results obtained.

86. (231) **MYD88 AND CXCR4 MUTATIONS IN PATIENTS WITH WALDENSTRÖM MACROGLOBULINEMIA AND IGM-MGUS**

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Waldenström Macroglobulinemia (WM) is a lymphoplasmacytic lymphoma with involvement of the bone marrow (BM) and the presence of a monoclonal IgM gammopathy. It is usually preceded by an IgM monoclonal gammopathy of undetermined significance (MGUS). WM and IgM-MGUS are associated to *MYD88* gene mutations, particularly $MYD88^{L265}$, and *CXCR4* gene mutations, being $CXCR4^{S338X}$ the most common variant. These mutations are of importance in diagnosis, treatment selection and response evaluation. We have analyzed *MYD88* and *CXCR4* mutations in patients with WM and IgM-MGUS in order to established their frequency and distribution in our cohort. BM or peripheral blood genomic DNA was used; ASO-PCR and bidirectional Sanger sequencing were performed. The study was approved by the local Ethic Committee; all individuals provided their informed consent. Thirty-one patients with WM: 22 at diagnosis, 4 in relapse, 5 during post treatment control (13 males; mean age 67.5 years) and 12 with IgM-MGUS (5 males; mean age 76.9 years) were evaluated. The activating mutation $MYD88^{L265P}$ was found in 81.8% WM patients at diagnosis, 100% at relapse, 0% in post treatment control and in 41.6% IgM-MGUS. *CXCR4* mutations were found in 2/22 (9%) cases with WM: one patient showed $CXCR4^{S338}$ C>G transversion at nucleotide 1013 and the other $CXCR4^{R334X}$ C>T, c.1000C<T variant, both resulting in the generation of a stop codon. Analysis of data showed the following distribution: $MYD88^{MUT}/CXCR4^{WT}$ (85.7% cases), $MYD88^{MUT}/CXCR4^{MUT}$ (9.5%) and $MYD88^{WT}/CXCR4^{WT}$ (4.8%). No *CXCR4* mutations in the IgM-MGUS patients were found. Our cohort showed *MYD88* positivity within reported values, instead we found a low frequency of *CXCR4* mutations. Although ASO-PCR is highly sensitive, it is advisable to analyze BM samples in relapse evaluation. To our knowledge, this is the first analysis of both mutations in patients with WM and IgM-MGUS from our country, being of significance in the way of a personalized medicine.

87. (234) **IMPACT OF HYPERGLYCAEMIA AND THE THERAPEUTIC ACTION OF METFORMIN ON THE LENGTH OF THE TELOMERES.**

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Objectives: To analyze the absolute telomere length (LTa) in individuals with altered fasting glucose levels compared to individuals with normal fasting glucose levels. Also, we performed a prospective controlled study to evaluate the variation in LTa in patients with decompensated type 2 Diabetes (T2D) before and after a treatment metabolic compensation.

Materials and Methods: The study included 246 individuals of both genders, which were divided according to normal fasting glucose levels <110 mg/dl (NFG group) and alterated fasting glucose levels ≥110 mg/dl (AFG group). In addition, they were divided by age groups into: under 25 years (<25Y), between 25 and 50 years (25-50Y) and over 50 years (>50Y). A subgroup of 30 patients with newly diagnosed T2D was studied, at the beginning (T0), and at 6 months (T6) of a pharmacological treatment and hygienic-dietary measures. Biochemical and clinical variables were analyzed for all the individuals. The LTa were determined by qPCR. Statistical analyzes were performed with GraphPad Prism and SPSS.

Results: LTa significantly correlated with age (r=-0.21, p=0.009) and the increase in blood glucose ranges (r=-0.32, p<0.001). The NFG group showed a significantly higher LTa than the AFG group (p<0.001), also when comparing the same age group: <25Y (p=0.013); 25-50Y (p=0.002) and> 50Y (p=0.002).

The T2D subgroup showed a negative association between the variation in LTa and age (r=-0.12, p=0.02) after 6 months of treatment. The most relevant result was the positive and significant association found between the variation of LTa and the treatment of dose of Metformin (r=0.003, p=0.007).

Conclusion: Glycemic control could prevent accelerated telomere shortening and reduce the risk of developing age-related diseases. The increase in LTa after treatment in T2D was associated with younger individuals and the use of higher doses of Metformin. LTa can be an effective marker for early intervention in hyperglycemia.

88. (274) **GENETIC VARIANTS OF CYP2E1 AND ITS RELATIONSHIP WITH PORPHYRIA CUTANEA TARDA DEVELOPMENT**

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Porphyria Cutanea Tarda (PCT) is due to a partial deficiency in uroporphyrinogen decarboxylase (URO-D); there are two main types: hereditary (H-PCT) or acquired (A-PCT). The cytochrome variants P-450, CYP1A1 and CYP1A2 alter their drug metabolizing capacity generating metabolites that can inhibit URO-D, increasing susceptibility to trigger Porphyria. The product of the CYP2E1 variant metabolizes ethanol, known as a porphyrinogenic agent. The objective was to investigate the role of CYP2E1*5B (NG_008383.1:g.3979C>T; rs2031920) and CYP2E1*7B (NG_008383.1:g.4963G>T; rs6413420) variants in PCT development. H-PCT (30), A-PCT (31) and control (33) groups were genotyped by RFLP-PCR and sequenced when the band pattern was unclear. When we analized CYP2E1*5B, the frequencies of the reference homozygote were similar to those of the heterozygote, the alternative homozygote were not present and C allele was the most common. There was no significant risk association between this variant and PCT. Studying CYP2E1*7B, the reference homozygotes genotypes were more frequent than heterozygotes and both have higher frequencies than alternative homozygotes; the frequency of G/T was significantly higher in H-PCT individuals compared to A-PCT (p=0.045), being the reference allele the most frequent. Comparing H-PCT vs A-PCT, G/T vs G/G gave a significant risk association (OR=4.11; 1.01<CI<17.2; p=0.044), being T allele for these same groups of not significant risk. The study of risk haplotypes for CYP2E1*5B/*7B in both types of PCT vs control gave T-T (non-significant differences). Since both variants are associated with an increase in transcriptional activity of CYP2E1 gene, it is suggested that they could be a risk factor to trigger PCT. These studies are valuable for personalized medical advice in order to prevent carriers from being exposed to porphyrinogenic agents.

89. (305) **DESIGN OF A CRISPR CAS9-BASED METHOD TO ASSESS THE FUNCTIONAL PATHOGENICITY OF LDL RECEPTOR GENE VARIANTS IN FAMILIAL HYPERCHOLESTEROLEMIA**

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