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Real-world treatment patterns and clinical outcomes of HCV treatment-naïve patients in China: an interim analysis from the CCgenos study

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Abstract

Background and Aim: In China, chronic hepatitis C virus (HCV) infection represents a considerable healthcare burden. Although interferon-based therapy has been the standard-of-care for many years, few long-term, real-life studies have assessed interferon-based treatment in China. The objective of CCgenos follow-up study was to analyze long-term treatment patterns and outcomes in a cohort of treatment-naïve, Han ethnic, patients with chronic HCV infection.

Methods: Patients who had participated in the CCgenos cross-sectional study were invited to enter this 5-year follow up. Clinical information and centralized HCV-RNA measures were collected at scheduled study visits every 6 months for untreated patients and every 3 months for treated patients.

Results: Among 512 patients enrolled, 334 (65.2%) received interferon-based treatment and 178 (34.8%) remained untreated over a median of 4.1 (1.2–4.3) years. A total of 82.8% (424/512) of patients had an IL28B CC genotype (GT); 60.7% (311/512) had HCV GT1b infection, including 121 (38.9%) untreated. Most patients with baseline cirrhosis were untreated (26/46, 56.5%). Among patients who completed treatment and 24 weeks of post-treatment follow up, the duration of interferon-based therapy was frequently longer than recommended (52.9% [92/174] of GT1b-infected were treated for > 1 year). Rates of sustained virologic response (SVR24) were 71.1% (226/318) overall; 62.4% (111/178) among patients with both GT1b infection and cirrhosis. 42.9% (15/35) among patients with cirrhosis.

Conclusions: There remains a high unmet need for effective HCV treatment in China, evidenced by a high proportion of patients remaining untreated by the current standard-of-care and relatively low SVR24 rates for patients with both GT1b infection and cirrhosis.

Introduction

Globally, more than 185 million people have been infected with the hepatitis C virus (HCV), of whom 350 000 die each year.1 Chronic HCV infection is associated with progressive liver disease that can lead to cirrhosis, hepatocellular carcinoma (HCC), and death.2 In China, the prevalence of HCV is estimated at 1–1.9% of the total population, representing around 25 million people,3,4 or 15% of the total HCV-infected population worldwide.5 According to the Chinese Ministry of Health annual reports on health statistics, newly reported cases of hepatitis C have been increasing steadily, from 20 000 cases in 2003 to over 200 000 in 2012.4

Hepatitis C virus treatment has evolved substantially over recent years with the introduction of direct antiviral agents (DAAs) in 2011 and the approval of the first all-oral DAA combinations in early 2014.6 However, no DAA has yet been approved in mainland China, where the current standard-of-care remains (pegylated) interferon alfa (pegIFN-α) and ribavirin (RBV).7 In China, the dominant HCV genotype (GT) is GT1 (73% in 2002,8 58% in 2014) most of which (98%) is subtype 1b.5,8 GT1b is associated with faster progression to cirrhosis and HCC compared with other HCV GTs.9,10 GT1 is associated with lower response rates to interferon-based therapy compared with other GTs,
although GT1b may be more likely to respond than GT1a.\textsuperscript{1,11} HCV GT1-infected patients with an \textit{IL28B} (rs12979860) CC GT are also more likely to achieve a sustained virologic response (SVR) following treatment with pegIFN-α/RBV.\textsuperscript{1,2} Over 80% of Chinese HCV patients are \textit{IL28B} GT CC; however, reported SVR rates with pegIFN-α/RBV in China, predominately in patients with GT1b infection, vary from 44% to 83%.\textsuperscript{5,13–19}

There are few long-term, real-life studies reporting treatment patterns and outcomes of interferon-based therapy in China. This is partly because the determination of true SVR rates is hindered by variation in treatment (regimens, doses, formulations, and durations), widespread use of low sensitivity HCV-RNA assays, and inconsistent use of SVR definitions. The cross-sectional phase of the CCgenos study (AI425-009/NCT01293279) generated data on the demographic and clinical characteristics of HCV in treatment-naïve Han Chinese across mainland China\textsuperscript{5} and provided a good foundation for follow-up analysis; a 5-year follow-up study (AI425-018/NCT01594554) was initiated with the objective of analyzing long-term, real-life outcomes in these patients. We present here the results of a 4-year follow up (cut-off date 31 May 2015) in this long-term study.

**Methods**

**Study design and patients.** In the cross-sectional phase of the CCgenos study, Han ethnic Chinese adults (≥18 years old) with recently confirmed chronic HCV infection (anti-HCV-antibody positive and HCV-RNA positive), who were naïve to HCV or HBV antiviral interferon treatment, were enrolled at 28 university hospitals across China. HCV GT and host \textit{IL28B} GTs were determined and compared with patient demographic and clinical parameters as previously described.\textsuperscript{5} Patients from the cross-sectional phase were invited to consent to enter a 5-year follow up (ClinicalTrials.gov identifier NCT01594554; BMS study ID AH452-018ST). No other exclusion criteria were applied for the follow-up phase, and no randomization or protocol-driven treatment was implemented.

For each patient, information on anti-HCV treatments received between completion of the cross-sectional phase (June 2011) and enrolment into the follow-up phase (April 2012) was collected retrospectively. Clinical information during follow up was collected following a schedule intended to match real-life practice in China and recommendations in the relevant clinical guidelines. Follow-up visits were carried out every 3 ± 1 months for patients on active anti-HCV treatment and every 6 ± 2 months for patients who remained treatment-naïve and those who had completed treatment. Study visits were scheduled from the time of enrolment into the follow-up study. Because treatment initiation may have occurred at various time points before or after enrolment, the visit schedule did not always correspond to a specified treatment duration. SVR24 was based on the HCV-RNA result collected at the closest time point occurring following 24 weeks, respectively, after the last dose of treatment.

**Assessments and endpoints.** At all scheduled study visits, HCV-RNA was analyzed at a central laboratory (the Peking University People’s Hospital) using the Abbott RealTime HCV assay (Abbott Laboratories, Des Plaines, IL, USA; lower limit of detection 12 IU/mL), and biochemistry, hematology, and blood coagulation functions were performed at local laboratories (i.e. treating hospitals).

Evidence of hepatic cirrhosis (compensated or decompensated) was based on biopsy results wherever possible. In the absence of biopsy results, diagnosis of decompensated cirrhosis was based on the following criteria: ascites, hepatic encephalopathy, upper gastrointestinal bleeding, or Child–Turcotte–Pugh score ≥7. If none of these criteria were met, evidence of hepatic cirrhosis could be based on any two of the following: imaging showing features of cirrhosis (nodular liver or splenomegaly), platelet count < 100×10^9/L in the absence of other explanations, liver stiffness measurement > 13 kPa, and gastro-esophageal varices in endoscopy.

**Statistical analysis.** Descriptive statistics was used to summarize treatment duration for treated patients by GT. Treatment duration was applied as a categorical variable (≤12 weeks, > 12 and ≤24 weeks, > 24 and ≤36 weeks, > 36 and ≤47 weeks, > 47 and ≤52 weeks, > 1 and ≤1.5 years, >1.5 and ≤2 years, > 2 and ≤3 years, and > 3 years) and as a continuous variable in the analyses. T-tests or Wilcoxon rank-sum tests were used to compare continuous variables at baseline between treated and untreated groups. Chi-square or Fisher’s exact tests were used for comparison of categorical variables.

The risk of disease progression (liver cirrhosis and HCC) was determined using a risk calculator based on the Risk Evaluation of Viral Load Elevation and Associated Liver Disease (REVEAL)-HCV cohort study, as previously described.\textsuperscript{20,21} Because this risk calculator was based on analysis of data from patients aged between 30 and 65 years, only patients within this age group were included in the risk analysis. Time to development of cirrhosis and HCC were estimated by Kaplan–Meier product limit method. Comparison of time with cirrhosis or HCC across treated and untreated patients was based on log-rank test.

**Results**

**Patient dispositions and baseline characteristics.** Out of 997 patients included in the cross-sectional phase, 512 were enrolled in the follow-up phase from 25 university hospitals across China (Fig. 1). One subject was excluded from the full analysis population because this patient started antiviral treatment before informed consent for the follow-up phase. Most of the 484 patients who did not participate in the follow-up phase were not permanent residents of the areas where participating hospitals were located and could not be contacted before follow up was initiated. There were no apparent differences between patients in the cross-sectional phase who were enrolled in the follow-up phase and those who were not, except for a slightly higher level of education ($P = 0.0180$) and slightly higher hemoglobin level among patients in the follow up ($141.0 \text{ g/L} vs 138.6 \text{ g/L}$, $P = 0.0488$, Supplemental Table 1). By the cut-off date (31 May 2015), the median duration of follow up was 4.1 (1.2–4.3) years; 334 (65.2%) had received anti-HCV treatment, and 178 (34.8%) had not.

Baseline demographics and disease characteristics are shown in Table 1. Most patients were infected with HCV GT1 (62.1% [318/512]), 60.7% with subtype GT1b (311/512); the remaining patients were infected with HCV GT2, 3, or 6. A greater proportion
of untreated patients had GT1b HCV infection (121/178, 68.0%) compared with treated patients (190/334, 56.9%); thus, a large proportion of patients with HCV GT1b remained untreated (121/311, 38.9%, compared with 43/163, 26.4% for HCV GT2/3). A greater proportion of untreated patients had cirrhosis at baseline compared with treated patients (14.6% vs 6.0% \( P = 0.0012 \)), and the treated group had higher baseline mean alanine aminotransferase (ALT) levels, platelet counts, and hemoglobin levels compared with the untreated group.

In addition, a greater proportion of untreated patients met \( \geq 1 \) (56.7%) or \( \geq 2 \) (25.3%) criteria for interferon ineligibility (older than 70 years old, cytopenia, cirrhosis, hypertension, diabetes, autoimmune disease, and thyroid dysfunction) compared with treated patients (35.9% and 9.3%, respectively, \( P < 0.0001 \) for both). The most frequent reasons cited for interferon ineligibility were low platelet count (\( \leq 90 \times 10^9/L \), 29.2% untreated, 10.8% treated), hypertension (17.4% untreated, 12.3% treated), cirrhosis (14.6% untreated, 6.0% treated), and diabetes (10.7% untreated, 5.7% treated).

**Treatment patterns.** The most common specified reasons for not receiving treatment by the cut-off date (Supplemental Table 2) were “patient did not agree to receive treatment temporarily” (30.3% [54/178]) and “other contraindications to treatment” (19.7% [35/178]). “Financial reasons” were cited for 7.9% (14/178) of patients, “decompensated hepatic cirrhosis” for 9.6% (17/178), and “other” reasons for 32.0% (57/178; in the clinical report form, it was not mandatory to specify other reasons).

Among patients who initiated HCV treatment, 313/334 (93.7%) completed treatment by the cut-off date, 11 patients (3.3%) were still on treatment, and 10 (3.0%) had dropped out during treatment. Treatments received were pegIFN-\( \alpha \)/RBV (70.4% [235/334]), conventional IFN-\( \alpha \)/RBV (25.4% [85/334]), pegIFN-\( \alpha \) monotherapy (2.1% [7/334]), conventional IFN-\( \alpha \) monotherapy (1.8% [6/334]), or other (0.3% [1/334]). Treatment durations by HCV GT are shown in Supplemental Table 3. Among 174 HCV GT1b-infected patients who completed treatment, 164 (94.3%) received treatment for 1.5 years or less, with most receiving treatment for at least 48 weeks; 82 (47.1%) were treated for \( \geq 1 \) and \( \leq 1.5 \) years; and 35 (20.1%) for 48–52 weeks. Total treatment durations were similar between pegylated and conventional IFN-\( \alpha \) (data not shown). Among 116 HCV GT2/3-infected patients who completed treatment, 114 (98.3%) completed treatment in 1.5 years or less; 29 (25.0%) were treated for \( \geq 1 \) and \( \leq 1.5 \) years, 29 (25.0%) for 48–52 weeks, 18 (15.5%) for 36–48 weeks, and 27 (23.3%) for 24–36 weeks. There was a trend of slightly longer treatment durations with conventional compared with pegIFN-\( \alpha \) (data not shown).

**Treatment effectiveness.** Of the 334 patients who initiated anti-HCV treatment, 312 (93.4%) completed 12 weeks of post-treatment follow up, and 308 (92.2%) completed 24 weeks of follow up. For ITT analysis, 318 patients were included with 308 patients who completed 24 weeks of follow up and 10 patients who dropped out the study, SVR24 was achieved by 226 (71.1%) patients (Table 2). The SVR24 rates were higher among patients with GT2 (87.1% [81/93]) or GT 3 (87.0% [20/23]) infection than among patients with GT1b (62.4% [111/178]), including those with an IL28B CC GT (65.5% [93/142]). Among patients with IL28B, non-CC GTs SVR24 was achieved by 50.0% (18/36) of those with HCV GT1 infection and 76.9% (10/13) of those with HCV of other
### Table 1  Baseline demographics and disease characteristics

| Parameter                                                                 | Untreated (n = 178) | Treated (n = 334) | Difference (P value)* |
|---------------------------------------------------------------------------|---------------------|------------------|-----------------------|
| Mean age, years (SD)                                                     | 52.8 (12.19)        | 43.2 (12.94)     | <0.0001               |
| Older than 65 years                                                      | 27 (15.2)           | 12 (3.6)         | <0.0001               |
| Male, n (%)                                                              | 94 (52.8)           | 199 (59.6)       | 0.1402                |
| BMI                                                                       | 23.3 (3.2)          | 23.6 (3.7)       | 0.4562                |
| HCV viral genotype/subtype, n (%)                                        |                     |                  |                       |
| 1                                                                        | 125 (70.2)          | 193 (57.8)       | **0.0180**            |
| 2/3                                                                      | 43 (24.2)           | 120 (35.9)       |                       |
| 6                                                                        | 10 (5.6)            | 21 (6.3)         |                       |
| 1b                                                                       | 121 (68.0)          | 190 (56.9)       | **0.0016**            |
| 2                                                                        | 26 (14.6)           | 96 (28.7)        |                       |
| 3                                                                        | 17 (9.6)            | 24 (7.2)         |                       |
| **IL28B SNP rs12979860 CC, n (%)**                                        | 143 (80.3)          | 281 (84.1)       | 0.2784                |
| Cirrhosis, n (%)                                                         | 26 (14.6)           | 20 (6.0)         | **0.0012**            |
| Among genotype subgroups                                                |                     |                  |                       |
| 1                                                                        | 18 (10.1)           | 14 (4.2)         | 0.5726                |
| 2/3                                                                      | 6 (3.4)             | 6 (1.8)          |                       |
| 6                                                                        | 2 (1.1)             | 0 (0.0)          |                       |
| 1b                                                                       | 18 (10.1)           | 14 (4.2)         | 0.8786                |
| 2                                                                        | 4 (2.2)             | 5 (1.5)          |                       |
| 3                                                                        | 2 (1.1)             | 1 (0.3)          |                       |
| CTP score ≥ 7, n (%)                                                     | 18 (10.1)           | 6 (1.8)          | **0.0001**            |
| HCV-RNA, mean Log_{10} IU/mL (SD)                                        | 5.9 (0.9)           | 5.9 (0.9)        | 0.3606                |
| ALT, mean U/L (SD)                                                       | 61.9 (42.0)         | 90.1 (112.4)     | **<0.0001**           |
| ALT ≥ ULN,† n (%)                                                       | 159 (88.8)          | 300 (89.8)       | 0.7110                |
| ALT ≥ 2 x ULN,† n (%)                                                   | 91 (51.1)           | 195 (58.4)       | 0.1152                |
| AST, mean U/L (SD)                                                       | 61.6 (36.4)         | 62.0 (57.8)      | 0.9230                |
| Platelets, mean × 10^9/L (SD)                                            | 134.5 (72.4)        | 167.0 (64.4)     | **<0.0001**           |
| Platelets ≤ 90 × 10^9/L, n (%)                                           | 52 (29.2)           | 36 (10.8)        | **<0.0001**           |
| Platelets ≤ 50 × 10^9/L, n (%)                                           | 19 (10.7)           | 4 (1.2)          | **<0.0001**           |
| AST/platelets, mean (SD)                                                 | 0.8 (1.0)           | 0.5 (0.6)        | **0.0002**            |
| APRI, mean (SD)                                                          | 1.9 (2.5)           | 1.2 (1.6)        | **0.0002**            |
| APRI categories,‡ n (%)                                                  | 0.0068              |                  |                       |
| < 0.5                                                                   | 42 (23.6)           | 119 (35.6)       |                       |
| ≥ 0.5, < 1.0                                                             | 46 (25.8)           | 92 (27.5)        |                       |
| ≥ 1.0, < 1.5                                                             | 23 (12.9)           | 41 (12.3)        |                       |
| ≥ 1.5, < 2.0                                                             | 16 (9.0)            | 29 (8.7)         |                       |
| ≥ 2.0                                                                   | 50 (28.1)           | 53 (15.9)        |                       |
| GGT, mean IU/L (SD)                                                      | 53.7 (64.7)         | 63.3 (85.8)      | 0.1249                |
| Hemoglobin, mean g/dL (SD)                                               | 13.8 (1.9)          | 14.3 (1.9)       | **0.0024**            |
| Hemoglobin < 8 g/dL, n (%)                                               | 0 (0.0)             | 2 (0.6)          | 0.5463                |
| Neutrophils, mean × 10^9/L (SD)                                          | 3.0 (1.5)           | 3.0 (1.3)        | 0.7945                |
| Neutrophils < 1.5 × 10^9/L, n (%)                                        | 17 (9.6)            | 22 (6.6)         | 0.2215                |
| Diabetes, n (%)                                                          | 19 (10.7)           | 19 (5.7)         | **0.0404**            |
| Hypertension                                                             | 31 (17.4)           | 41 (12.3)        | Not tested            |
| HBV co-infection, n (%)                                                  | 8 (4.5)             | 10 (3.0)         | 0.3800                |
| Interferon ineligibility criteria§                                        |                     |                  |                       |
| Met 1 criteria                                                           | 56 (31.5)           | 89 (26.6)        | 0.2496                |
| Met ≥ 1 criteria                                                         | 101 (67.7)          | 120 (35.9)       | **<0.0001**           |
| Met ≥ 2 criteria                                                         | 45 (25.3)           | 31 (9.3)         | **<0.0001**           |

*T-tests or Wilcoxon rank sum tests were used to compare continuous variables between groups. Chi-square or Fisher’s exact tests were used for comparison of categorical variables.

†ALT ≥ ULN defined for female as ALT ≥ 19 U/L or for male ALT ≥ 30 U/L.

‡APRI = 100 × AST/platelets/40.

§Older than 70 years old, cytopenia, cirrhosis, hypertension, diabetes, autoimmune disease, and thyroid dysfunction.

ALT, alanine aminotransferase; APRI, AST to platelet ratio index; AST, aspartate aminotransferase; BMI, body mass index; CTP, Child–Turcotte–Pugh; GGT, gamma-glutamyl transpeptidase; HBV, hepatitis B virus; HCV, hepatitis C virus; SNP, single nucleotide polymorphism.
GTs. Among patients with cirrhosis at treatment initiation, 45.5% (15/33) achieved SVR24. Patients treated in spite of having at least one interferon ineligibility criteria achieved low SVR24 rates (59.8% [67/112]). HCV GT1b is reported among untreated patients. Notably, there was a high proportion of patients with HCV GT1b infection (311/512 [60.7%]). HCV GT1b is reported among untreated patients. Notably, there was a high proportion of patients with HCV GT1b infection (311/512 [60.7%]). HCV GT1b is reported among untreated patients. Notably, there was a high proportion of patients with HCV GT1b infection (311/512 [60.7%]).

Discussion

This interim analysis of a long-term observational study provides important information about real-life treatment patterns and outcomes of interferon-based therapy for patients with chronic hepatitis C in China. The data demonstrate that there is currently an unmet medical need for effective, better tolerated, treatment options for many patients infected with HCV.

Among 512 patients followed up in the study, 34.8% (178) did not receive anti-HCV treatment over the 4.3-year follow-up period. Comparison of baseline characteristics between untreated and treated groups showed higher proportions of patients with HCV GT1b, cirrhosis, and multiple interferon ineligibility criteria among untreated patients. Notably, there was a high proportion of HCV GT1b infection (311/512 [60.7%]). HCV GT1b is reported to increase the rate of SVR24 regardless of HCV GT.

Disease progression. Risk scores derived from the risk prediction model20,21 for cirrhosis and HCC at baseline and at the last follow up are shown in Figures 2 and 3. For both cirrhosis and HCC, the distribution of risk scores among treated patients showed a significant shift towards lower scores at baseline and last visit (P < 0.0001; Fig 2A,3A). In contrast, there was no shift in risk score among untreated patients (Fig 2B,3B). Among treated patients, this shift towards lower risk scores was larger among those who achieved SVR24 (P < 0.0001 for cirrhosis and HCC) than among those who did not achieve SVR24 (P = 0.0082 for cirrhosis; P = 0.0109 for HCC; Fig 2C,D and 3C,D).

Figure 4 shows the Kaplan–Meier curves of time to disease development (cirrhosis and HCC) from baseline according to treatment status. The probability of progression to cirrhosis over time was significantly lower in the treated compared with untreated group (P < 0.0001). Kaplan–Meier analysis suggests a 29% probability that a patient left untreated would develop cirrhosis within 5 years of study baseline (probability of remaining free of cirrhosis 0.709, 95% confidence interval 0.448, 0.970). The corresponding probability for patients who received treatment was approximately 4% (probability of remaining free of cirrhosis 0.962, 95% confidence interval 0.930, 0.993). For HCC, the Kaplan–Meier curve implies a trend towards reduced probability of progression among treated patients; however, the difference was not significant (P = 0.4411).
to be an independent predictor HCC risk in both Western and Asian populations.\textsuperscript{22–24} Given the low treatment rate observed in this study, and the prevalence of HCV GT1b in China, in the next 10 to 20 years, a large proportion of patients with chronic HCV infection in China are likely to develop cirrhosis and/or HCC. In North America, the shifting age distribution of HCV infection as the “baby boomer” generation aged (born between 1945 and 1964 and exposed to infection during the 1970s)\textsuperscript{1,25} was paralleled, prior to the introduction of DAAs, with dramatic increases in HCV-associated liver disease and mortality.\textsuperscript{26,27} A similar trend could emerge in China, where the current age distribution of HCV infection is younger than in North America, with a shorter duration of infection.\textsuperscript{28}

Among untreated patients, 25.3% had ≥2 contraindications to interferon-based therapy; similarly, “patient did not agree to receive treatment temporarily” or “contraindications to treatment” accounted for the lack of treatment initiation in 50.0% of patients. New treatments are needed to provide viable treatment options for these patients. Notably 35.9% of the treated group had ≥1 contraindication for interferon, most frequently hypertension or low platelet count. Because of a lack of alternative options, these patients received interferon-based treatment in spite of contraindications but achieved low response rates, particularly those with HCV GT1b infection (42%). Given this low response rate, it may be better for these patients to wait for new treatment options to achieve better clinical outcomes.

The duration of interferon-based therapy was frequently extended beyond recommendations, yet despite a high proportion of patients with $\text{IL28B CC GT}$ ($\geq$80%), SVR24 rates were relatively low, 71.1% overall and 62.4% among HCV GT1b-infected patients. These rates are consistent with those reported in other studies in Chinese populations with predominately $\text{IL28B CC GT}$ (44% to 83%).\textsuperscript{5,13–19} Relatively low response rates may encourage physicians to treat for longer than that recommended by Chinese treatment guidelines.\textsuperscript{7} For GT1, 48 weeks of treatment is recommended for treatment-naive patients; approximately half of
the GT1b-infected patients with 24 weeks of post-treatment follow up in this study were treated for >1 year (52.9% [92/174]). For GT2/3, 24 weeks of treatment is recommended for treatment-naive patients; most GT2/3-infected patients who completed 24 weeks of post-treatment follow up in this study were treated for >36 weeks (67.2% [78/116]). The lack of high sensitivity HCV-RNA assays in local laboratories in most hospitals in China may have contributed to this extended treatment because clinical decisions could have been based on misleading virologic response results. Extended treatment did not appear to increase SVR24 rates, suggesting that there are no clinical or economic benefits to prolonging interferon-based treatment beyond the recommended duration.

Successful anti-HCV treatment reduces the risk of developing cirrhosis and HCC for HCV-infected patients. In this study, mean risk scores for cirrhosis and HCC were reduced between baseline and follow up in treated patients but not in untreated patients, with the largest reductions seen among treated patients who achieved SVR24. Kaplan–Meier analysis also showed that treatment significantly reduced the probability of progression to cirrhosis compared with no treatment ($P < 0.0001$). In this interim analysis, no significant difference was observed between treated and untreated patient groups for probability of progression to HCC; however, a trend towards reduced progression to HCC among treated patients appeared to be emerging that may become more apparent over a longer duration of follow up.

As with all real-life observational studies, the CCgenos follow-up study is subject to some limitations. For example, because of the low prevalence of FibroScan in 2010 in China, the diagnosis of cirrhosis was based on clinical criteria, rather than on the current “gold standard” of histology supplemented by FibroScan. Nevertheless, the specified clinical criteria are the same as those used during the Peking University–University of Michigan Joint Program and are an accepted method used by both Chinese and US investigators.

In conclusion, this study provides a good understanding of clinical outcomes with interferon-based therapy in China. There

![Figure 3](https://example.com/figure3.png)

**Figure 3**  Hepatocellular carcinoma (HCC) risk scores generated by the risk prediction model at baseline and last follow up for a) all treated patients (Baseline ($n=265$), mean ± SD = 11.98 ± 3.21; Last follow-up ($n=229$), mean ± SD = 7.05 ± 4.51; T-test, $P < 0.001$, paired t-test ($n=222$), $P < 0.0001$), b) all untreated patients (Baseline ($n=139$), mean ± SD = 13.41 ± 3.77; Last follow-up ($n=82$), mean ± SD = 13.17 ± 4.15; T-test, $P = 0.6611$, paired t-test ($n=60$), $P = 1.000$), c) treated patients who achieved SVR24 (Baseline ($n=179$), mean ± SD = 11.41 ± 2.87; Last follow-up ($n=168$), mean ± SD = 5.84 ± 3.56; T-test, $P < 0.001$, paired t-test ($n=165$), $P < 0.0001$), and d) treated patients who did not achieve SVR24 (Baseline ($n=50$), mean ± SD = 15.64 ± 2.26; Last follow-up ($n=41$), mean ± SD = 13.00 ± 4.67; T-test, $P = 0.0117$, paired t-test ($n=45$), $P = 0.0109$). Risk scores were calculated for patients who were aged 30 to 65 years and had no HCC at baseline and who had data available at the relevant time point for alanine aminotransferase, aspartate aminotransferase, hepatitis C virus-RNA, hepatitis C virus genotype, and cirrhosis and hepatocellular carcinoma status. SVR, sustained virologic response.
is a high-unmet medical need for effective treatment in China, especially in patients with GT1b infection, as evidenced by the low-treatment rate and relatively low-SVR24 rates for these patients. Given GT1b is the predominant GT in China and is associated with an increased risk of HCC, the prevalence of HCV-associated liver cirrhosis and HCC in China is likely to increase by the end of the next decade, creating a considerable economic burden. Successful anti-HCV treatment can reduce the risk of developing cirrhosis and HCC for HCV-infected patients. With the approval of more effective and better tolerated DAA regimens with shorter treatment durations, it is hoped that more patients will benefit from HCV treatment.

Disclosures
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Supporting information

Additional Supporting Information may be found in the online version of this article at the publisher’s web-site:

Table S1. Comparisons between patients in the cross-sectional phase (AI452-009ST) but not in the follow-up phase (AI452-018ST) and those enrolled in the follow-up phase (AI452-018ST).

Table S2. Reasons for not receiving treatment (by visit and current location).

Table S3. Treatment duration among who completed treatment.