UF Health Personalized Medicine Program

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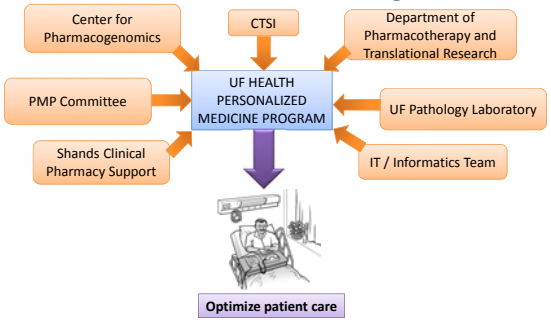
UF Health Personalized Medicine Program

- Program Objectives
  - Establish UF Health as leaders in genetic-guided care
  - Develop informatics systems to handle increasingly complex genomic data linked to EMR
  - Define when and how to use genetic data in patient care
  - Evaluate impact on patient safety, outcomes and costs of care
- Patient centric goal - Use genetic information to individualize drug therapy to:
  - Improve treatment outcomes
  - Improve safety
  - Potentially reduce costs of medical care

Make-up of the UF Health Personalized Medicine Program



Genomic Medicine Implementation Grant (IGNITE) awarded in 2013

Goals are to contribute to the evidence base regarding outcomes of incorporating genomic information into clinical care; and define and share the processes of genomic medicine implementation, diffusion, and sustainability in diverse settings.

CPIC Guidelines Applied at UF Health

Genes	Drug/ Drug class	Year of Publication
TPMT	Thiopurines	2011, 2013, 2015
CYP2C19	Clopidogrel	2011, 2013
CYP2C9, VKORC1	Warfarin	2011
CYP2D6	Codeine	2011, 2015
HLA-B	Abacavir	2012, 2014
HLA-B	Allopurinol	2012, 2015
SLCO1B1	Simvastatin	2012, 2014
CYP2C19, CYP2D6	TCAs	2013, 2015
HLA-B	Carbamazepine	2013
DPYD	Fluoropyrimidines	2014
IFNL3	Peginterferon alfa	2014
CFTR	Ivacaftor	2014
G6PD	Rasburicase	2014
CYP2C9, HLA-B	Phenytoin	2014
CYP2C19	SSRIs	2015
CYP3A5	Tacrolimus	2015

Personalized Medicine Program- Launched June 25, 2012

https://ufandshands.org/news/2012/uf-delivers-promise-personalized-medicine-heart-patients#/-1/

CYP2C19 and Clopidogrel

- CYP2C19 was built as a standard lab order
  - Run in UF Health Pathology Laboratories and includes *2, *3, *4, *5, *6, *8, *10, and *17 alleles
  - Results placed in EHR and recommendations for alternative therapy provided for loss-of-function (LOF) allele carriers
- Initially added to standard pre-cath order sets, later changed to post cath order set once billing began
- Epic Best Practice Advisories to created to support drug prescribing
- Epic Inbasket alerts created for Pharmacy monitoring

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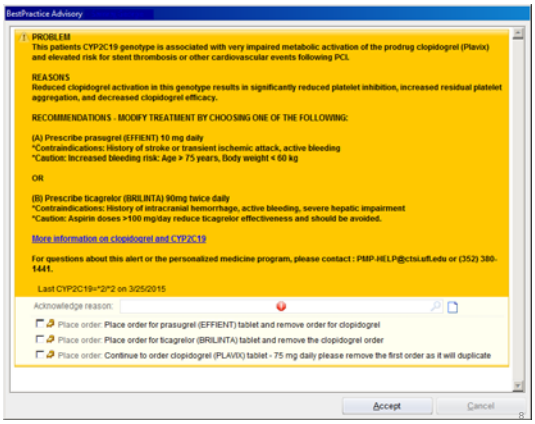
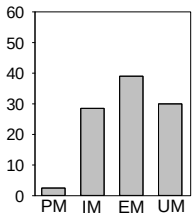


Clinical Implementation of *CYP2C19* Testing for Clopidogrel: CV Outcomes

- Reviewed EHR for patients who underwent PCI and *CYP2C19* genotyping
  - June 2012 – June 2014
  - Collected data through 6 months post PCI
- Major adverse cardiovascular events (MACE): composite of cardiovascular death, myocardial infarction, stroke, or stent thrombosis
- Compared patient characteristics and MACE between:
  - LOF allele carriers treated with alternative APT vs. clopidogrel
  - LOF allele carriers treated with alternative APT vs. non-LOF carriers

Circulation 2015;132:Suppl 3 A11802.

Percent of Patients with each CYP2C19 Phenotype

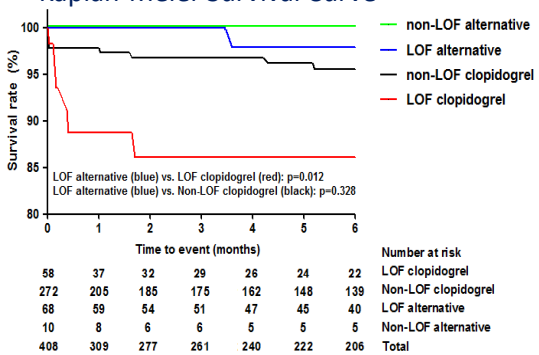


N= 408 patients

Actionable genotypes:
PM: 10 (2.5%)
IM: 116 (28.4%)
Total: 126 (30.9%)

Circulation 2015;132:Suppl 3 A11802.

Kaplan-Meier Survival Curve



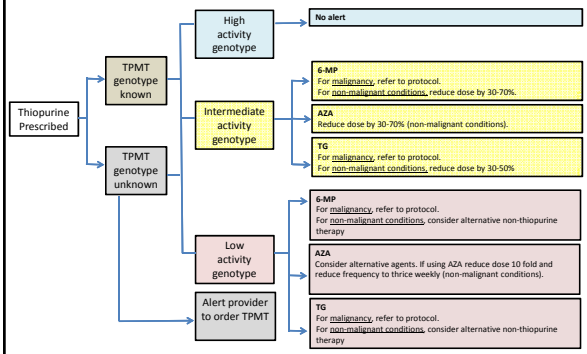
Circulation 2015;132:Suppl 3 A11802.

Clinician/Bedside Perspective: CYP2C19 - Clopidogrel

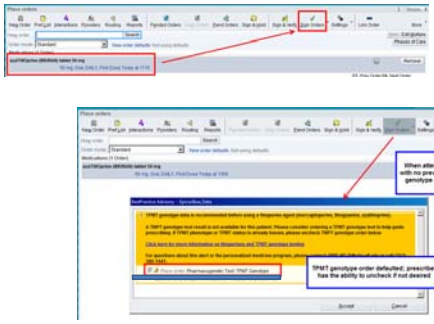
- Clinical test – standard on post-PCI order set
- Pharmacy alert and consult process
- Education
  - Clinicians and staff
  - Pre-implementation and ongoing (e.g., cardiology fellows)
  - Importance of discussing emerging evidence

TPMT and Thiopurines

- In February 2014, launched TPMT testing to dose thiopurines in the inpatient setting of Pediatric Hematology/Oncology
- Follow by an inpatient/outpatient launch in July in Adult and Pediatric GI for IBD patients
- Coordinated through the standard medication use processes within UF Health
- Associated with
  - Clinical decision support in Epic
  - Availability of consultation for interpreting and applying TPMT test results



BPA if TPMT drug ordered for a patient with no reported TPMT genotype



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Clinician/Bedside Perspective: TPMT – Thiopurines

- Outpatient vs. inpatient testing and alerting within Epic
- Clinical use of test differs with various specialties
- Education
  - Primarily pre-implementation
  - Use of and need for different types of TPMT testing
  - Broad and diverse target audience

CYP2D6 and Codeine & Tramadol

- Received significant interest from Family Medicine physicians
- April 2015 rolled out clinical CYP2D6 genotyping to guided opioid analgesics followed shortly with a research protocol focused in Family Medicine
- CDS created for codeine (outpatient) and tramadol (inpatient/outpatient)

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CYP2D6 now offered via UFHPL

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To: All involved in patient care

From:
Dr. Petr Starostik
Molecular Pathology Director
UF Health Pathology Laboratories

Dr. Robert Allan
Medical Director
UF Health Pathology Laboratories

Re: CYP2D6 Genotyping at UF Health Pathology Laboratories, Start date 4/6/15

Starting April 6, 2015, the UF Health Pathology Laboratory at Rocky Point in collaboration with the UF Health Personalized Medicine Program is pleased to offer CYP2D6 genetic testing. CYP2D6 genotype has important relevance for response to codeine and tramadol and possibly hydrocodone and oxycodone, which depend on CYP2D6 for bioactivation. CYP2D6 genotype may also have relevance for additional drugs metabolized by the CYP2D6 pathway.

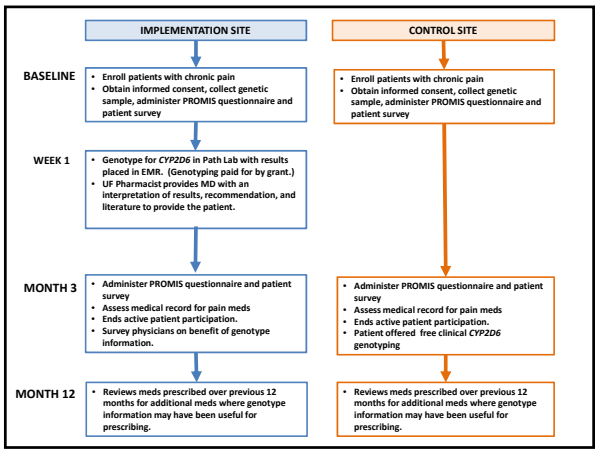
Approximately 6% to 10% of patients have a genotype leading to no CYP2D6 activity and are called Poor Metabolizers (PMs). PMs cannot metabolize codeine or tramadol into their more active forms (morphine or O-desmethyltramadol, respectively) and therefore have insufficient pain relief from codeine- or tramadol-containing analgesics. At the other end of the spectrum, another 6% of patients have too much CYP2D6 activity, and are called Ultrarapid Metabolizers (URMs). URMs quickly convert codeine or tramadol to their more active compounds, which can lead to toxic opioid levels with usual drug doses. Hydrocodone and oxycodone are also metabolized to more active forms by CYP2D6, but the impact of genetic variability on these agents is less clear.

Additional drugs metabolized by the CYP2D6 pathway include SSRIs (e.g., paroxetine), SNRIs (e.g., venlafaxine), TCAs (e.g., nortriptyline), and other psychiatric medications (e.g., aripiprazole). Consultation with a clinical pharmacist is recommended if the results indicate an abnormal CYP2D6 genotype and you would like assistance with interpretation and/or therapeutic options.

SPECIMEN REQUIREMENTS
This test could be collected as either a buccal or blood sample. Blood is preferable but buccal will suffice if it is in the best interest of the patient. Both will return the same accuracy of results. Blood Purple Top 3ml, 1ml minimum; Buccal: 4 brushes

RESULTS REPORTED:
Genotype and Phenotype with a detailed report will be available in Epic in the lab result section. The projected turn-around-time is 7-10 days.

INTERPRETATION OF RESULTS:



Provider Education Program

- Free CE program on pharmacogenetics to be offered through the UF Health PMP
- Participants will be offered free personalized genotyping Involves buccal cell collection (Research Informed Consent)
  - Includes *CYP2D6, CYP2C19, TPMT, CYP2C9, VKORC1, SLCO1B1* and other genes related to drug response.
- Educational program will be online
  - Interpreting genotype results
  - Genotype implications for drug response

Clinician/Bedside Perspective: CYP2D6 – Pain management

- Implementation
  - Gene and test complexity
  - Need to consider other clinical factors (e.g., drug-drug interactions)
  - Broad administrative and clinical implications of test (CDS, workflow, cost considerations)
- Education
  - Pre-implementation and ongoing
  - How to use Pgx testing in busy, generalist practice setting
  - Continual feedback
- What has worked, what has not?

Next CPIC implementations at UF Health

- CYP2C19/CYP2D6 for SSRIs and TCAs guided-antidepressant implementation and study in Pediatric Psychiatry
- Discussions underway with Oncology and Infectious Disease for clinical implementation of CYP2C19 for voriconazole

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UF Health PMP: Key Roles in a Successful Implementation

- Physician/prescriber champion in targeted patient population
- Pharmacogenetics program administration and leadership
- Integration within the larger system
- Institutional buy-in
- Education
  - Diverse needs and target audiences

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UF Health PMP: Key Roles in a Successful Implementation

- Regulatory/approval processes
  - Clinical and/or research activities
  - Implementation
  - Developing alerts or other clinical decision support
- Pathology/laboratory – clinical and/or research testing
- Pharmacy – clinical and/or research
- IT/Informatics support and personnel

Acknowledgements

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