S56-4 Pharmacogenomic mechanisms of interinvididual variability in anticoagulation responses to vitamin K antagonists and advances in individualized medicine

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There is a large interindividual variability in the anticoagulation responses to vitamin K-antagonists. While mechanistic explanations for this finding had remained unsolved for long time, recent advances in pharmacogenomics have unveiled that genetic polymorphisms of *CYP2C9* and vitamin K epoxide reductase complex 1 (*VKORC1*) and possibly *CYP4F2* would be involved in the interindividual variability. A whole-genome analysis has confirmed that SNPs of these genes may be genetic factors associated with the interindividual variability of warfarin doses. A multivariate analysis also showed that these genetic factors and clinical variability (age, body weight and concomitant administration of drugs that may be associated with metabolic interaction) would account for approximately 60% of interindividual variability of warfarin doses. A prospective randomized clinical study performed mainly in Caucasians has demonstrated that the induction of anticoagulation therapy with a genomic information assisted-warfarin dosing regimen was largely equivalent to one of the most sophisticated empirical dosing algorithms in terms of safety and efficacy. Because there are population differences in the genetic polymorphisms of *CYP2C9* and *VKORC1*, confirmative clinical studies should be carried out in Asian patients before the genomic information assisted-warfarin induction therapy is introduced in clinical use.