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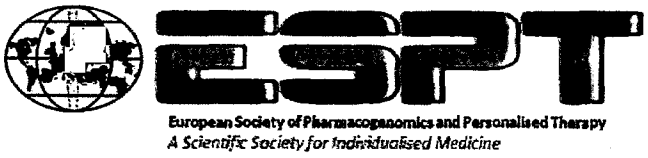
Poster Abstracts*)



Integration of Pharmacogenomics in clinical decision support

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enzyme-coupled detection scheme resulting in a genotype-specific precipitation pattern. Evaluation is done automatically by a software analysis system within seconds.

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1 Bank et al., Pharmacogenomics 2015;16(7):681-7; in this study the former OEM product name GenoChip CYP2D6 was used.

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Effects of CYP3A5 *3 polymorphism of both donors and recipients over chronic nephropathy in adult recipients of liver transplant treated with tacrolimus: cohort study

ABSTRACT n° 67

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Background: Calcineurin inhibitors (CI) metabolites in tissues can greatly exceed CI levels in blood, being potentially toxic. The most relevant polymorphism of their main metabolizing enzime, CYP3A5 *3 vs. *1, usually shows an association of higher metabolites concentration and risk of chronic CI nephrotoxicity (CN) in expressers (*1/*1 or *1/*3) compared with non-expressers (*3/*3) [1]. However, there are studies with opposite results.

Objective: To evaluate the impact of CYP3A5 *1 or *3 genotypes of donors and recipients over CN in adults liver transplant recipients treated with tacrolimus.

Design: Patients with at least three years post-transplant follow-up, that gave their written consent were included. Patients were genotyped using MassArray (Sequenom) and consequently divided in two groups, expressers and non-expressers of CYP3A5, correlating these data with their clinical data retrospectively obtained from electronic medical records. Multivariable Ridge regression was performed to assess the contribution of clinical variables.

Results: 77 patientes were included. Genotype frequencies were as follows: CYP3A5 *1/*1, *1/*3, and *3/*3 in 4, 12, and 61 of donors, and in 3, 10 and 64 of recipients, respectively. The incidence of CN was affected by the CYP3A5 expresser genotype in donors (expresser vs no-expressers: 37.5% vs. 11%, P =0.01; OR 4.2, 95% CI 1.02 -19.8]. This effect was higher if the recipient was also CYP3A5 expresser.

Conclusions: CYP3A5 *1 donors provide susceptibility for developing CN associated with tacrolimus. This efect is more pronounced in *1 recipients. This could be the result of a toxic action of tacrolimus metabolites in renal tissue, with lower tacrolimus blood concentrations.

[1] Rojas L, Neumann I, Herrero MJ, Bosó V, Reig J, Poveda JL et al. Effect of CYP3A5*3 on kidney transplant recipients treated with tacrolimus: A systematic review and meta-analysis of observational studies. Pharmacogenomics J. 2015;15(1):38-48.

The application of a new HPLC-FL method in determination of ALDH1 activity in plasma and serum

ABSTRACT n° 68

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Abstract

Introduction: ALDH1 is ubiquitously distributed in the adult epithelium of testis, brain, eye lens, kidney, lungs. It is also found in the liver, pancreas and stomach mucosa. In blood is located mainly in erythrocytes. According to various researches aldehyde dehydrogenase class 1 (ALDH1) is an enzyme with no

detectable activity in plasma/serum of healthy people using fluorimetric method due to low sensitivity. Thus we have previously created and optimized the HPLC-FL method for determination of this enzyme activity in plasma.

Methods: In this paper this HPLC-FL method (using 6-methoxy-2-naphthaldehyde as a substrate and NAD+ as a coenzyme) was applied to determination of ALDH activity in serum and plasma of healthy people (n=25) and people with elevated liver enzymes (n=15). The influence of hemolysis on the results was evaluated as well (n=5).

Results: Our results showed relatively low level of ALDH1 activity in healthy people with median ± IQR of 0.32±0.58 mU in plasma and 0.65±0.90 mU in serum. As predicted the level of the enzyme was significantly higher in group with elevated liver enzymes ($p<0.00001$) with median ± IQR of 4.8±4.6 mU in serum and 4.8±5.8 mU in plasma, respectively. The hemolysis also affected the ALDH1 level ($p<0.00001$).

Conclusion: The activity of ALDH1 was measurable using the new HPLC method in plasma and serum of both healthy and liver disease group. Since the ALDH level is significantly higher in group with higher liver enzymes, further research is needed to indicate the possible diagnostic or prognostic value of this marker. The rejection of hemolyzed samples is recommended.