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Genotype-guided dosing of old anticoagulants V/s direct dosing newer anticoagulants

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Coumarin derivatives such as warfarin, acenocoumarol and phenprocoumon constitute the world-wide oral anticoagulant treatment of thromboembolic disorders. Response to therapy to these drugs exhibits significant variation among patients. A significant part of this variation is due to the genetic background of individuals. Specifically, variations both in the genes of cytochrome P450 enzyme *CYP2C9* and vitamin K reductase *VKORC1* influence individual responses to anticoagulant therapy. *CYP2C9**2 and *3 variant alleles result in decreased *CYP2C9* activity affecting coumarin pharmacokinetics, while *VKORC1*-1639G>A polymorphism influences drug effectiveness. Lower doses of coumarins may be best for patients with variations in one or both of these genes and efforts are made to incorporate this knowledge in currently used dosing regimens. Towards this direction, pharmacogenetic-based dosing algorithms are currently tested in large prospective, randomized, pharmacogenetic clinical trials both in Europe and the USA, including EU-PACT (European Union-Pharmacogenetics of Anticoagulant Therapy) Trial. Some of these trials have been completed and their results have recently been published in New England Journal of Medicine. These studies will be presented and placed in context in comparison with clinical studies on effectiveness and safety of newer anticoagulants such as dabigatran and apixaban. The aim is to reduce bleeding or thrombotic events and increase effectiveness of anticoagulant agents, a drug class of major clinical significance.

Biography

Vangelis G Manolopoulos completed his PhD in Patras University, Greece, in 1991. He did Postdoctoral studies at the University of Wisconsin, USA (1992-1995), and the Catholic University of Leuven, Belgium (1995-1998). Since then he belongs to the faculty of Democritus University of Thrace Medical School in Alexandroupolis, Greece where he is Professor at the Department of Pharmacology. He has authored more than 80 indexed publications with approx 1400 citations and serves at the editorial board of several reputed journals. He is vice president of the European Society for Pharmacogenomics and Theranostics (ESPT) and also chairs its Education and Courses Division.

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