Journal of the Formosan Medical Association (2017) xx, 1–9

Available online at www.sciencedirect.com

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journal homepage: www.jfma-online.com

ORIGINAL ARTICLE

# Identification of treatment-experienced hepatitis C patients with poor cost-effectiveness of pegylated interferon plus ribavirin from a real-world cohort

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Received 13 December 2016; received in revised form 21 February 2017; accepted 23 February 2017

**KEYWORDS**
chronic hepatitis C;
cost-effectiveness analysis;
pegylated interferon;
ribavirin;
treatment-experienced

*Background/Purpose:* Pegylated interferon (PegIFN) plus ribavirin (RBV) combination therapy has been the standard of care since 2002. Although a better viral response has been achieved among chronic hepatitis C (CHC) patients in Taiwan, approximately 25% of hepatitis C virus (HCV) genotype 1 (G1) patients and 15% of G2 patients failed to achieve a sustained virological response (SVR) at the first therapy. The actual cost-effectiveness of the retreatment remains elusive. The present study conducted a real-world cost-effectiveness analysis of a large cohort among different pre-specified subgroups of treatment-experienced CHC patients.
*Methods:* A total of 117 patients with CHC who failed to achieve SVR at the first IFN-based therapy and received a second IFN-based therapy were enrolled. The inpatient and outpatient costs were acquired from National Health Insurance Research Database of Taiwan. The related medical care costs per treatment and per SVR were calculated.

Conflicts of interest: The authors certify that they have NO involvement in any organization or entity with any financial or non-financial interest in the subject matter or materials discussed in this manuscript.

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http://dx.doi.org/10.1016/j.jfma.2017.02.013

*Results:* We demonstrated that the average cost per SVR achieved was $13,722 in treatment-experienced CHC patients. Especially, patients with HCV G1 infection, baseline viral loads > 400,000 IU/mL, advanced hepatic fibrosis, not achieving a rapid viral response at week 4 or complete early viral response at week 12, had poorer cost-effectiveness for PegIFN/RBV retherapy, ranging from around $15,520 to as high as $72,546 per SVR achieved.
*Conclusion:* In the current study, we explored the real-world cost-effectiveness data of PegIFN/RBV for different subgroups of treatment-experienced HCV patients. These findings provide information for policy-makers for making decisions on treatment strategies of costly direct-acting antiviral agents for retreating CHC patients.


## Introduction

Over 185 million people are infected with hepatitis C virus (HCV) worldwide.[1–3] Persistent HCV infection leads to cirrhosis in 20% of patients who may develop hepatocellular carcinoma (HCC) and hepatic decompensation with an annual incidence of 1–5% and 2–6%, respectively.[4,5] In Taiwan, not only hepatitis B but also hepatitis C is prevalent with an age- and sex-adjusted prevalence rate of antibodies to HCV of approximately 3.3%,[6] primarily due to several HCV hyperendemic areas in the southwestern coastal region.[7,8]

Pegylated interferon (PegIFN) plus ribavirin (RBV) combination therapy has been the standard of care since 2002. Achievement of a sustained virological response (SVR) reduces the risk of liver cirrhosis, HCC, and liver-related mortality.[9–12] Although Taiwanese patients tend to respond better to PegIFN/RBV than patients in Western countries[13,14] due to the higher frequency of favorable interleukin-28B (IL28B) genotypes in East Asian patients,[15,16] around 25% patients are positive for naive HCV genotype 1 (G1), whereas approximately 15% of naive G2 patients failed to achieve an SVR.[17–19]

A second course of PegIFN/RBV (48 weeks and 24 weeks for HCV G1 and G2, respectively) was effective in the retreatment of a substantial group of treatment-experienced HCV G1[20] and G2 patients[21] in Taiwan. Although numerous studies have reported the treatment efficacy of PegIFN/RBV in the retreatment of patients who failed prior IFN-based therapy,[22–27] little is known about the cost-effectiveness of the treatment. Moreover, PegIFN/RBV treatment has been associated with frequent adverse events, leading to increased costs of close monitoring and management. In contrast, dose reductions and early discontinuation[28] may reduce medical expenses. Therefore, it is necessary to develop a model to represent the real-world cost-effectiveness of the retreatment. Since 1995, the Taiwan National Health Insurance (NHI) has covered over 99.7% of the population. The Taiwan National Health Insurance Administration first started to reimburse for PegIFN/RBV retreatment for chronic hepatitis C (CHC) in 2009. Therefore, this comprehensive database may offer the best resource of the real-world cost-effectiveness of this treatment. In our previous study, we reported its real-world cost-effectiveness in a population of treatment-naive patients within the outpatient database.[29] The present study conducted a real-world cost-effectiveness analysis of a large cohort that included both outpatient and inpatient information by linking a clinical cohort in a real-world clinical practice to the national database of the NHI research database (NHIRD) in Taiwan to explore factors associated with the cost-effectiveness of PegIFN/RBV among different pre-specified subgroups of treatment-experienced CHC patients. Although the newly introduced IFN-free direct-acting antivirals (DAA) provide very high treatment efficacy, shorter treatment duration, and good safety profiles for the treatment of patients who fail prior IFN-based therapy,[30–32] the very high costs of DAA make it unavailable and/or unaffordable in many resource-constrained areas.[33]

## Material and methods

### Study population

In the hospital-based cohort study, a total of 519 patients with CHC who failed prior IFN-based therapy and received a second IFN-based therapy were consecutively enrolled in a medical center and two core regional hospitals. All treatment courses with available on-treatment clinical data were assessed. However, 103 patients with HCC before antiviral treatment or coinfected with hepatitis B virus or HIV were excluded. The subsequent 416 treatment-experienced patients were further linked to the entire population of outpatient/inpatient expenditures and order in the NHIRD. Patients were further excluded if they met the following criteria: (1) the date of outpatient visits were not within the assessed HCV management period; (2) the treatment starting date was after January 1, 2013; (3) the patients were not administered PegIFN/RBV at each visit; and (4) a lack of SVR information. Finally, 117 treatment-experienced CHC patients retreated with PegIFN/RBV were enrolled in the cost-effectiveness analysis (Figure 1).

All patients provided written informed consent. The institutional review boards at the participating hospitals approved the protocols, which conformed to the guidelines of the International Conference on Harmonization for Good Clinical Practice costs.

### Clinical data from laboratory tests and SVR assessment

Serum HCV RNA levels were measured using a qualitative real-time polymerase chain reaction (PCR) with a detection

Please cite this article in press as: Liu T-W, et al., Identification of treatment-experienced hepatitis C patients with poor cost-effectiveness of pegylated interferon plus ribavirin from a real-world cohort, Journal of the Formosan Medical Association (2017), http://dx.doi.org/10.1016/j.jfma.2017.02.013