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Current and emerging pharmacogenomic tests for clinical practice

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Primary Topic: Pharmacogenomics
Primary Topic Other: Clinical Pharmacogenomics
Secondary Topic: Personalized Medicine
Presentation Level: Intermediate

Session Overview: Pharmacogenomics testing continues to gain foothold in clinical practice. CYP2C19 genotyping to predict responsiveness to clopidogrel, emerging markers for hepatitis C therapy and combinatorial CYP450 genotyping for psychotropics are some examples. Wider translation of these new pharmacogenomic tests would have a major impact on efficacy and safety.

Target Audience: Physicians, Pathologists, Lab Directors, Clinical Chemists, Technologists, IVD Industry Scientists, and Clinical Pharmacists.

Needs Assessment: Increasingly, there are new and emerging pharmacogenomic markers for personalizing drug therapies in cardiology, infectious diseases and psychiatry. In 2010, the FDA issued a "black box" warning regarding the use of clopidogrel in patients who are poor metabolizers for cytochrome P450 2C19, the principal enzyme involved in converting clopidogrel to the active drug. Clopidogrel inhibits platelet aggregation and is used to treat patients with cardiac disease, especially after percutaneous coronary intervention. Retrospective studies have shown that patients who are slow or intermediate metabolizers have a higher rate of adverse outcomes after stent placement than patients who are wild-type for CYP 2C19. In addition to the role of genotyping for assessing the pharmacokinetic effect, measurement of platelet function is important for assessing the pharmacodynamic effect of clopidogrel. There may also be a role for direct measurement of the active clopidogrel metabolite. Clopidogrel is scheduled to go off patent in 2012, which will widen the gap of drug costs between it and new anti-platelet medications such as prasugrel. Hepatitis C virus infects 170 million people worldwide, and can lead to permanent liver damage and cancer. Interferon alpha plus ribavirin is the standard treatment, effective in 80% of patients with genotype 2 or 3, and 50% effective for type 1b. Dual therapy has severe side effects often requiring dose modification or discontinuation. Recently, GWAS have identified that SNPs near IL28B are strongly associated with outcome of combination therapy. Protective IL28B SNPs are strongly associated with on-treatment viral kinetics and approximately 2-fold increased sustained viral response rates in HCV genotype 1 and 4. New therapies based on protease inhibitors are expected to be soon available and may be used as a triple drug therapy, requiring new pharmacogenomic studies. Psychotropics are metabolized by multiple CYP450 pathways, each of which, in isolation may inadequately account for a drug's pharmacokinetic properties. Emerging research points to the value of a combinatorial approach that considers CYP2C9, CYP2C19 and CYP2D6 as integrative components of a hepatic enzyme system for drug metabolism. This could be employed for patient-specific selection of psychotropics optimized to the innate drug metabolism reserve of each individual. This proposed symposium will explain how integration of clinical and genetic data may be needed for personalizing drug therapy.

Learning Objectives: After this this session, participants will be able to: 1)Understand the potential impacts of pharmacogenomics in the personalized drug therapies of common diseases; 2)Explain the need for pharmacogenomic testing for clopidogrel, Hep C drugs and psychotropics; 3)Identify commercial technologies for these pharmacogenomic testing.

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