PERSISTENT VIREMIA ON DAA THERAPY: REAL-WORLD EXPERIENCE, INTERVENTIONS, AND OUTCOMES

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INTRODUCTION

- Current treatment for hepatitis C virus (HCV) infection includes a variety of oral direct-acting antiviral (DAA) medications, which typically result in rapid viral response (RVR) and ultimately sustained virologic response rates (SVR) nearing 100%.
- The clinical impact of persistent viremia (PV) after day 21 of therapy has not been consistently demonstrated in clinical trials.[1-2]
- Despite the paucity of data, the AASLD and IDSA do provide guidance on the management of PV, recommending rechecking a viral load 2 weeks following a detectable week 4 viral load. Treatment discontinuation is recommended if this value is increased by greater than 10 fold.[3]
- In addition to the gap in published evidence for these recommendations, there is also a lack of knowledge in regards to the patient population with positive viral loads at week 4 and week 8.

RESEARCH QUESTIONS

- Among HCV-infected patients experiencing PV on DAA treatment, does PV impact SVR rate? Do real-world interventions align with current guideline recommendations?

METHODS

- Single center, descriptive, retrospective cohort study of HCV-infected patients evaluated and initiated on HCV treatment by the Vanderbilt University Medical Center (VUMC) Division of Gastroenterology, Hepatology, and Nutrition or the Division of Infectious Diseases.

Study Population:

- **Inclusion criteria**: Initiation of DAA treatment between October 2014 and September 2017.
- **Exclusion criteria:** Absence of on-treatment initial positive HCV RNA (>15 IU/mL) measured by polymerase chain reaction (PCR) between day 21 (week 3 start) and day 62 (week 8 end) of therapy; previous DAA treatment; and failure to complete prescribed therapy.

Endpoints:

- **Primary endpoint:** SVR rates in patients with PV stratified by the presence and type of intervention.
- **Secondary endpoints:** Percentage of patients receiving guideline-recommended interventions and patient factors related to patients receiving interventions.

RESULTS

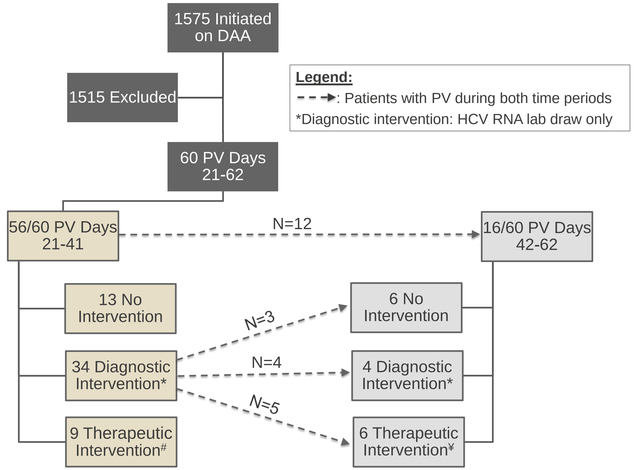
Baseline Characteristics	Overall Number (%) N=60	Days 21-41* Number (%) N=56	Days 42-62* Number (%) N=16
Male	48 (80%)	47 (83.9%)	10 (62.5%)
White	45 (75%)	42 (75%)	8 (50%)
Age (mean +/- SD)	52.8 +/- 9.8	52.5 +/- 9.8	53.6 +/- 10.4
HIV co-infection	14 (23.3%)	14 (25%)	6 (3.75%)
Degree of fibrosis			
F0-F1	14 (23.3%)	14 (25%)	3 (18.7%)
F2-F3	18 (30%)	15 (26.8%)	7 (43.8%)
F4	28 (46.7%)	27 (48.2%)	6 (37.5%)
CTP A	22 (78.5%)	22 (81.5%)	5 (83.3%)
CTP C	1 (3.6%)	1 (3.7%)	0
Genotype			
1a	44 (73.3%)	41 (73.2%)	12 (75%)
1b	3 (5%)	2 (3.6%)	1 (6.25%)
2	3 (5%)	3 (5.3%)	1 (6.25%)
3	9 (15%)	9 (16.1%)	2 (12.5%)
4	1 (1.7%)	1 (1.8%)	0
Previous treatment			
Naïve	48 (80%)	44 (78.6%)	15 (93.7%)
IFN +/- RBV	12 (20%)	12 (21.4%)	1 (6.3%)
Concomitant PPI use€	6 (10%)	6 (10.7%)	0
Immunosuppressed§	6 (10%)	6 (10.7%)	1 (6.3%)
Liver transplant recipient	1 (1.7%)	1 (1.8%)	0
Ongoing illicit substance use	12 (20%)	12 (21.4%)	5 (31.3%)
Treatment regimen			
SOF + RBV	3 (5%)	3 (5.3%)	0
LDV/SOF	33 (55%)	30 (53.6%)	9 (56.2%)
LDV/SOF + RBV	9 (15%)	8 (14.3%)	3 (18.7%)
SOF/VEL	6 (10%)	6 (10.7%)	1 (6.3%)
SOF/VEL + RBV	6 (10%)	6 (10.7%)	2 (12.5%)
PrOD + RBV	2 (3.3%)	2 (3.6%)	1 (6.3%)
EBR/GZR	1 (1.7%)	1 (1.8%)	0
Adherence:			
<7 missed doses	52 (86.6%)	49 (87.5%)	12 (75%)
≥7 missed doses	7 (11.7%)	6 (10.7%)	4 (25%)
Data not available	1 (1.7%)	1 (1.8%)	0

*Groups are not mutually exclusive

€ Concomitant PPI use: ≤20mg of omeprazole or equivalent

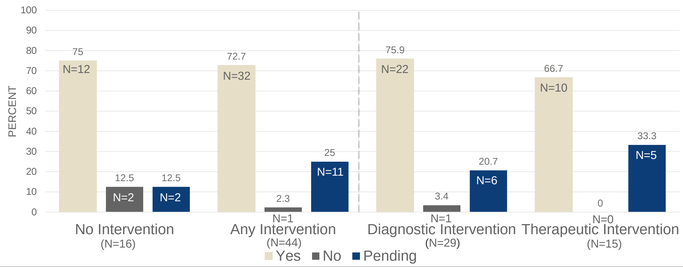
§Immunosuppressed: CD4 count <200#/mm^3, use of calcineurin inhibitors, use of antiproliferative and antimetabolic agents, T-cell costimulatory blocker use, administration of antibodies or immune globulins, and chronic glucocorticoid use

FIGURE 1: PATIENT DISTRIBUTION AND INTERVENTION



#Therapeutic Interventions Days 21-41 (n=9)		¥Therapeutic Interventions Days 42-62 (n=6)	
Ribavirin (RBV) added	3	RBV added	1
Treatment extended	2	Treatment extended	3
RBV added + treatment extended	2	RBV added + treatment extended	2
PPI held + treatment extended	1		
Increased RBV dose	1		

FIGURE 2: SVR RATES



RESULTS (CONTINUED)

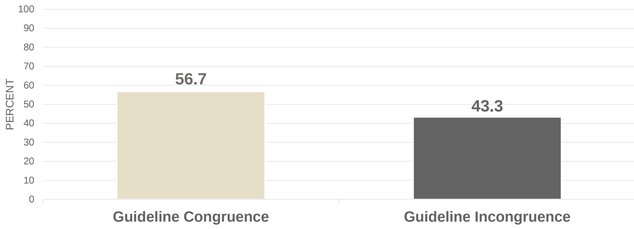
INTERVENTIONS

	UNIVARIATE*		MULTIVARIATE§	
Baseline Factor	OR (95% CI)	p-value	OR (95% CI)	p-value
Cirrhosis	2.4 (0.74 - 7.81)	0.144	5.8 (1.37 - 24.38)	***0.017***
Treatment Experienced	0.2 (0.024 - 1.69)	0.140	0.1 (0.01 - 0.81)	***0.033***
Immunosuppressed	1.4 (0.24 - 8.67)	0.698	3.7 (0.49 - 28.41)	0.205
Genotype 3	1.4 (0.12 - 16.58)	0.790	2.9 (0.20 - 40.55)	0.433

*Univariate analysis assessed using chi-squared test

§ Multivariate analysis assessed using logistic regression

FIGURE 3: GUIDELINE RECOMMENDED INTERVENTIONS



CONCLUSIONS

- Although still in process, the majority of PV patients have achieved SVR thus far regardless of intervention or type.
- Current AASLD/IDSA guideline recommendations for PV management are inconsistently adhered to and a wide variance in practice exists in both diagnostic and therapeutic interventions for HCV infected patients with PV.
- Accounting for other baseline factors, the presence of cirrhosis or treatment experience at baseline was more likely to result in a therapeutic intervention, though these were not significant on univariate analysis.
- Pharmacists and pharmacy benefit managers may play a role in streamlining care for this challenging population.

References:

1. Malespin M, Benyashvili T, Uprichard S, et al. Prevalence of end of treatment RNA-positvie/sustained viral response in HCV patients treated with sofosbuvir combination therapies. *Ther Adv Gastroenterol.* 2017;10(1): 68-73.
2. Sidharthan S, Kohi A, Sims Z, et al. Utility of Hepatitis C Viral Load Monitoring on Direct-Acting Antiviral Therapy. *Clin Infect Dis.* 2015;60 (12):1743-51.
3. American Association for the Study of Liver Diseases and Infectious Diseases Society of America (AASLD-IDSA). 2016. *Recommendations for testing, managing, and treating hepatitis C.* http://www.hcvguidelines.org.