HCV Treatment Among Active Inner City Drug Users With Glecaprevir/Pibrentasvir (G/P): The Grand Plan Study

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Background

The combination of Glecaprevir/Pibrentasvir (G/P) is approved for the treatment of chronic hepatitis C (HCV) infection (Figure 1). In registrational trials, cure rates of 95% or more were achieved when G/P was administered for a period of 8 weeks regardless of genotype or disease stage (1-3)[1,2,3]. In data pooled from 7 phase III trials, cure rates of 93% (n/N = 91/98) and 97% (n/N = 591/610) were achieved among recent and former drug users, respectively (intention-to-treat analysis), with <1.5% incidence of virologic failure[4]. In a study of more-difficult-to-treat drug users, administration of G/P under direct observation along with opiate agonist therapy (OAT) led to a cure rate of 94.6% (n/N=70/74), with 3 subjects lost to follow-up and one non-response to therapy [5]. In order to achieve HCV elimination by 2030, there is a need to develop and evaluate systems of care in populations that are even more difficult to treat, such as those who use fentanyl and have unstable housing and determine if the efficacy of G/P is maintained in such settings. We describe the efficacy of G/P in the treatment of chronic HCV infection within a community-based program targeting inner-city residents with multiple vulnerabilities, including unstable housing and active fentanyl use.

Methods

The Grand Plan Study evaluated HCV-infected subjects meeting all inclusion and none of the exclusion criteria for enrollment (Table 1). Subjects were identified through weekly events held in the inner city of Vancouver, Canada as well as targeted follow-up events to engage inner-city residents previously identified as having chronic HCV infection. We provided HCV treatment with Glecaprevir/Pibrentasvir (G/P) within the context of a multidisciplinary program of care , which aims to meet medical, psychological, social and addiction-related needs. HCV medications were administered in a way to maximize the likelihood of adherence and follow-up to the sustained virologic response (SVR) 12 time point. Medication administration included daily dispensing with OAT or weekly delivery of medications to the place of residence. If a subject was unavailable for weekly check-ins, interventions such as additional outreach events to places of residence were implemented to re-integrate them into care in a timely manner. This analysis presents the rate of documented cure (achievement of SVR12) in the target population to date.

Results

Figure 1. Glecaprevir/ Pibrentasvir tablet

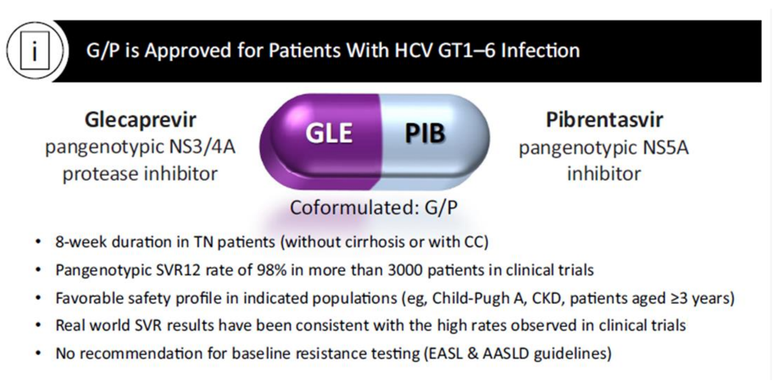

Table 1. Key inclusion and exclusion criteria

Key Inclusion Criteria	• Male or female, at least 19 years of age at time of screening. • HCV RNA positive with any HCV genotype at the time of engagement in care • Active PWUD: ongoing drug use, or documented use within the previous 3 months • F0-3/compensated liver disease (FibroScan <12 kPa) • HCV treatment naive
Key Exclusion Criteria	• Previous DAA-based HCV treatment • Pregnant or breast-feeding • Indication of cirrhosis or decompensated liver disease • Positive test result at time of screening for hepatitis B surface antigen (HBsAg) • Frequent injecting drug use that is judged by the treating physician to compromise subsequent HCV treatment adherence • Inability or unwillingness to provide informed consent or abide by the requirements of the study • Any medical contraindication or allergy to the G/P regimen

Results (continued)

Figure 3: Cascade of Treatment

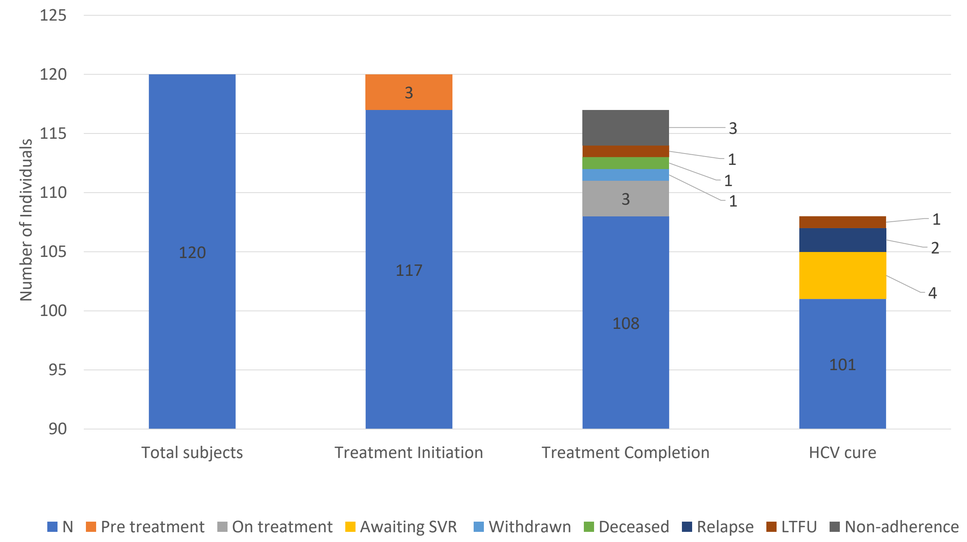

Table 2. Patient Demographics and Characteristics

Demographics	Characteristics (n=120)
Age (Median years, range)	49 (25-68)
Female (n,%)	34 (28.3%)
Ethnicity (n,%)	
white	88 (73.3%)
Indegenous	26 (21.7%)
Unstably housed (n,%)	55 (45.8%)
Active Fentanyl Use (n,%)	86 (71.7%)
FibroScan Score (n,%)	
F0/F1	70 (58.3%)
F2	19 (15.8%)
F3	6 (5%)
HIV co-infected (n,%)	3 (2.3%)
Genotype (n,%)	
GT1	67 (55.8%)
GT3	38 (31.7%)

We have identified 120 eligible subjects, with 46%unstably housed, and 72% actively using fentanyl (Table 2). 28.3% of subjects identified as female (Table 2). Very few subjects had advanced liver fibrosis, by study design. Opiates were the most commonly used substance (Figure 2). Treatment was not yet initiated in 3 subjects but will be shortly. The inception cohort for study purposes was thus 117 subjects, of which 108 have completed treatment. Reasons for treatment non-completion were: non-adherence (3), LTFU (1), early withdrawn (1) and being still on treatment (3). During the post-treatment phase, HCV RNA values were not available for 3 subjects due to accidental death (1), LTFU (1) and awaiting SVR 4 and/or 12 (4). Of the 101 subjects for whom post-treatment viral load measurements are available, SVR 12 and/or SVR 24 has been achieved in 99/101 (98%) subjects, with both treatment failures being attributed to virologic relapse (Figure 3).

Conclusion

Among inner city residents living with HCV infection, most of whom were active fentanyl users and unstably housed, the administration of G/P in the context of a robust program of engagement in care has led to HCV cure rates that exceed those achieved in clinical trials. This validates programs aimed at eliminating HCV in such populations that many consider more challenging to treat. Programs such as the one we have developed will play a significant role in reaching a key group of core transmitters of HCV infection, an important step in achieving the World Health Organization goal of eliminating HCV infection as a public health concern by 2030.

References

1.Brown, RS Jr, et al. *J Hepatol*. 2020;72(3):441-9
2.Foster et al, Drug Alcohol Depend 2019 Jan 1;194:487-494
3.Kwo, Paul Y., et al. *J Hepatol*. 2017; 263(71)
4.MAVIRET (SmPC): AbbVie 2021/Mavyret (US Package Insert): Abbvie 2021
5.Schmidbaueret al, PLoSOne.2020; 15(3): e0229239
6.Zeuzem, Stefan, et al. N EnglJ Med 2018; 378:354(69)

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