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Prevalence and Predictors of Important Telaprevir Drug Interactions Among Patients Coinfected With Hepatitis C and Human Immunodeficiency Virus

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Abstract

Background: Among patients with HIV and hepatitis C (HCV) coinfection, drug–drug interactions involving nonstructural protein 3/4 (NS3/4A) serine protease inhibitors for HCV infection are an important concern because these drugs affect cytochrome P450 metabolism and p-glycoprotein transporters. **Objectives:** The primary objective was to determine the prevalence of clinically significant drug–drug interactions (CSDDIs) in HIV/HCV coinfected patients if telaprevir-based HCV therapy is added to patients' medication regimens. Secondary objectives were to identify antiretroviral therapy (ART) regimens associated with the lowest risk of CSDDI and determine the clinical risk factors. **Methods:** A cross-sectional study was performed among adult HIV/HCV coinfected patients. Demographics, comorbidities, social history, and medication lists were extracted from medical records. For each patient, CSDDIs were identified by entering all medications and pegylated interferon, ribavirin, and telaprevir into Lexi-Interact drug interaction software. The number and nature of CSDDIs were recorded before and after addition of telaprevir-based therapy. **Results:** There were 335 patients included. Prior to the addition of telaprevir-based HCV therapy, there was a high frequency (82.1%) of any CSDDI. After the addition of telaprevir-based HCV therapy, the frequency of any CSDDI increased to 97% ($P < .001$). Contraindicated interactions rose from 20.0% to 38.2% of patients after addition of telaprevir-based therapy. Use of ≥10 non-HIV medications, dyslipidemia, and HIV protease inhibitors were independently associated with the occurrence of a contraindicated interaction. **Conclusions:** Clinicians considering initiating telaprevir in HIV/HCV coinfected patients should be vigilant of drug–drug interactions, particularly among patients with dyslipidemia, those using ≥10 non-HIV medications, and those using HIV protease inhibitors.

Keywords
hepatitis C, HIV, antiretroviral, drug interaction

Introduction

Direct-acting treatment modalities for chronic hepatitis C have dramatically increased the frequency of sustained virologic response (SVR).[1-7] Nonstructural protein 3/4 (NS3/4A) serine protease inhibitors represent the first available class of direct acting hepatitis C virus (HCV) agents, and treatment guidelines have incorporated these therapies into the standard HCV treatment regimen among patients infected with genotype 1 virus.[8]

Despite the availability of direct acting agents, use of these medications introduces increased drug toxicity risks and drug cost.[9] Drug–drug interactions represent another important concern since the currently available NS3/4A protease inhibitors, boceprevir, telaprevir, and simeprevir, affect cytochrome P450 metabolism and p-glycoprotein transporters.[10] Numerous proven and theoretical pharmacokinetic drug interactions have been associated with these agents, and careful consideration for drug interaction presence and management is necessary.[11]

Patients coinfected with human immunodeficiency virus (HIV) and HCV are likely to have an even greater risk for drug–drug interactions when receiving therapy with

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NS3/44A protease inhibitors. HIV/HCV coinfected patients must remain on antiretroviral therapy during HCV treatment to optimize HCV treatment outcomes and sustain HIV virologic suppression. Numerous drug interactions have been documented between antiretrovirals and NS3/4A protease inhibitors, and there are only a select number of antiretrovirals that can be coadministered with these agents.[12] Despite this information, there are currently limited data to describe the prevalence, risk factors, and feasibility of coadministration of NS3/4A protease inhibitors with antiretroviral agents in HIV/HCV coinfected patients.

Given this gap in the literature, the primary objective of this study was to determine the prevalence of clinically significant drug–drug interactions (CSDDI) in HIV/HCV coinfected patents if telaprevir-based HCV therapy is added to patients' medication regimens. As a secondary objective, we were interested in quantifying which ART regimens are associated with the lowest risk of CSDDI involving telaprevir. Giving the increased use of non-ART medications for other comorbidities among HIV patients, we also wanted to determine the clinical risk factors that are associated with a higher probability of a contraindicated medication combination involving telaprevir.

For this study, we chose to focus on telaprevir over boceprevir and simeprevir because of clear contradictions to coadministration with primary ART agents.[13-15] Based on these data, telaprevir appears to be among the more viable NS3/4A protease inhibitor for treating patients who are HIV/HCV coinfected and receiving concomitant antiretroviral therapy to manage their HIV infection.

Methods

Study Design and Population

A cross-sectional study of patients coinfected with HCV and HIV was performed at the Upstate New York Veterans' Healthcare Administration (VISN-2) and Upstate University Hospital (Syracuse, NY). Patients receiving care at these institutions between January 1, 2000, and July 31, 2012, and infected with both HCV and HIV were eligible for inclusion. Inclusion criteria were the following: (*a*) age ≥ 18 years, (*b*) documented HIV infection, and (*c*) laboratory-confirmed diagnosis of HCV infection. Patients with no medication history were excluded from the analyses.

Data Collection

Trained reviewers extracted information from the patients' medical records on demographics, comorbidities, social history, and medication lists. Demographic covariates included age, year of HCV and HIV diagnosis, sex, race, height, and weight. Episodic illnesses such as oropharangeal candidiasis, pneumonia, and various other opportunistic infections were not considered comorbid conditions.

Laboratory data included the most recent CD4 cell count, HIV-RNA, and HCV-RNA. Because of the nonparametric distributions of HIV-RNA and HCV-RNA, both these variables were log-transformed to assess them as a continuous variable. For patients with an undetectable HIV-RNA or HCV-RNA, the next digit below the threshold of detection was imputed before log-transformation to a continuous variable. For instance, a value of 49 would be imputed for a patient with an undetectable HIV RNA (<50 copies/mL).

The drug name, dose, strength, and frequency were abstracted from the most recent outpatient medication list.

Outcome Assessment

The primary outcome of this study was the prevalence of CSDDIs between the medications in the patient's profile and the addition of telaprevir-based HCV therapy. Telaprevir-based HCV therapy was defined as telaprevir, pegylated interferon-α (PegIFN), and ribavirin.

For each patient, CSDDIs were identified by entering all medications into Lexi-Interact drug interaction software. Once their medication profile was added, the number and nature of CSDDIs were recorded. Subsequently, telaprevir-based HCV therapy was added to the medication profile in Lexi-Interact to assess the potential for a CSDDI and the number and nature of CSDDIs were recorded. For the purposes of these analyses, CSDDIs were those that Lexi-Interact ranked as D-rated (interactions requiring enhanced monitoring or dosage modification) or X-rated (contraindicated interactions).[16]

For both outcomes (D/X-rated and X-rated interactions), the output from Lexi-Interact was cross-matched with the current prescribing information for telaprevir (Incivek).[14] If new drug–drug interaction data emerged during the study period, these data were included in the drug interaction analysis.

Statistical Analyses

Categorical variables were compared by the χ^2 or Fisher's exact test. Continuous variables were evaluated using the Student's *t* or Mann–Whitney *U* test. McNemar's test was used to assess the frequency of drug–drug interactions because the data are inherently matched (before/after adding telaprevir therapy). Breakpoints in the distribution of continuous variables were determined using classification tree (CART) analysis.[17]

All variables associated with the outcomes of interest in the bivariate analysis ($P < .2$) were considered for inclusion in the multivariate regression model. Multiplicative effect measure modification was assessed through the use of interaction terms. Due to the high proportion (>10%) of patients who were expected to achieve the outcome, a log-binomial regression with robust variance estimates was used.[18] A backwards stepwise approach was used to derive the most

parsimonious model. Variables remained in the final model if the associated *P* value was less than .05. Once the final model was derived, potential confounders were put back into the model and only retained if their presence changed the resulting prevalence ratios by more than 10%. All calculations were computed using SPSS version 11.5 (SPSS Inc, Chicago, IL), SAS version 9.3 (SAS Institute, Cary, NC), and CART software (Salford Systems, San Diego, CA).

Sample Size Justification

Assuming a type I error frequency of 5% and 80% power, a minimum of 234 patients were required to detect an effect size of 20% for the specified outcome.

Ethics

This study was approved by institutional review boards at the Stratton Veterans' Affairs Medical Center (Albany, NY) and Upstate Medical University (Syracuse, NY). Given the retrospective nature of the study, a waiver of consent was obtained.

Results

There were 4794 adult Veterans' Affairs patients with laboratory-confirmed HCV during the study period. Of these, only 250 patients were coinfected with HIV/HCV. Among these patients, 6 did not have medication histories available and were excluded, leaving 244 patients from the VAMC eligible for analysis. An additional 91 patients from Upstate Medical University satisfied inclusion criteria. The final analysis included a total of 335 HIV/HCV coinfected patients.

The majority of patients were male (87.2%) and disproportionately distributed by study site: 239 (98.0%) males from the VAMC study site and 53 (58.2%) males from Upstate University Hospital, $P < .001$. The mean (standard deviation [SD]) age of patients was 55.6 (7.3) years. The median (interquartile range [IQR]) durations of HIV and HCV infections for these patients were 18 (13-23) and 13 (10-17) years, respectively. The patients had a median (IQR) of 8 (6-12) underlying comorbidities. The patients were using a mean (SD) of 11.2 (4.9) medications. There were 306 (91.3%) patients receiving combination antiretroviral therapy (ART). The most commonly used ART regimen types were composed of 2 nucleoside reverse transcriptase inhibitors (NRTI) plus a: non-nucleoside reverse transcriptase inhibitor (NNRTI; 39.9%), protease inhibitor (PI; 38.6%), mixed/multiple class ART regimen (17.0%), and integrase strand transfer inhibitor (ISTI; (4.6%). Antidepressants (30.7%) and central nervous system (CNS) depressants (47.8%) were the most frequently used non-HIV drug classes.

The distribution and nature of CSDDIs are displayed in Figure 1A. The addition of telaprevir-based HCV therapy resulted in a statistically significant increase in the frequency of each type of CSDDI. Prior to the addition of telaprevir-based HCV therapy, there was a high frequency (82.1%) of any CSDDI (D- or X-rated interactions). After the addition of telaprevir-based HCV therapy to the patients' medication regimens, the frequency of any CSDDI increased to 97% ($P < .001$). Drug–drug interactions requiring a dose change of at least one medication occurred in 88 (26.3%) patients prior to the addition of telaprevir-based HCV therapy. This increased to 120 (35.8%) patients after the addition of telaprevir-based HCV therapy. The prevalence of contraindicated (X-rated) drug–drug interactions increased significantly from 20% to 38.2% after the addition of telaprevir-based HCV therapy ($P < .001$).

Interactions involving ART occurred frequently and significantly increased with the addition of telaprevir-based HCV therapy. Contraindicated interactions involving ART occurred in 95 (28.4%) patients after addition of telaprevir-based HCV therapy. The prevalence of contraindicated drug–drug interactions before and after addition of telaprevir-based hepatitis C therapy, stratified by type of ART regimen, is displayed in Figure 1B. There was no difference in the frequency (14.3%) of contraindicated drug–drug interactions before or after addition of telaprevir-based HCV therapy for patients receiving ISTI-based ART regimens to patients' medication profiles ($P = 1.00$). The probability of contraindicated drug–drug interactions for recipients of NNRTI-based ART regimens did not significantly differ before (17.2%) and after (26.2%) addition of telaprevir-based HCV therapy ($P = .08$). For patients receiving PI-based regimens and mixed class ART regimens, there was a statistically significant 2-fold increased frequency of contraindicated drug–drug interactions after the addition of telaprevir-based HCV therapy.

The bivariate analyses comparing the clinical covariates and occurrence of a contraindicated drug–drug interaction are displayed in Table 1. The CART-derived breakpoints were identified for age (≥52 years), duration of HIV infection (≥21 years), total number of medications (≥14), and total number of non-HIV medications (≥10). The probability of contraindicated drug–drug interactions was significantly higher for patients above these thresholds. The proportion of patients receiving ART was higher among patients with a contraindicated drug–drug interaction than those without, and the distributions of ART regimen types varied. Among patients with a contraindicated drug–drug interaction, PI-based ART was the most common regimen. Classes of medications that significantly differed between patients with and without a contraindicated drug–drug interaction were calcium channel blockers, corticosteroids, erectile dysfunction drugs, and HMG Co-A reductase inhibitors. Comorbidities that differed between patients with and without contraindicated drug–drug interactions were depression, substance abuse, dyslipidemia, and neuropathy.

The results of the multivariate regression analyses are displayed in Table 2. The use of at least 10 non-HIV medications and protease inhibitors were independently associated

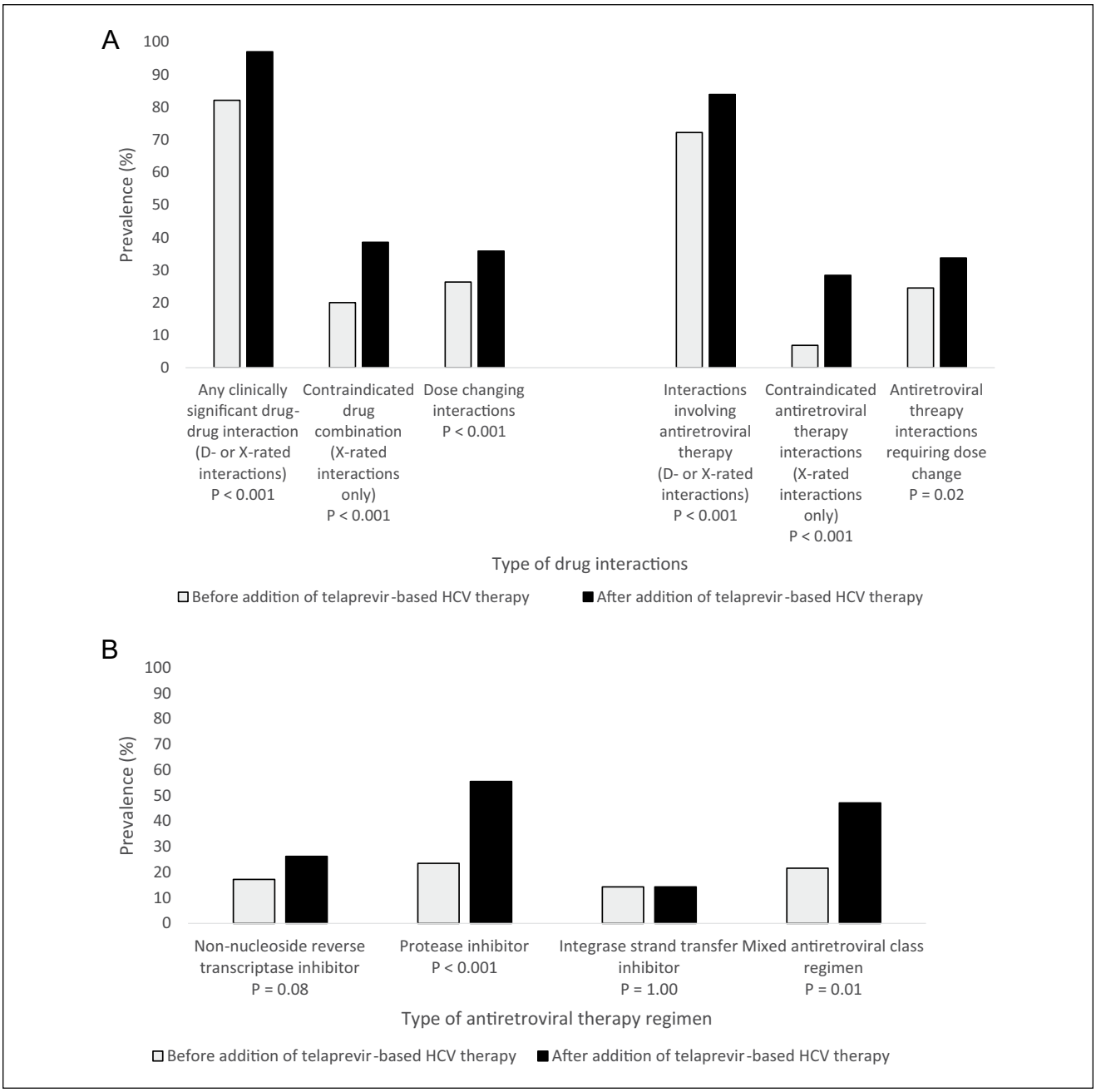

Figure 1. (A) Distribution of drug–drug interactions before and after addition of telaprevir-based hepatitis C therapy. (B) Prevalence of contraindicated drug–drug interactions before and after addition of telaprevir-based hepatitis C therapy, stratified by type of antiretroviral therapy regimen.

with the occurrence of a contraindicated drug–drug interaction involving telaprevir-based HCV therapy. Additionally, dyslipidemia was the only comorbidity that was associated with a contraindicated drug–drug interaction. In a separate model, use of protease inhibitors was removed from the model and replaced with each of the individual protease inhibitors. Use of darunavir, fosamprenavir, and lopinavir were the only protease inhibitors to remain in the final model and continued to be independently associated with a contraindicated drug–drug interaction.

Discussion

There were several notable findings from this investigation. First, we observed a high frequency of CSDDI (82.1%) prior to the addition of telaprevir-based HCV therapy to

Table 1. Bivariate Analyses of Clinical Covariates Associated With Contraindicated Drug–Drug Interactions Involving Telaprevir-Based HCV Therapy[a].

Covariate	No Contraindicated Drug–Drug Interaction (N = 206)	Contraindicated Interaction Present (N = 129)	*P* Value
Age, mean ± SD	55.0 ± 7.8	56.6 ± 6.3	.04
Age ≥ 52 years[b]	146 (70.9)	106 (82.2)	.02
Male sex	175 (85.0)	117 (90.7)	.13
Race			.07
African American	111 (54.4)	85 (66.4)	
Hispanic	27 (13.2)	18 (14.1)	
White	60 (29.4)	24 (18.8)	
Other	6 (2.9)	1 (0.8)	
Weight, mean ± SD	80.8 ± 18.6	78.3 ± 15.8	.21
Duration of HIV infection, median (IQR)	17 (11-22)	19 (15-24)	.009
Duration of HIV ≥ 21 years[b]	60 (29.1)	54 (41.9)	.02
Duration of HCV infection, median (IQR)	13 (8-16)	15 (11-19)	.002
Most recent CD4 count, median (IQR)	511 (288-688)	380 (187-542)	<.001
Most recent log-transformed HIV-RNA, mean ± SD	2.3 ± 1.1	2.4 ± 1.1	.32
Most recent log-transformed HCV-RNA, mean ± SD	5.0 ± 1.8	5.4 ± 1.5	.11
Antiretroviral therapy treatment experienced	191 (92.7)	124 (96.1)	.20
Receiving antiretroviral therapy	182 (88.3)	124 (96.1)	.01
Antiretroviral regimen type			<.001
Non-nucleoside reverse transcriptase inhibitor	90 (49.5)	32 (25.8)	
Protease inhibitor	53 (29.1)	66 (53.2)	
Integrase strand transfer inhibitor	12 (6.6)	2 (1.6)	
Other/mixed class regimen	27 (14.8)	24 (19.4)	
None	24 (11.6)	5 (3.9)	
Use of nucleoside reverse transcriptase inhibitors	176 (85.4)	107 (82.9)	.54
Zidovudine	45 (21.8)	20 (15.5)	.15
Lamivudine	77 (37.4)	38 (29.5)	.16
Emtricitabine	89 (43.2)	53 (41.1)	.70
Tenofovir	90 (43.7)	62 (48.1)	.43
Abacavir	26 (12.6)	15 (11.6)	.79
Didanosine	6 (2.9)	10 (7.8)	.06
Stavudine	23 (11.2)	11 (8.5)	.44
Use of non-nucleoside reverse transcriptase inhibitor	104 (50.5)	43 (33.3)	0.002
Efavirenz	81 (39.3)	31 (24.0)	.004
Nevirapine	20 (9.7)	4 (3.1)	.03
Rilpivirine	3 (1.5)	2 (1.6)	.95
Etravirine	0 (0.0)	6 (4.7)	.003
Use of protease inhibitor	63 (30.6)	87 (67.4)	<.001
Atazanavir	43 (20.9)	14 (10.9)	.02
Darunavir	0 (0.0)	20 (15.5)	<.001
Fosamprenavir	0 (0.0)	6 (4.7)	.003
Lopinavir	0 (0.0)	46 (35.7)	<.001
Saquinavir	3 (1.5)	2 (1.6)	.95
Indinavir	4 (1.9)	0 (0.0)	.30
Nelfinavir	13 (6.3)	2 (1.6)	.06
Ritonavir	36 (17.5)	80 (62.0)	<.001
Cobicistat	2 (1.0)	0 (0.0)	.53
Integrase inhibitor	22 (10.7)	17 (13.2)	.49
Raltegravir	20 (9.7)	17 (13.2)	.32
Elvitegravir	2 (1.0)	0 (0.0)	.53

(continued)

Table 1. (continued)

Covariate	No Contraindicated Drug–Drug Interaction (N = 206)	Contraindicated Interaction Present (N = 129)	*P* Value
Enfuvirtide	1 (0.5)	1 (0.8)	.0
Maraviroc	0 (0)	1 (0.8)	.39
Non-HIV medication usage			
Total number of medications, median (IQR)	10 (7-13)	13 (10-16)	<.001
Use of ≥ 14 medications[b]	39 (18.9)	57 (44.2)	<.001
Number of non-HIV medications, median (IQR)	7 (4-9)	9 (6-13)	<.001
Use of ≥ 10 non-HIV medications[b]	50 (24.3)	60 (46.5)	<.001
Antipsychotics	43 (20.9)	25 (19.4)	.74
Antibiotics	12 (5.8)	8 (6.2)	.88
Antidepressants	58 (28.2)	45 (34.9)	.19
Azole antifungals	7 (3.4)	7 (5.4)	.37
Statins	12 (5.8)	26 (20.2)	<.001
Calcium channel blockers	21 (10.2)	29 (22.5)	.002
Central nervous system depressants	94 (45.6)	66 (51.2)	.32
Erectile dysfunction drugs	9 (4.4)	49 (38.0)	<.001
Corticosteroids	28 (13.6)	28 (21.7)	.05
Comorbidities			
Alcoholism	65 (31.6)	53 (41.1)	.08
Anxiety	17 (8.3)	18 (14.0)	.10
Asthma	10 (4.9)	3 (2.3)	.38
Bipolar/mood/personality disorder	28 (13.6)	10 (7.8)	.10
Cardiovascular disease	17 (8.3)	14 (10.4)	.42
Chronic kidney disease	11 (5.3)	11 (8.5)	.25
Chronic obstructive pulmonary disease	20 (9.7)	14 (10.9)	.74
Depression	72 (35.0)	64 (49.6)	.008
Diabetes	26 (12.6)	21 (16.3)	.35
Dyslipidemia	23 (11.2)	31 (24.0)	.002
Epilepsy/seizures	11 (5.3)	7 (5.4)	.97
Gastroesophageal reflux disease	25 (12.1)	15 (11.6)	.88
Hepatitis B infection	13 (6.3)	14 (10.9)	.14
History of cancer	17 (8.3)	14 (10.9)	.42
History of substance abuse	117 (56.8)	88 (68.2)	.04
Hypertension	70 (34.0)	52 (40.3)	.24
Insomnia	13 (6.3)	13 (10.1)	.21
Neuropathy	15 (7.3)	19 (14.7)	.03
Osteoporosis/osteoarthritis/osteogenesis	20 (9.7)	14 (10.9)	.74
Posttraumatic stress disorder	22 (10.7)	22 (17.1)	.09
Prostate disease	16 (7.8)	15 (11.6)	.24
Schizophrenia/psychosis	17 (8.3)	12 (9.3)	.74
Vitamin D deficiency	21 (10.2)	22 (17.1)	.07

Abbreviations: SD, standard deviation; IQR, interquartile range; HCV, hepatitis C virus.
[a]All data presented as n (%), mean (SD), or median (IQR), unless noted otherwise.
[b]CART-derived breakpoint.

patients' medication profiles. Consistent with the literature, this is a population of patients that are already at high risk for CSDDI.[16,19] The use of multiple medications, polypharmacy, is common among patients with HIV and will continue to become problematic as this population continues to age.[20] After the addition of telaprevir-based HCV therapy, almost all patients (97%) had a CSDDI. This finding is important because drug–drug interactions can lead to harmful, yet preventable, patient outcomes including drug toxicity or inadequate clinical response. Our results demonstrate that nearly all coinfected individuals considering telaprevir-based therapy are vulnerable. Given their similarities in drug metabolism, comparable findings are likely with boceprevir- and simepravir-based HCV therapies.

Table 2. Clinical Covariates Independently Associated With Presence of Contraindicated Drug–Drug Interactions After Addition of Telaprevir-Based Hepatitis C Virus Therapy to Patients' Medication Regimens.

Covariate	Prevalence Ratio	95% Confidence Interval	*P* Value
Model 1			
Use of a protease-inhibitor	2.49	1.87-3.32	<.001
Use of ≥10 non-HIV medications	1.74	1.36-2.22	<.001
Dyslipidemia	1.53	1.17-1.99	.002
Model 2			
Darunavir	4.36	3.26-5.84	<.001
Fosamprenavir	4.15	3.14-5.48	<.001
Lopinavir	3.96	3.11-5.05	<.001
Use of ≥10 non-HIV medications	1.80	1.44-2.24	<.001
Dyslipidemia	1.62	1.26-2.08	.002

The majority of drug–drug interactions observed after the addition of telaprevir-based HCV therapy involved antiretroviral therapy. While the treatment guidelines recommend reviewing ART prior to the addition of HCV agents, this study illustrates that a high proportion of patients would require alterations to their ART regimens. It is important to note that the risk of contraindicated drug–drug interactions varied between and within different classes of ART regimens when telaprevir-based HCV therapy is added. In this study, PI-based ART was the most problematic and independently associated with the occurrence of a contraindicated drug–drug interaction. To refine this risk assessment, we replaced the use of PIs with the individual PI agents; the only PIs to remain in the model and continue to be independently associated with a contraindicated drug–drug interaction were darunavir, lopinavir, and fosamprenavir.

In addition to considering the ART, the risk of contraindicated drug–drug interactions was dependent on the full complement of medications received. Unsurprising, polypharmacy was an important predictor and use of ≥10 non-HIV medications was independently associated with an increase probability of contraindicated drug–drug interactions. This underscores the obvious risk of contraindicated drug–drug interactions among populations in which polypharmacy is crucial to optimizing management of comorbidities, especially as life expectancy increases and more drugs are utilized.

Dyslipidemia was also an independent predictor of CSDDIs. Dyslipidemia may have been a proxy for medication use patterns among the patients studied. Treatment of dyslipidemia is most often with an HMG CoA reductase inhibitor, and many drugs in this class are known to interact with telaprevir.

While this study is the first to quantify the prevalence of interactions involving telaprevir, several limitations should be considered. First, the exposure variable, telaprevir-based HCV therapy, was theoretical. None of the patients in the study actually received telaprevir therapy. Rather, the data were meant to quantify the magnitude of interactions that would occur had these patients initiated telaprevir-based HCV therapy. The theoretical design is also an asset. It is statistically more efficient to study theoretical risk, and from a bioethical perspective, we did not wait for drug interactions to occur before studying them. Second, we used an automated software program, Lexi-Interact, to define the presence of CSDDI and contraindicated drug–drug interactions. The gold standard would have been to convene an expert panel. However, in practice, most pharmacists rely on automated programs to screen for drug–drug interactions and use clinical judgment to determine the existence of a truly clinically significant drug–drug interaction. The use of Lexi-Interact to define our outcome is objective, reproducible, and not vulnerable to interpharmacist variability. In a survey of hospital pharmacists, it was also the most preferred program by pharmacists on the basis of database quality and performance.[21] Third, our 2 outcomes (CSDDI and contraindicated drug–drug interactions) were limited to interactions that Lexi-Interact considered D- or X-rated. We limited our outcomes to these interactions because they are the more serious potential drug–drug interactions. However, we recognize that pharmacists' opinions on the importance of C-rated interactions may vary and some require pharmacotherapeutic intervention. From a statistical perspective, perfect specificity and imperfect sensitivity that is nondifferentially distributed will lead to unbiased prevalence ratios. We anticipate that our prevalence estimates of CSDDI are conservative and more interactions, of lesser severity, may indeed exist. Fourth, we included all HIV/HCV coinfected patients and did not restrict to patients with solely genotype 1 HCV infection. Genotype was documented in the medical charts of only 92 patients. Furthermore, there is no biologically plausible reason to expect patients with non–genotype 1 HCV infection to have different medication use patterns than patients with genotype 1 HCV infection. Because there is no heterogeneity expected, the interactions identified are still pertinent

and preserve statistical efficiency. Finally, our data do not provide any comparative context on the frequency of CSDDI or contraindicated interactions that would occur with other NS3/4A serine protease inhibitors to treat HCV infection like boceprevir or simeprevir. Although only telaprevir was used in this analysis, similar drug interaction concerns are likely with the other available NS3/4A protease inhibitors. With the rapid approval of several other agents from different medications classes on the horizon, it is unclear what the population-based risk of drug–drug interactions would be, and similar studies would need to be performed on market entry. Since neither of these agents are recommended for coadministration with any available first-line HIV protease inhibitors or non-nucleoside reverse transcriptase inhibitors, drug interaction management is likely to be even more challenging for HIV/HCV coinfected patients.[13,15] A similar analysis with boceprevir and simeprevir might be equally valuable to compare to the current results, as well as with other drugs from other classes like sofosbuvir. An understanding of the drug interaction potential with these drugs will aid in the selection of safe and appropriate drug therapy.

In summary, the availability of telaprevir-based HCV therapy is changing the therapeutic landscape for patients with HIV/HCV coinfection. Clinicians considering initiating HCV therapy with telaprevir for HIV/HCV coinfected patients should be vigilant of drug–drug interactions, particularly among patients with dyslipidemia, those using ≥10 non-HIV medications, and those using a protease inhibitor. Pharmacists can help prevent adverse events associated with drug–drug interactions. Future research should evaluate strategies to avoid drug–drug interactions, such as switching ART regimens and minimizing polypharmacy.

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Declaration of Conflicting Interests

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