Hepatitis C Direct Acting Antiviral Therapies in a New York City HIV/AIDS Special Needs Plan: Uptake and Barriers

Mark H. Kuniholm, PhD,¹ Terry Leach, PharmD,² Joseph Lunievicz, BA,³ Noemí Olivo, MSN,²
Kathryn Anastos, MD,^{1,4} Yvette Vazquez, BS,² Mark Brennan-Ing, PhD,^{3,5} Stephen E. Karpiak, PhD,^{3,5}
Oladipo Alao, MD,² Denis Nash, PhD,⁶ and Jerome Ernst, MD^{2,3}

To the Editor:

HEPATITIS C VIRUS (HCV) co-infection is common among HIV-infected (HIV⁺) patients in the United States (US) and worldwide, with HCV prevalence rates >20% seen in some HIV patient populations.^{1–3} HCV-related liver disease progression is accelerated in HIV⁺ patients compared to HCV mono-infected patients, and liver decompensation and hepatocellular carcinoma (HCC) have emerged as leading causes of morbidity and mortality in many HIV⁺ patient populations.^{4,5} Until recently, HCV was an incurable chronic infection for most HIV⁺ patients. Recently, however, clinical trials have shown that >90% of HCV/HIV co-infected patients can eradicate HCV with interferon (IFN)-free direct acting antiviral (DAA) regimens.^{6–8}

It is believed—but not yet shown in long-term follow-up studies—that most patients co-infected with HCV and HIV will benefit from receipt of DAA therapy. Consequently clinicians show considerable interest in providing DAAs to their HIV⁺ patients, with an eventual goal of eradicating HCV from their patient populations. However, because of the great expense and limited availability—in some settings—of DAAs, it is not well understood what types of HIV⁺ patients are being prioritized for DAA therapy and whether current clinical practices are most effective in terms of reducing morbidity, mortality, and HCV-associated medical care costs. To provide insight into these questions, we used insurance claims data from a not-for-profit Medicaid Special Needs Health Plan designed exclusively for persons living with HIV/AIDS in New York City to: (a) assess the uptake of DAAs among HIV/HCV co-infected persons, and (b) compare patients receiving DAAs to those who are not to identify potential barriers and enablers to DAA uptake.

We used insurance claims data from Amida Care, a not-for-profit Medicaid Special Needs Health Plan exclusively designed

for persons living with HIV/AIDS in New York City. Amida Care began approving claims for DAAs in December 2013. We examined the Amida Care claims database for demographic, clinical, and pharmacy information among persons with claims consistent with chronic HCV infection (CPT-4, ICD-9, or ICD-10) during December 1, 2013 to September 30, 2014, and entered into the claims database through March 1, 2015. T-tests and chi-square tests were used for statistical comparisons. The study procedures were approved by the institutional review board of the Albert Einstein College of Medicine.

Current New York State Department of Health (NYSDOH) Medicaid fee-for-service guidelines related to DAA therapy stipulate that patients who are HIV⁺ should have HIV viral load levels below the lower limit of quantification (LLQ) for 6 months before authorization for DAA therapy is sought on their behalf by their clinical care providers. These NYSDOH guidelines are, to our knowledge, not shared directly with clinical care providers but are shared with approved Medicaid Managed Care health plans such as Amida Care.

Medicaid health plans including Amida Care have the authority to set their own DAA authorization criteria but reimbursement by the NYSDOH Medicaid program for DAA costs may be based on the NYSDOH Medicaid guidelines. When clinical providers communicate with Amida Care to seek prior authorization for DAA therapy, Amida Care staff provides information on the types of documentation it needs to evaluate the prior authorization request. For Amida Care claims, this includes documentation of HIV viral load levels.

During the study time period, 1756 individuals were active Amida Care participants, with a diagnosis consistent with chronic HCV infection based on claims data. Of these participants, 6% ($n=109$) received sofosbuvir (SOF) and/or simeprevir (SIM) during the study time period. Approval requests submitted to Amida Care by clinical care providers included evidence that all of these patients—with one exception—were

¹Department of Epidemiology and Population Health, Albert Einstein College of Medicine, Bronx, New York.

²Amida Care, New York, New York.

³ACRIA, New York, New York.

⁴Department of Medicine, Montefiore Medical Center, Bronx, New York.

⁵New York University College of Nursing, New York, New York.

⁶City University of New York School of Public Health, Hunter College Campus, New York, New York.

TABLE 1. PARTICIPANTS IN NEW YORK CITY HIV/AIDS HEALTH PLAN^a

	Received DAAs (n = 109)	No DAAs (n = 1647)	p
Sex			0.06
Male	83 (76%)	1111 (67%)	
Female	26 (24%)	536 (33%)	
Race/ethnicity			0.64
Black or African American	17 (16%)	310 (19%)	
White	3 (3%)	72 (4%)	
Other ^b	36 (33%)	538 (33%)	
Unknown	53 (49%)	727 (44%)	
History of AIDS	12 (11%)	432 (26%)	0.0004
Received opiate medication ^c	55 (50%)	803 (49%)	0.73
	Median (IQR)	Median (IQR)	
Age	53.2 (49.6–59.1)	52.8 (47.3–57.8)	0.007
CD4+ count ^d	467 (399–644)	420 (232–649)	0.06

^aPatients had diagnosis consistent with chronic HCV infection, December 1, 2013 to September 30, 2014.

DAA, direct acting antiviral; IQR, interquartile range.

^bIncludes Hispanics/Latinos.

^cThe most common opiate medications included: oxycodone, methadone, and tramadol.

^dCD4+ count comparisons were based on: [Received DAAs group: 33 unique participants with 93 CD4+ measurements during the study period] and [No DAAs group: 517 unique participants with 1114 CD4+ measurements during the study period].

receiving combination antiretroviral therapy (ART) and had HIV viral load levels below the LLQ of available virologic assays. The one exception was an elite controller who by definition had an HIV viral load level below the LLQ without ART.

As compared to those who did not receive SOF and/or SIM, patients treated with a DAA were significantly older (median age: 53.2 vs. 52.8; $p=0.007$), less likely to have a history of AIDS (11% vs. 26%; $p=0.0004$) and were non-significantly more likely to be male (76% vs. 67%, $p=0.06$). CD4+ T-cell levels for patients who received DAA therapy were nonsignificantly higher than for patients who did not (median CD4+: 467 vs. 420; $p=0.06$). Race/ethnicity and receipt of opiate-based medications did not differ significantly by receipt of DAAs (Table 1).

One hundred nine patients in a HIV/AIDS Medicaid health plan in New York City received DAA therapy for chronic HCV infection during 2013–2014. However, per NYSDOH guidelines, during that time period clinical care providers only requested approval to treat patients with well controlled HIV. Predictions of rapid eradication of HCV from HIV patient populations may therefore be unrealistic. HCV treatment guidelines published by the American Association for the Study of Liver Diseases (AASLD)/Infectious Diseases Society of America (IDSA)⁹ state that HIV+ patients are at “High Priority for Treatment Owing to High Risk for Complications” but make no mention of different treatment strategies based on HIV viral load. For HIV/HCV co-infected patients insured through Amida Care, and likely through other Medicaid health plans in New York, state Medicaid guidelines strongly influence access to DAA therapies.

The evidence upon which to base clinical and payer decisions related to provision of DAA therapy for HIV/HCV co-infected patients is very limited and is rapidly changing. For example, until very recently, almost all HIV/HCV co-infected patients receiving DAAs in efficacy trials were also receiving ART and/or had well controlled HIV.^{7,8} However, in a very recent, albeit small, efficacy trial there were no significant differences in HCV RNA decay or SVR rates between HIV/HCV co-infected patients who were or were not receiving ART during the time period of DAA administration.⁶ Understanding of drug–drug interactions between DAAs and ART is also incomplete.

There may come a time in the near future when HIV clinical care providers have completed treatment with DAAs of most/all HIV/HCV co-infected patients with well controlled HIV infection. An important dilemma for providers is therefore how to successfully treat HIV/HCV co-infected patients with detectable HIV viremia, a marker which in the opinion of some but not all providers and payers suggests that adherence to DAAs may be <100%. Directly observed therapy (DOT) and other interventions (e.g., peer-based models of treatment) have previously been considered as modalities to increase the effectiveness of interferon (IFN)-based HCV therapies.¹⁰ However, it is unclear if these same strategies will also be relevant for DAA-based HCV therapy which is taken for a short interval (e.g., 8–24 weeks) and is associated with many fewer side effects than IFN-based regimens. Comprehensive HCV care coordination initiatives which include DAA therapy are currently being evaluated in New York City but the effectiveness of these new programs for HIV/HCV co-infected patients is not yet known.

In conclusion, all 109 participants who received DAAs in a Medicaid health plan designed for persons living with HIV/AIDS in New York City in 2013–2014 had well controlled HIV. It is now important that clinical care providers and payers consider evidence-based strategies to treat HIV/HCV co-infected patients with inadequately controlled HIV replication. We speculate that such strategies will not only reduce HCV-associated morbidity and mortality but will also be cost effective, especially at low CD4+ T-cell levels, which are also a significant risk factor for serious and costly conditions such as HCC and decompensated cirrhosis.^{11,12}

Acknowledgments

No funding was received to support the project.

Author Disclosure Statement

TL, NO, YV, OA, and JE are employed by Amida Care which receives research funding from Gilead Sciences. JL, M. B-I, and SK are employed by ACRIA which receives research funding from Gilead Sciences. MK, KA, and DN report no conflicts.

References

1. Kuehlkamp VM, Schuelter-Trevisol F. Prevalence of human immunodeficiency virus/hepatitis C virus co-infection in Brazil and associated factors: A review. *Braz J Infect Dis* 2013;17:455–463.
2. Matthews PC, Geretti AM, Goulder PJ, et al. Epidemiology and impact of HIV coinfection with hepatitis B and

- hepatitis C viruses in Sub-Saharan Africa. *J Clin Virol* 2014; 61:20–33.
3. Zhang F, Zhu H, Wu Y, et al. HIV, hepatitis B virus, and hepatitis C virus co-infection in patients in the China National Free Antiretroviral Treatment Program, 2010–12: A retrospective observational cohort study. *Lancet Infect Dis* 2014;14:1065–1072.
 4. Puoti M, Moioli MC, Travi G, et al. The burden of liver disease in human immunodeficiency virus-infected patients. *Semin Liver Dis* 2012;32:103–113.
 5. Smith C, Sabin CA, Lundgren JD, et al. Factors associated with specific causes of death amongst HIV-positive individuals in the D:A:D Study. *AIDS* 2010;24:1537–1548.
 6. Osinusi A, Townsend K, Kohli A, et al. Virologic response following combined ledipasvir and sofosbuvir administration in patients with HCV genotype 1 and HIV co-infection. *JAMA* 2015;313:1232–1239.
 7. Sulkowski M, Hezode C, Gerstoft J, et al. Efficacy and safety of 8 weeks versus 12 weeks of treatment with grazoprevir MK-5172 and elbasvir MK-8742 with or without ribavirin in patients with hepatitis C virus genotype 1 mono-infection and HIV/hepatitis C virus co-infection C-WORTHY: A randomised, open-label phase 2 trial. *Lancet* 2015;385:1087–1097.
 8. Sulkowski MS, Naggie S, Lalezari J, et al. Sofosbuvir and ribavirin for hepatitis C in patients with HIV coinfection. *JAMA* 2014;312:353–361.
 9. ASLD, IDSA. Recommendations for Testing, Managing and Treating Hepatitis C. <http://www.hcvguidelines.org>. 2015 (Last accessed May 15, 2015).
 10. Bruggmann P, Litwin AH. Models of care for the management of hepatitis C virus among people who inject drugs: One size does not fit all. *Clin Infect Dis* 2013;57: S56–S61.
 11. Fernandez-Montero JV, Barreiro P, Vispo E, et al. Liver stiffness predicts liver-related complications and mortality in HIV patients with chronic hepatitis C on antiretroviral therapy. *AIDS* 2013;27:1129–1134.
 12. Kramer JR, Kowalkowski MA, Duan Z, et al. The effect of HIV viral control on the incidence of hepatocellular carcinoma in veterans with hepatitis C and HIV coinfection. *J Acquir Immune Defic Syndr* 2015;68:456–462.

Address correspondence to:

Mark H. Kuniholm, PhD

Department of Epidemiology and Population Health

Albert Einstein College of Medicine

Belfer Building, Room 1308

1300 Morris Park Ave

Bronx, NY 10461

E-mail: mark.kuniholm@einstein.yu.edu