AMP recommends minimum set of alleles for all clinical CYP2C9 genotyping testing

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The Association for Molecular Pathology (AMP), the premier global, molecular diagnostic professional society, today published consensus, evidence-based recommendations to aid in the design and validation of clinical CYP2C9 assays, promote standardization of testing across different laboratories and improve patient care. The report, "Recommendations for Clinical CYP2C9 Genotyping Allele Selection: A Joint Recommendation of the Association for Molecular Pathology and College of American Pathologists," was released online ahead of publication in *The Journal of Molecular Diagnostics*.

The AMP Pharmacogenetics (PGx) Working Group is developing a series of guidelines designed to help standardize clinical testing for frequently used genotyping assays. Developed with organizational representation from the College of American Pathologists (CAP) and the Clinical Pharmacogenetics Implementation Consortium (CPIC), the latest report follows a set of recommendations for clinical CYP2C19 genotyping allele selection that was previously published in May 2018. These reports define a minimum set of alleles/variants that should be included in clinical genotyping panels for two of the most important PGx genes. Currently, CYP2C9 tests can produce variable results due to factors such as the choice of tested alleles, targeted testing of populations with varying ethnic backgrounds, as well as the technical performance of the various platforms. These recommendations are intended to facilitate testing by laboratories and improve genotyping concordance across laboratories.

"The AMP PGx Working Group started with CYP2C19 and CYP2C9 genotyping panels due to the widespread adoption of these tests and our desire to help physicians, pharmacists, researchers, and other stakeholders better understand what these panels include and what the test results mean," said Victoria M. Pratt, Ph.D., FACMG, Associate Professor, Director of Pharmacogenetics and Molecular Genetics Laboratories, Indiana University School of Medicine, AMP President and PGx Working Group Chair. "Since these genes are involved in the phase I metabolism of many commonly prescribed medications, this series of recommendations should be implemented with other clinical guidelines such as those issued by CPIC, which focus primarily on the interpretation of genotyping results and therapeutic recommendations for specific drugs."

This new report offers a two-tier categorization of CYP2C9 alleles as an aid for designing CYP2C9 genotyping assays. Using criteria such as allele frequencies in different populations and ethnicities, the availability of reference materials and other technical considerations, the AMP PGx Working Group recommended a minimum set of alleles and their defining variants that should be included in all clinical CYP2C9 PGx tests (Tier 1). The team also defined a Tier 2 list of optional CYP2C9 alleles that do not currently meet one or more of the criteria for inclusion in Tier 1. These recommendations are not to be interpreted as restrictive but to provide a reference guide.

"Pharmacogenetics is a rapidly changing field, and we intend to update these recommendation documents as new data and/or reference materials become available," said Karen E. Weck, MD, Professor of Pathology and Laboratory Medicine, Professor of Genetics and Director, Molecular Genetics and Pharmacogenomics at University of North Carolina Chapel Hill, AMP President-Elect and PGx Working Group Member. "AMP members are among the early adopters of molecular diagnostic testing in clinical settings, and we are committed to

continuously improving professional practice and patient care."

AMP plans on publishing the third companion paper in this series focusing on recommendations on CYP2C9 alleles and additional warfarin sensitivity-associated genes/alleles early next year.

More information: Victoria M. Pratt et al, Recommendations for Clinical CYP2C9 Genotyping Allele Selection: A Joint Recommendation of the Association for Molecular Pathology and College of American Pathologists, *The Journal of Molecular Diagnostics* (2019). DOI: 10.1016/j.jmoldx.2019.04.003