

Warfarin Sensitivity Pharmacogenomics

INTRODUCTION

Detects genetic variations of CYP2C9/VKORC1 that directly affect warfarin mode of action and catabolism

INDICATIONS

- Useful for guiding warfarin dosage when initiating therapy
- Reduces risks associated with under/overdosage of warfarin

SPECIMEN REQUIREMENTS

- 5 ml blood in standard EDTA tube shipped at room temperature within 24 hours

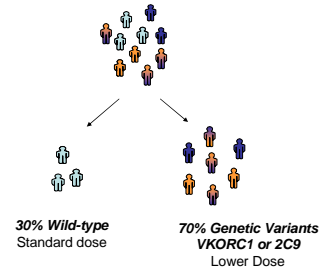
CONSULTATIVE SERVICES PROVIDED

- Suggested starting and maintenance warfarin dosing based on a multivariate regression dosing algorithm that incorporates the usual demographic variables (height, weight, age, medications) and genomic information
- Typically the algorithm suggests on average a 17% reduction in warfarin dose where *2 allele is present, a 30% reduction where the *3 allele is present, or where 1 (heterozygous) VKORC1 allele is present, and a 50% reduction in warfarin dose where the patient is homozygous for the VKORC1 allele

CONSIDERATIONS

- Although commonly prescribed (30 million warfarin prescriptions/year), warfarin can be a dangerous drug, since it is metabolized slowly and has a narrow therapeutic index that is poorly related to serum or tissue concentrations
- Major bleeding complications from warfarin are common and can be deadly—87,000 major bleeding events/year, including 17,000 strokes and 10,000 deaths
- Approximately 70% of the population carries variant CYP2C9 and/or VKORC1 alleles
- In August 2007, the FDA updated warfarin labeling with genetic information on CYP2C9 and VKORC1
- The AACC has issued Laboratory Practice Management Guidelines for CYP2C9 and VKORC1 evaluation and use
- Wide utilization of warfarin sensitivity pharmacogenomics is anticipated to improve patient care significantly
- The dosing algorithm is not a substitute for periodic INR monitoring and individual dose optimization is based on measured INR results

VKORC1 & CYP2C9 Inter-individual Genetic Variation



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