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, PhD[2]; James M. Hoffman, PharmD, MS[2]; Kristine R. Crews, PharmD[2]; Mary V. Relling, PharmD[2]; Cyrine E. Haidar, PharmD[2]

[1]Department of Pharmacy Practice, MCPHS University School of Pharmacy, Boston, MA
[2]Department 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).

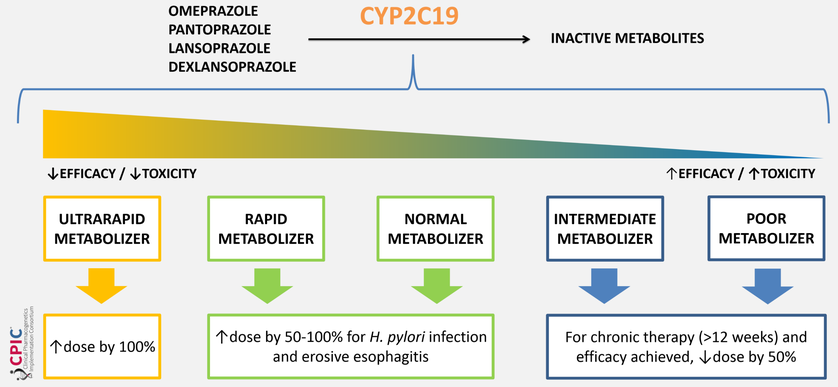


Figure 1. CPIC recommendations for *CYP2C19*-guided proton pump inhibitor therapy

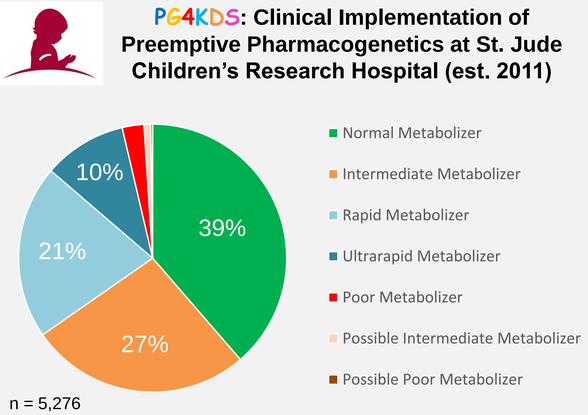
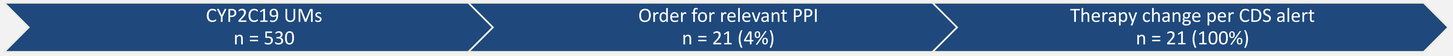


Figure 2. Frequency of CYP2C19 phenotypes at St. Jude

CYP2C19/PPI IMPLEMENTATION



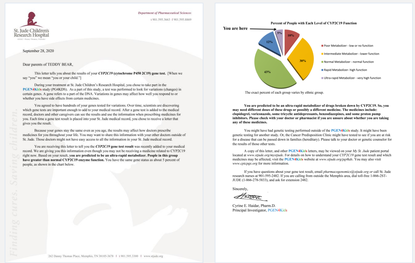


Figure 3. Sample *CYP2C19* result letter posted to online patient portal

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

	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

CPIC Clinical Pharmacogenetics Implementation Consortium

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

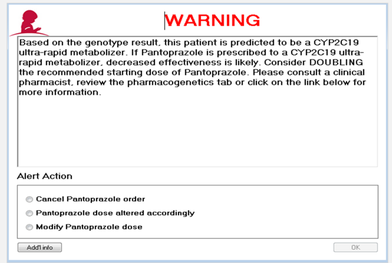


Figure 4. Sample *CYP2C19*/PPI clinical decision support (CDS) alert