683: Treatment with DCV Plus ASV Reduces Immune Activation in HIV/HCV Co-Infected Patients

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Background

HIV/HCV co-infected subjects have higher levels of immune activation and are traditionally more difficult to treat with immune-based therapy for HCV compared to those with HCV mono-infection. Directly-acting antivirals have shown promising results in treating subjects with HCV mono-infection in the absence of interferon and ribavirin. Here we describe changes in immune activation associated with rapid decline in HCV RNA levels in HIV/HCV co-infected subjects receiving treatment for HCV with daclatasvir (DCV) and asunaprevir (ASV).

Methodology

CONQUER is an ongoing prospective single center, phase 2 study conducted at the NIH Clinical Center of HIV/HCV co-infected subjects with genotype 1b HCV, naïve to DAAs, on antiretroviral therapy with HIV viral load (VL) <50. Participants received DCV and ASV for 24 weeks. HCV VL, measured using the Abbott assay, lower limit of quantification (LLOQ) 12 IU/ml; immune parameters, including CD4$^+$ T cell counts, HLA-DR/CD38 co-expression on CD4$^+$ and CD8$^+$ T cells; and liver function tests were followed prospectively. Median values and interquartile ranges (IQR) are reported; comparisons were made using Wilcoxon Rank tests.

Results

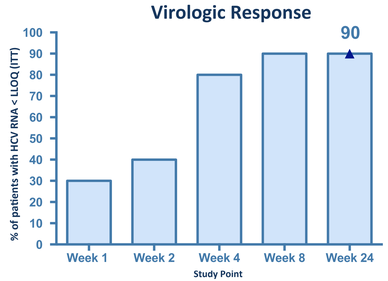
Subjects (n=10) were predominantly female (70%) and black (100%), with average age of 59 years and advanced liver disease (HAI fibrosis score ≥2, 67%); 20% were treatment-experienced, with previous pegylated interferon and ribavirin. HIV disease was well controlled, with HIV VL <50 on ART in 100%, average CD4 T-cell count of 855 cells/μL, and mean baseline HCV VL of 6.01 Log_{10} IU/mL.

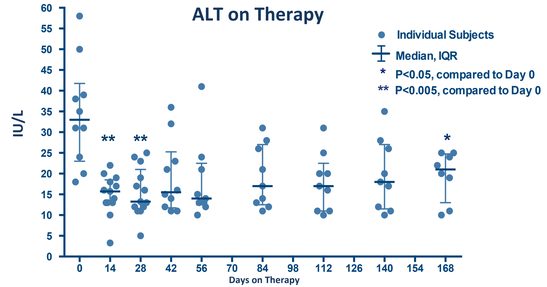
Table 1: Clinical Characteristics of Study Participants

Clinical Characteristic	n=10	
Age, median yrs (IQR)	59	(55.8 - 60.0)
Male sex, n (%)	3	(30%)
Ethnicity, n (%)		
Non-Hispanic white	0	(0)
Non-Hispanic black	10	(100.0)
BMI, median kg/m^2 (IQR)	28	(25 - 35.5)
Current tobacco use, n (%)	6	(60)
Baseline Hepatitis C Viral Load, median log_{10} (IQR)	5.9	(5.7-6.2)
Plasma HIV RNA <40 copies/mL, n (%)	10	(100)
Current CD4 count, median cells/mm^3 (IQR)	805	(644 - 884)
Baseline ALT (U/L)	34.4	(25.8-38.5)
HAI Fibrosis Stage* n (%)		*n=9
Stage 0-1:	3	(33.3)
Stage 2:	2	(22.2)
Stage 3- 4:	4	(44.4)
IVDU, n (%)	6	(60)
ART exposure, median years (IQR)	8	(8-12)

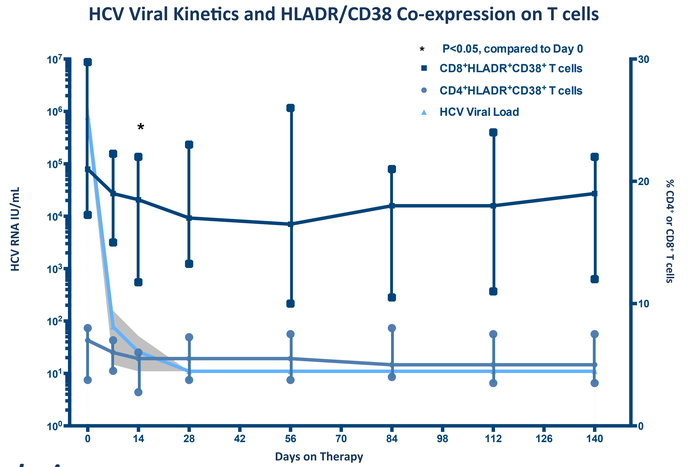
Results, Continued

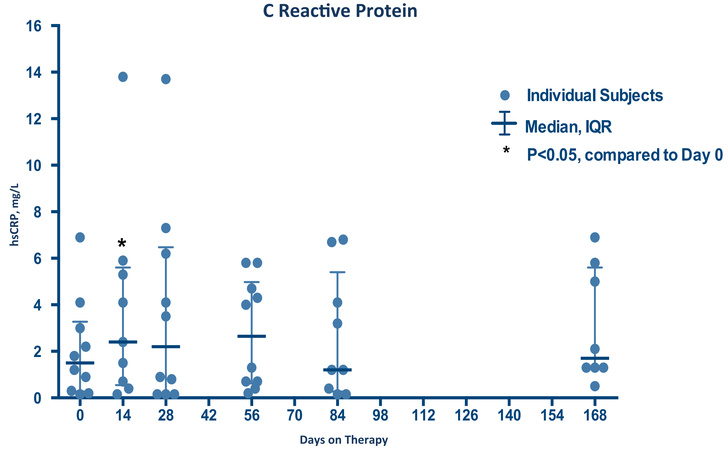
On therapy, HCV VL was below LLOQ in 40% by Week 2 and 80% by Week 4, and 90% by Week 24 (end of therapy). ALT was within the normal range at baseline, decreased by 54% (P=0.002) after Week 2, 53% (P=0.002) by Week 4, and a 39% (P=0.04) decrease by Week 24.





After 2 weeks on therapy, CD4 remained unchanged (P>0.99), while co-expression of HLADR/CD38 declined by 21% and 12% respectively on CD4$^+$ (P=0.023) and CD8$^+$ T cells (P=0.018), and Furthermore, CRP increased slightly at week 2 of therapy (+0.6mg/L, P=0.0234) but returned to baseline by week 4 (P=0.3125) and week 24, EOT (P=0.2500).





Conclusion

Consistent with the decline in Hepatitis C viral load, therapy with DCV plus ASV in HIV/HCV co-infected subjects is associated with a substantial decline in immune activation.
The impact of this decline on non-AIDS defining morbidities in HIV infected subjects will need to be assessed in larger clinical studies.

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