Micro-elimination of Chronic Hepatitis C by Universal Screening plus Direct Acting Antivirals for Incarcerated Persons in Taiwan

Tsung-Hua Yang¹², Yu-Jen Fang¹², Shih-Jer Hsu¹², Ji-Yuh Lee¹², Min-Chin Chiu¹², Jian-Jyun Yu¹², Chia-Chi Kuo¹², Chien-Hung Chen¹³

¹ Department of Internal Medicine, National Taiwan University Hospital Yunlin Branch, Douliu City, Yunlin County, Taiwan
² Hepatology Medical Center, National Taiwan University Hospital, Yunlin Branch, Douliu City, Yunlin County, Taiwan
³ College of Medicine, National Taiwan University, Taipei City, Taiwan

Corresponding Author

Chien-Hung Chen, MD, PhD
Department of Internal Medicine, National Taiwan University Hospital Yunlin Branch and National Taiwan University College of Medicine
No.579, Sec. 2, Yunlin Rd., Douliu City, Yunlin County, 640, Taiwan
Tel: +886-2-23123456 ext. 65923 Fax: +886-2-23819723
E-mail: chenhcc@ntu.edu.tw

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Summary: We established a special hepatitis C clinic in prison and offered universal hepatitis C screening for incarcerated persons. The prevalence of anti-HCV positivity was 33.5% and the viremic rate (detectable HCV RNA) was 69.2%. All treated patients achieved sustained virologic response.
Abstract

Background: Incarcerated persons are a special population with higher hepatitis C virus (HCV) prevalence and should be prioritized for micro-elimination. This study aimed to investigate the seroprevalence and to evaluate the effectiveness and safety of direct acting antiviral (DAA) therapy in the custodial settings.

Methods: Incarcerated persons in Yunlin Prison were recruited to receive anti-HCV antibody screening. Patients with positive HCV ribonucleic acid (HCV RNA) were treated with glecaprevir/pibrentasvir (GLE/PIB) in our special chronic hepatitis C (CHC) clinic in prison. The primary endpoint was sustained virologic response at week 12 off therapy (SVR12).

Results: A total of 1402 incarcerated persons were invited to anti-HCV screening and 824 (58.7%) accepted. The prevalence of anti-HCV positivity was 33.5% (276/824) and the viremic rate (detectable HCV RNA) was 69.2% (191/276). According to FIB-4 index, patients with F3 stage were six (3.1%), but none met the criteria of F4 stage. However, six (3.1%) had liver cirrhosis with splenomegaly, confirmed by findings of ultrasonography. The median \( \log_{10} \) HCV RNA level at baseline was 6.235 (2.394-7.403). Genotype (GT) 6 was predominant (39.3%), followed by GT 1a (22.0%) and 1b (14.1%). Mixed genotype HCV infection accounted for 3.6% of total infections. In total, 165 patients received GLE/PIB therapy. The overall SVR12 rates were 100%.

Conclusions: DAA therapy is highly effective and safe for incarcerated patients in Taiwan. Our special prison-based CHC clinic, linking universal screening to medical care, can serve as a model for micro-elimination of HCV in custodial settings.
**Key words:** hepatitis C virus, chronic hepatitis C, direct acting antiviral agent, prison, Taiwan
Introduction

Chronic hepatitis C virus (HCV) infection is a significant cause of liver-related morbidity and mortality worldwide. In 2015, an estimated 71.1 million people had chronic HCV infection globally, corresponding to a prevalence of 0.1% [1]. Taiwan has one of the highest HCV prevalence rates in Northeast Asia [2]. From 1996 to 2005, the prevalence of anti-HCV antibody (anti-HCV) in the general population of Taiwan was 4.4% [3]. HCV infection remains one of serious public issues in Taiwan’s healthcare system.

In most countries, the prevalence of HCV infection is higher in the incarcerated population than in the general population, with estimated prevalence ranging from 3% to 38% [4]. This phenomenon is probably related to the chaotic life of this special population, specifically, the frequent injection substance use among incarcerated persons [5]. Tattooing and risky sexual behavior also expose this vulnerable group to risk of HCV infection. A large proportion of the prison population in Taiwan is composed of criminalized persons with injection substance use. In 2019, 27,893 incarcerated persons were convicted of substance use-related crimes, accounting for 49.5% of the total prison population. Injection substance use is prohibited in Taiwan’s prison system. Those incarcerated patients got HCV infection before they entered the prison. In Taiwan, HIV screen testing is routinely performed for all incarcerated persons, but HCV is not included. Therefore, without routine anti-HCV screening, the prevalence of HCV infection in the custodial setting of Taiwan is unknown.

Given the high prevalence of HCV infection in custodial settings, the World Health Organization Hepatitis C 2018 guidelines classified people in prison as a priority group
for HCV treatment [6]. In fact, incarceration can be viewed as an opportunity for providing HCV screening and therapeutic interventions. The adequate duration of prison sentences permits the completion of a full-course antiviral treatment. However, a previous study indicated that loss to follow-up upon release from prison is a significant barrier to HCV treatment for incarcerated patients [7]. Therefore, early and effective HCV elimination in prison facilitates improving linkage to care and increasing the treatment rates of this vulnerable group, which is a key goal that is unmet and necessary for HCV elimination.

In the past, few studies have evaluated the efficacy of pegylated interferon (Peg-IFN) plus ribavirin (RBV) in HCV-infected incarcerated patients worldwide. The overall sustained virologic response (SVR) rate was approximately 36–69% [8, 9]. In Taiwan, the overall SVR rate of Peg-IFN/RBV therapy in prison population varied from 65.3 to 84.5% [10, 11]. Incarcerated patients have been shown to be as likely to be treated for HCV and as likely to achieve SVR as non-incarcerated patients [12]. Unfortunately, incarcerated patients in most countries have fewer opportunities to receive medical assistance than do other citizens [5, 13]. In fact, healthcare system in prison cannot be effectively used to develop general screening programs or diagnostic and therapeutic approaches for HCV-infected incarcerated populations. The HCV-infected incarcerated patients used to receive out-of-prison medical treatment on bail for their CHC. This process needed a lot of guard manpower and had some guarding risks.

Recently, the introduction of direct acting antivirals (DAAs) has revolutionized the management of CHC with high SVR rate and favorable tolerability in general
population [14-19]. DAA therapy is preferred in custodial settings because DAAs are more effective and safer and allow for shorter treatment courses, compared with Peg-IFN/RBV therapy. However, only few reports have evaluated the outcomes of HCV DAA treatment in the prison environment [20-24].

To the best of our knowledge, no studies have been conducted to examine DAA use in the custodial settings of Taiwan. DAA treatment response in incarcerated patients with HCV infection remains unknown. The current study aimed to investigate the seroprevalence and genotype distribution of HCV and to evaluate the effectiveness and safety of DAA therapy in Taiwan’s custodial settings.

**Methods**

**Study population**

In this prospective cohort study, incarcerated persons in Yunlin Prison were invited to HBsAg and anti-HCV screening between February and June 2019. Written informed consent was obtained prior to screening. All anti-HCV positive incarcerated persons were referred to the special CHC clinic in Yunlin Prison for further evaluation. Patients with positive HCV RNA were treated with glecaprevir/pibrentasvir (GLE/PIB) and followed up according to the Taiwan National Health Insurance (NHI) clinical practice guidelines. GLE/PIB was selected for this study because it was the only available pangenotypic DAA in our hospital during the study period. In addition, pangenotypic DAA is the choice of treatment for possible mixed genotype HCV infections in prison. Patients with less than 6 months remaining on their sentence were excluded from this study because they would be released from prison before completing the study protocol.
Special clinic for CHC in prison

Since January 2017, DAAs have been reimbursed by the Taiwan NHI program for CHC patients with advanced hepatic fibrosis or compensated cirrhosis. On January 1, 2019, the Taiwan NHI authorized the prescription of DAAs to all Taiwanese citizens with CHC. Currently in Taiwan, DAAs can only be prescribed by hepatologists and infection specialists. However, healthcare services in prison clinics in Taiwan are generally provided by family physicians instead of hepatologists, rendering DAA therapy inaccessible to incarcerated patients with HCV infection in Taiwan. To address this issue, we established a special CHC clinic in Yunlin Prison in February 2019, following universal screening for HCV infection. Two hepatologists, one registered nurse, one case manager, and two assistants were stationed at the clinic. We also equipped the prison clinic with a portable ultrasound machine for abdominal ultrasonography.

This study was approved by the Ethics Committee of the National Taiwan University Hospital (201810078RINC). Confidentiality of the enrolled patients was protected in accordance with the principles of Declaration of Helsinki and the International Conference on Harmonization for Good Clinical Practice.

Assessments

We collected demographic and clinical characteristics at baseline, including HCV viral load and genotype, stage of hepatic fibrosis, prior HCV treatment experience, past injection substance use, human immunodeficiency virus (HIV), and hepatitis B virus (HBV) infection for risk factor analysis. HIV positive patients were referred to infection subspecialist for further medical care.
Serum HCV RNA level was determined by Cobas® TaqMan® HCV Test v2.0 (Roche Molecular Diagnostics, CA, USA) with a lower limit of quantification (LLOQ) of 15 IU/mL. HCV genotype was determined by Cobas® HCV GT (Roche Molecular Diagnostics, CA, USA). Advanced hepatic fibrosis (fibrosis stage F3) was assessed using fibrosis index based on 4 factors (FIB-4) test ≥3.25. Abdominal ultrasonography was performed to detect the presence of liver cirrhosis and for hepatocellular carcinoma surveillance. Baseline laboratory tests were performed within 3 months prior to the initiation of GLE/PIB treatment. Patients were followed every 4 weeks until the end of treatment (EOT) and at Week 12 after treatment completion. Treatment-emergent adverse events (AEs) were recorded at every follow-up appointment. Safety data and laboratory abnormalities were graded using the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE).

**Statistical analysis**

Statistical analyses were performed using SPSS Statistics version 22.0 (IBM Corp., NY, USA). Baseline characteristics were reported in median (range) and frequencies (percentages), as appropriate. The on-treatment and off-treatment viral response rates and safety data were expressed in number and percentage. Univariate analysis was performed using the $\chi^2$ test, the Fisher’s exact test, or the Student’s t test, as appropriate. A two-sided $P<0.05$ was considered statistically significant.
Results

Demographic characteristics

During February to June 2019, we conducted three thorough briefings at Yunlin Prison and approached the potential participants of this study with an offer of enrollment. A total of 1,402 incarcerated persons, including those imprisoned during the study period, were invited. It equaled the full number of incarcerated individuals during study period. Among them, 824 incarcerated persons (58.8%) agreed to enrollment for HCV screening, and 276 incarcerated persons (33.5%, 276/824) were anti-HCV positive, of which 191 (69.2%, 191/276) were viremic. The baseline demographic and risk factor characteristics of the incarcerated persons with positive anti-HCV are shown in Table 1. Less IFN and DAA experience is found in positive HCV RNA group. HBV coinfection is more prominent in negative HCV RNA group. The baseline demographics and clinical characteristics of those CHC patients with positive HCV RNA are shown in Table 2. The median age of the CHC population was 45.6 years. Five (2.6%) patients were IFN-experienced. Six (3.1%) patients had a fibrosis stage of F3, according to the FIB-4 index. None of the patients met the F4 stage criteria of the FIB-4 index. However, six (3.1%) patients had liver cirrhosis with splenomegaly, as confirmed by ultrasonography findings. One patient showed prolonged INR (2.12) due to concomitant warfarin use.

The median log_{10} HCV RNA level at baseline was 6.235 (2.394-7.403). The genotype (GT) distribution was 39.3% (75/191) GT 6, 22.0% (42/191) GT 1a, 14.1% (27/191) GT 1b, 10.5% (20/191) GT 2, and 10.5% (20/191) GT 3. Seven patients had mixed genotype HCV infections, including three with GT 2+6 (1.6%), two with GT 1a+1b (1.0%), and two with GT 1b+2 (1.0%). Seventy-four (38.7%) patients had
elevation of alanine aminotransferase prior to treatment. The genotype distribution of treated patients is shown in Figure 1. Genotype 6 was predominant in treated patients of persons who inject drugs (PWID), followed by genotypes 1a, 1b, and 3.

Nine (4.7%) and seventeen (8.9%) patients were co-infected with HBV and HIV, respectively; during the interview, 166 patients (86.9%) admitted to injection substance use in the past. One patient had a confirmed diagnosis of advanced colon cancer with multiple liver metastases.

A total of 165 CHC patients received GLE/PIB therapy between February and June 2019. Twenty-six patients were excluded in this study, including twenty-four patients who will be released from prison in 6 months, one who refused antiviral therapy, and one who was transferred to a hospital for advanced cancer therapy. We excluded incarcerated patients who had less than 6 months sentence remaining because their SVR12 data cannot be obtained. The NHI would not reimburse the cost of treatments if these data are not available. However, further treatment after release was recommended. In univariate analyses, no statistically significant differences in baseline demographic characteristics were found among those who were treated and those who were not treated. All enrolled patients were treated according to the NHI clinical practice guidelines; 159 (96.4%) and six (3.6%) patients were treated for 8 and 12 weeks, respectively.

**Treatment effectiveness**

All 165 patients completed the treatment course. All (100%) patients had HCV RNA level below LLOQ at EOT. The overall SVR12 rates were 100%, regardless of
baseline characteristics or treatment duration. The patient selection protocol and treatment outcome of patients treated for HCV infection in Yunlin Prison are summarized in Figure 2.

**Safety profile**

In our study, sixteen (9.7%) patients experienced pruritis as the only AE. No anorexia and fatigue were reported during the course of treatment and no severe AEs occurred. Regarding laboratory abnormalities, only one Grade ≥3 (>5 × upper limit of normal, ULN) elevation in alanine aminotransferase (ALT) and aspartate aminotransferase (AST) level was observed. The ALT and AST level peaked at 304 and 179 U/L, respectively and dropped to normal limits at EOT. Elevation in total bilirubin level (>1.5 x ULN) during the treatment period was detected in 19 patients (11.5%). Among them, two patients exhibited Grade 3 (> 3 × ULN) elevation in total bilirubin level (1.2%), which peaked at 3.59 mg/dL and 3.33 mg/dL, respectively, and both patients completed the treatment without interruption. All enrolled patients completed treatment without premature termination. None of the patients experienced death or hepatic encephalopathy in our cohort. The AEs and laboratory abnormalities are summarized in Table 3.
Discussion

This study showed that micro-elimination of CHC in prison is possible with universal screening of anti-HCV for incarcerated persons. Additionally, we linked universal screening to the standard of care for incarcerated patients with positive HCV RNA.

Several studies reported that in most countries, the prevalence of HCV infection is higher in prisons than in community settings. The estimated prevalence varies from 3% to 38% [4]. However, the true seroprevalence and genotype distribution of HCV in Taiwan’s prison system are unknown due to the lack of research data. In Taiwan, the anti-HCV prevalence among incarcerated persons without substance use disorder was estimated to be 8.4% [25]. Among incarcerated persons with intravenous heroin dependence, the prevalence of HCV infection was 78.1% [26]. These studies focused on the HCV seroprevalence of subgroups rather than of all incarcerated persons in prisons. Our study is the first in Taiwan to use opt-in screening inside a prison to evaluate the seroprevalence and genotype distribution of HCV. The results showed that the prevalence of HCV infection in the prison population was 33.5%, which was considerably higher than that of the general population.

The distribution of HCV genotypes might vary between prison and general populations. Genotypes 1b and 2 are predominant in the general population of Taiwan [27]. Previous studies conducted outside of Taiwan showed that HCV genotypes 1 and 3 are more predominant in prison [28-34]. By contrast, one study in Taiwan reported that genotype 2a was the most predominant (58.9%), followed by 1a (17.3%), among incarcerated persons with intravenous heroin use [26]. Another study in Taiwan
indicated that genotype 1 was the most predominant (41.4%), followed by 3 (25.9%), among incarcerated patients who received Peg-IFN/RBV treatment [11]. Most of the incarcerated patients, who were enrolled in these studies, were transferred out of prison to receive medical therapy at medical facilities. Selection bias might exist in these studies.

Our universal screening showed that genotype 6 (39.3%) was predominant, followed by genotype 1a (22.0%). This result differs from the findings of other countries and previous studies in Taiwan. The mode of viral transmission may influence the predominance of certain genotypes in incarcerated persons. In our study, incarcerated persons with past substance dependency accounted for 86.9% of chronic HCV-infected prison population. According to previous research, a higher prevalence of HCV genotype 6 (41.0%), followed by 1a (18.5%) and 1b (13.8%), was reported in people with injection substance use in Taiwan [35]. This result highlights the association between the route of HCV transmission and genotype distribution. In addition, the coinfection rates of HBV and HIV were 4.7% and 8.9% respectively, probably because of similarities in the viral transmission routes. In Taiwan, the prevalence of HCV and HIV coinfection among people with injection substance use is relatively high and is gradually increasing [36]. As a result of high-risk behaviors, PWID might commonly harbor mixed genotype HCV infection and at risk of reinfection after treatment. Our study also found the relationship between mixed genotype infection and PWID. In treated patient group, mixed genotype infection was 3.5% among PWID, but none among non-PWID. These findings indicate that injection substance use is a crucial risk factor. Therefore, effective strategies, such as syringe services program and opioid agonist therapy, are required to prevent HCV transmission.
among PWID. Moreover, aggressive diagnostic and therapeutic approaches for HCV-infected incarcerated populations are also required, particularly in the new era of DAA therapy, which provides shorter treatment regimens in correctional settings.

Previously, CHC incarcerated patients have limited access to medical treatments because of obstacles such as medical accessibility, lack of disease awareness and low financial support. However, therapeutic effect wouldn’t change in prison. Some studies showed comparable or more favorable treatment responses to Peg-IFN/RBV therapy in incarcerated persons than in community-based patients [11, 12]. In the new era of DAA therapy, SVR, virologic failure, and discontinuation rates were reported to be similar in patients in the prison and community settings [23]. Because of its fewer side effects and improved efficacy, DAA therapy is more preferred to IFN-based therapy for incarcerated patients. The NHI authorized the prescription of DAAs to all Taiwanese citizens, including incarcerated patients, with confirmed CHC, drug availability no longer poses a problem for treating CHC in prisons. However, DAAs can only be prescribed by hepatologists or infection specialists, and this limitation is possibly a major barrier to CHC treatments for incarcerated patients. We addressed this issue by establishing a special CHC clinic in prison. This special CHC clinic, linking HCV screening to care, can be used as a model for treating incarcerated patients with CHC.

In our study, the overall SVR rates were 100% and no discontinuation of therapy was reported. This superior treatment response was probably attributed to favorable medical compliance in prison, which is partly due to the effective administration works in prison. No severe AEs were observed and pruritis (9.7%) was the only AE in our study. Although anorexia and fatigue (approximately 5%) during GLE/PIB therapy
were reported in real-world studies in Taiwan [37, 38], no such complaint was recorded in our study group, possibly because younger age, less comorbidities, and the simple prison life of our treated group might have alleviated such side effects. Regarding laboratory abnormalities, overall Grade ≥2 elevation in aminotransferase and total bilirubin level occurred in 12.7% of our patients. All patients recovered to normal limits after completing therapy. These findings indicate that GLE/PIB is effective, safe and well-tolerated in incarcerated patients with chronic HCV infection in Taiwan. Our study demonstrates that prison is an ideal place for micro-elimination of CHC; otherwise, incarcerated patients with CHC may have limited access to therapy once they are released from prison.

Incarcerated patients, particularly those with injection substance use, were reported to have high overall incidence of reinfection after successful treatment [39, 40]. This issue warrants further investigation. In our study, we could not estimate the reinfection rate after SVR, because a few of our treated patients were lost to regular follow-up after being released from prison or transferred to other prisons. Nevertheless, released incarcerated patients are presumed to have a high risk of reinfection due to their chaotic post-prison lifestyle in the community. Therefore, community-based health interventions for the elimination of HCV must be provided to this vulnerable group.

This study has several limitations. First, more than 40% of incarcerated persons in Yunlin Prison did not agree to participate in this study because the opt-in screening approach was adopted. Routine screening for all incarcerated persons is recommended as the aggressive diagnostic approach for HCV-infected incarcerated populations.
Second, to comply with the Taiwan NHI program, several patients were excluded from treatment because of the short length of their remaining sentence. Third, we did not assess the total direct medical and nonmedical costs. Therefore, the cost-effectiveness of IFN-free DAA therapy for the prison population could not be analyzed.

**Conclusion**

We determined that the prevalence of HCV infection in the prison population was 33.5%, which was considerably higher than that of the general population in Taiwan. Genotype 6 (39.3%) was predominant. DAA therapy was highly effective and safe for incarcerated patients with CHC in Taiwan. Our special CHC clinic in prison, linking HCV screening to care, can serve as a model for HCV micro-elimination.
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Conflict of Interest

All authors have no conflicts of interest to declare.

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| Characteristics                  | All patients (n = 276) | Positive HCV RNA (n = 191) | Negative HCV RNA (n = 85) | \( p \) value<sup>a</sup> |
|---------------------------------|------------------------|-----------------------------|---------------------------|--------------------------|
| Age, years                      | 45.5(30-73)            | 45.6(30-73)                 | 45.3(30-64)               | 0.5843                   |
| IFN-experienced                 | 14(5.1%)               | 5(2.6%)                     | 9(10.6%)                  | 0.0133                   |
| DAA-experienced                 | 1(0.4%)                | 0(0%)                       | 1(1.2%)                   | 0.3080                   |
| Hepatic fibrosis on Fibrosis-4 score |                       |                             |                           |                          |
| F3                              | 8(2.9%)                | 6(3.1%)                     | 2(2.4%)                   | 1                        |
| F4                              | 0                      | 0                           | 0                         |                          |
| HBV                             | 35(12.7%)              | 9(4.7%)                     | 26(30.6%)                 | <.0001                   |
| HIV                             | 23(8.3%)               | 17(8.9%)                    | 6(7.1%)                   | 0.6093                   |
| PWID                            | 233(84.4%)             | 166(86.9%)                  | 67(78.8%)                 | 0.0872                   |

HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; IFN, interferon; DAA, direct acting antiviral. PWID, people who inject drugs.

Data are expressed as n (%) or median (range). Categorical variables were compared by the \( \chi^2 \) test or the Fisher’s exact test; continuous variables were compared by the Student’s \( t \) test.

<sup>a</sup>Comparison was made between positive HCV RNA and negative HCV RNA groups; significant \( p \)-values are shown in bold text.
Table 2. Descriptive characteristics of the incarcerated persons with positive HCV RNA

| Characteristics                        | All patients (n = 191) | Treated patients (n = 165) | Untreated patients (n = 26) | P-valuea |
|----------------------------------------|------------------------|---------------------------|-----------------------------|----------|
| Age (years)                            | 45.6 (30-73)           | 45.8 (30-73)              | 44.3 (33-63)                | 0.38219776 |
| IFN-experienced                        | 5 (2.6%)               | 5 (3.0%)                  | 0 (0%)                      | 1        |
| Hepatic fibrosis on Fibrosis-4 score   |                        |                           |                             |          |
| F3                                     | 6 (3.1%)               | 6 (3.6%)                  | 0 (0%)                      | 1        |
| F4                                     | 0                      | 0                         | 0                           |          |
| Liver cirrhosis with splenomegaly on ultrasonography | 6 (3.1%) | 6 (3.6%) | 0 | 1 |
| HCV genotype                           |                        |                           |                             |          |
| 1a                                     | 42 (22.0%)             | 36 (21.8%)                | 6 (23%)                     | 0.8855   |
| 1b                                     | 27 (14.1%)             | 24 (14.5%)                | 3 (11.5%)                   | 1        |
| 2                                      | 20 (10.5%)             | 17 (10.3%)                | 3 (11.5%)                   | 0.7397   |
| 3                                      | 20 (10.5%)             | 19 (11.5%)                | 1 (3.8%)                    | 0.3203   |
| 6                                      | 75 (39.3%)             | 64 (38.7%)                | 11 (42.3%)                  | 0.7327   |
| 1a+1b                                  | 2 (1.0%)               | 1 (0.6%)                  | 1 (3.8%)                    | 0.2543   |
| 1b+2                                   | 2 (1.0%)               | 1 (0.6%)                  | 1 (3.8%)                    | 0.2543   |
| 2+6                                    | 3 (1.6%)               | 3 (1.8%)                  | 0 (0%)                      | 1        |
| HCV RNA (log_{10} IU/mL)               | 6.235                  | 6.246                     | 6.165                       | 0.67385888 |
| Platelet count (k/μL)                  | 218.1 (50-408)         | 218.2 (50-408)            | 216.9 (93-349)              | 0.90530737 |
| ALT (U/L)                              | 49.2 (7-350)           | 47.9 (7-350)              | 58.0 (10-315)               | 0.44189620 |
| AST (U/L)                              | 34.2 (9-175)           | 34.0 (9-175)              | 35.5 (14-115)               | 0.78307864 |
| Test                | Median (Range)       | Median (Range)       | Median (Range)       | p-Value       |
|---------------------|----------------------|----------------------|----------------------|---------------|
| Total bilirubin (mg/dL) | 0.77 (0.37-1.97)      | 0.77 (0.37-1.97)      | 0.73 (0.44-1.41)      | 0.44094274    |
| Albumin (g/dL)      | 4.47 (3.6-5.3)        | 4.47 (3.6-5.1)        | 4.45 (4.0-5.3)        | 0.77880776    |
|                     | 0.97 (0.88-2.12)      | 0.98 (0.88-2.12)      | 0.96 (0.91-1.07)      | 0.08209333    |
| INR                 | 0.92 (0.6-2.2)        | 0.92 (0.6-2.2)        | 0.89 (0.7-1.1)        | 0.17604307    |
|                     | 0.97 (0.88-2.12)      | 0.98 (0.88-2.12)      | 0.96 (0.91-1.07)      | 0.08209333    |
| Creatinine (mg/dL)  | 0.92 (0.6-2.2)        | 0.92 (0.6-2.2)        | 0.89 (0.7-1.1)        | 0.17604307    |
| CKD stage 4-5       | 0                    | 0                    | 0                    |               |
| HBV                 | 9 (4.7%)              | 7 (4.2%)              | 2 (7.6%)              | 0.3528        |
| HIV                 | 17 (8.9%)             | 16 (9.6%)             | 1 (3.8%)              | 0.4766        |
| PWID                | 166 (86.9%)           | 143 (86.6%)           | 23 (88.4%)            | 1             |

Data are presented as no. (%) or median (range). Categorical variables were compared using the χ² test or the Fisher’s exact test. Continuous variables were compared using the Student’s t test.

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; CKD, chronic kidney disease; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HIV, human immunodeficiency virus; IFN, interferon; INR, international normalized ratio, PWID, people who inject drugs; RNA, ribonucleic acid.

*Comparison was made between treated and untreated patient groups. Significant P-values are shown in bold text.
Table 3. Safety summary of the 165 patients treated with GLE/PIB

|                      | All treated patients (n = 165) |
|----------------------|---------------------------------|
| **Adverse events**   |                                 |
| Pruritus             | 16 (9.7)                        |
| Anorexia             | 0 (0)                           |
| Fatigue              | 0 (0)                           |
| Deaths               | 0 (0)                           |
| **Laboratory abnormalities**a |                     |
| ALTb > 5 × ULN       | 1 (0.6)                         |
| ASTb > 5 × ULN       | 1 (0.6)                         |
| **Total bilirubin**  |                                 |
| > 1.5-3 × ULN        | 17 (10.3)                       |
| > 3 × ULN            | 2 (1.2)                         |

Data are presented as no. (%).

Abbreviations: AST, Aspartate aminotransferase; ALT, Alanine aminotransferase; AE, adverse event; ULN, upper limit of normal.

a Post-baseline laboratory abnormalities.

b Post-nadir increase to >5 × ULN.
Figure Legends

Figure 1. CHC genotype distribution of treated patient group in Yunlin prison.
Abbreviations: PWID, people who inject drugs.

Figure 2. Selection protocol and outcome of patients treated for HCV infection in prison.
Abbreviations: PWID, persons who inject drugs; HCV, hepatitis C virus; RNA, ribonucleic acid; SVR, sustained virologic response.
Figure 1

Genotype distribution (All patients, N=165)

Genotype distribution (PWID, N=143)

Genotype distribution (non-PWID, N=22)
Figure 2

- Incarcerated persons attended the thorough briefings of this study (n = 1,402)
- Incarcerated persons agreed to enrollment for HCV screening (n = 824)
- Patients with positive anti-HCV (n = 276)
- Patients with positive HCV RNA (n = 191)
- Patients received direct-acting antivirals (n = 165)
- Patient achieved SVR 12 (n = 165)

24 will be released from prison in 6 months.
1 Refused treatment
1 hospitalized for advanced cancer treatment.