Primary Intended Outcomes

1. Facilitate the appropriate use of proactive pharmacogenomic tests as the standard of care for St. Jude patients.

2. Incorporate clinical decision support (CDS) tools linking pharmacogenetic testing to medication use, and characterize their use in the electronic medical record (EMR).

Relevant PPMI Recommendation(s)

B23. The following characteristics or activities should be considered essential to pharmacist-provided drug-therapy management in optimal pharmacy practice models:

   B23f. Adjustment of medication regimens based on genetic characteristics of the patient.

Situation Analysis

Although pharmacogenetics has existed as a discipline since at least the 1950s, the adoption of genetic testing to guide the safe and effective use of medication remains the exception. While there has been considerable progress in the technical ability to perform genomic testing, various barriers exist that limit the adoption of pharmacogenetic tests as the standard of care. Examples of barriers include fragmentation of health care systems, especially for lifetime genetic results, complexity of the underlying laboratory results, and the immaturity of CDS and EMR systems to facilitate point of care use of pharmacogenetic data when making drug therapy decisions. At St. Jude, we are able to overcome many of these barriers to implementing pharmacogenetics. We provide all the medications for our patients, have decades of experience performing pharmacogenetics, and have an integrated, comprehensive EMR with customized decision support.

Our philosophy is that pharmacogenetic tests results should be a part of the EMR prior to drug prescribing. If a genetic test is ordered at the time a drug is prescribed, clinicians must wait for the test results, which are often only available after the patient has already started therapy. A preemptive approach allows time for the reporting and interpretation of genetic test results so that
the information is available to guide clinicians making drug therapy decisions.

A few pharmacogenetic test results, including TPMT and CYP2D6, have been used for clinical care in a limited number of St. Jude patients since 2004. To expand our implementation of preemptive pharmacogenetics, we are using an array based genotyping platform that will interrogate 225 genes for over 1900 polymorphisms. The cost to perform array based testing is now similar to the cost of one or two single gene tests. Additionally, one test will provide data on several clinically relevant genes. However, data to support the clinical implementation of many of these genes are not available, and the process for deciding which genes to move into the EMR is not well defined. Our ongoing efforts will help us set up processes so we can determine which genes are important enough to be released to the EMR.

The preemptive use of pharmacogenetic test results by clinicians can be facilitated by developing tools and CDS within the EMR. Consults that interpret the patient’s genetic test result for busy clinicians are documented in a dedicated pharmacogenetic section of the EMR. These pharmacogenetic consults are similar to consults for pharmacokinetics that our department has performed for many years. High-risk pharmacogenetic results, which are results that require a change in drug therapy, are clearly documented in the EMR. Actionable patient-specific results are then linked to prescribing of relevant medications via CDS at point of care to guide dose modification or selection of alternative drugs. We are evaluating how clinicians accept the use of pharmacogenetics by monitoring how they respond to CDS alerts at the point of care.

Beyond St. Jude, there has been a gradual increase in compelling evidence to support increased adoption of pharmacogenetic tests into clinical practice. Much of this evidence is now organized into peer reviewed gene/drug guidelines through the Clinical Pharmacogenetics Implementation Consortium (CPIC), which was formed in 2009 as a shared project between PharmGKB and the NIH’s Pharmacogenomics Research Network. CPIC’s goal is to overcome some of the barriers to implementation of pharmacogenetic tests into clinical practice.

**Service Description**

Because we elected to implement only a subset of genes assayed, the complexity of interpretation of pharmacogenetics results, a heightened level of scrutiny for the use of genetic tests in patient care, and to manage patient education and consent, we are implementing pre-emptive pharmacogenetics in the context of a clinical research protocol. We have engaged a wide variety of physicians and others throughout our hospital as co-investigators. We continuously identify barriers and solutions, assess acceptance by clinicians and research participants, and share our knowledge outside of St. Jude.

Pharmacists lead all aspects of the implementation, including selecting the genotyping platform, prioritizing drug/gene pairs for implementation, developing consults to interpret and document results, and developing CDS and other informatics tools to manage and use the results at the
point of care. For a drug/gene pair that has been implemented into routine patient care at our hospital, there is an automated process to add pharmacogenetic consults to the EMR. These consults translate technical reports from the clinical laboratory into concise summaries that provide general dosing recommendations.

CDS is an essential component of our implementation efforts. A post-test alert fires when a drug is prescribed for a patient who has a high-risk pharmacogenetic result already in the EMR. In cases where the pharmacogenetic testing has not been measured for the patient or the result has not yet been posted to the EMR, pre-test alerts fire when orders are placed for drugs we consider high risk (e.g. thiopurines and codeine), to encourage that pharmacogenetic testing be ordered.

We established the Pharmacogenomics Oversight Committee (POC), a subcommittee of the St. Jude Pharmacy and Therapeutics Committee. The POC prioritizes which drug/gene pairs should be placed in the EMR and provides feedback on CDS and other aspects of our ongoing implementation.

**Key Elements for Success**

1. Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines,

2. Previous experience with pharmacogenetics through prior research,

3. Close collaboration with a clinical laboratory with extensive experience in clinical genetics,

4. Dedicated team within the Pharmaceutical Department working closely with many others in the health system, and

5. Mature and readily customizable computerized prescriber order entry (CPOE) and EMR systems – both inpatient and outpatient.

**Resource Utilization**

**Personnel:** Staff from the Pharmaceutical Department and Information Sciences. Key people worked on different aspects of the implementation. For example, our Pharmacogenetics resident coordinated the creation of the consults for each genetic result. Two Clinical Pharmacy Specialists provided ongoing feedback on many aspects, including consults, decision support, and patient education. Our hospital’s Clinical Decision Support Officer, who is a pharmacist working in Information Sciences, has been integral to informatics aspects. We are in the process of hiring a full time Clinical Pharmacogenetics Coordinator position to manage the entire process. Two bioinformaticists and two senior database analysts assisted with quality control process for genetic test interpretation. Department research nurses enroll all patients.

**IT and other infrastructure:** CPOE and EMR that is readily customizable; lab at Medical College of Wisconsin accredited to do array based genetic testing through the Clinical Laboratory Improvement Amendments program; clinically licensed laboratory within the Pharmaceutical Department.

**Supply Expense:** Cost of array-based testing (with 225 genes) is approximately equal to that of testing for 1 or 2 single genes.

**Return on Investment:** We are currently discussing options to obtain reimbursement.
Recognized Intangible Benefits
1. We work to save clinicians time and limit frustration. Alerts that are targeted only for high-risk or actionable genetic results decrease the risk of alert fatigue.
2. Further developing our expertise in pharmacogenetics has extended clinical pharmacists’ role as experts in drug therapy management at our hospital.

Outcome Measures
1. Through March 31, 2012, 210 patients have been genotyped, resulting in 420 TPMT and CYP2D6 gene test results (210 for TPMT and 210 for CYP2D6).
2. Ten Pharmacogenetic CDS rules have been developed for the drug/gene pairs implemented to date (5 Pre-test alerts and 5 Post-test).

Lessons Learned
1. CPIC guidance is crucial because it gives specific and actionable clinical information for drug therapy when genetic information is available. As of May 2012, six CPIC guidelines have been published in the journal Clinical Pharmacology and Therapeutics and on the PharmGKB website (www.pharmgkb.org).
2. Pharmacogenetic test results have lifetime implications, but the typical manner EMRs present laboratory data can make it difficult to find results from years ago. As laboratory tests are typically organized by date, it can be time-consuming for clinicians to find a lifetime result in the EMR. We developed a pharmacogenetics tab within our EMR as a way to readily access lifetime results in the EMR.

Other Considerations
1. It may not be feasible for all hospitals to take our array based approach that genotypes multiple genes at one time. Many hospitals may want to start small with well-established drug/gene pairs such as the ones in the CPIC guidelines. Major clinical laboratories offer genotyping for single genes (e.g. TPMT, CYP2C19).
2. Our protocol-driven approach fits with St. Jude’s focus on research. A research protocol is not necessarily a requirement to implement pharmacogenetics, especially for well-established drug/gene pairs.

Suggestions for Other Hospitals/Health Systems
1. Give careful thought to overall governance and structure. Tie the project in with both your P&T Committee (and other relevant hospital committees) and the overall mission of the hospital or health system. Start your initial efforts in focused areas where your hospital has focused expertise.
2. Develop thoughtful clinical decision support, especially because you are working with lifetime results. The information in the EMR will be used by clinicians of varying backgrounds and experience for years to come.
Helpful References


4. PG4KDS Clinical Implementation of Pharmacogenetics at St. Jude http://www.stjude.org/pg4kds


Team Members

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