Disease Progression During Advanced Fibrosis: IL28B Genotype Or HCV RNA Levels?

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We appreciate the insightful comments by Grebely et al. regarding the role of HCV RNA levels on disease outcome among persons with advanced chronic hepatitis C. We have performed the requested analysis to address the issue. HCV RNA levels were available on all patients from the HALT-C cohort but only from 108 of the 246 patients from the NIH cohort. In the cross-sectional analysis, the mean HCV RNA level was higher between the HALT-C cohort compared to the NIH cohort, 6.40 log_{10} IU/ml (SD 0.56) versus 5.58 log_{10} IU/ml (SD 0.90), p<0.0001, respectively. For both cohorts combined, HCV RNA levels were higher among patients with IL28B CC genotype (6.39 log_{10} IU/ml, SD 0.78) compared to IL28B TT genotype (6.23 log_{10} IU/ml, SD 0.53), p=0.0013, but not IL28B CT genotype (6.34 log_{10} IU/ml, SD 0.59), p=0.28. When CC was compared to CT and TT combined (mean 6.31, SD 0.78), the p-value was 0.087. Analyzing the two cohorts separately revealed no difference between IL28B genotypes CC and CT/TT in the NIH cohort, 5.51 log_{10} IU/ml (SD 1.00) for those with CC and 5.63 log_{10} IU/ml (SD 0.83) for those with IL28B CT/TT, p=0.52. However, in the HALT-C cohort the mean was 6.53 log_{10} IU/ml (SD 0.64) for those with IL28B genotype CC and 6.35 (SD 0.53) for those with genotype CT/TT, p<0.0001. The observation that HCV RNA levels did not differ between IL28B CC and non-CC genotypes in the NIH cohort could have been due to the small sample size.

Importantly, in multivariate analysis, HCV RNA levels were neither associated with fibrosis progression (p=0.61) nor clinical outcomes (p=0.75). Thus, while we found HCV RNA levels to be higher among patients with IL28CC genotype, as demonstrated previously by Grebely et al., they did not influence fibrosis progression or clinical outcomes. Further
studies are needed to investigate why patients with IL28 CC genotype have worse clinical outcomes compared to non-CC patients.

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**Abbreviations:**

| Abbreviation | Definition |
|--------------|------------|
| HCV          | Hepatitis C virus |
| HALT-C       | Hepatitis C Long-Term Treatment Against Cirrhosis |
| NIH          | National Institutes of Health |
| SD           | Standard Deviation |

**References:**

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