

Prevention of Liver-Related Complications With Elbasvir/Grazoprevir in Hepatitis C Infected Patients Who Are Receiving Opioid Agonist Therapy (OAT)

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Background

Background

- The World Health Organization (WHO) estimates that 130-150 million people are infected with hepatitis C virus (HCV) worldwide,¹ with 1.1% of the world's population chronically infected²
- However, among people who inject drugs (PWID), the prevalence of HCV infection is estimated at 67%³
- WHO recommends that all adults and children with chronic HCV infection, including PWID, should be assessed for antiviral treatment⁴
- The C-EDGE CoSTAR trial compared immediate treatment with elbasvir/grazoprevir (EBR/GZR), a direct-acting antiviral, to delayed treatment (control group) in treatment-naïve patients with genotype (GT) 1, 4, or 6 chronic hepatitis C (CHC) who were receiving opioid agonist therapy (OAT)⁵⁻⁶

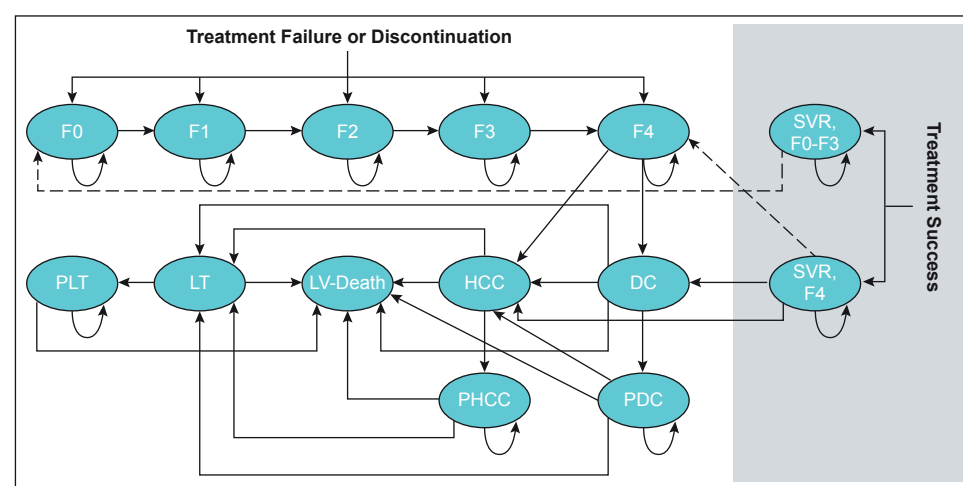
Objective

- The objective of this study was to model the long-term impact of EBR/GZR on the incidence of liver-related complications in patients receiving OAT by extending the results of C-EDGE CoSTAR over a 30-year time horizon

Methods

- A Markov model was constructed to evaluate the cost and effectiveness of EBR/GZR±ribavirin (RBV) over a 30-year time horizon
- The target population was patients infected with CHC GT1 or 4, stratified by presence of cirrhosis
- The model consists of 16 health states encompassing METAVIR fibrosis score (F0-F4), treatment success or failure, decompensated cirrhosis (DC), hepatocellular carcinoma (HCC), liver transplant, and liver-related death (Figure 1)

Figure 1: State transition model for chronic HCV and liver disease model



Hepatic fibrosis stage was based on METAVIR fibrosis scoring system: F0 = no fibrosis; F1 = portal fibrosis without septa; F2 = portal fibrosis with few septa; F3 = portal fibrosis with numerous septa without cirrhosis; and F4 = compensated cirrhosis; DC = decompensated cirrhosis; HCC = hepatocellular carcinoma; PDC = one-year post decompensated cirrhosis; PHCC = one-year post hepatocellular carcinoma; SVR12 = sustained virologic response 12 weeks after cessation of treatment.

Methods (continued)

Model Inputs

- Baseline patient characteristics, treatment regimens, and rates of sustained virologic response at 12 weeks (SVR12) and reinfection were obtained from C-EDGE CoSTAR (Tables 1-2)⁵⁻⁶
 - Results from the immediate and delayed treatment groups were pooled for use in the model
- Cost and utility inputs were obtained from published sources (Table 3)⁷⁻⁸
- Wholesale acquisition cost of \$4,550 per week was used for EBR/GZR

Model Outputs

- The primary outcome was incremental cost-utility ratio (ICUR) for EBR/GZR vs no treatment
- Other outcomes included cumulative proportion of patients developing cirrhosis, DC, and HCC; receiving liver transplants; and dying of liver-related causes over the time horizon, and the number of these events prevented per 1000 patients treated with EBR/GZR

Table 1: Baseline characteristics, C-EDGE CoSTAR⁵⁻⁶

Characteristic	Proportion
Baseline fibrosis stage	
F0	0.244
F1	0.244
F2	0.244
F3	0.070
F4	0.199
Males	0.764
Age at baseline	
18-35	0.15
36-50	0.458
51-64	0.382
≥65	0.01

Table 2: Treatment and outcomes, C-EDGE CoSTAR⁵⁻⁶

Variable	Base Case (95% CI)
SVR12, base case (95% CI)	
GT1a	0.938 (0.898-0.966)
GT1b	0.932 (0.813-0.986)
GT4	0.944 (0.727-0.999)
Treatment discontinuation, base case (95% CI)	0.007 (0.001-0.024)
Reinfection, rate per 100 person-years	2.5 (0.8-5.9)

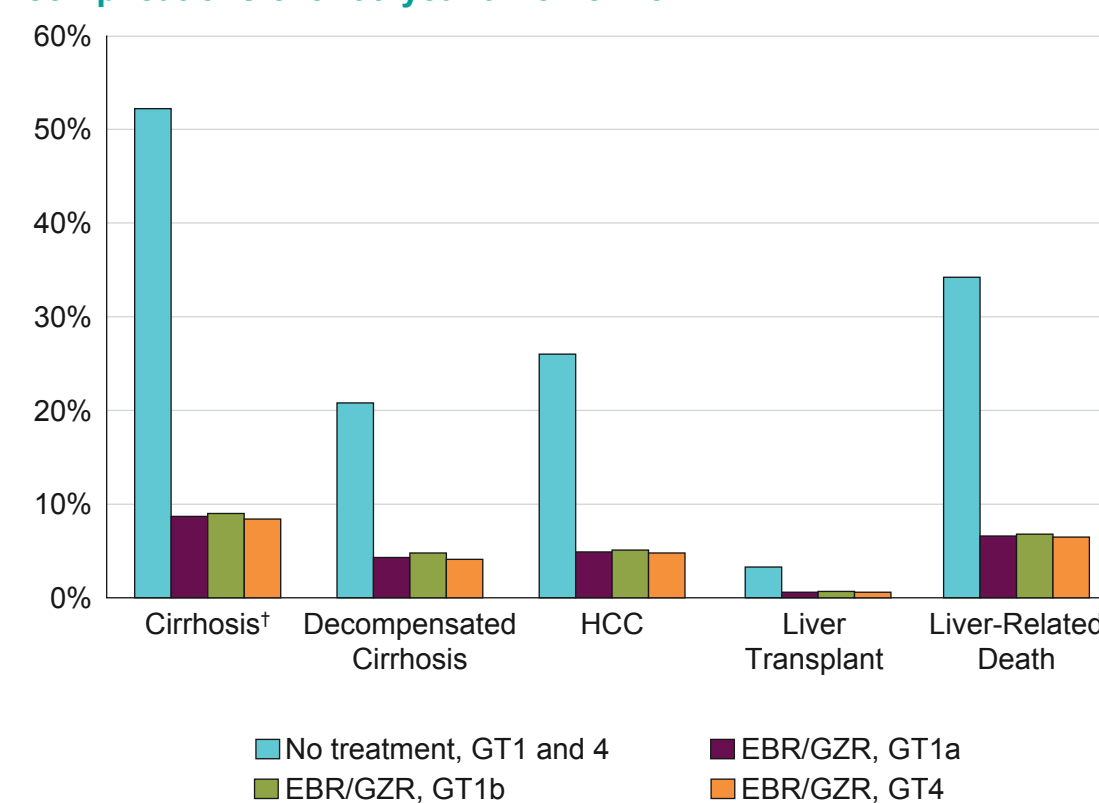
Table 3: Annual health state cost and utility inputs⁷⁻⁸

Input	Utility		Cost	
	Base Case	Range (±5%)	Base Case	95% CI
F0-F1	0.77	0.73-0.81	\$793	\$595-\$991
F2	0.77	0.73-0.81	\$803	\$602-\$1,004
F3	0.66	0.63-0.69	\$1,630	\$1,223-\$2,038
F4	0.55	0.52-0.58	\$1,901	\$1,426-\$2,376
DC	0.45	0.43-0.47	\$21,122	\$15,842-\$26,403
HCC	0.45	0.43-0.47	\$38,841	\$29,131-\$48,551
Post liver transplant, year 1	0.45	0.43-0.47	\$112,217	\$84,163-\$140,271
Post liver transplant, subsequent years	0.67	0.64-0.70	\$29,475	\$22,106-\$36,844
Post SVR, F0-F2	0.82	0.78-0.86	0	-
Post SVR, F3-F4	0.72	0.68-0.76	0	-
Annual discount rate	0.03	0-0.05	0.03	0-0.05

Results

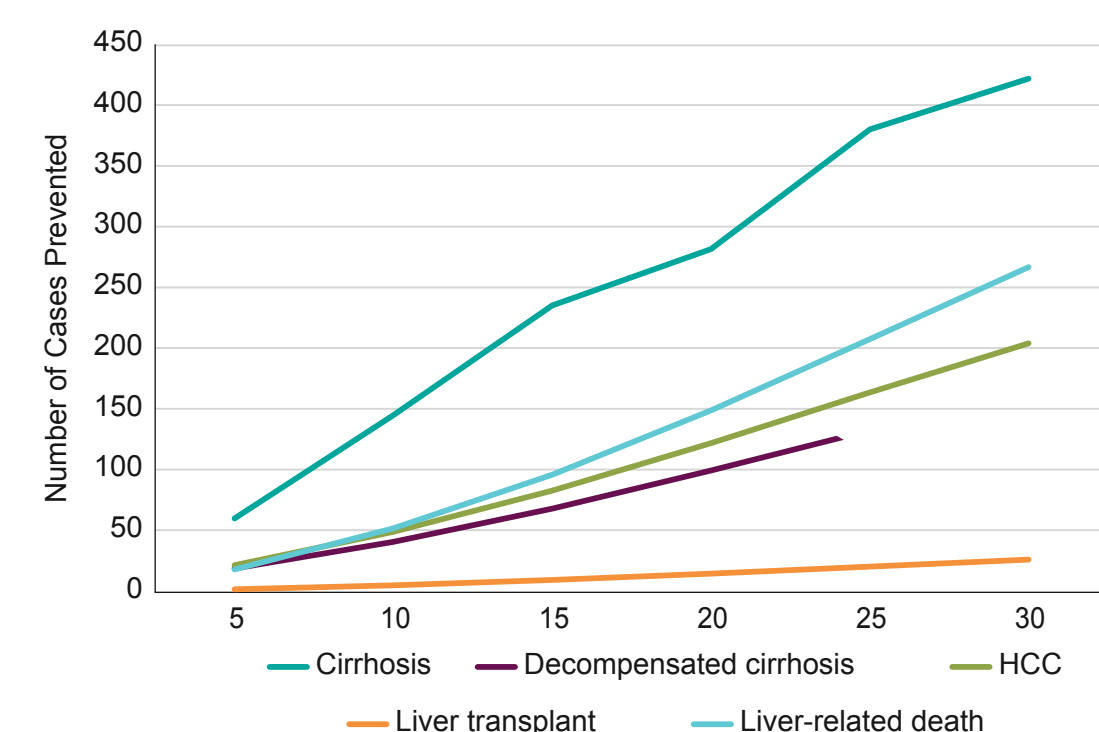
- Over 30 years, the proportion of patients developing liver-related complications was substantially reduced in patients receiving EBR/GZR compared to no treatment (Figures 2 and 3)

Figure 2: Proportion of patients developing liver-related complications over 30-year time horizon



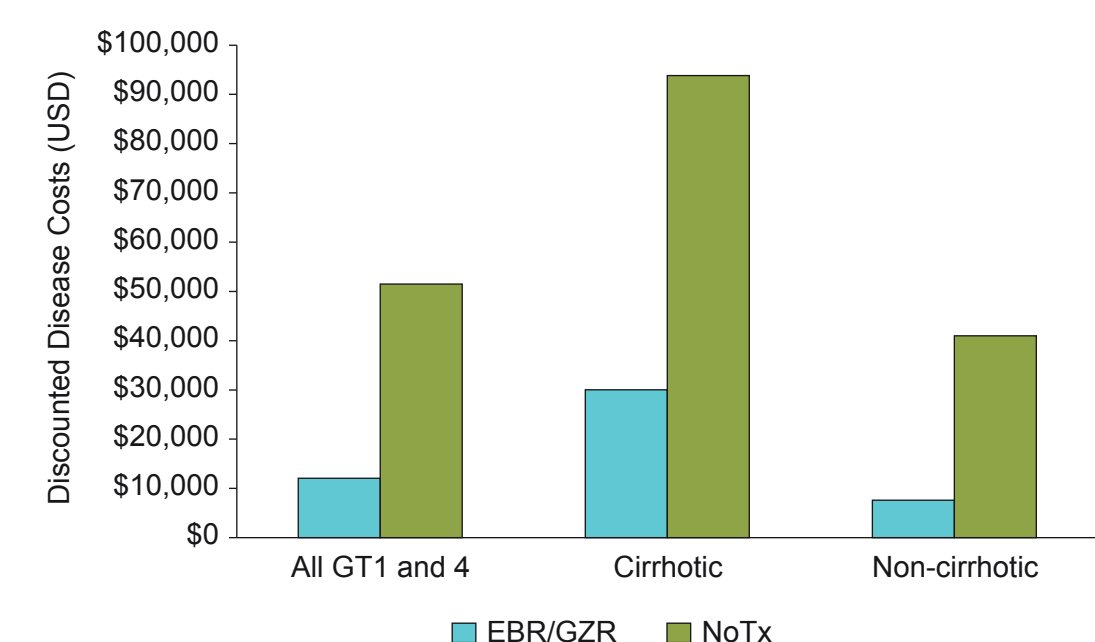
†Among those noncirrhotic at baseline.

Figure 3: Cases of liver complications prevented per 1000 GT1 and 4 patients treated with EBR/GZR vs no treatment over 30-year horizon



- Of all subgroups, cirrhotic patients had the highest cumulative disease incidence (Figure 3) and therefore accrue the highest cumulative disease cost (Figure 4)

Figure 4: 30-year disease costs, overall and by subgroup GT1 and 4 patients treated with EBR/GZR vs no treatment



- EBR/GZR was associated with more quality-adjusted life years (QALYs) than no treatment in all genotypes studied, and ICURs were less than \$6000/QALY for all genotypes over 30 years (Table 4), and \$1500/QALY over lifetime

Table 4: Base case results over 30-year time horizon

Result	No Treatment	EBR/GZR			
	GT1 and 4	GT1a	GT1b	GT4	
Discounted QALYs	10.8146	13.4935	13.4761	13.5131	
Discounted costs (\$)	\$51,513	\$66,567	\$66,814	\$66,291	
ICUR vs no treatment (\$/QALYs)	--	\$5,620	\$5,749	\$5,477	

Conclusions

- Use of EBR/GZR for the treatment of CHC in patients receiving OAT in the United States was projected to prevent a considerable number of cases of cirrhosis, decompensated cirrhosis, HCC, liver transplants, and liver-related death over 30 years compared to no treatment
- Thus EBR/GZR was projected to be a cost-effective therapy for CHC GT1- and 4-infected patients on OAT in the United States

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Sponsorship
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