Type: Poster Presentation

Final Abstract Number: 57.007
Session: Virology and Viral Infections (Non-HIV) I
Date: Friday, April 4, 2014
Time: 12:45-14:15
Room: Ballroom

Expression of Mx1, OAS1, PKR (EIF2AK2) and TP53 genes during treatment of chronic HCV patients

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Background: Interferon stimulated genes (ISGs) - *Mx1*, *OAS1* and *PKR* (*EIF2AK2*) play a key role in antiviral response against HCV infection. It is suggested that ISGs pre-activation is associated with anti-HCV treatment failure. Moreover, it was observed that interferon may stimulate transcription of *TP53*gene. The aim of this prospective study was to examine the association between *Mx1*, *OAS1*, *PKR* (*EIF2AK2*) and *TP53* expression and response to pegIFN+RBV treatment in CHC patients.

Methods & Materials: Genomic RNA was obtained from 35 CHC patients (genotype 1b) treated with pegIFN-α + RBV. *Mx1*, *OAS1*, *PKR* and *TP53* expression levels were quantified by real-time PCR using TaqMan probes. Serum HCV-RNA was measured by quantitative RT-PCR with specific primers from 5'noncoding region. Analyses were performed before pegIFN+RBV administration and then at 4. and 12. week of treatment.

Results: RVR and cEVR was achieved by 13 (37.1%) and 10 (28.6%) patients, respectively. 12 (34.3%) did not response to pegIFN+RBV treatment during 12 weeks (PNR). The mean values of baseline viral loads were comparable in RVR, cEVR and PNR group (6.7, 7.3 and $3.5x10^4$ IU/ml, respectively). Median expression levels of classical ISG (*Mx1*, *OAS1*, *PKR*), but not *TP53*: increased during CHC treatment; was higher in RVR compared to cEVR and PNR group before therapy; more noticeable increased in cEVR and PNR and than in RVR patients at week 4., was stable or poorly decreased in RVR, was stable or poorly increased in cEVR and noticeable decreased in PNR group between week 4. and 12. of therapy.

Conclusion: Increase in ISGs expression at week 4. of therapy might depend on baseline HCV-RNA level. ISGs expression may predict outcome of pegIFN + RBV treatement – pre-activation of the endogenous interferon system is associated with RVR and thereby with high likehood of achieving SVR. Treatment failure during the first 12 weeks of anti-HCV therapy (PNR) may be related to noticeable decrease in ISG expression between week 4. and 12. There is no association between TP53 expression and interferon action during treatment of CHC patients.

This research was supported by National Science Centre grant no 2011/01/B/N26/04258

http://dx.doi.org/10.1016/j.ijid.2014.03.1068

Type: Poster Presentation

Final Abstract Number: 57.008
Session: Virology and Viral Infections (Non-HIV) I
Date: Friday, April 4, 2014
Time: 12:45-14:15
Room: Ballroom

IL28B polymorphism and virological responseduring 12 weeks of pegylated interferon and ribavirin treatment in Polish chronic hepatitis C patients

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Background: Identification of molecular markers playing role in predicting anti-HCV treatment outcome would facilitate therapy optimizing. GWAS has demonstrated that genetic polymorphism at rs12979860 (C/T) near IL28B gene is a strong predictor of Sustained Virological Response (SVR) in chronic hepatitis C (CHC) patients treated with pegylated interferon α and ribavirin (pegIFN-α + RBV). Moreover, monitoring viral kinetics can help identify patients with high chances of treatment success. The aim of this study was to examine predictive value of IL28B SNP rs12979860 (C/T) for on-treatment virological response in Polish CHC patients treated with pegIFN-α and RBV.

Methods & Materials: The study involved 35 CHC patients (HCV genotype 1b). To determine treatment effect, serum HCV-RNA was measured on the first day of therapy and then after 4 and 12 weeks of treatment by one-step quantitative RT-PCR. Genomic DNA, isolated from peripheral blood lymphocytes, was used for IL28B rs12979860 (C/T) genotyping by High Resolution Melting (HRM) method.

Results: Results were confirmed by DNA sequencing. 13 patients (37.1%) became HCV RNA negative at week 4. (RVR - Rapid Virological Response) and 10 (28.6%) at week 12. (cEVR - complete Early Virological Response). 12 patients (34.3%) did not achieve virological response until 12. weeks (PNR - Primary Non-Response). The mean baseline viral load values were comparable among three groups - $6.69x10^4$ IU/ml *vs* $7.32x10^4$ IU/ml *vs* $3.51x10^4$IU/ml in RVR, cEVR and PNR group, respectively. The rs12979860 CC, CT and TT genotypes were found in 8 (22.9%), 23 (65.7%), 4 (11.4%) patients, respectively. Among patients with genotype CC, 75% achieved RVR and 25% achieved cEVR. Among CT genotype, RVR, cEVR and PNR were observed in 30.5%, 30.5% and 39% of patients, respectively. 25% of patients with the genotype TT achieved cEVR and 75% achieved PNR. Favorable CC was not observed in PNR and unfavorable TT genotype was not observed in RVR group.

Conclusion: The results confirm thatIL28Brs12979860 C/T polymorphism may predicts virological response in CHC during early phase of pegIFN + RBV treatment.

Research was supported by National Science Centre grant no 2011/01/B/N26/04258.

http://dx.doi.org/10.1016/j.ijid.2014.03.1069