Background: Chronic liver disease is frequently observed in HIV-infected patients and is multifactorial. Attenuation of fibrotic progression may improve liver-related morbidity and mortality. Cenicriviroc (CVC) is an oral, dual antagonist of CCR2/CCR5, which are involved in key pro-inflammatory and fibrogenic pathways. We evaluated effects of 2 doses of CVC on serum hepatic fibrosis biomarkers in HIV+ subjects treated in a Phase 2b trial (NCT01338883).

Methods: Patients with CCR5-tropic HIV-1 were randomized to receive CVC 100 mg (n=59), CVC 200 mg (n=56) or Efavirenz (EFV) (n=28), each combined with emtricitabine/tenofovir for 48 weeks. The Enhanced Liver Fibrosis (ELF) biomarker index was validated previously in patients with NASH, HCV and HBV infection, and by our lab in HIV patients with liver disease. The ELF index was calculated from the results of 3 serum biomarkers of collagen and extracellular matrix deposition: hyaluronic acid, propeptide of type III procollagen, and tissue inhibitor of metalloproteinase-1.

Results: Paired baseline and 48-week samples were randomly selected for 89/100 subjects completing the study: CVC 100 mg arm (n=37 /42), CVC 200 mg arm (n=36/41) and EFV controls (n=16/17). The ELF index was significantly different between the 5 groups using the Kruskal-Wallis test (p=0.0002). The ELF index in the F0 group was significantly different from F2,F3 and F4 group (p≤0.05). There was a significant linear correlation between the Metavir fibrosis score and the ELF Index (r=0.645, p<0.0001). The ELF score decreased significantly in patients who received CVC 200 mg after 48 weeks of treatment (p=0.0002) but remained unchanged in patients who received EFV or CVC 100 mg. HIV suppression was similar in all groups.

Conclusion: Daily administration of CVC 200 mg for 48 weeks was associated with a significant decrease in specific biomarkers of hepatic fibrosis encompassed by the ELF index. The difference in ELF is not explained by HIV response which was comparable between groups. Clinical trials of CVC are currently underway in adults with NASH and liver fibrosis, using a new single tablet formulation of CVC 100 mg and 150 mg providing drug levels comparable to CVC 200 mg utilized in the HIV Phase 2 trial. Evaluation of this CVC formulation in HIV patients who are at risk of liver fibrosis progression from any etiology appears warranted.