Implementing CYP2C19-guided proton pump inhibitor therapy has the potential to improve clinical outcomes.

CLINICAL IMPLEMENTATION OF CYP2C19 GENOTYPE-GUIDED PROTON PUMP INHIBITOR THERAPY

Roseann S. Gammal, PharmD^{1,2}; Kelly E. Caudle, PharmD, PhD²; James M. Hoffman, PharmD, MS²; Kristine R. Crews, PharmD²; Mary V. Relling, PharmD²; Cyrine E. Haidar, PharmD²

¹Department of Pharmacy Practice, MCPHS University School of Pharmacy, Boston, MA ²Department of Pharmaceutical Sciences, St. Jude Children's Research Hospital, Memphis, TN

SERVICE

As part of the preemptive clinical pharmacogenomics program at St. Jude Children's Research Hospital (St. Jude), gene/drug pairs with sufficient evidence for implementation, generally determined by the availability of Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines, are integrated into the electronic health record (EHR) and coupled with clinical decision support (CDS). In 2018, CDS alerts for CYP2C19 ultrarapid metabolizers (UMs) were developed to inform proton pump inhibitor (PPI) (omeprazole, pantoprazole, and lansoprazole) dosing to maximize the likelihood of therapeutic efficacy.

JUSTIFICATION

PPIs are metabolized primarily by CYP2C19 into inactive metabolites. Patients who are CYP2C19 UMs are at risk for subtherapeutic plasma concentrations and treatment failure with standard doses. Doubling the starting dose of omeprazole, pantoprazole, and lansoprazole in CYP2C19 UMs is recommended to improve efficacy. Among the 5,276 patients genotyped at St. Jude to date, 10% (n=530) are CYP2C19 UMs. Of these patients, 4% (n=21) had an order for omeprazole, lansoprazole, or pantoprazole which triggered a CDS alert in the past two years. CPIC recently drafted a guideline for CYP2C19-guided PPI dosing that includes further recommendations for patients with other CYP2C19 phenotypes beyond CYP2C19 UM. These new recommendations are being implemented at St. Jude, which will have clinical implications for many patients.

ADAPTABILITY

St. Jude is one of many institutions worldwide that have adopted CPIC guidelines for clinical implementation. The CPIC guideline for CYP2C19 and PPIs provides informatics resources, including a CYP2C19 genotype to phenotype translation table; examples of interpretive consults with CDS language pertaining to CYP2C19/PPIs; and workflows for implementing CYP2C19/PPIs into the EHR that any institution can modify for its own use.

FUNDING

CPIC is funded through the National Institutes of Health (R24GM115264 and U24HG010135).

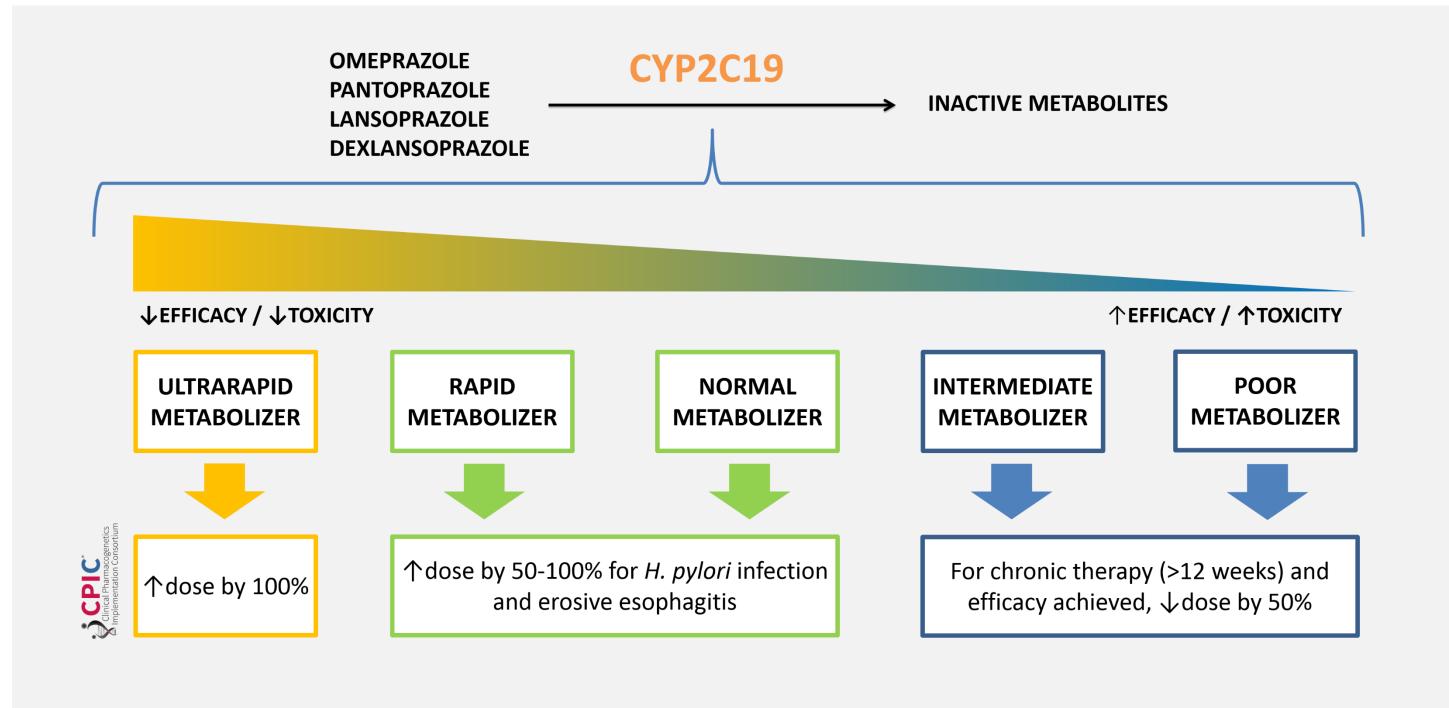


Figure 1. CPIC recommendations for *CYP2C19*-guided proton pump inhibitor therapy

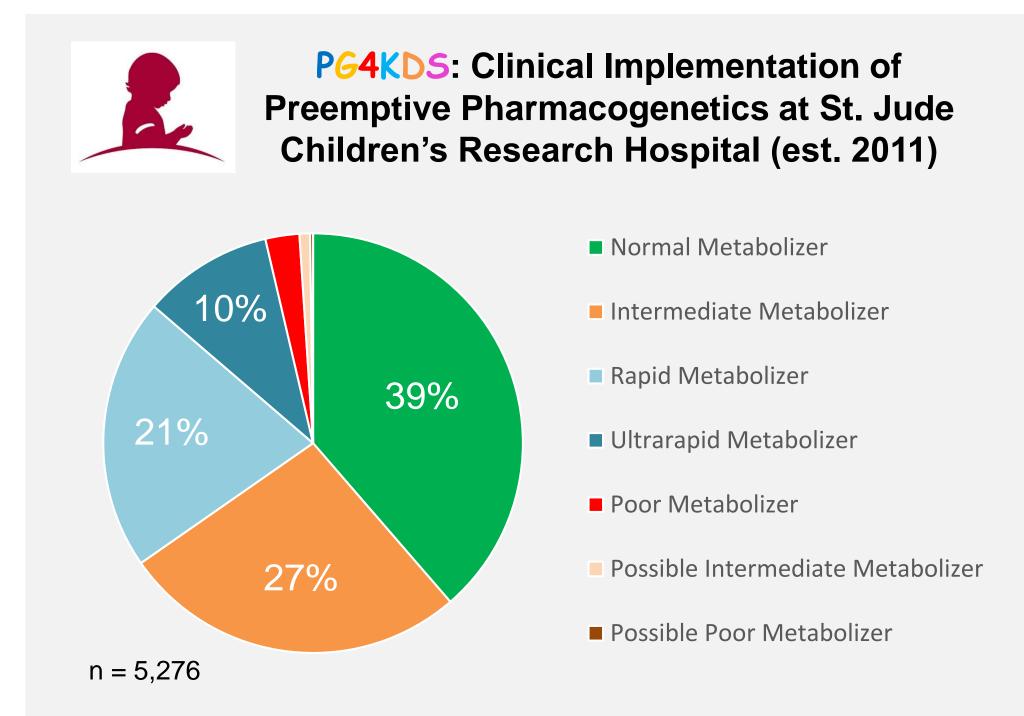


Figure 2. Frequency of CYP2C19 phenotypes at St. Jude

Therapy change per CDS alert

n = 21 (100%)



CYP2C19 UMs n = 530St. Jude Children's Research Hospital ■ Intermediate Metabolizer - lower function You are predicted to be an ultra-rapid metabolizer of drugs broken down by CYP2C19, So, yo need different doses of these drugs or possibly a different medicine. The medicines include: logrel, voriconazole, some tricyclic antidepressants, benzodiazepines, and some proton pump itors. Please check with your doctor or pharmacist if you are unsure about whether you are takin You might have had genetic testing performed outside of the PGENAKids study. It might have been tic testing for another study. Or, the Cancer Predisposition Clinic might have tested to see if you are at ris disease that can be passed down in families (hereditary). Please talk to your doctor or genetic counselor f esults of those other tests. A copy of this letter, and other PGEN4Kids letters, may be viewed on your My St. Jude patient portal twww.stjude.org/mystjude. For details on how to understand your CYP2C19 gene test result and whice s may be affected, visit the PGEN4Kids website at www.stjude.org/pg4kds. You may also visit ppgc.org for more information. If you have questions about your gene test result, email pharmacogenomics@stjude.org or call St. Jud research nurses at 901-595-2482. If you are calling from outside the Memphis area, dial toll-free 1-866-2ST-JIDF (1-866-2ST-SS33), and sk for extension 2482. Cyrine E. Haidar, Pharm.D. Principal Investigator, PGEN4Kids **Figure 3.** Sample *CYP2C19* result letter

posted to online patient portal

Table 1. Number of patients who received a PPI prescription based on CYP2C19 phenotype (July 2018-October 2020)

Order for relevant PPI

n = 21 (4%)

	Lansoprazole	Omeprazole	Pantoprazole	Total
UM	0	11	10	21
RM	5	48	76	129
NM	4	73	131	208
IM	7	53	91	151
PM	0	6	7	13



Each CYP2C19 phenotype is actionable for PPIs per the new CPIC recommendations (Figure 1).

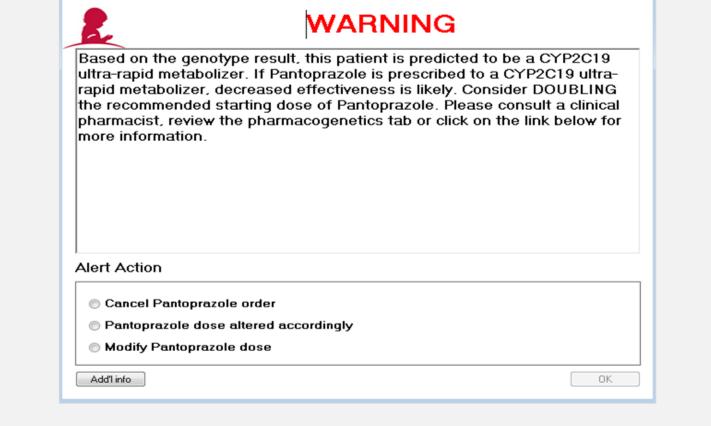


Figure 4. Sample CYP2C19/PPI clinical decision support (CDS) alert