Hepatitis C Following Liver Transplantation: Evaluation Of Response In British Columbia (HEP-CLEAR)

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Background

- Approximately 50% of liver transplant will develop recurrent hepatitis C within 1 year and 75% within 3 years.[1]
- 5-10% of recurrences are fibrosing cholestatic hepatitis (FCH), which is more aggressive and characterized by severe cholestatic injury and rapid liver dysfunction.[2]
- Therapy for recurrent hepatitis C is a combination of pegylated interferon and ribavirin (PEG-RBV).
- PEG-RBV is less effective post-liver transplant compared to pre-liver transplant (4-19% vs. 40-50% for genotype 1).[3]
- Response rate in our British Columbia population has not been previously studied.

Objectives

- Primary Objective:
  - To assess the response rates to PEG-RBV treatment in post-transplant liver patients with recurrent HCV.
- Secondary Objectives:
  - To determine HCV recurrence rates and time to recurrence.
  - To assess our primary outcome in the subgroup of recurrent HCV patients with documented FCH.

Methods

- **Design:** Single-center, retrospective chart review
- **Setting:** Vancouver General Hospital
- **Inclusion criteria:**
  - All patients who received a liver transplant for HCV-related liver failure between January 1, 2001 and December 31, 2008
- **Exclusion criteria:**
  - Co-infection with other viral hepatitis or HIV
  - Multi-organ transplants
  - Lost to follow-up
- **Data collection:** Until December 31, 2011

Results

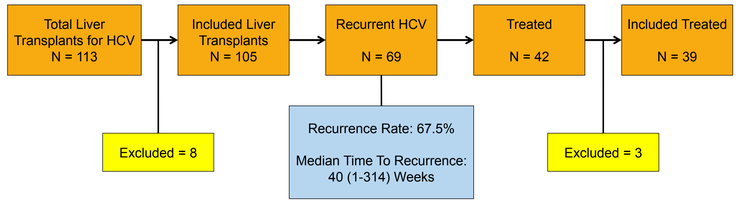

Figure 1: Patient inclusion and exclusion

	Total Treated (N = 39)	Non-FCH (N = 34)	FCH (N = 5)
Subject Characteristics			
Mean age at transplant (years)	51.0 ± 4.0	50.5 ± 4.7	53.0 ± 1.0
Gender (male)	30 (76.9%)	28 (82.4%)	2 (40.0%)
Mean weight (kg)	87.2 ± 16.7	88.4 ± 16.5	77.3 ± 16.8
Genotype			
Genotype 1	31 (79.5%)	27 (79.4%)	4 (80.0%)
Genotype 2, 3	8 (20.5%)	7 (20.6%)	1 (20.0%)
Fibrosis Grade			
Fibrosis 0, 1	13 (33.3%)	13 (38.2%)	N/A
Fibrosis 2	16 (41.0%)	16 (47.1%)	N/A
Fibrosis 3	5 (12.8%)	5 (14.7%)	N/A
Therapy			
INFα2b-RBV	2 (5.2%)	1 (2.9%)	1 (20.0%)
PEGα2a-RBV	27 (69.2%)	23 (67.6%)	4 (80.0%)
PEGα2b-RBV	10 (25.6%)	10 (28.4%)	0 (0.0%)
Donor Characteristics			
Deceased donor*	34 (87.2%)	29 (85.3%)	5 (100.0%)
Mean donor age (yrs)	41.3 ± 16.1	39.0 ± 15.3	57.0 ± 13.4
Timing			
From transplant to PEG-RBV therapy (median; weeks)	70.0 (12.0-330.0)	82.0 (17.0-330.0)	20.0 (12.0-23.0)
Induction Therapy			
IL-2RA	12 (30.8%)	10 (29.4%)	2 (40.0%)
ATG	1 (2.6%)	1 (2.9%)	0 (0.0%)
Baseline IMS Therapy			
Tac + MMF	22 (56.4%)	20 (58.8%)	2 (40.0%)
Tac + AZA	13 (33.3%)	12 (35.3%)	1 (20.0%)
Other	4 (10.3%)	2 (5.9%)	2 (40.0%)
CMV Status			
Donor-/Recipient-	6 (15.4%)	6 (17.6%)	0 (0.0%)
Donor+/Recipient-	5 (12.8%)	3 (8.8%)	2 (40.0%)
Recipient+	28 (71.8%)	25 (73.5%)	3 (60.0%)

Table 1: Baseline characteristics of patients treated with PEG-RBV (*All standard criteria brain death donors)

	SVR (N = 16)	No SVR (N = 18)	FCH (N = 5)
Virologic Response			
Neg at Wk12	13 (81.3%)	2 (11.1%)	0 (0.0%)
≥ 2 log drop HCV RNA Wk12 and -ve at Wk24	3 (18.8%)	0 (0.0%)	0 (0.0%)
≥ 2 log drop HCV RNA Wk12 and +ve at Wk24	0 (0.0%)	5 (27.8%)	1 (20.0%)
< 2 log drop HCV RNA Wk12	0 (0.0%)	11 (61.1%)	4 (80.0%)
Graft Outcomes			
Bx-confirmed rejection post-PEG-RBV initiation	0 (0.0%)	3 (16.7%)	0 (0.0%)
Mortality	0 (0.0%)	5 (27.8%)	5 (100.0%)
Median treatment to death time (weeks)	N/A	52 (8-124)	5 (1-92)
Median follow-up time (weeks)	370 (180-565)	320 (60-563)	29 (19-205)

Table 2: Virologic response and graft outcomes

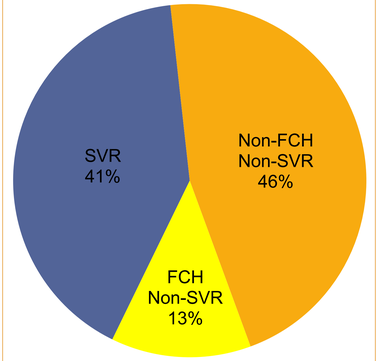

Figure 2: Sustained virologic response (SVR) to PEG-RBV

	SVR (N = 16)	No SVR (N = 18)	FCH (N = 5)
Prednisone Dose (2 yrs post-transplant)			
Mean prednisone (mg)	3942.2 ± 2203.1	4979.9 ± 2896.0	4610.0 ± 3561.8
0 prednisone pulses	11 (68.8%)	9 (50.0%)	3 (60.0%)
≥ 1 prednisone pulse	5 (31.3%)	9 (50.0%)	2 (40.0%)
Dose Adjustments			
↓INF dose	6 (37.5%)	6 (33.3%)	2 (40.0%)
↓RIB dose	11 (68.8%)	11 (61.1%)	3 (60.0%)
Supportive Meds			
Erythropoiesis-stimulating agent	5 (31.3%)	10 (55.6%)	1 (20.0%)
G-CSF	3 (18.8%)	7 (38.9%)	2 (40.0%)
CMV Infections			
CMV viremia > 1000 copies/mL	4 (25.0%)	2 (11.1%)	2 (40.0%)

Table 3: Potential factors affecting sustained virologic response (SVR)

Conclusion

- Our recurrence rate was 67.5% over a mean follow-up time of 4.5 years, which is similar compared to 75% over 3 years quoted in a previous trial.[1]
- Our SVR rate was 41%, which is higher compared to 4-19% quoted in a previous trial.[3]
- FCH had the poorest outcome as none in this subgroup achieved SVR and had 100% mortality.
- Small sample size and the limited number of patients who achieved SVR precluded regression analysis for significance of risk factors.

References

1. Gopal D. Liver Transplantation 2001; 7(3): 181-190.
2. Cimsit B. Transplantation Proceedings 2011; 43(3): 905-908.
3. Burton J. Liver Transplantation 2006; 12(2): 1044-1048.

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