

P0512 **Resistance to NS5A inhibitors in chronic hepatitis C patients infected with subtype 1a and 1b from Croatia**

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**Background:** NS5A inhibitors are one of the treatment options for chronic hepatitis C in Croatia, in combination with other direct acting antivirals (DAA). Testing for NS5A inhibitors resistance associated substitutions (RAS) is not part of the recommended pretreatment workup. Baseline prevalence of resistance to NS5A inhibitors varies in different geographical regions (6-16%) while there are no literature data for Croatia. The aim of this study was to analyze the frequency of RAS in persons infected with HCV subtype 1a and 1b prior to treatment with DAA.

**Materials/methods:** The study included 64 persons with chronic hepatitis C, 33 infected with HCV subtype 1a and 31 infected with subtype 1b receiving clinical care at the Department of Viral Hepatitis of the University Hospital for Infectious Diseases, Zagreb and Croatian Reference Center for Viral Hepatitis. HCV subtype was determined by using Inno LiPA genotyping test. Detection of substitutions associated with resistance to NS5A inhibitors was performed by population-based sequencing. Geno2Pheno algorithm was used for the interpretation of resistance analysis results.

**Results:** Resistance to NS5A inhibitors was detected in 10 of 64 (15.6%) of patients, 4 patients with subtype 1a (12.1%) and 7 patients with subtype 1b (22.6%). Additionally, five patients carried mutations that cause reduced susceptibility to NS5A inhibitors, 4 patients in subtype 1a and 1 patient in subtype 1b. Clade I of subtype 1a was detected in 18, and clade II in 15 patients. Mutations were equally distributed between clades. Three patients infected with subtype 1a carried the same RAS, Q30R which is associated with resistance to daclatasvir, elbasvir, ledipasvir and ombitasvir, and one patient carried M28T mutation. M28V mutation that causes reduced susceptibility to ombitasvir was detected in 4 patients. L31I mutation that causes reduced susceptibility to daclatasvir was detected in one subtype 1b patient as a single mutation and in additional 3 patients along with other RAS. Y93H RAS was found in 7 patients infected with subtype 1b.

**Conclusions:** The results of this study have shown a high prevalence of RAS to NS5A inhibitors in patients with chronic hepatitis C. Different resistance patterns were observed for subtypes 1a and 1b.