Prevention of Hepatitis C Virus (HCV) Recurrence with Peri-Transplant Hepatitis C Immune Globulin Combined with Pre-Transplant (Pre-LT) Antiviral Therapy (AVT)

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Background and Aims: Safer HCV AVTs are available to treat wait-listed patients to prevent post-LT HCV recurrence, but such therapies are not uniformly effective and the optimal duration of pre-LT AVT unknown. We evaluated the safety and efficacy of Biotest-HCIG, a human hepatitis C immune globulin to prevent HCV recurrence by neutralizing remaining HCV reservoirs in patients on pre-LT HCV AVT at the time of LT. Methods: In this phase 3, open-label randomized study, wait-listed patients with chronic HCV infection (all genotypes) treated with any AVT and who achieved HCV RNA <100 IU/ml prior to LT were eligible. In total, 84 patients will be randomized 1:1:1 to Biotest-HCIG (200 mg/kg or 300 mg/kg given on the day of LT and for 10 weeks post-LT) or observation. The primary endpoint is post-LT sustained virologic response (pTVR), defined as HCV RNA <43 IU/ml at 12 wks post-LT treatment. Post-transplant immunosuppression is site-specific. Results: To date, 17 subjects (all male, median age 59 yrs, 100% genotype 1, 94% with hepatocellular carcinoma, 12% with living donors) have undergone LT. Pre-LT AVT was telaprevir/peginterferon/ribavirin (RBV) (12%), sofosbuvir/RBV (76%) or sofosbuvir/simeprevir (12%) given for a median of 51 days (range 14-164 days) pre-LT with all patients achieving HCV RNA <43 IU/mL pre-LT (71% also undetectable). With median post-LT follow-up of 8 wks, post-LT HCV recurrence has been documented in 2 patients - at wk 2 (control) and wk 3 (200 mg Biotest-HCIG) post-LT. Overall, 11/12 (92%) of Biotest-HCIG-treated patients have maintained undetectable HCV RNA compared to 4/5 (80%) of controls (Table). Among 4 patients who were viremic at the time of LT and randomized to Biotest-HCIG, all have undetectable HCV RNA at median 9 wks follow-up. Biotest-HCIG-related side effects were infrequent and there were no discontinuations due to adverse events. Conclusion: Biotest-HCIG is safe and well-tolerated. To date, HCV recurrence rates in patients on pre-LT AVT are lower in Biotest-HCIG-treated patients compared with controls (8% vs 20%) and all patients viremic at LT who received Biotest-HCIG have undetectable HCV RNA. These preliminary results suggest Biotest-HCIG may be beneficial as an adjuvant therapy for HCV patients on AVT undergoing LT.

Treatment Group	N	Median Duration AVT Pre-LT (days)	HCV RNA negative Post-LT Last F/U			Median F/U Post-:T (days)
			Overall N (%)	Among HCV RNA undetectable at LT	Among HCV RNA detectable at LT	
Control	5	79	4/5 (80)	4/4	0/1	56
Biotest-HCIG 200mg/kg	6	49	5/6 (83)	3/4	2/2	49
Biotest-HCIG 300mg/kg	6	46	6/6 (100)	4/4	2/2	77

Disclosures:

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