including how to place an order in the EHR, integrate discrete PGx results into EHR, utilize results over time and minimize future out of pocket patient cost

- **Having a Personalized Medicine Consult Service can help adoption and implementation**
  - PCPs, pre-and post-study, wanted access to a personalized medicine consult service to help with complex cases and better identify patients most likely to benefit from PGx testing
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PACE pilot study
  - July 2018

Palliative care pilot study
  - Nov 2018

HLA-B and carbamazepine
  - March 2017
Alerts regarding the use of carbamazepine due to potential severe toxicity

• FDA boxed warning: dangerous and fatal skin reactions (Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN), have been reported with use of carbamazepine, especially in patients with a certain genetic variation (HLA-B*15:02)

• Greater than 15% of the population is reported positive in Hong Kong, Thailand, Malaysia, and parts of the Philippines, compared to about 10% in Taiwan and 4% in North China

• Testing should be performed for HLA-B*15:02 genetic variation in at risk populations prior to initiating carbamazepine (CBZ) treatment or use alternative therapy

• Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline recommending against use
For carbamazepine-naïve patients with positive HLA-B*15:02 result:

• Hard-Stop Alert: advises against use of CBZ (carbamazepine); use alternative meds

For carbamazepine-naïve patients who are Asian or Pacific Islander:

• Alert explains increased risk of CBZ-induced SJS/TEN
• Alert options:
  • Order HLA-B*15:02 testing
  • Order alternative medication
  • Over-ride: adherent on drug >3 months with no adverse cutaneous responses

For carbamazepine-naïve patients with no race or unknown race reported:

• Alert will explain increased risk of carbamazepine-induced SJS/TEN in specific populations
• Alert options: order HLA-B*15:02 testing; Order alternate medication; over-ride if race is known to be other than Asian/Pacific Islander.

For carbamazepine-naïve patients with race other than Asian/Pacific Islander:

• No alert will fire; normal carbamazepine dosing.

†Note: several drugs which might be considered alternatives to carbamazepine also have some association with drug-induced adverse cutaneous reactions and the HLA-B*15:02 allele. Specifically, phenytoin/fosphenytoin, oxcarbazepine, eslicarbazepine, and lamotrigine, if used, should be used with caution and monitored carefully.
Carbamazepine pre-test alert

HLA-B*15:02 Alert

Patients of Asian or Pacific Islander ethnicity and must be negative for HLA-B*15:02 to minimize risk of life-threatening reactions with carbamazepine. There is no result on file.

Click the Reference button to view additional information.

You must select an option in the Alert Action window. You can also add the order for HLA-B*15.02 by selecting the order in the Add order for: window.

Alert Action

- Cancel carbAMazepine
- Acknowledge Alert - must select reason

Add Order for:

- HLA-B*15:02 Genotyping, Carbamazepine Hypersensitivity
**HLA-B*1502 alert for carbamazepine**

This patient has a positive HLA-B*15:02 result. The use of carbamazepine in individuals carrying the HLA-B*15:02 variant allele is associated with a significantly high risk of drug-induced Stevens-Johnson Syndrome (SJS) and/or Toxic Epidermal Necrolysis (TEN).

DO NOT USE carbamazepine. Consider other alternatives.*

Click OK to cancel this order. Click the Reference button to view additional information.

*Note: several drugs which might be considered alternatives to carbamazepine also have some association with drug-induced adverse cutaneous reactions and the HLA-B*15:02 allele. Specifically, phenytoin/fosphenytoin, oxcarbazepine, eslicarbazepine, and lamotrigine, if used, should be used with caution and monitored carefully.
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Alerts regarding the use of mercaptopurine and potential severe myelosuppression

- Azathioprine (Aza), mercaptopurine (6MP), and thioguanine (TG) are all prodrugs inactivated by thiopurine methyltransferase (TPMT)
- ~3–14% of patients are TPMT intermediate metabolizers and may need dose adjustments upon initiation
- Small percentage are TPMT poor metabolizers and at risk for severe myelosuppression with standard dosing
- Mercaptopurine used in maintenance of ALL treatment
- Testing common in pediatric oncology, part of most protocols
- Decided to target mercaptopurine vs. azathioprine; also targeted pediatric oncology providers
First step: Need discrete field to trigger alerts
Mercaptopurine pre-test alert

TPMT Genotype Not Found

TPMT genotype testing is recommended before using mercaptopurine in acute leukemia to identify patients at increased risk for severe myelosuppression. A TPMT genotype test has not been ordered for this patient.

If there are results from another source then you can enter them by selecting "Enter Results" below. You can also order genotype testing by selecting the order below and you can cancel the mercaptopurine order by selecting Cancel Order.

Alert Action

- Cancel mercaptopurine
- Continue ordering mercaptopurine

Add Order for:

- TPMT genotype

Enter Results
TPMT Poor Metabolizer prescribed mercaptopurine

This patient is predicted to have low TPMT activity. The patient is at high risk for severe myelosuppression with normal doses of mercaptopurine and should receive greatly reduced doses. Start with 10% of the target dose and administer three times a week instead of daily.

Alert Action

- Cancel mercaptopurine
- Continue ordering mercaptopurine
- Modify mercaptopurine
Clinical Implementation at Mission Health

Assessment of drug use, planning

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Clinical Implementation at Mission Health
Challenges to implementing pharmacogenetic testing at Mission

- Who and when to test?
- Clinician awareness and engagement
- Choice of lab to perform testing
- Cost of testing
- Electronic health record integration
- Patient education
Preemptive vs. Reactive testing

- Healthy patient on no medications being tested with multi-gene panel
- Patient starting antidepressant therapy being tested with multi-gene panel
- Patient starting abacavir being tested for HLA-B*57:01
- Patient who has failed all known therapies being tested to explain why

Preemptive

Reactive
Getting the Message Out at Mission Health!

- Provider awareness initiatives
  - Grand Rounds
  - Personalized Medicine Conference for Pharmacists
  - Monthly staff meetings/leadership meetings
  - Family Practice Office visits
  - Digital media (screensaver and website)
  - Podcasts
  - Mailings
  - Institutional newsletters
- Community education initiatives
  - Health fairs
  - Local radio/newspapers
  - Blogs/social media
  - Speaking at community organizations
Genomic results are different from other lab results!

- Complex results in an unfamiliar nomenclature, require interpretation
- Increasing number of genes being tested
- Increasing volume of knowledge
- Results can be used over a person’s lifetime
- Need a way to tie results to prescribing for pharmacogenomic results
Key concepts to integrating pharmacogenomics into the EHR

- Document pharmacogenomics results in a consistent and time-independent manner
- Represent genomic results and interpretation as discrete data
- Provide a clinical interpretation based on expected phenotype that includes drug-specific pharmacotherapy recommendations
- Deploy clinical decision support so pharmacogenomic information is reliably used at the point of care

Adapted from Hoffman JM, Dunnenberger HM, Hicks JK. J Am Med Inform Assoc. 2016 Jul;23(4):796-801.
Interpretation and therapeutic recommendations

• Manual vs. automated
• Needs to be scalable and updatable
• Need a multipronged approach
  – Results on the flow sheet with phenotype interpretation
  – Problem list entry?
  – Consultation with interpretation and recommendations for therapy
    • Static
  – Clinical decision support
    • Can be modified
Pharmacogenetics tab added to EHR; all clinically eligible results are entered

<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>CYP2D6 Allele 1</td>
<td></td>
<td>*41</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CYP2D6 Allele 2</td>
<td></td>
<td>f Negative</td>
<td></td>
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<tr>
<td>CYP2D6 Genotype</td>
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<tr>
<td>PGKDS CYP2D6 Consult</td>
<td>f Routine</td>
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<tr>
<td>PGKDS CYP2D6 Letter</td>
<td>PGKDS CYP2D6</td>
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</tr>
<tr>
<td>Thiopurine 5 Methyl Genotype Result</td>
<td>f *1/*1</td>
<td></td>
<td></td>
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<tr>
<td>TPMT Genotype</td>
<td></td>
<td>f Normal</td>
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<td>f *1/*1</td>
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<td>PGKDS TPMT L</td>
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<td>Glucose-6-Phosphate Dehydrogenase</td>
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Slide courtesy of St. Jude Children’s Research Hospital
Result and interpretation interfaced from reference laboratory

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<thead>
<tr>
<th>CHEMISTRY RESULTS</th>
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<tbody>
<tr>
<td>CYP2C19 Specimen</td>
<td>Whole Blood</td>
</tr>
<tr>
<td>CYP2C19 Variant</td>
<td>*2 (A)</td>
</tr>
<tr>
<td>CYP2C19 Variant.</td>
<td>Negative</td>
</tr>
<tr>
<td>CYP2C19 Predicted Phenotype</td>
<td>Intermediate * (A)</td>
</tr>
</tbody>
</table>
Long interpretation; no therapeutic recommendations
Can put recommendations in a note but not discrete
Coded entries for actionable result can be created in a manual form
Pharmacogenomic Results

Result Type: Genetics/Personalized Medicine
Result Date: December 06, 2018 18:14 EST
Result Status: Asht (Verified)
Result Title: Pharmacogenomic Results
Verified By: Trkt. Evdgelph Aqebveyld on December 06, 2018 18:14 EST
Encounter info: 302068480614, CDWVNC Asheville, Ambulatory, 07/13/2018 -

Pharmacogenomic Results Entered On: 12/06/18 18:14 EST
Performed On: 12/06/18 18:14 EST by Trkt. Evdgelph Aqebveyld

General Information

Laboratory: OneOme

CYP2C19 Results
CYP2C19 Genotype: *1/*2
CYP2C19 Predicted Phenotype: Intermediate Metabolizer
CYP2C19 Result Interpretation: This result is consistent with decreased CYP2C19 enzymatic activity

Drugs to use with caution or that may need dose adjustments based on the CYP2C19 result:
Clopixol: Consider alternative antiplatelet medication, if no contraindication (e.g., prasugrel and ticagrelor), due to increased risk for reduced platelet inhibition in patients with ACS/PCI. The data for this recommendation is strongest in patients prescribed clopixol for acute coronary syndromes managed by percutaneous coronary intervention (ACS/PCI).

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CYP2D6 Results
CYP2D6 Diploidy Type: *1/*10
CYP2D6 Diploidy Activity Score: 1.25
CYP2D6 Predicted Phenotype Type: Normal Metabolizer
CYP2D6 Result Interpretation: This result is consistent with normal enzymatic activity

Drugs to use with caution or that may need dose adjustments based on the CYP2D6 result:
None

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CYP2C9 Results
CYP2C9 Result TR: *1/*2
CYP2C9 Predicted Phenotype TR: Intermediate Metabolizer
CYP2C9 Result Interpretation: This result is consistent with decreased CYP2C9 enzymatic activity

Drugs to use with caution or that may need dose adjustments based on the CYP2C9 result:
Phenobarb: Standard loading dose but consider a reduction in the recommended starting MAINTENANCE dose (based on patient's clinical characteristics). Subsequent maintenance doses should be adjusted accordingly to therapeutic drug monitoring and response. Same recommendation for fosphenytoin though given that it is IV only, it is less likely to be used for maintenance therapy.

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Warfarin: Based on the combined results of CYP2C9, VKORC1, CYP4F2, and CYP2C cluster no specific warfarin recommendations are available. Warfarin dose is dependent on numerous other clinical factors such as age, race, weight, sex, concomitant medications and comorbidities. Calculate dose based on validated published pharmacogenetic algorithms (warfarin dosing.org).
Results now discrete events on the flow sheet

<table>
<thead>
<tr>
<th>Navigator</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>PHARMACOGENOMIC RESULTS</td>
<td></td>
</tr>
<tr>
<td>CYP2C19 Genotype TR</td>
<td>*1/*2</td>
</tr>
<tr>
<td>CYP2C19 Predicted Phenotype TR</td>
<td>Intermediate Metabolizer</td>
</tr>
<tr>
<td>CYP2D6 Diployte TR</td>
<td>*1/*10</td>
</tr>
<tr>
<td>CYP2D6 Diployte Activity Score</td>
<td>1.25</td>
</tr>
<tr>
<td>CYP2D6 Predicted Phenotype TR</td>
<td>Normal Metabolizer</td>
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<tr>
<td>CYP2C9 Result TR</td>
<td>*1/*2</td>
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<tr>
<td>CYP2C9 Predicted Phenotype TR</td>
<td>Intermediate Metabolizer</td>
</tr>
<tr>
<td>CYP3A5 Result TR</td>
<td>*3/*3</td>
</tr>
<tr>
<td>CYP3A5 Predicted Phenotype TR</td>
<td>Poor Metabolizer</td>
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<tr>
<td>CYP2B6 Result TR</td>
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</tr>
<tr>
<td>CYP2B6 Predicted Phenotype TR</td>
<td>Normal Metabolizer</td>
</tr>
<tr>
<td>CYP3A4 Result TR</td>
<td>*1/*1</td>
</tr>
<tr>
<td>CYP3A4 Predicted Phenotype TR</td>
<td>Normal Metabolizer</td>
</tr>
<tr>
<td>CYP1A2 Result TR</td>
<td>*1F/*1F</td>
</tr>
<tr>
<td>CYP1A2 Predicted Phenotype TR</td>
<td>N/A</td>
</tr>
<tr>
<td>HLA-A Result TR</td>
<td>HLA-A*31:01 negative</td>
</tr>
<tr>
<td>HLA-B Result TR</td>
<td>HLA-B*58:01 positive</td>
</tr>
<tr>
<td>Factor II Result TR</td>
<td>rs1799963 GG</td>
</tr>
<tr>
<td>Factor V Result TR</td>
<td>rs6025 GG</td>
</tr>
</tbody>
</table>

Mission Health
Preventing Alert Fatigue

• Too much of a good thing can be bad
  – Alert fatigue a well-recognized dilemma with computerized medical systems
  – Review of 17 published studies reported 49% to 96% of medical alerts were overridden

• Suggestions for preventing alert fatigue
  – Targeted alerts
  – Limit who receives alerts
  – Present clear information
  – Other technologies?
Summary

• Implementation of pharmacogenomics is possible in a community health system
• Need top down and bottom up support
• Awareness and engagement of providers and patients is key
• Start with low-hanging fruit and utilize existing infrastructure when possible
• After developing process for first gene-drug pair, the rest will be easier
• IT infrastructure is crucial as we implement a pre-emptive testing strategy
Thank you!!!!
Clinical Implementation at Mission Health

- Assessment of drug use, planning
- Codeine Alerts Dec 2015
- Primary Care Pilot Study Sept 2016
- Pilots study in Supportive Care August 2017
- TPMT and mercaptopurine May 2018
- HLA-B and abacavir Nov 2018

- 2014
- 2015
- 2016
- 2017
- 2018

PM Clinic April 2016
HLA-B and carbamazepine March 2017
Updated codeine and tramadol alerts May 2018
PACE pilot study July 2018
Palliative care pilot study Nov 2018
Mission PM Supportive Care Pilot Study

- **Research participants:**
  - Oncologists: 9 clinicians/2 practices
  - Pre and post-testing Surveys on perceptions, knowledge and barriers to providing PGx testing in their practice
  - Education prior to ordering tests, offered testing to oncologists as part of education

- **Patient eligibility for testing:**
  - > 18yo, new diagnosis of cancer with chemotherapy planned
  - Moderately to highly emetogenic chemo (per NCCN guidelines)
  - Has not had Personalized Medicine testing previously

- **Testing as a clinical care test ordered by oncologist**
  - Testing provided by a commercial lab
  - Patients were consented to the study since results could affect other medications
  - Met with patients who wanted to discuss results

- **Mission IRB approval**
# Patient Demographics

<table>
<thead>
<tr>
<th>Variable</th>
<th>N (%)</th>
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<tbody>
<tr>
<td><strong>Sex:</strong></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>40 (77%)</td>
</tr>
<tr>
<td>Male</td>
<td>12 (23%)</td>
</tr>
<tr>
<td><strong>Age:</strong></td>
<td></td>
</tr>
<tr>
<td>under 20</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>21-40</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>41-60</td>
<td>23 (44%)</td>
</tr>
<tr>
<td>61-80</td>
<td>27 (52%)</td>
</tr>
<tr>
<td>Over 80</td>
<td>0 (0%)</td>
</tr>
<tr>
<td><strong>Cancer Type:</strong></td>
<td></td>
</tr>
<tr>
<td>Breast</td>
<td>21 (40%)</td>
</tr>
<tr>
<td>Lung</td>
<td>12 (23%)</td>
</tr>
<tr>
<td>Colon</td>
<td>4 (8%)</td>
</tr>
<tr>
<td>Endometrial/Ovarian</td>
<td>5 (6%)</td>
</tr>
<tr>
<td>Liver (all types)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Other</td>
<td>8 (15%)</td>
</tr>
</tbody>
</table>
Supportive Care Study Results

• 35/52 (67%) had a variation that would affect treatment or supportive care medications
  – Almost all of these were SSRIs, TCAs, PPIs
  – Some oral opioids (n=5)
  – 4 patients with Factor II deficiency, 1 with Factor V Leiden deficiency

• 9/52 (17%) had a variation that could affect current medication
  – CYP2D6 UM and ondansetron (n=2)
  – CYP2D6 PM and hydrocodone/oxycodone (n=2)
  – CYP2C19 UM/RM and PPIs (n=3)
  – CYP2C19 UM/PM and citalopram/escitalopram (n=2)
  – Drug-gene-gene interaction with 5FU and glimepiride
## Physician Responses: Pre- vs. Post-testing Surveys

<table>
<thead>
<tr>
<th>Question</th>
<th>Pre-Testing</th>
<th>Post-Testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Testing a cancer patient’s inherited genetic profile may influence his/her response to medications used in supportive care (pain, CINV, anxiety, depression)</td>
<td>89% SA/A 11% Disagree</td>
<td>100% SA/A</td>
</tr>
<tr>
<td>I am comfortable with my knowledge of how a patient’s inherited genetic profile may influence their response to supportive care medications.</td>
<td>22% Agree 44% Neutral 33% SD/D</td>
<td>89% SA/A 11% SD/D</td>
</tr>
<tr>
<td>I am comfortable interpreting results of inherited pharmacogenetic tests to predict response to supportive drug therapy in cancer patients.</td>
<td>22% SA/A 33% SD/D</td>
<td>66% SA/A 11% Disagree</td>
</tr>
<tr>
<td>Having participated in the study, I feel more comfortable discussing the results of inherited PGx testing to guide supportive care medications with a patient.</td>
<td></td>
<td>100% SA/A</td>
</tr>
</tbody>
</table>
Problem list entries can act as discrete fields for results

CYP2B6, CYP2C9, CYP2C19, CYP2D6, CYP3A5, DPYD, HLA-A*31:01, HLA-B*15:02, HLA-B*57:01, HLA-B*58:01, SLCO1B1, TPMT, UGT1A1
Diagnosis Search

Search: CYP2D6

Starts with: Within: Terminology

Terminology: ICD-10-CM, IMO
Terminology Axis: All terminology axes

<table>
<thead>
<tr>
<th>Term</th>
<th>Code</th>
<th>Terminology</th>
<th>Terminology Axis</th>
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<tbody>
<tr>
<td>CYP2D6 deficiency</td>
<td>50777692</td>
<td>IMO</td>
<td></td>
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<tr>
<td>CYP2D6 intermediate metabolizer</td>
<td>1493483176</td>
<td>IMO</td>
<td></td>
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<tr>
<td>CYP2D6 normal metabolizer</td>
<td>1493484783</td>
<td>IMO</td>
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<tr>
<td>CYP2D6 poor metabolizer</td>
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<td>IMO</td>
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<td>CYP2D6 ultra rapid metabolizer</td>
<td>1493474866</td>
<td>IMO</td>
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</tbody>
</table>

Add to Favorites
Consolidated Problems

Add new as: This Visit

Priority: This Visit (1)

- Diffuse large B-cell lymphoma, lymph nodes of multiple sites

Chronic (6)

- Anemia, pernicious
- CYP2C19 ultra-rapid metabolizer
- CYP2D6 poor metabolizer
- DM (diabetes mellitus)
- Malignant neoplasm of lower lobe of left lung
- Tobacco use

Historical (0)

Home Medications (4)

- Hct: aspirin (aspirin 325 mg oral tablet) 1 tab, PO (by Mouth), Daily, 0 Refill(s)

Vital Signs

All Visits: Last 18 months

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<th>Previous</th>
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<td>08/23/19 09:32</td>
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<td>08/23/19 09:32</td>
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<tr>
<td>Body Mass Index</td>
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<td>08/21/18 21:05</td>
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<td>Weight - kg</td>
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<td>08/21/18 21:05</td>
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<td>Weight, Measured - lb</td>
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<td>121.3</td>
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