Poster #P260 HIV/Hepatitis C Co-Infected Patients Are Significantly more Complex to Manage than HIV Mono-Infected Patients in a Large Cohort of Treatment-Naive, HIV-Positive Individuals

OPERA®
The Longitudinal Cohort

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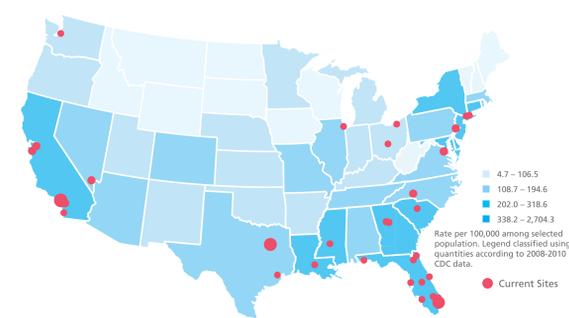
BACKGROUND

Hepatitis C virus (HCV) co-infection is common in patients with HIV due to shared modes of transmission.[1] Understanding differences between HIV mono-infected and HIV/HCV co-infected patient populations may lead to earlier identification of HCV co-infection, more effective management, and better clinical outcomes.

OBJECTIVE:
To evaluate differences between HIV mono-infected and HIV/HCV co-infected patient populations.

METHODS

Figure 1: U.S. Map of OPERA HIV+ Population & CDC (2010) State-by-State Estimates

Rate per 100,000 among selected population. Legend classified using quantities according to 2008-2010 CDC data.

- The Observational Pharmaco-Epidemiology Research & Analysis (OPERA) database follows 67,500 HIV+ patients through their electronic health records from 79 US community-based outpatient clinics in 15 states. [Figure 1]
- The OPERA population represents ~7% of all HIV+ patients linked to care in the US. It is the largest continuously operating cohort of HIV+ patients in the US, refreshed daily.
- The analysis included HIV+ individuals initiating HIV antiretroviral therapy (ART) for the first time between 1/1/2007 and 3/31/2015. Patients were followed from HIV treatment initiation to discontinuation of regimen, loss to follow-up, death or study end (3/31/2016).
- Demographics and clinical characteristics were compared between HIV/HCV co-infected and HIV mono-infected patients using Pearson chi-square or Wilcoxon rank-sum tests. Differences in time to HIV viral suppression (<50 copies/mL) with and without HCV co-infection were assessed using multivariable Cox proportional hazards regression.

RESULTS

- Of 9,190 HIV+ treatment-naïve patients, 7,837 (85.3%) were HCV antibody negative and 472 (5.1%) were HCV-positive; 881 (9.6%) patients had a history of HCV clearing or no testing prior to baseline and were excluded.
- HIV/HCV co-infected patients were significantly older (median age: 46.7 vs. 34.0 years), less likely to be male (76.9% vs. 86.6%), Hispanic (16.9% vs. 25.5%), or MSM (39.8% vs. 59.8%) than HIV mono-infected patients (p< 0.0001) (Table 1, Figure 2).
- Baseline CD4 cell counts were lower for HIV/HCV co-infected patients (279 vs. 330 cells/μL, p=0.0029) who were also more likely to have an AIDS defining event at baseline (9.7% vs. 6.3%, p=0.0037); there were no differences between groups in baseline HIV viral load.

Characteristic	HIV+ N= 7837	HIV+/HCV+ N= 472	P-value
Age (Median, IQR)	34.0 (26,7, 43.5)	46.7 (38.5, 52.2)	<0.0001
Gender, Male	6782 (86.6%)	363 (76.9%)	<0.0001
Risk of Infection, MSM*	4687 (59.8%)	188 (39.8%)	<0.0001
Race, African American	3065 (39.1%)	182 (38.6%)	0.8120
Ethnicity, Hispanic	1999 (25.5%)	80 (16.9%)	<0.0001
Log[10] HIV-1 Viral Load, Median (IQR)	4.7 (4.2, 5.1)	4.7 (4.2, 5.1)	0.4079
CD4 Count (Median, IQR)	330 (192, 479)	279 (161, 442)	0.0029
AIDS Defining Event at Baseline	497 (6.3%)	46 (9.7%)	0.0037
History of Syphillis at Baseline	2044 (26.1%)	126 (26.7%)	0.7682

*Only patients with HCV testing were included. Patients with a history of HCV that was resolved at baseline were excluded from this analysis. MSM=men who have sex with men

- Patients 50 or more years of age made up a significantly larger proportion of the HIV/HCV co-infected population than the HIV mono-infected population (36.2% vs. 11.2%, p<0.0001). Few adolescents or young adults (13-25 years old) were co-infected (n=16, 3.4%). (Figure 2)

Figure 2: Age by HCV Co-Infection Status

Legend: 13-25 Years Old | 26-49 Years Old | 50+ Years Old
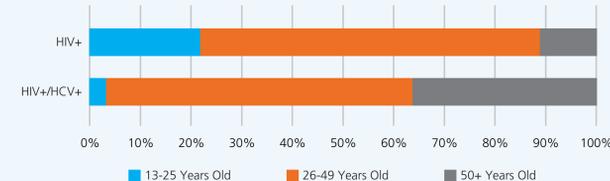
- HIV/HCV co-infected patients had significantly (p<0.05) more comorbid conditions (e.g., cardiovascular, cancer, endocrine, liver and renal disease; neuropathy; hypertension) and higher pill burden for their non-HIV medications (Table 2, Figures 3 and 4).
- Co-infected patients were twice as likely to present with mental illness (25.6% vs. 13.4%, p<0.0001) and a third had documented substance abuse (32.0% vs. 13.7%, p<0.0001).

Table 2: Comorbid Conditions with Significant Differences between HIV+ and HIV+/HCV+

	HIV+ N= 7837	HIV+/HCV+ N= 472	P-value
Any Comorbidity at Baseline	3374 (43.1%)	472 (100.0%)	<0.0001
Substance Abuse	1074 (13.7%)	151 (32.0%)	<0.0001
Mental Health Conditions	1048 (13.4%)	121 (25.6%)	<0.0001
Hypertension	1028 (13.1%)	106 (22.5%)	<0.0001
Endocrine Disorders	1002 (12.8%)	80 (16.9%)	0.0090
Liver Diseases	290 (3.7%)	472 (100.0%)	<0.0001
Peripheral Neuropathy	185 (2.4%)	30 (6.4%)	<0.0001
Invasive Cancer	132 (1.7%)	15 (3.2%)	0.0168
Cardiovascular Disease	111 (1.4%)	22 (4.7%)	<0.0001
Renal Disease	35 (0.4%)	9 (1.9%)	<0.0001

* Only patients with HCV testing were included. Patients with a history of HCV that was resolved at baseline were excluded from this analysis.

- Co-infected patients had median VACS Index scores 12 points higher than HIV mono-infected patients (p<0.0001). The impact of a 5-point change in the VACS index on 5-year mortality has been estimated at 30%.[2]

### Figure 3: Median (IQR) VACS Index by HCV Co-Infection Status
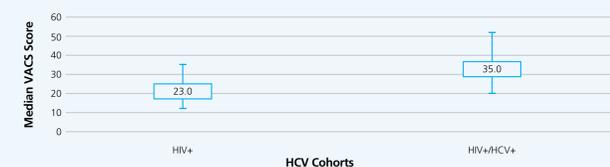
* The Veterans Aging Cohort Study (VACS) Index predicts all-cause mortality, cause-specific mortality and other outcomes through a score of including age, CD4 count, HIV-1 RNA levels, indices of organ system dysfunction and HCV infection. It was developed in veterans with HIV and has been validated in other populations including non-veterans, non-HIV, and other countries.[2]

Figure 4: Non-HIV Pills Per Day by HCV Co-Infection Status

HIV+: 5+ Pills 11%, 1-4 Pills 49%, 0 Pills 40%
HIV+/HCV+: 5+ Pills 21%, 1-4 Pills 52%, 0 Pills 27%
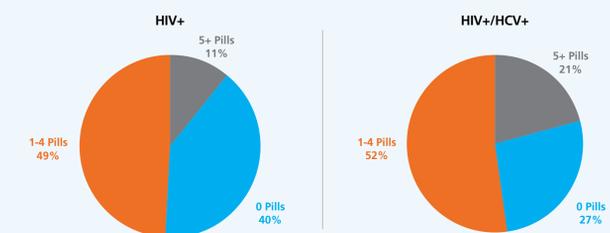
- HIV/HCV co-infected patients were more likely to receive Medicaid and Medicare and less likely to have ADAP/Ryan White or commercial insurance than HIV mono-infected patients (Figure 5).

Figure 5: Healthcare Payers at Baseline

Legend: HIV+ | HIV/HCV
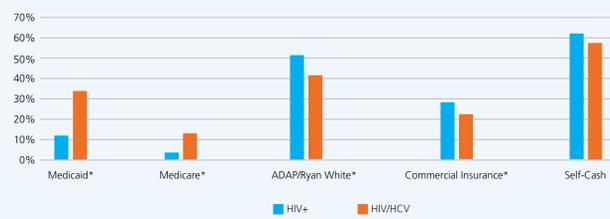
Patients had multiple payers at baseline.
*Payers that were significantly (p<.05) different between HIV mono-infected and HIV/HCV co-infected groups.

- HIV treatment was less successful in HIV/HCV co-infected patients, both in achieving suppression (HIV/HCV: 55.5% vs. HIV: 65.4%, p<0.0001) and avoiding rebound (HIV/HCV: 22.1% vs. HIV: 14.4%, p<0.0001) during initial treatment. In crude and adjusted models, those with HIV/HCV co-infection were significantly less likely to suppress their HIV VL to undetectable during their initial regimen (cHR=0.78 (95% CI=0.69, 0.89) aHR=0.80 (0.70, 0.91)). (Table 3)
- HIV mono-infected patients were less likely to virologically rebound once suppressed in both crude and adjusted models. HIV/HCV co-infected patients were significantly more likely to rebound (cHR=1.67 (1.30, 2.22) aHR=1.56 (1.18, 2.07)).

Table 3: Virologic Outcomes of Patients Initiating ART by HCV Co-Infection Status

	HIV+	HIV+/HCV+
Achieved Virologic Supression[1]	65.4%	55.5%
Unadjusted HR (95% CI)		0.78 (0.69,0.89)
Adjusted HR (95% CI)[2,3]		0.80 (0.70, 0.91)
Experienced Rebound[4]	14.4%	22.1%
Unadjusted HR (95% CI)		1.67 (1.30, 2.22)
Adjusted HR (95% CI)[4,5,6]		1.56 (1.18, 2.07)

[1] Suppression Defined as VL<50 copies/mL
[2] Referent= HIV+; HR > 1.0 indicates increased likelihood of suppression
[3] Cox regression adjusted for age at baseline, sex, African American race, , baseline VL, baseline CD4, AIDS, syphilis, substance abuse, mental illness, and total comorbid conditions at baseline
[4] Only among patients who first achieved suppression; rebound defined as 1 VL >200 copies/mL followed by discontinuation or 2 VL's >200 copies/mL
[5] Referent= HIV+; HR <1.0 indicates decreased risk of rebound after suppression
[6] Cox regression adjusted for age at baseline, sex, African American race, Hispanic ethnicity, baseline VL, baseline CD4, AIDS, syphilis, substance abuse, mental illness, and total comorbid conditions at baseline

DISCUSSION

- HIV/HCV co-infected patients tend to be older, have more comorbid conditions, receive more medications, and be more medically frail (higher mortality risk) than HIV mono-infected patients.
- Co-infected patients present with more advanced HIV disease (lower CD4 counts and more AIDS defining Illness) and are less likely to suppress and more likely to rebound virologically while receiving their initial HIV antiretroviral therapy.
- Psychologically, HIV/HCV patients suffer disproportionately from mental illness and substance abuse.
- HIV/HCV co-infected patients tend to be socioeconomically disadvantaged relying on Medicaid significantly more than HIV mono-infected patients.
- Strategies to simplify HIV treatment in HIV/HCV co-infected patients by optimizing pill count (lower pill burden) and limiting or avoiding complex drug interactions will be particularly important as more HIV/HCV co-infected patients are offered interferon (IFN) free, direct acting antiviral (DAA) treatment for their HCV infection. Moreover, during HCV treatment, continued management of multiple co-morbid conditions will also be necessary and reinforces the importance of simplification of HIV treatment in co-infected individuals.

KEY FINDINGS

HIV/HCV co-infected patients differ significantly from HIV mono-infected patients. Co-infected patients are more complex and pose unique treatment challenges for clinicians. Strategies to simplify co-infected patients' HIV care and avoid complications will be particularly important for this population as clinicians begin HCV treatment with DAA-based therapies while continuing to simultaneously manage the treatment of multiple co-morbid conditions.

REFERENCES

1. CDC: Sexually Transmitted Disease Treatment Guidelines 2015. MMWR 2015; 64 (No.3).
2. Cohen MH et al. Gender-Related Risk Factors Improve Mortality Predictive Ability of VACS Index Among HIV-Infected Women. J Acquir Immune Defic Syndr. 2015 Dec 15;70(5):538-44

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