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Projected impact of elbasvir/grazoprevir in patients with hepatitis C virus genotype 1 and chronic kidney disease in Vietnam

Chizoba Nwankwo [a], Shelby L. Corman [b,*], Elamin H. Elbasha [c]

[a] Center for Observational and Real-World Evidence (CORE), Merck & Co., Inc., Kenilworth, NJ, USA
[b] Health Economics and Outcomes Research, Pharmerit International, Bethesda, MD, USA
[c] Predictive and Economic Modeling, Merck & Co., Inc., North Wales, PA, USA

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ABSTRACT

Background: Hepatitis C virus (HCV) infection is an important cause of morbidity and mortality in patients with chronic kidney disease (CKD). The objective of this study was to predict the impact of EBR/GZR on the incidence of liver and kidney related complications compared with no treatment (NoTx) and pegylated interferon plus ribavirin (pegIFN/RBV) in patients with CKD stage 4/5 in Vietnam.
Methods: We developed a mathematical model of the natural history of chronic HCV, CKD, and liver disease. Efficacy of EBR/GZR and pegIFN/RBV were derived from the C-SURFER trial and a meta-analysis, respectively. We calculated lifetime cumulative morbidity and mortality rates, including incidence of decompensated cirrhosis (DC), hepatocellular carcinoma (HCC), and life expectancy.
Results: Estimated lifetime incidence of DC was significantly reduced in patients receiving EBR/GZR (3.47%) compared to NoTx (18.14%) and pegIFN/RBV (9.01%). Estimated incidence of HCC was 1.02%, 21.64%, and 8.90%, and 1.02% in patients receiving EBR/GZR, NoTx, and pegIFN/RBV. EBR/GZR was estimated to extend life expectancy by 4.2 and 2.0 years compared with NoTx and pegIFN/RBV.
Conclusions: Our model predicted that EBR/GZR will significantly reduce the incidence of liver-related complications and prolong life in patients with chronic HCV GT1 infection and CKD compared with NoTx or pegIFN/RBV.

Introduction

An estimated 185 million people are infected with the hepatitis C virus (HCV) worldwide, with over 2.4 million residing in the Asia-Pacific region [1]. Healthcare-associated disease transmission is common in this part of the world, with blood transfusion identified as a major risk factor for HCV infection [2]. Patients with chronic kidney disease (CKD) requiring hemodialysis are at high risk of HCV infection due in part to a lack of standardized infection control practices, reuse of dialysis filters, and contamination of hemodialysis machines [3,4]. An estimated 6 million patients (6.73%) in Vietnam are diagnosed with CKD, of which 80,000 (1.3%) have end-stage renal disease (ESRD) [5]. The national prevalence of HCV in dialysis patients is 27% and is high in all regions of Vietnam (11–43%) [6]. Among these patients, the odds of being HCV infected increased by 31% for each year on dialysis.

Regardless of whether renal dysfunction is present at the time of infection, chronic hepatitis C (CHC) is associated with declining renal function and development of CKD. In a systematic review and meta-analysis of longitudinal and cross-sectional studies, risk of CKD was increased by 23% in HCV-infected patients compared with uninfected controls [7]. Furthermore, in patients with CKD, estimated glomerular filtration rate (GFR) declines more rapidly over time among HCV-infected patients compared with those without HCV [8]. All-cause mortality risk is increased by 34% in HCV-positive dialysis patients compared with those without HCV [9], with cardiovascular disease being the most common cause of death [10].

Given the increased prevalence of HCV in patients with CKD and the increased morbidity and mortality in infected patients, treatment of this population with effective antiviral therapies is an

Abbreviations: CKD, chronic kidney disease; CVD, cardiovascular disease; DAA, direct-acting antiviral; DC, decompensated cirrhosis; EBR, elbasvir; ESRD, end-stage renal disease; GFR, glomerular filtration rate; GT, genotype; GZR, grazoprevir; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HD, hemodialysis; LMIC, low- to middle-income country; LVH, left ventricular hypertrophy; MI, myocardial infarction; NNT, number needed to treat; NoTx, no treatment; pegIFN, pegylated interferon; PSA, probabilistic sensitivity analysis; QALY, quality-adjusted life year; RBV, ribavirin; SBP, systolic blood pressure; SVR, sustained virologic response; TCHDL, total to high-density lipoprotein ratio; UI, uncertainty interval.

* Corresponding author at: 4350 East-West Highway, Suite 1100, Bethesda, MD 20814, USA.
E-mail address: scorman@pharmerit.com (S.L. Corman).

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important public health issue in Vietnam. Treatment of HCV with interferon-based therapy has been shown to reduce the risk of CKD by 58% [11], but these regimens are falling out of favor worldwide in both CKD and non-CKD populations due to the availability of all-oral direct-acting antivirals (DAAs) with simpler dosing regimens, shorter treatment durations, and more favorable adverse event profiles. However, both access to DAAs in the Asia-Pacific region and clinical data for DAAs in patients with CKD are limited; and thus pegylated interferon plus ribavirin (pegIFN/RBV) may still be the standard of care in patients with CKD [12].

Elbasvir/grazoprevir (EBR/GZR) is a fixed-dose combination of an HCV NS3/4A protease inhibitor (grazoprevir), and an HCV NS5A inhibitor (elbasvir) that is indicated for the treatment of CHC genotypes (GT) 1 and 4, including those with CKD. The safety and efficacy of EBR/GZR in CKD patients was established in the C-SURFER trial, a randomized, double-blind, placebo-controlled trial of patients with CKD stage 4/5, including those receiving dialysis [13]. In the per-protocol population, 99.1% of patients receiving EBR/GZR for 12 weeks achieved sustained virologic response (SVR) 12 weeks after completion of therapy. The aim of this analysis was to translate short-term findings from the C-SURFER trial into long-term predictions of the clinical impact of EBR/GZR on the incidence of specific liver and kidney related complications, life expectancy, and discounted quality-adjusted life years (QALYs) in Vietnam compared with no treatment and pegIFN/RBV. The target population is GT1 patients, which comprise 51% of HCV-infected dialysis patients in Vietnam [6].

Material and methods

We constructed a Markov state-transition model to assess the impact of treatment with EBR/GZR-based regimens on patients with CKD and CHC GT1 in Vietnam. The model was programmed in Excel (Microsoft Corp., Redmond, WA) supplemented with Visual Basic programming. The model combines major complications of both CKD and liver disease, in addition to cardiovascular disease complications that increase in frequency among patients with CKD.

Target population

The model simulated cohorts of CKD patients infected with CHC GT1. Baseline characteristics of the model cohort were obtained from published literature. The distribution of baseline CKD stage and risk factors for cardiovascular disease (systolic blood pressure [SBP], total to high-density lipoprotein ratio [TCHDL], and prevalence of smoking, diabetes, and left ventricular hypertrophy [LVH]) were obtained from the National Health and Nutrition Examination Survey [14,15]. METAVIR fibrosis stage at baseline was obtained from local market research data (unpublished). Patients were assumed to be 49 years old at baseline [16,17].

Model structure

The model structure is based on our previously published model of HCV treatment in patients with CKD [18], which drew from our validated Markov cohort model of liver disease progression [19–21], and previous models in CKD [22–26]. The model uses an annual cycle to predict the incidence and progression of CKD and liver disease and complications in a cohort of patients stratified by liver fibrosis status and CKD status.

Liver disease progression was modeled according to the natural history of HCV disease, including degree of fibrosis (METAVIR F0–4), decompensated cirrhosis (DC), hepatocellular carcinoma (HCC), liver transplant, and liver-related death (Fig. 1A). The progressive disease model assumes that a person with a given fibrosis score may progress to more severe stages of liver disease or may remain in that health state. In the absence of successful treatment, regression to less severe health states is not permitted. Patients who achieve SVR enter one of two health states determined by degree of fibrosis (SVR, F0–3 or SVR, F4), with no further progression of liver disease in non-cirrhotic patients (F0-3) and excess risk of DC and HCC in cirrhotic patients (F4).

The CKD model structure similarly reflects the natural history of CKD, with patients progressing through stages as defined by the National Kidney Foundation K/DOQI guidelines: CKD1 (GFR $\geq$ 90 mL/min), CKD2 (GFR 60–89 mL/min), CKD3a (GFR 45–59 mL/min), CKD3b (GFR 30–44 mL/min), CKD4 (GFR 15–29 mL/min) and CKD5 (GFR < 15 mL/min). Separate health states are incorporated for patients who require hemodialysis (HD) and kidney transplant (Fig. 1B).

Because CKD increases the risk of cardiovascular disease (CVD) complications, we explicitly modeled the incidence of myocardial infarction (MI) and stroke. Baseline probabilities of MI and stroke are derived from the age- and sex-based Framingham risk equations [27]. Model risk factors include diabetes status, systolic blood pressure (SBP) and hypertension, left ventricular hypertrophy (LVH), total and high-density lipoprotein cholesterol levels, and smoking status. Baseline probabilities of MI and stroke obtained from the Framingham risk equations were adjusted by CKD stage-specific hazard ratios. To account for the increased risk of developing ESRD or death from HCV infection among CKD patients, we adjusted the baseline CKD progression probabilities and other-cause mortality using hazard ratios obtained by comparing progression and mortality rates among HCV infected with rates among patients without HCV.

The evolution of the concomitant (HCV and CKD) of the CKD patient is modeled as follows. Each health state is defined with respect to HCV disease and CKD. A patient can progress to more severe HCV disease only, CKD disease only, or both. For example, a patient with CKD3a and fibrosis level F0 (CKD3a-F0) can progress to CKD3b-F0, CKD3a-F1, CKD3b-F1, can suffer an MI or stroke, can die from all causes or MI or stroke, or remain in CKD3a-F0.

Model assumptions

It was assumed that progression to DC and/or HCC only occurs in cirrhotic patients (F4 health states), and liver transplantation is performed for patients with DC or HCC only. Risk of reactivation in patients who received liver transplant was not included. The health states for CKD are defined according to GFR only, without incorporation of albuminuria or proteinuria. It was assumed that kidney transplants occur only after CKD5, and that patients with kidney transplants who experience graft failure may return to dialysis. Only hemodialysis is included in the model, and it is assumed that no patients use peritoneal dialysis. Because utilization of peritoneal dialysis is estimated in Vietnam to be 16.4% of all dialysis [28], inclusion of peritoneal dialysis would further complicate the model without having any significant impact on the results. We assume that chronic HCV accelerates progression to advanced CKD and CKD death, but CKD has no impact on liver disease progression.

Model comparators

The clinical and economic impact of using EBR/GZR was compared against that of no treatment and pegIFN/RBV in CKD patients with chronic HCV GT1 infection.

Model inputs

Efficacy of EBR/GZR was obtained from C-SURFER [13]. Efficacy of pegIFN/RBV was based on the results of a meta-analysis of clinical trials in dialysis patients [29].

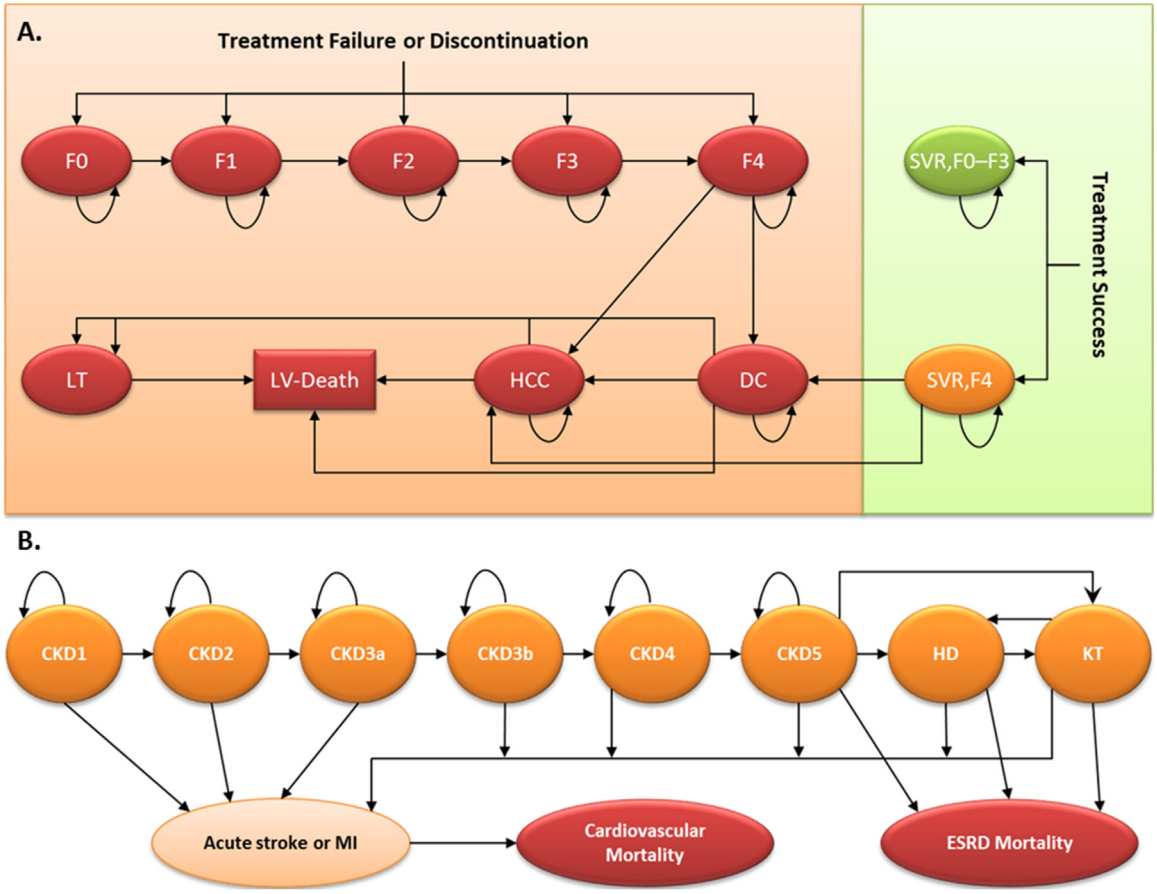

Fig. 1. State transition diagram for chronic HCV and liver disease model.
(A) State-transition diagram for chronic hepatitis C and liver disease model. The liver disease model consists of the following health states: no fibrosis (F0), portal fibrosis without septa (F1), portal fibrosis with few septa (F2), portal fibrosis with numerous septa without cirrhosis (F3), compensated cirrhosis (F4), decompensated cirrhosis (DC), hepatocellular carcinoma (HCC), liver transplant state (LT), end-stage liver disease death (ESLD Death), death from all other causes (not shown here) and two sustained virologic response (SVR) status states stratified by fibrosis stage—"SVR, F0–F3" and "SVR, F4."
(B) Simplified state-transition diagram for the chronic kidney disease (CKD) model. CKD stages are as follows: CKD1 (GFR ≥ 90), CKD2 (GFR 60–89), CKD3a (GFR 45–59), CKD3b (GFR 30–44), CKD4 4 (GFR 15–29), stage 5 (GFR < 15), hemodialysis (HD) and kidney transplantation (KT)

Clinical inputs that describe the rate of liver disease and CKD progression, the probability of receiving a liver or kidney transplantation, and all-cause and disease-related mortality were sourced from the published literature (Tables 1 and 2). Patients can have a stroke event or an MI event. Baseline probabilities of MI and stroke are derived from the age- and sex-based Framingham risk equations multiplied by a CKD stage multiplier.

Age- and gender-specific utility weights were obtained from the published literature [30]. Utility weights during the treatment phase and for each of the HCV health states and liver disease conditions were used to adjust quality of life of survivors. An on-treatment disutility was applied to RBV-containing regimens; no disutility was applied to RBV-free regimens.

Model analyses

The model projects the lifetime incidence of liver-related complications (DC, HCC, liver transplant, and end-stage liver disease [ESLD] mortality), kidney-related complications (kidney transplant, ESRD mortality), cardiovascular outcomes (stroke, MI), life expectancy, and QALYs. QALYs and disease costs were discounted at 3% per year, while other outcomes were not discounted.

In order to quantify the impact of uncertainty in the estimated values of transition probabilities, efficacy, and utility weights on the impact of EBR/GZR treatment strategies compared with comparators, we performed probabilistic sensitivity analysis (PSA). Using Monte Carlo simulations methods, we drew 1000 random samples from predefined distributions. Results of the PSA were summarized using 95% uncertainty intervals (UIs).

Results

The model predicted that the lifetime risk of liver disease complications would be reduced significantly in patients with CHC and comorbid CKD treated with EBR/GZR compared with those who are untreated or treated with pegIFN/RBV. The incidence of DC was reduced from 18.14% in untreated patients compared with 3.47% in patients treated with EBR/GZR, corresponding to a number needed to treat (NNT) of 7 patients to prevent one case of DC (Table 3, Fig. 2A). Compared with pegIFN/RBV, 18 patients would need to be treated with EBR/GZR to prevent one case of DC. The incidence of HCC was reduced from 21.64% in untreated patients to 8.9% in patients treated with pegIFN/RBV, and 1.02% in patients treated with EBR/GZR (NNT, 5 for EBR/GZR vs. no treatment and 13 for EBR/GZR vs. pegIFN/RBV) (Fig. 2B). ESLD mortality was also substantially lower in patients receiving EBR/GZR (0.24%) compared with pegIFN/RBV (10.63%) and no treatment (27.53%), and life expectancy was prolonged (18.1, 16.1, and 13.9 years, respectively). Differences in the proportion of patients with HCC and liver-related deaths emerged as early in the model time horizon and persisted throughout year 30, by which time all simulated patients had died (Fig. 2a, b).

Table 1
CKD model inputs.

Input	Value	Probability distribution	Source
Distribution of CKD stages at baseline			
CKD1	0.084		[14,15]
CKD2	0.319		
CKD3a	0.286		
CKD3b	0.286		
CKD4	0.017		
CKD5	0.003		
HD	0.003		
KT	0.003		
Risk factors for CVD			[15]
Systolic blood pressure	135		
Total to high density lipoprotein ratio	4.79		
Prevalence of smoking	0.62		
Prevalence of diabetes	0.117		
Prevalence of left ventricular hypertrophy	0.16		
Transition probabilities			
CKD1 to CKD2	0.083		[35]
CKD2 to CKD3a	0.096		[36]
CKD3a to CKD3b	0.096	Beta(228.42,1438.88)	[36]
CKD3b to CKD4	0.137	Beta(110.09,1249.03)	[24]
CKD4 to CKD5	0.081	Beta(126.69,75.69)	[24]
CKD5 to HD	0.626	Beta(77.08,8487.72)	[24]
CKD5 to KT	0.009	Beta(67.16,3467.81)	[24]
HD to KT	0.019	Beta(19.34,401.12)	[24]
KT to HD	0.046	Beta(105,867.26)	[24]
CKD5 to death	0.108	Beta(348.45,1738.08)	[24]
HD to death	0.167	Beta(16.04,556.64)	[24]
KT to death	0.028	Beta(23.92,175.41)	[24]
Acute stroke to death	0.12	Beta(23.92,175.41)	[22]
Acute MI to death	0.07	Beta(27.94,371.2)	[22]
Hazard rates			
Risk of death given HCV (all stages)	1.24	LogNormal(0.22,0.08)	[37]
Risk of progression of CKD given HCV (all stages)	1.32	LogNormal(0.28,0.11)	[7,38]
Risk of MI and stroke (CKD stage 3a)	1.40	LogNormal(0.34,0.02)	[39]
Risk of MI and stroke (CKD stage 3b)	2.00	LogNormal(0.69,0.03)	[38]
Risk of MI and stroke (CKD stage 4)	2.80	LogNormal(1.03,0.03)	[38]
Risk of MI and stroke (CKD stage 5)	3.40	LogNormal(1.22,0.05)	[38]
Risk of all-cause mortality (CKD stage 3a)	1.20	LogNormal(0.18,0.02)	[38]
Risk of all-cause mortality (CKD stage 3b)	1.80	LogNormal(0.59,0.03)	[38]
Risk of all-cause mortality (CKD stage 4)	3.20	LogNormal(1.16,0.02)	[38]
Risk of all-cause mortality ESRD (CKD stage 5, HD)	5.90	LogNormal(1.77,0.05)	[38]
Health state utilities			
CKD1	0.900	Beta(152.76,16.97)	[40]
CKD2	0.900	Beta(152.76,16.97)	[7]
CKD3a	0.870	Beta(198.89,29.72)	[7]
CKD3b	0.870	Beta(198.89,29.72)	[7]
CKD4	0.850	Beta(229.65,40.53)	[40]
CKD5	0.775	Beta(344.97,100.15)	[21,40]
HD	0.525	Beta(729.38,659.91)	[41]
Post-KT	0.840	Beta(245.02,46.67)	[42]

CKD, chronic kidney disease; CVD, cardiovascular disease; ESRD, end-stage renal disease; HCV, hepatitis C virus; HD, hemodialysis; KT, kidney transplant; MI, myocardial infarction.

Patients who are treated for CHC and subsequently achieve SVR (i.e., cure) are less likely to die of ESLD but experience a longer life expectancy over which renal and cardiovascular complications may develop. As such, the proportion of patients projected to experience MI or stroke was higher in patients receiving EBR/GZR compared with pegIFN/RBV and no treatment. In addition, given the lifetime time horizon in which all patients eventually die, ESRD mortality was higher in EBR/GZR patients than comparators, representing a shift from ESLD to ESRD mortality rather than an increase in ESRD mortality associated with EBR/GZR.

Discussion

The model projected that treatment of patients with CHC and CKD with EBR/GZR would reduce the incidence of liver-related complications and death, and prolong life expectancy, compared with pegIFN/RBV or no treatment. Due to this increased life expectancy, patients receiving EBR/GZR would experience more renal and cardiovascular complications that develop over a longer time period. Life expectancy gains in this model were similar to that reported in the US, with minor differences attributable to the target population. In the US model, all patients were CKD stage 1–4 at baseline, with no patients already receiving dialysis or kidney transplant [18]. In addition, patients in the US model had less severe hepatic fibrosis at baseline, with 30% in F3–F4 compared to 48% in this model. As such, the life expectancy in the EBR/GZR, pegIFN/RBV, and no treatment groups (22.94, 20.59, and 16.98 years, respectively) was greater than in this model (18.13, 16.10, and 13.88 years). A similar model in France estimated substantially lower life expectancy (6.28 life years for EBR/GZR and 5.09 for no treatment), in a target population of only CKD stage 4 and 5 patients [31].

Table 2
Liver disease model inputs.

Input	Value	Range or probability distribution	Source
Distribution of METAVIR fibrosis stages at baseline			Internal market research
F0	0.010		
F1	0.300		
F2	0.210		
F3	0.240		
F4	0.240		
Fibrosis progression			
F0 to F1	0.117	Beta(2.3,11.33)	[43]
F1 to F2	0.085	Beta(1.64,10.6)	[43]
F2 to F3	0.120	Beta(10.02,35.53)	[43]
F3 to F4	0.116	Beta(4.48,24.22)	[43]
F4 to DC	0.029	Beta(14.89,498.62)	[44–48]
F4 to HCC	0.028	Beta(2.43,84.41)	[43–53]
DC to HCC	0.068	Beta(23.51,322.19)	[54]
SVR, F4 to DC	0.008	Beta(0.84,103.66)	[55]
SVR, F4 to HCC	0.005	Beta(0.5,251.98)	[53]
Probability of receiving a liver transplant			
DC	0.023	Beta(1.42,87.06)	[56,57]
HCC	0.040	Beta(0.15,18.89)	[58]
Mortality rates			
All-cause mortality	Age/sex specific		
DC-related mortality	0.142	0.065–0.190	[29,59]
HCC-related mortality	0.427	0.330–0.860	[29,59]
LT-related mortality	0.116	0.060–0.420	[29,59]
Sustained viral response			
EBR/GZR	0.991	Beta(51.09,0.44)	[13]
PegIFN/RBV	0.60	Beta(4.05,2.7)	[29,59]

DC, decompensated cirrhosis; EBR/GZR, elbasvir/grazoprevir; HCC, hepatocellular carcinoma; LT, liver transplant; pegIFN/RBV, pegylated interferon/ribavirin; SVR, sustained virologic response.

Table 3
Projected lifetime incidence (95% uncertainty interval) of liver and kidney complications, life expectancy, and discounted quality-adjusted life years (QALYs).

Outcome	EBR/GZR	PegIFN/RBV	Difference, EBR/GZR vs. pegIFN/RBV	No treatment	Difference, EBR/GZR vs. no treatment
Liver-related outcomes					
Decompensated cirrhosis (%)	3.47 (0.17, 13.17)	9.01 (3.13, 16.67)	−5.54 (−11.59, 0.34)	18.14 (9.04, 26.21)	−14.67 (−23.38, −1.15)
Hepatocellular carcinoma (%)	1.02 (0.04, 4.21)	8.90 (2.27, 17.46)	−7.88 (−16.60, −1.54)	21.64 (7.01, 36.56)	−20.62 (−35.42, −6.00)
Liver transplant (%)	0.01 (0.00, 0.05)	0.51 (0.02, 1.43)	−0.49 (−1.42, −0.02)	1.31 (0.08, 3.43)	−1.30 (−3.41, −0.08)
End-stage liver disease mortality (%)	0.24 (0.00, 0.88)	10.63 (3.44, 19.08)	−10.40 (−18.78, −3.27)	27.53 (13.89, 39.04)	−27.79 (−38.86, −13.79)
Kidney-related outcomes					
Kidney transplant (%)	1.79 (1.41, 2.23)	2.20 (1.59, 3.09)	−0.42 (−1.18, 0.03)	3.18 (1.98, 4.77)	−1.40 (−2.89, −0.31)
End-stage renal disease mortality (%)	17.04 (14.79, 19.17)	15.88 (13.26, 19.05)	1.16 (0.53, 1.40)	16.65 (12.14, 22.45)	0.40 (−4.93, 4.31)
Cardiovascular outcomes					
Myocardial infarction (%)	31.48 (30.45, 32.53)	27.35 (24.94, 29.41)	4.13 (2.38, 6.51)	23.82 (20.86, 26.95)	7.66 (4.70, 10.47)
Stroke (%)	5.61 (5.41, 5.82)	4.70 (4.20, 5.13)	0.91 (0.53, 1.40)	3.95 (3.36, 4.59)	1.66 (1.04, 2.23)
Life expectancy (years)	18.13 (17.87, 18.40)	16.10 (14.80, 17.21)	2.03 (1.04, 3.38)	13.88 (12.43, 15.39)	4.25 (2.82, 5.68)
Discounted QALYs	9.96 (9.83, 10.09)	8.70 (8.02, 9.28)	1.26 (0.73, 1.96)	7.68 (7.00, 8.33)	2.28 (1.66, 2.96)

EBR/GZR, elbasvir/grazoprevir; pegIFN/RBV, pegylated interferon/ribavirin; QALYs, quality-adjusted life years.

The prevalence of HCV infection in the general population of Vietnam appears to be region-specific and has been reported at 0.38–4.7% [32]. Until recently, only interferon-based regimens were available in low- to middle-income countries (LMICs), including Vietnam, and access to these treatments has been limited [1]. Efforts to improve access to care in HCV-infected patients in LMICs include voluntary licensing between pharmaceutical patent-holders and local generic drug manufacturers, tiered pricing, and direct negotiating with government payers [1,33].

Due to limited resources, the healthcare system in Vietnam can provide care to only 10% of the 80,000 people with ESRD [5]. An increasing demand for hemodialysis has prompted a transition from hemodialysis administered at tertiary care hospitals to administration in decentralized hemodialysis clinics. A lack of training in infection control practices has been identified as a possible reason for the high prevalence of HCV infection within hemodialysis units in Vietnam, ranging from 6–54% [32].

To our knowledge, this is the first analysis aiming to establish the lifetime burden of CHC and to demonstrate the benefits of treatment in Vietnam. Other strengths include the incorporation of renal, hepatic, and cardiovascular complications into the model, providing a comprehensive picture of the disease burden avoided with treatment.

Our analysis also has some limitations. Due to low prevalence of peritoneal dialysis in Vietnam, we assumed that patients only received hemodialysis. We were unable to conduct a cost-effectiveness analysis that includes the cost of CHC treatment with EBR/GZR, or the subsequent complications avoided, because of the lack of local cost and pricing information in Vietnam. While EBR/GZR has been shown to be cost-effective compared to no treat-

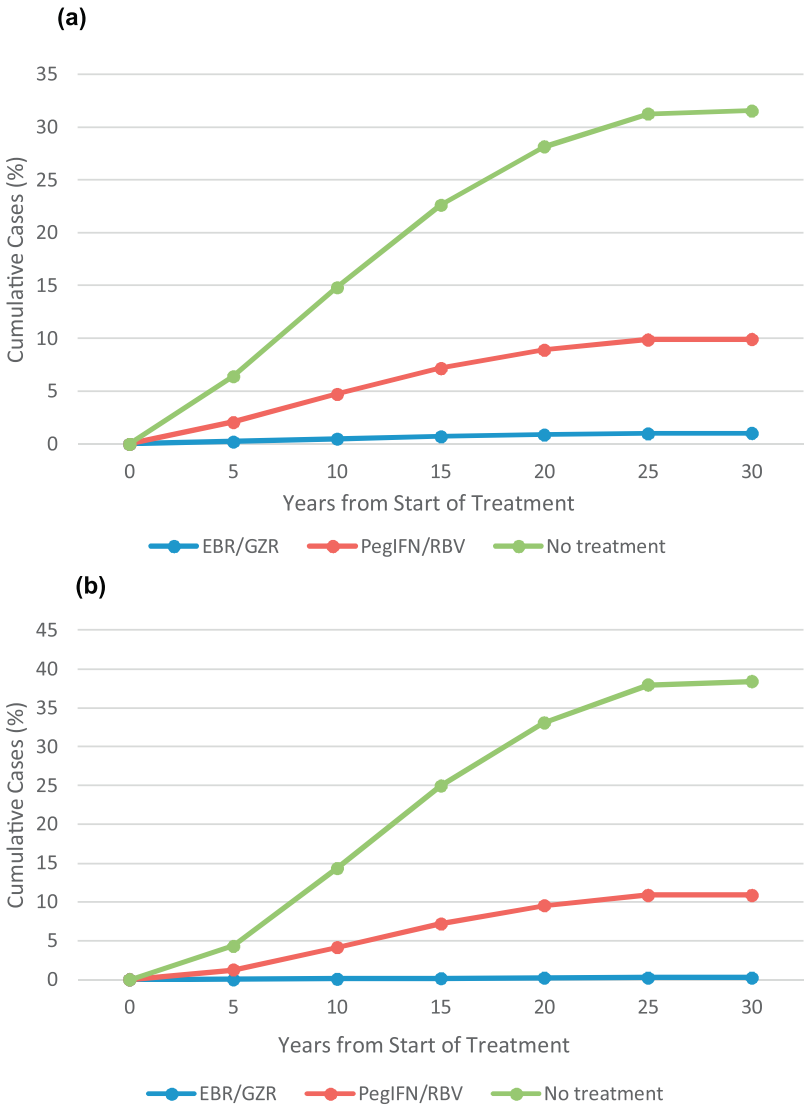

Fig. 2. Projected cumulative incidence of hepatocellular carcinoma (a) and liver-related death (b) by regimen (base case analysis).

ment in France [31], and compared to pegIFN/RBV and no treatment in the United States [18], these findings cannot be extrapolated to Vietnam due to differences in healthcare systems and payment. Further, it should be noted that even if EBR/GZR is cost-effective in this population, a substantial investment would need to be made to provide treatment to the estimated 20,000 HCV-infected patients in Vietnam who have ESRD [5,6]. Relationships between HCV infection and risk of ESRD death, and between progression of CKD and cardiovascular death, have been established and thus are explicitly modeled. However, the impact of HCV infection and cure on other leading causes of death in CKD patients, such as malignancies, infections, and chronic pulmonary disease [34], is not known. Therefore, deaths due to these causes are captured as part of all-cause mortality in CKD patients and not modeled explicitly. Finally, the model does not account for the risk of viral transmission between patients, which is of particular interest for patients receiving hemodialysis, who are at risk for healthcare-associated transmission.

In conclusion, this model projected that EBR/GZR will substantially reduce the lifetime incidence of liver-related complications and increase life expectancy and QALYs compared with pegIFN/RBV and no treatment in patients with CKD and concomitant CHC in Vietnam.

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