SAFETY AND EFFICACY OF THE COMBINATION OF PEGYLATED INTERFERON, RIBAVIRIN AND TELAPREVIR IN TREATMENT–NAÏVE AND TREATMENT-FAILURE GENOTYPE 1 CHRONIC HEPATITIS C PATIENTS WITH ADVANCED HEPATIC FIBROSIS OR COMPENSATED LIVER CIRRHOSIS

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Introduction. Telaprevir is a member of new class of drugs being developed for chronic hepatitis C (CHC): Direct Acting Antiviral (DAA) agents. Unlike pegylated interferon and ribavirin, DAA agents act directly on

hepatitis C virus replication cycle. Telaprevir is a specific inhibitor of the hepatitis C virus (HCV) NS34A serine protease, which is essential for viral replication. Clinical studies in treatment-naïve and treatment-failure subjects have demonstrated a statistically significant benefit (higher rate of sustained virological response (SVR)) by adding Telaprevir to the pegylated interferon and ribavirin standard regimen for the treatment of subjects chronically infected with genotype 1. Patients with advanced hepatic fibrosis or cirrhosis have a lower likelihood of SVR and also have the greatest risk of liver failure, hepatocellular carcinoma and death. Making Telaprevir available to this difficult-to-treat population may reduce the risk of long-term complications associated with HCV infection.

Aim. To examine the safety and virologic response of treatment with telaprevir in combination with pegylated interferon and ribavirin in genotype 1 CHC treatment-naïve and treatment–failure patients with bridging fibrosis or liver cirrhosis.

Results. 54(17 treatment-naïve/37 treatment–failure) genotype 1 CHC patients with average age 45.17±10.55 years, BMI 28.15±5,53 were included in to the retrospective cohort study. F3/F4 stage of fibrosis (METAVIR) was found in 37(68.5%)/17(31.5%) subjects, respectively. 39(72.2%) patients had hepatosteatosis. High baseline viral loud (HCV-RNA≥600,000 IU/ml) was found in 46(85.2%) patients. Out of 37 treatment-failure subjects: 15(40.5%) were previously non-responders, 10(27.0%) achieved a partial response and 12(32.4%) were relapsers. SVR was achieved in 12(70.6%) treatment-naïve patients and in 24(64.9%) treatment-failures. 4(26.7%) previous non-responders, 9(90.0%) partial responders and 11(91.7%) previous relapsers achieved SVR, respectively. For 1(1.9%) patient treatment was discontinued due to drug induced severe skin rash, 3(5.6%) patients discontinued treatment by themselves. The lowest average hemoglobin (117g/l±15.1) and platelet count ($152x10^9$/l±60.3) was observed at week 12, neutrophil count ($1.6x10^9$/l±0.65) – at week 24. Due to drug-induced anemia at week 4, 12 and 24 ribavirin dose was reduced in 9, 9 and 2 patients, respectively. Pegylated interferon dose was adjusted in 3 and 2 patients at week 12 and 24, respectively.

Conclusions. Significantly improved SVR (70.6%) with triple therapy was achieved in treatment-naïve patients as compared with historical SVR results (44%) in dual therapy (ADVANCE study). In treatment-failure group statistically significant benefit in achievement of SVR was demonstrated in previous relapsers (p=0,001) and partial responders (p=0,004) in compare to previous non-responders. Most common adverse effects (anemia, rash,

pruritus, thrombocytopenia, neutropenia) gradually resolved after the treatment completion. Monitoring of blood count at regular intervals and ribavirin and/or pegylated interferon dose reduction is valuable for management of drug induced hematological side effects.