Journal of Virus Eradication 10 (2024) 100388

Contents lists available at ScienceDirect

Journal of Virus Eradication

journal homepage: www.sciencedirect.com/journal/journal-of-virus-eradication

Original research

A comparison of sofosbuvir/velpatasvir and glecaprevir/pibrentasvir for the treatment of hepatitis C infection among people who inject drugs

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ARTICLE INFO

Keywords:
DAA
Hepatitis C
Glecaprevir/pibrentasvir
Sofosbuvir/velpatasvir
People who inject drugs

ABSTRACT

Background: To eliminate hepatitis C (HCV) infection as a public health concern by 2030, there is a need to develop comprehensive programs among key populations such as people who use drugs (PWUD). Two highly effective regimens are available for initial therapy: glecaprevir/pibrentasvir (G/P) given as 3 tablets/day for 8 weeks and sofosbuvir/velpatasvir (S/V) given as 1 tablet/day for 12 weeks. Data evaluating the safety and efficacy comparing one regimen over another in a population of PWUD is limited.

Methods: Patients were identified through outreach events. Viremic patients were offered HCV treatment within a multidisciplinary program. This retrospective comparison analysis focuses on the first 120 sequential individuals who chose either treatment and in whom a definitive outcome of treatment was available between March 1, 2019 and February 29, 2024. The primary outcomes of the analysis were cure of HCV infection and its corelates, as well as safety of the individual regimens.

Results: We successfully identified 120 within each of the G/P and S/V treatment groups. Of those on G/P, we note 28.3 % female, 20.9 % Indigenous, 70.8 % using fentanyl, and 51.3 % with unstable housing. Of those on S/V, we note 25.8 % female, 20.8 % Indigenous, and 75 % using fentanyl and 56.7 % with unstable housing. Overall, 118 and 115 patients completed therapy on G/P and S/V, respectively. A total of 118 and 115 completed therapy on G/P and S/V, with virologic relapse documented in 3 and 2 participants on G/P and S/V, respectively. The ITT/mITT cure rates for G/P and S/V were 95.0 %/97.4 % and 94.2 %/98.3 %, respectively. There were 5 drug overdose deaths among those who initiated treatment, one on G/P and 4 on S/V. **Conclusion**: We have evaluated two highly effective regimens in a group of inner-city PWUD, with comparable success rates well in excess of 90 %. Our data supports the offer of both options for the treatment of PWUD with HCV infection.

1. Introduction

In 2016, the World Health Organization (WHO) put forward the ambitious goal to eliminate HCV infection as a public health concern by 2030. To do so, 90 % of infected individuals would need to be diagnosed and 80 % successfully treated.[1] In this way, incident infections would be reduced by 90 % and disease-associated mortality would be reduced by 65 %. Globally, an estimated 71 million people are living with chronic HCV infection, including at least 5.8 million people who use or inject drugs (PWUD).[1] In addition, approximately 1.5 million new infections are recorded per year.[2] Treatment coverage among PWUD is still challenging with less than 20 % HCV treatment coverage for this marginalized population in Canada,[3] confirming that this issue will remain a significant public health burden for years to come.

Several population-specific approaches will be required to increase the rate of diagnosis and treatment of HCV infection. This is particularly true for vulnerable inner-city residents, many of whom are active drug users. This key population encounters specific challenges that limit meaningful engagement in care which reduces their HCV treatment uptake.[4] Meaningful provision of services to marginalized populations needs to be addressed via focused outreach programs to provide point-of-care interventions linked to strategies to immediately engage viremic individuals in care to receive treatment.

With effective development of direct-acting antiviral agents (DAA), HCV is almost universally curable,[5,6] We are fortunate, in many countries (including Canada), to have equal, low-barrier access to two different regimens to achieve this goal. The combination of sofosbuvir and velpatasvir (S/V) is given as one pill once a day for 12 weeks.[5,7–10]

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https://doi.org/10.1016/j.jve.2024.100388
Received 8 July 2024; Received in revised form 14 August 2024; Accepted 29 August 2024
Available online 31 August 2024

Its use has led to cure rates exceeding 95 % in a broad range of previously untreated individuals, including all patients with cirrhosis. Among PWUD, the SIMPLIFY study was conducted, with 97/103 (94 %) participants cured with S/V.[10] The combination of glecaprevir and pibrentasvir (G/P) is given as 3 pills once a day with food for 8 weeks.[11–13] Its use has led to cure rates exceeding 95 % in a broad range of previously untreated individuals, including all patients with compensated cirrhosis.[14] Among PWUD, the GRAND PLAN study was conducted, with 108/111 (97 %) participants cured with G/P.[15]

The HCV management guidelines highlight crucial differences between the DAA regimens of G/P and S/V, particularly in terms of drug-drug interactions, pharmacokinetics, and patient-specific factors, such as possible interactions between G/P and statins and anticonvulsants. Conversely, there remains some concern about the interaction between S/V and proton pump inhibitors as well as other acid-reducing agents. For a given patient, the selection of a specific regimen should be made to maximize both safety and efficacy. As such, the discussion on the use of DAAs in treating HCV infection must be fully aligned with these considerations.

There has not been a head-to-head comparison of S/V and G/P as first line therapy, among PWUD or otherwise. It is unlikely that such a study would ever be conducted. Given the high degree of efficacy for each regimen individually demonstrated in a broad range of clinical trials and no demonstration of reduced efficacy of one or the other in any specific group (other than G/P being contraindicated in patients with decompensated cirrhosis) many would argue that it is not needed. However, there would be some value in comparing their relative efficacies in a real-world setting, where both therapies are offered equally to large numbers of individuals over time. With this in mind, we undertook a retrospective evaluation of the efficacy of S/V and G/P among PWUD offered therapy in the context of a specific high-volume community-based program designed to promote diagnosis and engagement in care.

2. Methods

2.1. Study design

This is a retrospective chart review-based study to evaluate the efficacy and safety of two antiviral regimens, G/P and S/V, prescribed for the treatment of HCV infection at the Vancouver Infectious Diseases Centre (VIDC) in Vancouver, Canada. Individuals with HCV infection living in the inner-city were identified through dedicated outreach programs conducted at their place of residence. Point-of-care testing for HCV antibodies was performed, If positive, phlebotomy was immediately done on site for HCV RNA testing, with results available within one week. In some cases, historical positive HCV RNA tests were identified in the provincial laboratory database and used to confirm the presence of viremia. An offer of treatment was then made within the context of a multidisciplinary program to address medical, social, mental health and addiction-related needs. With the exception of patients with decompensated cirrhosis, an offer of both S/V and G/P therapy was made. Both are fully funded by governmental authorities. Patient preference generally guided the therapeutic selection, with approximately equal preference for either treatment. Among the prescribers within the program, there was no evidence, in clinical practice, of preference of one regimen over the other. Participants were 19 years or older, documented to be viremic with any HCV genotype at the time of enrollment, previously untreated for HCV infection and actively using or injecting drugs or having been documented to be doing so in the previous 3 months. Individuals with a specific contraindication to the use of S/V or G/P were excluded. Antiviral medications were dispensed weekly, with the possibility of daily dispensing if there were adherence concerns. Additionally, during treatment, a participant could be evaluated by a physician for acute medical conditions, to discuss issues of side effects or adherence or to assess any other concerns. Additional clinical and laboratory evaluations were completed as indicated, as part of routine medical care. After treatment was completed, individuals remained within the multidisciplinary care program to ensure that the outcome of HCV therapy could be ascertained.

Counting back from August 2022, the chart review was conducted in the first 120 sequential individuals receiving either G/P or S/V regimens in whom a definitive outcome of HCV treatment had been ascertained. The primary endpoint of the study was the proportion of participants achieving cure of HCV infection (undetectable HCV RNA 12 or more weeks after the end of S/V or G/P treatment, or SVR12). Secondary endpoints of interest included comparability of subjects selecting either S/V or G/P as their preferred regimen, correlates of not achieving SVR12 with either regimen, rate of premature treatment discontinuation, loss to follow up during the study, and mortality.

Relapse and reinfection were differentiated through review of HCV RNA measures at the end of treatment (EOT), as well as 4 and 12 weeks later. In the absence of sequencing and genotypic data, relapse or virologic failure was the assumed outcome if HCV RNA was detected at the end of treatment or within 12 weeks thereafter. Reinfection was identified when the HCV RNA bloodwork at EOT, SVR 4, and/or SVR 12 showed negative results, but subsequently indicated a positive HCV RNA result.

3. Statistical analysis

For this retrospective comparison study, descriptive statistics were utilized to report on the primary and secondary outcomes.

3.1. Patient consent

The study protocol was approved by Advarra and was conducted according to the Declaration of Helsinki and International Conference on Harmonization Good Clinical Practice guidelines. In addition, all participants provided specific written consent for the utilization of their demographic information in this research study.

4. Results

By pre-established design, 240 subjects were included, 120 each in the S/V and G/P treatment groups. To generate this dataset, treatment outcomes confirmed between March 1, 2019 and February 29, 2024 were considered among all participants. In our subjects, we noted a median age of 47 (IQR 38–55, range 22–77) years, 27 % female and 20.8 % Indigenous (Table 1). 72.9 % of the participants in this study were active fentanyl users and 53.3 % experiencing unstable housing defined by living in shelters, temporary single room accommodation centers (SRAs), or experiencing homelessness. In comparing demographic characteristics between participant in the G/P treatment group or in the S/V treatment group (Table 1), age, and sex were comparable. The median age at the time of enrollment was 45 years (IQR: 36.5–54) for the G/P group and 50 years (IQR: 39–56) for the S/V group, with age ranging from a minimum of 22 to a maximum of 75 years for G/P and 27 to 77 years for S/V, respectively (Table 1). We noted 34 (28.3 %) and 31 (25.8 %) of the participants were female in G/P and S/V groups, respectively. Additionally, 20.9 % of participants in G/P group and 20.8 % of participants in S/V group self-identified as Indigenous. Participants' drug use profiles, ascertained through self-reports, revealed a predominant utilization of fentanyl in both groups, 85 (70.8 %) and 90 (75 %) of participants on G/P and S/V. Lower rates of stimulant (amphetamine/cocaine) use were noted in subjects receiving G/P, as well as lower rates of alcohol use. The prevalence of HCV genotype 1 infection was predominant in both treatment cohorts, accounting for 64 (54.7 %) in the G/P treatment group and 62 (51.7 %) in the S/V treatment group, with genotype 3 being the second most prevalent one, representing 38 (32.5 %) in the G/P group and 49 (40.8 %) in the S/V group. Notably, higher FibroScan scores indicating stages F3-F4 were prevalent in the S/V group 25 (29.2 %).

Table 1
Baseline characteristics of participants who completed either G/P or S/V treatment regimens.

Characteristics		G/P	S/V	All
		N = 120	N = 120	N = 240
Age (years)	Median	45	50	47
	Min	22	27	22
	Max	75	77	77
	IQR	36.5–54	39–56	38–55
Sex	Female	34 (28.3 %)	31 (25.8 %)	65 (27 %)
	Male	86 (71.7 %)	89 (74.2 %)	175 (72.9 %)
Ethnicity	Caucasian	90 (75.0 %)	90 (75 %)	180 (75 %)
	Indigenous	25 (20.9 %)	25 (20.8 %)	50 (20.8 %)
	Others	5 (4.1 %)	5 (4.2 %)	10 (4.2 %)
Genotype	1	64 (54.7 %)	62 (51.7 %)	126 (52.5 %)
	2	13 (11.1 %)	4 (3.3 %)	17 (7 %)
	3	38 (32.5 %)	49 (40.8 %)	87 (36.2 %)
	N/A	5 (4.2 %)	5 (4.2 %)	10 (4.2 %)
Fibrosis Stage	F0-F2	109 (91.6 %)	82 (68.3 %)	191 (79.6 %)
	F3-F4	10 (8.4 %)	35 (29.2 %)	45 (18.8 %)
	N/A	1 (0.8 %)	3 (2.5 %)	4 (1.6 %)
Drug use profile	Amphetamine	47 (39.2 %)	77 (64.2 %)	124 (51.6 %)
	Benzodiazepine	5 (4.2 %)	21 (17.5 %)	26 (10.8 %)
	Cocaine	19 (15.8 %)	59 (49.2 %)	78 (32.5 %)
	Fentanyl	85 (70.8 %)	90 (75 %)	175 (72.9 %)
	Methadone	34 (28.3 %)	53 (44.2 %)	87 (36.2 %)
Alcohol	Yes	36 (30 %)	59 (49.2 %)	95 (39.5 %)
	No	81 (69.2 %)	59 (49.2 %)	140 (58.3 %)
Unstable housing	Yes	60 (51.3 %)	68 (56.7 %)	128 (53.3)
	No	54 (46.1 %)	52 (43.3 %)	106 (44.2 %)

Table 2
Baseline characteristics of participants who self identified as Indigenous who completed G/P or S/V treatment regimens.

		G/P	S/V	All
Indigenous characteristics		N=26	N=25	N=51
Age (years)	Median	46	51	47
	Min	23	31	23
	Max	63	69	69
	IQR	38–52	38–57	38–55.5
Sex	Female	10 (38.4 %)	5 (20 %)	15 (29.4 %)
	Male	16 (64 %)	20 (80 %)	36 (70.6 %)
Genotype	1	14 (56 %)	17 (68 %)	31 (60.8 %)
	2	5 (20 %)	2(8 %)	7 (13.7 %)
	3	6 (24 %)	6 (24 %)	12 (23.5 %)
	N/A	1 (3.85 %)		1 (1.2 %)
Fibrosis Stage	F0-F2	24 (96 %)	14 (56 %)	38 (74.5 %)
	F3-F4	2 (8 %)	10 (40 %)	12 (23.5 %)
	N/A		1 (4 %)	1 (1.2 %)
Drug use profile	Amphetamine	11 (44 %)	15 (60 %)	26 (51 %)
	Benzodiazepine	4 (16 %)	3 (12 %)	7 (13.7 %)
	Cocaine	7 (28 %)	12 (48 %)	19 (37.2 %)
	Fentanyl	18 (72 %)	17 (68 %)	35 (68.6 %)
	Methadone	11 (44 %)	10 (40 %)	21 (41.2 %)
Alcohol	Yes	10 (40 %)	18 (72 %)	28 (54.9 %)
	No	15 (60 %)	7 (28 %)	22 (43.1 %)
Unstable housing	Yes	16 (64 %)	17 (68 %)	33 (64.7 %)
	No	10 (40 %)	8 (32 %)	18 (35.3 %)

A focused examination of the indigenous subset within our study revealed a total of 26 subjects receiving treatment with G/P and 25 subjects receiving treatment with S/V (Table 2). In our total indigenous cohort, the median age was 47 (IQR = 38–55.5, range 23–69) years. The distribution of sex at birth resulted in 15 (29.4 %) females and 36 (70.6 %) males. More specifically, more females were enrolled in the G/P treatment group, with 10 (38.4 %) females compared to 5 (20 %) females in the S/V group. The prevalence of FibroScan scores denoting stages F3-F4 was notably higher in the S/V treatment group, accounting for 10 (40 %), as opposed to 2 (8 %) in the G/P group. Fentanyl emerged as the predominant drug of choice in both treatment groups, with rates of 18 (72 %) and 17 (68 %) for G/P and S/V, respectively. The indigenous subset exhibited elevated levels of amphetamine and cocaine use in the S/V treatment groups, registering at 48 % cocaine use, in contrast to 28 % for G/P, and 60 % amphetamine use in the S/V group, in contrast to 44 % for G/P, respectively. Furthermore, similar to the broader demographic cohort, unstable housing conditions were prevalent among over half of the indigenous participants, with proportions of 64 % and 68 % for G/P and S/V, respectively.

Next, we investigated the cascades of care for each treatment group (Fig. 1A and B). Out of 120 subjects who initiated G/P treatment, 118 completed the 8 weeks treatment, while one participant was lost to follow up during treatment and one withdrew from the study. Out of 118 subject who completed the G/P treatment, 114 achieved HCV cure, 1 subject died due to overdose, and 3 showed relapse (Fig. 1A). The G/P

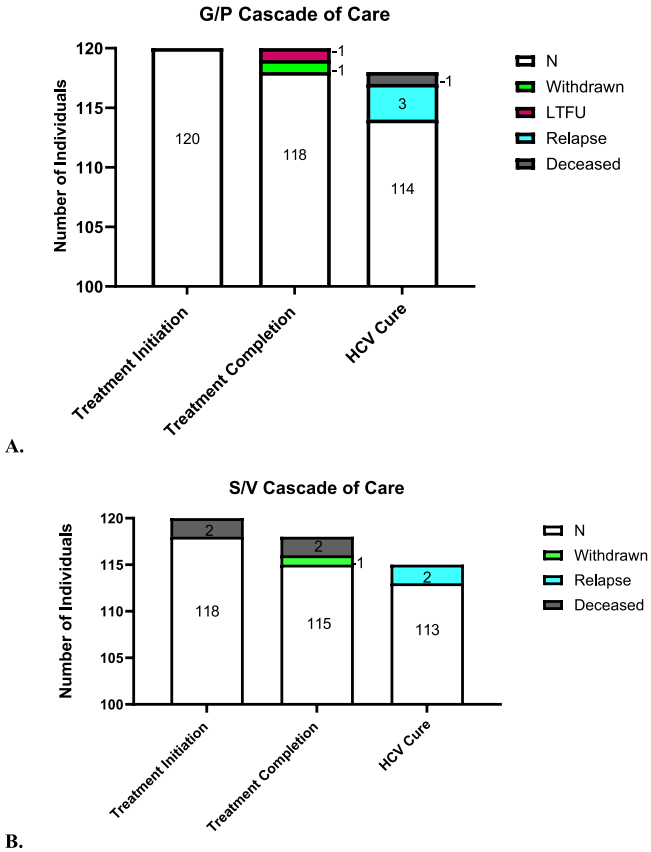

Fig. 1. HCV cascade of care for G/P and S/V treatments. A) Cascade of care for G/P. B) Cascade of care for S/V. LTFU: Lost to follow up.

treatment resulted in 95.0 % (114/120) cure rate by ITT, 97.4 % (114/117) by mITT. We also investigated the cascade of care for the S/V treatment group (Fig. 1B). Out of 120 subjects who were enrolled in the S/V treatment group, 118 initiated treatment and 2 subjects died due to

drug-related causes before initiating treatment. Out of 118 subjects who initiated S/V treatment, 115 completed 12 weeks treatment with 2 subjects dying due to overdose after initiating treatment and 1 subject withdrawing from the study. Out of 115 subjects who completed the S/V treatment, 113 achieved SVR12 and were cured, 2 subjects showed relapse (Fig. 1B). The S/V treatment resulted in 94.2 % (113/120) cure rate by ITT, 98.3 % (113/115) by mITT. These results indicate that both treatment regimens, G/P and S/V, show high efficacy in achieving SVR12 with no significant differences among marginalized population such as PWUD.

Instances of virologic relapse are summarized in Table 3. We have investigated the characteristics of 5 documented cases: 3 were on G/P, and 2 on S/V. The 5 individuals were aged between 33 and 56 years at enrollment, comprising 4 males and 1 female, all with unstable housing and actively utilizing fentanyl. FibroScan scores ranged from F0 to F2, and HCV genotypes included 1A, 2, and 3A. For those in whom a virologic relapse was documented, second-line HCV treatment with the combination of sofosbuvir, velpatasvir, and voxilaprevir was offered as retreatment, free of charge. To date, 3 individuals have achieved SVR12 through successful retreatment (see Table 4).

5. Discussion

Numerous studies have substantiated the effectiveness and safety of DAA therapy in the treatment of HCV within populations characterized as PWUD, even when concurrent substance use persists.[10,15–20] Interventions using currently available regimens have demonstrated high sustained virologic cure rates, comparable to those observed in cohorts without a history of drug use.[21,22] This is true of both S/V and G/P in clinical trials of PWUD with HIV infection. As such, both are commonly offered in parallel to each other, especially in high volume centers such as ours. There is no comparative data for G/P vs. S/V in clinical trials or otherwise. We therefore aimed to address this issue by identifying large numbers of treated patients in whom the result of treatment was known to attempt to discern if outcomes were comparable in a setting where patients were identified and treated in a uniform and systematic way. In addition, this analysis should allow us to evaluate whether our perceived practice of offering both treatments equally (excluding decompensated cirrhotic individuals) was borne out in clinical practice, or whether a more directed assignment of patients with certain characteristics to one regimen or the other should be implemented.

Baseline characteristics were quite comparable between those who received either G/P or S/V. It is not expected that minor difference in non-opiate drug use pattern and sex distribution between the two groups (most noted among indigenous women) would have affected treatment outcomes. Similarly, an imbalance with a slight excess of those with more advanced fibrosis on S/V had no impact on our findings, given that all virologic relapses were documented among individuals with mild liver fibrosis. By strict ITT analysis, cure rate among PWUD undergoing treatment with G/P was 95.0 % (114/120), 97.4 % (114/117) by mITT analysis. This compares to 94.2 % (113/120) and 98.3 % (113/115) on S/V. These figures are consistent to those reported in the medical literature, including among PWUD.[15,21,22,23–28] The results from this retrospective comparison study seem to indicate that both G/P and S/V are highly effective in treating PWUD cohorts and neither is inherently superior to this other.

In our study, among our cohort of PWUD, treatment adherence was high in subjects enrolled in both treatment regimens, with 118 out of 120 completing the G/P treatment course and 115 out of 120 the S/V treatment course. This aligns with prior studies demonstrating low treatment discontinuation rates in people who inject drugs,[29–31,32] especially if they are treated in appropriate settings. Out of a total of 240 subjects in this retrospective study, we documented only five overdose deaths in the setting of an opioid crisis where three deaths/day are reported within the inner city of Vancouver, with a population of about 15,000 individuals.[33] There was one from the G/P treatment group and four from the S/V treatment group. This data suggests that engagement in care may play a role in reducing opioid-related mortality and reassures us about the use of G/P in this population, where there was a concern about a drug interaction with fentanyl, possibly increasing its toxicity. A recent observational study observed no link between recorded adverse events and any specific drug administration regimen among PWUD who use fentanyl.[34]

The lower withdrawal and lost-to-follow-up (LTFU) rates in the present study compared to other cohorts can be largely attributed to the model of care and the multidisciplinary approach employed in our program. This approach plays a crucial role in enhancing participant engagement and retention by providing comprehensive longitudinal support. The multidisciplinary team, which includes physicians, nurses, and outreach workers, offers holistic care that addresses not only the medical needs of participants but also their social, psychological, and substance use-related challenges. This comprehensive support structure is likely a significant factor in keeping withdrawal and LTFU rates low. Another key aspect is the emphasis on personalized care plans tailored to each participant's unique needs. This approach helps build trust with participants, making them more likely to stay engaged in care, complete treatment and remain engaged so that the outcome of HCV therapy can be ascertained. If an individual is not present for a scheduled follow-up visit, strategies for engagement through our outreach programs are immediately implemented. Lastly, culturally sensitive care, which considers the cultural and social context of PWUD, plays a significant role in fostering a sense of belonging and reducing stigma.

To achieve the WHO goal of HCV elimination by 2030, a systematic approach to the diagnosis and treatment of infection in all target populations will be needed, including among PWUD. In many cases, the availability of different individualized therapeutic options will be important. We have evaluated two highly effective regimens in a group of inner-city PWUD enriched for fentanyl use and unstable housing. Although this was not a randomized trial, we will note that among 240 subjects included in this analysis (120 per treatment arm), baseline demographic and disease characteristics were highly comparable, as noted above. Our data supports the offer of both G/P and S/V regimens within the setting of a multidisciplinary program for the treatment of PWUD with HCV infection, irrespective of the level of stability.

Table 3
Participants with documented virological relapse.

Treatment	ID	Age at baseline	Sex	Ethnicity	Genotype	Fibrescore	Active Drug Use	Type of Drug	Unstable Housing	Baseline Viral Load (IU/ml)	Confirmation Viral Load at Point of Relapse
	22	**44**	**M**	**Caucasian**	**1A**	**F0**	**Y**	**F,M**	**Y**	**3,038,030**	**61,826**
G/P	**99**	**52**	**M**	**Caucasian**	**3A**	**F0**	**Y**	**A,F**	**y**	**10,969,093**	**14,858,439**
	124	**40**	**F**	**Indigenous**	**2**	**F2**	**Y**	**C,F**	**Y**	**2,942,871**	**8,479,148**
S/V	**5**	**56**	**M**	**Caucasian**	**1A**	**F1**	**Y**	**A,C**	**Y**	**1277837**	**566997**
	87	**33**	**M**	**Indigenous**	**1A**	**F1**	**Y**	**A,C,O**	**Y**	**399678**	**370532**

Baseline characteristics of participants with documented virologic relapse and their baseline and confirmation viral loads at point of relapse. All patients were active drug users and had unstable housing.
[a]A, Amphetamines; B, Benzodiaspan; C, Cocaine; M, Methadone; O, Opiates; F, Fentanyl; CAN, Cannabis.

Table 4
Participants with documented viral re-infection.

Treatment	ID	Age at baseline	Sex	Ethnicity	Genotype	Fibrescore	Active Drug Use	Type of Drug	Unstable Housing	Re-infected confirmation viral load (IU/ml)	Current RNA status
	16	**63**	**M**	**Indigenous**	**3A**	**F1**	**Y**	**O**	**Y**	**245**	**2591**
	38	**29**	**M**	**Caucasian**	**1A**	**F0**	**Y**	**A,B,C, CAN,M, O**	**Y**	**79090**	**50**
G/P	**43**	**29**	**M**	**Caucasian**	**3A**	**F0**	**Y**	**A,M,O**	**Y**	**552987**	**Undetectable -Cured by S/V**
	51	**38**	**M**	**Indigenous**	**2B**	**F0**	**Y**	**A,B,M,O**	**Y**	**7688**	**Undetectable -Cured by S/V**
	52	**27**	**M**	**Caucasian**	**1A**	**F1**	**Y**	**M**	**Y**	**3911**	**94890**
	2	**56**	**M**	**Caucasian**	**3A**	**F4**	**Y**	**A,M,O**	**Y**	**103**	**104151**
	11	**35**	**F**	**Caucasian**	**1A**	**F0**	**Y**	**O**	**Y**	**275760**	**2295924**
S/V	**32**	**49**	**M**	**Caucasian**	**1A**	**F1**	**Y**	**C,CAN, M,O**	**Y**	**11521881**	**14331977**
	38	**57**	**M**	**Caucasian**	**1A**	**F1**	**Y**	**A,C,O**	**Y**	**160096**	**Undetectable -Cured by S/V**
	90	**29**	**M**	**Caucasian**	**1A**	**F0**	**Y**	**A,C, CAN,O**	**Y**	**850263**	**Undetectable -Cured by G/P**
	120	**51**	**F**	**Caucasian**	**1B**	**F0**	**Y**	**A,C, CAN,M, O**	**Y**	**2281**	**Undetectable -Cured by S/V**

Baseline characteristics of participants with documented virologic re-infection. All patients were active drug users and had unstable housing.
[a]A, Amphetamines; B, Benzodiazepine; C, Cocaine; M, Methadone; O, Opiates; F, Fentanyl; CAN, Cannabis.

6. Limitations

One of the limitations of our findings is that they were generated as part of a retrospective chart review, not a randomized clinical trial. We are therefore relying on non-directed prescribing of either regimen in a way that could affect the outcome. This is not a major concern here, as the groups were comparable according to key parameters of interest. Further, very high success rates were observed in all cases. The key predictors of failure were factors of vulnerability (ongoing fentanyl use and unstable housing), issues completely unrelated to the choice of treatment. Secondly, the reporting and collection of patient-level data in self-reported drug use, history of overdose, and alcohol use are subject to considerable bias arising from incomplete information or stigma associated with substance use and may underestimate vulnerability. In our experience, our low-threshold community-based program mitigates this risk, as reflected in the very high reported rates of drug use here. Studies conducted at centers similar to ours have suggested that collection of substance use data and other stigmatized behaviors yield reliable results.[31] Thirdly, the scope and comprehensive nature of the services we offer would yield higher success rates and reduce our ability to detect any differences in treatment efficacy should they exist. As an example, without adherence support (which may not be available in all clinics treating PWUD with HCV infection), treatment discontinuations would be more frequent and disproportionately reduce the measured cure rates for individuals receiving a longer course of treatment. If this is correct, it backs the need to have such adherence support in place to ensure that the benefits of intervention are maximized and that something approaching the infrastructure that we provide should be the standard for health care delivery to inner city populations.

7. Conclusion

We have demonstrated that high and consistent treatment outcomes can be achieved with either treatment option (G/P or S/V) in individuals who are active drug users and who are committed to starting HCV treatment. With appropriate support, treatment completion rates were equally high with both approaches, and there were no concerns about the safety of G/P or S/V in this population.

Funding statements

The funder had no role in the analysis or interpretation of the study results and did not have access to the raw data. VIDC staff designed and implemented the study and evaluated its outcome under the supervision of Brian Conway<a name = "Line_manuscript_53">

Informed consent statement

All cohort participants provided written informed consent to the access of their personal health numbers, linkage to vaccination status and history, and the questionnaire survey.

CRediT authorship contribution statement

Shana Yi: Writing – review & editing, Writing – original draft, Visualization, Formal analysis, Data curation, Conceptualization. **David Truong:** Writing – review & editing, Supervision, Investigation. **Brian Conway:** Writing – review & editing, Writing – original draft, Supervision, Investigation, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests.

- SY has no conflict of interest to declare.
- DT has received honoraria and/or acted as remunerated advisor for AbbVie and Gilead Sciences.
- BC has received research grants, honoraria and/or acted as a remunerated advisor for AbbVie, Astra Zeneca, Gilead Sciences, GSK, Indivior Canada, Merck, Moderna, Sanofi Pasteur, Seqirus, and ViiV Healthcare. In particular, AbbVie and Gilead Sciences have funded the community pop-up clinic program in a direct way.

Data availability

Data will be made available on request.

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