

Determinants of Response to Pegylated Interferon and Ribavirin for Acute Hepatitis C Infection in Patients with Human Immunodeficiency Virus

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No disclosures



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Icahn School of Medicine at
Mount Sinai

Acute HCV in HIV

- Since 2000, there have been reported epidemics of acute HCV in HIV-infected MSM predominantly in Western Europe, Australia, and the USA
- Acute HCV takes a chronic course more frequently in HIV infected individuals
- Positive HCV RNA 12 weeks into acute infection is associated with transition to chronic HCV
 - Treatment recommended with persistent viremia >12 weeks after onset of symptoms or known exposure

Acute HCV in HIV

- Of those treated, sustained virologic response (SVR) rates are approximately 60-80%.
 - Australian Trial in Acute Hepatitis C (ATAHC) 2009 (N=20)*
 - European Collaborative Cohort Study 2010 (N=111)*
 - Japanese cohort 2013 (N=12)*
- Achievement of rapid virologic response (RVR) has been shown to be an important factor for achievement of SVR

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Ishikane M. ICAAC Sep 2013. Abstract H-1268

Acute HCV Treatment

Current guidelines recommend a combination of pegylated-interferon (pIFN) and weight-based ribavirin (RBV), with the duration of treatment based on achievement of RVR

- If RVR, treatment duration should be 24 weeks
- If no RVR, treatment duration of 48 weeks should be considered
 - If $<2 \log_{10}$ drop in HCV RNA at week 12, treatment can be discontinued

Direct Acting Antivirals (DAAs)

- The study of DAA use for acute HCV infection in HIV co-infected patients is limited but appears to be efficacious*
 - shortens treatment duration and increases SVR rates
- However, the use of DAAs can lead to added cost, drug interactions, and side effects
- Ideally, the addition of a DAA would be reserved for patients unlikely to achieve SVR with pegIFN + RBV alone

**Fierer D. CROI 2013. Abstract 156LB*

Methods

- **Our study aimed to describe treatment outcomes in a relatively large NYC cohort with acute HCV and HIV**
- **From January 2004 – January 2013, 75 HIV-infected males with acute HCV were treated with pIFN + RBV via ongoing cohort studies at Weill Cornell Medical Center and Mount Sinai**
- **Subjects were identified through referral from primary care and HIV physicians, city STD and public health clinics, and community outreach in high-risk populations**

Methods

Eligibility criteria:

- Male and female patients ≥ 18 years of age
- Acute hepatitis C infection defined as:
 - First anti-HCV antibody or HCV RNA positive within the previous 6 months and
 - Documented anti-HCV antibody negative or HCV RNA negative within the 12 months prior to anti-HCV antibody positive result
- OR
- Acute clinical hepatitis (jaundice or $ALT > 5X$ ULN) within the 6 months prior to first positive HCV antibody or HCV RNA, with no other cause of acute hepatitis identifiable
- Initiated treatment with peginterferon and ribavirin

Methods

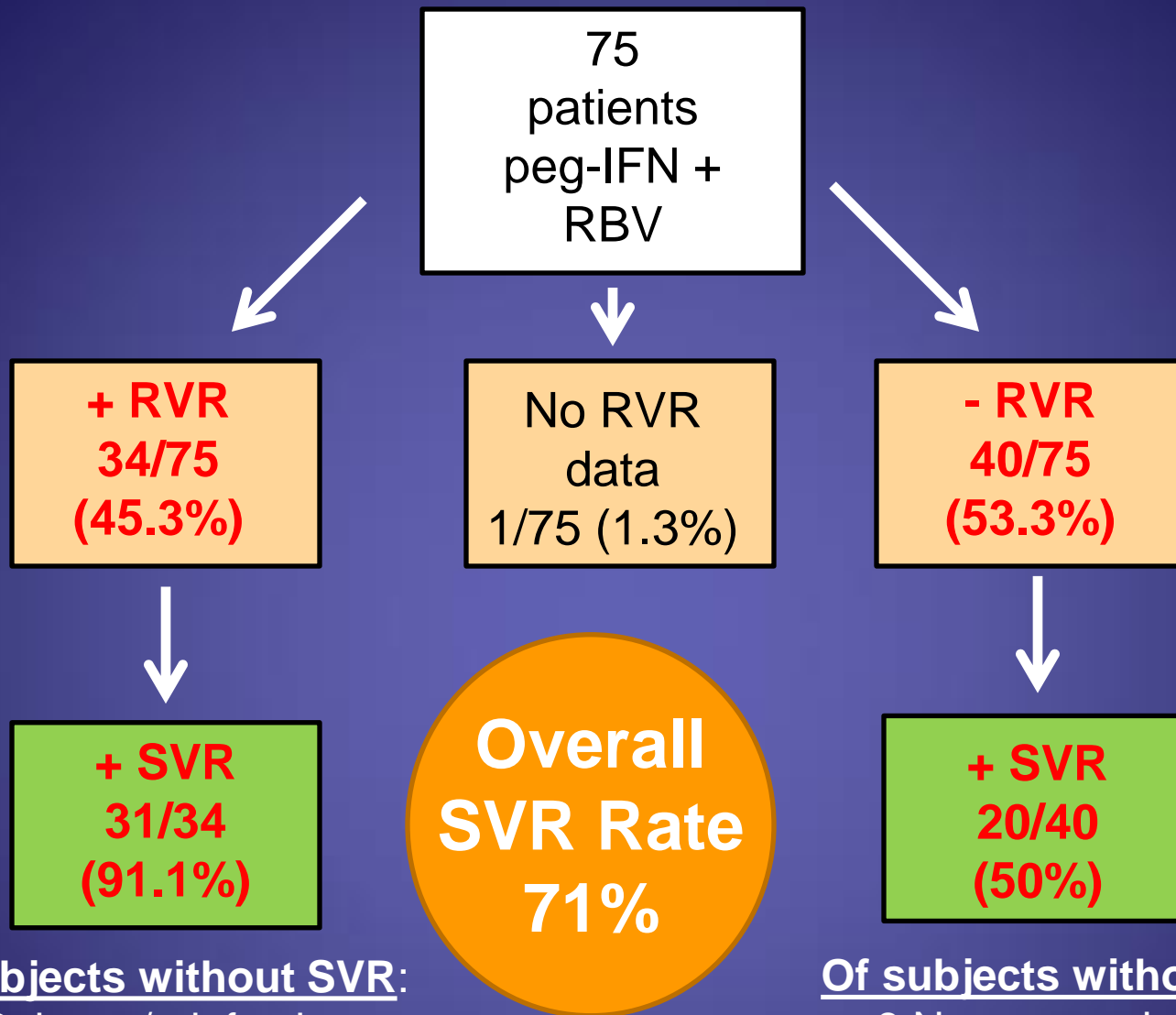
- Retrospective analyses were performed to determine which factors were associated with RVR or SVR
 - SVR defined as undetectable HCV RNA 12 and/or 24 weeks after treatment cessation

Baseline Characteristics (n=75)

(n=75)	# subjects (percent) or median (IQR)
Age (years)	42 (35 - 46)
Race/Ethnicity:	
White non-Hispanic	46 (61%)
Hispanic	17 (23%)
Black non-Hispanic	12 (16%)
MSM	66/67 (99%)
IVDU ever	24/67 (36%)
Duration HIV (years)	7 (3-10)
Baseline CD4 (cells/mm ³)	551 (351 – 723)
HIV RNA < 200 copies/mL	45 (63%)
On ARVs at diagnosis	51 (74%)

Baseline Characteristics - Cont

(n=75)	# subjects (percent) or median (IQR)
HCV Genotype 1	66 (92%)
IL28B CC	21/51 (41%)
Time to treatment (weeks from clinical onset)	17 (13 – 24)
Peak pre-treatment ALT	718 (390 – 1317)
Baseline pre-treatment HCV RNA > 1,000,000 IU/mL	35 (47%)



Of subjects without SVR:

- 2 Relapse/reinfection
- 1 Missing data

Of subjects without SVR:

- 8 Nonresponders
- 4 Rebound on treatment
- 7 Relapse/reinfection
- 1 Missing data

Predictors of RVR in G1 Acute

(n=59)	Univariate OR	P-value	Multivariate OR	P-value
Baseline pre-treatment HCV RNA \leq 1,000,000 IU/mL *	16.949	<0.001	17.241	<0.001
Peak pre-treatment ALT >600 IU/mL *	2.353	0.103	5.697	0.036
CD4 > 500 cells/mm³*	3.536	0.023	4.877	0.047
Black Race *	4.125	0.034		
Time to treatment > 20 wks*	2.910	0.039		
Hispanic *	2.143	0.193		
No h/o IVDU ever	1.894	0.240		
HIV VL >200 copies/mL	1.721	0.314		
Age >40 years	1.071	0.891		
Duration HIV \leq 8 years	1.037	0.363		

* Included in stepwise logistic regression

Pre- Rx Predictors of SVR G1 Acute

(n=59)	Univariate OR	P-value	Multivariate OR	P-value
Baseline pre-treatment HCV RNA \leq 1,000,000 IU/mL*	2.809	0.073	6.173	<0.001
Age \leq 40 years *	4.717	0.009	5.682	0.010
Non-Black Race *	1.822	0.344	5.051	0.058
Hispanic *	5.185	0.043		
CD4 > 500 cells/mm ³ *	2.083	0.178		
Duration HIV > 8 years	1.694	0.322		
Peak pre-treatment ALT >600 IU/mL	1.694	0.322		
HIV VL >200 copies/mL	1.417	0.535		
Time to treatment > 20 wks	1.256	0.667		
RF IVDU ever	1.106	0.978		

* Included in stepwise logistic regression

RVR as predictor of SVR

- Odds ratio = 13.5 (p=.003)
- When included in MV model, age ≤ 40 was the only other significant predictor of SVR (OR 5.8, p 0.01)

Limitations

- Our study is limited by the small number of total subjects, although this represents largest described North American cohort.
- Race was used in statistical analyses rather than IL28B, as IL28B data was only available for a subset of patients.

Conclusions

- The majority of HIV-infected patients respond favorably to treatment with peginterferon plus ribavirin in the acute stage of HCV infection.
 - RVR is the most important predictor of SVR
- However, there is a need for improved identification and optimization of therapy in those who are at high risk of acute HCV treatment failure.

Conclusions

Consideration should be made to the addition of a DAA to pIFN + RBV:

1) Prior to initiating treatment if poor prognostic factors

- CD4 \leq 500 cells/mm³, peak pre-treatment ALT \leq 600 IU/mL, age > 40 years, baseline pre-treatment HCV RNA of > 1,000,000 IU/mL, black race

OR

2) On treatment if no RVR

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- **ID Week Committee**



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