Direct-Acting Antivirals Improve Access to Care and Cure for Patients with HIV and chronic Hepatitis C Virus from 2011-2015

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Background

- Prior to the approval of direct-acting antivirals (DAA), uptake of curative hepatitis C virus (HCV) therapy was low, particularly for HIV/HCV co-infected patients[1]
- DAA offers >95% sustained virologic response (SVR) for the vast majority of HCV-infected patients, regardless of HIV-1 infection[2,3]
- Although safety and efficacy of HCV therapies have improved, challenges have emerged including high rates of insurance denials and drug interactions between antiretroviral therapy (ART) and DAA[4,5]

Primary Objective

To measure rates of HCV treatment uptake for active HIV/HCV co-infected and HCV mono-infected patients at Duke University Health System per year of study follow-up by treatment era [DAA + pegylated-interferon with ribavirin (PEG-IFN/RBV) versus IFN-free DAA] from 2011 to 2015.

Methods

STUDY DESIGN / POPULATION

- Retrospective cohort study at Duke University Health System
- January 1, 2011 to December 31, 2015
- Subjects age ≥ 18 with documented HCV and HIV-HCV by ICD-9 or ICD-10 were identified by the Duke Enterprise Data Unified Content Explorer (DEDUCE)
- HIV and HCV diagnoses were confirmed by direct evidence of viral infection or named HIV or HCV on problem list with corresponding antiviral regimen(s) on medication list
- Prescriptions for DAA were queried to determine the treatment numbers for each year
- Demographic and clinical data were extracted by DEDUCE and supplemented by manual chart review
- Cirrhosis and hepatitis B virus (HBV) determined by ICD-9/10
- Time to DAA approval and insurance status were provided by Duke Specialty Pharmacy records

STUDY DEFINTIONS

- SVR 12 = undetectable HCV RNA viral load at 12 ± 2 weeks following completion of HCV treatment
- Treatment uptake = prescription for any HCV therapeutic regimen on medication list for patient with confirmed HCV
- ART switch = change in ART due to initiation of DAA
- Treatment (Tx) experienced = any prior HCV therapy
- Time to DAA approval = # of days between receipt of DAA prescription and approval after prior authorization

STATISTICS

- Comparisons among cohorts employed the Fisher's exact test, the chi-square test, and Student's t-test as appropriate
- Statistical analysis was performed with SAS version 9.4

Treatment Uptake

Figure 1. Treatment uptake for all patients with HCV and HIV/HCV presenting to care by study year

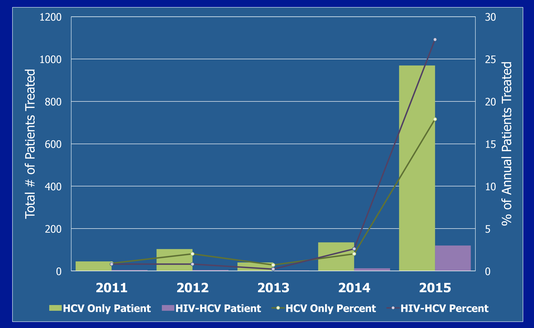


Table 1. Demographics of all patients presenting for HCV care from 2011-2015

Characteristic	Treated (n=1242)	Not treated (n=8718)	P-value	HCV mono-infection (n=9245)	HIV/HCV co-infection (n=715)	P-value
Age (median, range)	61 (55-65)	60 (54-65)	p=0.0007	60 (54-65)	58 (52-62)	p<0.0001
% Male	60.4%	60.8%	p=0.78	60.1%	69.8%	p<0.0001
Race						
African-American	482 (38.8%)	3345 (38.4%)	p=0.78	3314 (35.8%)	513 (71.8%)	p<0.0001
Caucasian	684 (55.1%)	4641 (53.2%)	p=0.24	5160 (55.8%)	165 (23.1%)	p<0.0001
Other	44 (3.5%)	448 (5.1%)	p=0.01	466 (5.1%)	26 (3.6%)	p=0.11
Unknown/declined	32 (2.6%)	284 (3.3%)	p=0.23	305 (3.3%)	11 (1.5%)	p=0.008
Ethnicity						
Hispanic	11 (0.9%)	151 (1.8%)	p=0.03	143 (1.6%)	19 (2.6%)	p=0.03
Non-Hispanic	1187 (95.6%)	7038 (80.7%)	p<0.0001	7593 (82.1%)	632 (88.4%)	p<0.0001
Unknown/declined	44 (3.5%)	1529 (17.5%)	p<0.0001	1509 (16.3%)	64 (9.0%)	P<0.0001

Table 2. Treatment uptake by era and infection status

	HCV mono-infection (n=9245)	HIV/HCV co-infection (n=715)	Total (n=9960)	P-value
Treatment uptake				
DAA+PEG-IFN/RBV	185 (2.0%)	7 (1.0%)	192	p=0.055
IFN-free DAA	936 (10.1%)	114 (15.9%)	1050	p=0.001
Total treated	1121 (12.1%)	121 (16.9%)	1242	p=0.001

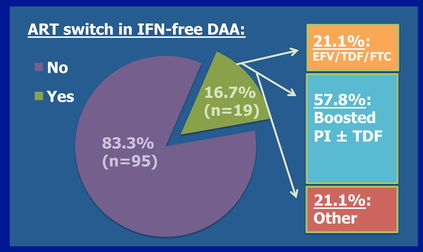
Table 3. Demographics of all patients treated with HCV therapeutics during study period

Characteristic	HCV mono-infection (n=1121)	HIV-HCV co-infection (n=121)	P-value
Age (median, range)	61 (56-65)	57 (52-62)	p=0.0002
% Male	59.1%	72.7%	p=0.003
Race			
African-American	394 (35.1%)	88 (72.7%)	p<0.0001
Caucasian	652 (58.2%)	32 (26.5%)	p<0.0001
Other	43 (3.8%)	1 (0.8%)	p=0.12
Unknown/declined	32 (2.9%)	0	N/A
Ethnicity			
Hispanic	10 (0.9%)	1 (1.5%)	p=1.00
Non-Hispanic	1069 (95.4%)	118 (97.0%)	p=0.36
Unknown/declined	42 (3.7%)	2 (1.5%)	p=0.31
HCV Genotype			
1	119 (10.6%)	4 (3.3%)	p=0.009
1a	552 (49.2%)	91 (75.2%)	p<0.0001
1b	228 (20.3%)	19 (15.7%)	p=0.28
2	89 (8.0%)	3 (2.5%)	p=0.03
3	56 (5.0%)	0	N/A
4	16 (1.4%)	0	N/A
6	1 (0.1%)	0	N/A
Unknown	60 (5.4%)	4 (3.3%)	p=0.51
% Cirrhosis	49.0%	47.1%	p=0.70
% HBV infection	1.6%	6.6%	p=0.002
% Tx-experienced	23.1%	18.4%	p=0.29

HIV patients – ART switches

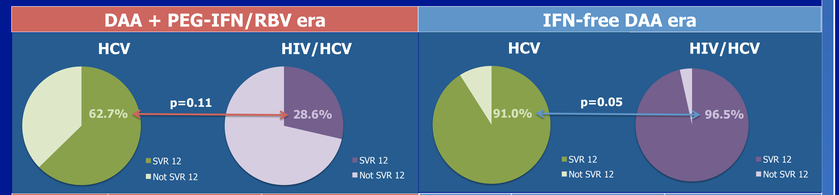
Table 4. Hepatic comorbidities by infection status, 2011-2015

Liver-related comorbidities	HCV (n=9245)	HIV-HCV (n=715)	P-value
Esophageal varices	7.1%	5.3%	p=0.04
Hepatic decompensation			
Ascites	10.9%	10.5%	p=0.80
Spontaneous bacterial peritonitis	1.4%	1.0%	p=0.50
Hepatic encephalopathy	4.9%	3.1%	p=0.03
Death	5.7%	6.2%	p=0.62



Treatment success – SVR 12

Figure 2. Treatment success by treatment era for HCV vs HIV/HCV patients



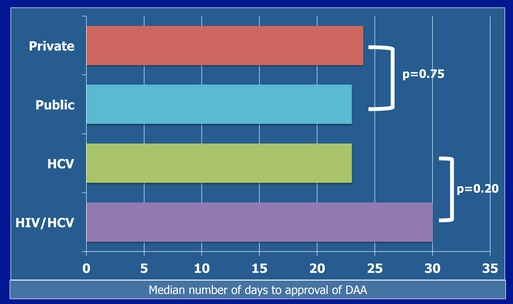
	HCV (n=185)	HIV/HCV (n=7)
Genotype		
1	16/21 (76.2%)	N/A
1a	53/91 (58.2%)	1/1 (100%)
1b	13/25 (52.0%)	0/2 (0%)
2	24/35 (68.6%)	1/1 (100%)
3	8/9 (88.9%)	N/A
4	2/3 (66.7%)	N/A
6	N/A	N/A
Unknown	0/1 (0%)	0/3 (0%)

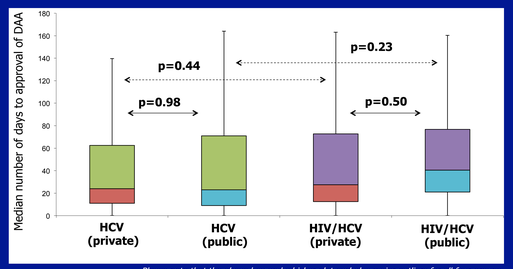
	HCV (n=936)	HIV/HCV (n=114)
Genotype		
1	95/98 (96.9%)	4/4 (100%)
1a	447/461 (96.9%)	87/90 (96.7%)
1b	197/203 (97.0%)	17/17 (100%)
2	53/54 (98.2%)	2/2 (100%)
3	47/47 (100%)	N/A
4	12/13 (92.1%)	N/A
6	1/1 (100%)	N/A
Unknown	0/59 (0%)	0/1 (0%)

SVR 12 rates in patients with:	HCV mono-infection	HIV/HCV co-infection	P-value
Cirrhosis	382/433 (88.2%)	52/54 (96.3%)	p=0.10
Tx-experienced	195/210 (92.9%)	5/5 (100%)	p=1.00
Cirrhosis + Tx-experienced	121/133 (91.0%)	2/2 (100%)	p=1.00

Access to DAA therapy

Figure 3. Time to DAA approval by infection and insurance status





Please note that the above box-and-whisker plot excludes major outliers for all four groups

Conclusions

- Treatment uptake for HIV/HCV compared to HCV mono-infected patients has improved significantly in the IFN-free DAA era
- Patients with HIV/HCV who are treated with DAA are more likely to be younger, male and African-American compared to HCV mono-infected counterparts
- Antiretroviral therapy switching prior to HCV therapy is common for HIV/HCV patients
- DAA provide similar rates of SVR 12 for patients with HCV mono-infection and HIV co-infection
- There was no difference in time to approval for DAA therapy when compared by insurance status, nor when compared by infectious status (HCV vs HIV/HCV) including stratifying infection status by payer source

References

(1) Torriani, F. J. *et al.* Peginterferon Alfa-2a plus ribavirin for chronic hepatitis C virus infection in HIV-infected patients. *N. Engl. J. Med.* **351,** 438–450 (2004). (2) Osinusi, A. *et al.* Virologic response following combined ledipasvir and sofosbuvir administration in patients with HCV genotype 1 and HIV co-infection. *JAMA* **313,** 1232–1239 (2015). (3) Sulkowski, M. S. *et al.* Ombitasvir, paritaprevir co-dosed with ritonavir, dasabuvir, and ribavirin for hepatitis C in patients co-infected with HIV-1: a randomized trial. *JAMA* **313,** 1223–1231 (2015). (4) Lo Re V. 3rd *et al.* Disparities in Absolute Denial of Modern Hepatitis C Therapy by Type of Insurance. *Clin Gastroenterol Hepatol.* **14**, 1035—1043 (2016). (5) Childs, K. *et al.* Directly acting antivirals for hepatitis C virus arrive in HIV/hepatitis C virus co-infected patients: from 'mind the gap' to 'where's the gap?'. *AIDS.* **30**, 975—989 (2016).