

## **Association of IL28B genotype with fibrosis progression and clinical outcomes in patients with chronic hepatitis C: A longitudinal analysis.**

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**Background:** IL28B polymorphisms are associated with spontaneous clearance of HCV infection and response to therapy. Whether IL28B genotype affects fibrosis progression or clinical outcome is unclear. **Aims:** To study the relationship between IL28B genotype and both histological and clinical outcomes in patients with chronic hepatitis C (CHC). **Methods:** Hepatic fibrosis was scored using the Ishak (0-6) scale; progression was defined as a 2-point increase in Ishak score between biopsies. Multiple logistic and Cox regressions were used to identify variables associated with fibrosis progression. **Results:** 1483 patients were included in a baseline cross-sectional analysis, from which 276 were eligible for a paired biopsy analysis (median time between biopsies-4 years), and 400 for a clinical outcome analysis. At baseline biopsy, patients with IL28B CC genotype had significantly higher portal inflammation (2.4 vs. 2.2) and ALT levels (133 vs. 105 U/L),  $p < 0.05$  for all. In the paired biopsy analysis, there was no difference in the frequency of fibrosis progression between patients with IL28B CC and non-CC genotypes (17% vs. 23%). In logistic regression, only higher baseline alkaline phosphatase, lower platelets and greater hepatic steatosis were associated with fibrosis progression. Patients with IL28B CC were twice as likely to develop adverse clinical outcomes compared to non-CC (32% vs. 16%),  $P = 0.007$ . **Conclusions:** IL28B CC genotype was associated with greater hepatic necroinflammation, higher ALT, and worse clinical outcomes in CHC patients. This suggests that IL28B CC is associated with a state of enhanced immunity that on one hand can promote viral clearance, but alternately, can increase necroinflammation and hepatic decompensation without enhancing fibrosis progression. (HEPATOLOGY 2013.).