HIV Coinfected Have Similar SVR Rates as HCV Monoinfected With DAAs: It’s Time to End Segregation and Integrate HIV Patients Into HCV Trials

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Phase 3 trials of direct acting antiviral drugs (DAAs) for hepatitis C virus (HCV) excluded patients coinfected with human immunodeficiency virus (HIV). After approval, small trials were done in HIV-HCV coinfected patients. The status quo results in delayed access to DAAs for HIV coinfected patients, a group with more rapid progression of liver disease. This article reviews all approved DAAs and compares sustained virological response (SVR) rates in the HIV coinfected with those in the HCV monoinfected treated with the same regimen for the same HCV genotype. SVR rates in HCV genotype 1 to 4 are virtually identical in the HIV co-infected as in the HCV monoinfected, regardless of whether the regimens contain interferon. Because HIV coinfection does not affect SVR rates or toxicity with DAA-containing therapy, excluding HIV coinfected patients from clinical trials of DAA-containing anti-HCV therapy is discriminatory and unnecessary. Rather, HIV coinfection is one of many comorbidities that occur in some patients with HCV infection.

Keywords. HIV; HCV; HIV exceptionalism; clinical trials.

The World Health Organization estimates that there are 35 million people living with human immunodeficiency virus (HIV) globally [1], of whom approximately 25% or 8.75 million are coinfected with hepatitis C virus (HCV). On the other hand, the 8.75 million people with HIV-HCV coinfec tion constitute only 6%–11% of the 80 to 135 million people estimated to be HCV-infected globally [2, 3].

HIV coinfec tion accelerates the natural history of HCV-induced hepatic fibrosis [4, 5], and liver disease is a major cause of death in the HIV-HCV coinfected [6]. Two factors contributing to the significant morbidity and mortality of HCV in the HIV coinfected are the facts that a low percentage of HIV-HCV coinfected patients have been treated for HCV [7, 8], and that prior to the introduction of direct acting antivirals (DAAs) for HCV, virological cure of HCV infection (sustained virological response [SVR]) occurred at a low rate, especially in HCV genotype 1 [7, 9–12]. However, treatment-induced SVR of HCV infection reduces liver-related mortality and all-cause mortality in the HIV coinfected [13], just as it does in the HCV monoinfected [14]. Hence, it is important to treat and more importantly to cure HCV infection in all patients, whether HIV coinfected or not.

To date, registration trials for HCV therapies have excluded patients with HIV coinfection. In the case of dual therapy with pegylated interferon alfa plus ribavirin (PR), the phase 3 registration trials, published in 2001 for pegylated interferon alfa-2b [15] and 2002 for pegylated interferon alfa-2a [16], excluded HIV-infected individuals, and studies of PR in the HIV coinfected were not published until 2004 [9, 11, 12]. The manufacturers of all HCV DAAs approved to date have similarly excluded HIV coinfected patients from the phase 3 clinical trials.
and have subsequently undertaken dedicated clinical trials in the HIV-HCV coinfected population. In many cases, the trials in the HIV coinfected had small samples sizes and were not powered for statistical comparisons. Some studies in the HIV coinfected have excluded patients who failed prior anti-HCV therapy [17, 18]. Accordingly, some prescription drug plans have not funded the use of these HCV treatments in the coinfected until dedicated clinical trials are subsequently undertaken in the HIV co-infected. In Canada, public funding of boceprevir was first recommended in October 2011, with the proviso that the HIV-coinfected patients were excluded due to the absence of data in this population (https://www.cadth.ca/sites/default/files/cdr/complete/cdr_complete_Victrelis_Oct-26-11.pdf). Coverage for boceprevir in the HIV coinfected was not recommended until 20 months later based on data in the HIV-HCV coinfected (https://www.cadth.ca/sites/default/files/cdr/complete/cdr_complete_SF0312-Victrelis_RFA_June-14-13.pdf).

In this article, the clinical trials of DAA-containing therapy for HCV in the HIV-coinfected are reviewed. These demonstrate that SVR rates are remarkably similar in the HIV coinfected compared with HCV monoinfected patients treated with the same regimen for the same HCV genotype, and support the view that the current state of knowledge supports enrolling HIV-coinfected patients within the “parent” HCV clinical trials rather than conducting small, statistically underpowered studies in a subset of patients constituting 5%–10% of the HCV-infected population, potentially delaying their access to new HCV treatments.

METHODS

The phase 3 registration trials for DAAs approved to date (boceprevir, telaprevir, simeprevir, sofosbuvir, sofosbuvir/ledipasvir, paritaprevir/ombitasvir/ritonavir plus dasabuvir), plus faldaprevir were reviewed. Studies were identified by searching PubMed and clinicaltrials.gov for the names of all licensed DAAs plus faldaprevir. Although faldaprevir is not approved and its commercialization will not be pursued, faldaprevir was included in this study because phase 3 registration trials have been completed, including one of the largest published studies to date involving a DAA in a HIV-coinfected population (n = 308). In addition to the phase 3 registration studies, clinical trials of the same DAA-containing anti-HCV regimens in a dedicated HIV-coinfected population were reviewed, and SVR rates are compared between the HCV monoinfected and the HIV-HCV coinfected. Abstract data were used only when a publication was not yet available.

RESULTS

The results are reviewed according to specific DAA-containing regimen and summarized in Table 1. The most frequently used interferon-free regimens for HCV genotypes 1, 2, and 3 are depicted in Figure 1. There were few to no differences in inclusion/exclusion criteria in the studies of the same DAA-containing regimens in the HCV monoinfected compared with the HIV-HCV coinfected, apart from HIV infection.

Pegylated Interferon Plus Ribavirin Plus Boceprevir

Two large clinical trials evaluated the efficacy and safety of PR plus boceprevir in HCV genotype 1 monoinfected treatment naive patients [19, 20]. Using a response-guided treatment paradigm, SVR rates were 63% in both studies, 233/368 in SPRINT-2 [19], and 431/687 in the “anemia” study [20]. Using a fixed 48-week duration of PR plus boceprevir given from week 4 to 48, the SVR rate was 66% (242/354) in SPRINT-2 [19]. In a small phase 2 study of 64 HIV-HCV genotype 1 coinfected patients naïve to prior HCV therapy, the SVR rate with a 48-week course of PR plus boceprevir added from week 4 to 48 was 63% (40/64) [17].

Pegylated Interferon Plus Ribavirin Plus Telaprevir

Three large clinical trials evaluated the efficacy and safety of PR plus telaprevir in HCV genotype 1 monoinfected treatment naive patients [21–23]. Using a response-guided treatment paradigm, SVR rates were 75% (271/363) in ADVANCE [21] and 74% (544/740) in OPTIMIZE [23]. In a small phase 2 study of 38 HIV-HCV genotype 1 coinfected patients naïve to prior HCV therapy, the SVR rate with a 48-week course of PR plus telaprevir added for the first 12 weeks was 74% (28/38) [18].

Pegylated Interferon Plus Ribavirin Plus Simeprevir

Two trials evaluated PR plus simeprevir in HCV genotype 1 monoinfected treatment naive patients [24, 26]. Using a response-guided treatment paradigm, SVR rates were 80% (210/264) in QUEST-1 [24] and 81% (209/257) in QUEST-2 [26]. In patients with HCV genotype 1 monoinfection who relapsed after previous treatment with interferon with or without ribavirin, the SVR rate with simeprevir plus response-guided PR was 79% (206/260) in the PROMISE study [27]. In patients with HCV genotype 1 monoinfection who were partial or null responders to a prior course of PR, who were treated with 48 weeks of PR with simeprevir added for the first 12 weeks, the SVR rate was 70% (101/145) in prior partial responders and 44% (102/234) in prior null responders in the ATTAIN study [28].

PR plus simeprevir was evaluated in 106 HIV--HCV genotype 1 coinfected patients [25]. Simeprevir was given for the first 12 weeks of therapy. The duration of PR therapy was response-guided in noncirrhotic treatment naive and prior relapse patients, and 48 weeks in all others. SVR rates were 79% (42/53) in the treatment naive, 87% (13/15) in prior relapsers, 70% (7/10) in prior partial responders, and 54% (15/28) in prior null responders [25].

Pegylated Interferon Plus Ribavirin Plus Faldaprevir

Two trials (STARTVerso-1 and STARTVerso-2) evaluated PR plus faldaprevir in HCV genotype 1 monoinfected treatment
<table>
<thead>
<tr>
<th>Study</th>
<th>SVR Rate % (n/N)</th>
<th>Study</th>
<th>SVR Rate % (n/N)</th>
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</thead>
<tbody>
<tr>
<td>Pegylated interferon + ribavirin + boceprevir in HCV treatment naive (TN), genotype 1</td>
<td></td>
<td>Pegylated interferon + ribavirin + telaprevir in HCV TN, genotype 1</td>
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<tr>
<td>Pegylated interferon + ribavirin + telaprevir in HCV TN, genotype 1</td>
<td></td>
<td>OPTIMIZE [23]</td>
<td>74 (544/740)</td>
</tr>
<tr>
<td>Pegylated interferon + ribavirin + simeprevir in HCV TN, genotype 1</td>
<td></td>
<td>Pegylated interferon + ribavirin + simeprevir in prior relapsers, genotype 1</td>
<td></td>
</tr>
<tr>
<td>Phase 2 [17]</td>
<td>63 (40/64)</td>
<td>C212 [25]</td>
<td>87 (13/15)</td>
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<tr>
<td>Phase 2 [18]</td>
<td>74 (28/38)</td>
<td>ATTAIN [28]</td>
<td>70 (101/145)</td>
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<tr>
<td>OPTIMIZE [23]</td>
<td>74 (544/740)</td>
<td>ATTAIN [28]</td>
<td>44 (102/234)</td>
</tr>
<tr>
<td>Pegylated interferon + ribavirin + simeprevir in prior null responders, genotype 1</td>
<td></td>
<td>Pegylated interferon + ribavirin + faldaprevir in HCV TN, genotype 1</td>
<td></td>
</tr>
<tr>
<td>Pegylated interferon + ribavirin + simeprevir in prior relapsers, genotype 1</td>
<td></td>
<td>STARTVerso-3 [31]</td>
<td>70 (140/201)</td>
</tr>
<tr>
<td>Pegylated interferon + ribavirin + simeprevir, all x 12 wks, genotype 1</td>
<td></td>
<td>NEUTRINO [32]</td>
<td>89 (260/291)</td>
</tr>
<tr>
<td>Sofosbuvir + ribavirin x 24 wks, genotype 1</td>
<td></td>
<td>Sofosbuvir + ribavirin x 24 wks, genotype 2 (mainly TN)</td>
<td></td>
</tr>
<tr>
<td>SPARE [34]</td>
<td>68 (17/25)</td>
<td>FISSION [32]</td>
<td>97 (68/70)</td>
</tr>
<tr>
<td>PHOTON-1 [35]</td>
<td>75 (86/114)</td>
<td>POSITRON [37]</td>
<td>93 (101/109)</td>
</tr>
<tr>
<td>PHOTON-2 [36]</td>
<td>85 (95/112)</td>
<td>VALENCE [38]</td>
<td>93 (68/73)</td>
</tr>
<tr>
<td>Sofosbuvir + ribavirin, genotype 2, treatment experienced (TE)</td>
<td></td>
<td>Sofosbuvir + ribavirin, genotype 2, treatment experienced (TE)</td>
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<tr>
<td>PHOTON-1 [35]</td>
<td>92 (22/24)</td>
<td>PHOTON-2 [36]</td>
<td>92 (22/24)</td>
</tr>
<tr>
<td>24-week</td>
<td>83 (5/6)</td>
<td>PHOTON-1 [35]</td>
<td>92 (22/24)</td>
</tr>
<tr>
<td>PHOTON-2 [36]</td>
<td>92 (22/24)</td>
<td>PHOTON-1 [35]</td>
<td>92 (22/24)</td>
</tr>
<tr>
<td>Sofosbuvir + ribavirin x 12 wks, genotype 3, TN</td>
<td></td>
<td>Sofosbuvir + ribavirin x 12 wks, genotype 3, TN</td>
<td></td>
</tr>
<tr>
<td>POSITRON [37]</td>
<td>67 (28/42)</td>
<td>POSITRON [37]</td>
<td>61 (60/98)</td>
</tr>
<tr>
<td>Sofosbuvir + ribavirin + simeprevir x 12 wks, genotype 1</td>
<td></td>
<td>Sofosbuvir + ribavirin + simeprevir x 12 wks, genotype 1</td>
<td></td>
</tr>
<tr>
<td>VALENCE [38]</td>
<td>85 (213/250)</td>
<td>VALENCE [38]</td>
<td>85 (213/250)</td>
</tr>
<tr>
<td>(58% TE)</td>
<td></td>
<td>PHOTON-1 [35]</td>
<td>94 (16/17)</td>
</tr>
<tr>
<td>24-week</td>
<td>91 (52/57)</td>
<td>91 (52/57)</td>
<td></td>
</tr>
<tr>
<td>ION-3 [43]</td>
<td>96 (455/473)</td>
<td>TURQUOISE-I [45]</td>
<td>94 (29/31)</td>
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</table>
Using a response-guided treatment paradigm, the SVR rate in the combined studies was 73% (760/1045) [29]. PR plus faldaprevir was also studied in patients who failed prior PR therapy in the STARTVerso-3 study [29]. Relapsers to prior PR therapy who received faldaprevir with response-guided PR achieved a SVR rate of 70% whether they received 12 weeks (69/99) or 24 weeks of faldaprevir (71/102) [31].

PR plus faldaprevir was evaluated in 308 HIV-HCV genotype 1 coinfected patients who were either HCV treatment naïve (n = 239) or prior relapsers to PR (n = 69) in the STARTVerso-4 study [31]. SVR rates were 69% (164/239) in the treatment naïve patients and 83% (57/69) in relapsers to prior PR therapy [30].

**Pegylated Interferon Plus Ribavirin Plus Sofosbuvir**

A 12-week regimen of PR plus sofosbuvir was evaluated in 327 treatment naïve HCV monoinfected patients, of whom 291 (89%) were infected with HCV genotype 1 in the NEUTRINO study [32]. The SVR rate in patients with HCV genotype 1 was 89% (260/291) [32]. The same regimen was tested in 19 HIV-HCV genotype 1 coinfected patients, and the SVR rate was also 89% (17/19) [33].

### Table 1 continued.

<table>
<thead>
<tr>
<th>Study</th>
<th>SVR Rate % (n/N)</th>
<th>Study</th>
<th>SVR Rate % (n/N)</th>
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</thead>
<tbody>
<tr>
<td>PEARL-III [48] TN (genotype 1b)</td>
<td>99 (209/210)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PEARL-IV [48] TN (genotype 1a)</td>
<td>97 (97/100)</td>
<td></td>
<td></td>
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<tr>
<td>TURQUOISE-II [49] (all cirrhotic)</td>
<td>92 (191/208)</td>
<td></td>
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</tr>
<tr>
<td>Sofosbuvir + daclatasvir × 12 wks, genotype 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AI444040 [50]</td>
<td>100 (41/41)</td>
<td>ALLY-2 [51]</td>
<td>97 (123/127)</td>
</tr>
<tr>
<td>Sofosbuvir + daclatasvir × 12 wks, genotype 3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALLY-3 [52]</td>
<td>89 (135/152)</td>
<td>ALLY-2 [51]</td>
<td>100 (10/10)</td>
</tr>
</tbody>
</table>

Abbreviations: HCV, hepatitis C virus; HIV, human immunodeficiency virus; SVR, sustained virological response.

**Figure 1.** Sustained virological response rates in the hepatitis C virus (HCV) monoinfected and the human immunodeficiency virus (HIV)-HCV coinfected with interferon-free therapy in HCV genotypes 1, 2, and 3.
Sofosbuvir Plus Ribavirin
The interferon-free regimen of sofosbuvir plus ribavirin was studied in 4 phase 3 studies in HCV genotype 2 and 3 monoinfected patients called FISSION [32], POSITRON [37], FUSION [37], and VALENCE [38], one pilot study in HCV genotype 1 monoinfection [34], one study in HCV genotypes 1, 2, and 3 in the HIV coinfected called PHOTON-1 [35], and another study in HCV genotype 1–4 in the HIV coinfected called PHOTON-2 [36].

Sofosbuvir Plus Ribavirin in HCV Genotype 1
In a pilot study in HCV genotype 1 monoinfected patients treated with sofosbuvir plus ribavirin for 24 weeks, the SVR rate was 68% (17/25) [38]. In HIV-HCV genotype 1 coinfected patients treated with the same 24-week regimen of sofosbuvir plus ribavirin, the SVR rate was 75% (86/114) in PHOTON-1 [35] and 85% (95/112) in PHOTON-2 [36].

Sofosbuvir Plus Ribavirin in HCV Genotype 2
In HCV genotype 2 monoinfected patients, a 12-week regimen of sofosbuvir plus ribavirin resulted in SVR rates of 97% (68/70) in FISSION [32], 93% (101/109) in POSITRON [37], and 93% (68/73) in VALENCE [38]. In HCV genotype 2 monoinfected patients who failed prior PR therapy, the SVR was 86% (31/36) with 12 weeks and 94% (30/32) with 16 weeks of sofosbuvir plus ribavirin in FUSION [37]. In HIV-HCV genotype 2 coinfected patients, the SVR rate was 88% (23/26) in prior HCV treatment naïve patients treated with sofosbuvir plus ribavirin for 12 weeks in PHOTON-1 [35] and 89% (17/19) in PHOTON-2 [36] and 90% (27/30) in prior HCV treatment failure patients who were treated with sofosbuvir plus ribavirin for 24 weeks [35, 36].

Sofosbuvir Plus Ribavirin in HCV Genotype 3
In HCV genotype 3 monoinfected patients, a 12-week regimen of sofosbuvir plus ribavirin resulted in suboptimal SVR rates of 56% (102/183) in FISSION [32], and 61% (60/98) in POSITRON [37]. In HCV genotype 3 monoinfected patients who failed prior PR therapy, the SVR rate was 30% (10/32) with 12 weeks and 62% (39/63) with 16 weeks of sofosbuvir plus ribavirin in FUSION [37]. However, a 24-week course of sofosbuvir resulted in a SVR rate of 85% (213/250) in VALENCE [38]. In HIV-HCV genotype 3 coinfected patients naïve to prior HCV treatment, the SVR rate was 67% (28/42) in patients treated with sofosbuvir plus ribavirin for 12 weeks, and 94% (16/17) in PHOTON-1 [35] and 91% in PHOTON-2 (52/57) when treated for 24 weeks [36]. SVR rates were 86% (57/66) in prior HCV treatment failure patients who were treated for 24 weeks [35, 36].

Sofosbuvir Plus Ribavirin in HCV Genotype 4
In HCV genotype 4 monoinfected patients, a 12-week regimen of sofosbuvir plus ribavirin resulted in suboptimal SVR rates of 68% (21/31) [53], but a 24-week course yielded a SVR rate of 93% (27/29). In HIV-HCV genotype 4 coinfected patients, the SVR rate with a 24-week course of sofosbuvir plus ribavirin was 84% (26/31) [36].

Sofosbuvir/ledipasvir
The fixed-dose combination of sofosbuvir 400 mg and ledipasvir 90 mg was evaluated in three phase 3 clinical trials in patients with HCV genotype 1 monoinfection [39, 41, 43]. When administered for 12 weeks, SVR rates were 97% (417/430) in treatment naïve patients and 94% (102/109) in patients who failed prior treatment. In a phase 2 study, 50 noncirrhotic HCV treatment naïve patients with HIV-HCV genotype 1 coinfection were treated with 12 weeks of sofosbuvir plus ledipasvir and 49 (98%) achieved an SVR [40]. In a phase 3 study of 335 HIV-HCV genotype 1 coinfection patients, the SVR rate with a 24-week course of sofosbuvir plus ledipasvir was 96% (213/217), with no appreciable difference in cirrhotic (SVR 94%) and noncirrhotic (SVR 96%) patients [42]. The SVR rate in those with HCV genotype 1 infection was also 96% (313/327).

Paritaprevir/ombitasvir/ritonavir Plus Dasabuvir Plus + Ribavirin
The all-oral, interferon-free regimen of coformulated paritaprevir/ombitasvir/ritonavir plus dasabuvir plus ribavirin was evaluated in 5 clinical trials in noncirrhotic patients [44, 46–48] and one clinical trial in exclusively cirrhotic patients with HCV genotype 1 monoinfection [43]. When administered for 12 weeks, this regimen resulted in a SVR rate of 97% (1132/1168) in noncirrhotic patients [44, 46–48] and 92% (191/208) in cirrhotic patients [49]. The same 3 DAA-containing 5-drug regimen was administered to 63 HIV-HCV genotype 1 coinfected patients and the SVR rate was 94% (29/31) in patients treated for 12 weeks and 91% (29/32) in patients treated for 24 weeks [45].

Sofosbuvir Plus Daclatasvir
Sofosbuvir plus daclatasvir with or without ribavirin was first evaluated in 211 HCV monoinfected patients [50]. Only 41 patients in that study, all treatment-naïve with genotype 1 infection, received 12 weeks of sofosbuvir plus daclatasvir, and all achieved SVR. Recently, a 12-week course of sofosbuvir plus ribavirin was demonstrated to achieve SVR rates of 96% (80/83) in treatment naïve and 98% (43/44) in treatment-experienced patients with HIV-HCV genotype 1 coinfection [51]. In genotype 3, a 12-week course of sofosbuvir plus daclatasvir resulted in a SVR rate of 89% (135/152) in HCV monoinfected patients in the ALLY-3 study [52] and in 10 of 10 HIV coinfected patients in the ALLY-2 study [51].

DISCUSSION
In the pre-DAA era, when HCV was treated with dual PR therapy, SVR rates were low in the HIV-coinfected, at least with
HCV genotype 1 [7, 9–12] compared with SVR rates in the HCV mono-infected. However, when DAAs are used as part of HCV therapy, SVR rates appear to be virtually identical to those achieved in HCV monoinfected patients with the same HCV genotype who receive the same DAA-containing regimen, whether the regimen contains interferon or not [17-53]. There is also no evidence that adverse effects of HCV therapy occur at a different frequency or with different severity in the HIV coinfectected. In addition, loss of control of HIV viremia has not been a problem in patients treated for HCV infection who continue to receive anti-HIV therapy [17, 18, 25, 30, 33, 35, 36, 42, 45, 51, 54].

In consideration of the above, the time has come to stop considering HIV-HCV coinfection as a unique subpopulation of HCV infection requiring dedicated anti-HCV clinical trials, and instead HIV infection should be considered as a comorbidity that occurs in a small proportion of HCV-infected persons, similar to diabetes mellitus. The example of diabetes mellitus as an HCV comorbidity is worthy of more discussion. Similar to HIV coinfection, diabetics experience more severe HCV-related outcomes [55, 56]. The World Health Organization estimates the prevalence of diabetes mellitus in persons over 25 years of age to be 10% [57], similar to the prevalence of HIV infection in HCV-infected persons. Yet there have not been clinical trials of anti-HCV therapy restricted to diabetics. Instead, HCV-infected diabetics are permitted in clinical trials of anti-HCV therapy with the proviso that their diabetes mellitus is under reasonable control.

Many comorbidities other than diabetes mellitus are permitted in HCV clinical trials, as long as these medical conditions are controlled, such as hypertension, hyperlipidemia, coronary artery disease, valvular heart disease, asthma, chronic obstructive pulmonary disease, and gastroesophageal reflux disease, to name common ones. Although serious mental illness was excluded from interferon-containing clinical trials, even if controlled, this restriction has been removed in most interferon-free clinical trials. Lower limits for platelet counts have also been adopted for clinical trials of interferon-free therapy, further demonstrating that enrollment criteria for HCV clinical trials can be liberalized over time.

HIV infection should be considered as yet another permissible comorbidity in HCV clinical trials. As with other permissible comorbidities, HIV infection needs to be controlled, and drug-drug interactions need to be appropriately managed. Clinically significant drug-drug interactions are particularly problematic between HIV protease inhibitors and HCV NS3 protease inhibitors [58]. However, these drug-drug interactions are usually manageable, in many cases by avoiding the use of HIV protease inhibitors. Although some anti-HIV drugs are incompatible with some anti-HCV regimens, a number of non-HIV drugs, including statins, are also incompatible with some anti-HCV regimens, and in the developed world, many more people are taking statins than are taking anti-HIV therapy. Multivariate analyses of clinical trials can examine whether or not HIV coinfection influences SVR or other clinical trial outcomes, just as multivariate analysis is used to examine the role of other baseline factors.

Including HIV-infected persons in clinical trials of anti-HCV therapy is beneficial from several perspectives. First, it makes the clinical trial population more representative of the “true” HCV-infected population. Second, it accelerates access to anti-HCV therapies for those co-infected with HIV. Third, it is another step toward ending HIV exceptionalism, a concept that argues that HIV/AIDS merits a different public health response than all other public health issues, a view that has been criticized as not scientifically, ethically, or fiscally justifiable [59]. Arguably, denying patients access to HCV clinical trials for which they meet all the study criteria, except for being HIV-infected, is discriminatory, and could conceivably be challenged legally.

A first step toward integration of HIV-infected persons into clinical trials is occurring in the phase 3 program of the grazoprevir-elsabvir fixed-dose combination. On the basis of similar SVR and safety outcomes in HCV genotype 1 monoinfected patients and HIV-HCV genotype 1 coinfected patients in the phase 2 clinical trial program C-WORTHY [54], three of the phase 3 trials include HIV coinfected patients with HCV monoinfected participants (NCT02105688, NCT02105701, and NCT02252016), although three other phase 3 trials of grazoprevir-elsabvir continue to exclude HIV coinfection (NCT02092350, NCT02105454, NCT02105467), and one phase 3 trial is exclusively for the HIV coinfected (NCT02105662). I propose that all future phase 3 anti-HCV clinical trial programs should include HIV coinfected participants with HCV mono-infected patients, with the proviso that their HIV disease be controlled and that drug-drug interactions are appropriately managed. Both regulators and research ethics committees should challenge pharmaceutical companies and/or researchers who propose to exclude HIV-infected participants to provide a valid scientific reason for their exclusion, and to simultaneously explain why a myriad of other comorbidities can be included. The time to “mainstream” HIV-infected persons into HCV clinical trials is now. It is the “right thing to do,” both scientifically and ethically.

Notes

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Potential conflict of interest. The author’s institution has received funding for Hepatitis C Virus clinical trials from AbbVie, Boehringer Ingelheim, Bristol-Myers Squibb, Gilead, Merck, Pfizer, Roche and Vertex, for which the author has been an investigator, and the author has served on Advisory Boards for the same 8 companies plus Janssen.

The author has submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.
References


