Pharmacogenetic Testing in a Community Cancer Center

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Published in final edited form as:

Annu Rev Pharmacol Toxicol. 2015 ; 55: 89–106. doi:10.1146/annurev-pharmtox-010814-124835.

Preemptive Clinical Pharmacogenetics Implementation: Current programs in five United States medical centers

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Abstract

Although the field of pharmacogenetics has existed for decades, the implementation of, pharmacogenetic testing in clinical care has been slow. There are numerous publications, describing the barriers to clinical implementation of pharmacogenetics. Recently, several freely, available resources have been developed to help address these barriers. In this review we, discuss current programs that use preemptive genotyping to optimize the pharmacotherapy of, patients. Array-based preemptive testing includes a large number of relevant pharmacogenes, that impact multiple high-risk drugs. Using a preemptive approach allows genotyping results to, be available prior to any prescribing decision so that genomic variation may be considered as, an inherent patient characteristic in the planning of therapy. This review describes the common, elements among programs that have implemented preemptive genotyping and highlights key, processes for implementation, including clinical decision support.

Keywords

Pharmacogenomics; Precision medicine; Individualized medicine; Personalized medicine; Clinical decision support

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Clinical delivery of pharmacogenetic testing services: a proposed partnership between genetic counselors and pharmacists

One of the basic questions in the early uses of pharmacogenetic (PGx) testing revolves around the clinical delivery of testing. Because multiple health professionals may play a role in the delivery of PGx testing, various clinical delivery models have begun to be studied. We propose that a partnership between genetic counselors and pharmacists can assist clinicians in the delivery of comprehensive PGx services. Based on their expert knowledge of pharmacokinetics and pharmacodynamics, pharmacists can facilitate the appropriate application of PGx test results to adjust medication use as warranted and act as a liaison to the healthcare team recommending changes in medication based on test results and patient input. Genetic counselors are well-trained in genetics as well as risk communication and counseling methodology, but have limited knowledge of pharmaceuticals. The complementary knowledge and skill set supports the partnership between genetic counselors and pharmacists to provide effective PGx testing services.

KEYWORDS: delivery models ▪ pharmacogenetic testing ▪ team-based care

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Drug response may be improved through adjustment of drug selection and dosing based on information from a patient's genotype regard-

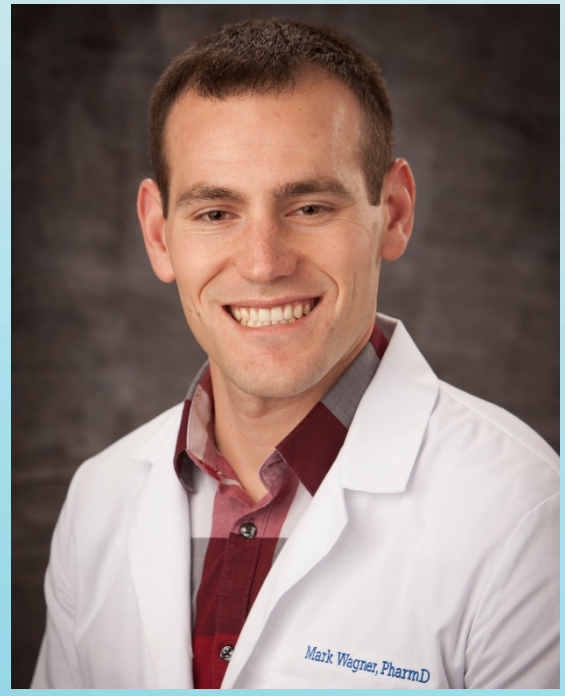
and communicate results to patients [8]. A UK study reported that patients do not appear to have a preference about which health provider(s)

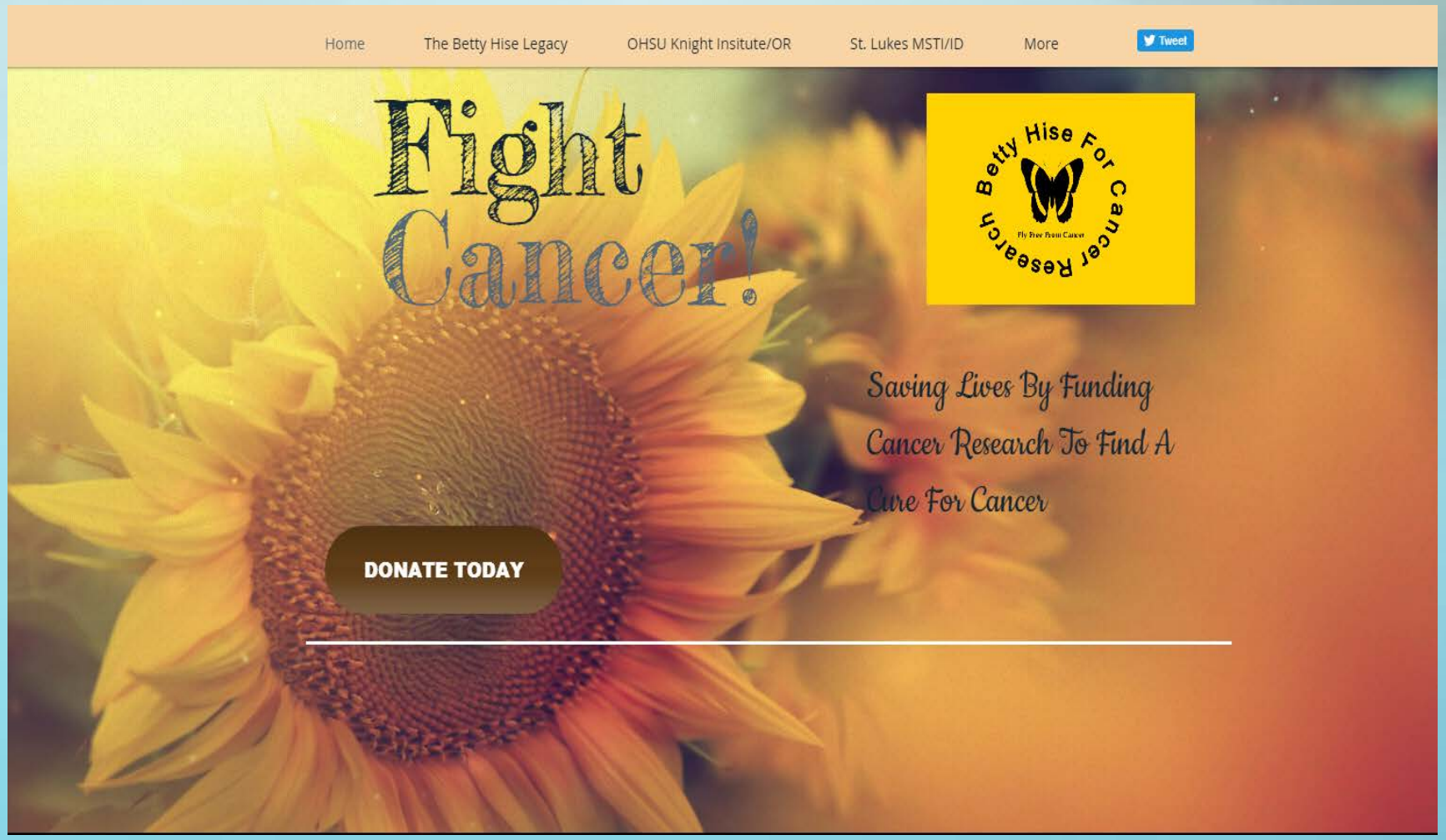
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3731754/ Accessed 29 Aug 2016.

St. Luke's Health System
Mountain States Tumor Institute

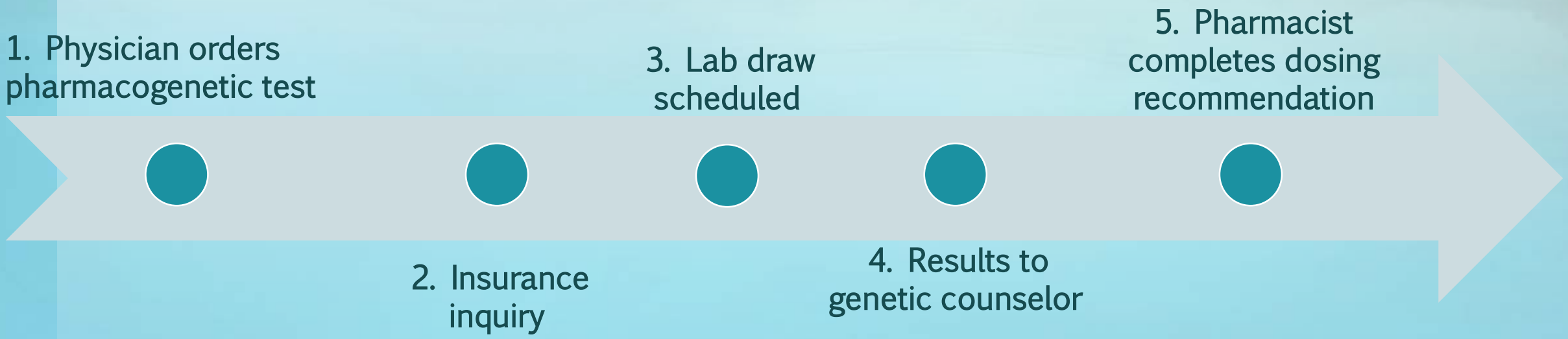
- Established in 1972
- Regional Community Cancer Center
- 5 sites
  - **Boise**
    - Meridian, Nampa, Fruitland and Twin Falls
- Serves southern Idaho, eastern Oregon and northern Nevada

Mark Wagner
Post-Graduate Year 2 Oncology Resident

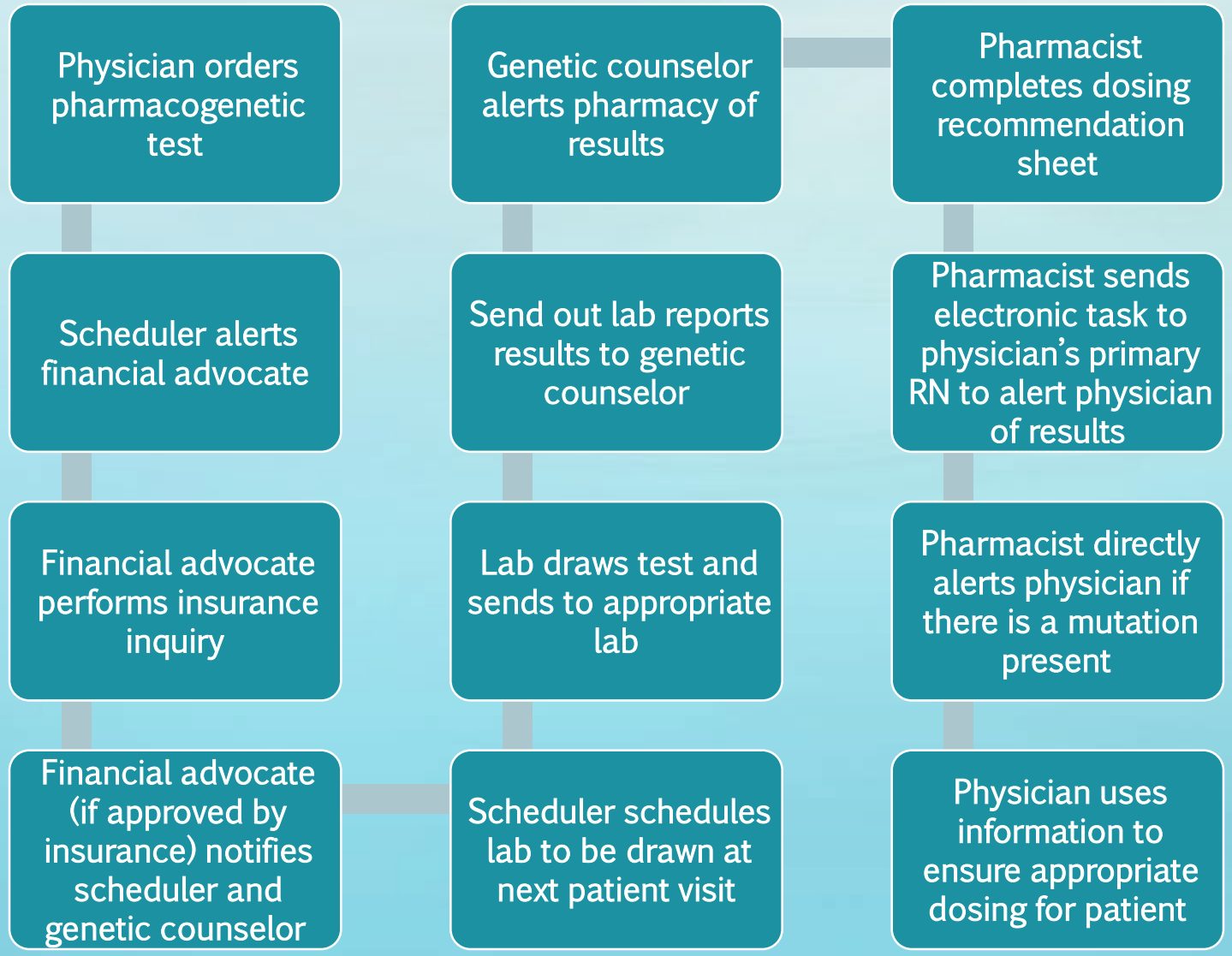




Pharmacogenetic Testing Process

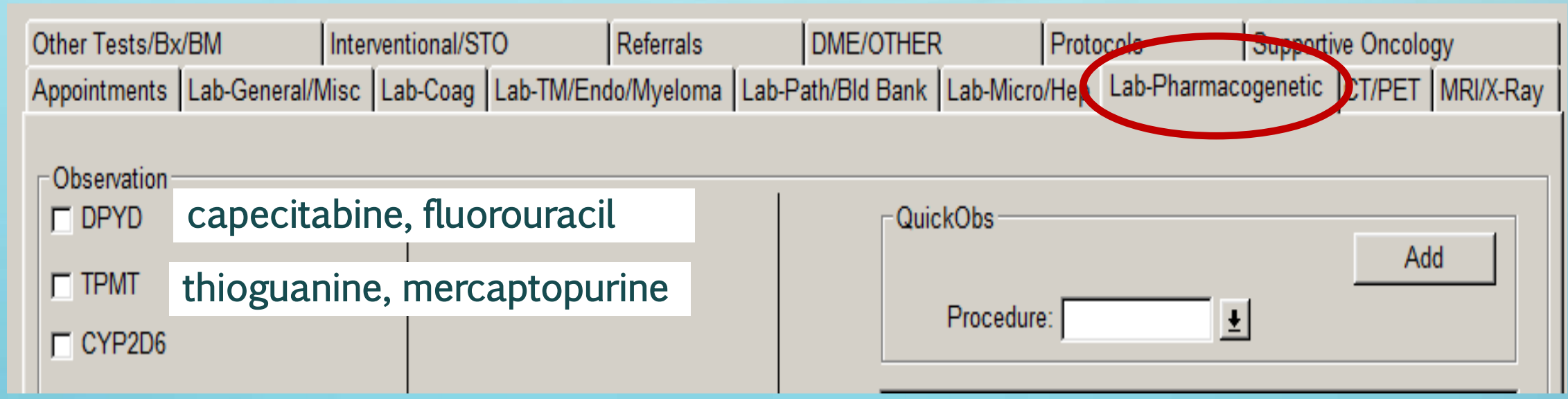


The Real World



Selection of Pharmacogenetic Tests

- Dosing recommendations available in the CPIC guidelines
- Frequency of prescribing
- Significance/incidence of genetic mutations
- Cost and test availability



Result Dissemination

- Genetic Counselor
  - Receives results from contract lab
  - Communicates results with pharmacist
- Pharmacist
  - Fills out dosing recommendation sheet
  - Sends electronic message to physician’s primary nurse
  - Alerts physician of results if necessary

St Luke's
Mountain States
Tumor Institute

NAME: Test, Boise
MEDICAL RECORD NUMBER: A090004
Date of Birth: 2/4/2003
Date: October 14, 2014

Test	Drug	Result	Recommendation
☐ **DPYD**	☐ Fluorouracil (5-FU)	☐ Homozygous Wild Type (No mutation detected)	☐ No dose adjustment
		☐ Heterozygous (One copy of the IVS14+1 G>A mutation)	☐ Start at 50% of the initial recommended dose - titrate dose based on toxicity
		☐ Homozygous Variant (Two copies of the IVS14+1 G>A mutation)	☐ **CONTRAINDICATED** – select alternative therapy
	☐ Capecitabine	☐ Homozygous Wild Type (No mutation detected)	☐ No dose adjustment
		☐ Heterozygous (One copy of the IVS14+1 G>A mutation)	☐ Start at 50% of the initial recommended dose - titrate dose based on toxicity
		☐ Homozygous Variant (Two copies of the IVS14+1 G>A mutation)	☐ **CONTRAINDICATED** – select alternative therapy

Table 2. Number of Pharmacogenetic Tests Ordered on Eligible Patients
(Results from November 4, 2014 to April 1, 2016)

DRUG	# OF TESTS ORDERED	ELIGIBLE PATIENTS	PERCENT ORDERED
Fluorouracil	73	148	49.3%
Capecitabine	63	125	50.4%
Mercaptopurine	5	5	100%
Thioguanine	0	0	N/A
Total	141	278	50.7%

Table 3. Number of Pharmacogenetic Tests Ordered on Eligible Patients
(Results from February 1, 2016 to April 1, 2016)

DRUG	# OF TESTS ORDERED	ELIGIBLE PATIENTS	PERCENT ORDERED
Fluorouracil	14	17	82.4%
Capecitabine	13	14	92.9%
Mercaptopurine	1	1	100%
Thioguanine	0	0	N/A
Total	28	32	87.5%

Results

Test	Homozygous Wild Type	Heterozygous Variant	Homozygous Variant
DPYD	186	3	0
TPMT	5	0	0

- DPYD variants - *2A, *13, rs67376798A

Cost of Testing & Contract Labs

- Individual genes vs alleles (~$200)
  - DPYD
  - TPMT
- Variants of unknown significance
- Test turn around time
  - Send out
  - Insurance requirement
  - Batched labs – twice weekly
  - 13 days for DPYD; 9 days for TPMT
- Multiple genes and cost effectiveness

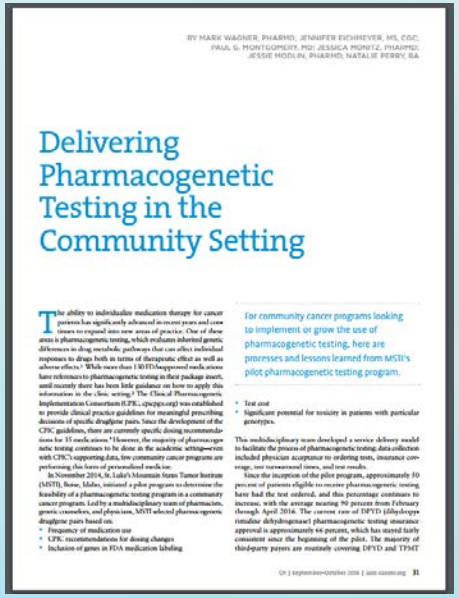
Insurance Coverage

Insurance Company	# of Tests Ordered	# Approved	# Denied
Medicare	36	35	1
Blue Cross	22	8 (6 out of state)	14 (3 out of state)
Regence	7	2	3 (2 pending)
AARP Medicare CMPLT HMO	7	7	0
United Healthcare	6	6	0
Medicaid	6	5	1
True Blue	6	1	5
Select Health	6	3	3
Tricare	5	1	4
Pacific Source	5	3	2
20 other companies (≤4 tests ordered)	28	14	14
Self Pay	5	3 payed	2 opted out

EMR Challenges

- Epic Go-Live Oct 1, 2016
  - Admin support not available to establish new workflow
    - Reports
    - Pharmacy recommendations
    - Patient identification

Oncology Issues Sep/Oct 2016



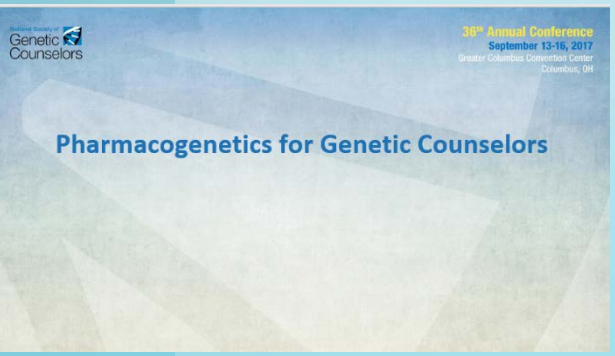
Delivering Pharmacogenetic Testing in the Community Setting

BY MARK WAGNER, PHARMD; JENNIFER EICHMEYER, MS, CGC; PAUL G. MONTGOMERY, MD; JESSICA MONITZ, PHARMD; JESSIE MODLIN, PHARMD; NATALIE PERRY, BA

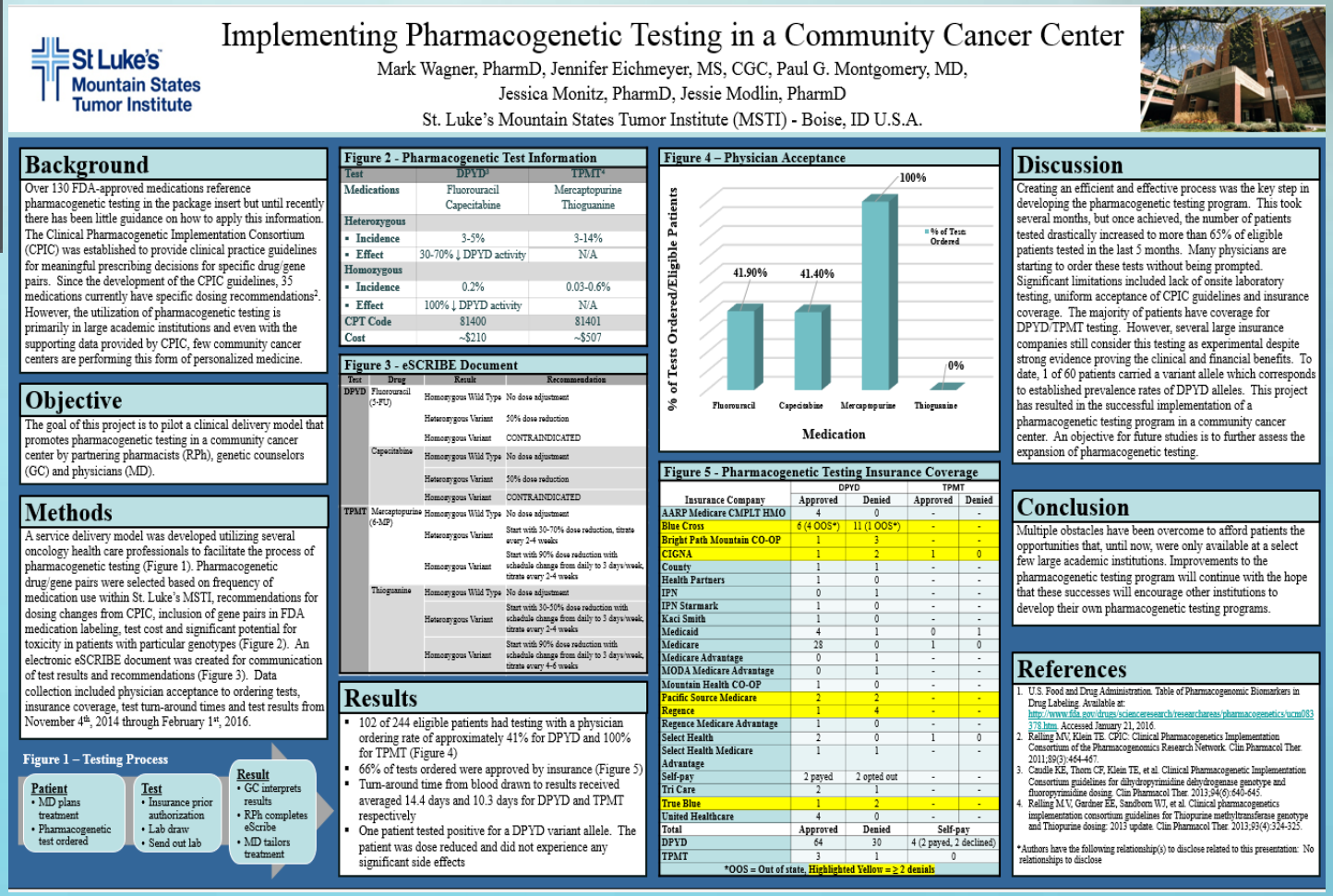
For community cancer programs looking to implement or grow the use of pharmacogenetic testing, here are processes and lessons learned from MSTI's pilot pharmacogenetic testing program.

Idaho Society of Clinical Oncology 2016

National Society of Genetic Counseling Education Conference Sept 2017



Hematology/Oncology Pharmacy Association 2016



St Luke's Mountain States Tumor Institute

Implementing Pharmacogenetic Testing in a Community Cancer Center

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Jessica Monitz, PharmD, Jessie Modlin, PharmD
St. Luke's Mountain States Tumor Institute (MSTI) - Boise, ID U.S.A.

Background

Over 130 FDA-approved medications reference pharmacogenetic testing in the package insert but until recently there has been little guidance on how to apply this information. The Clinical Pharmacogenetic Implementation Consortium (CPIC) was established to provide clinical practice guidelines for meaningful prescribing decisions for specific drug/gene pairs. Since the development of the CPIC guidelines, 35 medications currently have specific dosing recommendations[2]. However, the utilization of pharmacogenetic testing is primarily in large academic institutions and even with the supporting data provided by CPIC, few community cancer centers are performing this form of personalized medicine.

Objective

The goal of this project is to pilot a clinical delivery model that promotes pharmacogenetic testing in a community cancer center by partnering pharmacists (RPh), genetic counselors (GC) and physicians (MD).

Methods

A service delivery model was developed utilizing several oncology health care professionals to facilitate the process of pharmacogenetic testing (Figure 1). Pharmacogenetic drug/gene pairs were selected based on frequency of medication use within St. Luke's MSTI, recommendations for dosing changes from CPIC, inclusion of gene pairs in FDA medication labeling, test cost and significant potential for toxicity in patients with particular genotypes (Figure 2). An electronic eSCRIBE document was created for communication of test results and recommendations (Figure 3). Data collection included physician acceptance to ordering tests, insurance coverage, test turn-around times and test results from November 4th, 2014 through February 1st, 2016.

Figure 1 – Testing Process

Figure 2 - Pharmacogenetic Test Information

Test	DPYD[3]	TPMT[4]
Medications	Fluorouracil Capecitabine	Mercaptopurine Thioguanine
Heterozygous		
▪ Incidence	3-5%	3-14%
▪ Effect	30-70% ↓ DPYD activity	N/A
Homozygous		
▪ Incidence	0.2%	0.03-0.6%
▪ Effect	100% ↓ DPYD activity	N/A
CPT Code	81400	81401
Cost	~$210	~$507

Figure 3 - eSCRIBE Document

Test	Drug	Result	Recommendation
DPYD	Fluorouracil (5-FU)	Homozygous Wild Type	No dose adjustment
		Heterozygous Variant	50% dose reduction
		Homozygous Variant	CONTRAINDICATED
	Capecitabine	Homozygous Wild Type	No dose adjustment
		Heterozygous Variant	50% dose reduction
		Homozygous Variant	CONTRAINDICATED
TPMT	Mercaptopurine (6-MP)	Homozygous Wild Type	No dose adjustment
		Heterozygous Variant	Start with 30-70% dose reduction, titrate every 2-4 weeks
		Homozygous Variant	Start with 90% dose reduction with schedule change from daily to 3 days/week, titrate every 2-4 weeks
	Thioguanine	Homozygous Wild Type	No dose adjustment
		Heterozygous Variant	Start with 30-50% dose reduction with schedule change from daily to 3 days/week, titrate every 2-4 weeks
		Homozygous Variant	Start with 90% dose reduction with schedule change from daily to 3 days/week, titrate every 4-6 weeks

Results

- 102 of 244 eligible patients had testing with a physician ordering rate of approximately 41% for DPYD and 100% for TPMT (Figure 4)
- 66% of tests ordered were approved by insurance (Figure 5)
- Turn-around time from blood drawn to results received averaged 14.4 days and 10.3 days for DPYD and TPMT respectively
- One patient tested positive for a DPYD variant allele. The patient was dose reduced and did not experience any significant side effects

Figure 4 – Physician Acceptance

Figure 5 - Pharmacogenetic Testing Insurance Coverage

	DPYD		TPMT	
Insurance Company	Approved	Denied	Approved	Denied
AARP Medicare CMPLT HMO	4	0	-	-
Blue Cross	6 (4 OOS*)	11 (1 OOS*)	-	-
Bright Path Mountain CO-OP	1	3	-	-
CIGNA	1	2	1	0
County	1	1	-	-
Health Partners	1	0	-	-
IPN	0	1	-	-
IPN Starmark	1	0	-	-
Kaci Smith	1	0	-	-
Medicaid	4	1	0	1
Medicare	28	0	1	0
Medicare Advantage	0	1	-	-
MODA Medicare Advantage	0	1	-	-
Mountain Health CO-OP	1	0	-	-
Pacific Source Medicare	2	2	-	-
Regence	1	4	-	-
Regence Medicare Advantage	1	0	-	-
Select Health	2	0	1	0
Select Health Medicare Advantage	1	1	-	-
Self-pay	2 payed	2 opted out	-	-
Tri Care	2	1	-	-
True Blue	1	2	-	-
United Healthcare	4	0	-	-
Total	Approved	Denied	Self-pay	
DPYD	64	30	4 (2 payed, 2 declined)	
TPMT	3	1	0	

*OOS = Out of state, Highlighted Yellow = ≥ 2 denials

Discussion

Creating an efficient and effective process was the key step in developing the pharmacogenetic testing program. This took several months, but once achieved, the number of patients tested drastically increased to more than 65% of eligible patients tested in the last 5 months. Many physicians are starting to order these tests without being prompted. Significant limitations included lack of onsite laboratory testing, uniform acceptance of CPIC guidelines and insurance coverage. The majority of patients have coverage for DPYD/TPMT testing. However, several large insurance companies still consider this testing as experimental despite strong evidence proving the clinical and financial benefits. To date, 1 of 60 patients carried a variant allele which corresponds to established prevalence rates of DPYD alleles. This project has resulted in the successful implementation of a pharmacogenetic testing program in a community cancer center. An objective for future studies is to further assess the expansion of pharmacogenetic testing.

Conclusion

Multiple obstacles have been overcome to afford patients the opportunities that, until now, were only available at a select few large academic institutions. Improvements to the pharmacogenetic testing program will continue with the hope that these successes will encourage other institutions to develop their own pharmacogenetic testing programs.

References

1. U.S. Food and Drug Administration. Table of Pharmacogenomic Biomarkers in Drug Labeling. Available at: http://www.fda.gov/drugs/scienceresearch/researchareas/pharmacogenetics/ucm083378.htm. Accessed January 21, 2016.
2. Relling MV, Klein TE. CPIC: Clinical Pharmacogenetics Implementation Consortium of the Pharmacogenomics Research Network. Clin Pharmacol Ther. 2011;89(3):464-467.
3. Caudle KE, Thorn CF, Klein TE, et al. Clinical Pharmacogenetic Implementation Consortium guidelines for dihydropyrimidine dehydrogenase genotype and fluoropyrimidine dosing. Clin Pharmacol Ther. 2013;94(6):640-645.
4. Relling M.V, Gardner EE, Sandborn WJ, et al. Clinical pharmacogenetics implementation consortium guidelines for Thiopurine methyltransferase genotype and Thiopurine dosing: 2013 update. Clin Pharmacol Ther. 2013;93(4):324-325.

*Authors have the following relationship(s) to disclose related to this presentation: No relationships to disclose

Mountain States Conference 2015 and 2016

Pharmacogenetic Testing in Community Cancer Centers

- Lab does not perform this test
- We don’t know if insurance will pay
- Pharmacy does not know how to interpret the results
- EMR is not set up to order this testing pre-emptively before treatment starts
- Lack of staffing of genetic counselors
- Genetic counselors have limited training (non-traditional role)

Thank you