(LDL), high density lipoprotein (HDL), triglycerides (TG), alanine- aminotransferase (ALT) and aspartate aminotransferase (AST), liver size and fibrosis before and during treatment with sebelipase alfa, and adverse events. From the outpatient programme were obtained dose, administrations and weeks of treatment. The efficacy was evaluated by normalising the analytical values of the lipidic and liver profiles in three patients who participated in the clinical trial until April 2018.

Results Three male brothers 12, 15 and 17 years' old diagnosed with LALD before 5 years, heterozygous for mutation in the LIPA gene c.894G>A, c.256C>T. Before the trial, patients presented abnormal analytical values (except TG), hepatomegaly and fibrosis. Patients received continuous treatment with sebelipase-alfa at a dose of 1 mg/kg/2 weeks intravenously. Preparation of the medication was carried out by the hospital pharmacy service. In April 2018, after 225, 183 and 114 weeks of treatment respectively, all three patients maintained the values analysed in the range of normality (except HDL in two and TG in one patient). Hepatomegaly reversed in all patients. The means of the values and of the percentages of variation to the basal were: cholesterol 150.66 ± 22.89 mg/dL (−34.19%), LDL 89.33 ± 12.20 mg/dL (−46.90%), HDL 35.66 ± 6.35 mg/dL (+1.55%), AST 30.66 ± 4.04 IU/L (−64.88%), ALT 21.33 ± 4.93 mg/dL (−65.99%) and TG 130 ± 85.91 mg/dL (+2.12%). Concerning safety, two patients who suffered diarrhoea, and adverse effects related to the infusion were not reported.

Conclusion LALD is a rare disease, and sebelipase-alfa is the first drug authorised for its treatment. The response to treatment with sebelipase-alfa has been favourable from the beginning, with an improvement in the studied variables and a good safety profile in the reported cases.

REFERENCES AND/OR ACKNOWLEDGEMENTS

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No conflict of interest.

5PSQ-008 CYP2C19 SNP'S INFLUENCE ON CLOPIDOGREL RESPONSE IN PERIPHERAL ARTERY DISEASE PATIENTS

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Background Clopidogrel is a prodrug, metabolised to its active metabolite especially by the CYP2C19 enzyme. The effect of CYP2C19 polymorphisms on clopidogrel efficacy in coronary disease had been widely researched. The clopidogrel label recommends testing the CYP2C19 loss of function alleles before the start of the treatment and the DPWG and CPIC pharmacogenetic dosing guidelines recommend switching clopidogrel in case of carrying the CYP2C19*2 SNP in coronary patients with stent. This remains unstudied in peripheral artery disease (PAD) patients.

Purpose Explore the influence of CYP2C19 genetic polymorphisms on clopidogrel response in PAD patients.

Material and methods Peripheral artery disease patients treated with clopidogrel after percutaneous transluminal angioplasty were recruited. They were tested for carrying the CYP2C19*2, *3 (loss of function (LOF)) and *17 (gain of function (GOF))

allele. The primary endpoint was the occurrence of atherothrombotic ischaemic events, diagnosed by ultrasound imaging, during 12 months' follow-up. Furthermore, we collected data about clinical parameters (age, sex, ethnicity), co-medication during follow-up, vascular risk factors and surgical parameters.

We tested the association between carrying LOF or GOF alleles and the primary endpoint in a univariate analysis, and multivariate analysis including those clinical parameters previously related to clopidogrel response. OR and HR were calculated and P-values<0.05 were considered statistically significant.

Results Seventy-two patients were recruited, mean age 67.4 ± 9.4 years, 22.2 females and 100% were caucasians. Carrying CYP2C19 LOF alleles was significantly associated with the primary endpoint in the single analysis (OR=4.49; 95% CI: 1.45 to 13.84; p=0.009), in the multivariate analysis (OR=4.89; 95% CI: 1.32 to 12.83; p=0.018). This association remains significant if we perform a survival analysis (HR=4.07; 95% CI: 1.80 to 9.20; p≤0.001). On the other hand, carrying CYP2C19 GOF alleles was not related to the primary endpoint.

Conclusion CYP2C19 LOF polymorphisms show a higher effect on clopidogrel response in PAD patients than that provided in acute coronary syndrome patients. These SNPs may be used as genetic markers of clopidogrel response in PAD patients. Clopidogrel treatment may be guided by CYP2C19 genotyping, although further analysis should be performed.

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No conflict of interest.

5PSQ-009 CYP2C19 SNP'S INFLUENCE ON CLOPIDOGREL RESPONSE IN CEREBROVASCULAR DISEASE PATIENTS: FINAL RESULTS

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Background Clopidogrel is a prodrug, which is metabolised to its active metabolite especially by the CYP2C19 enzyme. Carrying some polymorphisms, contained in the DNA region encoding the CYP2C19 expression, have shown a significant association with a lack of clopidogrel efficacy among coronary patients. This association had been widely researched and the clopidogrel label recommends testing the CYP2C19 loss of function alleles before the start of the treatment, even DPWG and CPIC pharmacogenetic dosing guidelines, and recommend switching clopidogrel in case of carrying the CYP2C19 loss of function alleles in coronary patients with stent. This remains unstudied in cerebrovascular-disease patients.

Purpose Explore the influence of CYP2C19 genetic polymorphisms on clopidogrel response in cerebrovascular disease patients.

Material and methods Patients after stroke or transient ischaemic event (TIA) treated with clopidogrel after hospitalisation were recruited. These were tested for carrying the CYP2C19*2, *3 (loss of function (LOF)) and *17 (gain of function (GOF)) alleles. As primary endpoint we considered