Results: In the study group, allele A was 8%, in the control group 4% (p = 0.1; chi-square). The following genotypes distribution was observed in the study group: AA – 0.02; AG – 0.13; GG – 0.83. In the control group the following genotype distribution was observed: AA – 0.01; AG – 0.05; GG – 0.94. Distributions corresponded to Hardy-Weinberg equilibrium.

Conclusion: In our prospective study, we observed tendency to genetic predisposition to higher activity of CYP3A5 in women with stillbirth compared with matched women with normal pregnancy. The results, however, did not reach statistical significance, which may demonstrate either lack of real association or insufficient number of subjects recruited. The observation needs to be proved or disproved in a larger population.

Disclosure of Interest: None declared.

PP153—EVALUATION OF THE RELATIONSHIPS BETWEEN ABCB1 C3435T AND G2677T/A POLYMORPHISMS AND CLINICAL RESPONSE TO VENLAFAXINE IN PATIENTS WITH MAJOR DEPRESSIVE DISORDER

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Introduction: Venlafaxine, as a substrate of p-glycoprotein, is a widely used serotonin-noradrenaline reuptake inhibitor (SNRI). The aim of the study is to investigate the influence of ABCB1 G2677T/A, C3435T polymorphisms on efficacy of venlafaxine.

Patients (or Materials) and Methods: Patients (n = 52) who met the Diagnostic and Statistical Manual of Mental Disorders Fourth Edition-IV criteria for major depressive disorder (MDD) were enrolled in the study. All patients had affirmed for once a day administration of venlafaxine at 8:00 to 9:00 AM during the study. Protocol visits were completed at baseline, 1st, 2nd, 4th, and 6th weeks. The clinical response to venlafaxine was evaluated by psychiatrists using 17-item Hamilton Rating Scale for Depression (HAM-D17).

Results: Our results showed that there is no correlation between efficacy and tolerability of venlafaxine and ABCB1 gene C3435T > A and C3435T > T polymorphisms. But carriers of the TT genotype for 3435C>T polymorphism could be tended to be poor responder (Table).

Conclusion: Although our results showed that there is no correlation between efficacy of venlafaxine and ABCB1 G2677T/A, C3435T polymorphisms, we couldn’t reach the sufficient patient number. There is need for studies with sufficient patient number and haplotype analysis including also ABCB1 C1236T polymorphism in MDD patients.


PP154—PERSONALISING HEALTH CARE: FEASIBILITY AND FUTURE IMPLICATIONS FOR ALL STAKEHOLDER GROUPS INCLUDING AUTHORITIES, PHYSICIANS AND PATIENTS

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Introduction: The promise of personalized care has not always translated into improvements in patient care. There are concerns among payers that advice for certain genetic tests has been revoked, diagnostic tests can be costly, and there is fragmentation of funding of care including tests. In addition, pharmaceutical companies are seeking high prices for new targeted drugs through designating them as orphan drugs. Consequently, there is a need to integrate current knowledge about the value of genetic, biomarkers, prognostic tests and targeted drug therapies from a health authority perspective to provide future guidance.

Patients (or Materials) and Methods: This will be achieved by (1) reviewing the current literature regarding personalized medicine; (2) appraising key funding, organizational, and health care issues that need to be addressed especially from a health authority perspective; and (3) suggesting future avenues for all key stakeholder groups to enhance future funding and utilization of new personalized approaches to improve future patient care. The latter will be achieved through an iterative process.

Results: Multiple findings are consolidated under headings. These include (1) general considerations incorporating definitions and the need for different approaches to progress personalized medicine; (2) knowledge about the influence of pharmacogenomics on response and toxicity of drug therapies using current examples including cases where recommendations have recently been revoked; (3) knowledge of the value of biomarker tests to target treatment approaches; (4) challenges and concerns including the potentially high cost of tests and targeted therapies and current fragmentation of funding; and (5) key issues for health care funding bodies to address to enhance funding for new diagnostic/prognostic tests as well as new targeted therapies. Guidance is given on potential ways forward for all key stakeholder groups including reviewing key medical, ethical, legal,
PP155—PREVALENCE OF GENE POLYMORPHISM SLC01B1 IN PATIENTS WITH DYSLIPIDEMIA AND SYSTEMIC ATHEROSCLEROSIS IN RUSSIAN POPULATION

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Introduction: The statin lipid-lowering efficacy and safety varies widely among patients. This is mainly interpersonal differences can be explained by genetic factors. The purpose of this study was to investigate the prevalence of allelic variants (polymorphism) of the gene SLC01B1 *5 (c.521T>C, rs4149056), which encodes a polypeptide involved in the removal of statins by the liver into the bile, as well as prediction of myopathy in patients who are to use of statins. The frequency of genotypes in SLC01B1 in the Russian population is not known in other European ethnic groups is 8% to 20%.

Patients (or Materials) and Methods: The study is based AGL Hospital Road station Yaroslavl OJSC “Russian Railways” GBOU VPO Yaroslavl State Medical Academy, Russian Ministry of Health in 2012–2013. The study included 377 patients with dyslipidemia and systemic atherosclerosis. Of these, 226 men (59.95%) and 151 women (40.05%); the mean age was 52.58 ± 12.21. All patients underwent determination of single nucleotide polymorphisms SLC01B1 *5 using real-time PCR thermocycler with IQ 5 (firma Bio-Rad).

Results: Identified gene polymorphisms SLC01B1 *5: heterozygous genotype s.521 vehicle in 106 patients (28.12%) and homozygous genotype CC s.521 - in 14 patients (3.71%), which is associated with an increased risk of myopathy with statins and the need for correction of the maximum dose to be lower compared with the TT genotype s.521 ("wild" type).

Conclusion: The frequency of the heterozygous genotype (s.521TS) is 28%, and homozygous genotype (s.521SS) - 4% of patients with dyslipidemia and systemic atherosclerosis, which requires a reduction of the therapeutic dose of statins to one half and one quarter, respectively. Thus, the holding of pharmacogenetic testing can be useful for your personal selection of the dose of statin to maximize the effectiveness and safety of treatment.

Disclosure of Interest: None declared.

PP156—CYP2D6 GENOTYPES AND PREDICTION OF METABOLIC PROFILES IN THE PORTUGUESE POPULATION: CLINICAL IMPLICATIONS

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Introduction: CYP2D6 codes for a protein that is vastly involved in metabolism of various substances. Different metabolic profiles determine the processing of xenobiotics and endobiotics, thereby influencing disease risk, therapeutic efficacy and side effects, or toxicity of xenobiotics. The aim of this work was to characterize CYP2D6 polymorphisms and predict metabolic profiles in the Portuguese population.

Patients (or Materials) and Methods: A total of 300 Portuguese unrelated adult healthy volunteers were studied. Genetic analysis included allelic discrimination and copy number determination with TaqMan® probes by real-time PCR and allele duplications of CYP2D6*, CYP2D6*2, CYP2D6*4, and CYP2D6*10 were confirmed by long PCR and PCR-RFLP.

Results: The percentages of poor and ultrarapid metabolizers found in this Portuguese population were 6.3% and 4.7%, respectively. Accordingly, it is estimated that, taking into account the number of inhabitants estimated by CENSUS 2011 (10,562,178), there are ~665,417 poor metabolizers (PM) and 496,422 ultrarapid metabolizers (UM) in Portugal. The frequency of extensive metabolizers (EM) and intermediate metabolizers (IM) is in agreement with previous studies.

Conclusion: The allelic frequencies were similar to other studies of European populations, with some exceptions, such as for CYP2D6*10, which is higher in Portuguese population and for CYP2D6*6 and duplication of *1 and *2, that present lower frequencies in the present study. After this study, we could evaluate the most important CYP2D6 variants in the Portuguese population and predict metabolic profiles. The data presented here are noteworthy for determination of the genetic variability influencing CYP2D6 activity, to improve the effectiveness and safety in the xenobiotics exposure, working also as a strong tool for clinical practice and development of individualized pharmacotherapy.

Disclosure of Interest: None declared.

PP157—CYP2C9 ALLELE FREQUENCIES AMONG THREE COSTA RICAN ETHNIC GROUPS COMPARED WITH HISPANIC POPULATIONS

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Introduction: CYP2C9 is involved in the metabolism of drugs such as warfarin, losartan, fluoxetine, and NSAIDs. The frequency of CYP2C9*2, allele causing decreased enzyme activity, has been reported to be lower in Amerindian and Admixed populations (from Cuba, Nicaragua, Ecuador, and Mexico), than in Spanish-Caucasian populations.1,2 The aim of this study was to determine CYP2C9 allele frequencies in 3 Costa Rican ethnic groups and to compare the results with frequencies previously reported for Hispanic populations.

Patients (or Materials) and Methods: The CYP2C9 alleles (*2, *3 and *6) were analyzed by real-time-PCR among 375 healthy individuals belonging to 3 ethnic groups living in Costa Rica: Amerindians (AM; n = 193), Afro-Caribbean (AC: n = 45) and Costa Rican Mestizo population (CRM; n = 137). These frequencies were compared with a population of Spaniards (SP n = 327) 2 previously published.

Results: The frequency of CYP2C9*2 was significantly lower in the AM (2.8%) and CRM (7.7%) than in the SP group (16%; P < 0.05).