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Short Communication

Short Communication: Heterogeneity in Drug and Alcohol use-Related Exclusion Criteria in Direct Acting Antiviral Agent Hepatitis C Treatment Trials for Individuals Coinfected with Hepatitis C Virus and HIV

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Abstract

Coinfection with HIV and Hepatitis C virus (HCV) is often an infectious complication of drug use. People who use or have used drugs have been excluded from manyof the clinical trials evaluating safety and efficacy of directacting antiviral agents (DAAs).

We sought to systematically evaluate exclusion criteria concerning drug and alcohol use in DAA-based HCV treatment trials for HIV/HCV coinfected persons by searching the clinicaltrials.gov website of the U.S. National Library of Medicine and National Institutes of Health for DAA-based HCV treatment trials in HIV/HCV coinfected individuals for all available trials through May 2013. (Clinicaltrials.gov maintains a record of trials conducted in the U.S. and 185 other countries). Exclusion criteria referencing drug and/or alcohol use were tabulated and analyzed.Eighteen completed, ongoing and recruiting clinical trials were identified, involving nine DAAs (protease, polymerase and NS5A inhibitors). Nine trials (50%) excluded individuals with either current or prior alcohol, "substance," or "drug" use. In a majority of these trials (78%), exclusion was also based upon site investigators' perceptions of capacity or suitability to participate in the trial. We conclude that there is heterogeneity in exclusion criteria concerning substance use in clinical trials of DAAs in coinfection, and that the potential to exclude patients is based on subjective perceptions. Developing consistent, evidence-based criteria concerning substance use could permit greater, more equitable access to DAA trials for the HIV/HCV coinfected population.

INTRODUCTION

Hepatitis C virus (HCV) coinfection is prevalent among HIV-infected persons who inject drugs (PWIDs), with estimates ranging from 50% to upwards of 90% in many countries [1]. Coinfection with HCV typically leads to accelerated fibrosis progression, leading to more rapid progression to cirrhosis and liver failure, and higher rates of liver-related, AIDS-related and all-cause morbidity and mortality among this population [2-4].

Despite the severity of HCV coinfection, only a minority of coinfected PWID have received treatment for HCV [5]. This trend

is due both to formidable socioeconomic access barriers, and to provider perceptions of this population as being too unstable for treatment, despite a lack of evidence to date to support this practice. Both U.S. and European recommendations endorse considering all coinfected PWIDs as eligible for treatment, and data for HCV monoinfection has confirmed no difference in sustained virologic response (SVR) between PWID and non-PWID [6]. The WHO has also endorsed this principle as "efficacious and cost-effective in PWID" and recommends "that all adults and children with chronic HCV infection, including PWID, should be assessed for antiviral treatment[7]."WHO has also stated that "treatment may also be effective as prevention, due to a reduction in transmission", a recommendation based on modeling studies which have demonstrated the utility of antiviral treatment in reducing the prevalence of HCV among PWID [7].

Since 2011, approval of multiple direct-acting antiviral agents (DAAs) for HCV has rapidly changed the HCV treatment landscape, offering higher cure rates, fewer adverse effects, and a shorter duration of therapy over traditional interferon-based therapy. Though these medicines are part of a new, interferon-free treatment era, perceptions about HCV treatment as complex, prolonged, and risky remain entrenched in clinical practice, and prevent PWID from accessing treatment.

This explosion in therapeutic candidates for HCV provides numerous opportunities for enrolling coinfected PWID and coinfected persons who use alcohol and non-injection drugs in clinical trials evaluating safety and efficacy of DAAs. However, many coinfected persons have been excluded from these trials based on individual drug-and-alcohol-use histories. We performed a systematic evaluation of active DAA-based HCV treatment trials in HCV/HIV coinfected persons to determine the extent and nature of their exclusion, and to help inform future research among this important patient population.

METHODS

We performed a search of the clinicaltrials.gov website of the U.S. National Library of Medicine and National Institutes of Health during May 2013 for DAA-based HCV treatment trials for HIV/HCV coinfected individuals through May 2013. (Clinicaltrials.gov maintains a record of trials conducted in the U.S. and 185 other countries). We searched the database combining various terms including "HIV", "HCV", "coinfection", and specific names of DAAs. We identified all completed, ongoing, and recruiting DAA-based HCV treatment trials enrolling HIV/HCV coinfected patients as of May 2013 we identified all DAAs involved in these clinical trials and detailed the rationale behind exclusions based on drug-and-alcohol related histories. Two researchers cross-checked the findings to ensure accuracy.

RESULTS

We identified 18 completed, ongoing, and recruiting DAA-based HCV treatment trials enrolling HIV/HCV coinfected patients (Table 1). Overall, the trials ranged in nature from Phase 1 to Phase 3 trials, with each enrolling between 20 and 310 participants. The trials investigated safety and efficacy of DAAs, and drug-drug interactions between DAAs and antiretroviral therapies for HIV. The trials involved 9 DAAs (protease, polymerase, and NS5A inhibitors) (Table 2).

Table 1: DAA Agents in HCV Treatment Trials Enrolling HIV/HCV Coinfected Individuals.

Protease Inhibitor	Polymerase Inhibitor	Other
Telaprevir	Sofosbuvir	Daclatasvir (NS5A inhibitor)
Boceprevir	Silibinin	
Faldaprevir	Silymarin	
Simeprevir (TMC435)		
Asunaprevir		

A variety of criteria excluded patients with drug-and-alcohol-related histories from these trials (Table 3). Nine (50%) excluded individuals with current or prior alcohol, "substance" or "drug" use. Of these, 6 (33%) excluded individuals with current use, while 3 (17%) and 2 (11%) excluded individuals with history of drug or alcohol use, respectively, requiring a period of pre-treatment abstinence ranging from 6 months to 3 years prior to screening. In 7 of the 9 trials, exclusion was also based upon site investigators' perceptions (e.g. subject to their "opinion" of an individual's substance use, whether substance use was "clinically relevant," "excessive," or "may represent an obstacle to trial participation."). No trial defined which drugs were considered exclusionary, but for 1 specifying marijuana. It was not evident whether or not these trials actively drug tested participants.

Of note, in several instances, exclusion criteria were discordant with the drug-and-alcohol-use criteria in trials by the same sponsors (e.g., Gilead trials NCT01565889 compared to NCT01667731, and Janssen trials NCT01332955 compared to NCT01513941). Additionally, four trials specifically mentioned opiate substitution therapy (OST) in their exclusion criteria. Two studies (NCT00959699 and NCT01718301) excluded individuals on OST that were not in an opiate substitution maintenance program (OSMP).

DISCUSSION

There is significant heterogeneity and inconsistency – even among trials from the same sponsor – in exclusion criteria concerning alcohol and substance use in DAA clinical trials of for people with HIV/HCV coinfection. It was notable that 4 out of 9 trials applied interferon-era exclusion criteria to interferon-free trial regimens. There are several possible reasons for these exclusions. First and foremost may be practice-based fears about substance use history serving as a proxy for social "instability" in this population, which may considered an impediment to trial participation, completion, adherence and follow-up given the significant side effects and close laboratory monitoring required for interferon-based HCV therapy – concerns based not on interferon therapy itself, but rather on people who use drugs and alcohol. Second may be concerns that this population will be at high risk for HCV reinfection following successful treatment and sustained virologic response (SVR), a marker for HCV clearance, or cure. Finally, there may be concerns about drug-resistant HCV among "unstable" patients who quit before completing treatment [8].

Though these rationales are widespread in clinical care of HCV patients today, little evidence exists to validate their use.

Table 2: HCV DAA Clinical Trials Involving HIV/HCV Coinfected Participants.

Clinicaltrials.gov Identifier Trial Sponsor; Phase (Sample Size); Current Status	Official Trial Title	Drug- and Alcohol-related Exclusion Criteria
NCT00246363 Henry Sacks, Mount Sinai School of Medicine; Phase 1 and 2 (n=40); Completed	A Pilot Randomized Placebo-Controlled Trial Designed to Determine the Tolerability and Efficacy of Silymarin (Milk Thistle) vs. Placebo for the Treatment of Chronic Hepatitis C in HIV Infected Patients	• Problems with alcohol of illegal drugs within one year of study entry
NCT01565889 Gilead; Phase 1 and 2 (est. n=80); Ongoing, not recruiting	Part A: Drug Interaction Study Between GS-7977 and Antiretroviral Therapy (ARV) Combinations of Efavirenz, Tenofovir and Emtricitabine; Efavirenz, Zidovudine and Lamivudine; Atazanavir/Ritonavir, Tenofovir and Emtricitabine; Darunavir/Ritonavir, Tenofovir and Emtricitabine; Raltegravir, Tenofovir and Emtricitabine in Human Immunodeficiency Virus and Hepatitis C Virus (HIV/HCV) Co-infected Patients. Part B: A Phase 2, Open-Label Study to Investigate the Efficacy and Safety of GS-7977 With Peginterferon Alfa 2a and Ribavirin for 12 Weeks in Treatment-Naïve HIV/HCV Co-infected Patients.	• Clinically relevant drug or alcohol abuse
NCT01816490 University of Zurich; Phase 2 (est. n=20); Currently recruiting	A Phase II, Multi-center, Open-label, Interventional Study to Evaluate the Safety of Intravenous Silibinin (iSIL) and Its Effect on the Hepatitis C Virus Load in Treatment-experienced HCV-HIV Co-infected Individuals With Advanced Liver Fibrosis in the Swiss HIV Cohort Study (SHCS)	No mention
NCT00983853 Vertex; Phase 2 (n=68); Completed	A Phase 2a, 2-Part, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Multicenter Study of Telaprevir in Combination With Peginterferon Alfa-2a (Pegasys®) and Ribavirin (Copegus®) in Subjects Who Have Chronic HCV-1/HIV-1 Co-Infection and Are Treatment-Naïve for Hepatitis C	No mention
*NCT00959699 Merck, Phase 2; (n=99); Completed	A Phase 2b, Safety and Efficacy Study of Boceprevir in Patients Coinfected With HIV and Hepatitis C (Protocol No. P05411)	- Current evidence of substance abuse within 3 years of the Screening Visit. - History of marijuana use deemed excessive by the Investigator. - History of a clinical diagnosis within the past 6 months of substance abuse prior to Day 1.
NCT01332955Janssen, Phase 2 ;(n=70); Ongoing, not recruiting	Pilot Study of PegInterferon-Ribavirin-Telaprevir Efficacy and Tolerability in HIV-HCV Coinfected Patients Who Had Previously Failed a PegInterferon-Ribavirin Regimen. (ANRS HC26 TelapreVIH)	• Alcohol intake and/or substance abuse that may represent an obstacle for participation of the subject
*NCT01335529 French National Institute for Health and Medical Research-French National Agency for Research on AIDS and Viral Hepatitis (Inserm-ANRS); Phase 2 (n=69); Ongoing, not recruiting	Pilot Study to Assess the Efficacy and Safety of Boceprevir, in Combination With Peg-Interferon Alfa and Ribavirin, in Patients With HIV/HCV Co-infection Who Have Failed to a Previous Therapy With Peg-Interferon/Ribavirin	• Drug addiction which may disturb the study participation according to the investigator. • Alcohol consumption which may disturb the study participation according to the investigator.
*NCT01725542 French National Institute for Health and Medical Research-French National Agency for Research on AIDS and Viral Hepatitis (Inserm-ANRS); Phase 2 (est. n=65); Currently recruiting	Pilot Study to Assess the Efficacy and Tolerance to a QUadruple Therapy With Asunaprevir , Daclatasvir, Ribavirin and Pegylated Interferon Alpha-2a, in HIV-HCV Genotype 1 or 4 Coinfected Patients Previously Null Responders to a Standard Pegylated Interferon -Ribavirin Regimen	• Alcohol intake that may represent an obstacle for the participation of the subject in the study • Substance abuse that may represent an obstacle for the participation of the subject in the study.
NCT01471574 Bristol-Myers Squibb; Phase 3 (est. n=300); Currently recruiting	A Phase 3, Open Label Study of Safety and Efficacy With BMS-790052 Plus Peg-Interferon Alfa 2a and Ribavirin in Previously Untreated HCV Patients Coinfected With Human Immunodeficiency Virus (HIV) and Hepatitis C Virus (HCV)	No mention
NCT01479868 Janssen R&D Ireland; Phase 3 (n=109); Ongoing, not recruiting	A Phase III Open-Label Study to Evaluate the Safety, Tolerability and Efficacy of TMC435 Plus PegIFNα-2a (Pegasys) and Ribavirin (Copegus) Triple Therapy in Chronic Hepatitis C Genotype-1 Infected Subjects Who Are Co-infected With Human Immunodeficiency Virus Type 1 (HIV-1)	No mention
NCT01667731 Gilead; Phase 3 (est. n=230); Ongoing, not recruiting	A Phase 3, Open-label Study to Investigate the Efficacy and Safety of GS-7977 Plus Ribavirin in Chronic Genotype 1, 2 and 3 Hepatitis C Virus (HCV) and Human Immunodeficiency Virus (HIV) Co-infected Subjects	No mention

NCT01783678 Gilead; Phase 3 (est. n=270); Currently recruiting	A Phase 3, Open-label Study to Investigate the Efficacy and Safety of Sofosbuvir Plus Ribavirin in Chronic Genotype 1, 2, 3 and 4 Hepatitis C Virus (HCV) and Human Immunodeficiency Virus (HIV) Co-infected Subjects	• Clinically-relevant drug or alcohol abuse within 12 months of screening.
NCT01482767 NIAID; Phase 3 (est. n=310); Currently recruiting	A Prospective, Phase III, Open-Label Study of Boceprevir, Pegylated-Interferon Alfa 2b and Ribavirin in HIV/HCV Coinfected Subjects	• Active drug or alcohol use or dependence that, in the opinion of the site investigator, would interfere with adherence to study requirements
*NCT01718301 Anna Cruceta; Phase 3 (est. n=128); Not yet open for recruitment	A Study to Evaluate Safety and Efficacy of Boceprevir-response Guided Therapy in Controlled HIV Patients with Chronic Hepatitis C Genotype 1 Infection Who Failed Previously to Peginterferon/Ribavirin	• Any current evidence of substance abuse of alcohol or other drugs
NCT01467479 Vertex; Phase 3 (est. n=160); Ongoing, not recruiting	An Open Label, Phase 3 Study of Telaprevir in Combination with Peginterferon Alfa 2a (Pegasys®) and Ribavirin (Copegus®) in Subjects Coinfected with Genotype 1 Hepatitis C Virus and Human Immunodeficiency Virus Type 1 (HIV/HCV-1)	No mention
NCT01513941Janssen; Phase 3 (n=163); Ongoing, not recruiting	An Open-Label, Phase 3b Study to Determine Efficacy and Safety of Telaprevir, Pegylated-Interferon-alfa-2a and Ribavirin in Hepatitis C Virus Treatment-Naïve and Treatment-Experienced Subjects with Genotype 1 Chronic Hepatitis C and Human Immunodeficiency Virus Type 1 (HCV-1/HIV-1) Coinfection	No mention
NCT01500616Janssen; Phase 3 (n=122); Ongoing, not recruiting	Multicenter, Open-Label, Study of Telaprevir in Combination With Peginterferon Alfa and Ribavirin in Human Immunodeficiency Virus/Genotype 1 Chronic Hepatitis C Coinfected Subjects With Severe Fibrosis or Compensated Cirrhosis	No mention
NCT01399619 Boehringer; Phase 3 (est. n=310); Ongoing, not recruiting	Safety and Efficacy of 120mg and 240mg BI 201335 Once Daily in Combination With Pegylated Interferon Alpha and Ribavirin for Treatment of Chronic Hepatitis C (HCV) Genotype 1 Infection in HIV/HCV Co-infected Patients. A Multinational, Randomised, Parallel Group, Open-label Trial.	No mention

Table 3: Types of Drug-and-Alcohol Related Exclusion Criteria in HCV DAA Clinical Trials Involving HIV/HCV Coinfected Participants.

Exclusion Criteria	Number of Trials with Exclusion Criteria (n=18)
History of Alcohol Use/Abuse	2
History of Drug or Substance Use/Abuse	3
Current Alcohol Use/Abuse	6
Current Drug or Substance Use/Abuse	6
"Opinion" or "Judgment" of Investigator	3
Subjective Judgment of Use ("Clinically Relevant" or "May Represent an Obstacle")	4
"Drug" or "Substance" not defined	18

Many studies have shown that when current or former HCV-monoinfected PWID are enrolled in comprehensive HCV care, rates of SVR do not substantially differ from those of non-PWID [9,10]. Although study data on SVR rates in coinfected PWID is scarcer, to date there are no data supporting any difference in SVR rates between coinfected PWID and non-PWID [11]. Additionally, regardless of injection drug use status, coinfected patients have been shown to have more rapid HCV progression and thus stand to benefit from antiviral treatment [12]. While risk for post-treatment HCV reinfection among PWID has been cited as a concern, little data exists to support exclusion criteria, given the widespread availability of needle-exchange programs and the substantial benefits to long-term mortality on treating and curing HCV. Untreated PWID also increase the risk of HCV infection to others in injecting drug networks; the benefits of treatment to decreasing forward transmission of HCV therefore represent an additional counterweight to concerns that a small minority of PWID may become reinfected if treated [13,14]. Furthermore, the successful treatment of patients with HCV who are currently or have recently injected drugs plays an important role in public health by reducing the risk of transmission to other PWIDs, and has been shown to be cost effective [14,15].

Inconsistent exclusion criteria also raises ethical concerns about withholding treatment from persons with current or former substance use histories, many of whom are stigmatized. Comparisons have aptly been drawn between this population and that of patients with chronic obstructive pulmonary disease, diabetes, and other chronic medical illnesses who are not routinely denied therapy despite possible poor treatment compliance or ongoing risk behavior such as smoking and alcohol consumption[8]. With so many patients progressing towards hepatic decompensation, there is no ethical justification for denying access to trials testing DAAs whose future approval – even if rapid – may still come too late for thousands of patients in need today [16].

Finally, it is important to consider the implications of these exclusions on the quality of the data derived from the clinical trials themselves. Coinfected patients with current or recent injecting drug histories make up 80% of the total coinfected patient population [17]. Denying such a large group equitable access to clinical trials may create a selection bias for a patient population that is healthier, and with less advanced liver disease.

As a result, critical data on the safety and efficacy of new DAA therapies may be overly optimistic when applied to the majority of coinfected patients. Inconsistent exclusion of coinfected PWIDs would also adversely affect comparison of outcomes data across clinical trials, if not making it difficult to impossible altogether. Additionally, many trials that provide allowances for exclusion leave precise criteria qualifications to individual investigators. Therefore, even within certain clinical trials, enrollment of coinfected PWIDs is inconsistent at best, and at worst creates and perpetuates substantive disparities in equitable enrollment between clinical trial locations.

The era of DAA-based therapies has already revolutionized the field of HCV treatment, and the tremendous improvement in treatment uptake, simplicity, safety, tolerability and cure rates will continue. Numerous clinical trials of DAA regimens in coinfected patients are planned or ongoing. It is critical to ensure that enrollment criteria for these trials do not fall prey to old misconceptions regarding treatment of patients with current or former drug-and-substance abuse. The exclusion of PWID from treatment for HCV, as was commonly the case during the interferon-era, must not shape the new, promising era of interferon-free regimens.Unfortunately, this precedent may already be shaping the HCV treatment landscape for PWIDs [18,19]. Developing consistent, evidence-based inclusion and exclusion criteria concerning substance use will permit greater, more equitable access to DAA trials for this population and increase the clinical relevance of their results.

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REFERENCES

1. Aceijas C, Rhodes T. Global estimates of prevalence of HCV infection among injecting drug users. Int J Drug Policy. 2007; 18: 352-358.
2. Hernando V, Perez-Cachafeiro S, Lewden C, Gonzalez J, Segura F, Oteo JA. All-cause and liver-related mortality in HIV positive subjects compared to the general population: differences by HCV co-infection. J Hepatol. 2012; 57: 743-751.
3. van der Helm J, Geskus R, Sabin C, Meyer L, Del Amo J, Chêne G. Effect of HCV infection on cause-specific mortality after HIV seroconversion, before and after 1997. Gastroenterology. 2013; 144: 751-760.
4. Wada N, Jacobson LP, Cohen M, French A, Phair J, Muñoz A. Cause-specific life expectancies after 35 years of age for human immunodeficiency syndrome-infected and human immunodeficiency syndrome-negative individuals followed simultaneously in long-term cohort studies, 1984-2008. Am J Epidemiol. 2013 Jan 15; 177:116-125.
5. Walsh N, Maher L. HIV and viral hepatitis C coinfection in people who inject drugs: implications of new direct acting antivirals for hepatitis C virus treatment. Curr Opin HIV AIDS. 2012; 7: 339-344.
6. Aspinall EJ, Corson S, Doyle JS, Grebely J, Hutchinson SJ, Dore GJ. Treatment of hepatitis C virus infection among people who are actively injecting drugs: a systematic review and meta-analysis. Clin Infect Dis. 2013; 57 Suppl 2: S80-89.
7. Guidelines for the screening, care and treatment of persons with hepatitis C infection. Geneva: World Health Organization: 2014 Apr. 2015.
8. Edlin BR, Seal KH, Lorvick J, Kral AH, Ciccarone DH, Moore LD. Is it justifiable to withhold treatment for hepatitis C from illicit-drug users? N Engl J Med. 2001; 345: 211-215.
9. Seal KH, Currie SL, Shen H, Anand BS, Bini EJ, Brau N. Hepatitis C treatment candidacy and outcomes among 4318 US veterans with chronic hepatitis C virus infection: does a history of injection drug use matter? J Clin Gastroenterol. 2007; 41: 199-205.
10. Matthews G, Kronborj IJ, Dore GJ. Treatment for hepatitis C virus infection among current injection drug users in Australia. Clin Infect Dis 2005; 40: S325-329.
11. Taylor LE, Swan T, Matthews GV. Management of hepatitis C virus/HIV coinfection among people who use drugs in the era of direct-acting antiviral-based therapy. Clin Infect Dis. 2013; 57 Suppl 2: S118-124.
12. Garg S, Taylor LE, Grasso C, Mayer KH. Prevalent and incident hepatitis C virus infection among HIV-infected men who have sex with men engaged in primary care in a Boston community health center. Clin Infect Dis. 2013; 56: 1480-1487.
13. Grebely J, Dore GJ. Prevention of hepatitis C virus in injecting drug users: a narrow window of opportunity. J Infect Dis. 2011; 203: 571-574.
14. Martin NK, Vickerman P, Miners A, Foster GR, Hutchinson SJ, Goldberg DJ. Cost-effectiveness of hepatitis C virus antiviral treatment for injection drug user populations. Hepatology. 2012; 55: 49-57.
15. Martin NK, Vickerman P, Foster GR, Hutchinson SJ, Goldberg DJ, Hickman M. Can antiviral therapy for hepatitis C reduce the prevalence of HCV among injecting drug user populations? A modeling analysis of its prevention utility. J Hepatol. 2011; 54: 1137-1144.
16. Davis GL, Alter MJ, El-Serag H, Poynard T, Jennings LW. Aging of hepatitis C virus (HCV)-infected persons in the United States: a multiple cohort model of HCV prevalence and disease progression. Gastroenterology. 2010; 138: 513-52, 521.
17. The Center for Disease Control and Prevention. HIV and Viral Hepatitis Fact Sheet.
18. Sofosbuvir for the Treatment of Hepatitis C and Evaluation of the 2014 American Association for the Study of Liver Diseases Treatment Guidelines. Center for Evidence-based Policy, Oregon Health & Sciences University.
19. Evidence-Based Reporting Critical to Decisions on Sofosbuvir and Health Care Innovations. Statement of the National Association of Medicaid Directors. 20 May 2014.

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