Pan-Genotypic Hepatitis C Treatment With Glecaprevir/Pibrentasvir Achieves Greatest Improvements in Quality-Adjusted Life-Years and Lifetime Risk Reductions in Liver-Related Morbidity and Mortality vs Standards of Care: A Cost-Utility Analysis

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BACKGROUND

- As new treatments for hepatitis C virus (HCV) encompass a pan-genotypic indication, no study to date has compared the impact of different treatment strategies on patient outcomes across all genotypes (GTs) and the cost-effectiveness of such strategies

OBJECTIVE

- To report the quality-adjusted life-years (QALYs), sustained virologic response (SVR), cost-effectiveness, and lifetime liver morbidity and mortality outcomes in patients with GT1–6 chronic HCV infection treated with glecaprevir (identified by AbbVie and Enanta) and pibrentasvir (G/P) compared with other standards of care over a lifetime horizon

METHODS

MODEL DESIGN

- A Markov model of the natural history of HCV was developed based on previous literature (**Figure 1**)[1,2]
- Patients with any genotype (GTs1–6) of HCV initiated treatment in one of five initial liver fibrosis states (F0, F1, F2, F3, and F4) according to a baseline fibrosis distribution
- From initial fibrosis states, progression to more severe states depended on virus GT and achievement (or not) of SVR
  - Patients who did not achieve SVR were assumed to face the same risks for liver disease progression as untreated patients
  - Transitions between health states could occur every year in the model
- The model was run over a lifetime horizon
- Patients with fibrosis stage F0–F3 who achieved SVR were assumed to be cured and did not progress to a more advanced liver disease stage, whereas patients with compensated cirrhosis (CC) were assumed to face an excess risk of hepatocellular carcinoma (HCC), even after achieving SVR
- Liver-related death (LrD) could occur from the decompensated cirrhosis (DCC), HCC, and liver transplant (LT) states; death from non-hepatic causes could occur from any state
- Transition probabilities for GT1 patients were derived from previously published cost-effectiveness studies in the United States (**Table 1**)
  - Progression rates for GTs2, 3, 4, 5, and 6 were estimated by multiplying those for GT1 by multipliers shown in **Table 1**

Table 1. Annual Transition Probabilities

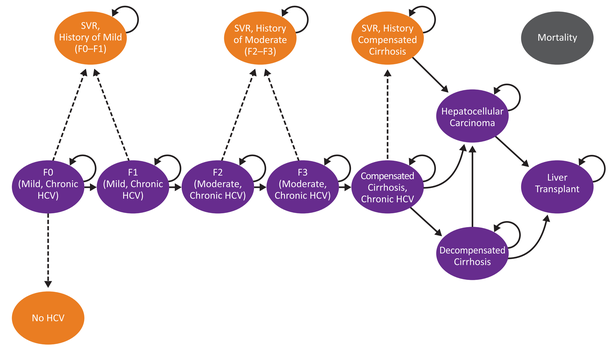
Fibrosis Progression: Annual Probabilities and GT-specific multipliers			
Age-Dependent GT1 TPs[3]		GT-Specific Fibrosis Progression Multiplier	
	Base case		Base case
F0 to F1	0.110	GT2[4]	0.68
F1 to F2	0.088	GT3[4]	1.30
F2 to F3	0.176	GT4[4]	0.94
F3 to F4	0.143	GT5*	0.94
		GT6*	0.94

*Assumption – same as GT4. GT, genotype; TP, transition probability.

Non-fibrosis Disease Progression, Annual Probabilities	
	Base case
SVR, history of severe fibrosis (CC) to HCC[5]	0.012
CC to DCC[6]	0.040
CC to HCC (first year)[6]**	0.020
DCC to HCC (first year)[6]**	0.020
Liver transplant	
DCC to liver transplant (first year)[6]	0.050
HCC to liver transplant (first year)[6]	0.150
Liver-related mortality	
DCC to LrD[6]	0.260
Liver transplant to LrD[6]	0.140
After liver transplant to LrD[6]	0.050
HCC first year to LrD[6]	0.720
HCC subsequent year to LrD[6]	0.250
Spontaneous remission from F0[6]	0.012

**GT-specific multipliers[4]: GT2, 0.62; GT3, 1.44; GT4, 0.96; GT5/6, assumed the same as GT4.
CC, compensated cirrhosis; DCC, decompensated cirrhosis; GT, genotype; HCC, hepatocellular carcinoma, LrD, liver-related death; SVR, sustained virologic response.

Figure 1. Model Structure



Note: Health states are depicted by ellipses; arrows represent permissible transitions between health states while loops represent no transition. Dashed arrows depict the possibility of achieving SVR (recovered). Death is possible from any health state. Liver-related death is possible from DCC, HCC, and LT. HCV, hepatitis C virus; SVR, sustained virologic response.

POPULATION CHARACTERISTICS

- Baseline characteristics of the target population were based on US-based real-world data (**Table 2**)

TREATMENT EFFICACY

- Regimen-specific SVR rates, adverse event rates, and treatment durations were based primarily on Phase 3 clinical trials of the regimens analyzed, as detailed in US prescribing information

TREATMENT STRATEGY COMPARISONS

- A portfolio approach was used to compute pan-genotypic outcomes for the overall HCV population by aggregating outcomes across patient segments based on GT, cirrhosis status, and treatment history weighted by the distribution of each segment
- The model compared a cohort of patients (all GTs) treated with G/P vs two treatment strategies
  - Strategy 1: sofosbuvir/ledipasvir (SOF/LDV) for GTs1 and 4, and sofosbuvir/velpatasvir (SOF/VEL) for GTs2, 3, 5, and 6
  - Strategy 2: grazoprevir/elbasvir (GZR/EZR) for GTs1 and 4, and SOF/VEL for GTs2, 3, 5, and 6

Table 2. Baseline Patient Characteristics

Treatment History Distribution*			
Naïve 98.3%			
Experienced 1.7%			
Patient Characteristics – Naïve		**Patient Characteristics – Experienced**	
Age (in years)*	49.9	Age (in years)*	57.2
% male*	57.6%	% male*	68.3%
% GT1a among GT1 patients**	44.4%	% GT1a among GT1 patients**	44.4%
Initial fibrosis distribution (%)*		Initial fibrosis distribution (%)*	
F0	32.2%	F0	13.7%
F1	17.7%	F1	13.2%
F2	29.2%	F2	28.0%
F3	10.0%	F3	15.2%
F4	11.0%	F4	29.9%

*AbbVie data on file (H17.DoF.021, H17.DoF.033), HCV epidemiology on patients who are available for treatment (i.e., not including cures or ongoing treatment). HCV patient epidemiology estimates are based on 2016 data from two large US lab service providers that cover about 80% of lives in the United States.
**G/P Phase 3 trials (ENDURANCE-1, ENDURANCE-3, and EXPEDITION-1). GT, genotype; HCV, hepatitis C virus.

OUTCOMES

- Health outcome measures included lifetime risks of CC, DCC, HCC, LT, and LrD, and life expectancy (LE)
- Other outcome measures included QALYs, SVR and cost per SVR; the number needed to treat (NNT) to achieve a QALY, SVR, or avoid an adverse liver event; incremental cost-effectiveness ratios; and incremental net monetary benefit (INMB)
  - Costs and QALYs were discounted at a rate of 3%

SENSITIVITY ANALYSIS

- A probabilistic sensitivity analysis (PSA) was carried out using a cost-effectiveness acceptability curve (CEAC) to determine the likelihood that each treatment strategy was cost-effective at different willingness-to-pay (WTP) thresholds

RESULTS

- Across all GTs, treatment with G/P resulted in higher overall SVR rates (98.6%) compared with Strategies 1 (96.0%) and 2 (96.1%); treatment with G/P resulted in lower costs per SVR ($35,209) compared with Strategies 1 ($83,537) and 2 ($70,598) (**Table 3**)

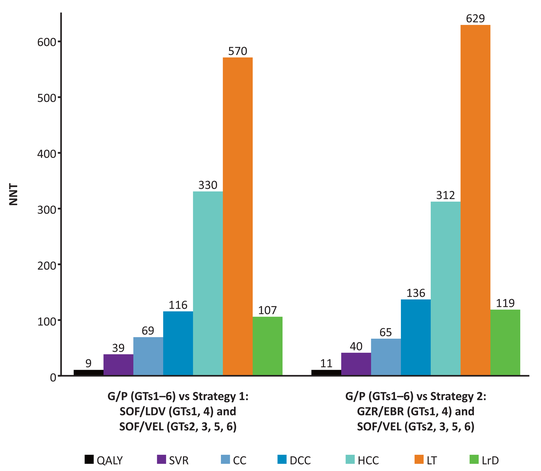
Table 3. Patient Outcomes and Cost-effectiveness of Treatment With G/P vs Standards of Care

Outcome (all costs in USD, $)	G/P (GTs1–6)	Strategy 1: SOF/LDV (GTs1, 4) SOF/VEL (GTs2, 3, 5, 6)	G/P vs Strategy 1	Strategy 2: GZR/EBR (GTs1, 4) SOF/VEL (GTs2, 3, 5, 6)	G/P vs Strategy 2
Total costs	34,703	80,169	−45,466	67,832	−33,129
QALYs	18.16	18.05	0.11	18.06	0.09
ICER			−417,950		−353,036
Is G/P dominant?			Yes		Yes
INMB			56,345		42,513
Is G/P cost-effective at maximum WTP?*			Yes		Yes
Overall SVR	98.6%	96.0%	2.6%	96.1%	2.5%
Total costs per SVR	35,209	83,537	−48,328	70,598	−35,389
Total regimen cost per SVR	28,336	75,146	−46,810	62,398	−34,062
LE at baseline age, years	79.2	79.0	0.1	79.0	0.2
LYG, years	18.8	18.7	0.1	18.8	0.1
Breakdown of total costs					
Regimen cost	27,929	72,116	−44,188	59,953	−32,025
Ribavirin	0	3	−3	78	−78
DAA	27,929	72,114	−44,185	59,875	−31,946
Medical/other cost	6,774	8,053	−1,278	7,879	−1,104
Treatment-related AE	20	21	−1	40	−20
Medical	6,754	8,032	−1,277	7,838	−1,084

AE, adverse event; DAA, direct-acting antiviral; EBR, elbasvir; G/P, glecaprevir/pibrentasvir; GT, genotype; GZR, grazoprevir; ICER, incremental cost-effectiveness ratio; INMB, incremental net monetary benefit; LDV, ledipasvir; LE, life expectancy; LYG, life-year gain; QALY, quality-adjusted life-year; SOF, sofosbuvir; SVR, sustained virologic response; USD, United States dollar; VEL, velpatasvir; WTP, willingness to pay. *WTP = $100,000.

- The NNT to achieve an additional SVR when treated with G/P, compared with Strategy 1 or 2, was 39 and 40, respectively (**Figure 2**)
- The NNT to achieve an additional QALY when treated with G/P, compared with Strategy 1 or 2, was 9 and 11, respectively (**Figure 2**)

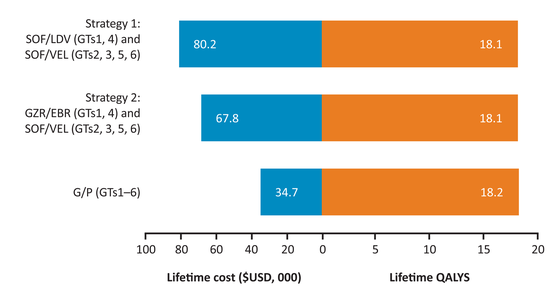
Figure 2. NNT to Achieve/Avoid Health Outcomes With G/P Treatment Compared With Strategies 1 and 2



CC, compensated cirrhosis; DCC, decompensated cirrhosis; EBR, elbasvir; G/P, glecaprevir/pibrentasvir; GT, genotype; GZR, grazoprevir; HCC, hepatocellular carcinoma; LDV, ledipasvir; LrD, liver-related death; LT, liver transplant; NNT, number needed to treat; QALY, quality-adjusted life-year; SOF, sofosbuvir; SVR, sustained virologic response; VEL, velpatasvir.

- Treatment with G/P was the dominant option, resulting in an increase in lifetime QALYs (18.2) compared with Strategies 1 (18.1) and 2 (18.1) at a lower lifetime cost of $34,703 for G/P vs $80,169 and $67,832 for Strategies 1 and 2, respectively (**Figure 3**)

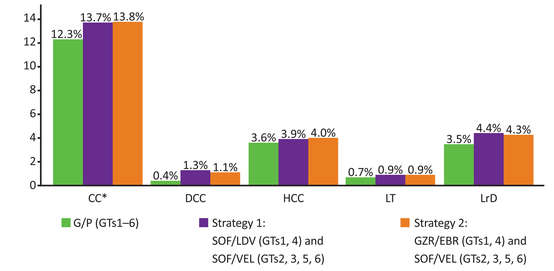
Figure 3. Lifetime Costs and QALYs With G/P Treatment Compared With Strategies 1 and 2



EBR, elbasvir; G/P, glecaprevir/pibrentasvir; GT, genotype; GZR, grazoprevir; LDV, ledipasvir; QALY, quality-adjusted life-year; SOF, sofosbuvir; SVR, sustained virologic response; VEL, velpatasvir.

- Treatment with G/P was associated with lower lifetime risks of liver-related morbidity and mortality compared with Strategies 1 and 2 (**Figure 4**)

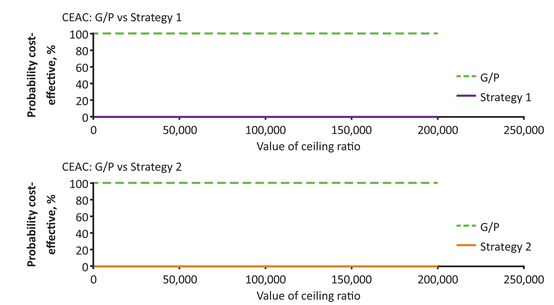
Figure 4. Lifetime Risk of CC, DCC, HCC, LT, and LrD With HCV Treatment With G/P (all GTs) Compared With Strategies 1 and 2



*The model's baseline input includes 11.3% cirrhotic patients.
CC, compensated cirrhosis; DCC, decompensated cirrhosis; EBR, elbasvir; G/P, glecaprevir/pibrentasvir; GT, genotype; GZR, grazoprevir; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; LDV, ledipasvir; LrD, liver-related death; LT, liver transplant; SOF, sofosbuvir; VEL, velpatasvir.

- Results from 500 Monte Carlo simulations in PSA of selected treatment strategies showed that G/P was the most cost-effective strategy in 100% of the simulations at each WTP threshold (**Figure 5**)

Figure 5. Cost-effectiveness Acceptability Curves for G/P vs Strategies 1 and 2



CEAC, cost-effectiveness acceptability curve, G/P, glecaprevir/pibrentasvir.

DISCUSSION

- The model compared pan-genotypic treatment with G/P to current standards of care in an assessment of QALYs; SVR; lifetime risks of liver-related morbidity and mortality; the NNT to achieve a QALY, SVR, or avoid an adverse event; and treatment cost-effectiveness
  - These results were similar in a sensitivity analysis where GT5 and 6 patients were treated with SOF/LDV
- Despite the lack of evidence from randomized controlled trial settings showing that treatment with direct-acting antivirals improves long-term health outcomes (and SVR), a large body of evidence indicates associations between SVR and improvements in liver function, fibrosis, cirrhosis-related complications, extrahepatic outcomes, and all-cause mortality[7]
- This analysis suggests G/P is a dominant treatment option and should be considered for use in patients infected with all HCV GTs

LIMITATIONS

- SVR inputs are based on rates from Phase 3 clinical trials and may differ from rates observed in real-world settings
- Transition probabilities and costs were obtained from the best available estimates in the literature; actual values for these may differ across other settings and patient subgroups
- This model does not include fibrosis stage improvement (i.e., regression) after achieving SVR
- Results may not be generalizable to specific real-world settings

CONCLUSIONS

- Compared with current standards of care, pan-genotypic treatment with G/P offers the most favorable improvements in quality-adjusted survival, SVR, and lifetime risk reductions in liver-related morbidity and mortality
- The G/P regimen proved a dominant treatment option compared with current standard practices, providing most favorable health outcomes at the lowest cost

DISCLOSURES

Design, study conduct, and financial support for the study were provided by AbbVie Inc. AbbVie Inc. participated in the interpretation of data and review and approval of the poster. All authors contributed to the development of the publication and maintained control over the final content.

Sammy Saab is a consultant to and serves on speakers' bureaus for AbbVie Inc., BMS, Gilead, Janssen, and Merck. **Suchin Virabhak** and **Scott Johnson** are employees of Medicus Economics, LLC. **Helene Parise** is a contractor to Medicus Economics, LLC. Medicus Economics, LLC, received consulting fees for research from AbbVie Inc. **Brett Pinsky** and **Yuri Sanchez Gonzalez** are employees of AbbVie Inc. and may own stocks and/or options of the company.

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Pan-genotypic Hepatitis C Treatment With Glecaprevir + Pibrentasvir Resulted in Improvement in Cardiovascular and Metabolic Extrahepatic Manifestations and Stable Renal Function: Results From Phase 3 Clinical Trials

Poster # 1177

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BACKGROUND

- Hepatitis C virus (HCV) is both a hepato- and lymphotropic virus
- While HCV-infected patients are at risk of developing liver-related complications, HCV infection is also associated with the development of extrahepatic manifestations (EHMs)
- Studies have shown that approximately two-thirds of HCV-infected patients experience EHMs[1]
- In the era of direct acting antiviral (DAA) regimens, US-based retrospective studies have observed that treated patients had reduced risk of cardiovascular and cerebrovascular events.[2]
- These extrahepatic benefits of treatment may extend to a broad range of EHMs and translate into cost savings of approximately $25,000 in all-cause medical costs per patient per year[3]
- An analysis of registrational trial of 3D±RBV (ombitasvir/paritaprevir {identified by AbbVie and Enanta}/ritonavir + dasabuvir)-concluded that treatment resulted in improvement in cardiovascular and metabolic EHMs and no worsening of renal function in genotype 1 patients[4]
- However, the impact of short-duration, all-oral pan-genotypic DAAs like glecaprevir + pibrentasvir (G/P) on EHMs is not well defined

G/P: Pan-genotypic Next Generation Direct-Acting Antiviral

Glecaprevir (formerly ABT-493) pangenotypic NS3/4A protease inhibitor

Coformulated: G/P

Pibrentasvir (formerly ABT-530) pangenotypic NS5A inhibitor

In vitro and PK:[5,6]
- High barrier to resistance; potent against most NS3 and NS5A polymorphisms
- Once-daily oral dosing with food

Clinical:
- Minimal metabolism and negligible renal excretion (<1%)
- Overall SVR12 rate of 98% in over 2000 patients in Phase 3 studies
- Favorable safety profile irrespective of baseline factors such as compensated liver cirrhosis and advance renal disease

G/P is co-formulated and dosed once daily as three 100 mg/40 mg pills for a total dose of 300 mg/120 mg Glecaprevir was identified by AbbVie and Enanta. *GT3 treatment experienced patients required 16 weeks of treatment. ^PRS = Prior treatment experience with regimens containing interferon, pegylated interferon, ribavirin, and/or sofosbuvir, but no prior treatment experience with an HCV NS3/4A PI or NS5A inhibitor. ^^In clinical trials, subjects were treated with prior regimens containing simeprevir and sofosbuvir, or simeprevir, boceprevir, or telaprevir with pegylated interferon and ribavirin.
#Indications for evaluated population

OBJECTIVES

- Determine the impact of treatment with G/P regimen on renal, cardiovascular and metabolic EHMs
- Investigate the differential impact of treatment by baseline EHM disease severity for patients treated with G/P, according to clinically relevant subgroups (Table 1)
- Investigate the differential effect of treatment by cirrhosis and treatment history status.

METHODS

Study Design

- Post-hoc analysis of clinical trial data from phase 3 trials of G/P

Study Cohorts

- Study cohorts were defined as follows:
  - Cohort 1: Patient data from 5 phase 3 trials were pooled to study the effect of treatment on select EHMs (ENDURANCE–1, ENDURANCE–2, ENDURANCE–3, ENDURANCE 4, EXPEDITION–1).
  - Cohort 2: EXPEDITION–4 trial was used to study the impact of treatment on renal EHMs in patients with advanced renal impairment at baseline (i.e. CKD stages 4 and 5).

METHODS (Continued)

Extrahepatic Manifestations

- The following EHMs were studied based on available biomarkers : cardiovascular (non-fasting triglyceride levels), metabolic (non-fasting glucose levels), and renal diseases (estimated glomerular filtration rates; eGFR)
- Improvement in cardiovascular and metabolic EHMs was defined as a decrease in the triglycerides and glucose values respectively, and improvement in renal EHM was defined as increase in eGFR.

Empirical Analysis

- Longitudinal mixed regression models (MM)[7] were used to assess the treatment effect on each EHM. The model controlled for patient baseline biomarker values, demographics and clinical characteristics (i.e. fibrosis stage, genotype, age, gender, BMI, presence of diabetes, HCV treatment history, viral load).
- The change from baseline to subsequent time points was estimated and plotted based on the regression coefficients from the MM.

Table 1. Clinically Relevant Subgroups For Each EHM

EHM Subgroup	Subgroup Definition	Sample Size (N, %)
Cardiovascular		
Normal triglyceride levels	Triglycerides levels < 175 mg/dL	1404 (90.4%)
Elevated triglyceride levels	Triglyceride levels ≥ 175 mg/dL	149 (9.6%)
Metabolic		
Normal glucose levels	Glucose levels < 140 mg/dL	1491 (96.2%)
Pre-diabetes	Glucose levels 140–200 mg/dL	46 (3.0%)
Diabetes	Glucose levels > 200 mg/dL	13 (0.8%)
Renal		
CKD stage 1	eGFR ≥ 90 mL/min/1.73 m^2	788 (50.8%)
CKD stage 2	eGFR 60–89 mL/min/1.73 m^2	741 (47.8%)
CKD stage 3 (moderate renal impairment)	eGFR 30–59 mL/min/1.73 m^2	22 (1.4%)
CKD stage 4 (severe) and stage 5 (end-stage)*	eGFR ≤ 29 ml/min/1.73 m^2	104 (100%)
Dialysis patients		86 (82.6%)
Stage 4, without dialysis		12 (11.5%)
Stage 5 without dialysis		6 (5.7%)

*All patients for this subgroup were from EXPEDITION–4 trial (cohort 2)

Table 2. Patient Demographics and Clinical Characteristics at Baseline

	Cohort 1: CV, metabolic and renal*	Cohort 2: Renal – patients with CKD Stage 4 or 5**
N	1561	104
Age (mean; years)	51.5	57.5
Gender - male	821 (52.6%)	79 (76.0%)
Race		
White	1255 (80.4%)	64 (61.5%)
Asian	213 (13.6%)	9 (8.7%)
Black or African American	62 (4.0%)	25 (24.0%)
Others	28 (1.8%)	6 (5.8%)
Fibrosis		
F0–F1	1174 (75.2%)	58 (55.8%)
F2	92 (5.9%)	11 (10.6%)
F3	145 (9.3%)	17 (16.3%)
F4	146 (9.4%)	17 (16.3%)
Genotype		
1	797 (51.1%)	55 (52.9%)
2	229 (14.7%)	16 (15.4%)
3	389 (24.9%)	11 (10.6%)
Others (4,5,6)	146 (9.4%)	22 (21.2%)
BMI (≥30)[a]	280 (17.9%)	25 (24.0%)
Prior diabetes history - Yes[b]	102 (6.5%)	43 (41.3%)
History of metabolic syndrome - Yes[c]	278 (17.8%)	45 (43.3%)
Prior cardiovascular disease - Yes[d]	442 (28.3%)	93 (89.4%)
HOMA - IR		
< 2	756 (48.4%)	27 (26.0%)
≥ 2	529 (33.9%)	42 (40.4%)
Missing	276 (17.7%)	35 (33.7%)
HCV History		
Naive-all	1158 (74.2%)	60 (57.7%)
Treatment experienced	403 (25.8%)	42 (40.4%)
Treatment arm		
12 weeks	1053 (67.5%)	104 (100.0%)
8 weeks	508 (32.5%)	-
SVR12		
Yes	1536 (98.4%)	102 (98.1%)
No	12 (0.8%)	1 (1.0%)
Missing	13 (0.8%)	1 (1.0%)

*Only patients with eGFR ≥30 included **Patients with eGFR < 30 included; Cohort 1 includes all patients treated with G/P regimen in phase 3 trials except those enrolled in EXPEDITION 4 trial. Cohort 2 includes patients enrolled in EXPEDITION 4 trial. [a]Rest of the proportion represents BMI < 30; [b]Rest of proportion represents patients with no prior diabetes history; [c]Rest of proportion represents patients with no prior metabolic syndrome; [d]Rest of proportion represents patients with no prior cardiovascular disease

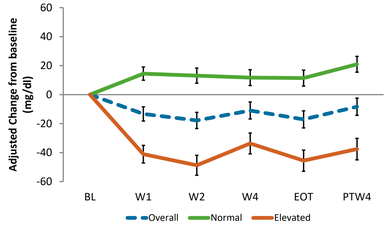
RESULTS

Cardiovascular Manifestations

- Among Cohort 1, treatment with G/P resulted in statistically significant decreases in triglyceride levels compared with baseline by end of treatment (–17.1 mg/dl; p = 0.0038; 95% CI: –28.7 mg/dl, –5.5 mg/dl) (**Figure 1A**)
  - Subgroup analysis by EHM severity showed that patients with elevated triglyceride levels at baseline had large and significant decreases from baseline in triglyceride levels by end of treatment (–45.5 mg/dl; p < 0.001; 95% CI: –59.8 mg/dl, –31.3 mg/dl)
  - Patients with normal triglyceride levels showed modest but significant increases in triglyceride levels by end of treatment (11.3 mg/dl; p = 0.03; 95% CI: 0.6 mg/dl, 22.1 mg/dl)
- Similar trend was observed across all treated patients regardless of treatment history and cirrhotic status (**Figure 1B**)

Figure 1. Cardiovascular EHMs – Predicted Change From Baseline in Triglyceride Levels

(A) Overall impact of treatment with G/P on triglycerides



(B) Overall impact of treatment with G/P on triglycerides by treatment history and cirrhotic status

	N	Adjusted baseline	Adjusted change from baseline				
			W1	W2	W4	EOT	PTW4
Naïve, F0–F3	1037	162.9	–21.1*	–22.2*	–14.9*	–19.4*	–8.7*
Naïve, F4	110	167.9	–18.1*	–38.4*	–40.7*	–37.3*	–38.3*
Experienced, F4	36	148.5	–26.3*	–32.1*	3.2	–29.7	–12.3
Experienced, F0–F3	364	140.8	–20.7*	–22.8*	–20.5*	–23.8*	–20.3*

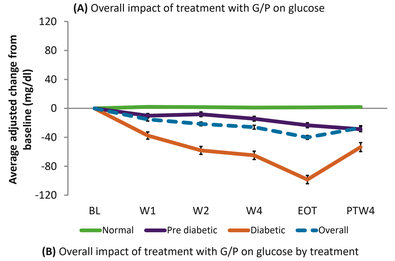
Non - Fasting baseline triglyceride levels ≥175 mg/dL were defined as elevated
Note: The graphs depict predicted change from baseline at individual time points based on longitudinal mixed model regression. The model for fig 1a modeled value of triglycerides at each time point. The key independent variable was longitudinal viral load and adjusted for baseline triglycerides level, fibrosis stages, genotype, age, BMI, history of diabetes, metabolic syndrome, cardiovascular disease, treatment history, study enrollment.
Error bars represent standard errors. *represents statistically significant change from baseline
W: week, EOT: end of treatment; PTW: post treatment week

Metabolic Manifestations

- Among Cohort 1, treatment with G/P resulted in statistically significant decreases in glucose levels compared with baseline by end of treatment (–40.1 mg/dl; p = 0.0038; 95% CI: –28.7 mg/dl, –5.5 mg/dl) (**Figure 2A**)
  - Patients with normal glucose levels demonstrated small but non-significant increases in glucose levels by end of treatment (1.8 mg/dL; p = 0.32; 95% CI: –1.7 mg/dl, 5.4 mg/dl)
  - Patients who were pre-diabetic at baseline had significant decreases from baseline in glucose levels by end of treatment (–23.3 mg/dL; p < 0.001; 95% CI: –30.1 mg/dl, –16.6 mg/dl)
  - Patients who were diabetic at baseline had the greatest decreases from baseline in glucose levels by end of treatment (–98.3 mg/dL; p < 0.0001; 95% CI: –109.7 mg/dl, –87.1mg/dl)
- Similar trend was observed across all G/P treated patients regardless of treatment history and cirrhotic status (**Figure 2B**)

Figure 2. Metabolic EHMs – Predicted Change From Baseline in Glucose Levels

(A) Overall impact of treatment with G/P on glucose



(B) Overall impact of treatment with G/P on glucose by treatment history and cirrhotic status

	N	Adjusted baseline	Adjusted change from baseline				
			W1	W2	W4	EOT	PTW4
Naïve, F0–F3	1037	159.3	1.6	–12.1*	–4.3	–35.4*	–42.7*
Naïve, F4	110	190.3	–39.5*	–43.8*	–46.8*	–63.1*	–34.3*
Experienced, F4	36	161.5	–5.2	–27.3*	–45.8*	–41.4*	–33.5*
Experienced, F0–F3	364	149.04	–9.8*	–6.1	–16.6*	–16.6*	–23.7*

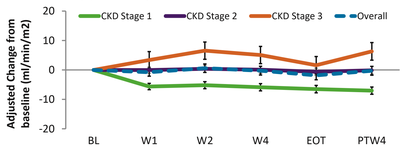
Non - Fasting baseline glucose levels between 140 and 200 mg/dL were defined as pre-diabetic and levels above 200 mg/dl were defined as diabetic
Note: The graphs depict predicted change from baseline at individual time points based on longitudinal mixed model regression. The model for fig 2a modeled value of glucose at each time point. The key independent variable was longitudinal viral load and adjusted for baseline glucose level, fibrosis stages, genotype, age, BMI, history of diabetes, metabolic syndrome, cardiovascular disease, treatment history, study enrollment.
Error bars represent standard errors. *represents statistically significant change from baseline
W: week, EOT: end of treatment; PTW: post treatment week

Renal Manifestations

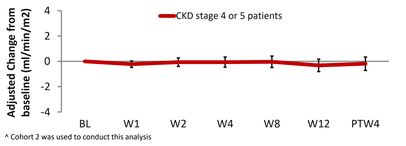
- Among Cohort 1, treatment with G/P resulted in a non-statistically significant decreases in eGFR levels compared with baseline by end of treatment (–1.8 ml/min/1.73 m^2; p = 0.22 95% CI: –4.8 ml/min/m^2; 1.1 ml/min/m^2) (**Figure 3A**)
  - Patients who had CKD stage 2 at baseline had a non-significant improvements from baseline in eGFR by end of treatment (0.6 ml/min/1.73m^2; 95% CI: –3.1 ml/min/1.73m^2, 1.8 ml/min/1.73m^2)
  - Patients who had CKD stage 3 at baseline had a non-significant improvements from baseline in eGFR by end of treatment (1.6 ml/min/1.73m^2; p = 0.58; 95% CI: –4.2 ml/min/1.73m^2, 7.4 ml/min/1.73m^2)
  - Among Cohort 2 (CKD stage 4 and 5 patients) G/P treated patients, experienced no statistically significant change by end of treatment (–0.3 ml/min/1.73m^2; p = 0.52; 95% CI: –1.3 ml/min/1.73m^2, 0.65 ml/min/1.73m^2) (**Figure 3B**)
- Across all treated patients, irrespective of treatment history and cirrhotic status, there was no statistically significant decline in eGFR, except for naïve cirrhotic in Cohort 2 (**Figure 3C**)

Figure 3. Renal EHMs – Predicted Change From Baseline in eGFR

(A) Overall impact of treatment with G/P on eGFR



(B) Overall impact of treatment with G/P on eGFR in renal impaired patients^



^ Cohort 2 was used to conduct this analysis

(C) Overall impact of treatment with G/P on eGFR by treatment history and cirrhotic status

	N	Adjusted baseline	Cohort 1 Adjusted change from baseline				
			W1	W2	W4	EOT	PTW4
Naïve, F0–F3	1037	86.8	3.3*	4.1*	3.3*	1.1	3.4*
Naïve, F4	110	79.5	–1.1	2.5	1.1	–0.9	0.2
Experienced, F4	36	84.9	–7.5	–3.9	–3.1	–5.5	–2.6
Experienced, F0–F3	364	82.8	–0.3	0.5	–0.4	–1.1	–1.1
			Cohort2 Adjusted change from baseline				
	N	**Adjusted baseline**	**W1**	**W2**	**W4**	**EOT**	**PTW4**
Naïve, F0–F3	53	9.2	–0.1	0.2	0.6	0.2	0.2
Naïve, F4	7	11.6	–0.1	–0.9	–0.5	–1.1	–2.8*
Experienced, F4	10	10.2	–0.6	–0.4	–1.7*	–2.1*	–1.6
Experienced, F0–F3	33	8.5	–0.4	0.4	0.2	0.3	0.7

Chronic kidney disease stages were defined based on guidelines as stage 1 (signs of kidney damage but normal or elevated eGFR ≥ 90 mL/min/1.73 m^2), stage 2 (eGFR 60–89 mL/min/1.73 m^2), stage 3 and higher (<59 mL/min/1.73 m^2)
Note: The graphs depict predicted change from baseline at individual time points based on longitudinal mixed model regression. The model for fig 3a and 3b modeled value of eGFR at each time point. The key independent variable was longitudinal viral load and adjusted for baseline eGFR level, fibrosis stages, genotype, age, BMI, history of diabetes, metabolic syndrome, cardiovascular disease, treatment history, study enrollment.
Error bars represent standard errors. *represents statistically significant change from baseline
W: week, EOT: end of treatment; PTW: post treatment week

DISCUSSION

Patient Population

- With the depleting pool of warehoused cirrhotic patients and higher efficacy of previous generation DAAs, the new pool of treatable patients is likely to be the treatment naïve non-cirrhotic population.[8]
- The benefits from treatment on EHM outcomes were also observed in treatment-naive, non-cirrhotic patients, with 36% of this population receiving 8-week treatment.

Cardiovascular EHMS

- Elevated triglycerides levels have been associated with increased risk of coronary heart disease and all cause mortality.[9,10] Treatment with interferon-based antiviral therapy has previously been shown to lower risk of cardiovascular complications[11]
- Thus, the overall decline in triglyceride levels observed in current study for all HCV patients treated with G/P regimen, especially in patients with elevated triglycerides at baseline; may translate into long-term clinical benefit.

Metabolic EHMs

- Elevation in glucose levels has been associated increased rates of cardiovascular events.[10,11] Treatment with interferon-based antiviral therapy has been associated with improvement in fasting glucose levels which may prevent or delay the onset of metabolic syndrome.[12,13]
- Thus, the overall decline in glucose levels observed in the current study for all HCV patients treated with G/P regimen, especially in pre-diabetic and diabetic population may translate into clinical benefits of delaying metabolic syndrome and associated cardiovascular events.

Renal EHMs

- A decline in eGFR has been associated with increased risk for end-stage renal disease (ESRD) and absolute all-cause mortality risk.[14]
- Treatment of HCV with interferon based triple therapy have been demonstrated to cause renal impairment.[15] Among newer DAA agents, sofosbuvir-based DAA regimens have also been shown to have a negative effect on renal function.[16-18]
- The stable eGFR function shown-by current study for HCV patients treated with a renally sparing regimen like G/P, could avoid the renal risks associated with sofosbuvir-based treatment.

LIMITATIONS

- This analysis used data from patients enrolled in clinical trials and therefore may have limited generalizability to the overall HCV-infected population
- The majority of patients in Cohort 2 were on hemodialysis, thus limiting the ability to observe true improvements or changes to eGFR.
- Unobserved confounding variables not included as covariates in the regression analysis could potentially bias the study results.
- The relationship between the biomarkers used in the analysis and clinical EHM outcomes was inferred based on prior published literature and further analyses (e.g. long term real-world data with confirmed diagnoses or outcomes) are warranted to validate such effects.
- The current study followed patients during the treatment period only. Therefore, the persistency of the EHM outcomes post-treatment was not established. However a prior study has established persistency of these effects at least 52 weeks post treatment with an all oral sofosbuvir-free DAA regimen.[4]
- Not all patients in the current analysis, received treatment as per the current approved USFDA label.

CONCLUSIONS

- HCV treatment with G/P had a positive impact on cardiovascular and metabolic EHM biomarkers, especially in patients with elevated triglycerides and pre-diabetes or diabetes at baseline.
- Patients with CKD stages 2–5 had stable eGFR during and post-treatment.
- The beneficial effects of HCV treatment on EHM outcomes were maintained in patients irrespective of their treatment history and cirrhosis status.

DISCLOSURES AND CONFLICTS OF INTEREST

Design and study conduct for the study was approved by AbbVie, Inc. AbbVie Inc. participated in the interpretation of data, and review and approval of the abstract. All authors contributed to the development of the publication and maintained control over the final content.
Tram Tran received consulting, advisor/speaker fees and research grants from Gilead Sciences, Bristol-Myers Squibb, and AbbVie.
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Federico Mensa, Caroline Park and Yuri Sanchez Gonzalez are employees of AbbVie Inc. and may own stocks and/or options of the company.

ACKNOWLEDGEMENTS

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Chronic kidney disease and hepatitis C mutually advance liver and renal disease progression: real-world evidence from the United States

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BACKGROUND

- Based on a comprehensive review of recent epidemiologic literature, the global prevalence of chronic hepatitis C virus (HCV) infection is estimated to be 1.1% (0.9–1.4%), corresponding to approximately 80 (64–103) million people infected, resulting in substantial burden for society and healthcare systems[1]
- Extrahepatic manifestations (EHMs) associated with chronic HCV infection are common and varied, frequently increasing the burden of HCV[2]
- Among a broad range of EHMs, HCV infection has been associated with increased incidence of chronic kidney disease (CKD)[3,4]
- Evidence suggests that patients comorbid for both HCV-related liver disease and CKD may have increased morbidity and mortality[4]
- However, there is limited evidence on the extent to which having HCV and CKD may mutually advance time to renal and liver disease progression

OBJECTIVE

- To assess how CKD affects liver disease progression in patients with HCV, and how HCV infection affects renal disease progression in patients with CKD

METHODS

DATA SOURCE: OPTUM CLINFORMATICS® DATA MART

- Large de-identified database of physician- and patient-level data including medical claims, pharmacy claims, lab results, and administrative data in the United States from 2000 to present day
- Database covers 16 million lives annually and is updated semi-annually/quarterly

DATA ANALYSIS

- Disease progression was analyzed using Kaplan-Meier plots for up to 10 years post-index, between 2006–2016

STATISTICAL ANALYSIS

- McNemars, paired *t*-test, and regression with negative-binomial distribution were used for statistical analysis of categorical, continuous, and count variables, respectively

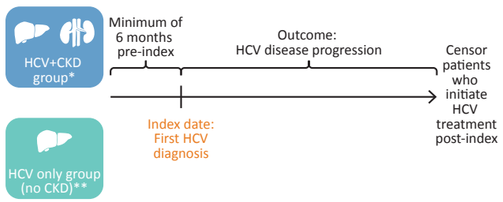
STUDY DESIGN: LIVER DISEASE PROGRESSION (FIGURE 1)

- To assess the influence of CKD on liver disease progression, a cohort of patients with HCV was identified
- Index date: date of first HCV diagnosis between 2006–2016
- The subgroup of HCV patients with a CKD diagnosis at or prior to HCV was compared to HCV patients without a CKD diagnosis
- Patients were matched 1:2 on propensity score (±0.0005) controlling for age, gender, HCV duration, and state
- Liver disease progression:
  - Patients with ≥2 liver FIB4 fibrosis scores at least 6 months apart
    - Categorical changes in FIB4 fibrosis stages (F0–1, F2, F3–F4) calculated from FIB4 fibrosis score
    - Increase in FIB4 score ≥0.4, which is associated is associated with a higher incidence of fibrosis progression to cirrhosis[5]

STUDY DESIGN: RENAL DISEASE PROGRESSION (FIGURE 2)

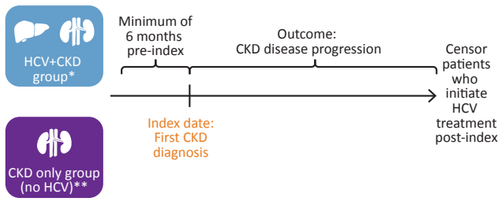
- To assess the influence of HCV on renal disease progression, a cohort of CKD patients was identified
- Index date: date of first CKD diagnosis between 2006–2016
- The subgroup of CKD patients with a HCV diagnosis at or prior to CKD was compared to CKD patients without a HCV diagnosis
- Patients were matched 1:2 on propensity score (±0.0005) controlling for age at baseline, gender, CKD duration (follow-up), and geographic state
- Renal disease progression
  - Patients with ≥2 serum creatinine levels at least 6 months apart
    - Change in CKD stage (3a, 3b, 4, and 5)
    - Annualized decrease in estimated glomerular filtration rate (eGFR) ≥4 mL/min/1.73 m² [http://www2.kidney.org/professionals/kdoqi/guidelines_ckd/p7_risk_g13.htm; Accessed 2/13/2016]

Figure 1. Study Design: Liver Disease Progression



*Pre-index CKD diagnosis at or prior to HCV
**Pre-index without CKD diagnosis
CKD, chronic kidney disease; HCV, hepatitis C virus

Figure 2. Study Design: Renal Disease Progression



*Pre-index HCV diagnosis at or prior to CKD
**Pre-index without HCV diagnosis
CKD, chronic kidney disease; HCV, hepatitis C virus

RESULTS

LIVER PROGRESSION COHORT (TABLE 1)

- A total of 4,758 patients with a diagnosis of HCV between 2006–2016 were identified
- Of these, 1,586 (33.3%) had a pre-index diagnosis of CKD within 1 year prior to HCV
- A significantly higher percentage of HCV patients with CKD than those without CKD demonstrated liver fibrosis progression as characterized by FIB4 group increase and by FIB4 score increase
- 25.1% of HCV patients with CKD demonstrated liver fibrosis progression, characterized by FIB4 group increase, within 10 years, compared with 14.3% of HCV patients without CKD (1.82 hazard ratio [HR], p<0.001) (**Figure 3**)
- Mean time to fibrosis stage progression was lower in patients with CKD vs those without CKD (827 vs 987 days, p=0.330)
- 43.0% of HCV patients with CKD demonstrated liver fibrosis progression, characterized by FIB4 score increase ≥0.4 within 10 years, compared with 26.6% of HCV patients without CKD (1.79 HR, p<0.001) (**Figure 4**)
- Mean time to FIB4 score increase ≥0.4 was lower in patients with CKD than those without (765 vs 890 days, p=0.994)

RENAL PROGRESSION COHORT (TABLE 2)

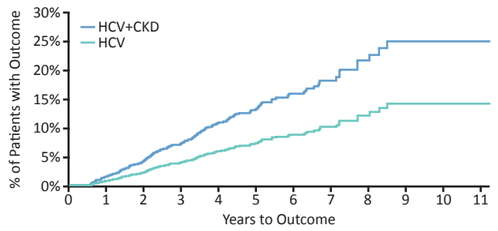
- A total of 1,620 patients with a diagnosis of CKD between 2006–2016 eligible for a CKD increase were identified, and 1,323 patients with a diagnosis of CKD between 2006–2016 eligible for an annualized eGFR decrease were identified
- A significantly higher percentage of CKD patients with HCV than those without HCV demonstrated renal disease progression as characterized by both CKD stage progression (p<0.001) and by an annualized decrease in eGFR (p<0.001)
- 77.3% of CKD patients with HCV demonstrated CKD stage progression within 10 years, compared with 48.8% of CKD patients without HCV (2.21 HR, p<0.001) (**Figure 5**)
- Mean time to progression was lower in patients with HCV vs those without HCV (506 vs 676 days, p=0.032)
- Kaplan-Meier curves demonstrated a gap in renal disease progression as early as one year post-index
- 46.8% of CKD patients with HCV demonstrated annualized eGFR decrease of ≥4 mL/min/1.73 m² within 10 years, compared with 28.3% of CKD patients without HCV (1.88 HR, p<0.001) (**Figure 6**)
- There was no significant difference in mean time to progression (as measured by annualized eGFR decrease) in CKD patients with HCV versus those without HCV (489 vs 470 days, p=0.648)

Table 1. Matched HCV/CKD and HCV Without CKD: Patient Characteristics and Fibrosis Progression

	Overall	Matched HCV/CKD patients	HCV patients without CKD
Patient characteristics			
Number of patients	4,758	1,586	3,172
Age of patient at first HCV diagnosis, mean (SD)	53.9 (10.4)	53.9 (10.6)	53.8 (10.4)
Male, n (%)	3,049 (64%)	1,008 (64%)	2,041 (64%)
Fibrosis progression			
Mean days to fibrosis stage increase (95% CI)	910 (819–1,000)	827 (720–934)	987 (844–1,130)
Patients with fibrosis stage increase, n (%)	205 (4.3%)	99 (6.2%)	106 (3.3%)
Mean days to FIB4 score increase (95% CI)	831 (769–893)	765 (682–847)	890 (799–980)
Patients with FIB4 score increase, n (%)	405 (8.5%)	190 (12.0%)	215 (6.8%)

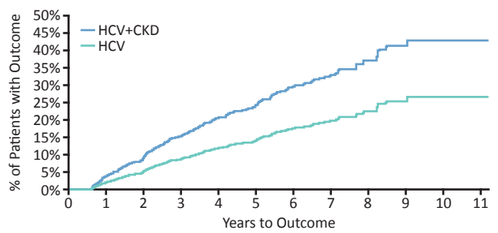
CI, confidence interval; CKD, chronic kidney disease; HCV, hepatitis C virus

Figure 3. Proportion of patients with fibrosis stage increase (Dx 2006–2016)



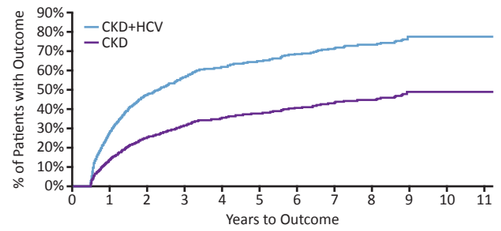
CKD, chronic kidney disease; HCV, hepatitis C virus

Figure 4. Proportion of patients with FIB4 score increase ≥0.4 (Dx 2006–2016)



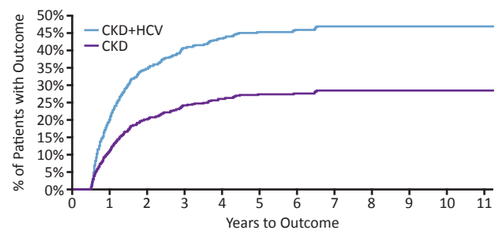
CKD, chronic kidney disease; HCV, hepatitis C virus

Figure 5. Proportion of patients with CKD stage increase (Dx 2006–2016)



CKD, chronic kidney disease; HCV, hepatitis C virus

Figure 6. Proportion of Patients With Renal Disease Progression (eGFR Annualized Decrease ≥4 mL/min/1.73 m²)



CKD, chronic kidney disease; eGFR, glomerular filtration rate; HCV, hepatitis C virus

Table 2. Matched CKD/HCV and CKD Without HCV: Patient Characteristics and Renal Disease Progression

	Overall	Matched CKD/HCV patients	CKD patients without HCV
Patients eligible for CKD stage increase			
Number of Patients	1,620	540	1,080
Age of patient at first CKD diagnosis, mean (SD)	56.9 (10.5)	56.3 (8.4)	57.2 (11.4)
Male, n (%)	1,104 (68.1%)	365 (67.6%)	739 (68.4%)
Index CKD Stage, n (%)			
CKD Stage 3a	895 (55.2%)	294 (54.4%)	601 (55.6%)
CKD Stage 3b	272 (16.8%)	105 (19.4%)	167 (15.5%)
CKD Stage 4	453 (28.0%)	141 (26.1%)	312 (28.9%)
CKD Stage 5	0 (0%)	0 (0%)	0 (0%)
Mean days to CKD stage increase (95% CI)	595 (553–637)	506 (456–555)	676 (611–741)
Patients with CKD stage increase, n (%)	607 (37.5%)	282 (52.2%)	325 (30.1%)
Patients eligible for eGFR decrease ≥4 mL/min/1.73 m²			
Number of patients	1,323	441	882
Age of patient at first CKD diagnosis, mean (SD)	55.9 (10.0)	56.4 (8.0)	55.7 (10.9)
Male, n (%)	919 (69.5%)	300 (68.0%)	619 (70.2%)
Mean days to eGFR decrease ≥4 mL/min/1.73 m²/year (95% CI)	479 (441–516)	489 (431–547)	470 (421–519)
Patients with annualized eGFR decrease, n (%)	351 (26.5%)	161 (36.5%)	190 (21.5%)

CI, confidence interval; CKD, chronic kidney disease; eGFR, glomerular filtration rate; HCV, hepatitis C virus

DISCUSSION

- Among a cohort of HCV patients, a significantly greater percentage of those with comorbid CKD demonstrated liver fibrosis progression within 10 years compared with HCV patients without CKD
- Among a cohort of CKD patients, a significantly greater percentage of those with comorbid HCV demonstrated renal disease progression within 10 years, compared with CKD patients without HCV
- Differences in disease progression between patients with or without the respective comorbidity in each cohort were apparent after one year
- These results suggest that early identification and treatment of chronic hepatitis C (CHC) could lead to mutual health benefits for liver and renal diseases
  - Recently, Mahale et al demonstrated that HCV treatment and sustained virologic response can reduce the clinical burden of extrahepatic manifestations (EHMs) of chronic HCV infection, including renal impairment (glomerulonephritis), particularly with early initiation after the HCV index date[6]
  - Results of a large claims database analysis demonstrated that CHC treatment initiated in early fibrosis stages significantly mitigates the economic burden from hepatic complications and EHMs including kidney disease[7]

LIMITATIONS

- This analysis was based on claims data, which are subject to several limitations as the primary purpose of claims data is reimbursement, not research. As such:
  - Records are often incomplete
  - Diagnoses may be inaccurate or incomplete as they are often extracted from the medical record for claims purposes by non-healthcare staff
  - By nature, claims data analysis is retrospective
- The potential role of CHC treatment to mitigate the burden of worsened liver fibrosis and CKD when they occur comorbidly was not analyzed in this study and remains an area of future research

CONCLUSIONS

- Liver fibrosis and CKD are worsened when both are present as comorbidities compared with when only one condition is present
- Early identification and treatment of HCV could lead to mutual health benefits for liver and renal diseases

DISCLOSURES

Design and study conduct for the study was approved by AbbVie Inc. AbbVie participated in the interpretation of data and review and approval of the poster. All authors contributed to the development of the poster and maintained control over the final content.

Tram Tran received consulting, advisor/speaker fees, and research grants from Gilead Sciences, Bristol-Myers Squibb, and AbbVie.

Yuri Sanchez Gonzalez, **Oscar Hayes**, and **Steven E. Marx** are employees of AbbVie and may own stocks and/or options of the company.

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Assessing Patient Preferences for and Relative Importance of Features of New Direct Acting Antiviral (DAA) Treatments for Chronic Hepatitis C Virus (HCV) Infections

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PREMISE

- Since 2013, an increasing number of all oral, interferon (IFN)-free direct acting antivirals (DAAs) have been made available to treat chronic hepatitis C, with increasingly improved efficacy, tolerability, and ease of use[1-2]
- Understanding patients' preferences for features of new DAAs could help improve the understanding of treatment adherence, and thereby potentially improve treatment outcomes
- This study aimed to: (a) quantify and evaluate HCV patient preferences for and trade off among features of new DAAs, and (b) examine whether preferences for treatment features vary among patient subgroups

METHODS

DISCRETE CHOICE EXPERIMENT (DCE) DESIGN

- DCE questions were designed to assess patients' preferences for features (ie, attributes) of new DAA treatments
- Nine features were determined based on a literature review and consultation with clinical experts (**Table 1**)
- An orthogonal design was used to develop 72 choice cards, each showing 2 hypothetical HCV treatment profiles (Treatment A vs. Treatment B) (**Figure 1**)
- The 72 choice cards were randomly divided into 8 groups; patients were randomly assigned to 1 group and asked to select their preferred profile between A and B on a given card
- A patient tutorial was provided to explain a patient's treatment journey and the choice task
- This study was approved under the exemption category by the New England Institutional Research Board

Table 1. Features and levels

Feature	Levels
Efficacy	
Cure rate	95%; 97%; 100%
Convenience	
Once-daily tablet count and packaging	• 1 tablet from a prescription bottle • 1 tablet in a single-dose blister pack • 3 tablets in a single-dose blister pack
Duration of treatment (weeks)	8; 12; 16; 24
Office visits for HCV treatment (all patients required to have 1 visit for treatment initiation and 1 visit for post-treatment viral evaluation)	• Simplified monitoring during HCV treatment (eg, telephone check-in by doctor or nurse) • One additional office visit during HCV treatment • Two additional office visits during HCV treatment
Drug-Drug Interactions	
Modification of concurrent statin use	• No modification to a statin • Temporarily reduce dose of a statin • Temporarily stop taking a statin • Switch to a different medication
Modification of concurrent PPI use	• No modification to a PPI • Temporarily reduce dose or modify timing of taking a PPI • Temporarily stop taking a PPI • Switch to a different medication
Adverse Events	
Risk of diarrhea	5%; 15%; 25%
Risk of headache	5%; 15%; 25%; 35%
Risk of nausea	5%; 15%; 25%

HCV, hepatitis C virus; PPI, proton pump inhibitor.

Figure 1. An example choice card

Treatment features	Treatment A	Treatment B
Treatment duration	16 weeks	8 weeks
Once-daily tablet count and packaging		
Cure rate	100% chance to be cured	97% chance to be cured
Follow-up monitoring during HCV treatment (all patients are required to have 1 visit for treatment initiation and 1 visit for post-treatment evaluation)	Simplified monitoring (no in-person visit, eg, telephone check-in by doctor or nurse) 	2 additional office visits during HCV treatment 
Modification of concurrent use of statins (medications to lower cholesterol level)	Temporarily reduce dose of a statin	No modification to a statin
Modification of concurrent use of PPIs (medications to reduce stomach acid)	Temporarily reduce dose or modify timing of taking a PPI	No modification to a PPI
Risk of diarrhea	5 out of 100 people	25 out of 100 people
Risk of headache	15 out of 100 people	25 out of 100 people
Risk of nausea	25 out of 100 people	5 out of 100 people
Please tell us which treatment you would prefer	I prefer Treatment A ☐	I prefer Treatment B ☐

HCV, hepatitis C virus; PPI, proton pump inhibitor.

SAMPLE SELECTION AND DATA COLLECTION

- Data were collected from adult patients with HCV in the US and EU5 countries (United Kingdom, France, Germany, Italy, Spain), who were the existing members of patient panels of Survey Sampling International, an established survey research firm
- Eligible patients were adults with self-reported HCV who confirmed having diagnosis assessments (blood test, liver biopsy, liver ultrasound scan, computed tomography scan, magnetic resonance imaging, or Home Access Hepatitis C Check kit), ≥6 years of education, and willingness to participate in the study
- The survey also collected patient baseline characteristics including demographics, HCV medical history, and treatment history
- Pre-tests (phone interviews with online simultaneous screen-sharing of questionnaire) were conducted before the start of the survey to confirm the relevance of treatment features of interest and the clarity of the patient tutorial

STATISTICAL METHODS

- Multivariable logistic regression models with generalized estimating equations were conducted
- Coefficients from the regression analysis indicated the relative importance of features in patient preferences
- Subgroup analyses were conducted by treatment experience (treatment naïve [TN], treatment experienced [TE] in IFN-free, and TE in IFN only) and by region (US, EU5), with Z-tests to compare between subgroups

RESULTS

Table 2. Participants' characteristics (N=328)

Age (years), mean ± SD	47.7 ± 14.4
Female, n (%)	168 (51.2)
Country/region, n (%)	
US	227 (69.2)
EU5	101 (30.8)
Highest level of formal education, n (%)	
Completed 6–12 years of education	103 (31.4)
Completed >12 years of education	225 (68.6)
Employment status, n (%)	
Employed	176 (53.7)
Not working	140 (42.7)
Student	8 (2.4)
Decline to answer	4 (1.2)
Selected key chronic comorbidities, n (%)	
Anxiety/depression	149 (45.4)
Cardiovascular disease (eg, ischemic heart disease)	29 (8.8)
Cirrhosis	47 (14.3)
Diabetes/insulin resistance	59 (18.0)
Fibrosis	33 (10.1)
Gastroesophageal reflux disease (GERD)	77 (23.5)
Hepatitis B virus infection	32 (9.8)
HIV infection/AIDS	23 (7.0)
Kidney disease	24 (7.3)
Liver cancer	17 (5.2)
Liver transplant	20 (6.1)
Injectable recreational drug use, n (%)	
Never used	154 (47.0)
Former/current user	162 (49.4)
Decline to answer	12 (3.7)
Patient motivation level (by PAM-13), n (%)	
Level 1 (not yet believe patients have active/important role)	27 (8.4)
Level 2 (lack confidence/knowledge to take action)	34 (10.6)
Level 3 (beginning to take action)	148 (46.0)
Level 4 (maintaining behavior over time)	113 (35.1)

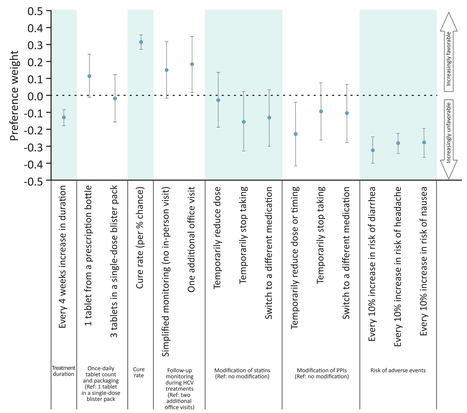
HCV DISEASE AND TREATMENT HISTORY

- Mean time since diagnosis was 11.2 years and 18.6% of patients were diagnosed with HCV in the 3 years prior to survey
- 37.2% of patients did not know their HCV genotype
- Patients had varied HCV treatment history:
  - TN: n=131 (39.9%)
  - TE with IFN-free: n=129 (39.3%), 47% of whom had exposure to IFN-containing treatments
  - TE with IFN-containing only: n=68 (11.6%)
- Nearly one-third of patients had GERD, or were on PPIs; almost half of patients had cardiovascular disease, diabetes, hyperlipidemia, hypertension, or were on statins

PATIENT PREFERENCES

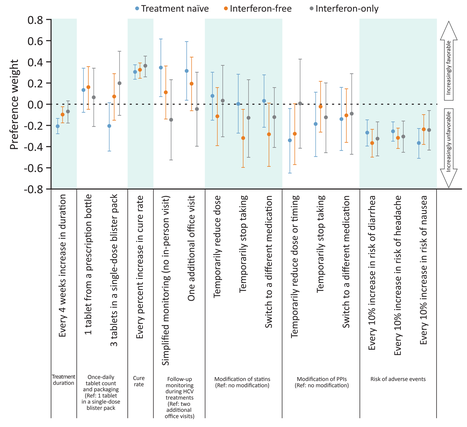
- Treatment features significantly preferred by patients (**Figure 2**) were
  - higher cure rate, shorter treatment duration, lower risks of diarrhea, headache, and nausea (all p<0.0001)
  - requiring only 1 rather than 2 additional office visits while on treatment (p=0.036)
  - not requiring dose reduction or change in timing of PPIs (p=0.016)
- Preferences for certain treatment features varied among the subgroups by treatment history (**Figure 3**)
  - All preferred shorter duration: greater among TN patients than among TE with IFN-free (p=0.046) or TE with IFN-only patients (p=0.042)
  - TN patients strongly preferred simplified monitoring relative to 2 additional office visits; TE IFN-only patients preferred having 2 additional visits relative to simplified monitoring (p=0.041)
  - For TN patients, having 3 tablets was less preferred than having 1 tablet; TE IFN-only patients preferred having 3 tablets rather than 1 tablet (p=0.035)
- Preferences were generally similar between US and EU5 patients with 1 exception: US patients had stronger preferences for having 1 rather than 2 additional office visits, whereas treatment visit frequency was not associated with preference in EU5 patients (p=0.022)

Figure 2. Importance of treatment features to patients (overall population)



HCV, hepatitis C virus; PPI, proton pump inhibitor.

Figure 3. Importance of treatment features to patients (by treatment experience subgroups)



HCV, hepatitis C virus; PPI, proton pump inhibitor.

DISCUSSION/LIMITATIONS

- Preferences for monitoring differed in TE IFN-only patients compared with TN and TE IFN-free patients, which should be considered when planning use of DAAs in these patients
- Preferences were generally similar between US and EU5 patients, although US patients preferred less monitoring burden during treatment
- Findings from this online, panel-based patient survey may not be generalizable to the broader population of HCV patients
- Recall bias of disease and treatment-related medical history may be present
- Patients' preferences for hypothetical HCV therapies may not represent their preferences for HCV treatments received in the real world

CONCLUSIONS

- Given the overall high efficacy of new DAAs, HCV patients' preferences for therapy may differ based on treatment features other than efficacy/effectiveness
- Less disruption to a patient's life (such as no modification in PPI use, lower risk of adverse events) and added convenience (such as shorter treatment duration, fewer office visits during treatment) seem to be important from HCV patients' perspective
- Improved understanding of patients' preferences for features of new DAA therapies can help facilitate communication with patients and inform other key stakeholders such as physicians and payers to potentially improve treatment outcomes

DISCLOSURES

The financial support for the study was provided by AbbVie. AbbVie participated in the interpretation of data, review, and approval of the publication. All authors contributed to the development of the publication and maintained control over the final content.

Tania M. Welzel is a member of advisory committees or review panels for Novartis, Janssen, Gilead, AbbVie, Boehringer-Ingelheim, and BMS. **Brett Pinsky**, **Yanjun Bao**, and **Yaozhu J. Chen** are stock shareholders and employees of AbbVie. **Darshan Mehta** is supported for graduate research work by a fellowship agreement between University of Southern California (USC) and AbbVie. **Min Yang**, **Gautam Sajeev**, and **Eric Q. Wu** are employees of Analysis Group, Inc., a consulting firm which consults to numerous payers, providers, and suppliers to the healthcare industry.

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An Analysis of Potential Elimination Strategies for Hepatitis C Using a Budget Optimization Model for the UK

Poster # 1077

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BACKGROUND

- The introduction of highly effective oral direct-acting antivirals (DAAs) offers countries an opportunity to cure hepatitis C virus (HCV) and meet the World Health Organization (WHO) targets for eliminating viral hepatitis as a public health threat in the population by 2030[1]
- Access to DAA treatment in the UK is increasing and is no longer restricted to the most severe cases but there remains a large percentage of patients estimated at 50%[2] who remain undiagnosed and making elimination a challenge
- These patients will continue to have a significant impact on the future burden of the disease

OBJECTIVES

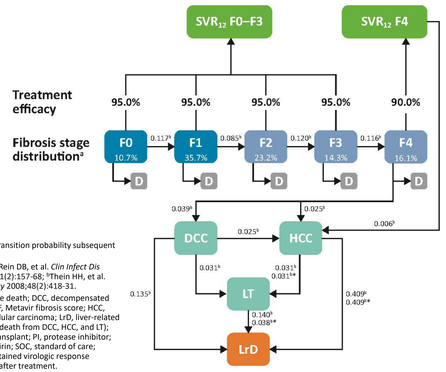
- To understand the optimal use of current HCV budget allocations for the United Kingdom (UK) based on liver fibrosis stage and the impact on the 2030 WHO elimination targets
- To assess what impact greater investment in treatment and screening will have on the care burden and speed of elimination of HCV in the UK

METHODS

Model Design

- A sequential, multi-cohort, health-state transition Markov model (**Figure 1**) was designed to assess the clinical and economic outcomes for the UK HCV population from 2017 until 2030
- The model used annual cycles for the eligible HCV population diagnosed across the five liver fibrosis stages (F0–F4)
- An incident cohort of newly diagnosed patients was added annually and adjusted proportionally to the size of the total HCV population over time

Figure 1. Model Schematic



*Annual transition probability subsequent to Year 1.

Sources: [a]Rein DB, et al. *Clin Infect Dis* 2015;15;61(2):157-68; [b]Thein HH, et al. *Hepatology* 2008;48(2):418-31.

D, all-cause death; DCC, decompensated cirrhosis; F, Metavir fibrosis score; HCC, hepatocellular carcinoma; LrD, liver-related death (ie, death from DCC, HCC, and LT); LT, liver transplant; PI, protease inhibitor; RBV, ribavirin; SOC, standard of care; SVR_{12}, sustained virologic response 12 weeks after treatment.

Treatment Strategies and Budget Allocation

- 12 treatment strategies encompassing possible treatment allocation by fibrosis stage were considered (**Table 1**)
- Strategies 1 to 10 assumed a budget allocation across different fibrosis groups proportional to the fibrosis distribution in the HCV population
- Strategies 11 and 12 assumed the sequential treatment of patients until the available budget was fully exhausted by either treating patients with F0 first (F0→F4) or treating patients with F4 first (F4→F0)

METHODS (Continued)

Data Inputs

- Data inputs related to the HCV natural history and treatment efficacy are denoted in **Figure 1**
- Epidemiologic data and cost inputs are described in **Table 1**.
- Cost inputs were obtained from published literature and included healthcare expenditures attributable to liver-related complications (including decompensated cirrhosis [DCC], hepatocellular carcinoma [HCC], liver transplant [LT] and liver-related death [LrD]) (**Table 1**)
- Drug costs were computed based on the list price all-oral direct-acting antiviral therapies and averaged at £15,000 per treatment course
- Screening costs were set at £1000 per diagnosed HCV patient
- Annual budget was set at £230 m to reflect current estimated UK HCV spend
- Patient outcomes and costs were discounted at 3.5%

Outcomes

- Health outcomes included the projected number of QALYs, patients treated and patients reaching SVR, end-stage liver disease (ie, DCC, HCC or LT) or LrD
- Economic outcomes included HCV treatment and liver-related medical costs

Analyses

- Firstly, we assessed the optimal treatment strategy that achieved the best possible liver outcomes (ie, highest number of SVRs and lowest number of DCC, HCC, LT and LrD cases) based on the current UK treatment budget of £230 million and the current diagnosis rate of 50%
- Secondly, we assessed the path to HCV elimination with the optimal treatment strategy under three scenarios:
  - Current fixed treatment budget and current diagnosis rate
  - Annual treatment budget remains fixed at £230 million but diagnosed population rate increased to 90%[2] by 2030 to meet WHO target
  - Annual treatment budget increased by 10% and diagnosed population increased to 90% by 2030
  - Analysis was conducted without extra hepatic costs included but they could add significant additional burden[3]

Table 1. Data Inputs

Data input	Base
Prevalence 2017	
Prevalent cases in 2017[a]	214,000
Fraction diagnosed[b]	50%
Average age (years)[c]	40
Annual incidence	
Annual incident cases[d]	4,603
Fraction diagnosed[b]	50%
Average age (years)[c]	40
Costs	
Treatment[c]	£15,000
Medical (annual costs)[e]	
SVR F0-F3	£58
SVR F4	£586
F0	£160
F1	£160
F2	£589
F3	£589
F4	£914
DCC	£12,333
HCC 1st y.	£10,990
HCC sub. y.	£10,990
LT 1st y.	£49,749

*Refers to "prior to transplant" health state.

Sources and assumptions: [a,b]Public Health England Hepatitis C in the UK 2016 report.pdf.

[c]Assumption.

[d]Polaris Observatory 2016

[e]Backx, et al. *Journal of viral hepatitis* 21.3 (2014):208-215.

CC, compensated cirrhosis (Metavir fibrosis score F4); DCC, decompensated cirrhosis; EHMs, extrahepatic manifestations; F, Metavir fibrosis score; HCC, hepatocellular carcinoma; LrD, liver-related death (ie, death from DCC, HCC, and LT); LT, liver transplant; SVR, sustained virologic response.

RESULTS

Optimal treatment: stepwise strategy F4→F0 (Strategy 12)

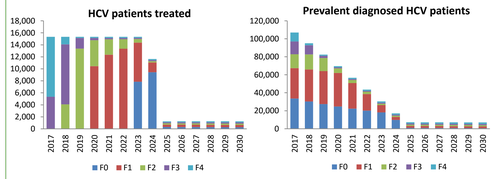
- Among all budget-feasible treatment options, the stepwise strategy to sequentially treat all fibrosis stages prioritizing the most advanced cases (F4→F0) maximised favorable liver outcomes and minimised adverse liver outcomes by 2030 (**Table 2**)
- In contrast a strategy of restricting treatment to stages F3–F4 (which historically was observed in UK) yielded 100,925 fewer SVR cases and an increase of 133 DCC, 64 HCC, 24 LT, and 149 LrD cases

Steps To Elimination By Increasing Diagnosis Rate and Budget (Figure 2 and 3)

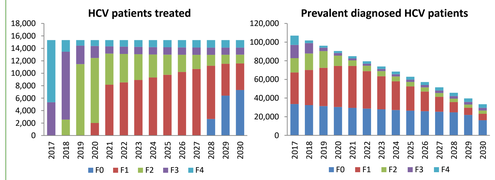
- Under current rates of diagnosis (50%) "elimination" amongst diagnosed HCV patients will be achieved by 2025 but the 112,551 undiagnosed patients will continue to pose a high healthcare burden cost, £54m annually by 2030
- Increasing diagnosis rates to 90% by 2030 would mean an additional 88,121 patients are treated of which 69,632 achieved SVR but the current budget is insufficient to achieve elimination targets by 2030
- A 10% increase in the initial budget to £253m would achieve elimination within WHO targets
  - 196,891 patients would have achieved SVR by 2030
  - The burden from the 16,530 undiagnosed prevalent patients is reduced to less than £10.7m per year by 2030

Figure 2. Path to HCV Elimination Under 3 Budget Scenarios (F4→F0, Strategy 12)

Budget fixed at £230m only 50% patients diagnosed



Budget maintained at £230m diagnosed population increased to 90% by 2030



Budget increased by 10% to 253m per year and 90% diagnosed by 2030

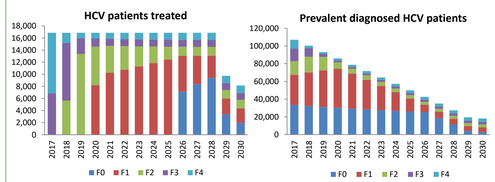
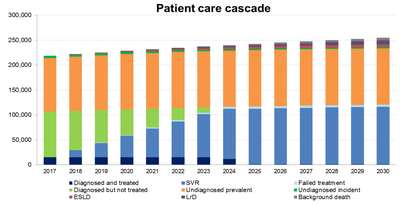
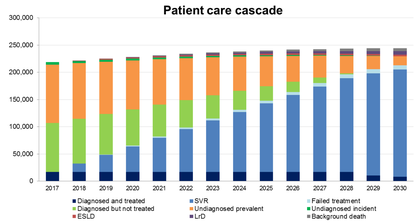


Figure 3. Dynamic Treatment Cascade (Current vs Elimination Strategy)

Current strategy (£230m annual budget and 50% diagnosis by 2030)



Elimination strategy (£253m annual budget and 90% diagnosis by 2030)



Cost Of Care and Avoidable Medical Costs In Path To Elimination

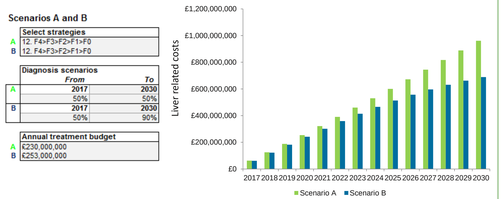
- Under current strategy annual total cost of care (treatment and medical costs but no screening) would reduce from £293m in 2017 to £96m in 2030
- Under elimination strategy (£253m budget and 90% diagnosis) the annual total cost of care, including screening costs would reduce from £315m to £125m by 2030 but with 81,483 more patients in SVR than current strategy
  - Over £272m would be saved in liver-related medical costs by 2030 compared to current strategy (**Figure 4**)
  - If costs for extra hepatic manifestations are included savings are increased to £528m[3]

Figure 4. Comparative Medical Costs (Current vs Elimination Strategy)

Savings made in liver-related medical costs using an elimination strategy vs current strategy

Scenario A = Current Strategy (50% diagnosis, no increase in screening and treatment budget, F4 → F0)

Scenario B = Elimination strategy (90% diagnosis by 2030, increased screening and treatment budget, F4 → F0)



DISCUSSION

- The sequential treatment of all fibrosis stages, prioritizing the most advanced cases, achieves the most favorable patient outcomes
- Restricting treatment to most severe patients while reducing treatment costs yields higher adverse outcomes and consequentially higher medical costs in the future
- Under current rates of diagnosis (50%) elimination amongst diagnosed HCV patients will be achieved by 2025 but undiagnosed patients will continue to impose a high healthcare burden and associated cost
- Improving diagnosis rates remains central to achieve elimination and requires better screening strategies

LIMITATIONS

- SVR inputs may differ from rates observed in real-world settings
- Transition probabilities and costs were obtained from estimates in the literature; actual values for these may differ across other settings and patient subgroups
- The model did not account for HCV transmission, reinfection, treatment compliance, retreatment or additional factors related to chronic HCV infection
- While treatment costs were assumed constant over time, changes in cost would affect number of patients able to access treatment and would have an impact on the path to HCV elimination
- While quality-adjusted life years (QALYs) based on utility weights used in previous UK-based health economic health assessments were part of the model, the cost per QALYs gained were not included in this analysis but are an important consideration for payers in considering elimination policies

CONCLUSIONS

- A stepwise strategy to treat all fibrosis stages prioritizing most advanced cases offers the most optimal use of treatment budget in UK
- However, at current diagnosis rates the number of patients achieving SVR will fall short of WHO 2030 targets for elimination
- Initial costs of HCV care are higher in an elimination strategy but reduce substantially by 2030 as more patients achieve SVR and future medical costs are reduced
- Current treatment budgets are sufficient to treat the entire diagnosed population by 2025, but to achieve WHO targets for elimination greater investments in HCV screening diagnosis and treatment are needed

DISCLOSURES AND CONFLICTS OF INTEREST

Design, study conduct and financial support for the study were provided by AbbVie Inc. AbbVie Inc. participated in the interpretation of data, and review and approval of the abstract. All authors contributed to the development of the publication and maintained control over the final content.

Olivier Ethgen owns SERFAN innovation and is a consultant for AbbVie Inc.

Yuri Sanchez Gonzalez is an employee of AbbVie Inc. and may own stocks and/or options of the company.

Andy Ingram is a contractor with Abbvie Ltd

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Impact of Hepatitis C Treatment With Glecaprevir + Pibrentasvir on Patient's Health Related Quality of Life: Results From Phase 3 CERTAIN Trials

Poster # 1187

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BACKGROUND

- Hepatitis C virus is the most common cause of chronic liver disease in Japan[1]
- Chronic hepatitis C (CHC) infected patients have diminished health related quality of life (HRQoL),[2-5] particularly driven by fatigue[6-10]
- Prior literature on the HRQoL in the Japanese population taking non pan genotypic sofosbuvir based regimen have concluded minor decrements due to ribavirin during treatment which did not continue during the post treatment period. The patients treated on RBV free regimen showed improvement in QoL both during the post treatment.[11-12]
- The pan-genotypic drug combination of glecaprevir (identified by AbbVie and Enanta) and pibrentasvir (GLE/PIB) reported 99% and 100% SVR rates in CERTAIN I and CERTAIN II trials respectively.[13-14] This pangenotypic regimen offers the first RBV-free therapy for GT2-6 Japanese HCV patients.
- However the effect of treatment with this regimen on health related quality of life (HRQoL) is not known

OBJECTIVES

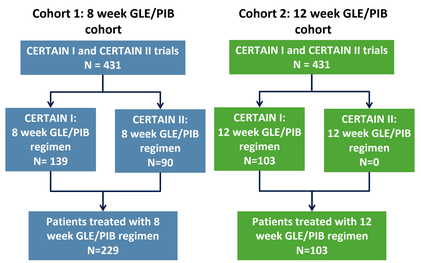
- This study aims to report on the impact of treatment with the GLE/PIB regimen on patient reported function and quality of life as measured by the EuroQol five dimensions questionnaire (EQ-5D-3L) and Fatigue Severity Scale (FSS) for patients treated with 8 weeks or 12 weeks GLE/PIB regimen

METHODS

Study design

- This analysis pooled PRO data (EQ-5D-3L and FSS) from two Japanese registration trials, CERTAIN I and CERTAIN II
- Two study cohorts were then defined based on GLE/PIB treatment regimen of 8 weeks or 12 weeks as described in **Figure 1**
- The study period comprised of treatment period, and 12 weeks of post treatment (PT) follow-up

Figure 1. Patient Selection



METHODS (Continued)

PRO Questionnaires

- PRO questionnaires utilized in this study are described in **Table 1**

Table 1. PRO Questionnaires

Measure	Description	Scoring
EQ-5D-3L	• Comprises of 5 dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression), each of which is rated on 3 levels of severity.[15] ○ Responses to the 5 items are used to derive a discrete health state that is mapped to a preference (utility) specific for different societies. ○ Participants also report their perception of their overall health on a separate visual analog scale (VAS).	• The total scores on EQ-5D-3L range from -0.11 to 1 and 1 represents the perfect health and on EQ-5D VAS range from 0 to 100. • Higher scores indicate a better HRQoL.
Fatigue Severity scale (FSS)	• The FSS is a 9 item questionnaire with questions related to how fatigue interferes with certain activities and rates its severity[16] • The items are scored on a 7-point scale with 1 = "strongly disagree" and 7= "strongly agree".	• The instrument is scored by taking the mean of all the scores; here the minimum score is 1 and maximum score is 7. • Higher scores indicate greater fatigue severity.

DATA ANALYSIS

Empirical analysis: Mixed models

- PRO scores at each time point were analyzed using linear mixed models independently for the two study cohorts
- An overall analysis and subgroup analysis by patient treatment history (i.e. treatment naïve or treatment experienced) was conducted for each study cohorts
- Models were adjusted for:
  - Fixed effects: baseline viral load, baseline FIB – 4 score, prior treatment history, patient`s age, gender, genotype, history of depression, time period.
  - Random effects: Subject
- The change from baseline was predicted based on the model coefficients and tested for statistical significance.

Proportional analysis

- Proportion of patients reporting perfect health on EQ-5D were studied at baseline, end of treatment and post treatment week 12.

RESULTS

Study Population

- A total of 229 8 week treated patients and 103 12 week treated patients from CERTAIN I and II trials were included for analysis
- Baseline demographics of the study population are shown in **Table 2**

Table 2. Demographics of Study Population

	Cohort 1: 8 Week Regimen	Cohort 2: 12 Week Regimen
N	229	103
Age	60.8	67.2
Gender		
Male	136	45
Female	93	58
Fibrosis		
F0 - F1	81	10
F2	10	0
F3	12	4
F4	1	42
Missing	125	47
Mean FIB - 4 score	2.19	5.03
Cirrhosis		
Yes	0	64
No	229	39
Genotype		
1	132	70
2	97	21
3		12
Treatment history		
Naïve	176	46
Peg-interferon/Ribavirin experienced	53	24
DAA experienced		33
Baseline Viral load		
<6,000,000	210	97
≥6,000,000	19	6
Depression or bipolar disorder		
Yes	4	8
No	225	95
Study		
CERTAIN I	139	103
CERTAIN II	90	

EMPIRICAL ANALYSIS: 8 WEEK GLE/PIB REGIMEN (TABLE 3)

Baseline HRQoL

- Baseline values on EQ-5D HUI were in line with the values observed in Japanese general population
- Patients who were treatment experienced had a comparatively lower QoL than naïve patients as measured by EQ-5D HUI and FSS

Treatment period HRQoL

- By the end of treatment period, all GLE/PIB treated patients experienced statistically significant improvements in QoL as compared to baseline
- The treatment naïve patients also experienced statistically significant improvements in QoL as compared to baseline, whereas the treatment experienced patients had a statistically insignificant increase in QOL.

Post-treatment HRQoL

- By post-treatment week 12, patients had no statistically significant change from baseline

Table 3. Longitudinal Mixed Model Results – 8 Week GLE/PIB Regimen

	Unadjusted baseline value (SD)	Average adjusted change from baseline at EOT (SE)	Average adjusted change from baseline at PTW12 (SE)
		Overall	
EQ-5D HUI	0.94 (0.11)	0.018* (0.008)	0.008 (0.007)
EQ-5D VAS	80.3 (14.1)	1.57 (0.8565)	1.14 (0.8584)
FSS	2.98(1.38)	–0.042 (0.07)	–0.001 (0.08)
		Treatment – Naive	
EQ-5D HUI	0.95 (0.11)	0.015* (0.008)	0.002 (0.008)
EQ-5D VAS	80.1 (14.1)	1.92* (0.9198)	1.26 (0.9613)
FSS	2.97(1.38)	–0.062 (0.088)	-0.006 (0.094)
		Treatment experienced^	
EQ-5D HUI	0.91 (0.13)	0.02 (0.002)	0.03 (0.018)
EQ-5D VAS	80.8 (14.1)	0.45 (2.0936)	0.71 (1.9291)
FSS	3.02 (1.41)	0.018 (0.134)	0.019 (0.155)

*p < 0.05
^ includes only patients experienced with peg-interferon and ribavirin
HUI = Health utility index; FSS = Fatigue sub scale; EOT = end of treatment; PTW = post treatment week; SE = standard error; SD = Standard deviation
The table presents predicted change from baseline at selected time points from linear mixed models.

EMPIRICAL ANALYSIS: 12 WEEK GLE/PIB REGIMEN (TABLE 4)

Baseline HRQoL

- Baseline values on EQ-5D HUI were in line with the values observed in Japanese general population

Treatment period HRQoL

- By the end of treatment period, all GLE/PIB treated patients experienced statistically significant improvements in QoL as compared to baseline
- The treatment naïve and treatment experienced patients experienced statistically insignificant increase in QOL.

Post-treatment HRQoL

- By post-treatment week 12, patients had no statistically significant change from baseline

Table 4. Longitudinal Mixed Model Results – 12 Week GLE/PIB Regimen

	Unadjusted baseline value (SD)	Average adjusted change from baseline at EOT (SE)	Average adjusted change from baseline at PTW12 (SE)
		Overall	
EQ-5D HUI	0.91 (0.131)	0.025* (0.012)	–0.003 (0.013)
EQ-5D VAS	80.8 (13.2)	0.855 (1.141)	–0.32 (1.2112)
FSS	2.86 (1.396)	0.073 (0.115)	0.159 (0.118)
		Treatment – Naïve	
EQ-5D HUI	0.89 (0.13)	0.024 (0.019)	–0.002 (0.019)
EQ-5D VAS	80.5 (12.5)	1.34 (1.9186)	–0.94 (2.1017)
FSS	2.89 (1.44)	0.047 (0.181)	0.181 (0.190)
		Treatment experienced^	
EQ-5D HUI	0.93 (0.127)	0.025 (0.015)	–0.004 (0.016)
EQ-5D VAS	81.1 (13.8)	0.47 (1.3792)	0.21 (1.3945)
FSS	2.83 (1.37)	0.096 (0.149)	0.142 (0.151)

*p < 0.05
^includes both peg-interferon and ribavirin experienced and prior direct acting antiviral experienced
HUI = Health utility index; VAS = visual analogue scale; W = week; EOT = end of treatment; PTW = post treatment week; SE = standard error; SD = Standard deviation
The table presents predicted change from baseline at selected time points from linear mixed models.

PROPORTION OF PATIENTS REPORTING PERFECT HEALTH ON EQ-5D-3L HUI

Proportional analysis

- Proportion of patients treated with 8 week and 12 week GLE/PIB regimen reporting perfect health on EQ-5D-3L are depicted in **Figures 2 and 3** respectively
- At baseline more than 50% of the population reported perfect health.
- The proportion of patients reporting perfect health increased by end of treatment irrespective of patient population considered. This was maintained during the post treatment period
- This proportion of patients reporting perfect health at each time point were consistently higher as compared to general population norm of 60%.[17]

FIG 2 and 3: Proportion of Patients Reporting Perfect Health on EQ-5D-3L

Fig 2. Proportion of Patients, Treated With 8 Weeks GLE/PIB Regimen, Reporting Perfect Health

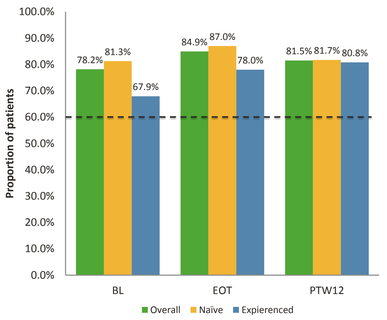
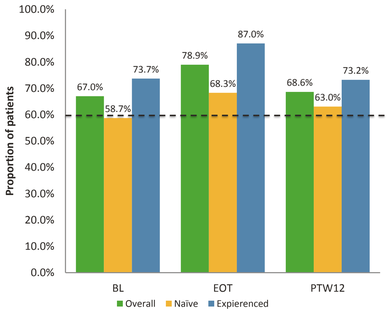


Fig 3. Proportion of Patients, Treated With 12 Weeks GLE/PIB Regimen, Reporting Perfect Health



Note: The dotted line represents the proportion of general population reporting full health on EQ-5D-3L[17] (60% for respondents aged between 60–70)
BL: baseline; EOT: End of treatment

DISCUSSION

- This study is the first comprehensive assessment of HRQoL in Japanese HCV patients treated with pan genotypic GLE/PIB regimen
- The study demonstrated, treatment with 8 or 12 weeks of GLE/PIB resulted in stable or improved HRQoL, as evidenced by increase in EQ-5D-3L score and reduction in FSS score
- Our results are consistent with HRQoL gains documented with other IFN/RBV-free DAA regimens in this population[11,12]
- Patients enrolled in the trials had a high HRQoL (mean EQ-5D-3L HUI > 0.9) at baseline with majority of population reporting perfect health. This is in line with the QoL of Japanese general population[17]. These high baseline score and ceiling effect with the EQ-5D-3L scale, resulted in very few patients reporting minimally important difference (MID) changes

STRENGHTS & LIMITATIONS

Strengths

- The current study is one of the first studies to report HRQoL in Japanese population treated with a pan-genotypic DAA regimen
- PRO instruments used in this study have been validated and used widely across indications and geographies

Limitations

- The study sampled patients enrolled in clinical trials, therefore generalizability to patients in routine clinical practice may be limited. Further real world studies may be warranted
- Unobservable factors, not collected in the database, may have influenced results

CONCLUSIONS

- Treatment with 8 or 12 weeks of GLE/PIB regimen resulted in no worsening or improvement in patient`s HRQoL.
- The results were similar irrespective of patient`s HCV treatment history

DISCLOSURES AND CONFLICTS OF INTEREST

Design and study conduct for the study was approved by AbbVie, Inc. AbbVie Inc. participated in the interpretation of data, and review and approval of the abstract. All authors contributed to the development of the publication and maintained control over the final content.

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Brett Pinsky is employee of AbbVie Inc. and may own stocks and/or options of the company.

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